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(54) **HPIV3 RNA VACCINES**

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(57) **ABSTRACT**

The disclosure relates to respiratory virus ribonucleic acid (RNA) vaccines and combination vaccines, as well as methods of using the vaccines and compositions comprising the vaccines.

Specification includes a Sequence Listing.

Fig. 1

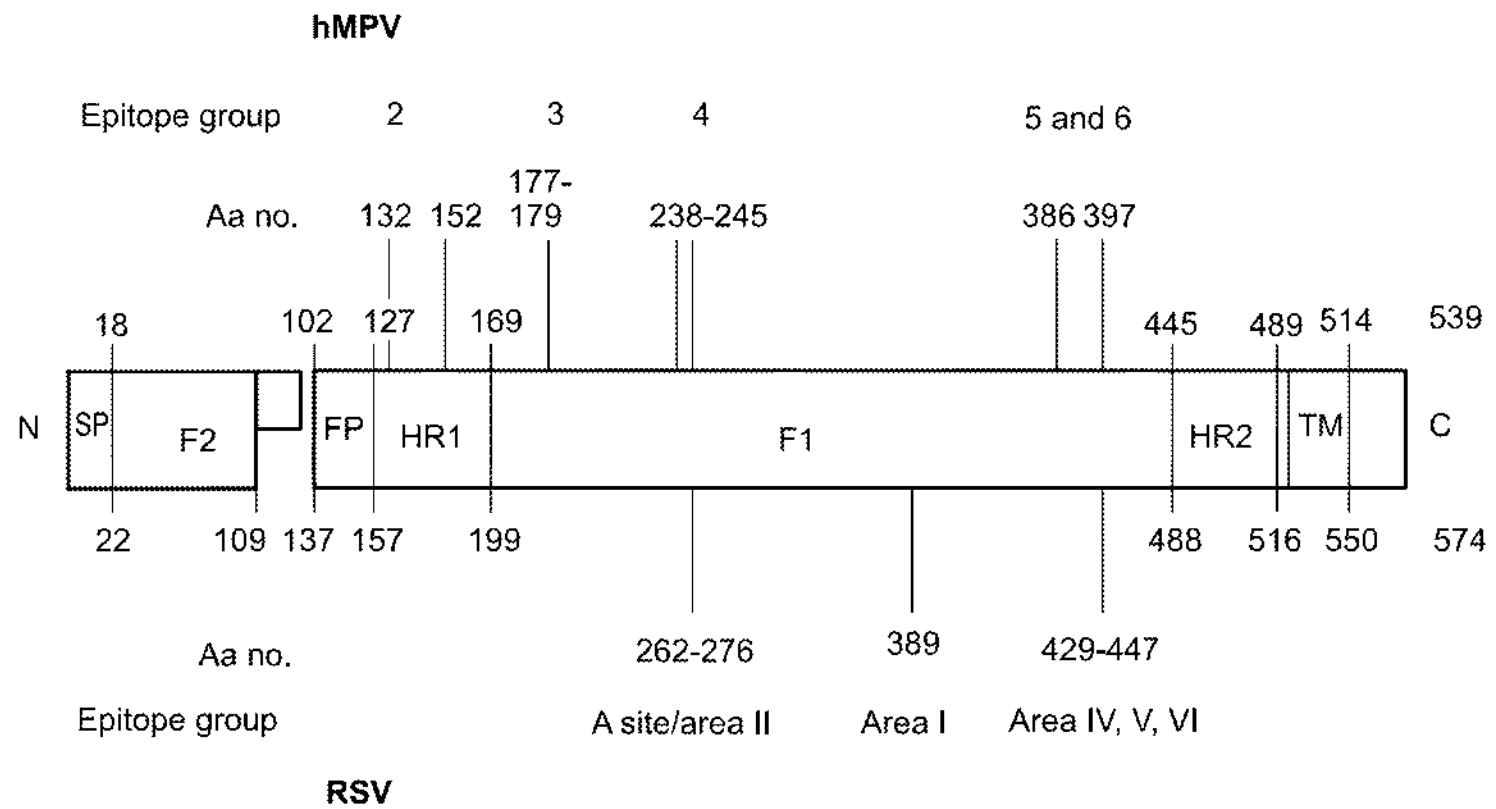


Fig. 2A

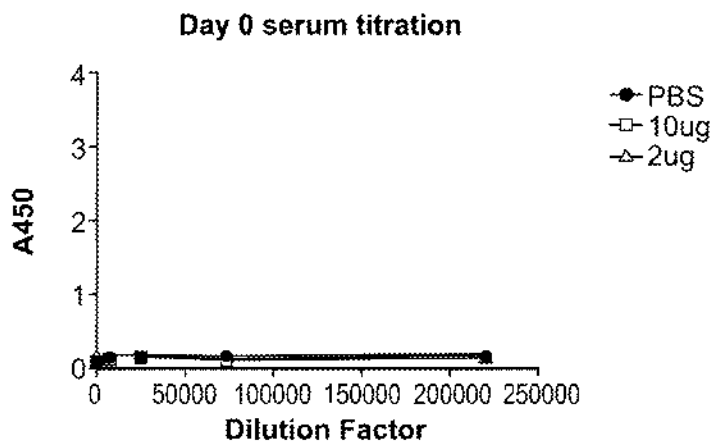


Fig. 2B

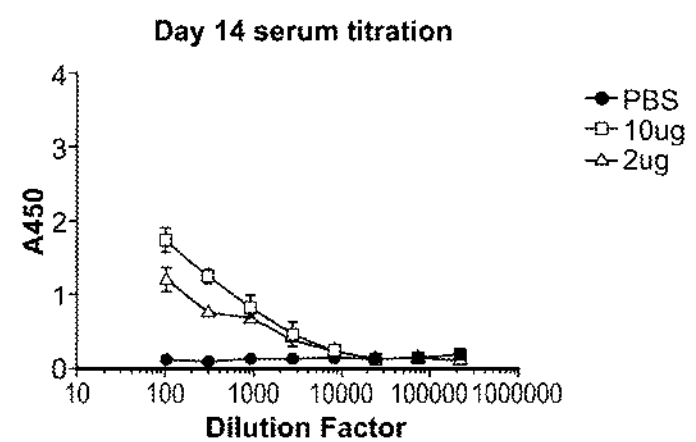
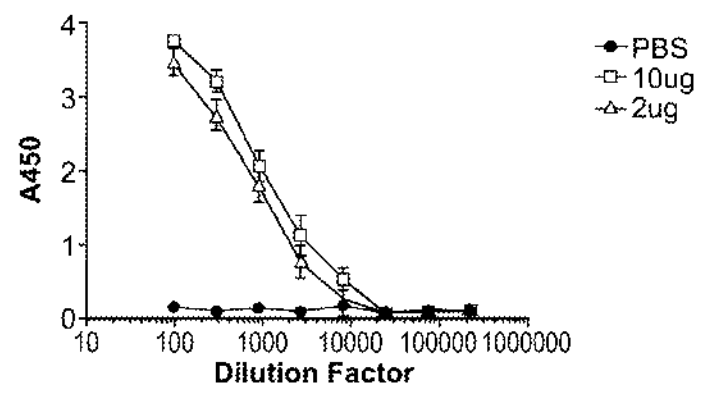


Fig. 2C Day 35 serum titration



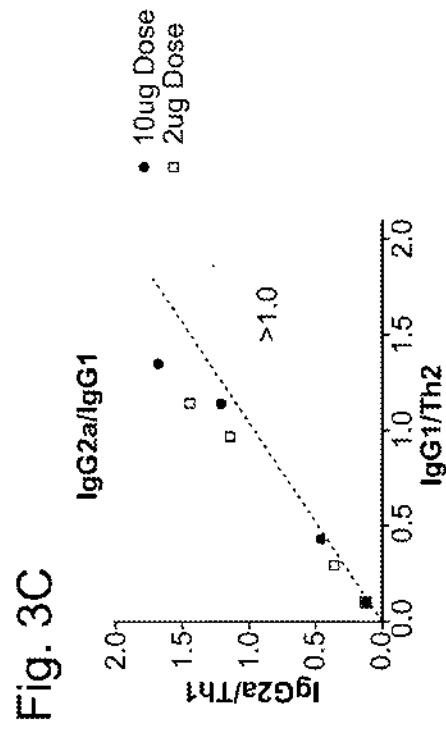
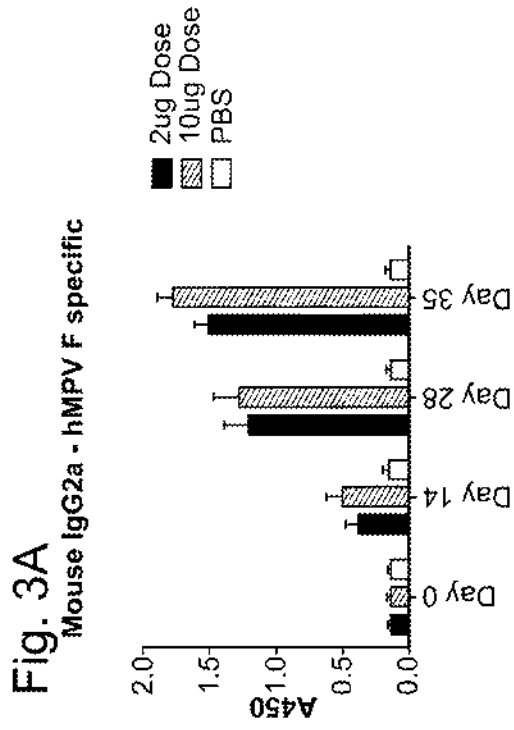
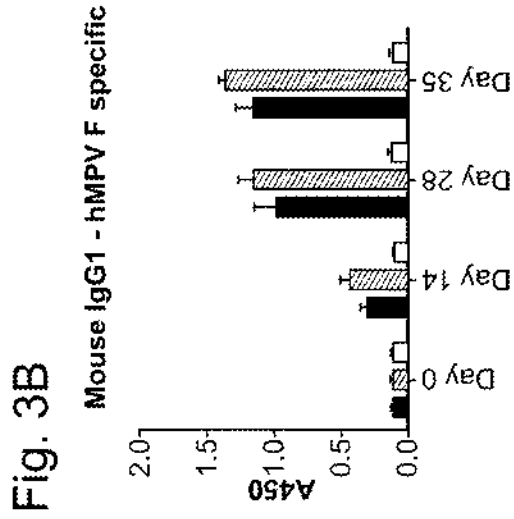
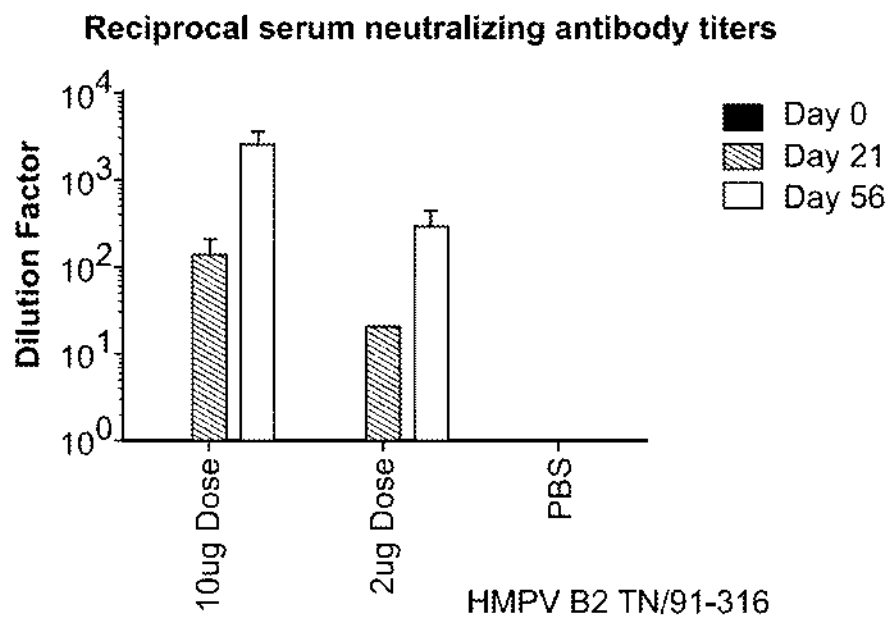


Fig. 4



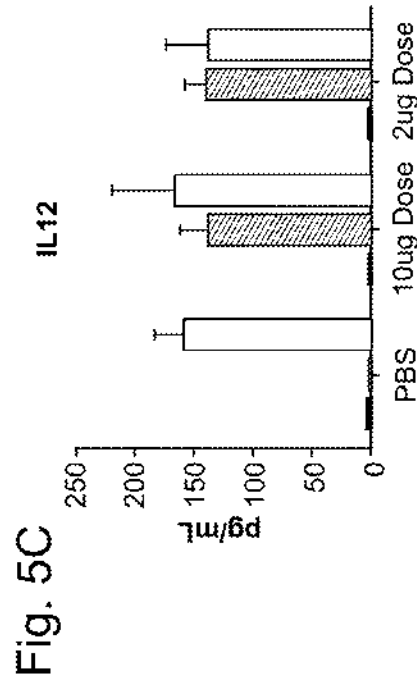
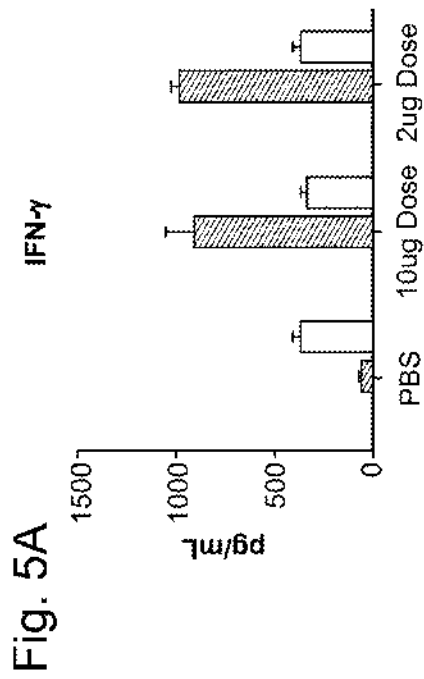
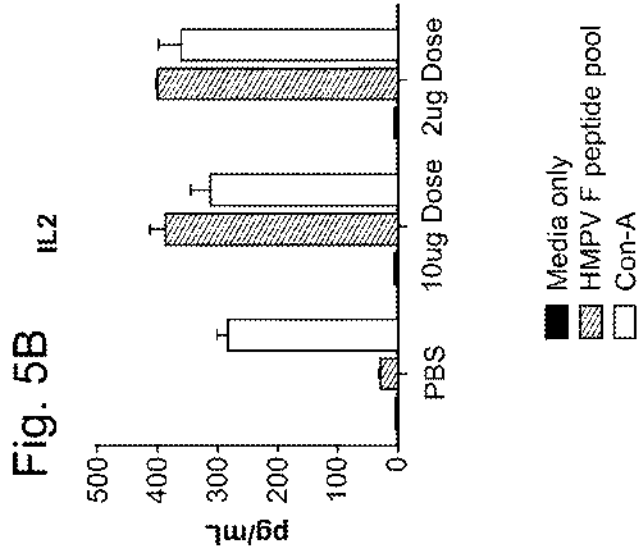


Fig. 6A

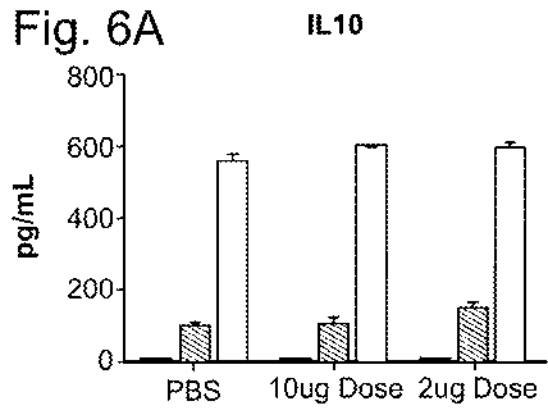
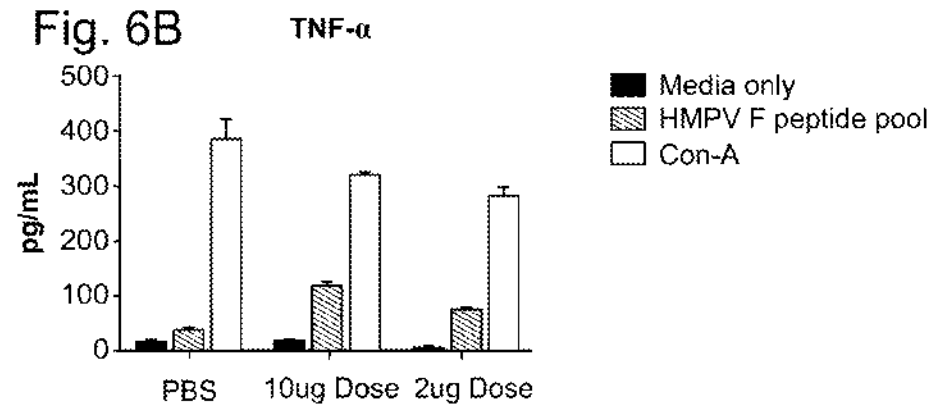


Fig. 6B



Media only
HMPV F peptide pool
Con-A

Fig. 6C

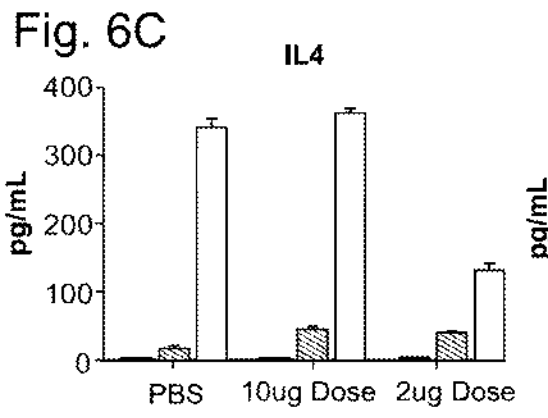


Fig. 6D

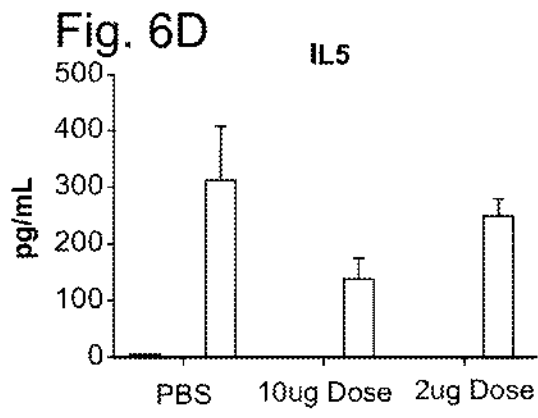
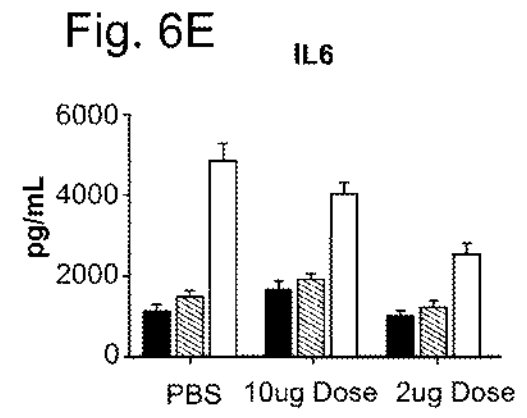


Fig. 6E



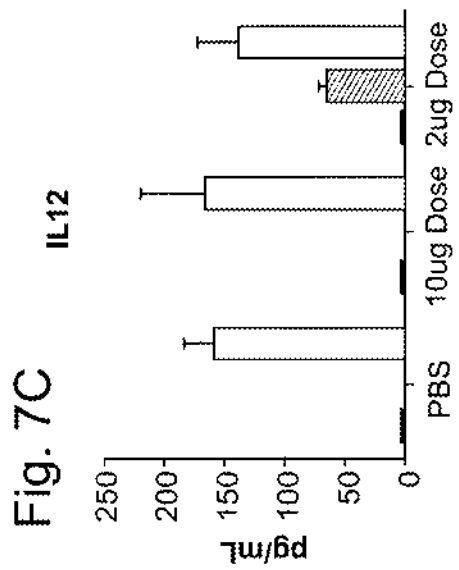
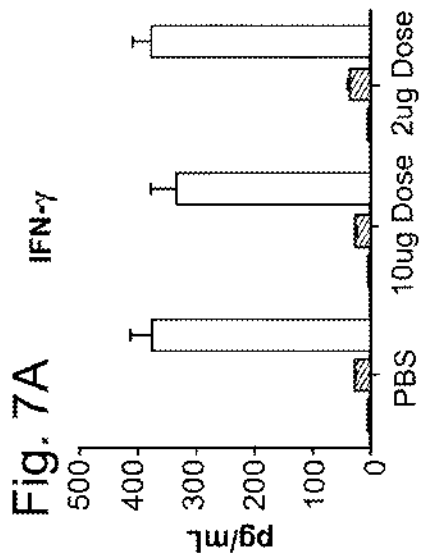
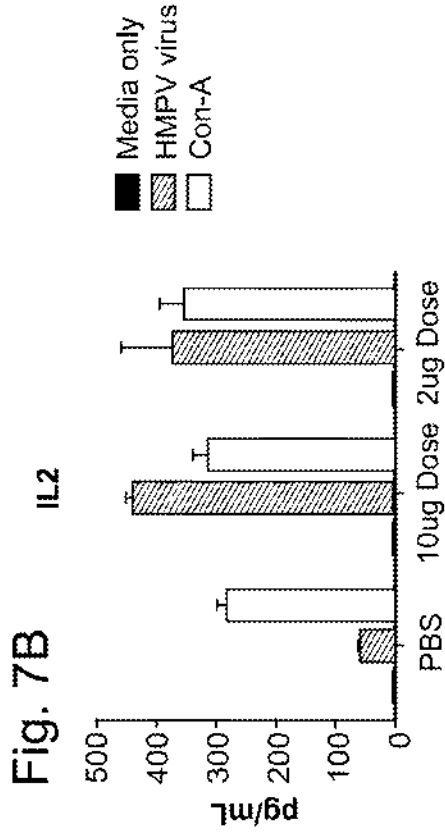


Fig. 8A IL10

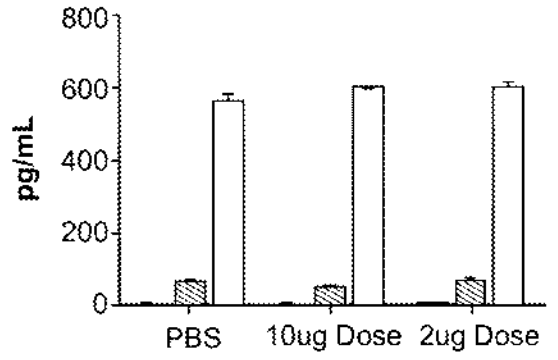


Fig. 8B TNF- α

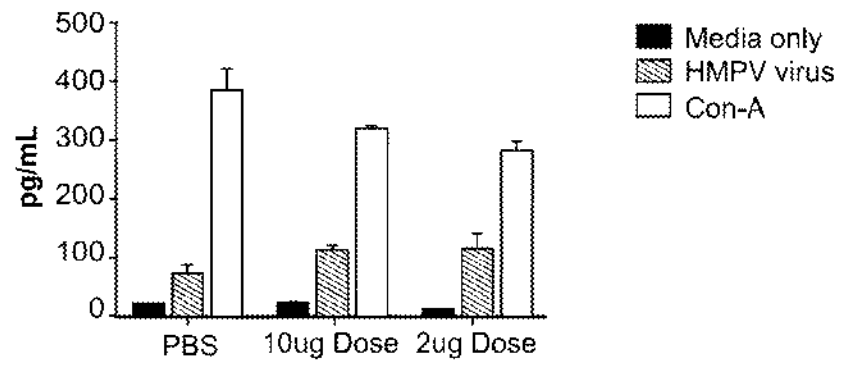


Fig. 8C IL4

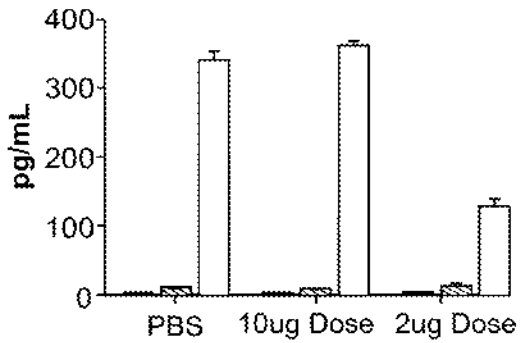


Fig. 8D IL5

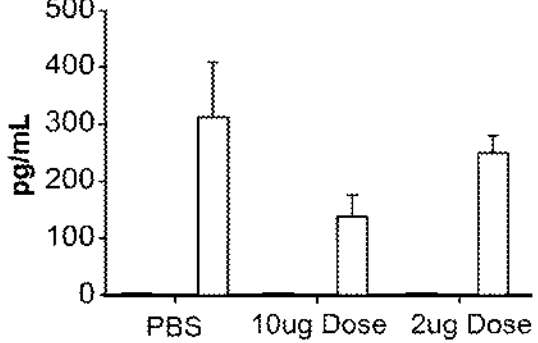


Fig. 8E IL6

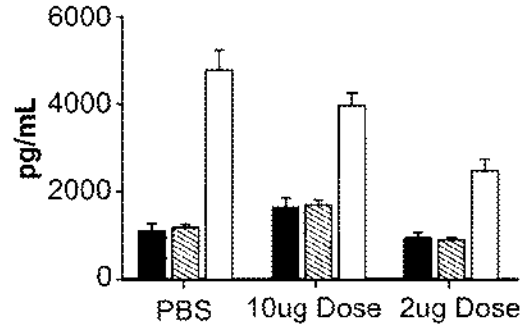


Fig. 9A

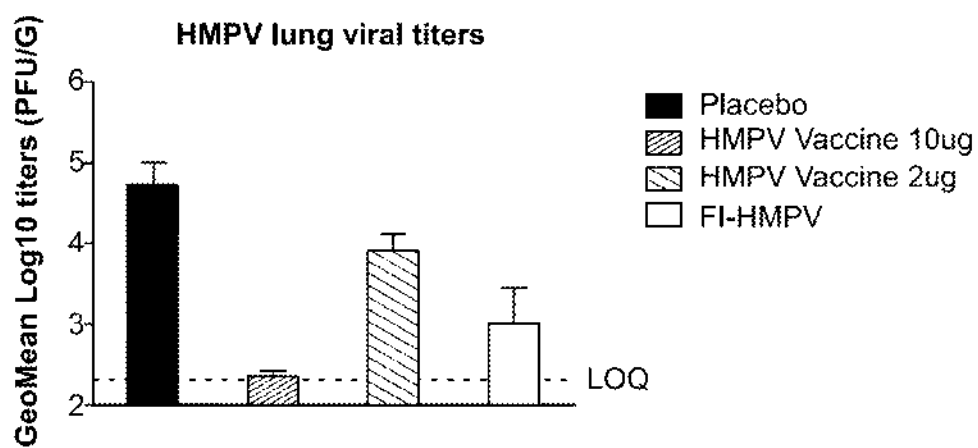


Fig. 9B

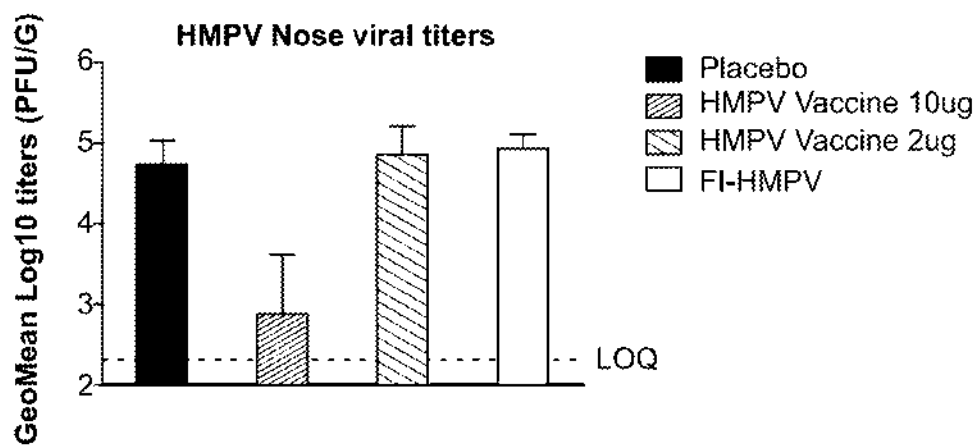


Fig. 10

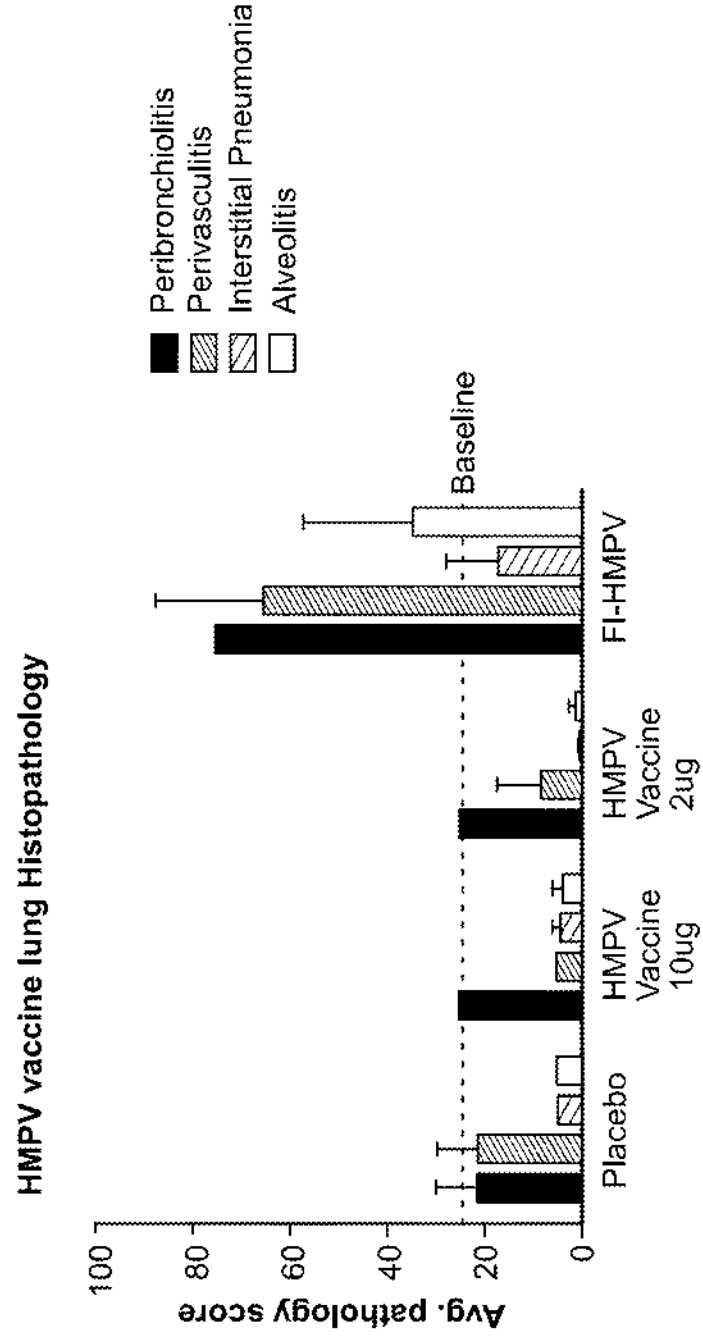
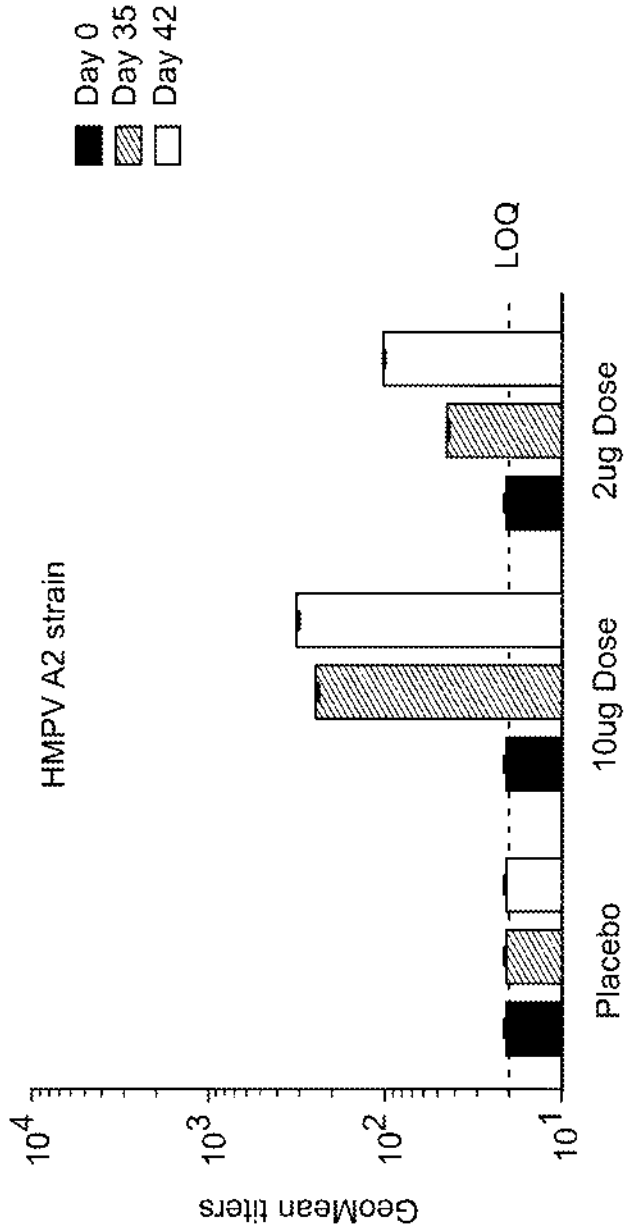
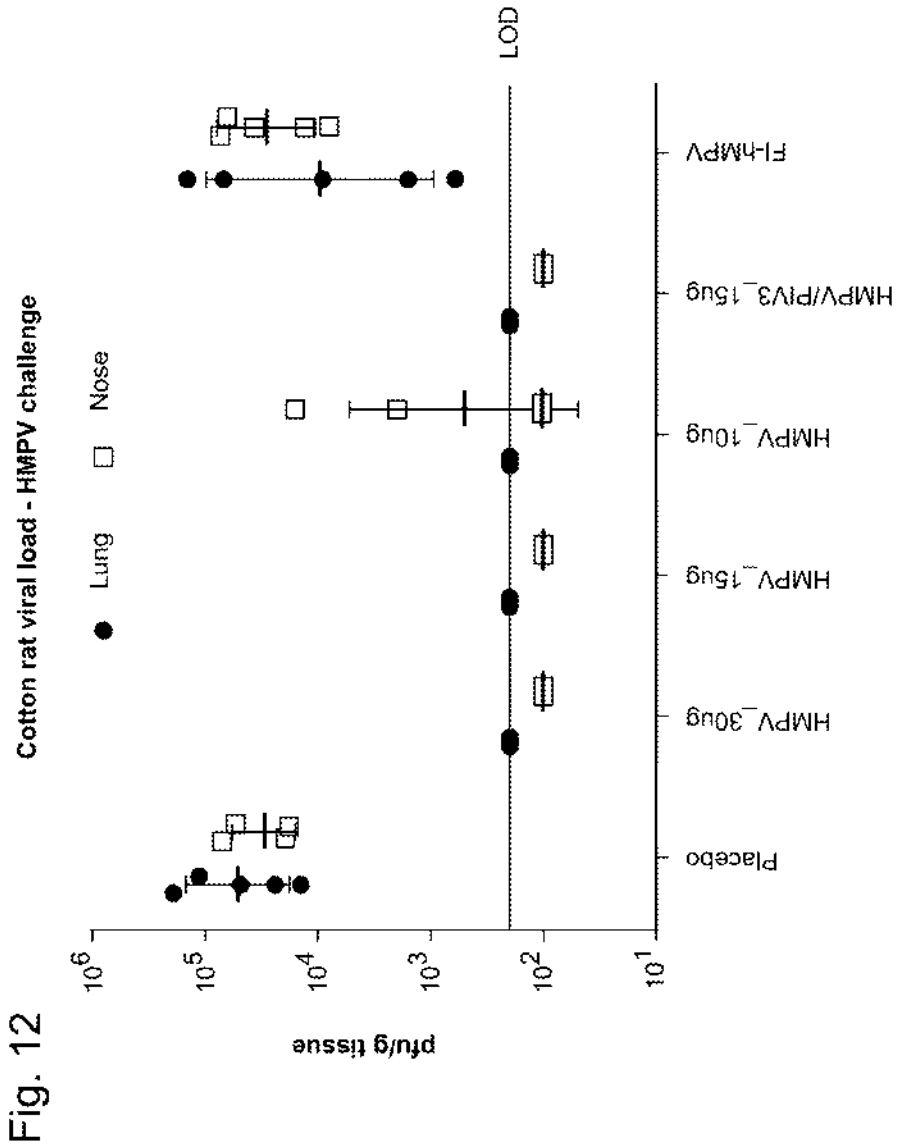


Fig. 11

HMPV neutralization antibody titers in cotton rats





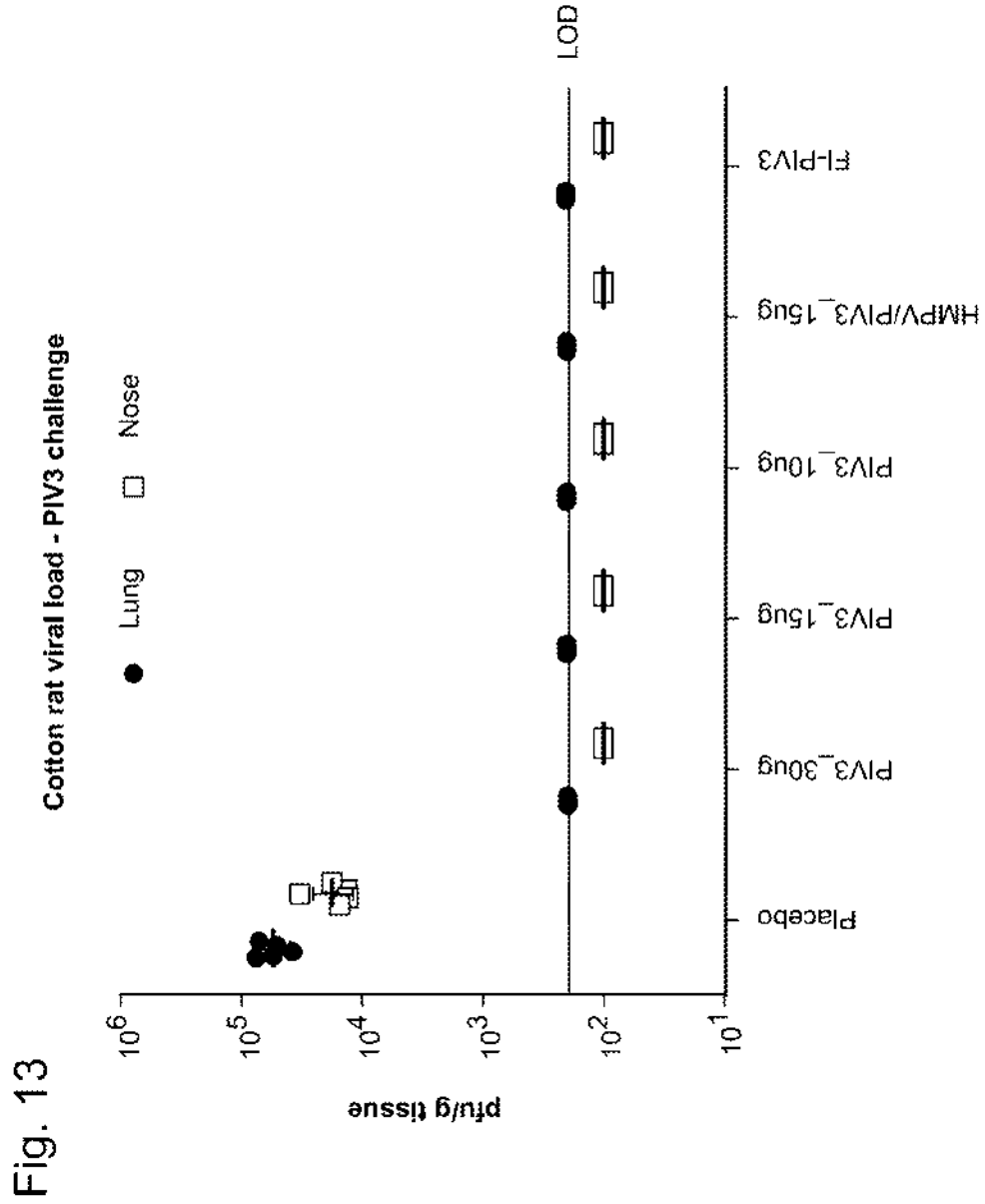


Fig. 14

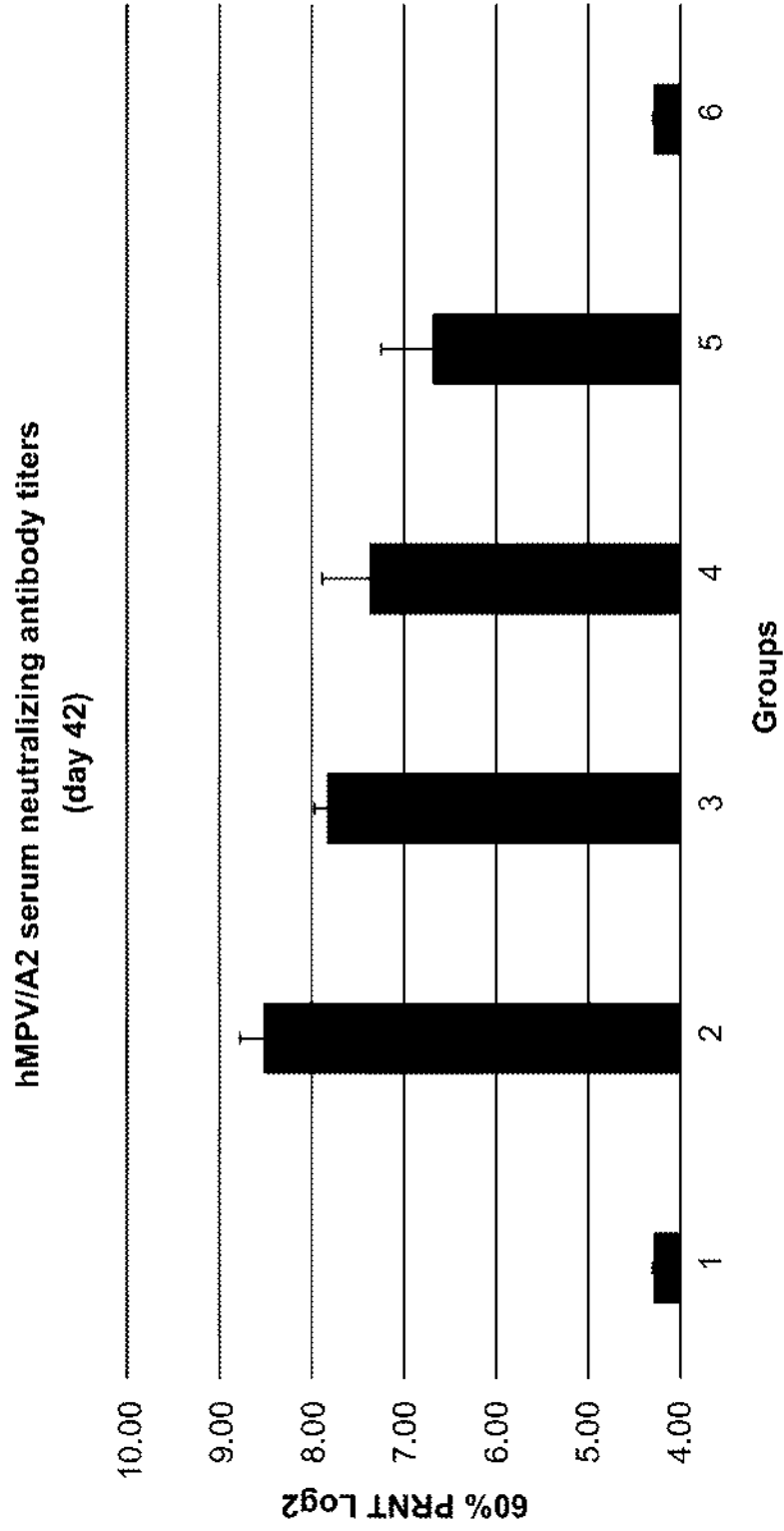


Fig. 15

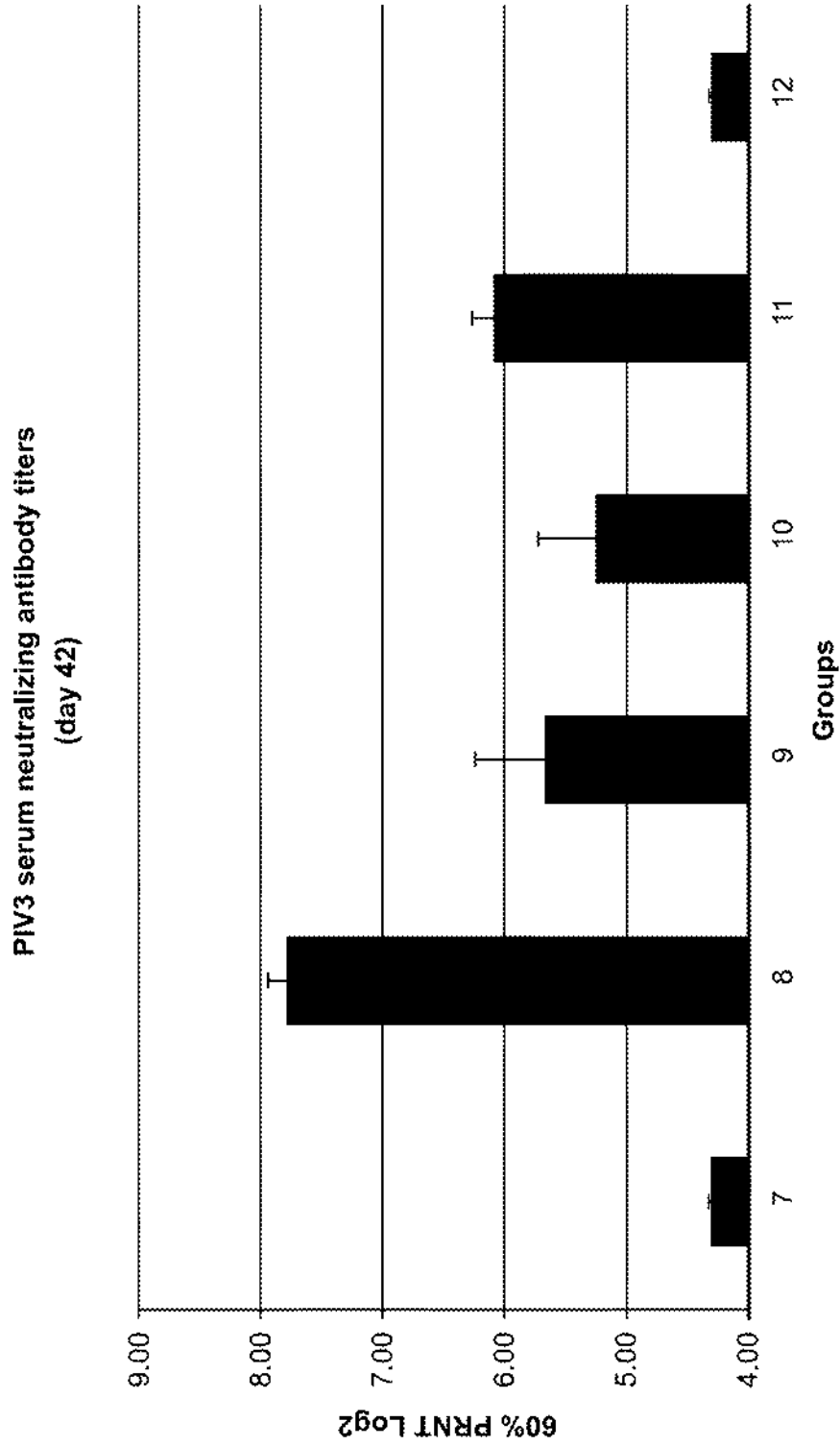


Fig. 16
Cotton rat lung histopathology

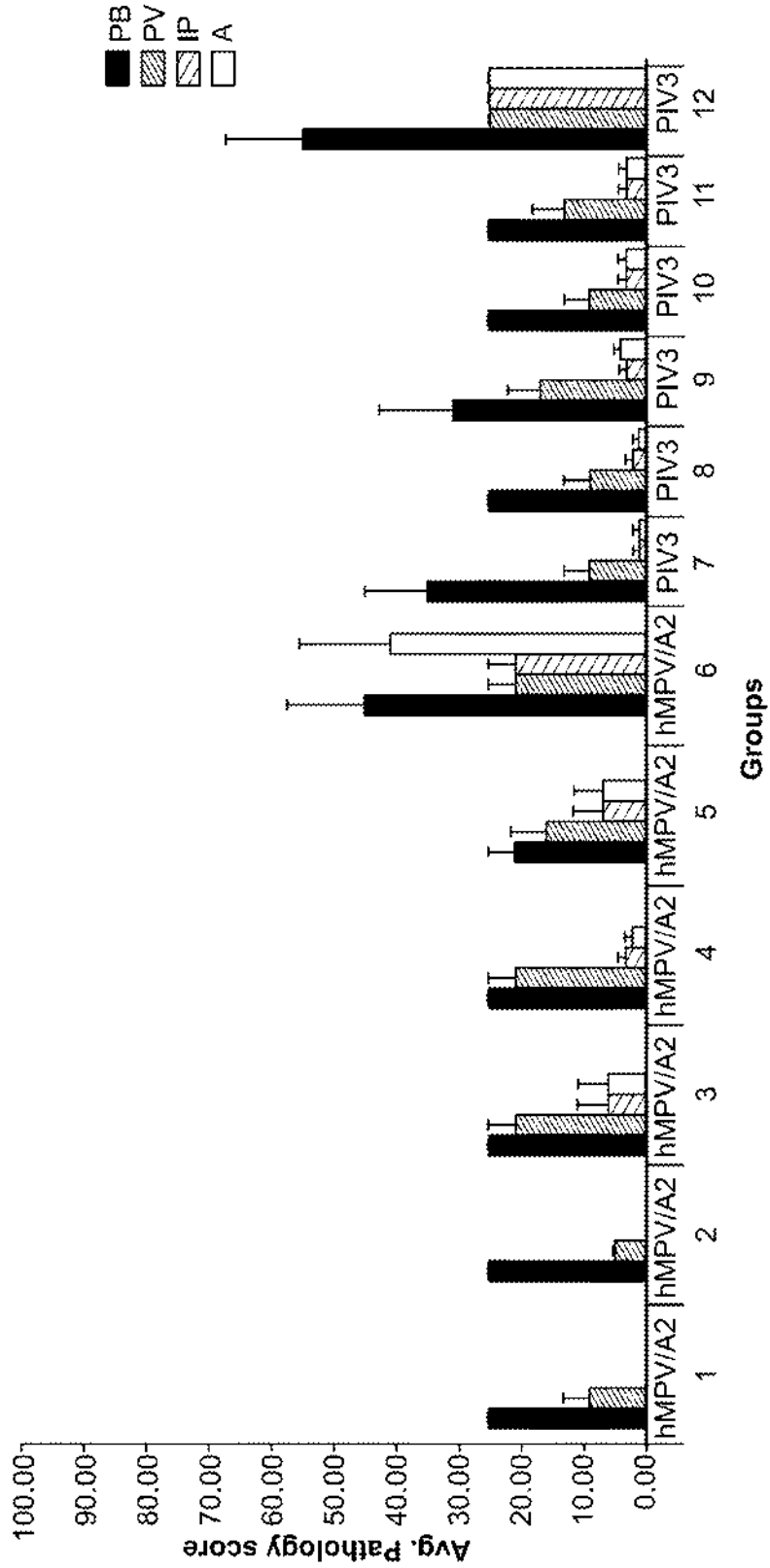


Fig. 17

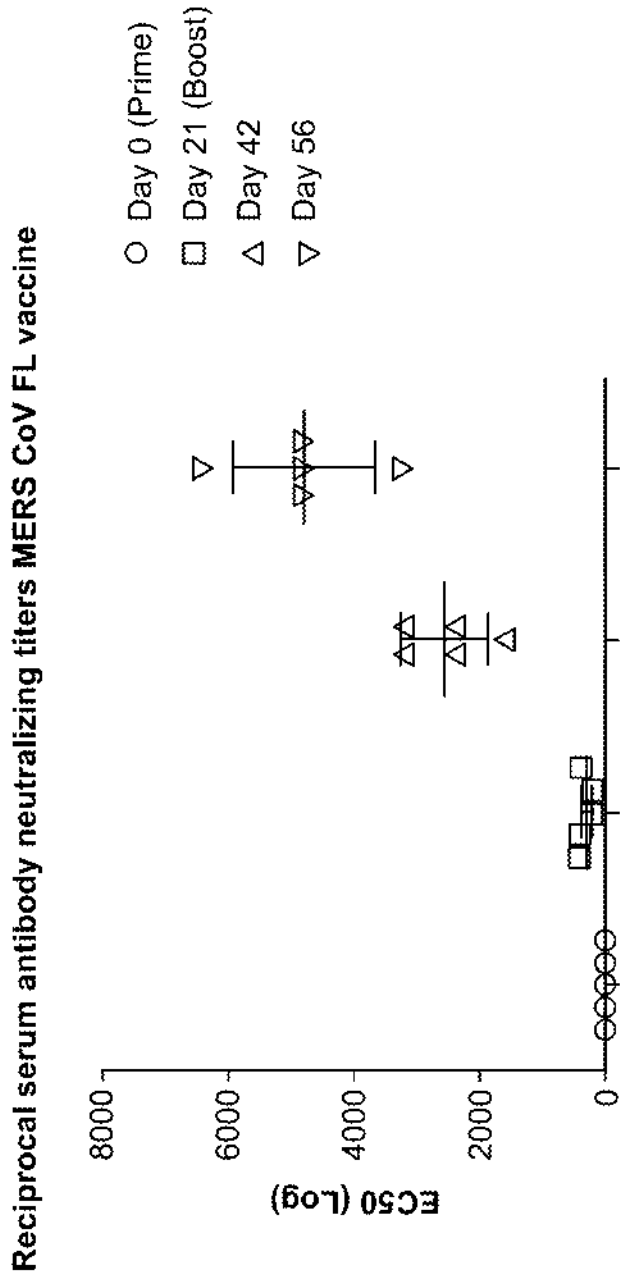


Fig. 18

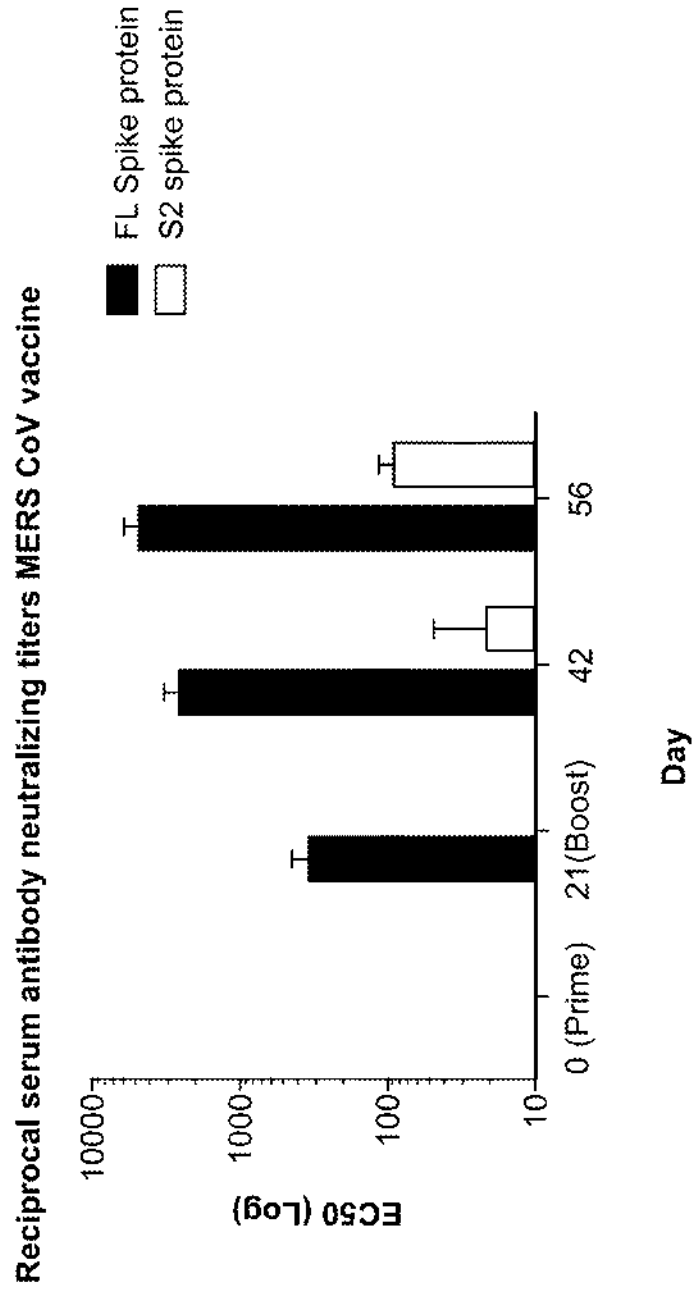


Fig. 19A

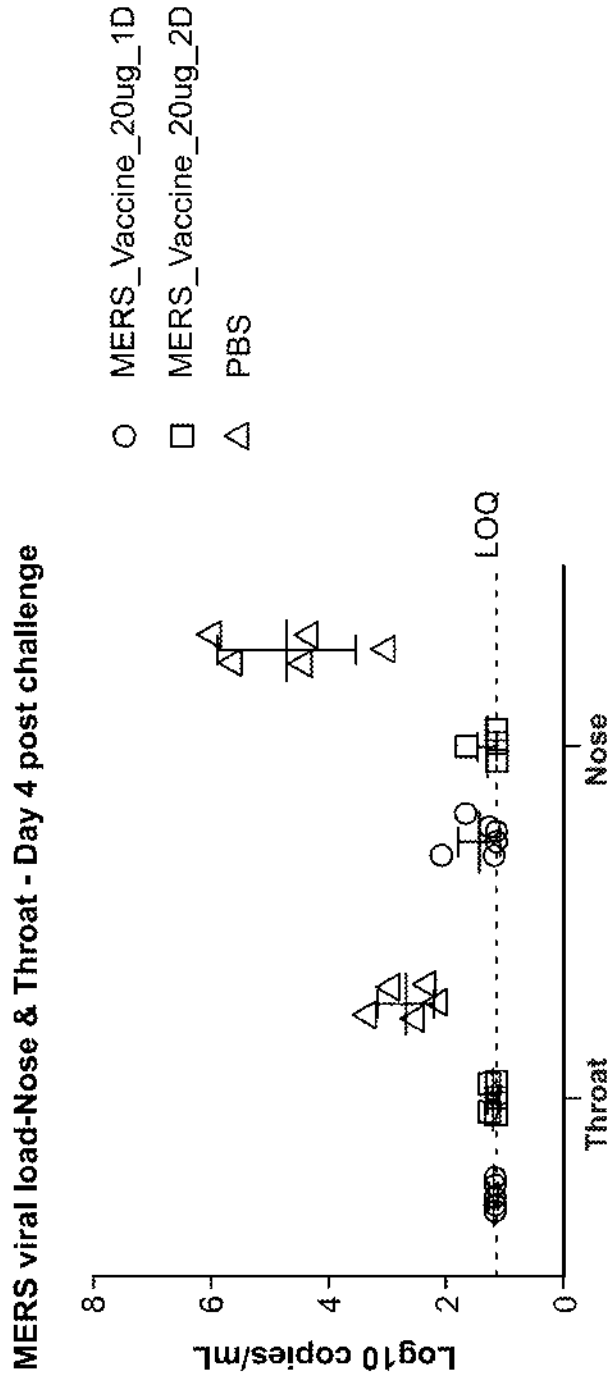


Fig. 19B

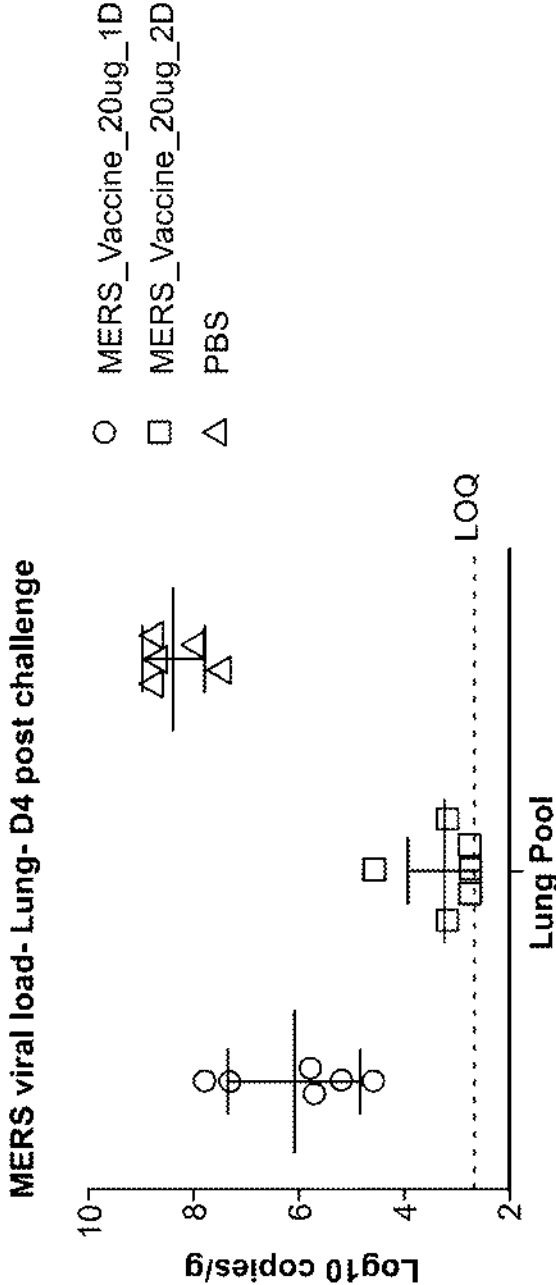


Fig. 19C

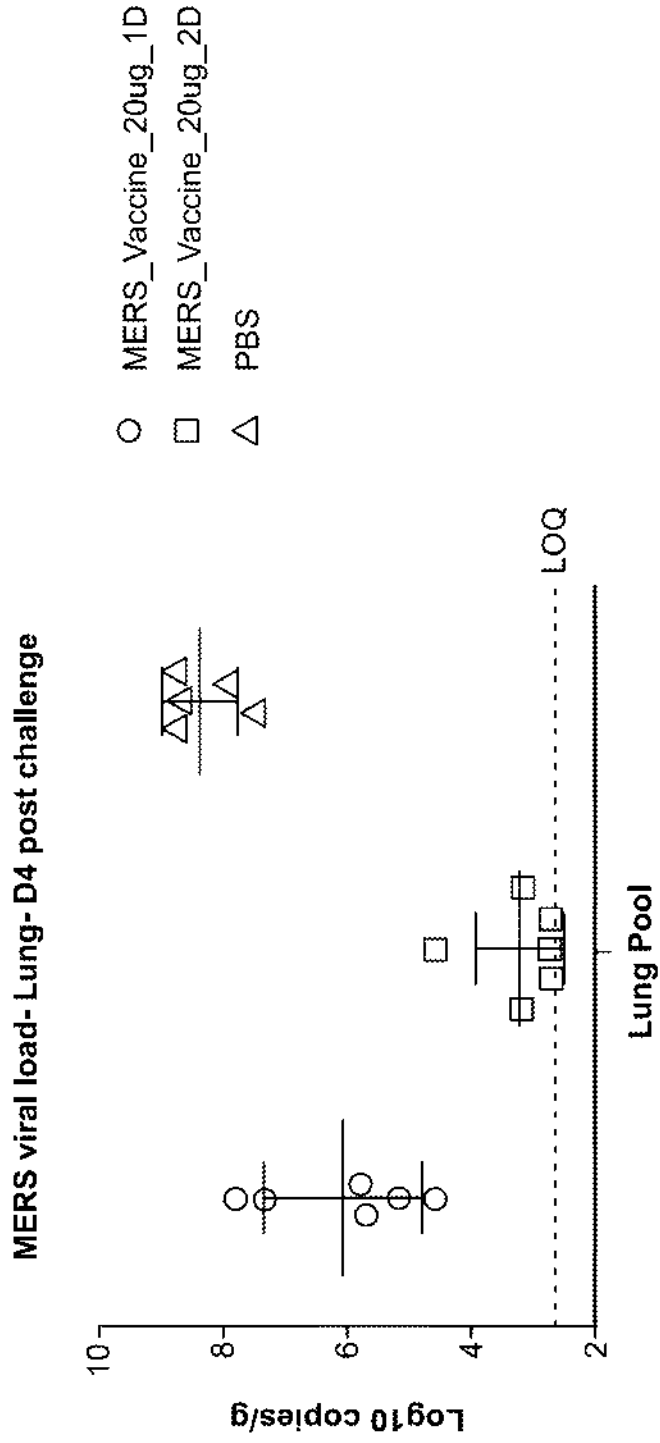
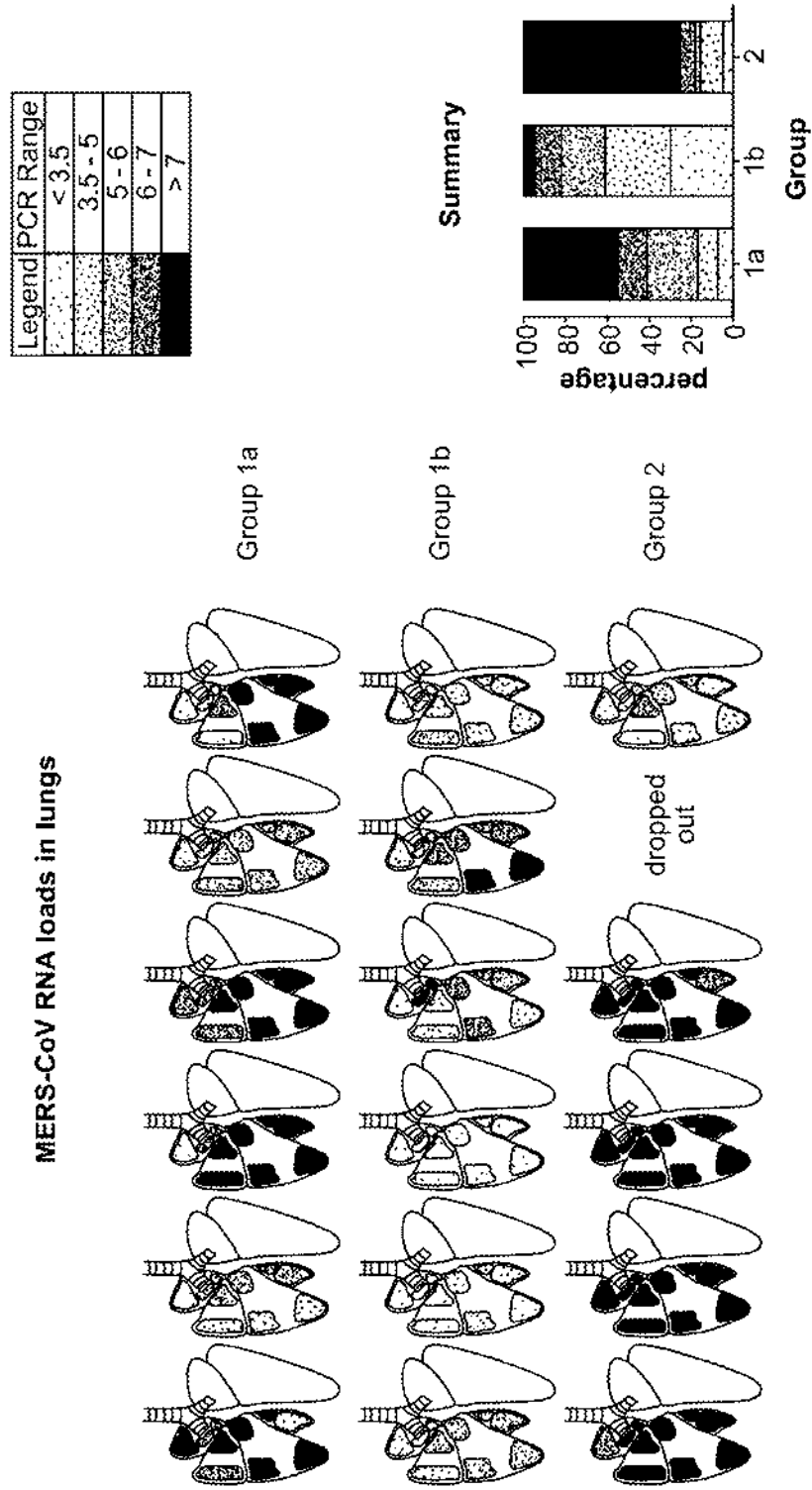


Fig. 20A



Group 1a

Group 1b

Group 2

dropped out

Summary

Group

Percentage

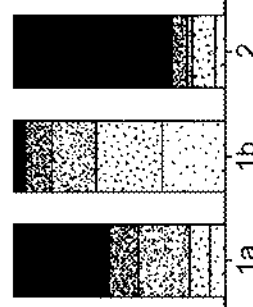


Fig. 20B

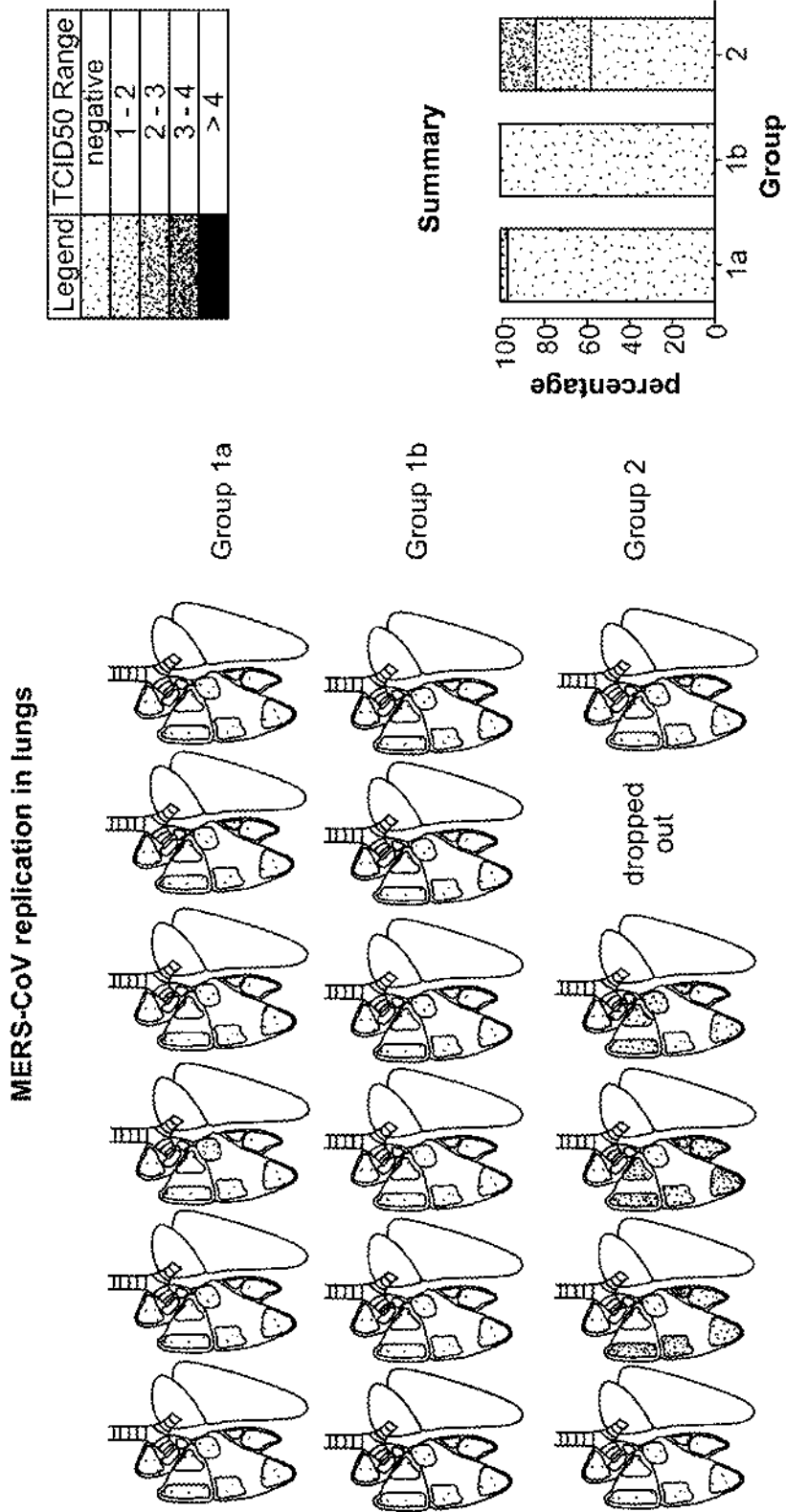
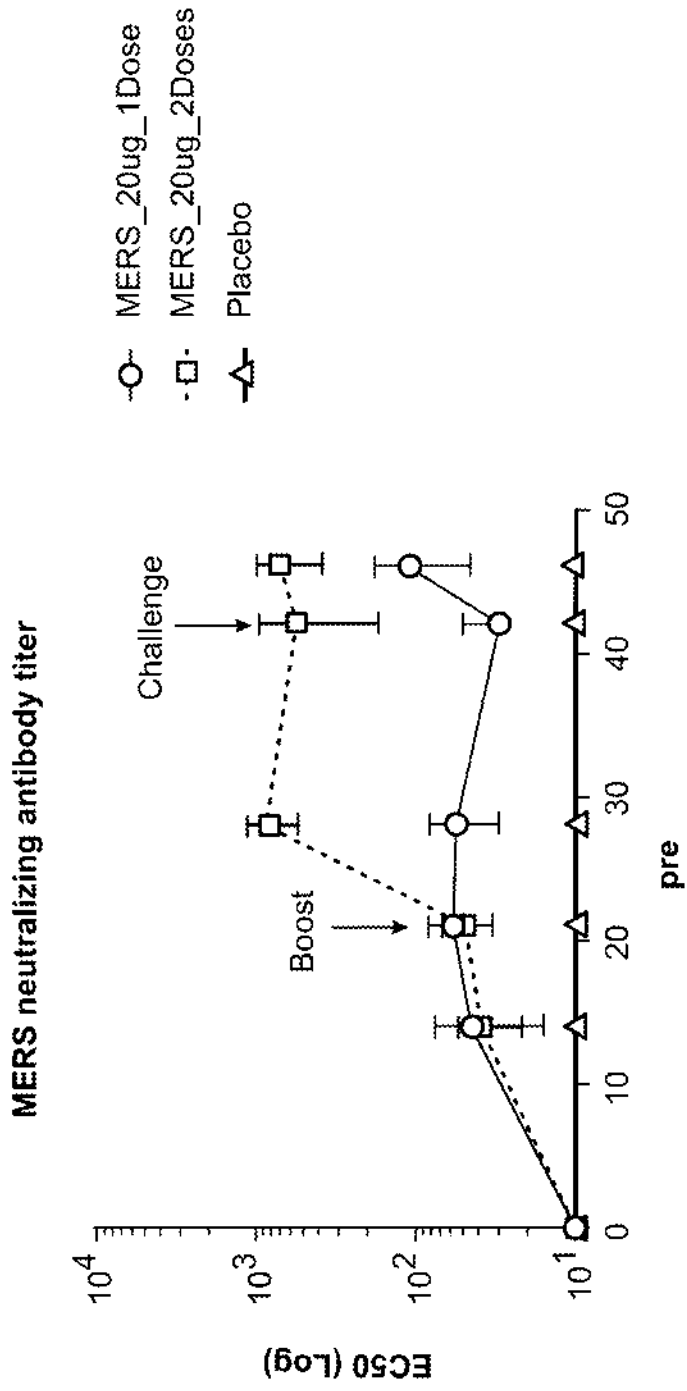


Fig. 21



HPIV3 RNA VACCINES

RELATED APPLICATIONS

[0001] This application is a continuation of U.S. application Ser. No. 16/040,981, filed Jul. 20, 2018, which is a continuation of U.S. application Ser. No. 15/674,599, now U.S. Pat. No. 10,064,934, filed Aug. 11, 2017, which is a continuation of international application number PCT/US2016/058327, which claims the benefit under 35 U.S.C. § 119(e) of U.S. provisional application No. 62/244,802, filed Oct. 22, 2015, U.S. provisional application No. 62/247,297, filed Oct. 28, 2015, U.S. provisional application No. 62/244,946, filed Oct. 22, 2015, U.S. provisional application No. 62/247,362, filed Oct. 28, 2015, U.S. provisional application No. 62/244,813, filed Oct. 22, 2015, U.S. provisional application No. 62/247,394, filed Oct. 28, 2015, U.S. provisional application No. 62/244,837, filed Oct. 22, 2015, U.S. provisional application No. 62/247,483, filed Oct. 28, 2015, and U.S. provisional application No. 62/245,031, filed Oct. 22, 2015, each of which is incorporated by reference herein in its entirety.

BACKGROUND

[0002] Respiratory disease is a medical term that encompasses pathological conditions affecting the organs and tissues that make gas exchange possible in higher organisms, and includes conditions of the upper respiratory tract, trachea, bronchi, bronchioles, alveoli, pleura and pleural cavity, and the nerves and muscles of breathing. Respiratory diseases range from mild and self-limiting, such as the common cold, to life-threatening entities like bacterial pneumonia, pulmonary embolism, acute asthma and lung cancer. Respiratory disease is a common and significant cause of illness and death around the world. In the US, approximately 1 billion "common colds" occur each year. Respiratory conditions are among the most frequent reasons for hospital stays among children.

[0003] The human metapneumovirus (hMPV) is a negative-sense, single-stranded RNA virus of the genus *Pneumovirinae* and of the family Paramyxoviridae and is closely related to the avian metapneumovirus (AMPV) subgroup C. It was isolated for the first time in 2001 in the Netherlands by using the RAP-PCR (RNA arbitrarily primed PCR) technique for identification of unknown viruses growing in cultured cells. hMPV is second only to RSV as an important cause of viral lower respiratory tract illness (LRI) in young children. The seasonal epidemiology of hMPV appears to be similar to that of RSV, but the incidence of infection and illness appears to be substantially lower.

[0004] Parainfluenza virus type 3 (PIV3), like hMPV, is also a negative-sense, single-stranded sense RNA virus of the genus *Pneumovirinae* and of the family Paramyxoviridae and is a major cause of ubiquitous acute respiratory infections of infancy and early childhood. Its incidence peaks around 4-12 months of age, and the virus is responsible for 3-10% of hospitalizations, mainly for bronchiolitis and pneumonia. PIV3 can be fatal, and in some instances is associated with neurologic diseases, such as febrile seizures. It can also result in airway remodeling, a significant cause of morbidity. In developing regions of the world, infants and young children are at the highest risk of mortality, either from primary PIV3 viral infection or a secondary consequences, such as bacterial infections. Human parainfluenza

viruses (hPIV) types 1, 2 and 3 (hPIV1, hPIV2 and hPIV3, respectively), also like hMPV, are second only to RSV as important causes of viral LRI in young children.

[0005] RSV, too, is a negative-sense, single-stranded RNA virus of the genus *Pneumovirinae* and of the family Paramyxoviridae. Symptoms in adults typically resemble a sinus infection or the common cold, although the infection may be asymptomatic. In older adults (e.g., >60 years), RSV infection may progress to bronchiolitis or pneumonia. Symptoms in children are often more severe, including bronchiolitis and pneumonia. It is estimated that in the United States, most children are infected with RSV by the age of three. The RSV virion consists of an internal nucleocapsid comprised of the viral RNA bound to nucleoprotein (N), phosphoprotein (P), and large polymerase protein (L). The nucleocapsid is surrounded by matrix protein (M) and is encapsulated by a lipid bilayer into which the viral fusion (F) and attachment (G) proteins as well as the small hydrophobic protein (SH) are incorporated. The viral genome also encodes two nonstructural proteins (NS1 and NS2), which inhibit type I interferon activity as well as the M-2 protein.

[0006] The continuing health problems associated with hMPV, PIV3 and RSV are of concern internationally, reinforcing the importance of developing effective and safe vaccine candidates against these virus.

[0007] Despite decades of research, no vaccines currently exist (Sato and Wright, *Pediatr. Infect. Dis. J.* 2008; 27(10 Suppl):S123-5). Recombinant technology, however, has been used to target the formation of vaccines for hPIV-1, 2 and 3 serotypes, for example, and has taken the form of several live-attenuated intranasal vaccines. Two vaccines in particular were found to be immunogenic and well tolerated against hPIV-3 in phase I trials. hPIV1 and hPIV2 vaccine candidates remain less advanced (Durbin and Karron, *Clinical Infectious Diseases: an official publication of the Infectious Diseases Society of America* 2003; 37(12):1668-77).

[0008] Measles virus (MeV), like hMPV, PIV3 and RSV, is a negative-sense, single-stranded RNA virus that is the cause of measles, an infection of the respiratory system. MeV is of the genus *Morbillivirus* within the family Paramyxoviridae. Humans are the natural hosts of the virus; no animal reservoirs are known to exist. Symptoms of measles include fever, cough, runny nose, red eyes and a generalized, maculopapular, erythematous rash. The virus is highly contagious and is spread by coughing.

[0009] In addition to hMPV, PIV, RSV and MeV, betacoronaviruses are known to cause respiratory illnesses. Betacoronaviruses (BetaCoVs) are one of four genera of coronaviruses of the subfamily Coronavirinae in the family Coronaviridae, of the order Nidovirales. They are enveloped, positive-sense, single-stranded RNA viruses of zoonotic origin. The coronavirus genera are each composed of varying viral lineages, with the *betacoronavirus* genus containing four such lineages. The BetaCoVs of the greatest clinical importance concerning humans are OC43 and HKU1 of the A lineage, SARS-CoV of the B lineage, and MERS-CoV of the C lineage. MERS-CoV is the first betacoronavirus belonging to lineage C that is known to infect humans.

[0010] The Middle East respiratory syndrome coronavirus (MERS-CoV), or EMC/2012 (HCoV-EMC/2012), initially referred to as novel coronavirus 2012 or simply novel coronavirus, was first reported in 2012 after genome sequencing of a virus isolated from sputum samples from a

person who fell ill during a 2012 outbreak of a new flu. As of July 2015, MERS-CoV cases have been reported in over 21 countries. The outbreaks of MERS-CoV have raised serious concerns world-wide, reinforcing the importance of developing effective and safe vaccine candidates against MERS-CoV.

[0011] Severe acute respiratory syndrome (SARS) emerged in China in 2002 and spread to other countries before brought under control. Because of a concern for reemergence or a deliberate release of the SARS coronavirus, vaccine development was initiated.

[0012] Deoxyribonucleic acid (DNA) vaccination is one technique used to stimulate humoral and cellular immune responses to foreign antigens, such as hMPV antigens and/or PIV antigens and/or RSV antigens. The direct injection of genetically engineered DNA (e.g., naked plasmid DNA) into a living host results in a small number of its cells directly producing an antigen, resulting in a protective immunological response. With this technique, however, comes potential problems, including the possibility of insertional mutagenesis, which could lead to the activation of oncogenes or the inhibition of tumor suppressor genes.

SUMMARY

[0013] Provided herein are ribonucleic acid (RNA) vaccines that build on the knowledge that RNA (e.g., messenger RNA (mRNA)) can safely direct the body's cellular machinery to produce nearly any protein of interest, from native proteins to antibodies and other entirely novel protein constructs that can have therapeutic activity inside and outside of cells. The RNA (e.g., mRNA) vaccines of the present disclosure may be used to induce a balanced immune response against hMPV, PIV, RSV, MeV, and/or BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-NH and/or HCoV-HKU1), or any combination of two or more of the foregoing viruses, comprising both cellular and humoral immunity, without risking the possibility of insertional mutagenesis, for example, hMPV, PIV, RSV, MeV, BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1) and combinations thereof are referred to herein as "respiratory viruses." Thus, the term "respiratory virus RNA vaccines" encompasses hMPV RNA vaccines, PIV RNA vaccines, RSV RNA vaccines, MeV RNA vaccines, BetaCoV RNA vaccines, and any combination of two or more of hMPV RNA vaccines, PIV RNA vaccines, RSV RNA vaccines, MeV RNA vaccines, and BetaCoV RNA vaccines.

[0014] The RNA (e.g., mRNA) vaccines may be utilized in various settings depending on the prevalence of the infection or the degree or level of unmet medical need. The RNA (e.g., mRNA) vaccines may be utilized to treat and/or prevent a hMPV, PIV, RSV, MeV, a BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1), or any combination of two or more of the foregoing viruses, of various genotypes, strains, and isolates. The RNA (e.g., mRNA) vaccines have superior properties in that they produce much larger antibody titers and produce responses earlier than commercially available anti-viral therapeutic treatments. While not wishing to be bound by theory, it is believed that the RNA (e.g., mRNA) vaccines, as mRNA polynucleotides, are better designed to produce the appropriate protein conformation upon translation as the RNA (e.g., mRNA) vaccines

co-opt natural cellular machinery. Unlike traditional vaccines, which are manufactured ex vivo and may trigger unwanted cellular responses, RNA (e.g., mRNA) vaccines are presented to the cellular system in a more native fashion.

[0015] In some aspects the invention is a respiratory virus vaccine, comprising at least one RNA polynucleotide having an open reading frame encoding at least one respiratory virus antigenic polypeptide, formulated in a cationic lipid nanoparticle.

[0016] Surprisingly, in some aspects it has also been shown that efficacy of mRNA vaccines can be significantly enhanced when combined with a flagellin adjuvant, in particular, when one or more antigen-encoding mRNAs is combined with an mRNA encoding flagellin.

[0017] RNA (e.g., mRNA) vaccines combined with the flagellin adjuvant (e.g., mRNA-encoded flagellin adjuvant) have superior properties in that they may produce much larger antibody titers and produce responses earlier than commercially available vaccine formulations. While not wishing to be bound by theory, it is believed that the RNA (e.g., mRNA) vaccines, for example, as mRNA polynucleotides, are better designed to produce the appropriate protein conformation upon translation, for both the antigen and the adjuvant, as the RNA (e.g., mRNA) vaccines co-opt natural cellular machinery. Unlike traditional vaccines, which are manufactured ex vivo and may trigger unwanted cellular responses, RNA (e.g., mRNA) vaccines are presented to the cellular system in a more native fashion.

[0018] Some embodiments of the present disclosure provide RNA (e.g., mRNA) vaccines that include at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide or an immunogenic fragment thereof (e.g., an immunogenic fragment capable of inducing an immune response to the antigenic polypeptide) and at least one RNA (e.g., mRNA polynucleotide) having an open reading frame encoding a flagellin adjuvant.

[0019] In some embodiments, at least one flagellin polypeptide (e.g., encoded flagellin polypeptide) is a flagellin protein. In some embodiments, at least one flagellin polypeptide (e.g., encoded flagellin polypeptide) is an immunogenic flagellin fragment. In some embodiments, at least one flagellin polypeptide and at least one antigenic polypeptide are encoded by a single RNA (e.g., mRNA) polynucleotide. In other embodiments, at least one flagellin polypeptide and at least one antigenic polypeptide are each encoded by a different RNA polynucleotide.

[0020] In some embodiments at least one flagellin polypeptide has at least 80%, at least 85%, at least 90%, or at least 95% identity to a flagellin polypeptide having a sequence identified by any one of SEQ ID NO: 54-56.

[0021] Provided herein, in some embodiments, is a ribonucleic acid (RNA) (e.g., mRNA) vaccine, comprising at least one (e.g., at least 2, 3, 4 or 5) RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one (e.g., at least 2, 3, 4 or 5) hMPV, PIV, RSV, MeV, or a BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide, or any combination of two or more of the foregoing antigenic polypeptides. Herein, use of the term "antigenic polypeptide" encompasses immunogenic fragments of the antigenic polypeptide (an immuno-

genic fragment that induces (or is capable of inducing) an immune response to hMPV, PIV, RSV, MeV, or a BetaCoV), unless otherwise stated.

[0022] Also provided herein, in some embodiments, is a RNA (e.g., mRNA) vaccine comprising at least one (e.g., at least 2, 3, 4 or 5) RNA polynucleotide having an open reading frame encoding at least one (e.g., at least 2, 3, 4 or 5) hMPV, PIV, RSV, MeV, and/or a BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NI.63, HCoV-NL, HCoV-NH, HCoV-IKU1) antigenic polypeptide or an immunogenic fragment thereof, linked to a signal peptide.

[0023] Further provided herein, in some embodiments, is a nucleic acid (e.g., DNA) encoding at least one (e.g., at least 2, 3, 4 or 5) hMPV, PIV, RSV, MeV, and/or a BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NI.63, HCoV-NL, HCoV-NH, HCoV-IKU1) RNA (e.g., mRNA) polynucleotide.

[0024] Further still, provided herein, in some embodiments, is a method of inducing an immune response in a subject, the method comprising administering to the subject a vaccine comprising at least one (e.g., at least 2, 3, 4 or 5) RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one (e.g., at least 2, 3, 4 or 5) hMPV, PIV, RSV, MeV, and/or a BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NI.63, HCoV-NL, HCoV-NH, HCoV-IKU1) antigenic polypeptide, or any combination of two or more of the foregoing antigenic polypeptides.

[0025] hMPV/PIV3/RSV

[0026] In some embodiments, a RNA (e.g., mRNA) vaccine comprises at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV, PIV3 or RSV antigenic polypeptide. In some embodiments, at least one antigenic polypeptide is a hMPV, PIV3 or RSV polypeptide. In some embodiments, at least one antigenic polypeptide is major surface glycoprotein G or an immunogenic fragment thereof. In some embodiments, at least one antigenic polypeptide is Fusion (F) glycoprotein (e.g., Fusion glycoprotein F0, F1 or F2) or an immunogenic fragment thereof. In some embodiments, at least one antigenic polypeptide is major surface glycoprotein G or an immunogenic fragment thereof and F glycoprotein or an immunogenic fragment thereof. In some embodiments, the antigenic polypeptide is nucleoprotein (N) or an immunogenic fragment thereof, phosphoprotein (P) or an immunogenic fragment thereof, large polymerase protein (L) or an immunogenic fragment thereof, matrix protein (M) or an immunogenic fragment thereof, small hydrophobic protein (SH) or an immunogenic fragment thereof, nonstructural protein1(NS1) or an immunogenic fragment thereof, or nonstructural protein 2 (NS2) and an immunogenic fragment thereof. In some embodiments, at least one hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 (Table 3; see also amino acid sequences of Table 4). In some embodiments, the amino acid sequence of the hMPV antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 5-8 (Table 3; see also amino acid sequences of Table 4).

[0027] In some embodiments, at least one hMPV antigenic polypeptide is encoded by a nucleic acid sequence identified by any one of SEQ ID NO: 1-4 (Table 2).

[0028] In some embodiments, at least one hMPV RNA (e.g., mRNA) polynucleotide is encoded by a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 1-4 (Table 2). In some embodiments, at least one hMPV RNA (e.g., mRNA) polynucleotide comprises a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 57-60 (Table 2).

[0029] In some embodiments, at least one antigenic polypeptide is obtained from hMPV strain CAN98-75 (CAN75) or the hMPV strain CAN97-83 (CAN83).

[0030] In some embodiments, at least one PIV3 antigenic polypeptide comprises hemagglutinin-neuraminidase, Fusion (F) glycoprotein, matrix protein (M), nucleocapsid protein (N), viral replicase (L), non-structural V protein, or an immunogenic fragment thereof.

[0031] In some embodiments, at least one PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 (Table 6; see also amino acid sequences of Table 7). In some embodiments, the amino acid sequence of the PIV3 antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 12-13 (Table 6; see also amino acid sequences of Table 7).

[0032] In some embodiments, at least one PIV3 antigenic polypeptide is encoded by a nucleic acid sequence identified by any one of SEQ ID NO: 9-12 (Table 5; see also nucleic acid sequences of Table 7).

[0033] In some embodiments, at least one PIV3 RNA (e.g., mRNA) polynucleotide is encoded by a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 9-12 (Table 5; see also nucleic acid sequences of Table 7). In some embodiments, at least one PIV3 RNA (e.g., mRNA) polynucleotide comprises a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 61-64 (Table 5).

[0034] In some embodiments, at least one antigenic polypeptide is obtained from PIV3 strain HPIV3/Homo sapiens/PER/FLA4815/2008.

[0035] In some embodiments, at least one RSV antigenic polypeptide comprises at least one antigenic polypeptide that comprises glycoprotein G, glycoprotein F, or an immunogenic fragment thereof. In some embodiments, at least one RSV antigenic polypeptide comprises at least one antigenic polypeptide that comprises glycoprotein F and at least one or at least two antigenic polypeptide selected from G, M, N, P, L, SH, M2, NS1 and NS2.

[0036] MeV

[0037] In some embodiments, a RNA (e.g., mRNA) vaccine comprises at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one MeV antigenic polypeptide. In some embodiments, at least one antigenic polypeptide is a hemagglutinin (HA) protein or an immunogenic fragment thereof. The HA protein may be from MeV strain D3 or B8, for example. In some embodiments, at least one antigenic polypeptide is a Fusion (F) protein or an immunogenic fragment thereof. The F protein may be from MeV strain D3 or B8, for example. In some embodiments, a MeV RNA (e.g., mRNA) vaccine comprises at least one RNA polynucleotide encoding a HA protein and a F protein. The HA and F proteins may be from MeV strain D3 or B8, for example.

[0038] In some embodiments, at least one MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 (Table 14). In some embodiments, the amino acid sequence of the MeV antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 47-50 (Table 14).

[0039] In some embodiments, at least one MeV antigenic polypeptide is encoded by a nucleic acid sequence of SEQ ID NO: 35-46 (Table 13).

[0040] In some embodiments, at least one MeV RNA (e.g., mRNA) polynucleotide is encoded by a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 35-46 (Table 13). In some embodiments, at least one MeV RNA (e.g., mRNA) polynucleotide comprises a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 69-80 (Table 13).

[0041] In some embodiments, at least one antigenic polypeptide is obtained from MeV strain B3/B3.1, C2, D4, D6, D7, D8, G3, H1, Moraten, Rubcovax, MVi/New Jersey, USA/45.05, MVi/Texas, USA/4.07, AIK-C, MVi/New York, USA/26.09/3, MVi/California, USA/16.03, MVi/Virginia, USA/15.09, MVi/California, USA/8.04, or MVi/Pennsylvania, USA/20.09.

[0042] BetaCoV

[0043] In some embodiments, a RNA (e.g., mRNA) vaccine comprises at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one BetaCoV antigenic polypeptide. In some embodiments, the BetaCoV is MERS-CoV. In some embodiments, the BetaCoV is SARS-CoV. In some embodiments, the BetaCoV is HCoV-OC43. In some embodiments, the BetaCoV is HCoV-229E. In some embodiments, the BetaCoV is HCoV-NL63. In some embodiments, the BetaCoV is HCoV-HKU1. In some embodiments, at least one antigenic polypeptide is a betacoronavirus structural protein. For example, a betacoronavirus structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, a betacoronavirus structural protein is a spike protein (S). In some embodiments, a betacoronavirus structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof.

[0044] BetaCoV RNA (e.g., mRNA) polynucleotides of the vaccines provided herein may encode viral protein components of betacoronaviruses, for example, accessory proteins, replicase proteins and the like are encompassed by the present disclosure. RNA (e.g., mRNA) vaccines may include RNA polynucleotides encoding at least one accessory protein (e.g., protein 3, protein 4a, protein 4b, protein 5), at least one replicase protein (e.g., protein 1a, protein 1b), or a combination of at least one accessory protein and at least one replicase protein. The present disclosure also encompasses RNA (e.g., mRNA) vaccines comprising RNA (e.g., mRNA) polynucleotides encoding an accessory protein and/or a replicase protein in combination with at least one structural protein. Due to their surface expression properties, vaccines featuring RNA polynucleotides encoding structural proteins are believed to have preferred immunogenic activity and, hence, may be most suitable for use in the vaccines of the present disclosure.

[0045] Some embodiments of the present disclosure provide betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1 or a combination thereof) vaccines that include at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide. Also provided herein are pan-betacoronavirus vaccines. Thus, a betacoronavirus vaccine comprising a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding any one, two, three or four of MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, and HCoV-HKU1, for example, may be effective against any one of, any combination of, or all of, MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1. Other betacoronaviruses are encompassed by the present disclosure.

[0046] In some embodiments, at least one antigenic polypeptide is a MERS-CoV structural protein. For example, a MERS-CoV structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, the MERS-CoV structural protein is a spike protein (S) (see, e.g., Coleman C M et al. *Vaccine* 2014; 32:3169-74, incorporated herein by reference). In some embodiments, the MERS-CoV structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof (Li J et al. *Viral Immunol* 2013; 26(2):126-32; He Y et al. *Biochem Biophys Res Commun* 2004; 324(2):773-81, each of which is incorporated herein by reference).

[0047] In some embodiments, at least one MERS-CoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-28 or 33 (Table 11). In some embodiments, the amino acid sequence of the MERS-CoV antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 24-28 or 33 (Table 11).

[0048] In some embodiments, at least one MERS-CoV antigenic polypeptide is encoded by a nucleic acid sequence identified by any one of SEQ ID NO: 20-23 (Table 10).

[0049] In some embodiments, at least one MERS-CoV RNA (e.g., mRNA) polynucleotide is encoded by a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 20-23 (Table 10). In some embodiments, at least one MERS-CoV RNA (e.g., mRNA) polynucleotide comprises a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 65-68 (Table 10).

[0050] In some embodiments, at least one antigenic polypeptide is obtained from MERS-CoV strain Riyadh_14_2013, 2c1MC/2012, or Hasa_1_2013.

[0051] In some embodiments, at least one antigenic polypeptide is a SARS-CoV structural protein. For example, a SARS-CoV structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, the SARS-CoV structural protein is a spike protein (S). In some embodiments, the SARS-CoV structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof.

[0052] In some embodiments, at least one SARS-CoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 29, 32 or 34 (Table 11). In some embodiments, the amino acid sequence of the SARS-CoV antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 29, 32 or 34 (Table 11).

[0053] In some embodiments, at least one antigenic polypeptide is a HCoV-OC43 structural protein. For example, a HCoV-OC43 structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, the HCoV-OC43 structural protein is a spike protein (S). In some embodiments, the HCoV-OC43 structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof.

[0054] In some embodiments, at least one HCoV-OC43 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 30 (Table 11). In some embodiments, the amino acid sequence of the HCoV-OC43 antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 30 (Table 11).

[0055] In some embodiments, an antigenic polypeptide is a HCoV-HKU1 structural protein. For example, a HCoV-HKU1 structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, the HCoV-HKU1 structural protein is a spike protein (S). In some embodiments, the HCoV-HKU1 structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof.

[0056] In some embodiments, at least one HCoV-HKU1 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 31 (Table 11). In some embodiments, the amino acid sequence of the HCoV-HKU1 antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 31 (Table 11).

[0057] In some embodiments, an open reading frame of a RNA (e.g., mRNA) vaccine is codon-optimized. In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and is codon optimized mRNA.

[0058] In some embodiments, a RNA (e.g., mRNA) vaccine further comprising an adjuvant.

[0059] Tables 4, 7, 12 and 15 provide National Center for Biotechnology Information (NCBI) accession numbers of interest. It should be understood that the phrase "an amino acid sequence of Tables 4, 7, 12 and 15" refers to an amino acid sequence identified by one or more NCBI accession numbers listed in Tables 4, 7, 12 and 15. Each of the amino acid sequences, and variants having greater than 95% identity or greater than 98% identity to each of the amino acid sequences encompassed by the accession numbers of Tables 4, 7, 12 and 15 are included within the constructs (polynucleotides/polypeptides) of the present disclosure.

[0060] In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 80% identity to wild-type mRNA sequence. In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 75%, 85% or 95% identity to a wild-type mRNA sequence. In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 50-80%, 60-80%, 40-80%, 30-80%, 70-80%, 75-80% or 78-80% identity to wild-type mRNA sequence. In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 40-85%, 50-85%, 60-85%, 30-85%, 70-85%, 75-85% or 80-85% identity to wild-type mRNA sequence. In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 40-90%, 50-90%, 60-90%, 30-90%, 70-90%, 75-90%, 80-90%, or 85-90% identity to wild-type mRNA sequence.

[0061] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to wild-type mRNA sequence, but does not include wild-type mRNA sequence.

[0062] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and has less than 95%, 90%, 85%, 80% or 75% identity to wild-type mRNA sequence. In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and has 30-80%, 40-80%, 50-80%, 60-80%, 70-80%, 75-80% or 78-80%, 30-85%, 40-85%, 50-805%, 60-85%, 70-85%, 75-85% or 78-85%, 30-90%, 40-90%, 50-90%, 60-90%, 70-90%, 75-90%, 80-90% or 85-90% identity to wild-type mRNA sequence.

[0063] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15). In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having 95%-99% identity to an amino acid sequence

identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15).

[0064] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and having membrane fusion activity. In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having 95%-99% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and having membrane fusion activity.

[0065] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) that attaches to cell receptors.

[0066] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) that causes fusion of viral and cellular membranes.

[0067] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide,

at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides), at least one 5' terminal cap and at least one chemical modification, formulated within a lipid nanoparticle.

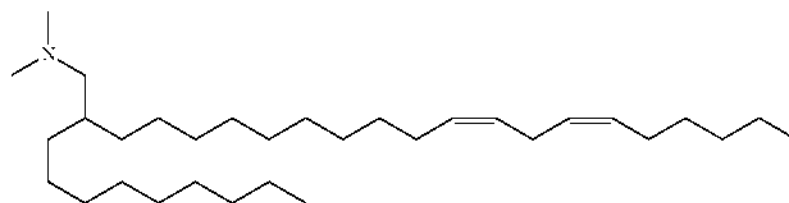
[0069] In some embodiments, a 5' terminal cap is 7mG (5')ppp(5')NmpNp.

[0070] In some embodiments, at least one chemical modification is selected from pseudouridine, N1-methylpseudouridine, N1-ethylpseudouridine, 2-thiouridine, 4'-thiouridine, 5-methylcytosine, 5-methyluridine, 2-thio-1-methyl-1-deaza-pseudouridine, 2-thio-1-methyl-pseudouridine, 2-thio-5-aza-uridine, 2-thio-dihydropseudouridine, 2-thio-dihydrouridine, 2-thio-pseudouridine, 4-methoxy-2-thio-pseudouridine, 4-methoxy-pseudouridine, 4-thio-1-methylpseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-methyluridine. In some embodiments, the chemical modification is in the 5-position of the uracil. In some embodiments, the chemical modification is a N1-methylpseudouridine. In some embodiments, the chemical modification is a N1-ethylpseudouridine.

[0071] In some embodiments, a lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid. In some embodiments, a cationic lipid is an ionizable cationic lipid and the non-cationic lipid is a neutral lipid, and the sterol is a cholesterol. In some embodiments, a cationic lipid is selected from the group consisting of 2,2-dilinoleyl-4-dimethylaminoethyl-1,3-dioxolane (DI.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DI.in-MC3-DMA), di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (I.319), (1Z,15Z)-N,N-dimethyl-2-nonylhenicosa-12,15-dien-1-amine (I.608), and N,N-dimethyl-1-[(1S,2R)-2-octylecyclopropyl]heptadecan-8-amine (I.530).

[0072] In some embodiments, the lipid is

(I.608)

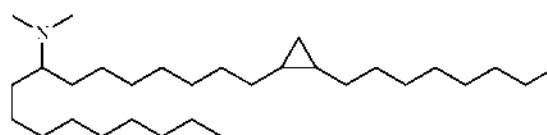


at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) that is responsible for binding of the virus to a cell being infected.

[0068] Some embodiments of the present disclosure provide a vaccine that includes at least one ribonucleic acid (RNA) (e.g., mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3

[0073] In some embodiments, the lipid is

(I.530)



[0074] In some embodiments, a lipid nanoparticle comprises compounds of Formula (I) and/or Formula (II), discussed below.

[0075] In some embodiments, a respiratory virus RNA (e.g., mRNA) vaccine is formulated in a lipid nanoparticle that comprises a compound selected from Compounds 3, 18, 20, 25, 26, 29, 30, 60, 108-112 and 122, described below.

[0076] Some embodiments of the present disclosure provide a vaccine that includes at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides), wherein at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) of the uracil in the open reading frame have a chemical modification, optionally wherein the vaccine is formulated in a lipid nanoparticle (e.g., a lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid).

[0077] In some embodiments, 100% of the uracil in the open reading frame have a chemical modification. In some embodiments, a chemical modification is in the 5-position of the uracil. In some embodiments, a chemical modification is a N1-methyl pseudouridine. In some embodiments, 100% of the uracil in the open reading frame have a N1-methyl pseudouridine in the 5-position of the uracil.

[0078] In some embodiments, an open reading frame of a RNA (e.g., mRNA) polynucleotide encodes at least two antigenic polypeptides (e.g., at least two hMPV antigenic polypeptides, at least two PIV3 antigenic polypeptides, at least two RSV antigenic polypeptides, at least two MeV antigenic polypeptides, or at least two BetaCoV antigenic polypeptides, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides). In some embodiments, the open reading frame encodes at least five or at least ten antigenic polypeptides. In some embodiments, the open reading frame encodes at least 100 antigenic polypeptides. In some embodiments, the open reading frame encodes 2-100 antigenic polypeptides.

[0079] In some embodiments, a vaccine comprises at least two RNA (e.g., mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides). In some embodiments, the vaccine comprises at least five or at least ten RNA (e.g., mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide or an immunogenic fragment thereof. In some embodiments, the vaccine comprises at least 100 RNA (e.g., mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide. In some embodiments, the vaccine

comprises 2-100 RNA (e.g., mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide.

[0080] In some embodiments, at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) is fused to a signal peptide. In some embodiments, the signal peptide is selected from: a HulgGk signal peptide (METPAQLLELLIWIPLDTIG; SEQ ID NO: 15); IgI heavy chain epsilon-1 signal peptide (MDWTWILFLVAAAIRVHS; SEQ ID NO: 16); Japanese encephalitis PRM signal sequence (MLGSNSGQRVVFTELLIIVAPAYS; SEQ ID NO: 17); VSVg protein signal sequence (MKCLLYLAFIFGVNCA; SEQ ID NO: 18) and Japanese encephalitis JEV signal sequence (MWLVSLAIVTACAGA; SEQ ID NO: 19).

[0081] In some embodiments, the signal peptide is fused to the N-terminus of at least one antigenic polypeptide. In some embodiments, a signal peptide is fused to the C-terminus of at least one antigenic polypeptide.

[0082] In some embodiments, at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) comprises a mutated N-linked glycosylation site.

[0083] Also provided herein is a RNA (e.g., mRNA) vaccine of any one of the foregoing paragraphs (e.g., a hMPV vaccine, a PIV3 vaccine, a RSV vaccine, a MeV vaccine, or a BetaCoV vaccine, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing vaccines), formulated in a nanoparticle (e.g., a lipid nanoparticle).

[0084] In some embodiments, the nanoparticle has a mean diameter of 50-200 nm. In some embodiments, the nanoparticle is a lipid nanoparticle. In some embodiments, the lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid. In some embodiments, the lipid nanoparticle comprises a molar ratio of about 20-60% cationic lipid, 0.5-15% PEG-modified lipid, 25-55% sterol, and 25% non-cationic lipid. In some embodiments, the cationic lipid is an ionizable cationic lipid and the non-cationic lipid is a neutral lipid, and the sterol is a cholesterol. In some embodiments, the cationic lipid is selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319).

[0085] In some embodiments, a lipid nanoparticle comprises compounds of Formula (I) and/or Formula (II), as discussed below.

[0086] In some embodiments, a lipid nanoparticle comprises Compounds 3, 18, 20, 25, 26, 29, 30, 60, 108-112, or 122, as discussed below.

[0087] In some embodiments, the nanoparticle has a polydispersity value of less than 0.4 (e.g., less than 0.3, 0.2 or 0.1).

[0088] In some embodiments, the nanoparticle has a net neutral charge at a neutral pH value.

[0089] In some embodiments, the respiratory virus vaccine is multivalent.

[0090] Some embodiments of the present disclosure provide methods of inducing an antigen specific immune response in a subject, comprising administering to the subject any of the RNA (e.g., mRNA) vaccine as provided herein in an amount effective to produce an antigen-specific immune response. In some embodiments, the RNA (e.g., mRNA) vaccine is a hMPV vaccine, a PIV3 vaccine, a RSV vaccine, a MeV vaccine, or a BetaCoV vaccine, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1 vaccines. In some embodiments, the RNA (e.g., mRNA) vaccine is a combination vaccine comprising a combination of any two or more of the foregoing vaccines.

[0091] In some embodiments, an antigen-specific immune response comprises a T cell response or a B cell response.

[0092] In some embodiments, a method of producing an antigen-specific immune response comprises administering to a subject a single dose (no booster dose) of a RNA (e.g., mRNA) vaccine of the present disclosure. In some embodiments, the RNA (e.g., mRNA) vaccine is a hMPV vaccine, a PIV3 vaccine, a RSV vaccine, a MeV vaccine, or a BetaCoV vaccine, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1 vaccines. In some embodiments, the RNA (e.g., mRNA) vaccine is a combination vaccine comprising a combination of any two or more of the foregoing vaccines.

[0093] In some embodiments, a method further comprises administering to the subject a second (booster) dose of a RNA (e.g., mRNA) vaccine. Additional doses of a RNA (e.g., mRNA) vaccine may be administered.

[0094] In some embodiments, the subjects exhibit a seroconversion rate of at least 80% (e.g., at least 85%, at least 90%, or at least 95%) following the first dose or the second (booster) dose of the vaccine. Seroconversion is the time period during which a specific antibody develops and becomes detectable in the blood. After seroconversion has occurred, a virus can be detected in blood tests for the antibody. During an infection or immunization, antigens enter the blood, and the immune system begins to produce antibodies in response. Before seroconversion, the antigen itself may or may not be detectable, but antibodies are considered absent. During seroconversion, antibodies are present but not yet detectable. Any time after seroconversion, the antibodies can be detected in the blood, indicating a prior or current infection.

[0095] In some embodiments, a RNA (e.g., mRNA) vaccine is administered to a subject by intradermal or intramuscular injection.

[0096] Some embodiments, of the present disclosure provide methods of inducing an antigen specific immune response in a subject, including administering to a subject a RNA (e.g., mRNA) vaccine in an effective amount to produce an antigen specific immune response in a subject.

Antigen-specific immune responses in a subject may be determined, in some embodiments, by assaying for antibody titer (for titer of an antibody that binds to a hMPV, PIV3, RSV, MeV and/or BetaCoV antigenic polypeptide) following administration to the subject of any of the RNA (e.g., mRNA) vaccines of the present disclosure. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased by at least 1 log relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased by 1-3 log relative to a control.

[0097] In some embodiments, the anti-antigenic polypeptide antibody titer produced in a subject is increased at least 2 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased at least 5 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased at least 10 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased 2-10 times relative to a control.

[0098] In some embodiments, the control is an anti-antigenic polypeptide antibody titer produced in a subject who has not been administered a RNA (e.g., mRNA) vaccine of the present disclosure. In some embodiments, the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine (see, e.g., Ren J, et al. *J of Gen. Virol.* 2015; 96: 1515-1520), or wherein the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some embodiments, the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a hMPV, PIV3, RSV, MeV and/or BetaCoV virus-like particle (VLP) vaccine (see, e.g., Cox R G et al., *J Virol.* 2014 June; 88(11): 6368-6379).

[0099] A RNA (e.g., mRNA) vaccine of the present disclosure is administered to a subject in an effective amount (an amount effective to induce an immune response). In some embodiments, the effective amount is a dose equivalent to an at least 2-fold, at least 4-fold, at least 10-fold, at least 100-fold, at least 1000-fold reduction in the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, wherein the anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, a purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, a live attenuated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine, an inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine, or a hMPV, PIV3, RSV, MeV and/or BetaCoV VLP vaccine. In some embodiments, the effective amount is a dose equivalent to 2-1000-fold reduction in the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, wherein the anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, a purified hMPV, PIV3, RSV, MeV and/or

BetaCoV protein vaccine, a live attenuated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine, an inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine, or a hMPV, PIV3, RSV, MeV and/or BetaCoV VLP vaccine.

[0100] In some embodiments, the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a virus-like particle (VLP) vaccine comprising structural proteins of hMPV, PIV3, RSV, MeV and/or BetaCoV.

[0101] In some embodiments, the RNA (e.g., mRNA) vaccine is formulated in an effective amount to produce an antigen specific immune response in a subject.

[0102] In some embodiments, the effective amount is a total dose of 25 μg to 1000 μg , or 50 μg to 1000 μg . In some embodiments, the effective amount is a total dose of 100 μg . In some embodiments, the effective amount is a dose of 25 μg administered to the subject a total of two times. In some embodiments, the effective amount is a dose of 100 μg administered to the subject a total of two times. In some embodiments, the effective amount is a dose of 400 μg administered to the subject a total of two times. In some embodiments, the effective amount is a dose of 500 μg administered to the subject a total of two times.

[0103] In some embodiments, the efficacy (or effectiveness) of a RNA (e.g., mRNA) vaccine is greater than 60%. In some embodiments, the RNA (e.g., mRNA) polynucleotide of the vaccine at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides.

[0104] Vaccine efficacy may be assessed using standard analyses (see, e.g., Weinberg et al., *J Infect Dis.* 2010 Jun. 1; 201(11):1607-10). For example, vaccine efficacy may be measured by double-blind, randomized, clinical controlled trials. Vaccine efficacy may be expressed as a proportionate reduction in disease attack rate (AR) between the unvaccinated (ARU) and vaccinated (ARV) study cohorts and can be calculated from the relative risk (RR) of disease among the vaccinated group with use of the following formulas:

$$\text{Efficacy} = (\text{ARU} - \text{ARV}) / \text{ARU} \times 100; \text{ and}$$

$$\text{Efficacy} = (1 - \text{RR}) \times 100.$$

[0105] Likewise, vaccine effectiveness may be assessed using standard analyses (see, e.g., Weinberg et al., *J Infect Dis.* 2010 Jun. 1; 201(11):1607-10). Vaccine effectiveness is an assessment of how a vaccine (which may have already proven to have high vaccine efficacy) reduces disease in a population. This measure can assess the net balance of benefits and adverse effects of a vaccination program, not just the vaccine itself, under natural field conditions rather than in a controlled clinical trial. Vaccine effectiveness is proportional to vaccine efficacy (potency) but is also affected by how well target groups in the population are immunized, as well as by other non-vaccine-related factors that influence the "real-world" outcomes of hospitalizations, ambulatory visits, or costs. For example, a retrospective case control analysis may be used, in which the rates of vaccination among a set of infected cases and appropriate controls are compared. Vaccine effectiveness may be expressed as a

rate difference, with use of the odds ratio (OR) for developing infection despite vaccination:

$$\text{Effectiveness} = (1 - \text{OR}) \times 100.$$

[0106] In some embodiments, the efficacy (or effectiveness) of a RNA (e.g., mRNA) vaccine is at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, or at least 90%.

[0107] In some embodiments, the vaccine immunizes the subject against hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses for up to 2 years. In some embodiments, the vaccine immunizes the subject against hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses for more than 2 years, more than 3 years, more than 4 years, or for 5-10 years.

[0108] In some embodiments, the subject is about 5 years old or younger. For example, the subject may be between the ages of about 1 year and about 5 years (e.g., about 1, 2, 3, 5 or 5 years), or between the ages of about 6 months and about 1 year (e.g., about 6, 7, 8, 9, 10, 11 or 12 months). In some embodiments, the subject is about 12 months or younger (e.g., 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2 months or 1 month). In some embodiments, the subject is about 6 months or younger. In some embodiments, the subject was born full term (e.g., about 37-42 weeks). In some embodiments, the subject was born prematurely, for example, at about 36 weeks of gestation or earlier (e.g., about 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26 or 25 weeks). For example, the subject may have been born at about 32 weeks of gestation or earlier. In some embodiments, the subject was born prematurely between about 32 weeks and about 36 weeks of gestation. In such subjects, a RNA (e.g., mRNA) vaccine may be administered later in life, for example, at the age of about 6 months to about 5 years, or older.

[0109] In some embodiments, the subject is pregnant (e.g., in the first, second or third trimester) when administered an RNA (e.g., mRNA) vaccine. Viruses such as hMPV, PIV3 and RSV causes infections of the lower respiratory tract, mainly in infants and young children. One-third of RSV related deaths, for example, occur in the first year of life, with 99 percent of these deaths occurring in low-resource countries. It's so widespread in the United States that nearly all children become infected with the virus before their second birthdays. Thus, the present disclosure provides RNA (e.g., mRNA) vaccines for maternal immunization to improve mother-to-child transmission of protection against the virus.

[0110] In some embodiments, the subject is a young adult between the ages of about 20 years and about 50 years (e.g., about 20, 25, 30, 35, 40, 45 or 50 years old).

[0111] In some embodiments, the subject is an elderly subject about 60 years old, about 70 years old, or older (e.g., about 60, 65, 70, 75, 80, 85 or 90 years old).

[0112] In some embodiments, the subject is has a chronic pulmonary disease (e.g., chronic obstructive pulmonary disease (COPD) or asthma). Two forms of COPD include chronic bronchitis, which involves a long-term cough with mucus, and emphysema, which involves damage to the

lungs over time. Thus, a subject administered a RNA (e.g., mRNA) vaccine may have chronic bronchitis or emphysema.

[0113] In some embodiments, the subject has been exposed to hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses; the subject is infected with hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses; or subject is at risk of infection by hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses.

[0114] In some embodiments, the subject is immunocompromised (has an impaired immune system, e.g., has an immune disorder or autoimmune disorder).

[0115] In some embodiments the nucleic acid vaccines described herein are chemically modified. In other embodiments the nucleic acid vaccines are unmodified.

[0116] Yet other aspects provide compositions for and methods of vaccinating a subject comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a first respiratory virus antigenic polypeptide, wherein the RNA polynucleotide does not include a stabilization element, and wherein an adjuvant is not coformulated or co-administered with the vaccine.

[0117] In other aspects the invention is a composition for or method of vaccinating a subject comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide wherein a dosage of between 10 µg/kg and 400 µg/kg of the nucleic acid vaccine is administered to the subject. In some embodiments the dosage of the RNA polynucleotide is 1-5 µg, 5-10 µg, 10-15 µg, 15-20 µg, 10-25 µg, 20-25 µg, 20-50 µg, 30-50 µg, 40-50 µg, 40-60 µg, 60-80 µg, 60-100 µg, 50-100 µg, 80-120 µg, 40-120 µg, 40-150 µg, 50-150 µg, 50-200 µg, 80-200 µg, 100-200 µg, 120-250 µg, 150-250 µg, 180-280 µg, 200-300 µg, 50-300 µg, 80-300 µg, 100-300 µg, 40-300 µg, 50-350 µg, 100-350 µg, 200-350 µg, 300-350 µg, 320-400 µg, 40-380 µg, 40-100 µg, 100-400 µg, 200-400 µg, or 300-400 µg per dose. In some embodiments, the nucleic acid vaccine is administered to the subject by intradermal or intramuscular injection. In some embodiments, the nucleic acid vaccine is administered to the subject on day zero. In some embodiments, a second dose of the nucleic acid vaccine is administered to the subject on day twenty one.

[0118] In some embodiments, a dosage of 25 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 100 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 50 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 75 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 150 micrograms of the RNA polynucleotide is included in the nucleic acid

vaccine administered to the subject. In some embodiments, a dosage of 400 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 200 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, the RNA polynucleotide accumulates at a 100 fold higher level in the local lymph node in comparison with the distal lymph node. In other embodiments the nucleic acid vaccine is chemically modified and in other embodiments the nucleic acid vaccine is not chemically modified.

[0119] Aspects of the invention provide a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide does not include a stabilization element, and a pharmaceutically acceptable carrier or excipient, wherein an adjuvant is not included in the vaccine. In some embodiments, the stabilization element is a histone stem-loop. In some embodiments, the stabilization element is a nucleic acid sequence having increased GC content relative to wild type sequence.

[0120] Aspects of the invention provide nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide is present in the formulation for in vivo administration to a host, which confers an antibody titer superior to the criterion for seroprotection for the first antigen for an acceptable percentage of human subjects. In some embodiments, the antibody titer produced by the mRNA vaccines of the invention is a neutralizing antibody titer. In some embodiments the neutralizing antibody titer is greater than a protein vaccine. In other embodiments the neutralizing antibody titer produced by the mRNA vaccines of the invention is greater than an adjuvanted protein vaccine. In yet other embodiments the neutralizing antibody titer produced by the mRNA vaccines of the invention is 1,000-10,000, 1,200-10,000, 1,400-10,000, 1,500-10,000, 1,000-5,000, 1,000-4,000, 1,800-10,000, 2,000-10,000, 2,000-5,000, 2,000-3,000, 2,000-4,000, 3,000-5,000, 3,000-4,000, or 2,000-2,500. A neutralization titer is typically expressed as the highest serum dilution required to achieve a 50% reduction in the number of plaques.

[0121] Also provided are nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide is present in a formulation for in vivo administration to a host for eliciting a longer lasting high antibody titer than an antibody titer elicited by an mRNA vaccine having a stabilizing element or formulated with an adjuvant and encoding the first antigenic polypeptide. In some embodiments, the RNA polynucleotide is formulated to produce a neutralizing antibodies within one week of a single administration. In some embodiments, the adjuvant is selected from a cationic peptide and an immunostimulatory nucleic acid. In some embodiments, the cationic peptide is protamine.

[0122] Aspects provide nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame comprising at least one chemical modification or optionally no nucleotide modification, the open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide is present in the formulation for in vivo administration to a host such that the level of antigen expression in the host significantly exceeds a level of

antigen expression produced by an mRNA vaccine having a stabilizing element or formulated with an adjuvant and encoding the first antigenic polypeptide.

[0123] Other aspects provide nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame comprising at least one chemical modification or optionally no nucleotide modification, the open reading frame encoding a first antigenic polypeptide, wherein the vaccine has at least 10 fold less RNA polynucleotide than is required for an unmodified mRNA vaccine to produce an equivalent antibody titer. In some embodiments, the RNA polynucleotide is present in a dosage of 25-100 micrograms.

[0124] Aspects of the invention also provide a unit of use vaccine, comprising between 10 ug and 400 ug of one or more RNA polynucleotides having an open reading frame comprising at least one chemical modification or optionally no nucleotide modification, the open reading frame encoding a first antigenic polypeptide, and a pharmaceutically acceptable carrier or excipient, formulated for delivery to a human subject. In some embodiments, the vaccine further comprises a cationic lipid nanoparticle.

[0125] Aspects of the invention provide methods of creating, maintaining or restoring antigenic memory to a respiratory virus strain in an individual or population of individuals comprising administering to said individual or population an antigenic memory booster nucleic acid vaccine comprising (a) at least one RNA polynucleotide, said polynucleotide comprising at least one chemical modification or optionally no nucleotide modification and two or more codon-optimized open reading frames, said open reading frames encoding a set of reference antigenic polypeptides, and (b) optionally a pharmaceutically acceptable carrier or excipient. In some embodiments, the vaccine is administered to the individual via a route selected from the group consisting of intramuscular administration, intradermal administration and subcutaneous administration. In some embodiments, the administering step comprises contacting a muscle tissue of the subject with a device suitable for injection of the composition. In some embodiments, the administering step comprises contacting a muscle tissue of the subject with a device suitable for injection of the composition in combination with electroporation.

[0126] Aspects of the invention provide methods of vaccinating a subject comprising administering to the subject a single dosage of between 25 ug/kg and 400 ug/kg of a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide in an effective amount to vaccinate the subject.

[0127] Other aspects provide nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame comprising at least one chemical modification, the open reading frame encoding a first antigenic polypeptide, wherein the vaccine has at least 10 fold less RNA polynucleotide than is required for an unmodified mRNA vaccine to produce an equivalent antibody titer. In some embodiments, the RNA polynucleotide is present in a dosage of 25-100 micrograms.

[0128] Other aspects provide nucleic acid vaccines comprising an LNP formulated RNA polynucleotide having an open reading frame comprising no nucleotide modifications (unmodified), the open reading frame encoding a first antigenic polypeptide, wherein the vaccine has at least 10 fold less RNA polynucleotide than is required for an unmodified

mRNA vaccine not formulated in a LNP to produce an equivalent antibody titer. In some embodiments, the RNA polynucleotide is present in a dosage of 25-100 micrograms.

[0129] The data presented in the Examples demonstrate significant enhanced immune responses using the formulations of the invention. Both chemically modified and unmodified RNA vaccines are useful according to the invention. Surprisingly, in contrast to prior art reports that it was preferable to use chemically unmodified mRNA formulated in a carrier for the production of vaccines, it is described herein that chemically modified mRNA-LNP vaccines required a much lower effective mRNA dose than unmodified mRNA, i.e., tenfold less than unmodified mRNA when formulated in carriers other than LNP. Both the chemically modified and unmodified RNA vaccines of the invention produce better immune responses than mRNA vaccines formulated in a different lipid carrier.

[0130] In other aspects the invention encompasses a method of treating an elderly subject age 60 years or older comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a respiratory virus antigenic polypeptide in an effective amount to vaccinate the subject.

[0131] In other aspects the invention encompasses a method of treating a young subject age 17 years or younger comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a respiratory virus antigenic polypeptide in an effective amount to vaccinate the subject.

[0132] In other aspects the invention encompasses a method of treating an adult subject comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a respiratory virus antigenic polypeptide in an effective amount to vaccinate the subject.

[0133] In some aspects the invention is a method of vaccinating a subject with a combination vaccine including at least two nucleic acid sequences encoding respiratory antigens wherein the dosage for the vaccine is a combined therapeutic dosage wherein the dosage of each individual nucleic acid encoding an antigen is a sub therapeutic dosage. In some embodiments, the combined dosage is 25 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the combined dosage is 100 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments the combined dosage is 50 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the combined dosage is 75 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the combined dosage is 150 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the combined dosage is 400 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the sub therapeutic dosage of each individual nucleic acid encoding an antigen is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 micrograms. In other embodiments the nucleic acid vaccine is chemically modified and in other embodiments the nucleic acid vaccine is not chemically modified.

[0134] The RNA polynucleotide is one of SEQ ID NO: 1-4, 9-12, 20-23, 35-46, 57-61, and 64-80 and includes at least one chemical modification. In other embodiments the RNA polynucleotide is one of SEQ ID NO: 1-4, 9-12, 20-23, 35-46, 57-61, and 64-80 and does not include any nucleotide modifications, or is unmodified. In yet other embodiments the at least one RNA polynucleotide encodes an antigenic protein of any of SEQ ID NO: 5-8, 12-13, 24-34, and 47-50 and includes at least one chemical modification. In other embodiments the RNA polynucleotide encodes an antigenic protein of any of SEQ ID NO: 5-8, 12-13, 24-34, and 47-50 and does not include any nucleotide modifications, or is unmodified.

[0135] In preferred aspects, vaccines of the invention (e.g., LNP-encapsulated mRNA vaccines) produce prophylactically- and/or therapeutically- efficacious levels, concentrations and/or titers of antigen-specific antibodies in the blood or serum of a vaccinated subject. As defined herein, the term antibody titer refers to the amount of antigen-specific antibody produced in a subject, e.g., a human subject. In exemplary embodiments, antibody titer is expressed as the inverse of the greatest dilution (in a serial dilution) that still gives a positive result. In exemplary embodiments, antibody titer is determined or measured by enzyme-linked immunosorbent assay (ELISA). In exemplary embodiments, antibody titer is determined or measured by neutralization assay, e.g., by microneutralization assay. In certain aspects, antibody titer measurement is expressed as a ratio, such as 1:40, 1:100, etc.

[0136] In exemplary embodiments of the invention, an efficacious vaccine produces an antibody titer of greater than 1:40, greater than 1:100, greater than 1:400, greater than 1:1000, greater than 1:2000, greater than 1:3000, greater than 1:4000, greater than 1:500, greater than 1:6000, greater than 1:7500, greater than 1:10000. In exemplary embodiments, the antibody titer is produced or reached by 10 days following vaccination, by 20 days following vaccination, by 30 days following vaccination, by 40 days following vaccination, or by 50 or more days following vaccination. In exemplary embodiments, the titer is produced or reached following a single dose of vaccine administered to the subject. In other embodiments, the titer is produced or reached following multiple doses, e.g., following a first and a second dose (e.g., a booster dose.)

[0137] In exemplary aspects of the invention, antigen-specific antibodies are measured in units of $\mu\text{g/ml}$ or are measured in units of IU/L (International Units per liter) or mIU/ml (milli International Units per ml). In exemplary embodiments of the invention, an efficacious vaccine produces $>0.5 \mu\text{g/ml}$, $>0.1 \mu\text{g/ml}$, $>0.2 \mu\text{g/ml}$, $>0.35 \mu\text{g/ml}$, $>0.5 \mu\text{g/ml}$, $>1 \mu\text{g/ml}$, $>2 \mu\text{g/ml}$, $>5 \mu\text{g/ml}$ or $>10 \mu\text{g/ml}$. In exemplary embodiments of the invention, an efficacious vaccine produces $>10 \text{ mIU/ml}$, $>20 \text{ mIU/ml}$, $>50 \text{ mIU/ml}$, $>100 \text{ mIU/ml}$, $>200 \text{ mIU/ml}$, $>500 \text{ mIU/ml}$ or $>1000 \text{ mIU/ml}$. In exemplary embodiments, the antibody level or concentration is produced or reached by 10 days following vaccination, by 20 days following vaccination, by 30 days following vaccination, by 40 days following vaccination, or by 50 or more days following vaccination. In exemplary embodiments, the level or concentration is produced or reached following a single dose of vaccine administered to the subject. In other embodiments, the level or concentration is produced or reached following multiple doses, e.g., following a first and a second dose (e.g., a booster dose.) In

exemplary embodiments, antibody level or concentration is determined or measured by enzyme-linked immunosorbent assay (ELISA). In exemplary embodiments, antibody level or concentration is determined or measured by neutralization assay, e.g., by microneutralization assay.

[0138] The details of various embodiments of the disclosure are set forth in the description below. Other features, objects, and advantages of the disclosure will be apparent from the description and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0139] The foregoing and other objects, features and advantages will be apparent from the following description of particular embodiments of the disclosure, as illustrated in the accompanying drawings in which like reference characters refer to the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating the principles of various embodiments of the disclosure.

[0140] FIG. 1 shows a schematic of one example of a RNA (e.g., mRNA) vaccine construct of the present disclosure. The construct depicts a human metapneumovirus and human respiratory syncytial virus full length fusion protein obtained from wild-type strains (*The Journal of General Virology*, 2008; 89(Pt 12):3113-3118, incorporated herein by reference).

[0141] FIGS. 2A-2C are graphs showing the levels of anti-hMPV fusion protein-specific antibodies in the serum of mice immunized with hMPV mRNA vaccines on day 0 (FIG. 2A), day 14 (FIG. 2B) and day 35 (FIG. 2C) post immunization. The mice were immunized with a single dose ($2 \mu\text{g}$ or $10 \mu\text{g}$) on day 0 and were given a boost dose ($2 \mu\text{g}$ or $10 \mu\text{g}$) on day 21. hMPV fusion protein-specific antibodies were detected at up to 1:10000 dilution of serum on day 35 for both doses.

[0142] FIGS. 3A-3C are graphs showing the result of IgG isotyping in the serum of mice immunized with hMPV mRNA vaccines. The levels of hMPV fusion protein-specific IgG2a (FIG. 3A) and IgG1 (FIG. 3B) antibodies in the serum are measured by ELISA. FIG. 3C shows that hMPV fusion protein mRNA vaccine induced a mixed Th1/Th2 cytokine response with a Th1 bias.

[0143] FIG. 4 is a graph showing in vitro neutralization of a hMPV B2 strain (TN/91-316) using the sera of mice immunized with a mRNA vaccine encoding hMPV fusion protein. Mouse serum obtained from mice receiving a $10 \mu\text{g}$ or a $2 \mu\text{g}$ dose contained hMPV-neutralizing antibodies.

[0144] FIGS. 5A-5C are graphs showing a Th1 cytokine response induced by a hMPV fusion peptide pool (15-mers-50) (overlap) in splenocytes isolated from mice immunized with the hMPV mRNA vaccines. Virus-free media was used as a negative control and Concanavalin A (ConA, a positive control for splenocyte stimulation) was included. The cytokines tested included IFN- γ (FIG. 5A), IL-2 (FIG. 5B) and IL-12 (FIG. 5C).

[0145] FIGS. 6A-6E are graphs showing the Th2 cytokine response induced by a hMPV fusion peptide pool (15-mers-50) in splenocytes isolated from mice immunized with the hMPV mRNA vaccines. Virus-free media was used as a negative control and Concanavalin A was also included. The cytokines tested included IL-10 (FIG. 6A), TNF- α (FIG. 6B), IL-4 (FIG. 6C), IL-5 (FIG. 6D) and IL-6 (FIG. 6E).

[0146] FIGS. 7A-7C are graphs showing the Th1 response induced by inactivated hMPV virus in splenocytes isolated

from mice immunized with hMPV mRNA vaccines. Virus-free media was used as a negative control and Concanavalin A was included. The cytokines tested included IFN- γ (FIG. 7A), IL-2 (FIG. 7B) and IL12 (FIG. 7C).

[0147] FIGS. 8A-8E are graphs showing the Th2 response induced by inactivated hMPV virus in splenocytes isolated from mice immunized with the hMPV mRNA vaccines. Virus-free media was used as a negative control and Concanavalin A was included. The cytokines tested include IL-10 (FIG. 8A), TNF- α (FIG. 8B), IL4 (FIG. 8C), IL-5 (FIG. 8D) and IL-6 (FIG. 8E).

[0148] FIGS. 9A-9B are graphs showing the results of cotton rat challenge experiments. Two different doses of the hMPV mRNA vaccines were used (2 μ g or 10 μ g doses) to immunize the cotton rats before challenge. The hMPV mRNA vaccines reduced the viral titer in the lung and nose of the cotton rat, with the 10 μ g dose being more effective in reducing viral titer. Use of a 10 μ g dose resulted in 100% protection in the lung and a -2 log reduction in nose viral titer. Use of a 2 μ g dose resulted in a 1 log reduction in lung viral titer and no reduction in nose viral titer. The vaccine was administered on Day 0, and a boost was administered on Day 21.

[0149] FIG. 10 is a graph showing the lung histopathology of cotton rats that received hMPV mRNA vaccines. Pathology associated with vaccine-enhanced disease was not observed in immunized groups.

[0150] FIG. 11 is a graph showing hMPV neutralization antibody titers in cotton rats that received hMPV mRNA vaccines (2 μ g or 10 μ g doses) on days 35 and 42 post immunization.

[0151] FIG. 12 is a graph showing the lung and nose viral load in cotton rats challenged with a hMPV/A2 strain after immunization with the indicated mRNA vaccines (hMPV mRNA vaccine or hMPV/PIV mRNA combination vaccine). Vaccinated cotton rats showed reduced lung and nose viral loads after challenge, compared to control.

[0152] FIG. 13 is a graph showing the lung and nose viral load in cotton rats challenged with PIV3 strain after immunization with indicated mRNA vaccines (PIV mRNA vaccine or hMPV/PIV combination vaccine). Vaccinated cotton rats showed reduced lung and nose viral loads after challenge, compared to control.

[0153] FIG. 14 is a graph showing hMPV neutralizing antibody titers in cotton rats that received different dosages of hMPV mRNA vaccines or hMPV/PIV combination mRNA vaccines on day 42 post immunization. The dosages of the vaccine are indicated in Table 9.

[0154] FIG. 15 is a graph showing PIV3 neutralizing antibody titers in cotton rats that received different dosages of PIV mRNA vaccines or hMPV/PIV combination mRNA vaccines on day 42 post immunization. The dosages of the vaccine are indicated in Table 9.

[0155] FIG. 16 is a graph showing the lung histopathology score of cotton rats immunized with hMPV mRNA vaccines, PIV mRNA vaccines or hMPV/PIV combination mRNA vaccines as indicated in Table 9. Low occurrence of alveolitis and interstitial pneumonia was observed, indicating no antibody-dependent enhancement (ADE) of hMPV associated diseases.

[0156] FIG. 17 is a graph showing the reciprocal MERS-CoV neutralizing antibody titers in mice immunized with

betacoronavirus mRNA vaccine encoding the MERS-CoV full-length Spike protein, on days 0, 21, 42, and 56 post immunization.

[0157] FIG. 18 is a graph showing the reciprocal MERS-CoV neutralizing antibody titers in mice immunized with betacoronavirus mRNA vaccine encoding either the MERS-CoV full-length Spike protein, or the S2 subunit of the Spike protein. The full length spike protein induced a stronger immune response compared to the S2 subunit alone.

[0158] FIGS. 19A-19C are graphs showing the viral load in the nose and throat, the bronchoalveolar lavage (BAL), or the lungs of New Zealand white rabbits 4 days post challenge with MERS-CoV. The New Zealand white rabbits were immunized with one 20 μ g-dose (on day 0) or two 20 μ g-doses (on day 0 and 21) of MERS-CoV mRNA vaccine encoding the full-length Spike protein before challenge. FIG. 19A shows that two doses of MERS-CoV mRNA vaccine resulted in a 3 log reduction of viral load in the nose and led to complete protection in the throat of the New Zealand white rabbits. FIG. 19B shows that two doses of MERS-CoV mRNA vaccine resulted in a 4 log reduction of viral load in the BAL of the New Zealand white rabbits. FIG. 19C show one dose of MERS-CoV mRNA vaccine resulted in a 2 log reduction of viral load, while two doses of MERS-CoV mRNA vaccine resulted in an over 4 log reduction of viral load in the lungs of the New Zealand white rabbits.

[0159] FIGS. 20A-20B are images and graphs showing viral load or replicating virus detected by PCR in the lungs of New Zealand white rabbits 4 days post challenge with MERS-CoV. The New Zealand white rabbits were immunized with a single 20 μ g dose (on day 0, Group 1a) of MERS-CoV mRNA vaccine encoding the full-length Spike protein, two 20 μ g doses (on day 0 and 21, Group 1b) of MERS-CoV mRNA vaccine encoding the full-length Spike protein, or placebo (Group 2) before challenge. FIG. 20A shows that two doses of 20 μ g a MERS-CoV mRNA vaccine reduced over 99% (2 log) of viruses in the lungs of New Zealand white rabbits. FIG. 20B shows that the group of New Zealand white rabbits that received 2 doses of 20 μ g MERS-CoV mRNA vaccine did not have any detectable replicating MERS-CoV virus in their lungs.

[0160] FIG. 21 is a graph showing the MERS-CoV neutralizing antibody titers in New Zealand white rabbits immunized with MERS-CoV mRNA vaccine encoding the full-length Spike protein. The results show that two doses of 20 μ g MERS-CoV mRNA vaccine induced a significant amount of neutralizing antibodies against MERS-CoV (IC₅₀ between 500-1000). The MERS-CoV mRNA vaccine induced antibody titer is 3-5 fold better than any other vaccines tested in the same model.

DETAILED DESCRIPTION

[0161] The present disclosure provides, in some embodiments, vaccines that comprise RNA (e.g., mRNA) polynucleotides encoding a human metapneumovirus (hMPV) antigenic polypeptide, a parainfluenza virus type 3 (PIV3) antigenic polypeptide, a respiratory syncytial virus (RSV) antigenic polypeptide, a measles virus (MeV) antigenic polypeptide, or a betacoronavirus antigenic polypeptide (e.g., Middle East respiratory syndrome coronavirus (MERS-CoV), SARS-CoV, human coronavirus (HCoV)-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH (New Haven) and HCoV-HKU1) (see, e.g., Jasper E. et al.

Emerging Infectious Diseases, 12(5), 2006; and Pyrc K, et al. *Journal of Virology*, 81(7):3051-57, 2007, the contents of each of which is here incorporated by reference in their entirety). The present disclosure also provides, in some embodiments, combination vaccines that comprise at least one RNA (e.g., mRNA) polynucleotide encoding at least two antigenic polypeptides selected from hMPV antigenic polypeptides, PIV3 antigenic polypeptides, RSV antigenic polypeptides, MeV antigenic polypeptides and BetaCoV antigenic polypeptides. Also provided herein are methods of administering the RNA (e.g., mRNA) vaccines, methods of producing the RNA (e.g., mRNA) vaccines, compositions (e.g., pharmaceutical compositions) comprising the RNA (e.g., mRNA) vaccines, and nucleic acids (e.g., DNA) encoding the RNA (e.g., mRNA) vaccines. In some embodiments, a RNA (e.g., mRNA) vaccine comprises an adjuvant, such as a flagellin adjuvant, as provided herein.

[0162] The RNA (e.g., mRNA) vaccines (e.g., hMPV, PIV3, RSV, MeV, BetaCoV RNA vaccines and combinations thereof), in some embodiments, may be used to induce a balanced immune response, comprising both cellular and humoral immunity, without many of the risks associated with DNA vaccination.

[0163] The entire contents of International Application No. PCT/US2015/02740 is incorporated herein by reference.

Human Metapneumovirus (hMPV)

[0164] hMPV shares substantial homology with respiratory syncytial virus (RSV) in its surface glycoproteins. hMPV fusion protein (F) is related to other paramyxovirus fusion proteins and appears to have homologous regions that may have similar functions. The hMPV fusion protein amino acid sequence contains features characteristic of other paramyxovirus F proteins, including a putative cleavage site and potential N-linked glycosylation sites. Paramyxovirus fusion proteins are synthesized as inactive precursors (F⁰) that are cleaved by host cell proteases into the biologically fusion-active F1 and F2 domains (see, e.g., Cseke G, et al. *Journal of Virology*, 2007; 81(2):698-707, incorporated herein by reference). hMPV has one putative cleavage site, in contrast to the two sites established for RSV F, and only shares 34% amino acid sequence identity with RSV F. F2 is extracellular and disulfide linked to F1. Fusion proteins are type I glycoproteins existing as trimers, with two 4-3 heptad repeat domains at the N- and C-terminal regions of the protein (H1R1 and H1R2), which form coiled-coil alpha-helices. These coiled coils become apposed in an antiparallel fashion when the protein undergoes a conformational change into the fusogenic state. There is a hydrophobic fusion peptide N proximal to the N-terminal heptad repeat, which is thought to insert into the target cell membrane, while the association of the heptad repeats brings the transmembrane domain into close proximity, inducing membrane fusion (see, e.g., Baker, K A et al. *Mol. Cell* 1999; 3:309-319). This mechanism has been proposed for a number of different viruses, including RSV, influenza virus, and human immunodeficiency virus. Fusion proteins are major antigenic determinants for all known paramyxoviruses and for other viruses that possess similar fusion proteins such as human immunodeficiency virus, influenza virus, and Ebola virus.

[0165] In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV fusion protein (F). In some

embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding a F1 or F2 subunit of a hMPV F protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV glycoprotein (G). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV matrix protein (M). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV phosphoprotein (P). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV nucleoprotein (N). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV SH protein (SH).

[0166] In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein, M protein, P protein, N protein and SH protein.

[0167] In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and G protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and M protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and P protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and N protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and SH protein.

[0168] In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and M protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and P protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and N protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and SH protein.

[0169] In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and M protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and P protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and N protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and SH protein.

[0170] A hMPV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV antigenic polypeptide identified by any one of SEQ ID NO: 5-8 (Table 3; see also amino acid sequences of Table 4).

[0171] A hMPV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 1-4 (Table 2).

[0172] The present disclosure is not limited by a particular strain of hMPV. The strain of hMPV used in a vaccine may be any strain of hMPV. Non-limiting examples of strains of hMPV for use as provide herein include the CAN98-75 (CAN75) and the CAN97-83 (CAN83) hMPV strains (Skidopoulos M H et al. *J Virol.* 20014; 78(13):6927-37, incorporated herein by reference), a hMPV A1, A2, B1 or B2 strain (see, e.g., de Graaf M et al. *The Journal of General Virology* 2008; 89:975-83; Peret T C T et al. *The Journal of Infectious Disease* 2002; 185:1660-63, incorporated herein by reference), a hMPV isolate TN/92-4 (e.g., SEQ ID NO: 1 and 5), a hMPV isolate NI/1/99 (e.g., SEQ ID NO: 2 and 6), or a hMPV isolate PI/R/CF10497/2010/B (e.g., SEQ ID NO: 3 and 7).

[0173] In some embodiments, at least one hMPV antigenic polypeptide is obtained from a hMPV A1, A2, B1 or B2 strain (see, e.g., de Graaf M et al. *The Journal of General Virology* 2008; 89:975-83; Peret T C T et al. *The Journal of Infectious Disease* 2002; 185:1660-63, incorporated herein by reference). In some embodiments, at least one antigenic polypeptide is obtained from the CAN98-75 (CAN75) hMPV strain. In some embodiments, at least one antigenic polypeptide is obtained from the CAN97-83 (CAN83) hMPV strain. In some embodiments, at least one antigenic polypeptide is obtained from hMPV isolate TN/92-4 (e.g., SEQ ID NO: 1 and 5). In some embodiments, at least one antigenic polypeptide is obtained from hMPV isolate NI/1/99 (e.g., SEQ ID NO: 2 and 6). In some embodiments, at least one antigenic polypeptide is obtained from hMPV isolate PI/R/CF10497/2010/B (e.g., SEQ ID NO: 3 and 7).

[0174] In some embodiments, hMPV vaccines comprise RNA (e.g., mRNA) polynucleotides encoding a hMPV antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with hMPV F protein and having F protein activity.

[0175] A protein is considered to have F protein activity if, for example, the protein acts to fuse the viral envelope and host cell plasma membrane, mediates viral entry into a host cell via an interaction with arginine-glycine-aspartate (RGD)-binding integrins, or a combination thereof (see, e.g., Cox R G et al. *J Virol.* 2012; 88(22):12148-60, incorporated herein by reference).

[0176] In some embodiments, hMPV vaccines comprise RNA (e.g., mRNA) polynucleotides encoding hMPV antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with hMPV G protein and having G protein activity.

[0177] A protein is considered to have G protein activity if, for example, the protein acts to modulate (e.g., inhibit) hMPV-induced cellular (immune) responses (see, e.g., Bao X et al. *PLoS Pathog.* 2008; 4(5):e1000077, incorporated herein by reference).

Human Parainfluenza Virus Type 3 (PIV3)

[0178] Parainfluenza viruses belong to the family Paramyxoviridae. These are enveloped viruses with a negative-sense single-stranded RNA genome. Parainfluenza viruses belong to the subfamily Paramyxoviridae, which is subdivided into three genera: Respirovirus (PIV-1, PIV-3, and Sendai virus (SeV)), Rubulavirus (PIV-2, PIV-4 and

mumps virus) and Morbillivirus (measles virus, rinderpest virus and canine distemper virus (CDV)). Their genome, a ~15 500 nucleotide-long negative-sense RNA molecule, encodes two envelope glycoproteins, the hemagglutinin-neuraminidase (HN), the fusion protein (F or F0), which is cleaved into F1 and F2 subunits, a matrix protein (M), a nucleocapsid protein (N) and several nonstructural proteins including the viral replicase (L). All parainfluenza viruses, except for PIV-1, express a non-structural V protein that blocks IFN signaling in the infected cell and acts therefore as a virulence factor (see, e.g., Nishio M et al. *J Virol.* 2008; 82(13):6130-38).

[0179] PIV3 hemagglutinin-neuraminidase (HN), a structural protein, is found on the viral envelope, where it is necessary for attachment and cell entry. It recognizes and binds to sialic acid-containing receptors on the host cell's surface. As a neuraminidase, HN removes sialic acid from virus particles, preventing self-aggregation of the virus, and promoting the efficient spread of the virus. Furthermore, HN promotes the activity of the fusion (F or F0) protein, contributing to the penetration of the host cell's surface.

[0180] PIV3 fusion protein (PIV3 F) is located on the viral envelope, where it facilitates the viral fusion and cell entry. The F protein is initially inactive, but proteolytic cleavage leads to its active forms, F1 and F2, which are linked by disulfide bonds. This occurs when the HN protein binds its receptor on the host cell's surface. During early phases of infection, the F glycoprotein mediates penetration of the host cell by fusion of the viral envelope to the plasma membrane. In later stages of the infection, the F protein facilitates the fusion of the infected cells with neighboring uninfected cells, which leads to the formation of a syncytium and spread of the infection.

[0181] PIV3 matrix protein (M) is found within the viral envelope and assists with viral assembly. It interacts with the nucleocapsid and envelope glycoproteins, where it facilitates the budding of progeny viruses through its interactions with specific sites on the cytoplasmic tail of the viral glycoproteins and nucleocapsid. It also plays a role in transporting viral components to the budding site.

[0182] PIV3 phosphoprotein (P) and PIV3 large polymerase protein (L) are found in the nucleocapsid where they form part of the RNA polymerase complex. The L protein, a viral RNA-dependent RNA polymerase, facilitates genomic transcription, while the host cell's ribosomes translate the viral mRNA into viral proteins.

[0183] PIV3 V is a non-structural protein that blocks IFN signaling in the infected cell, therefore acting as a virulence factor.

[0184] PIV3 nucleoprotein (N) encapsidates the genome in a ratio of 1 N per 6 ribonucleotides, protecting it from nucleases. The nucleocapsid (NC) has a helical structure. The encapsidated genomic RNA is termed the NC and serves as template for transcription and replication. During replication, encapsidation by PIV3 N is coupled to RNA synthesis and all replicative products are resistant to nucleases. PIV3 N homo-multimerizes to form the nucleocapsid and binds to viral genomic RNA. PIV3 N binds the P protein and thereby positions the polymerase on the template.

[0185] In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 fusion protein (F). In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding a

F1 or F2 subunit of a PIV3 F protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 hemagglutinin-neuraminidase (HN) (see, e.g., van Wyke Coelingh K I, et al. *J Virol.* 1987; 61(5):1473-77, incorporated herein by reference). In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 matrix protein (M). In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 phosphoprotein (P). In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 nucleoprotein (N).

[0186] In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, HN protein, M protein, P protein, and N protein.

[0187] In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and HN protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and M protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and P protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and N protein.

[0188] In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HN protein and M protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HN protein and P protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HN protein and N protein.

[0189] In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, HN protein and M protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, HN protein and P protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, HN protein and N protein.

[0190] A PIV3 vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one PIV3 antigenic polypeptide identified by any one of SEQ ID NO: 12-13 (Table 6; see also amino acid sequences of Table 7).

[0191] A PIV3 vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 9-12 (Table 5; see also nucleic acid sequences of Table 7).

[0192] The present disclosure is not limited by a particular strain of PIV3. The strain of PIV3 used in a vaccine may be any strain of PIV3. A non-limiting example of a strain of PIV3 for use as provide herein includes HPIV3/Homo sapiens/PI3R/FLA4815/2008.

[0193] In some embodiments, PIV3 vaccines comprise RNA (e.g., mRNA) polynucleotides encoding a PIV3 antigenic polypeptides having at least 95%, at least 96%, at least

97%, at least 98% or at least 99% identity with PIV3 F protein and having F protein activity.

[0194] In some embodiments, PIV3 vaccines comprise RNA (e.g., mRNA) polynucleotides encoding PIV3 antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with PIV3 hemagglutinin-neuraminidase (HN) and having hemagglutinin-neuraminidase activity.

[0195] A protein is considered to have hemagglutinin-neuraminidase activity if, for example, it is capable of both receptor binding and receptor cleaving. Such proteins are major surface glycoproteins that have functional sites for cell attachment and for neuraminidase activity. They are able to cause red blood cells to agglutinate and to cleave the glycosidic linkages of neuraminic acids, so they have the potential to both bind a potential host cell and then release the cell if necessary, for example, to prevent self-aggregation of the virus.

[0196] In some embodiments, PIV3 vaccines comprise RNA (e.g., mRNA) polynucleotides encoding PIV3 antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with PIV3 HN, F (e.g., F, F1 or F2), M, N, I, or V and having HN, F (e.g., F, F1 or F2), M, N, I, or V activity, respectively.

Respiratory Syncytial Virus (RSV)

[0197] RSV is a negative-sense, single-stranded RNA virus of the genus *Pneumovirinae*. The virus is present in at least two antigenic subgroups, known as Group A and Group B, primarily resulting from differences in the surface G glycoproteins. Two RSV surface glycoproteins G and F mediate attachment with and attachment to cells of the respiratory epithelium. F surface glycoproteins mediate coalescence of neighboring cells. This results in the formation of syncytial cells. RSV is the most common cause of bronchiolitis. Most infected adults develop mild cold-like symptoms such as congestion, low-grade fever, and wheezing. Infants and small children may suffer more severe symptoms such as bronchiolitis and pneumonia. The disease may be transmitted among humans via contact with respiratory secretions.

[0198] The genome of RSV encodes at least three surface glycoproteins, including F, G, and SH, four nucleocapsid proteins, including L, P, N, and M2, and one matrix protein, M. Glycoprotein F directs viral penetration by fusion between the virion and the host membrane. Glycoprotein G is a type II transmembrane glycoprotein and is the major attachment protein. SH is a short integral membrane protein. Matrix protein M is found in the inner layer of the lipid bilayer and assists virion formation. Nucleocapsid proteins L, P, N, and M2 modulate replication and transcription of the RSV genome. It is thought that glycoprotein G tethers and stabilizes the virus particle at the surface of bronchial epithelial cells, while glycoprotein F interacts with cellular glycosaminoglycans to mediate fusion and delivery of the RSV virion contents into the host cell (Krzyszaniak M A et al. *PLoS Pathog* 2013; 9(4)).

[0199] In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding I.

protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding P protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding N protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding M2 protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding M protein.

[0200] In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein, L protein, P protein, N protein, M2 protein and M protein.

[0201] In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and G protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and L protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and P protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and N protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and M2 protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and M protein.

[0202] In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and L protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and P protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and N protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and M2 protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and M protein.

[0203] In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and L protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and P protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and N protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and M2 protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and M protein.

[0204] The present disclosure is not limited by a particular strain of RSV. The strain of RSV used in a vaccine may be any strain of RSV.

[0205] In some embodiments, RSV vaccines comprise RNA (e.g., mRNA) polynucleotides encoding a RSV antigenic polypeptides having at least 95%, at least 96%, at least

97%, at least 98% or at least 99% identity with RSV F protein and having F protein activity.

[0206] In some embodiments, RSV vaccines comprise RNA (e.g., mRNA) polynucleotides encoding RSV antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with RSV G protein and having G protein activity.

[0207] A protein is considered to have G protein activity if, for example, the protein acts to modulate (e.g., inhibit) hMPV-induced cellular (immune) responses (see, e.g., Bao X et al. *PLoS Pathog.* 2008; 4(5):e1000077, incorporated herein by reference).

Measles Virus (MeV)

[0208] Molecular epidemiologic investigations and virologic surveillance contribute notably to the control and prevention of measles. Nearly half of measles-related deaths worldwide occur in India, yet virologic surveillance data are incomplete for many regions of the country. Previous studies have documented the presence of measles virus genotypes D4, D7, and D8 in India, and genotypes D5, D9, D11, H11, and G3 have been detected in neighboring countries. Recently, MeV genotype B3 was detected in India (Kuttiatt V S et al. *Emerg Infect Dis.* 2014; 20(10): 1764-66).

[0209] The glycoprotein complex of paramyxoviruses mediates receptor binding and membrane fusion. In particular, the MeV fusion (F) protein executes membrane fusion, after receptor binding by the hemagglutinin (HA) protein (Muhlebach M D et al. *Journal of Virology* 2008; 82(22): 11437-45). The MeV P gene codes for three proteins: P, an essential polymerase cofactor, and V and C, which have multiple functions but are not strictly required for viral propagation in cultured cells. V shares the amino-terminal domain with P but has a zinc-binding carboxyl-terminal domain, whereas C is translated from an overlapping reading frame. The MeV C protein is an infectivity factor. During replication, the P protein binds incoming monomeric nucleocapsid (N) proteins with its amino-terminal domain and positions them for assembly into the nascent ribonucleocapsid. The P protein amino-terminal domain is natively unfolded (Deveaux P et al. *Journal of Virology* 2004; 78(21): 11632-40).

[0210] In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding P protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding C protein.

[0211] In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein, F protein, P protein, V protein and C protein.

[0212] In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and F protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and P protein. In some embodiments, a MeV

vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and C protein.

[0213] In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and P protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and C protein.

[0214] In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein, F protein and P protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein, F protein and V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein, F protein and C protein.

[0215] In some embodiments, MeV vaccines comprise RNA (e.g., mRNA) encoding a MeV antigenic polypeptide having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with MeV HA protein and having MeV HA protein activity.

[0216] In some embodiments, MeV vaccines comprise RNA (e.g., mRNA) encoding a MeV antigenic polypeptide having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with MeV F protein and having MeV F protein activity.

[0217] A protein is considered to have HA protein activity if the protein mediates receptor binding and/or membrane fusion. MeV F protein executes membrane fusion, after receptor binding by the MeV HA protein.

[0218] A MeV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one MeV antigenic polypeptide identified by any one of SEQ ID NO: 47-50 (Table 14; see also amino acid sequences of Table 15).

[0219] A MeV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide identified by any one of SEQ ID NO: 37, 40, 43, 46 (Table 13).

[0220] A MeV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 35, 36, 38, 39, 41, 42, 44 and 45 (Table 13).

[0221] The present disclosure is not limited by a particular strain of MeV. The strain of MeV used in a vaccine may be any strain of MeV. Non-limiting examples of strains of MeV for use as provide herein include B3/B3.1, C2, D4, D6, D7, D8, G3, H1, Moraten, Rubeovax, MVi/New Jersey.USA/45.05, MVi/Texas.USA/4.07, AIK-C, MVi/New York.USA/26.09/3, MVi/California.USA/16.03, MVi/Virginia.USA/15.09, MVi/California.USA/8.04, and MVi/Pennsylvania.USA/20.09.

[0222] MeV proteins may be from MeV genotype D4, D5, D7, D8, D9, D11, H1, G3 or B3. In some embodiments, a MeV HA protein or a MeV F protein is from MeV genotype D8. In some embodiments, a MeV HA protein or a MeV F protein is from MeV genotype B3.

Betacoronaviruses (BetaCoV)

[0223] MERS-CoV. MERS-CoV is a positive-sense, single-stranded RNA virus of the genus *Betacoronavirus*. The genomes are phylogenetically classified into two clades, clade A and clade B. It has a strong tropism for non-ciliated bronchial epithelial cells, evades the innate immune response and antagonizes interferon (IFN) production in infected cells. Dipeptyl peptidase 4 (DPP4, also known as CD26) has been identified as a functional cellular receptor for MERS-CoV. Its enzymatic activity is not required for infection, although its amino acid sequence is highly conserved across species and is expressed in the human bronchial epithelium and kidneys. Most infected individuals develop severe acute respiratory illnesses, including fever, cough, and shortness of breath, and the virus can be fatal. The disease may be transmitted among humans, generally among those in close contact.

[0224] The genome of MERS-CoV encodes at least four unique accessory proteins, such as 3, 4a, 4b and 5, two replicase proteins (open reading frame 1a and 1b), and four major structural proteins, including spike (S), envelope (E), nucleocapsid (N), and membrane (M) proteins (Almazan F et al. *MBio* 2013; 4(5):e00650-13). The accessory proteins play nonessential roles in MERS-CoV replication, but they are likely structural proteins or interferon antagonists, modulating in vivo replication efficiency and/or pathogenesis, as in the case of SARS-CoV (Almazan F et al. *MBio* 2013; 4(5):e00650-13; Totura A L et al. *Curr Opin Virol* 2012; 2(3):264-75; Scobey T et al. *Proc Natl Acad Sci USA* 2013; 110(40):16157-62). The other proteins of MERS-CoV maintain different functions in virus replication. The E protein, for example, involves in virulence, and deleting the E-coding gene results in replication-competent and propagation-defective viruses or attenuated viruses (Almazan F et al. *MBio* 2013; 4(5):e00650-13). The S protein is particularly essential in mediating virus binding to cells expressing receptor dipeptidyl peptidase-4 (DPP4) through receptor-binding domain (RBD) in the S1 subunit, whereas the S2 subunit subsequently mediates virus entry via fusion of the virus and target cell membranes (Li F. *J Virol* 2015; 89(4):1954-64; Raj V S et al. *Nature* 2013; 495(7440):251-4).

[0225] In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding the S1 subunit of the S protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding the S2 subunit of the S protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding E protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding N protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding M protein.

[0226] In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein, N protein and M protein.

[0227] In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and E

protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and N protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and M protein.

[0228] In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and M protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and N protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), M protein and N protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding E protein, M protein and N protein.

[0229] A MERS-CoV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one MERS-CoV antigenic polypeptide identified by any one of SEQ ID NO: 24-38 or 33 (Table 11; see also amino acid sequences of Table 12).

[0230] A MERS-CoV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 20-23 (Table 10).

[0231] The present disclosure is not limited by a particular strain of MERS-CoV. The strain of MERS-CoV used in a vaccine may be any strain of MERS-CoV. Non-limiting examples of strains of MERS-CoV for use as provide herein include Riyadh_14_2013, and 2cJ:MC/2012, Hlasi_1_2013.

[0232] SARS-CoV. The genome of SARS-CoV includes of a single, positive-strand RNA that is approximately 29,700 nucleotides long. The overall genome organization of SARS-CoV is similar to that of other coronaviruses. The reference genome includes 13 genes, which encode at least 14 proteins. Two large overlapping reading frames (ORFs) encompass 71% of the genome. The remainder has 12 potential ORFs, including genes for structural proteins S (spike), E (small envelope), M (membrane), and N (nucleo-capsid). Other potential ORFs code for unique putative SARS-CoV-specific polypeptides that lack obvious sequence similarity to known proteins. A detailed analysis of the SARS-CoV genome has been published in *J Mol Biol* 2003; 331: 991-1004.

[0233] In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein, N protein and M protein.

[0234] In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and E protein. In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and N protein. In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and M protein.

[0235] In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and M protein. In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and N protein. In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and N protein. In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding E protein, M protein and N protein.

[0236] A SARS-CoV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one SARS-CoV antigenic polypeptide identified by any one of SEQ ID NO: 29, 32 or 34 (Table 11; see also amino acid sequences of Table 12).

[0237] The present disclosure is not limited by a particular strain of SARS-CoV. The strain of SARS-CoV used in a vaccine may be any strain of SARS-CoV.

[0238] HCoV-OC43. Human coronavirus OC43 is an enveloped, positive-sense, single-stranded RNA virus in the species *Betacoronavirus-1* (genus *Betacoronavirus*, subfamily Coronavirinae, family Coronaviridae, order Nidovirales). Four HCoV-OC43 genotypes (A to D), have been identified with genotype D most likely arising from recombination. The complete genome sequencing of two genotype C and D strains and bootscan analysis shows recombination events between genotypes B and C in the generation of genotype D. Of 29 strains identified, none belong to the more ancient genotype A. Along with HCoV-229E, a species in the *Alphacoronavirus* genus, HCoV-OC43 are among the known viruses that cause the common cold. Both viruses can cause severe lower respiratory tract infections, including pneumonia in infants, the elderly, and immunocompromised individuals such as those undergoing chemotherapy and those with HIV/AIDS.

[0239] HCoV-HKU1. Human coronavirus HKU1 (HCoV-HKU1) is a positive-sense, single-stranded RNA virus with the HE gene, which distinguishes it as a group 2, or betacoronavirus. It was discovered in January 2005 in two patients in Hong Kong. The genome of HCoV-HKU1 is a 29,926-nucleotide, polyadenylated RNA. The GC content is 32%, the lowest among all known coronaviruses. The genome organization is the same as that of other group II coronaviruses, with the characteristic gene order 1a, 1b, HE, S, E, M, and N. Furthermore, accessory protein genes are present between the S and E genes (ORF4) and at the position of the N gene (ORF5). The TRS is presumably located within the AAUCUAAAC sequence, which precedes each ORF except E. As in sialodacryoadenitis virus and mouse hepatitis virus (MHV), translation of the E protein possibly occurs via an internal ribosomal entry site. The 3' untranslated region contains a predicted stem-loop structure immediately downstream of the N ORF (nucleotide position 29647 to 29711). Further downstream, a pseudoknot structure is present at nucleotide position 29708 to 29760. Both RNA structures are conserved in group II coronaviruses and are critical for virus replication.

[0240] HCoV-NL63. The RNA genome of human coronavirus NL63 (HCoV-NL63) is 27,553 nucleotides, with a poly(A) tail (Fig. 1). With a GC content of 34%, HCoV-

NI.63 has one of the lowest GC contents of the coronaviruses, for which GC content ranges from 32 to 42%. Untranslated regions of 286 and 287 nucleotides are present at the 5' and 3' termini, respectively. Genes predicted to encode the S, E, M, and N proteins are found in the 3' part of the HCoV-NI.63 genome. The HE gene, which is present in some group II coronaviruses, is absent, and there is only a single, monocistronic accessory protein ORF (ORF3) located between the S and E genes. Subgenomic mRNAs are generated for all ORFs (S, ORF3, E, M, and N), and the core sequence of the TRS of HCoV-NI.63 is defined as AAC-UAAA. This sequence is situated upstream of every ORF except for the E ORF, which contains the suboptimal core sequence AACUAAU. Interestingly, a 13-nucleotide sequence with perfect homology to the leader sequence is situated upstream of the suboptimal E TRS. Annealing of this 13-nucleotide sequence to the leader sequence may act as a compensatory mechanism for the disturbed leader-TRS/body-TRS interaction.

[0241] HCoV-229E. Human coronavirus 229E (HCoV-229E) is a single-stranded, positive-sense, RNA virus species in the *Alphacoronavirus* genus of the subfamily *Coronavirinae*, in the family *Coronaviridae*, of the order *Nidovirales*. Along with Human coronavirus OC43, it is responsible for the common cold. HCoV-NI.63 and HCoV-229E are two of the four human coronaviruses that circulate worldwide. These two viruses are unique in their relationship towards each other. Phylogenetically, the viruses are more closely related to each other than to any other human coronavirus, yet they only share 65% sequence identity. Moreover, the viruses use different receptors to enter their target cell. HCoV-NI.63 is associated with croup in children, whereas all signs suggest that the virus probably causes the common cold in healthy adults. HCoV-229E is a proven common cold virus in healthy adults, so it is probable that both viruses induce comparable symptoms in adults, even though their mode of infection differs (HCoV-NI.63 and HCoV-229E are two of the four human coronaviruses that circulate worldwide. These two viruses are unique in their relationship towards each other. Phylogenetically, the viruses are more closely related to each other than to any other human coronavirus, yet they only share 65% sequence identity. Moreover, the viruses use different receptors to enter their target cell. HCoV-NI.63 is associated with croup in children, whereas all signs suggest that the virus probably causes the common cold in healthy adults. HCoV-229E is a proven common cold virus in healthy adults, so it is probable that both viruses induce comparable symptoms in adults, even though their mode of infection differs (Dijkman R, et al. *J Formos Med Assoc.* 2009 April; 108(4):270-9, the contents of which is incorporated herein by reference in their entirety).

Combination Vaccines

[0242] Embodiments of the present disclosure also provide combination RNA (e.g., mRNA) vaccines. A "combination RNA (e.g., mRNA) vaccine" of the present disclosure refers to a vaccine comprising at least one (e.g., at least 2, 3, 4, or 5) RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a combination of any two or more (or all of) antigenic polypeptides selected from hMPV antigenic polypeptides, PIV3 antigenic polypeptides, RSV antigenic polypeptides, MeV antigenic polypeptides, and BetaCoV antigenic polypeptides (e.g., selected from MERS-CoV,

CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NI.63, HCoV-NI., HCoV-NH and HCoV-HKU1).

[0243] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide, a RSV antigenic polypeptide, a MeV antigenic polypeptide, and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NI.63, HCoV-NI., HCoV-NH and HCoV-HKU1).

[0244] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a PIV3 antigenic polypeptide.

[0245] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a RSV antigenic polypeptide.

[0246] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a MeV antigenic polypeptide.

[0247] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a BetaCoV antigenic polypeptide.

[0248] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide and a RSV antigenic polypeptide.

[0249] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide and a MeV antigenic polypeptide.

[0250] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NI.63, HCoV-NI., HCoV-NH and HCoV-HKU1).

[0251] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a RSV antigenic polypeptide and a MeV antigenic polypeptide.

[0252] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a RSV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NI.63, HCoV-NI., HCoV-NH and HCoV-HKU1).

[0253] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NI.63, HCoV-NI., HCoV-NH and HCoV-HKU1).

[0254] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide, a RSV antigenic polypeptide and a MeV antigenic polypeptide.

[0255] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3

antigenic polypeptide, a RSV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-IKU1).

[0256] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-IKU1).

[0257] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a RSV antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-IKU1).

[0258] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide, a RSV antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-IKU1).

[0259] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide and a RSV antigenic polypeptide.

[0260] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide and a MeV antigenic polypeptide.

[0261] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-IKU1).

[0262] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a RSV antigenic polypeptide and a MeV antigenic polypeptide.

[0263] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a RSV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-IKU1).

[0264] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-IKU1). In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide, a RSV antigenic polypeptide and a MeV antigenic polypeptide.

[0265] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucle-

otide encoding a PIV3 antigenic polypeptide, a RSV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-IKU1).

[0266] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a RSV antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-IKU1).

[0267] Other combination respiratory virus RNA (e.g., mRNA) vaccines are encompassed by the present disclosure.

[0268] It has been discovered that the mRNA vaccines described herein are superior to current vaccines in several ways. First, the lipid nanoparticle (LNP) delivery is superior to other formulations including a protamine base approach described in the literature and no additional adjuvants are to be necessary. The use of LNPs enables the effective delivery of chemically modified or unmodified mRNA vaccines. Additionally it has been demonstrated herein that both modified and unmodified LNP formulated mRNA vaccines were superior to conventional vaccines by a significant degree. In some embodiments the mRNA vaccines of the invention are superior to conventional vaccines by a factor of at least 10 fold, 20 fold, 40 fold, 50 fold, 100 fold, 500 fold or 1,000 fold.

[0269] Although attempts have been made to produce functional RNA vaccines, including mRNA vaccines and self-replicating RNA vaccines, the therapeutic efficacy of these RNA vaccines have not yet been fully established. Quite surprisingly, the inventors have discovered, according to aspects of the invention a class of formulations for delivering mRNA vaccines in vivo that results in significantly enhanced, and in many respects synergistic, immune responses including enhanced antigen generation and functional antibody production with neutralization capability. These results can be achieved even when significantly lower doses of the mRNA are administered in comparison with mRNA doses used in other classes of lipid based formulations. The formulations of the invention have demonstrated significant unexpected in vivo immune responses sufficient to establish the efficacy of functional mRNA vaccines as prophylactic and therapeutic agents. Additionally, self-replicating RNA vaccines rely on viral replication pathways to deliver enough RNA to a cell to produce an immunogenic response. The formulations of the invention do not require viral replication to produce enough protein to result in a strong immune response. Thus, the mRNA of the invention are not self-replicating RNA and do not include components necessary for viral replication.

[0270] The invention involves, in some aspects, the surprising finding that lipid nanoparticle (LNP) formulations significantly enhance the effectiveness of mRNA vaccines, including chemically modified and unmodified mRNA vaccines. The efficacy of mRNA vaccines formulated in LNP was examined in vivo using several distinct antigens. The results presented herein demonstrate the unexpected superior efficacy of the mRNA vaccines formulated in LNP over other commercially available vaccines.

[0271] In addition to providing an enhanced immune response, the formulations of the invention generate a more

rapid immune response with fewer doses of antigen than other vaccines tested. The mRNA-LNP formulations of the invention also produce quantitatively and qualitatively better immune responses than vaccines formulated in a different carriers.

[0272] The data described herein demonstrate that the formulations of the invention produced significant unexpected improvements over existing antigen vaccines. Additionally, the mRNA-LNP formulations of the invention are superior to other vaccines even when the dose of mRNA is lower than other vaccines. Mice immunized with either 10 µg or 2 µg doses of an hMPV fusion protein mRNA LNP vaccine or a PIV3 mRNA LNP vaccine produced neutralizing antibodies which for instance, successfully neutralized the hMPV B2 virus. A 10 µg dose of mRNA vaccine protected 100% of mice from lethal challenge and drastically reduced the viral titer after challenge (~2 log reduction).

[0273] Two 20 µg doses of MERS-CoV mRNA LNP vaccine significantly reduced viral load and induced significant amount of neutralizing antibodies against MERS-CoV (IC₅₀ between 500-1000). The MERS-CoV mRNA vaccine induced antibody titer was 3-5 fold better than any other vaccines tested in the same model.

[0274] The LNP used in the studies described herein has been used previously to deliver siRNA in various animal models as well as in humans. In view of the observations made in association with the siRNA delivery of LNP formulations, the fact that LNP is useful in vaccines is quite surprising. It has been observed that therapeutic delivery of siRNA formulated in LNP causes an undesirable inflammatory response associated with a transient IgM response, typically leading to a reduction in antigen production and a compromised immune response. In contrast to the findings observed with siRNA, the LNP-mRNA formulations of the invention are demonstrated herein to generate enhanced IgG levels, sufficient for prophylactic and therapeutic methods rather than transient IgM responses.

Nucleic Acids/Polynucleotides

[0275] Respiratory virus vaccines, as provided herein, comprise at least one (one or more) ribonucleic acid (RNA) (e.g., mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide selected from hMPV, PIV3, RSV, MeV and BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1) antigenic polypeptides. The term "nucleic acid" includes any compound and/or substance that comprises a polymer of nucleotides (nucleotide monomer). These polymers are referred to as polynucleotides. Thus, the terms "nucleic acid" and "polynucleotide" are used interchangeably.

[0276] Nucleic acids may be or may include, for example, ribonucleic acids (RNAs), deoxyribonucleic acids (DNAs), threose nucleic acids (TNAs), glycol nucleic acids (GNAs), peptide nucleic acids (PNAs), locked nucleic acids (LNAs), including LNA having a β-D-ribo configuration, α-LNA having an α-L-ribo configuration (a diastereomer of LNA), 2'-amino-LNA having a 2'-amino functionalization, and 2'-amino-α-LNA having a 2'-amino functionalization), ethylene nucleic acids (ENAs), cyclohexenyl nucleic acids (CENAs) or chimeras or combinations thereof.

[0277] In some embodiments, polynucleotides of the present disclosure function as messenger RNA (mRNA). "Mes-

senger RNA" (mRNA) refers to any polynucleotide that encodes a (at least one) polypeptide (a naturally-occurring, non-naturally-occurring, or modified polymer of amino acids) and can be translated to produce the encoded polypeptide in vitro, in vivo, in situ or ex vivo. The skilled artisan will appreciate that, except where otherwise noted, polynucleotide sequences set forth in the instant application will recite "T"s in a representative DNA sequence but where the sequence represents RNA (e.g., mRNA), the "T"s would be substituted for "U"s. Thus, any of the RNA polynucleotides encoded by a DNA identified by a particular sequence identification number may also comprise the corresponding RNA (e.g., mRNA) sequence encoded by the DNA, where each "T" of the DNA sequence is substituted with "U."

[0278] The basic components of an mRNA molecule typically include at least one coding region, a 5' untranslated region (UTR), a 3' UTR, a 5' cap and a poly-A tail. Polynucleotides of the present disclosure may function as mRNA but can be distinguished from wild-type mRNA in their functional and/or structural design features, which serve to overcome existing problems of effective polypeptide expression using nucleic-acid based therapeutics.

[0279] In some embodiments, a RNA polynucleotide of an RNA (e.g., mRNA) vaccine encodes 2-10, 2-9, 2-8, 2-7, 2-6, 2-5, 2-4, 2-3, 3-10, 3-9, 3-8, 3-7, 3-6, 3-5, 3-4, 4-10, 4-9, 4-8, 4-7, 4-6, 4-5, 5-10, 5-9, 5-8, 5-7, 5-6, 6-10, 6-9, 6-8, 6-7, 7-10, 7-9, 7-8, 8-10, 8-9 or 9-10 antigenic polypeptides. In some embodiments, a RNA (e.g., mRNA) polynucleotide of a respiratory virus vaccine encodes at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 antigenic polypeptides. In some embodiments, a RNA (e.g., mRNA) polynucleotide of a respiratory virus vaccine encodes at least 100 or at least 200 antigenic polypeptides. In some embodiments, a RNA polynucleotide of a respiratory virus vaccine encodes 1-10, 5-15, 10-20, 15-25, 20-30, 25-35, 30-40, 35-45, 40-50, 1-50, 1-100, 2-50 or 2-100 antigenic polypeptides.

[0280] Polynucleotides of the present disclosure, in some embodiments, are codon optimized. Codon optimization methods are known in the art and may be used as provided herein. Codon optimization, in some embodiments, may be used to match codon frequencies in target and host organisms to ensure proper folding; bias GC content to increase mRNA stability or reduce secondary structures; minimize tandem repeat codons or base runs that may impair gene construction or expression; customize transcriptional and translational control regions; insert or remove protein trafficking sequences; remove/add post translation modification sites in encoded protein (e.g. glycosylation sites); add, remove or shuffle protein domains; insert or delete restriction sites; modify ribosome binding sites and mRNA degradation sites; adjust translational rates to allow the various domains of the protein to fold properly; or to reduce or eliminate problem secondary structures within the polynucleotide. Codon optimization tools, algorithms and services are known in the art—non-limiting examples include services from GeneArt (Life Technologies), DNA2.0 (Menlo Park Calif.) and/or proprietary methods. In some embodiments, the open reading frame (ORF) sequence is optimized using optimization algorithms.

[0281] In some embodiments, a codon optimized sequence shares less than 95% sequence identity, less than 90% sequence identity, less than 85% sequence identity, less than 80% sequence identity, or less than 75% sequence identity to a naturally-occurring or wild-type sequence (e.g., a natu-

rally-occurring or wild-type mRNA sequence encoding a polypeptide or protein of interest (e.g., an antigenic protein or antigenic polypeptide)).

[0282] In some embodiments, a codon-optimized sequence shares between 65% and 85% (e.g., between about 67% and about 85%, or between about 67% and about 80%) sequence identity to a naturally-occurring sequence or a wild-type sequence (e.g., a naturally-occurring or wild-type mRNA sequence encoding a polypeptide or protein of interest (e.g., an antigenic protein or polypeptide)). In some embodiments, a codon-optimized sequence shares between 65% and 75%, or about 80% sequence identity to a naturally-occurring sequence or wild-type sequence (e.g., a naturally-occurring or wild-type mRNA sequence encoding a polypeptide or protein of interest (e.g., an antigenic protein or polypeptide)).

[0283] In some embodiments a codon-optimized RNA (e.g., mRNA) may, for instance, be one in which the levels of G/C are enhanced. The G/C-content of nucleic acid molecules may influence the stability of the RNA. RNA having an increased amount of guanine (G) and/or cytosine (C) residues may be functionally more stable than nucleic acids containing a large amount of adenine (A) and thymine (T) or uracil (U) nucleotides. WO02/098443 discloses a pharmaceutical composition containing an mRNA stabilized by sequence modifications in the translated region. Due to the degeneracy of the genetic code, the modifications work by substituting existing codons for those that promote greater RNA stability without changing the resulting amino acid. The approach is limited to coding regions of the RNA.

Antigens/Antigenic Polypeptides

[0284] In some embodiments, an antigenic polypeptide (e.g., a hMPV, PIV3, RSV, MeV or BetaCoV antigenic polypeptide) is longer than 25 amino acids and shorter than 50 amino acids. Polypeptides include gene products, naturally occurring polypeptides, synthetic polypeptides, homologs, orthologs, paralogs, fragments and other equivalents, variants, and analogs of the foregoing. A polypeptide may be a single molecule or may be a multi-molecular complex such as a dimer, trimer or tetramer. Polypeptides may also comprise single chain polypeptides or multichain polypeptides, such as antibodies or insulin, and may be associated or linked to each other. Most commonly, disulfide linkages are found in multichain polypeptides. The term "polypeptide" may also apply to amino acid polymers in which at least one amino acid residue is an artificial chemical analogue of a corresponding naturally-occurring amino acid.

[0285] A "polypeptide variant" is a molecule that differs in its amino acid sequence relative to a native sequence or a reference sequence. Amino acid sequence variants may possess substitutions, deletions, insertions, or a combination of any two or three of the foregoing, at certain positions within the amino acid sequence, as compared to a native sequence or a reference sequence. Ordinarily, variants possess at least 50% identity to a native sequence or a reference sequence. In some embodiments, variants share at least 80% identity or at least 90% identity with a native sequence or a reference sequence.

[0286] In some embodiments "variant mimics" are provided. A "variant mimic" contains at least one amino acid that would mimic an activated sequence. For example, glutamate may serve as a mimic for phospho-threonine

and/or phospho-serine. Alternatively, variant mimics may result in deactivation or in an inactivated product containing the mimic. For example, phenylalanine may act as an inactivating substitution for tyrosine, or alanine may act as an inactivating substitution for serine.

[0287] "Orthologs" refers to genes in different species that evolved from a common ancestral gene by speciation. Normally, orthologs retain the same function in the course of evolution. Identification of orthologs is important for reliable prediction of gene function in newly sequenced genomes.

[0288] "Analog" is meant to include polypeptide variants that differ by one or more amino acid alterations, for example, substitutions, additions or deletions of amino acid residues that still maintain one or more of the properties of the parent or starting polypeptide.

[0289] The present disclosure provides several types of compositions that are polynucleotide or polypeptide based, including variants and derivatives. These include, for example, substitutional, insertional, deletion and covalent variants and derivatives. The term "derivative" is synonymous with the term "variant" and generally refers to a molecule that has been modified and/or changed in any way relative to a reference molecule or a starting molecule.

[0290] As such, polynucleotides encoding peptides or polypeptides containing substitutions, insertions and/or additions, deletions and covalent modifications with respect to reference sequences, in particular the polypeptide sequences disclosed herein, are included within the scope of this disclosure. For example, sequence tags or amino acids, such as one or more lysines, can be added to peptide sequences (e.g., at the N-terminal or C-terminal ends). Sequence tags can be used for peptide detection, purification or localization. Lysines can be used to increase peptide solubility or to allow for biotinylation. Alternatively, amino acid residues located at the carboxy and amino terminal regions of the amino acid sequence of a peptide or protein may optionally be deleted providing for truncated sequences. Certain amino acids (e.g., C-terminal residues or N-terminal residues) alternatively may be deleted depending on the use of the sequence, as for example, expression of the sequence as part of a larger sequence that is soluble, or linked to a solid support.

[0291] "Substitutional variants" when referring to polypeptides are those that have at least one amino acid residue in a native or starting sequence removed and a different amino acid inserted in its place at the same position. Substitutions may be single, where only one amino acid in the molecule has been substituted, or they may be multiple, where two or more (e.g., 3, 4 or 5) amino acids have been substituted in the same molecule.

[0292] As used herein the term "conservative amino acid substitution" refers to the substitution of an amino acid that is normally present in the sequence with a different amino acid of similar size, charge, or polarity. Examples of conservative substitutions include the substitution of a non-polar (hydrophobic) residue such as isoleucine, valine and leucine for another non-polar residue. Likewise, examples of conservative substitutions include the substitution of one polar (hydrophilic) residue for another such as between arginine and lysine, between glutamine and asparagine, and between glycine and serine. Additionally, the substitution of a basic residue such as lysine, arginine or histidine for another, or the substitution of one acidic residue such as

aspartic acid or glutamic acid for another acidic residue are additional examples of conservative substitutions. Examples of non-conservative substitutions include the substitution of a non-polar (hydrophobic) amino acid residue such as isoleucine, valine, leucine, alanine, methionine for a polar (hydrophilic) residue such as cysteine, glutamine, glutamic acid or lysine and/or a polar residue for a non-polar residue.

[0293] “Features” when referring to polypeptide or polynucleotide are defined as distinct amino acid sequence-based or nucleotide-based components of a molecule respectively. Features of the polypeptides encoded by the polynucleotides include surface manifestations, local conformational shape, folds, loops, half-loops, domains, half-domains, sites, termini and any combination(s) thereof.

[0294] As used herein when referring to polypeptides the term “domain” refers to a motif of a polypeptide having one or more identifiable structural or functional characteristics or properties (e.g., binding capacity, serving as a site for protein-protein interactions).

[0295] As used herein when referring to polypeptides the terms “site” as it pertains to amino acid based embodiments is used synonymously with “amino acid residue” and “amino acid side chain.” As used herein when referring to polynucleotides the terms “site” as it pertains to nucleotide based embodiments is used synonymously with “nucleotide.” A site represents a position within a peptide or polypeptide or polynucleotide that may be modified, manipulated, altered, derivatized or varied within the polypeptide-based or polynucleotide-based molecules.

[0296] As used herein the terms “termini” or “terminus” when referring to polypeptides or polynucleotides refers to an extremity of a polypeptide or polynucleotide respectively. Such extremity is not limited only to the first or final site of the polypeptide or polynucleotide but may include additional amino acids or nucleotides in the terminal regions. Polypeptide-based molecules may be characterized as having both an N-terminus (terminated by an amino acid with a free amino group (NH₂)) and a C-terminus (terminated by an amino acid with a free carboxyl group (COOH)). Proteins are in some cases made up of multiple polypeptide chains brought together by disulfide bonds or by non-covalent forces (multimers, oligomers). These proteins have multiple N- and C-termini. Alternatively, the termini of the polypeptides may be modified such that they begin or end, as the case may be, with a non-polypeptide based moiety such as an organic conjugate.

[0297] As recognized by those skilled in the art, protein fragments, functional protein domains, and homologous proteins are also considered to be within the scope of polypeptides of interest. For example, provided herein is any protein fragment (meaning a polypeptide sequence at least one amino acid residue shorter than a reference polypeptide sequence but otherwise identical) of a reference protein having a length of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 or longer than 100 amino acids. In another example, any protein that includes a stretch of 20, 30, 40, 50, or 100 (contiguous) amino acids that are 40%, 50%, 60%, 70%, 80%, 90%, 95%, or 100% identical to any of the sequences described herein can be utilized in accordance with the disclosure. In some embodiments, a polypeptide includes 2, 3, 4, 5, 6, 7, 8, 9, 10, or more mutations as shown in any of the sequences provided herein or referenced herein. In another example, any protein that includes a stretch of 20, 30, 40, 50, or 100 amino acids that are greater than 80%,

90%, 95%, or 100% identical to any of the sequences described herein, wherein the protein has a stretch of 5, 10, 15, 20, 25, or 30 amino acids that are less than 80%, 75%, 70%, 65% to 60% identical to any of the sequences described herein can be utilized in accordance with the disclosure.

[0298] Polypeptide or polynucleotide molecules of the present disclosure may share a certain degree of sequence similarity or identity with the reference molecules (e.g., reference polypeptides or reference polynucleotides), for example, with art-described molecules (e.g., engineered or designed molecules or wild-type molecules). The term “identity,” as known in the art, refers to a relationship between the sequences of two or more polypeptides or polynucleotides, as determined by comparing the sequences. In the art, identity also means the degree of sequence relatedness between two sequences as determined by the number of matches between strings of two or more amino acid residues or nucleic acid residues. Identity measures the percent of identical matches between the smaller of two or more sequences with gap alignments (if any) addressed by a particular mathematical model or computer program (e.g., “algorithms”). Identity of related peptides can be readily calculated by known methods. “% identity” as it applies to polypeptide or polynucleotide sequences is defined as the percentage of residues (amino acid residues or nucleic acid residues) in the candidate amino acid or nucleic acid sequence that are identical with the residues in the amino acid sequence or nucleic acid sequence of a second sequence after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent identity. Methods and computer programs for the alignment are well known in the art. Identity depends on a calculation of percent identity but may differ in value due to gaps and penalties introduced in the calculation. Generally, variants of a particular polynucleotide or polypeptide have at least 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% but less than 100% sequence identity to that particular reference polynucleotide or polypeptide as determined by sequence alignment programs and parameters described herein and known to those skilled in the art. Such tools for alignment include those of the BLAST suite (Stephen F. Altschul, et al. (1997), “Gapped BLAST and PSI-BLAST: a new generation of protein database search programs,” *Nucleic Acids Res.* 25:3389-3402). Another popular local alignment technique is based on the Smith-Waterman algorithm (Smith, T. F. & Waterman, M. S. (1981) “Identification of common molecular subsequences,” *J. Mol. Biol.* 147:195-197). A general global alignment technique based on dynamic programming is the Needleman-Wunsch algorithm (Needleman, S. B. & Wunsch, C. D. (1970) “A general method applicable to the search for similarities in the amino acid sequences of two proteins,” *J. Mol. Biol.* 48:443-453). More recently, a Fast Optimal Global Sequence Alignment Algorithm (FOGSA) was developed that purportedly produces global alignment of nucleotide and protein sequences faster than other optimal global alignment methods, including the Needleman-Wunsch algorithm. Other tools are described herein, specifically in the definition of “identity” below.

[0299] As used herein, the term “homology” refers to the overall relatedness between polymeric molecules, e.g. between nucleic acid molecules (e.g. DNA molecules and/or RNA molecules) and/or between polypeptide molecules.

Polymeric molecules (e.g. nucleic acid molecules (e.g. DNA molecules and/or RNA molecules) and/or polypeptide molecules) that share a threshold level of similarity or identity determined by alignment of matching residues are termed homologous. Homology is a qualitative term that describes a relationship between molecules and can be based upon the quantitative similarity or identity. Similarity or identity is a quantitative term that defines the degree of sequence match between two compared sequences. In some embodiments, polymeric molecules are considered to be "homologous" to one another if their sequences are at least 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% identical or similar. The term "homologous" necessarily refers to a comparison between at least two sequences (polynucleotide or polypeptide sequences). Two polynucleotide sequences are considered homologous if the polypeptides they encode are at least 50%, 60%, 70%, 80%, 90%, 95%, or even 99% for at least one stretch of at least 20 amino acids. In some embodiments, homologous polynucleotide sequences are characterized by the ability to encode a stretch of at least 4-5 uniquely specified amino acids. For polynucleotide sequences less than 60 nucleotides in length, homology is determined by the ability to encode a stretch of at least 4-5 uniquely specified amino acids. Two protein sequences are considered homologous if the proteins are at least 50%, 60%, 70%, 80%, or 90% identical for at least one stretch of at least 20 amino acids.

[0300] Homology implies that the compared sequences diverged in evolution from a common origin. The term "homolog" refers to a first amino acid sequence or nucleic acid sequence (e.g., gene (DNA or RNA) or protein sequence) that is related to a second amino acid sequence or nucleic acid sequence by descent from a common ancestral sequence. The term "homolog" may apply to the relationship between genes and/or proteins separated by the event of speciation or to the relationship between genes and/or proteins separated by the event of genetic duplication. "Orthologs" are genes (or proteins) in different species that evolved from a common ancestral gene (or protein) by speciation. Typically, orthologs retain the same function in the course of evolution. "Paralogs" are genes (or proteins) related by duplication within a genome. Orthologs retain the same function in the course of evolution, whereas paralogs evolve new functions, even if these are related to the original one.

[0301] The term "identity" refers to the overall relatedness between polymeric molecules, for example, between polynucleotide molecules (e.g. DNA molecules and/or RNA molecules) and/or between polypeptide molecules. Calculation of the percent identity of two polynucleic acid sequences, for example, can be performed by aligning the two sequences for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second nucleic acid sequences for optimal alignment and non-identical sequences can be disregarded for comparison purposes). In certain embodiments, the length of a sequence aligned for comparison purposes is at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, or 100% of the length of the reference sequence. The nucleotides at corresponding nucleotide positions are then compared. When a position in the first sequence is occupied by the same nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity

between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which needs to be introduced for optimal alignment of the two sequences. The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. For example, the percent identity between two nucleic acid sequences can be determined using methods such as those described in Computational Molecular Biology, Lesk, A. M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D. W., ed., Academic Press, New York, 1993; Sequence Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; Computer Analysis of Sequence Data, Part I, Griffin, A. M., and Griffin, H. G., eds., Humana Press, New Jersey, 1994; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991; each of which is incorporated herein by reference. For example, the percent identity between two nucleic acid sequences can be determined using the algorithm of Meyers and Miller (CABIOS, 1989, 4:11-17), which has been incorporated into the ALIGN program (version 2.0) using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. The percent identity between two nucleic acid sequences can, alternatively, be determined using the GAP program in the GCG software package using an NWSgapdna.CMP matrix. Methods commonly employed to determine percent identity between sequences include, but are not limited to those disclosed in Carillo, H., and Lipman, D., *SIAM J Applied Math.*, 48:1073 (1988); incorporated herein by reference. Techniques for determining identity are codified in publicly available computer programs. Exemplary computer software to determine homology between two sequences include, but are not limited to, GCG program package, Devereux, J., et al., *Nucleic Acids Research*, 12(1), 387 (1984), BLASTP, BLASTN, and FASTA. Altschul, S. F. et al., *J. Molec. Biol.*, 215, 403 (1990).

Multiprotein and Multicomponent Vaccines

[0302] The present disclosure encompasses respiratory virus vaccines comprising multiple RNA (e.g., mRNA) polynucleotides, each encoding a single antigenic polypeptide, as well as respiratory virus vaccines comprising a single RNA polynucleotide encoding more than one antigenic polypeptide (e.g., as a fusion polypeptide). Thus, a vaccine composition comprising a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a first antigenic polypeptide and a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a second antigenic polypeptide encompasses (a) vaccines that comprise a first RNA polynucleotide encoding a first antigenic polypeptide and a second RNA polynucleotide encoding a second antigenic polypeptide, and (b) vaccines that comprise a single RNA polynucleotide encoding a first and second antigenic polypeptide (e.g., as a fusion polypeptide). RNA (e.g., mRNA) vaccines of the present disclosure, in some embodiments, comprise 2-10 (e.g., 2, 3, 4, 5, 6, 7, 8, 9 or 10), or more, RNA polynucleotides having an open reading frame, each of which encodes a different antigenic polypeptide (or a single RNA polynucleotide encoding 2-10, or more, different antigenic polypeptides). The antigenic polypeptides may be selected from hMPV, PIV3, RSV, MIV and BetaCoV (e.g., selected from MERS-CoV, SARS-CoV,

HCov-OC43, HCov-229E, HCov-NL63, HCov-NL, HCov-NH and HCov-HKU1) antigenic polypeptides.

[0303] In some embodiments, a respiratory virus vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral capsid protein, a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral premembrane/membrane protein, and a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral envelope protein. In some embodiments, a respiratory virus vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral fusion (F) protein and a RNA polynucleotide having an open reading frame encoding a viral major surface glycoprotein (G protein). In some embodiments, a vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral F protein. In some embodiments, a vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral G protein. In some embodiments, a vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a HN protein.

[0304] In some embodiments, a multicomponent vaccine comprises at least one RNA (e.g., mRNA) polynucleotide encoding at least one antigenic polypeptide fused to a signal peptide (e.g., any one of SEQ ID NO: 15-19). The signal peptide may be fused at the N-terminus or the C-terminus of an antigenic polypeptide. An antigenic polypeptide fused to a signal peptide may be selected from hMPV, PIV3, RSV, MeV and BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCov-OC43, HCov-229E, HCov-NL63, HCov-NL, HCov-NH and HCov-HKU1) antigenic polypeptides.

Signal Peptides

[0305] In some embodiments, antigenic polypeptides encoded by respiratory virus RNA (e.g., mRNA) polynucleotides comprise a signal peptide. Signal peptides, comprising the N-terminal 15-60 amino acids of proteins, are typically needed for the translocation across the membrane on the secretory pathway and, thus, universally control the entry of most proteins both in eukaryotes and prokaryotes to the secretory pathway. Signal peptides generally include three regions: an N-terminal region of differing length, which usually comprises positively charged amino acids; a hydrophobic region; and a short carboxy-terminal peptide region. In eukaryotes, the signal peptide of a nascent precursor protein (pre-protein) directs the ribosome to the rough endoplasmic reticulum (ER) membrane and initiates the transport of the growing peptide chain across it for processing. ER processing produces mature proteins, wherein the signal peptide is cleaved from precursor proteins, typically by a ER-resident signal peptidase of the host cell, or they remain uncleaved and function as a membrane anchor. A signal peptide may also facilitate the targeting of the protein to the cell membrane. The signal peptide, however, is not responsible for the final destination of the mature protein. Secretory proteins devoid of additional address tags in their sequence are by default secreted to the external environment. During recent years, a more advanced view of signal peptides has evolved, showing that the functions and immunodominance of certain signal peptides are much more versatile than previously anticipated.

[0306] Respiratory virus vaccines of the present disclosure may comprise, for example, RNA (e.g., mRNA) polynucleotides encoding an artificial signal peptide, wherein the

signal peptide coding sequence is operably linked to and is in frame with the coding sequence of the antigenic polypeptide. Thus, respiratory virus vaccines of the present disclosure, in some embodiments, produce an antigenic polypeptide comprising an antigenic polypeptide (e.g., hMPV, PIV3, RSV, MeV or BetaCoV) fused to a signal peptide. In some embodiments, a signal peptide is fused to the N-terminus of the antigenic polypeptide. In some embodiments, a signal peptide is fused to the C-terminus of the antigenic polypeptide.

[0307] In some embodiments, the signal peptide fused to the antigenic polypeptide is an artificial signal peptide. In some embodiments, an artificial signal peptide fused to the antigenic polypeptide encoded by the RNA (e.g., mRNA) vaccine is obtained from an immunoglobulin protein, e.g., an IgE signal peptide or an IgG signal peptide. In some embodiments, a signal peptide fused to the antigenic polypeptide encoded by a RNA (e.g., mRNA) vaccine is an Ig heavy chain epsilon-1 signal peptide (IgE HC SP) having the sequence of: MDWTWILFTVAAATRVHS (SEQ ID NO: 16). In some embodiments, a signal peptide fused to the antigenic polypeptide encoded by the (e.g., mRNA) RNA (e.g., mRNA) vaccine is an IgGk chain V-III region HAH signal peptide (IgGk SP) having the sequence of MET-PAQLLFLILLWLPDITG (SEQ ID NO: 15). In some embodiments, the signal peptide is selected from: Japanese encephalitis PRM signal sequence (MIGSNSGQRV-VFIIILJLVAPAYS; SEQ ID NO: 17), VSVg protein signal sequence (MKCLLYLAFLFIGVNC; SEQ ID NO: 18) and Japanese encephalitis JEV signal sequence (MWIVS-LAIVTACAGA; SEQ ID NO: 19).

[0308] In some embodiments, the antigenic polypeptide encoded by a RNA (e.g., mRNA) vaccine comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, 47-50 or 54-56 (Tables 3, 6, 11, 14 or 17; see also amino acid sequences of Tables 4, 7, 12 or 15) fused to a signal peptide identified by any one of SEQ ID NO: 15-19 (Table 8). The examples disclosed herein are not meant to be limiting and any signal peptide that is known in the art to facilitate targeting of a protein to ER for processing and/or targeting of a protein to the cell membrane may be used in accordance with the present disclosure.

[0309] A signal peptide may have a length of 15-60 amino acids. For example, a signal peptide may have a length of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, or 60 amino acids. In some embodiments, a signal peptide has a length of 20-60, 25-60, 30-60, 35-60, 40-60, 45-60, 50-60, 55-60, 15-55, 20-55, 25-55, 30-55, 35-55, 40-55, 45-55, 50-55, 15-50, 20-50, 25-50, 30-50, 35-50, 40-50, 45-50, 15-45, 20-45, 25-45, 30-45, 35-45, 40-45, 15-40, 20-40, 25-40, 30-40, 35-40, 15-35, 20-35, 25-35, 30-35, 15-30, 20-30, 25-30, 15-25, 20-25, or 15-20 amino acids.

[0310] A signal peptide is typically cleaved from the nascent polypeptide at the cleavage junction during ER processing. The mature antigenic polypeptide produced by a respiratory virus RNA (e.g., mRNA) vaccine of the present disclosure typically does not comprise a signal peptide.

Chemical Modifications

[0311] Respiratory virus vaccines of the present disclosure, in some embodiments, comprise at least RNA (e.g., mRNA) polynucleotide having an open reading frame

encoding at least one antigenic polypeptide that comprises at least one chemical modification.

[0312] The terms “chemical modification” and “chemically modified” refer to modification with respect to adenosine (A), guanosine (G), uridine (U), thymidine (T) or cytidine (C) ribonucleosides or deoxyribonucleosides in at least one of their position, pattern, percent or population. Generally, these terms do not refer to the ribonucleotide modifications in naturally occurring 5'-terminal mRNA cap moieties. With respect to a polypeptide, the term “modification” refers to a modification relative to the canonical set 20 amino acids. Polypeptides, as provided herein, are also considered “modified” if they contain amino acid substitutions, insertions or a combination of substitutions and insertions.

[0313] Polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides), in some embodiments, comprise various (more than one) different modifications. In some embodiments, a particular region of a polynucleotide contains one, two or more (optionally different) nucleoside or nucleotide modifications. In some embodiments, a modified RNA polynucleotide (e.g., a modified mRNA polynucleotide), introduced to a cell or organism, exhibits reduced degradation in the cell or organism, respectively, relative to an unmodified polynucleotide. In some embodiments, a modified RNA polynucleotide (e.g., a modified mRNA polynucleotide), introduced into a cell or organism, may exhibit reduced immunogenicity in the cell or organism, respectively (e.g., a reduced innate response).

[0314] Modifications of polynucleotides include, without limitation, those described herein. Polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) may comprise modifications that are naturally-occurring, non-naturally-occurring or the polynucleotide may comprise a combination of naturally-occurring and non-naturally-occurring modifications. Polynucleotides may include any useful modification, for example, of a sugar, a nucleobase, or an internucleoside linkage (e.g., to a linking phosphate, to a phosphodiester linkage or to the phosphodiester backbone).

[0315] Polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides), in some embodiments, comprise non-natural modified nucleotides that are introduced during synthesis or post-synthesis of the polynucleotides to achieve desired functions or properties. The modifications may be present on an internucleoside linkages, purine or pyrimidine bases, or sugars. The modification may be introduced with chemical synthesis or with a polymerase enzyme at the terminal of a chain or anywhere else in the chain. Any of the regions of a polynucleotide may be chemically modified.

[0316] The present disclosure provides for modified nucleosides and nucleotides of a polynucleotide (e.g., RNA polynucleotides, such as mRNA polynucleotides). A “nucleoside” refers to a compound containing a sugar molecule (e.g., a pentose or ribose) or a derivative thereof in combination with an organic base (e.g., a purine or pyrimidine) or a derivative thereof (also referred to herein as “nucleobase”). A nucleotide” refers to a nucleoside, including a phosphate group. Modified nucleotides may be synthesized by any useful method, such as, for example, chemically, enzymatically, or recombinantly, to include one or more modified or non-natural nucleosides. Polynucleotides may comprise a region or regions of linked nucleosides. Such regions may have variable backbone linkages. The

linkages may be standard phosphodiester linkages, in which case the polynucleotides would comprise regions of nucleotides.

[0317] Modified nucleotide base pairing encompasses not only the standard adenosine-thymine, adenosine-uracil, or guanosine-cytosine base pairs, but also base pairs formed between nucleotides and/or modified nucleotides comprising non-standard or modified bases, wherein the arrangement of hydrogen bond donors and hydrogen bond acceptors permits hydrogen bonding between a non-standard base and a standard base or between two complementary non-standard base structures. One example of such non-standard base pairing is the base pairing between the modified nucleotide inosine and adenine, cytosine or uracil. Any combination of base/sugar or linker may be incorporated into polynucleotides of the present disclosure.

[0318] Modifications of polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) that are useful in the vaccines of the present disclosure include, but are not limited to the following: 2-methylthio-N6-(cis-hydroxyisopentenyl)adenosine; 2-methylthio-N6-methyladenosine; 2-methylthio-N6-(threonyl carbamoyl)adenosine; N6-glycylcarbamoyladenosine; N6-isopentenyladenosine; N6-methyladenosine; N6-threonylcarbamoyladenosine; 1,2'-O-dimethyladenosine; 1-methyladenosine; 2'-O-methyladenosine; 2'-O-ribosyladenosine (phosphate); 2-methyladenosine; 2-methylthio-N6 isopentenyladenosine; 2-methylthio-N6-hydroxynorvalyl carbamoyladenosine; 2'-O-methyladenosine; 2'-O-ribosyladenosine (phosphate); Isopentenyladenosine; N6-(cis-hydroxyisopentenyl)adenosine; N6,2'-O-dimethyladenosine; N6,2'-O-dimethyladenosine; N6,N6,2'-O-trimethyladenosine; N6,N6-dimethyladenosine; N6-acetyladenosine; N6-hydroxynorvalylcarbamoyladenosine; N6-methyl-N6-threonylcarbamoyladenosine; 2-methyladenosine; 2-methylthio-N6-isopentenyladenosine; 7-deaza-adenosine; N1-methyl-adenosine; N6, N6 (dimethyl)adenine; N6-cis-hydroxy-isopentenyl-adenosine; α -thio-adenosine; 2 (amino)adenine; 2 (aminopropyl)adenine; 2 (methylthio) N6 (isopentenyl)adenine; 2-(alkyl)adenine; 2-(aminoalkyl)adenine; 2-(aminopropyl)adenine; 2-(halo)adenine; 2-(halo)adenine; 2-(propyl)adenine; 2'-Amino-2'-deoxy-ATP; 2'-Azido-2'-deoxy-ATP; 2'-Deoxy-2'-a-aminoadenosine TP; 2'-Deoxy-2'-a-azidoadenosine TP; 6 (alkyl)adenine; 6 (methyl)adenine; 6-(alkyl)adenine; 6-(methyl)adenine; 7 (deaza)adenine; 8 (alkenyl)adenine; 8 (alkynyl)adenine; 8 (amino)adenine; 8 (thioalkyl)adenine; 8-(alkenyl)adenine; 8-(alkyl)adenine; 8-(alkynyl)adenine; 8-(amino)adenine; 8-(halo)adenine; 8-(hydroxyl)adenine; 8-(thioalkyl)adenine; 8-(thiol)adenine; 8-azido-adenosine; aza adenine; deaza adenine; N6 (methyl)adenine; N6-(isopentyl)adenine; 7-deaza-8-aza-adenosine; 7-methyladenine; 1-Deazaadenosine TP; 2'-fluoro-N6-Bz-deoxyadenosine TP; 2'-O Me-2-Amino-ATP; 2'-O-methyl-N6-Bz-deoxyadenosine TP; 2'-a-Ethynyladenosine TP; 2-aminoadenosine TP; 2-Amino-ATP; 2'-a-Trifluoromethyladenosine TP; 2-Azidoadenosine TP; 2'-b-I-thiynyladenosine TP; 2-Bromoadenosine TP; 2'-b-Trifluoromethyladenosine TP; 2-Chloroadenosine TP; 2'-Deoxy-2',2'-difluoroadenosine TP; 2'-Deoxy-2'-a-mercaptopadenosine TP; 2'-Deoxy-2'-a-thiomethoxyadenosine TP; 2'-Deoxy-2'-b-aminoadenosine TP; 2'-Deoxy-2'-b-azidoadenosine TP; 2'-Deoxy-2'-b-bromoadenosine TP; 2'-Deoxy-2'-b-chloroadenosine TP; 2'-Deoxy-2'-b-fluoroadenosine TP; 2'-Deoxy-2'-b-iodoadenosine

TP; 2'-Deoxy-2'-b-mercaptadenosine TP; 2'-Deoxy-2'-b-thiomethoxyadenosine TP; 2-Fluoroadenosine TP; 2-Iodo-adenosine TP; 2-Mercaptadenosine TP; 2-methoxy-adenine; 2-methylthio-adenine; 2-Trifluoromethyladenosine TP; 3-Deaza-3-bromoadenosine TP; 3-Deaza-3-chloroadenosine TP; 3-Deaza-3-fluoroadenosine TP; 3-Deaza-3-iodoadenosine TP; 3-Deazaadenosine TP; 4'-Azidoadenosine TP; 4'-Carbocyclic adenosine TP; 4'-Ethylnyladenosine TP; 5'-Homo-adenosine TP; 8-Aza-ATP; 8-bromo-adenosine TP; 8-Trifluoromethyladenosine TP; 9-Deazaadenosine TP; 2-aminopurine; 7-deaza-2,6-diaminopurine; 7-deaza-8-aza-2,6-diaminopurine; 7-deaza-8-aza-2-aminopurine; 2,6-diaminopurine; 7-deaza-8-aza-adenine; 7-deaza-2-aminopurine; 2-thiocytidine; 3-methylcytidine; 5-formylcytidine; 5-hydroxymethylcytidine; 5-methylcytidine; N4-acetylcytidine; 2'-O-methylcytidine; 2'-O-methylcytidine; 5,2'-O-dimethylcytidine; 5-formyl-2'-O-methylcytidine; Lysidine; N4,2'-O-dimethylcytidine; N4-acetyl-2'-O-methylcytidine; N4-methylcytidine; N4,N4-dimethyl-2'-OMe-Cytidine TP; 4-methylcytidine; 5-aza-cytidine; Pseudo-iso-cytidine; pyrrolo-cytidine; α -thio-cytidine; 2-(thio)cytosine; 2'-Amino-2'-deoxy-C'TP; 2'-Azido-2'-deoxy-C'TP; 2'-Deoxy-2'-aminocytidine TP; 2'-Deoxy-2'-azidocytidine TP; 3 (deaza) 5 (aza)cytosine; 3 (methyl)cytosine; 3-(alkyl)cytosine; 3-(deaza) 5 (aza)cytosine; 3-(methyl)cytidine; 4,2'-O-dimethylcytidine; 5 (halo)cytosine; 5 (methyl)cytosine; 5 (propynyl)cytosine; 5 (trifluoromethyl)cytosine; 5-(alkyl)cytosine; 5-(alkynyl)cytosine; 5-(halo)cytosine; 5-(propynyl)cytosine; 5-(trifluoromethyl)cytosine; 5-bromo-cytidine; 5-iodo-cytidine; 5-propynyl cytosine; 6-(azo)cytosine; 6-aza-cytidine; aza cytosine; deaza cytosine; N4 (acetyl) cytosine; 1-methyl-1-deaza-pseudoisocytidine; 1-methyl-pseudoisocytidine; 2-methoxy-5-methyl-cytidine; 2-methoxy-cytidine; 2-thio-5-methyl-cytidine; 4-methoxy-1-methyl-pseudoisocytidine; 4-methoxy-pseudoisocytidine; 4-thio-1-methyl-1-deaza-pseudoisocytidine; 4-thio-1-methyl-pseudoisocytidine; 4-thio-pseudoisocytidine; 5-azazebularine; 5-methyl-zebularine; pyrrolo-pseudoisocytidine; Zebularine; (E)-5-(2-Bromo-vinyl)cytidine TP; 2,2'-anhydro-cytidine TP hydrochloride; 2'Fluor-N4-Bz-cytidine TP; 2'Fluor-N4-Acetyl-cytidine TP; 2'-O-Methyl-N4-Acetyl-cytidine TP; 2'-O-methyl-N4-Bz-cytidine TP; 2'-a-Ethylnylcytidine TP; 2'-a-Trifluoromethylcytidine TP; 2'-b-Ethylnylcytidine TP; 2'-b-Trifluoromethylcytidine TP; 2'-Deoxy-2',2'-difluorocytidine TP; 2'-Deoxy-2'-a-mercaptocytidine TP; 2'-Deoxy-2'-a-thiomethoxycytidine TP; 2'-Deoxy-2'-b-aminocytidine TP; 2'-Deoxy-2'-b-azidocytidine TP; 2'-Deoxy-2'-b-bromocytidine TP; 2'-Deoxy-2'-b-chlorocytidine TP; 2'-Deoxy-2'-b-fluorocytidine TP; 2'-Deoxy-2'-b-iodocytidine TP; 2'-Deoxy-2'-b-mercaptocytidine TP; 2'-Deoxy-2'-b-thiomethoxycytidine TP; 2'-O-Methyl-5-(1-propynyl)cytidine TP; 3'-Ethylnylcytidine TP; 4'-Azidocytidine TP; 4'-Carbocyclic cytidine TP; 4'-Ethylnylcytidine TP; 5-(1-Propynyl)ara-cytidine TP; 5-(2-Chloro-phenyl)-2-thiocytidine TP; 5-(4-Amino-phenyl)-2-thiocytidine TP; 5-Aminoallyl-C'TP; 5-Cyanocytidine TP; 5-Ethylnylara-cytidine TP; 5-Ethylnylcytidine TP; 5-Homo-cytidine TP; 5-Methoxycytidine TP; 5-Trifluoromethyl-Cytidine TP; N4-Amino-cytidine TP; N4-Benzoyl-cytidine TP; Pseudoisocytidine TP; 7-methylguanosine; N2,2'-O-dimethylguanosine; N2-methylguanosine; Wyosine; 1,2'-O-dimethylguanosine; 1-methylguanosine; 2'-O-methylguanosine; 2'-O-ribosylguanosine (phosphate); 2'-O-methylguanosine; 2'-O-ribosylguanosine (phosphate); 7-aminomethyl-7-

deazaguanosine; 7-cyano-7-deazaguanosine; Archacosine; Methylwyo sine; N2,7-dimethylguanosine; N2,N2,2'-O-trimethylguanosine; N2,N2,7-trimethylguanosine; N2,N2-dimethylguanosine; N2,7,2'-O-trimethylguanosine; 6-thioguanosine; 7-deaza-guanosine; 8-oxo-guanosine; N1-methyl-guanosine; α -thio-guanosine; 2 (propyl)guanine; 2-(alkyl)guanine; 2'-Amino-2'-deoxy-GTP; 2'-Azido-2'-deoxy-GTP; 2'-Deoxy-2'-a-aminoguanosine TP; 2'-Deoxy-2'-a-azidoguanosine TP; 6 (methyl)guanine; 6-(alkyl)guanine; 6-(methyl)guanine; 6-methyl-guanosine; 7 (alkyl)guanine; 7 (deaza)guanine; 7 (methyl)guanine; 7-(alkyl)guanine; 7-(deaza)guanine; 7-(methyl)guanine; 8 (alkyl)guanine; 8 (alkynyl)guanine; 8 (halo)guanine; 8 (thioalkyl)guanine; 8-(alkenyl)guanine; 8-(alkyl)guanine; 8-(alkynyl)guanine; 8-(amino)guanine; 8-(halo)guanine; 8-(hydroxyl)guanine; 8-(thioalkyl)guanine; 8-(thiol)guanine; aza guanine; deaza guanine; N (methyl)guanine; N-(methyl)guanine; 1-methyl-6-thio-guanosine; 6-methoxy-guanosine; 6-thio-7-deaza-8-aza-guanosine; 6-thio-7-deaza-guanosine; 6-thio-7-methyl-guanosine; 7-deaza-8-aza-guanosine; 7-methyl-8-oxo-guanosine; N2,N2-dimethyl-6-thio-guanosine; N2-methyl-6-thio-guanosine; 1-Me-GTP; 2'Fluor-N2-isobutyl-guanosine TP; 2'-O-methyl-N2-isobutyl-guanosine TP; 2'-a-Ethylnylguanosine TP; 2'-a-Trifluoromethylguanosine TP; 2'-b-Ethylnylguanosine TP; 2'-b-Trifluoromethylguanosine TP; 2'-Deoxy-2',2'-difluoroguanosine TP; 2'-Deoxy-2'-a-mercaptoguanosine TP; 2'-Deoxy-2'-a-thiomethoxyguanosine TP; 2'-Deoxy-2'-b-aminoguanosine TP; 2'-Deoxy-2'-b-azidoguanosine TP; 2'-Deoxy-2'-b-bromoguanosine TP; 2'-Deoxy-2'-b-chloroguanosine TP; 2'-Deoxy-2'-b-fluoroguanosine TP; 2'-Deoxy-2'-b-iodoguanosine TP; 2'-Deoxy-2'-b-mercaptoguanosine TP; 2'-Deoxy-2'-b-thiomethoxyguanosine TP; 4'-Azidoguanosine TP; 4'-Carbocyclic guanosine TP; 4'-Ethylnylguanosine TP; 5'-Homo-guanosine TP; 8-bromo-guanosine TP; 9-Deazaguanosine TP; N2-isobutyl-guanosine TP; 1-methylinosine; Inosine; 1,2'-O-dimethylinosine; 2'-O-methylinosine; 7-methylinosine; 2'-O-methylinosine; Epoxyqueuosine; galactosyl-queuosine; Mannosylqueuosine; Queuosine; allylamino-thymidine; aza thymidine; deaza thymidine; deoxy-thymidine; 2'-O-methyluridine; 2-thiouridine; 3-methyluridine; 5-carboxymethyluridine; 5-hydroxyuridine; 5-methyluridine; 5-taurinomethyl-2-thiouridine; 5-taurinomethyluridine; Dihydrouridine; Pseudouridine; (3-(3-amino-3-carboxypropyl)uridine; 1-methyl-3-(3-amino-5-carboxypropyl)pseudouridine; 1-methylpseudouridine; 1-methyl-pseudouridine; 2'-O-methyluridine; 2'-O-methylpseudouridine; 2'-O-methyluridine; 2-thio-2'-O-methyluridine; 3-(3-amino-3-carboxypropyl)uridine; 3,2'-O-dimethyluridine; 3-Methyl-pseudo-Uridine TP; 4-thiouridine; 5-(carboxyhydroxymethyl)uridine; 5-(carboxyhydroxymethyl)uridine methyl ester; 5,2'-O-dimethyluridine; 5,6-dihydro-uridine; 5-aminomethyl-2-thiouridine; 5-carbamoylmethyl-2'-O-methyluridine; 5-carbamoylmethyluridine; 5-carboxyhydroxymethyluridine; 5-carboxyhydroxymethyluridine methyl ester; 5-carboxymethylaminomethyl-2'-O-methyluridine; 5-carboxymethylaminomethyl-2-thiouridine; 5-carboxymethylaminomethyl-2-thiouridine; 5-carboxymethylaminomethyluridine TP; 5-Carbamoylmethyluridine TP; 5-methoxycarbonylmethyl-2'-O-methyluridine; 5-methoxycarbonylmethyl-2-thiouridine; 5-methoxycarbonylmethyluridine; 5-methyl-2-thiouridine; 5-methylaminomethyl-2-selenouridine; 5-methylaminomethyl-2-

thiouridine; 5-methylaminomethyluridine; 5-Methyl-dihydrouridine; 5-Oxyacetic acid-Uridine TP; 5-Oxyacetic acid-methyl ester-Uridine TP; N1-methyl-pseudo-uridine; uridine 5-oxyacetic acid; uridine 5-oxyacetic acid methyl ester; 3-(3-Amino-3-carboxypropyl)-Uridine TP; 5-(iso-Pentenylaminomethyl)-2-thiouridine TP; 5-(iso-Pentenylaminomethyl)-2'-O-methyluridine TP; 5-(iso-Pentenylaminomethyl)uridine TP; 5-propynyl uracil; α -thio-uridine; 1 (aminoalkylamino-carbonylethylene)-2 (thio)-pseudouracil; 1 (aminoalkylaminocarbonylethylene)-2,4-(dithio)pseudouracil; 1 (aminoalkylaminocarbonylethylene)-4 (thio)pseudouracil; 1 (aminoalkylaminocarbonylethylene)-pseudouracil; 1 (aminocarbonylethylene)-2(thio)-pseudouracil; 1 (aminocarbonylethylene)-2,4-(dithio)pseudouracil; 1 (aminocarbonylethylene)-4 (thio)pseudouracil; 1 (aminocarbonylethylene)-pseudouracil; 1 substituted 2(thio)-pseudouracil; 1 substituted 2,4-(dithio)pseudouracil; 1 substituted 4 (thio) pseudouracil; 1 substituted pseudouracil; 1-(aminoalkylamino-carbonylethylene)-2-(thio)-pseudouracil; 1-Methyl-3-(3-amino-3-carboxypropyl) pseudouridine TP; 1-Methyl-3-(3-amino-3-carboxypropyl)pseudo-UTP; 1-Methyl-pseudo-UTP; 2 (thio)pseudouracil; 2' deoxy uridine; 2' fluorouridine; 2-(thio)uracil; 2,4-(dithio)pseudouracil; 2' methyl, 2' amino, 2' azido, 2' fluoro-guanosine; 2'-Amino-2'-deoxy-UTP; 2'-Azido-2'-deoxy-UTP; 2'-Azido-deoxyuridine TP; 2'-O-methylpseudouridine; 2' deoxy uridine; 2' fluorouridine; 2'-Deoxy-2'-a-aminouridine TP; 2'-Deoxy-2'-a-azidouridine TP; 2-methylpseudouridine; 3 (3 amino-3 carboxypropyl)uracil; 4 (thio)pseudouracil; 4-(thio)pseudouracil; 4-(thio)uracil; 4-thiouracil; 5 (1,3-diazole-1-alkyl)uracil; 5 (2-aminopropyl)uracil; 5 (aminoalkyl)uracil; 5 (dimethylaminoalkyl)uracil; 5 (guanidiniumalkyl)uracil; 5 (methoxycarbonylmethyl)-2-(thio)uracil; 5 (methoxycarbonyl-methyl)uracil; 5 (methyl) 2 (thio)uracil; 5 (methyl) 2,4 (dithio)uracil; 5 (methyl) 4 (thio)uracil; 5 (methylaminomethyl)-2 (thio)uracil; 5 (methylaminomethyl)-2,4 (dithio)uracil; 5 (methylaminomethyl)-4 (thio)uracil; 5 (propynyl)uracil; 5 (trifluoromethyl)uracil; 5-(2-aminopropyl)uracil; 5-(alkyl)-2-(thio)pseudouracil; 5-(alkyl)-2,4 (dithio)pseudouracil; 5-(alkyl)-4 (thio)pseudouracil; 5-(alkyl)pseudouracil; 5-(alkyl)uracil; 5-(alkynyl)uracil; 5-(allylamino)uracil; 5-(cyanoalkyl)uracil; 5-(dialkylaminoalkyl)uracil; 5-(dimethylaminoalkyl)uracil; 5-(guanidiniumalkyl)uracil; 5-(halo)uracil; 5-(1,3-diazole-1-alkyl)uracil; 5-(methoxy)uracil; 5-(methoxycarbonylmethyl)-2-(thio)uracil; 5-(methoxycarbonyl-methyl)uracil; 5-(methyl) 2(thio)uracil; 5-(methyl) 2,4 (dithio)uracil; 5-(methyl) 4 (thio)uracil; 5-(methyl)-2-(thio)pseudouracil; 5-(methyl)-2,4 (dithio)pseudouracil; 5-(methyl)-4 (thio)pseudouracil; 5-(methyl)pseudouracil; 5-(methylaminomethyl)-2 (thio)uracil; 5-(methylaminomethyl)-2,4(dithio)uracil; 5-(methylaminomethyl)-4-(thio)uracil; 5-(propynyl)uracil; 5-(trifluoromethyl)uracil; 5-aminoallyl-uridine; 5-bromo-uridine; 5-iodo-uridine; 5-uracil; 6 (azo)uracil; 6-(azo)uracil; 6-aza-uridine; ally-amino-uracil; aza uracil; deaza uracil; N3 (methyl)uracil; P pseudo-UTP-1-2-ethanoic acid; Pseudouracil; 4-Thio-pseudo-UTP; 1-carboxymethyl-pseudouridine; 1-methyl-1-deaza-pseudouridine; 1-propynyl-uridine; 1-taurinomethyl-1-methyl-uridine; 1-taurinomethyl-4-thio-uridine; 1-taurinomethyl-pseudouridine; 2-methoxy-4-thio-pseudouridine; 2-thio-1-methyl-1-deaza-pseudouridine; 2-thio-1-methyl-pseudouridine; 2-thio-5-aza-uridine; 2-thio-dihy-

dropseudouridine; 2-thio-dihydrouridine; 2-thio-pseudouridine; 4-methoxy-2-thio-pseudouridine; 4-methoxy-pseudouridine; 4-thio-1-methyl-pseudouridine; 4-thio-pseudouridine; 5-aza-uridine; Dihydropseudouridine; (\pm)-1-(2-Hydroxypropyl)pseudouridine TP; (2R)-1-(2-Hydroxypropyl)pseudouridine TP; (2S)-1-(2-Hydroxypropyl)pseudouridine TP; (E)-5-(2-Bromo-vinyl)ara-uridine TP; (E)-5-(2-Bromo-vinyl)uridine TP; (Z)-5-(2-Bromo-vinyl)ara-uridine TP; (Z)-5-(2-Bromo-vinyl)uridine TP; 1-(2,2,2-Trifluoroethyl)-pseudo-UTP; 1-(2,2,3,3,3-Pentafluoropropyl)pseudouridine TP; 1-(2,2,1-Diethoxyethyl)pseudouridine TP; 1-(2,4,6-Trimethylbenzyl)pseudouridine TP; 1-(2,4,6-Trimethyl-benzyl)pseudo-UTP; 1-(2,4,6-Trimethyl-phenyl)pseudo-UTP; 1-(2-Amino-2-carboxyethyl)pseudo-UTP; 1-(2-Amino-ethyl)pseudo-UTP; 1-(2-Hydroxyethyl)pseudouridine TP; 1-(2-Methoxyethyl)pseudouridine TP; 1-(3,4-Bis-trifluoromethoxybenzyl)pseudouridine TP; 1-(3,4-Dimethoxybenzyl)pseudouridine TP; 1-(3-Amino-3-carboxypropyl)pseudo-UTP; 1-(3-Amino-propyl)pseudo-UTP; 1-(3-Cyclopropyl-prop-2-ynyl)pseudouridine TP; 1-(4-Amino-4-carboxybutyl)pseudo-UTP; 1-(4-Amino-benzyl)pseudo-UTP; 1-(4-Amino-butyl)pseudo-UTP; 1-(4-Aminophenyl)pseudo-UTP; 1-(4-Azidobenzyl)pseudouridine TP; 1-(4-Bromobenzyl)pseudouridine TP; 1-(4-Chlorobenzyl)pseudouridine TP; 1-(4-Fluorobenzyl)pseudouridine TP; 1-(4-Iodobenzyl)pseudouridine TP; 1-(4-Methanesulfonylbenzyl)pseudouridine TP; 1-(4-Methoxybenzyl)pseudouridine TP; 1-(4-Methoxy-benzyl)pseudo-UTP; 1-(4-Methoxyphenyl)pseudo-UTP; 1-(4-Methylbenzyl)pseudouridine TP; 1-(4-Methyl-benzyl)pseudo-UTP; 1-(4-Nitrobenzyl)pseudouridine TP; 1-(4-Nitro-benzyl)pseudo-UTP; 1-(4-Nitro-phenyl)pseudo-UTP; 1-(4-Thiomethoxybenzyl)pseudouridine TP; 1-(4-Trifluoromethoxybenzyl)pseudouridine TP; 1-(4-Trifluoromethylbenzyl)pseudouridine TP; 1-(5-Amino-pentyl)pseudo-UTP; 1-(6-Amino-hexyl)pseudo-UTP; 1,6-Dimethyl-pseudo-UTP; 1-[3-(2-{2-[2-(2-Aminoethoxy)-ethoxy]-ethoxy}-propionyl)pseudouridine TP; 1-[3-[2-(2-Aminoethoxy)-ethoxy]-propionyl] pseudouridine TP; 1-Acetyl-pseudouridine TP; 1-Alkyl-6-(1-propynyl)-pseudo-UTP; 1-Alkyl-6-(2-propynyl)-pseudo-UTP; 1-Alkyl-6-allyl-pseudo-UTP; 1-Alkyl-6-ethynyl-pseudo-UTP; 1-Alkyl-6-homoallylpseudo-UTP; 1-Alkyl-6-vinyl-pseudo-UTP; 1-Allylpseudouridine TP; 1-Aminomethyl-pseudo-UTP; 1-Benzoylpseudouridine TP; 1-Benzoyloxymethylpseudouridine TP; 1-Benzyl-pseudo-UTP; 1-Biotinyl-PI(3)G2-pseudouridine TP; 1-Biotinylpseudouridine TP; 1-Butyl-pseudo-UTP; 1-Cyanomethylpseudouridine TP; 1-Cyclobutylmethylpseudouridine TP; 1-Cyclobutyl-pseudo-UTP; 1-Cycloheptylmethyl-pseudo-UTP; 1-Cycloheptyl-pseudo-UTP; 1-Cyclohexylmethyl-pseudo-UTP; 1-Cyclohexyl-pseudo-UTP; 1-Cyclooctylmethyl-pseudo-UTP; 1-Cyclooctyl-pseudo-UTP; 1-Cyclopentylmethyl-pseudo-UTP; 1-Cyclopentyl-pseudo-UTP; 1-Cyclopropylmethyl-pseudo-UTP; 1-Cyclopropyl-pseudo-UTP; 1-Ethyl-pseudo-UTP; 1-Hexyl-pseudo-UTP; 1-Homoallylpseudouridine TP; 1-Hydroxymethylpseudouridine TP; 1-iso-propyl-pseudo-UTP; 1-Me-2-thio-pseudo-UTP; 1-Me-4-thio-pseudo-UTP; 1-Me-alpha-thio-pseudo-UTP; 1-Methanesulfonylmethylpseudouridine TP; 1-Methoxymethylpseudouridine TP; 1-Methyl-6-(2,2,2-Trifluoroethyl)pseudo-UTP; 1-Methyl-6-(4-morpholino)-pseudo-UTP; 1-Methyl-6-(4-thiomorpholino)-pseudo-UTP; 1-Methyl-6-(substituted phenyl)pseudo-UTP; 1-Methyl-6-amino-pseudo-UTP; 1-Methyl-6-

azido-pseudo-UTP; 1-Methyl-6-bromo-pseudo-UTP; 1-Methyl-6-butyl-pseudo-UTP; 1-Methyl-6-chloro-pseudo-UTP; 1-Methyl-6-cyano-pseudo-UTP; 1-Methyl-6-dimethylamino-pseudo-UTP; 1-Methyl-6-ethoxy-pseudo-UTP; 1-Methyl-6-ethylcarboxylate-pseudo-UTP; 1-Methyl-6-ethyl-pseudo-UTP; 1-Methyl-6-fluoro-pseudo-UTP; 1-Methyl-6-formyl-pseudo-UTP; 1-Methyl-6-hydroxyamino-pseudo-UTP; 1-Methyl-6-hydroxy-pseudo-UTP; 1-Methyl-6-iodo-pseudo-UTP; 1-Methyl-6-iso-propyl-pseudo-UTP; 1-Methyl-6-methoxy-pseudo-UTP; 1-Methyl-6-methylamino-pseudo-UTP; 1-Methyl-6-phenyl-pseudo-UTP; 1-Methyl-6-propyl-pseudo-UTP; 1-Methyl-6-tert-butyl-pseudo-UTP; 1-Methyl-6-trifluoromethoxy-pseudo-UTP; 1-Methyl-6-trifluoromethyl-pseudo-UTP; 1-Morpholinomethylpseudouridine TP; 1-Pentyl-pseudo-UTP; 1-Phenyl-pseudo-UTP; 1-Pivaloylpseudouridine TP; 1-Propargylpseudouridine TP; 1-Propyl-pseudo-UTP; 1-propynyl-pseudouridine; 1-p-tolyl-pseudo-UTP; 1-tert-Butyl-pseudo-UTP; 1-Thiomethoxymethylpseudouridine TP; 1-Thiomorpholinomethylpseudouridine TP; 1-Trifluoroacetyl-pseudouridine TP; 1-Trifluoromethyl-pseudo-UTP; 1-Vinylpseudouridine TP; 2,2'-anhydro-uridine TP; 2'-bromo-deoxyuridine TP; 2'-H-5-Methyl-2'-deoxy-UTP; 2'-OMe-5-Me-UTP; 2'-OMe-pseudo-UTP; 2'-a-Ethynyluridine TP; 2'-a-Trifluoromethyluridine TP; 2'-b-Ethynyluridine TP; 2'-b-Trifluoromethyluridine TP; 2'-Deoxy-2',2'-difluorouridine TP; 2'-Deoxy-2'-a-mercaptopuridine TP; 2'-Deoxy-2'-a-thiomethoxyuridine TP; 2'-Deoxy-2'-b-aminouridine TP; 2'-Deoxy-2'-b-azidouridine TP; 2'-Deoxy-2'-b-bromouridine TP; 2'-Deoxy-2'-b-chlorouridine TP; 2'-Deoxy-2'-b-fluorouridine TP; 2'-Deoxy-2'-b-iodouridine TP; 2'-Deoxy-2'-b-mercaptopuridine TP; 2'-Deoxy-2'-b-thiomethoxyuridine TP; 2-methoxy-4-thio-uridine; 2-methoxyuridine; 2'-O-Methyl-5-(1-propynyl)uridine TP; 3-Alkyl-pseudo-UTP; 4'-Azidouridine TP; 4'-Carbocyclic uridine TP; 4'-Ethynyluridine TP; 5-(1-Propynyl)ara-uridine TP; 5-(2-Furanyl)uridine TP; 5-Cyanouridine TP; 5-Dimethylaminouridine TP; 5'-Homo-uridine TP; 5-iodo-2'-fluoro-deoxyuridine TP; 5-Phenylethynyluridine TP; 5-Trideuteromethyl-6-deuterouridine TP; 5-Trifluoromethyl-Uridine TP; 5-Vinylarauridine TP; 6-(2,2,2-Trifluoroethyl)-pseudo-UTP; 6-(4-Morpholino)-pseudo-UTP; 6-(4-Thiomorpholino)-pseudo-UTP; 6-(Substituted-Phenyl)-pseudo-UTP; 6-Amino-pseudo-UTP; 6-Azido-pseudo-UTP; 6-Bromo-pseudo-UTP; 6-Butyl-pseudo-UTP; 6-Chloro-pseudo-UTP; 6-Cyano-pseudo-UTP; 6-Dimethylamino-pseudo-UTP; 6-Ethoxy-pseudo-UTP; 6-Ethylcarboxylate-pseudo-UTP; 6-Ethyl-pseudo-UTP; 6-Fluoro-pseudo-UTP; 6-Formyl-pseudo-UTP; 6-Hydroxyamino-pseudo-UTP; 6-Hydroxy-pseudo-UTP; 6-Iodo-pseudo-UTP; 6-iso-Propyl-pseudo-UTP; 6-Methoxy-pseudo-UTP; 6-Methyl-amino-pseudo-UTP; 6-Methyl-pseudo-UTP; 6-Phenyl-pseudo-UTP; 6-Phenyl-pseudo-UTP; 6-Propyl-pseudo-UTP; 6-tert-Butyl-pseudo-UTP; 6-Trifluoromethoxy-pseudo-UTP; 6-Trifluoromethyl-pseudo-UTP; Alpha-thio-pseudo-UTP; Pseudouridine 1-(4-methylbenzenesulfonic acid) TP; Pseudouridine 1-(4-methylbenzoic acid) TP; Pseudouridine TP 1-[3-(2-ethoxy)propionic acid]; Pseudouridine TP 1-[3-{2-(2-[2-(2-ethoxy)-ethoxy]-ethoxy)-ethoxy}propionic acid]; Pseudouridine TP 1-[3-{2-(2-[2-(2-ethoxy)-ethoxy]-ethoxy)-ethoxy}propionic acid]; Pseudouridine TP 1-[3-{2-(2-[2-(2-ethoxy)-ethoxy]-ethoxy)-ethoxy}propionic acid]; Pseudouridine TP 1-methylphos-

phonic acid; Pseudouridine TP 1-methylphosphonic acid diethyl ester; Pseudo-UTP-N1-3-propionic acid; Pseudo-UTP-N1-4-butanoic acid; Pseudo-UTP-N1-5-pentanoic acid; Pseudo-UTP-N1-6-hexanoic acid; Pseudo-UTP-N1-7-heptanoic acid; Pseudo-UTP-N1-methyl-p-benzoic acid; Pseudo-UTP-N1-p-benzoic acid; Wybutosine; Hydroxywybutosine; Isowyosine; Peroxywybutosine; undermodified hydroxywybutosine; 4-demethylwyosine; 2,6-(diamino)purine: 1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl; 1,3-(diazia)-2-(oxo)-phenthiazin-1-yl; 1,3-(diazia)-2-(oxo)-phenoxazin-1-yl; 1,3,5-(triazia)-2,6-(dioxo)-naphthalene; 2 (amino) purine; 2,4,5-(trimethyl)phenyl; 2' methyl, 2' amino, 2' azido, 2' fluoro-cytidine; 2' methyl, 2' amino, 2' azido, 2' fluoro-adenine; 2' methyl, 2' amino, 2' azido, 2' fluoro-uridine; 2' amino-2'-deoxyribose; 2-amino-6-Chloro-purine; 2-aza-inosinyl; 2'-azido-2'-deoxyribose; 2'fluoro-2'-deoxyribose; 2'-fluoromodified bases; 2'-O-methyl-ribose; 2-oxo-7-aminopyridopyrimidin-3-yl; 2-oxo-pyridopyrimidine-3-yl; 2-pyridinone; 3 nitropropole; 3-(methyl)-7-(propynyl) isocarbostyryl; 3-(methyl)isocarbostyryl; 4-(fluoro)-6-(methyl)benzimidazole; 4-(methyl)benzimidazole; 4-(methyl)indolyl; 4,6-(dimethyl)indolyl; 5 nitroindole; 5 substituted pyrimidines; 5-(methyl)isocarbostyryl; 5-nitroindole; 6-(aza)pyrimidine; 6-(azo)thymine; 6-(methyl)-7-(aza)indolyl; 6-chloro-purine; 6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; 7-(aminoalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenthiazin-1-yl; 7-(aminoalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl; 7-(aminoalkylhydroxy)-1,3-(diazia)-2-(oxo)-phenoxazin-1-yl; 7-(aminoalkylhydroxy)-1,3-(diazia)-2-(oxo)-phenthiazin-1-yl; 7-(aminoalkylhydroxy)-1,3-(diazia)-2-(oxo)-phenoxazin-1-yl; 7-(aza)indolyl; 7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenoxazin-yl; 7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenthiazin-1-yl; 7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl; 7-(guanidiniumalkylhydroxy)-1,3-(diazia)-2-(oxo)-phenoxazin-1-yl; 7-(guanidiniumalkylhydroxy)-1,3-(diazia)-2-(oxo)-phenthiazin-1-yl; 7-(guanidiniumalkylhydroxy)-1,3-(diazia)-2-(oxo)-phenoxazin-1-yl; 7-(propynyl)isocarbostyryl; 7-(propynyl)isocarbostyryl, propynyl-7-(aza)indolyl; 7-deaza-inosinyl; 7-substituted 1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl; 7-substituted 1,3-(diazia)-2-(oxo)-phenoxazin-1-yl; 9-(methyl)-imidizopyridinyl; Aminoindolyl; Anthracenyl; bis-ortho-(aminoalkylhydroxy)-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; bis-ortho-substituted-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; Difluorotolyl; Hypoxanthine; Imidizopyridinyl; Inosinyl; Isocarbostyryl; Isoguanisine; N2-substituted purines; N6-methyl-2-amino-purine; N6-substituted purines; N-alkylated derivative; Naphthalenyl; Nitrobenzimidazolyl; Nitroimidazolyl; Nitroindazolyl; Nitroprazolyl; Nubularine; O6-substituted purines; O-alkylated derivative; ortho-(aminoalkylhydroxy)-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; ortho-substituted-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; Oxoformycin TP; para-(aminoalkylhydroxy)-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; para-substituted-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; Pentacenyl; Phenanthracenyl; Phenyl; propynyl-7-(aza)indolyl; Pyrenyl; pyridopyrimidin-3-yl; pyridopyrimidin-3-yl, 2-oxo-7-amino-pyridopyrimidin-3-yl; pyrrolo-pyrimidin-2-on-3-yl; Pyrrolopyrimidinyl; Pyrrolopyrimidinyl; Stilbenzyl; substituted 1,2,4-triazoles; Tetracenyl; Tubercidine; Xanthine; Xanthosine-5'-TP; 2-thio-zebularine; 5-aza-2-thio-zebularine; 7-deaza-2-amino-purine; pyridin-4-one ribo-

nucleoside: 2-Amino-riboside-TP; Formycin A TP; Formycin B TP; Pyrrolosine TP; 2'-OH-ara-adenosine TP; 2'-OH-ara-cytidine TP; 2'-OH-ara-uridine TP; 2'-OH-ara-guanosine TP; 5-(2-carbomethoxyvinyl)uridine TP; and N6-(19-Amino-pentaoxonanadecyl)adenosine TP.

[0319] In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) include a combination of at least two (e.g., 2, 3, 4 or more) of the aforementioned modified nucleobases.

[0320] In some embodiments, modified nucleobases in polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) are selected from the group consisting of pseudouridine (ψ), N1-methylpseudouridine ($m^1\psi$), N1-ethylpseudouridine, 2-thiouridine, 4'-thiouridine, 5-methylcytosine, 2-thio-1-methyl-1-deaza-pseudouridine, 2-thio-1-methyl-pseudouridine, 2-thio-5-aza-uridine, 2-thio-dihydropseudouridine, 2-thio-dihydrouridine, 2-thio-pseudouridine, 4-methoxy-2-thio-pseudouridine, 4-methoxy-pseudouridine, 4-thio-1-methyl-pseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-methyl uridine. In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) include a combination of at least two (e.g., 2, 3, 4 or more) of the aforementioned modified nucleobases.

[0321] In some embodiments, modified nucleobases in polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) are selected from the group consisting of 1-methyl-pseudouridine ($m^1\psi$), 5-methoxy-uridine (mo^5U), 5-methyl-cytidine (m^5C), pseudouridine (ψ), α -thio-guanosine and α -thio-adenosine. In some embodiments, polynucleotides includes a combination of at least two (e.g., 2, 3, 4 or more) of the aforementioned modified nucleobases.

[0322] In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise pseudouridine (ψ) and 5-methyl-cytidine (m^5C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 1-methyl-pseudouridine ($m^1\psi$). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 1-methyl-pseudouridine ($m^1\psi$) and 5-methyl-cytidine (m^5C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 2-thiouridine (s^2U). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 2-thiouridine and 5-methyl-cytidine (m^5C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise methoxy-uridine (mo^5U). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 5-methoxy-uridine (mo^5U) and 5-methyl-cytidine (m^5C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 2'-O-methyl uridine. In some embodiments polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 2'-O-methyl uridine and 5-methyl-cytidine (m^5C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise N6-methyl-adenosine (m^6A). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise N6-methyl-adenosine (m^6A) and 5-methyl-cytidine (m^5C).

[0323] In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) are uniformly modified (e.g., fully modified, modified throughout the entire sequence) for a particular modification. For example, a polynucleotide can be uniformly modified with 5-methyl-cytidine (m^5C), meaning that all cytosine residues in the mRNA sequence are replaced with 5-methyl-cytidine (m^5C). Similarly, a polynucleotide can be uniformly modified for any type of nucleoside residue present in the sequence by replacement with a modified residue such as those set forth above.

[0324] Exemplary nucleobases and nucleosides having a modified cytosine include N4-acetyl-cytidine ($ac4C$), 5-methyl-cytidine (m^5C), 5-halo-cytidine (e.g., 5-iodo-cytidine), 5-hydroxymethyl-cytidine (hm^5C), 1-methyl-pseudoisocytidine, 2-thio-cytidine (s^2C), and 2-thio-5-methyl-cytidine.

[0325] In some embodiments, a modified nucleobase is a modified uridine. Exemplary nucleobases and In some embodiments, a modified nucleobase is a modified cytosine, nucleosides having a modified uridine include 5-cyano uridine, and 4'-thio uridine.

[0326] In some embodiments, a modified nucleobase is a modified adenine. Exemplary nucleobases and nucleosides having a modified adenine include 7-deaza-adenine, 1-methyl-adenosine (m^1A), 2-methyl-adenine (m^2A), and N6-methyl-adenosine (m^6A).

[0327] In some embodiments, a modified nucleobase is a modified guanine. Exemplary nucleobases and nucleosides having a modified guanine include inosine (I), 1-methyl-inosine (m^1I), wyosine (imG), methylwyosine ($mimG$), 7-deaza-guanosine, 7-cyano-7-deaza-guanosine ($preQ0$), 7-aminomethyl-7-deaza-guanosine ($preQ1$), 7-methyl-guanosine (m^7G), 1-methyl-guanosine (m^1G), 8-oxo-guanosine, 7-methyl-8-oxo-guanosine.

[0328] The polynucleotides of the present disclosure may be partially or fully modified along the entire length of the molecule. For example, one or more or all or a given type of nucleotide (e.g., purine or pyrimidine, or any one or more or all of A, G, U, C) may be uniformly modified in a polynucleotide of the disclosure, or in a given predetermined sequence region thereof (e.g., in the mRNA including or excluding the polyA tail). In some embodiments, all nucleotides X in a polynucleotide of the present disclosure (or in a given sequence region thereof) are modified nucleotides, wherein X may any one of nucleotides A, G, U, C, or any one of the combinations A+G, A+U, A+C, G+U, G+C, U+C, A+G+U, A+G+C, G+U+C or A+G+C.

[0329] The polynucleotide may contain from about 1% to about 100% modified nucleotides (either in relation to overall nucleotide content, or in relation to one or more types of nucleotide, i.e., any one or more of A, G, U or C) or any intervening percentage (e.g., from 1% to 20%, from 1% to 25%, from 1% to 50%, from 1% to 60%, from 1% to 70%, from 1% to 80%, from 1% to 90%, from 1% to 95%, from 10% to 20%, from 10% to 25%, from 10% to 50%, from 10% to 60%, from 10% to 70%, from 10% to 80%, from 10% to 90%, from 10% to 95%, from 10% to 100%, from 20% to 25%, from 20% to 50%, from 20% to 60%, from 20% to 70%, from 20% to 80%, from 20% to 90%, from 20% to 95%, from 20% to 100%, from 50% to 60%, from 50% to 70%, from 50% to 80%, from 50% to 90%, from 50% to 95%, from 50% to 100%, from 70% to 80%, from 70% to 90%, from 70% to 95%, from 70% to 100%.

from 80% to 90%, from 80% to 95%, from 80% to 100%, from 90% to 95%, from 90% to 100%, and from 95% to 100%). Any remaining percentage is accounted for by the presence of unmodified A, G, U, or C.

[0330] The polynucleotides may contain at a minimum 1% and at maximum 100% modified nucleotides, or any intervening percentage, such as at least 5% modified nucleotides, at least 10% modified nucleotides, at least 25% modified nucleotides, at least 50% modified nucleotides, at least 80% modified nucleotides, or at least 90% modified nucleotides. For example, the polynucleotides may contain a modified pyrimidine such as a modified uracil or cytosine. In some embodiments, at least 5%, at least 10%, at least 25%, at least 50%, at least 80%, at least 90% or 100% of the uracil in the polynucleotide is replaced with a modified uracil (e.g., a 5-substituted uracil). The modified uracil can be replaced by a compound having a single unique structure, or can be replaced by a plurality of compounds having different structures (e.g., 2, 3, 4 or more unique structures). In some embodiments, at least 5%, at least 10%, at least 25%, at least 50%, at least 80%, at least 90% or 100% of the cytosine in the polynucleotide is replaced with a modified cytosine (e.g., a 5-substituted cytosine). The modified cytosine can be replaced by a compound having a single unique structure, or can be replaced by a plurality of compounds having different structures (e.g., 2, 3, 4 or more unique structures).

[0331] Thus, in some embodiments, the RNA (e.g., mRNA) vaccines comprise a 5'UTR element, an optionally codon optimized open reading frame, and a 3'UTR element, a poly(A) sequence and/or a polyadenylation signal wherein the RNA is not chemically modified.

[0332] In some embodiments, the modified nucleobase is a modified uracil. Exemplary nucleobases and nucleosides having a modified uracil include pseudouridine (ψ), pyridin-4-one ribonucleoside, 5-aza-uridine, 6-aza-uridine, 2-thio-5-aza-uridine, 2-thio-uridine (s^2U), 4-thio-uridine (s^4U), 4-thio-pseudouridine, 2-thio-pseudouridine, 5-hydroxy-uridine (ho^5U), 5-aminoallyl-uridine, 5-halo-uridine (e.g., 5-iodo-uridine or 5-bromo-uridine), 3-methyl-uridine (m^3U), 5-methoxy-uridine (mo^5U), uridine 5-oxoacetic acid (emo^5U), uridine 5-oxoacetic acid methyl ester ($memo^5U$), 5-carboxymethyl-uridine (cm^5U), 1-carboxymethyl-pseudouridine, 5-carboxyhydroxymethyl-uridine (chm^5U), 5-carboxyhydroxymethyl-uridine methyl ester ($mchm^5U$), 5-methoxycarbonylmethyl-uridine (mcm^5U), 5-methoxycarbonylmethyl-2-thio-uridine (mcm^5s^2U), 5-aminomethyl-2-thio-uridine (nm^5s^2U), 5-methylaminomethyl-uridine (mm^5U), 5-methylaminomethyl-2-thio-uridine (mm^5s^2U), 5-methylaminomethyl-2-seleno-uridine (mm^5se^2U), 5-carbamoylmethyl-uridine (nem^5U), 5-carboxymethylaminomethyl-uridine ($cmmm^5U$), 5-carboxymethylaminomethyl-2-thio-uridine ($cmmm^5s^2U$), 5-propynyl-uridine, 1-propynyl-pseudouridine, 5-taurinomethyl-uridine (tm^5U), 1-taurinomethyl-pseudouridine, 5-taurinomethyl-2-thio-uridine (tm^5s^2U), 1-taurinomethyl-4-thio-pseudouridine, 5-methyl-uridine (m^5U , i.e., having the nucleobase deoxythymine), 1-methyl-pseudouridine ($m^1\psi$), 5-methyl-2-thio-uridine (m^5s^2U), 1-methyl-4-thio-pseudouridine ($m^1s^4\psi$), 4-thio-1-methyl-pseudouridine, 3-methyl-pseudouridine ($m^3\psi$), 2-thio-1-methyl-pseudouridine, 1-methyl-1-deaza-pseudouridine, 2-thio-1-methyl-1-deaza-pseudouridine, dihydrouridine (D), dihydropseudouridine, 5,6-dihydrouridine, 5-methyl-dihydrouridine (m^5D), 2-thio-dihydrouridine, 2-thio-dihydropseudouridine, 2-methoxy-

uridine, 2-methoxy-4-thio-uridine, 4-methoxy-pseudouridine, 4-methoxy-2-thio-pseudouridine, N1-methyl-pseudouridine, 3-(3-amino-3-carboxypropyl)uridine (acp^3U), 1-methyl-3-(3-amino-3-carboxypropyl)pseudouridine ($acp^3\psi$), 5-(isopentenylaminomethyl)uridine (im^5U), 5-(isopentenylaminomethyl)-2-thio-uridine (im^5s^2U), α -thio-uridine, 2'-O-methyl-uridine (Um), 5,2'-O-dimethyl-uridine (m^5Um), 2'-O-methyl-pseudouridine (ψm), 2-thio-2'-O-methyl-uridine (s^2Um), 5-methoxycarbonylmethyl-2'-O-methyl-uridine (mcm^5Um), 5-carbamoylmethyl-2'-O-methyl-uridine (nem^5Um), 5-carboxymethylaminomethyl-2'-O-methyl-uridine ($cmmm^5Um$), 3,2'-O-dimethyl-uridine (m^3Um), and 5-(isopentenylaminomethyl)-2'-O-methyl-uridine (im^5Um), 1-thio-uridine, deoxythymidine, 2'-l-ara-uridine, 2'-l-uridine, 2'-OH-ara-uridine, 5-(2-carbomethoxyvinyl) uridine, and 5-[3-(1-*l*-propenylamino)] uridine.

[0333] In some embodiments, the modified nucleobase is a modified cytosine. Exemplary nucleobases and nucleosides having a modified cytosine include 5-aza-cytidine, 6-aza-cytidine, pseudoisocytidine, 3-methyl-cytidine (m^3C), N4-acetyl-cytidine (ac^4C), 5-formyl-cytidine (f^5C), N4-methyl-cytidine (m^4C), 5-methyl-cytidine (m^5C), 5-halo-cytidine (e.g., 5-iodo-cytidine), 5-hydroxymethyl-cytidine (hm^5C), 1-methyl-pseudoisocytidine, pyrrolo-cytidine, pyrrolo-pseudoisocytidine, 2-thio-cytidine (s^2C), 2-thio-5-methyl-cytidine, 4-thio-pseudoisocytidine, 4-thio-1-methyl-pseudoisocytidine, 4-thio-1-methyl-1-deaza-pseudoisocytidine, 1-methyl-1-deaza-pseudoisocytidine, zebularine, 5-aza-zebularine, 5-methyl-zebularine, 5-aza-2-thio-zebularine, 2-thio-zebularine, 2-methoxy-cytidine, 2-methoxy-5-methyl-cytidine, 4-methoxy-pseudoisocytidine, 4-methoxy-1-methyl-pseudoisocytidine, lysidine (k_2C), α -thio-cytidine, 2'-O-methyl-cytidine (Cm), 5,2'-O-dimethyl-cytidine (m^5Cm), N4-acetyl-2'-O-methyl-cytidine (ac^4Cm), N4,2'-O-dimethyl-cytidine (m^4Cm), 5-formyl-2'-O-methyl-cytidine (f^5Cm), N4,N4,2'-O-trimethyl-cytidine (m^42Cm), 1-thio-cytidine, 2'-l-ara-cytidine, 2'-l-cytidine, and 2'-OH-ara-cytidine.

[0334] In some embodiments, the modified nucleobase is a modified adenine. Exemplary nucleobases and nucleosides having a modified adenine include 2-amino-purine, 2, 6-diaminopurine, 2-amino-6-halo-purine (e.g., 2-amino-6-chloro-purine), 6-halo-purine (e.g., 6-chloro-purine), 2-amino-6-methyl-purine, 8-azido-adenosine, 7-deaza-adenine, 7-deaza-8-aza-adenine, 7-deaza-2-amino-purine, 7-deaza-8-aza-2-amino-purine, 7-deaza-2,6-diaminopurine, 7-deaza-8-aza-2,6-diaminopurine, 1-methyl-adenosine (m^1A), 2-methyl-adenine (m^2A), N6-methyl-adenosine (m^6A), 2-methylthio-N6-methyl-adenosine (ms^2m^6A), N6-isopentenyl-adenosine (i^6A), 2-methylthio-N6-isopentenyl-adenosine (ms^2i^6A), N6-(cis-hydroxyisopentenyl)adenosine (io^6A), 2-methylthio-N6-(cis-hydroxyisopentenyl)adenosine (ms^2io^6A), N6-glycylcarbamoyl-adenosine (g^6A), N6-threonylcarbamoyl-adenosine (t^6A), N6-methyl-N6-threonylcarbamoyl-adenosine (m^6t^6A), 2-methylthio-N6-threonylcarbamoyl-adenosine (ms^2g^6A), N6,N6-dimethyl-adenosine (m^62A), N6-hydroxyisovalylcarbamoyl-adenosine (hn^6A), 2-methylthio-N6-hydroxyisovalylcarbamoyl-adenosine (ms^2hn^6A), N6-acetyl-adenosine (ac^6A), 7-methyl-adenine, 2-methylthio-adenine, 2-methoxy-adenine, α -thio-adenosine, 2'-O-methyl-adenosine (Am), N6,2'-O-dimethyl-adenosine (m^6Am), N6,N6,2'-O-trimethyl-adenosine (m^62Am), 1,2'-

O-dimethyl-adenosine (m¹Am), 2'-O-ribosyladenosine (phosphate) (Ar(p)), 2-amino-N6-methyl-purine, 1-thio-adenosine, 8-azido-adenosine, 2'-F-ara-adenosine, 2'-F-adenosine, 2'-Oll-ara-adenosine, and N6-(19-amino-penta-oxanodecyl)-adenosine.

[0335] In some embodiments, the modified nucleobase is a modified guanine. Exemplary nucleobases and nucleosides having a modified guanine include inosine (I), 1-methyl-inosine (m¹I), wyosine (imG), methylwyosine (mimG), 4-demethyl-wyosine (imG-14), isowyosine (imG2), wybutosine (yW), peroxywybutosine (o2yW), hydroxywybutosine (OhyW), undermodified hydroxywybutosine (OhyW*), 7-deaza-guanosine, queuosine (Q), epoxyqueuosine (oQ), galactosyl-queuosine (galQ), mannosyl-queuosine (manQ), 7-cyano-7-deaza-guanosine (preQ₆), 7-aminomethyl-7-deaza-guanosine (preQ₁), archaeosine (G⁺), 7-deaza-8-aza-guanosine, 6-thio-guanosine, 6-thio-7-deaza-guanosine, 6-thio-7-deaza-8-aza-guanosine, 7-methyl-guanosine (m⁷G), 6-thio-7-methyl-guanosine, 7-methyl-inosine, 6-methoxy-guanosine, 1-methyl-guanosine (m¹G), N2-methyl-guanosine (m²G), N2,N2-dimethyl-guanosine (m²₂G), N2,7-dimethyl-guanosine (m^{2,7}G), N2, N2,7-dimethyl-guanosine (m^{2,2,7}G), 8-oxo-guanosine, 7-methyl-8-oxo-guanosine, 1-methyl-6-thio-guanosine, N2-methyl-6-thio-guanosine, N2,N2-dimethyl-6-thio-guanosine, α-thio-guanosine, 2'-O-methyl-guanosine (Gm), N2-methyl-2'-O-methyl-guanosine (m²Gm), N2,N2-dimethyl-2'-O-methyl-guanosine (m²₂Gm), 1-methyl-2'-O-methyl-guanosine (m¹Gm), N2,7-dimethyl-2'-O-methyl-guanosine (m^{2,7}Gm), 2'-O-methyl-inosine (Im), 1,2'-O-dimethyl-inosine (m¹Im), 2'-O-ribosyl-guanosine (phosphate) (Gr(p)), 1-thio-guanosine, O6-methyl-guanosine, 2'-F-ara-guanosine, and 2'-I-guanosine.

N-Linked Glycosylation Site Mutants

[0336] N-linked glycans of viral proteins play important roles in modulating the immune response. Glycans can be important for maintaining the appropriate antigenic conformations, shielding potential neutralization epitopes, and may alter the proteolytic susceptibility of proteins. Some viruses have putative N-linked glycosylation sites. Deletion or modification of an N-linked glycosylation site may enhance the immune response. Thus, the present disclosure provides, in some embodiments, RNA (e.g., mRNA) vaccines comprising nucleic acids (e.g., mRNA) encoding antigenic polypeptides that comprise a deletion or modification at one or more N-linked glycosylation sites.

In Vitro Transcription of RNA (e.g., mRNA)

[0337] Respiratory virus vaccines of the present disclosure comprise at least one RNA polynucleotide, such as a mRNA (e.g., modified mRNA). mRNA, for example, is transcribed in vitro from template DNA, referred to as an "in vitro transcription template." In some embodiments, an in vitro transcription template encodes a 5' untranslated (UTR) region, contains an open reading frame, and encodes a 3' UTR and a polyA tail. The particular nucleic acid sequence composition and length of an in vitro transcription template will depend on the mRNA encoded by the template.

[0338] A "5' untranslated region" (5'UTR) refers to a region of an mRNA that is directly upstream (i.e., 5') from the start codon (i.e., the first codon of an mRNA transcript translated by a ribosome) that does not encode a polypeptide.

[0339] A "3' untranslated region" (3'UTR) refers to a region of an mRNA that is directly downstream (i.e., 3') from the stop codon (i.e., the codon of an mRNA transcript that signals a termination of translation) that does not encode a polypeptide.

[0340] An "open reading frame" is a continuous stretch of DNA beginning with a start codon (e.g., methionine (ATG)), and ending with a stop codon (e.g., TAA, TAG or TGA) and encodes a polypeptide. A "polyA tail" is a region of mRNA that is downstream, e.g., directly downstream (i.e., 3'), from the 3' UTR that contains multiple, consecutive adenosine monophosphates. A polyA tail may contain 10 to 300 adenosine monophosphates. For example, a polyA tail may contain 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290 or 300 adenosine monophosphates. In some embodiments, a polyA tail contains 50 to 250 adenosine monophosphates. In a relevant biological setting (e.g., in cells, in vivo) the poly(A) tail functions to protect mRNA from enzymatic degradation, e.g., in the cytoplasm, and aids in transcription termination, export of the mRNA from the nucleus and translation.

[0341] In some embodiments, a polynucleotide includes 200 to 3,000 nucleotides. For example, a polynucleotide may include 200 to 500, 200 to 1000, 200 to 1500, 200 to 3000, 500 to 1000, 500 to 1500, 500 to 2000, 500 to 3000, 1000 to 1500, 1000 to 2000, 1000 to 3000, 1500 to 3000, or 2000 to 3000 nucleotides.

Flagellin Adjuvants Flagellin is an approximately 500 amino acid monomeric protein that polymerizes to form the flagella associated with bacterial motion. Flagellin is expressed by a variety of flagellated bacteria (*Salmonella typhimurium* for example) as well as non-flagellated bacteria (such as *Escherichia coli*). Sensing of flagellin by cells of the innate immune system (dendritic cells, macrophages, etc.) is mediated by the Toll-like receptor 5 (TLRS) as well as by Nod-like receptors (NLRs) Ipaf and Naip5. TLRS and NLRs have been identified as playing a role in the activation of innate immune response and adaptive immune response. As such, flagellin provides an adjuvant effect in a vaccine.

[0342] The nucleotide and amino acid sequences encoding known flagellin polypeptides are publicly available in the NCBI GenBank database. The flagellin sequences from *S. Typhimurium*, *H. Pylori*, *V. Cholera*, *S. marcescens*, *S. flexneri*, *T. Pallidum*, *L. pneumophila*, *B. burgdorferi*, *C. difficile*, *R. meliloti*, *A. tumefaciens*, *R. lupini*, *B. claridgeiae*, *P. Mirabilis*, *B. subtilis*, *L. monocytogenes*, *P. aeruginosa*, and *E. coli*, among others are known.

[0343] A flagellin polypeptide, as used herein, refers to a full length flagellin protein, immunogenic fragments thereof, and peptides having at least 50% sequence identity to a flagellin protein or immunogenic fragments thereof. Exemplary flagellin proteins include flagellin from *Salmonella typhi* (UniProt Entry number: Q56086), *Salmonella typhimurium* (A0A0C9DG09), *Salmonella enteritidis* (A0A0C9BA137), and *Salmonella choleraesuis* (Q6V2X8), and SEQ ID NO: 54-56 (Table 17). In some embodiments, the flagellin polypeptide has at least 60%, 70%, 75%, 80%, 90%, 95%, 97%, 98%, or 99% sequence identity to a flagellin protein or immunogenic fragments thereof.

[0344] In some embodiments, the flagellin polypeptide is an immunogenic fragment. An immunogenic fragment is a portion of a flagellin protein that provokes an immune response. In some embodiments, the immune response is a

T1RS immune response. An example of an immunogenic fragment is a flagellin protein in which all or a portion of a hinge region has been deleted or replaced with other amino acids. For example, an antigenic polypeptide may be inserted in the hinge region. Hinge regions are the hyper-variable regions of a flagellin. Hinge regions of a flagellin are also referred to as “D3 domain or region,” “propeller domain or region,” “hypervariable domain or region” and “variable domain or region.” “At least a portion of a hinge region,” as used herein, refers to any part of the hinge region of the flagellin, or the entirety of the hinge region. In other embodiments an immunogenic fragment of flagellin is a 20, 25, 30, 35, or 40 amino acid C-terminal fragment of flagellin.

[0345] The flagellin monomer is formed by domains D0 through D3. D0 and D1, which form the stem, are composed of tandem long alpha helices and are highly conserved among different bacteria. The D1 domain includes several stretches of amino acids that are useful for T1RS activation. The entire D1 domain or one or more of the active regions within the domain are immunogenic fragments of flagellin. Examples of immunogenic regions within the D1 domain include residues 88-114 and residues 411-431 (in *Salmonella typhimurium* FljC flagellin. Within the 13 amino acids in the 88-100 region, at least 6 substitutions are permitted between *Salmonella* flagellin and other flagellins that still preserve T1RS activation. Thus, immunogenic fragments of flagellin include flagellin like sequences that activate T1RS and contain a 13 amino acid motif that is 53% or more identical to the *Salmonella* sequence in 88-100 of FljC (LQRVRIEAVQSAN; SEQ ID NO: 84).

[0346] In some embodiments, the RNA (e.g., mRNA) vaccine includes an RNA that encodes a fusion protein of flagellin and one or more antigenic polypeptides. A “fusion protein” as used herein, refers to a linking of two components of the construct. In some embodiments, a carboxy-terminus of the antigenic polypeptide is fused or linked to an amino terminus of the flagellin polypeptide. In other embodiments, an amino-terminus of the antigenic polypeptide is fused or linked to a carboxy-terminus of the flagellin polypeptide. The fusion protein may include, for example, one, two, three, four, five, six or more flagellin polypeptides linked to one, two, three, four, five, six or more antigenic polypeptides. When two or more flagellin polypeptides and/or two or more antigenic polypeptides are linked such a construct may be referred to as a “multimer.”

[0347] Each of the components of a fusion protein may be directly linked to one another or they may be connected through a linker. For instance, the linker may be an amino acid linker. The amino acid linker encoded for by the RNA (e.g., mRNA) vaccine to link the components of the fusion protein may include, for instance, at least one member selected from the group consisting of a lysine residue, a glutamic acid residue, a serine residue and an arginine residue. In some embodiments the linker is 1-30, 1-25, 1-25, 5-10, 5, 15, or 5-20 amino acids in length.

[0348] In other embodiments the RNA (e.g., mRNA) vaccine includes at least two separate RNA polynucleotides, one encoding one or more antigenic polypeptides and the other encoding the flagellin polypeptide. The at least two RNA polynucleotides may be co-formulated in a carrier such as a lipid nanoparticle.

Broad Spectrum RNA (e.g., mRNA) Vaccines

[0349] There may be situations where persons are at risk for infection with more than one strain of hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). RNA (e.g., mRNA) therapeutic vaccines are particularly amenable to combination vaccination approaches due to a number of factors including, but not limited to, speed of manufacture, ability to rapidly tailor vaccines to accommodate perceived geographical threat, and the like. Moreover, because the vaccines utilize the human body to produce the antigenic protein, the vaccines are amenable to the production of larger, more complex antigenic proteins, allowing for proper folding, surface expression, antigen presentation, etc. in the human subject. To protect against more than one strain of hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1), a combination vaccine can be administered that includes RNA (e.g., mRNA) encoding at least one antigenic polypeptide protein (or antigenic portion thereof) of a first respiratory virus and further includes RNA encoding at least one antigenic polypeptide protein (or antigenic portion thereof) of a second respiratory virus. RNA (e.g., mRNA) can be co-formulated, for example, in a single lipid nanoparticle (LNP) or can be formulated in separate LNPs for co-administration.

Methods of Treatment

[0350] Provided herein are compositions (e.g., pharmaceutical compositions), methods, kits and reagents for prevention and/or treatment of respiratory diseases/infections in humans and other mammals. Respiratory virus RNA (e.g., mRNA) vaccines can be used as therapeutic or prophylactic agents, alone or in combination with other vaccine(s). They may be used in medicine to prevent and/or treat respiratory disease/infection. In exemplary aspects, the RNA (e.g., mRNA) vaccines of the present disclosure are used to provide prophylactic protection from hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). Prophylactic protection from hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) can be achieved following administration of a RNA (e.g., mRNA) vaccine of the present disclosure. Respiratory virus RNA (e.g., mRNA) vaccines of the present disclosure may be used to treat or prevent viral “co-infections” containing two or more respiratory infections. Vaccines can be administered once, twice, three times, four times or more, but it is likely sufficient to administer the vaccine once (optionally followed by a single booster). It is possible, although less desirable, to administer the vaccine to an infected individual to achieve a therapeutic response. Dosing may need to be adjusted accordingly.

[0351] A method of eliciting an immune response in a subject against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) is provided in aspects of the present disclosure. The method involves administering to the subject a respiratory virus RNA (e.g., mRNA) vaccine comprising at least one RNA (e.g., mRNA) polynucleotide having an open reading

frame encoding at least one hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide thereof, thereby inducing in the subject an immune response specific to hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide or an immunogenic fragment thereof, wherein anti-antigenic polypeptide antibody titer in the subject is increased following vaccination relative to anti-antigenic polypeptide antibody titer in a subject vaccinated with a prophylactically effective dose of a traditional vaccine against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). An "anti-antigenic polypeptide antibody" is a serum antibody that binds specifically to the antigenic polypeptide.

[0352] In some embodiments, a RNA (e.g., mRNA) vaccine (e.g., a hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) RNA vaccine) capable of eliciting an immune response is administered intramuscularly via a composition including a compound according to Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIE) (e.g., Compound 3, 18, 20, 25, 26, 29, 30, 60, 108-112, or 122).

[0353] A prophylactically effective dose is a therapeutically effective dose that prevents infection with the virus at a clinically acceptable level. In some embodiments the therapeutically effective dose is a dose listed in a package insert for the vaccine. A traditional vaccine, as used herein, refers to a vaccine other than the RNA (e.g., mRNA) vaccines of the present disclosure. For instance, a traditional vaccine includes but is not limited to live/attenuated microorganism vaccines, killed/inactivated microorganism vaccines, subunit vaccines, protein antigen vaccines, DNA vaccines, VLP vaccines, etc. In exemplary embodiments, a traditional vaccine is a vaccine that has achieved regulatory approval and/or is registered by a national drug regulatory body, for example the Food and Drug Administration (FDA) in the United States or the European Medicines Agency (EMA).

[0354] In some embodiments the anti-antigenic polypeptide antibody titer in the subject is increased 1 log to 10 log following vaccination relative to anti-antigenic polypeptide antibody titer in a subject vaccinated with a prophylactically effective dose of a traditional vaccine against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1).

[0355] In some embodiments the anti-antigenic polypeptide antibody titer in the subject is increased 1 log, 2 log, 3 log, 5 log or 10 log following vaccination relative to anti-antigenic polypeptide antibody titer in a subject vaccinated with a prophylactically effective dose of a traditional vaccine against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1).

[0356] A method of eliciting an immune response in a subject against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-

HKU1) is provided in other aspects of the disclosure. The method involves administering to the subject a respiratory virus RNA (e.g., mRNA) vaccine comprising at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide or an immunogenic fragment thereof, thereby inducing in the subject an immune response specific to hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide or an immunogenic fragment thereof, wherein the immune response in the subject is equivalent to an immune response in a subject vaccinated with a traditional vaccine against the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) at 2 times to 100 times the dosage level relative to the RNA (e.g., mRNA) vaccine.

[0357] In some embodiments, the immune response in the subject is equivalent to an immune response in a subject vaccinated with a traditional vaccine at 2, 3, 4, 5, 10, 50, 100 times the dosage level relative to the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) RNA (e.g., mRNA) vaccine.

[0358] In some embodiments the immune response in the subject is equivalent to an immune response in a subject vaccinated with a traditional vaccine at 10-100 times, or 100-1000 times, the dosage level relative to the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) RNA (e.g., mRNA) vaccine.

[0359] In some embodiments the immune response is assessed by determining [protein] antibody titer in the subject.

[0360] Some aspects of the present disclosure provide a method of eliciting an immune response in a subject against a In some embodiments the immune response in the subject is equivalent to an immune response in a subject vaccinated with a traditional vaccine at 2, 3, 4, 5, 10, 50, 100 times the dosage level relative to the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) RNA (e.g., mRNA) vaccine by administering to the subject a respiratory virus RNA (e.g., mRNA) vaccine comprising at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide, thereby inducing in the subject an immune response specific to the antigenic polypeptide or an immunogenic fragment thereof, wherein the immune response in the subject is induced 2 days to 10 weeks earlier relative to an immune response induced in a subject vaccinated with a prophylactically effective dose of a traditional vaccine against the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or

HCov-11KU1). In some embodiments, the immune response in the subject is induced in a subject vaccinated with a prophylactically effective dose of a traditional vaccine at 2 times to 100 times the dosage level relative to the RNA (e.g., mRNA) vaccine.

[0361] In some embodiments, the immune response in the subject is induced 2 days earlier, or 3 days earlier, relative to an immune response induced in a subject vaccinated with a prophylactically effective dose of a traditional vaccine.

[0362] In some embodiments the immune response in the subject is induced 1 week, 2 weeks, 3 weeks, 5 weeks, or 10 weeks earlier relative to an immune response induced in a subject vaccinated with a prophylactically effective dose of a traditional vaccine.

[0363] Also provided herein is a method of eliciting an immune response in a subject against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCov-OC43, HCov-229E, HCov-NL63, HCov-NL, HCov-NH and/or HCov-11KU1) by administering to the subject a respiratory virus RNA (e.g., mRNA) vaccine having an open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide does not include a stabilization element, and wherein an adjuvant is not co-formulated or co-administered with the vaccine.

Therapeutic and Prophylactic Compositions

[0364] Provided herein are compositions (e.g., pharmaceutical compositions), methods, kits and reagents for prevention, treatment or diagnosis of hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCov-OC43, HCov-229E, HCov-NL63, HCov-NL, HCov-NH and/or HCov-11KU1) in humans and other mammals, for example. Respiratory virus RNA (e.g., mRNA) vaccines can be used as therapeutic or prophylactic agents. They may be used in medicine to prevent and/or treat infectious disease. In some embodiments, the respiratory RNA (e.g., mRNA) vaccines of the present disclosure are used for the priming of immune effector cells, for example, to activate peripheral blood mononuclear cells (PBMCs) *ex vivo*, which are then infused (re-infused) into a subject.

[0365] In some embodiments, respiratory virus vaccine containing RNA (e.g., mRNA) polynucleotides as described herein can be administered to a subject (e.g., a mammalian subject, such as a human subject), and the RNA (e.g., mRNA) polynucleotides are translated *in vivo* to produce an antigenic polypeptide.

[0366] The respiratory virus RNA (e.g., mRNA) vaccines may be induced for translation of a polypeptide (e.g., antigen or immunogen) in a cell, tissue or organism. In some embodiments, such translation occurs *in vivo*, although such translation may occur *ex vivo*, in culture or *in vitro*. In some embodiments, the cell, tissue or organism is contacted with an effective amount of a composition containing a respiratory virus RNA (e.g., mRNA) vaccine that contains a polynucleotide that has at least one a translatable region encoding an antigenic polypeptide.

[0367] An "effective amount" of an respiratory virus RNA (e.g., mRNA) vaccine is provided based, at least in part, on the target tissue, target cell type, means of administration, physical characteristics of the polynucleotide (e.g., size, and extent of modified nucleosides) and other components of the vaccine, and other determinants. In general, an effective amount of the respiratory virus RNA (e.g., mRNA) vaccine composition provides an induced or boosted immune

response as a function of antigen production in the cell, preferably more efficient than a composition containing a corresponding unmodified polynucleotide encoding the same antigen or a peptide antigen. Increased antigen production may be demonstrated by increased cell transfection (the percentage of cells transfected with the RNA, e.g., mRNA, vaccine), increased protein translation from the polynucleotide, decreased nucleic acid degradation (as demonstrated, for example, by increased duration of protein translation from a modified polynucleotide), or altered antigen specific immune response of the host cell.

[0368] In some embodiments, RNA (e.g., mRNA) vaccines (including polynucleotides their encoded polypeptides) in accordance with the present disclosure may be used for treatment of hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCov-OC43, HCov-229E, HCov-NL63, HCov-NL, HCov-NH and/or HCov-11KU1).

[0369] Respiratory RNA (e.g., mRNA) vaccines may be administered prophylactically or therapeutically as part of an active immunization scheme to healthy individuals or early in infection during the incubation phase or during active infection after onset of symptoms. In some embodiments, the amount of RNA (e.g., mRNA) vaccine of the present disclosure provided to a cell, a tissue or a subject may be an amount effective for immune prophylaxis.

[0370] Respiratory virus RNA (e.g., mRNA) vaccines may be administered with other prophylactic or therapeutic compounds. As a non-limiting example, a prophylactic or therapeutic compound may be an adjuvant or a booster. As used herein, when referring to a prophylactic composition, such as a vaccine, the term "booster" refers to an extra administration of the prophylactic (vaccine) composition. A booster (or booster vaccine) may be given after an earlier administration of the prophylactic composition. The time of administration between the initial administration of the prophylactic composition and the booster may be, but is not limited to, 1 minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes, 6 minutes, 7 minutes, 8 minutes, 9 minutes, 10 minutes, 15 minutes, 20 minutes, 35 minutes, 40 minutes, 45 minutes, 50 minutes, 55 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 7 hours, 8 hours, 9 hours, 10 hours, 11 hours, 12 hours, 13 hours, 14 hours, 15 hours, 16 hours, 17 hours, 18 hours, 19 hours, 20 hours, 21 hours, 22 hours, 23 hours, 1 day, 36 hours, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 10 days, 2 weeks, 3 weeks, 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 1 year, 18 months, 2 years, 3 years, 4 years, 5 years, 6 years, 7 years, 8 years, 9 years, 10 years, 11 years, 12 years, 13 years, 14 years, 15 years, 16 years, 17 years, 18 years, 19 years, 20 years, 25 years, 30 years, 35 years, 40 years, 45 years, 50 years, 55 years, 60 years, 65 years, 70 years, 75 years, 80 years, 85 years, 90 years, 95 years or more than 99 years. In some embodiments, the time of administration between the initial administration of the prophylactic composition and the booster may be, but is not limited to, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, 3 months, 6 months or 1 year.

[0371] In some embodiments, respiratory virus RNA (e.g., mRNA) vaccines may be administered intramuscularly or intradermally, similarly to the administration of inactivated vaccines known in the art.

[0372] Respiratory virus RNA (e.g., mRNA) vaccines may be utilized in various settings depending on the prevalence

of the infection or the degree or level of unmet medical need. As a non-limiting example, the RNA (e.g., mRNA) vaccines may be utilized to treat and/or prevent a variety of respiratory infections. RNA (e.g., mRNA) vaccines have superior properties in that they produce much larger antibody titers and produce responses early than commercially available anti-viral agents/compositions.

[0373] Provided herein are pharmaceutical compositions including respiratory virus RNA (e.g., mRNA) vaccines and RNA (e.g., mRNA) vaccine compositions and/or complexes optionally in combination with one or more pharmaceutically acceptable excipients.

[0374] Respiratory virus RNA (e.g., mRNA) vaccines may be formulated or administered alone or in conjunction with one or more other components. For instance, hMPV/PIV3/RSV RNA (e.g., mRNA) vaccines (vaccine compositions) may comprise other components including, but not limited to, adjuvants.

[0375] In some embodiments, respiratory virus (e.g., mRNA) vaccines do not include an adjuvant (they are adjuvant free).

[0376] Respiratory virus RNA (e.g., mRNA) vaccines may be formulated or administered in combination with one or more pharmaceutically-acceptable excipients. In some embodiments, vaccine compositions comprise at least one additional active substances, such as, for example, a therapeutically-active substance, a prophylactically-active substance, or a combination of both. Vaccine compositions may be sterile, pyrogen-free or both sterile and pyrogen-free. General considerations in the formulation and/or manufacture of pharmaceutical agents, such as vaccine compositions, may be found, for example, in Remington: The Science and Practice of Pharmacy 21st ed., Lippincott Williams & Wilkins, 2005 (incorporated herein by reference in its entirety). In some embodiments, respiratory virus RNA (e.g., mRNA) vaccines are administered to humans, human patients or subjects. For the purposes of the present disclosure, the phrase "active ingredient" generally refers to the RNA (e.g., mRNA) vaccines or the polynucleotides contained therein, for example, RNA polynucleotides (e.g., mRNA polynucleotides) encoding antigenic polypeptides.

[0377] Formulations of the respiratory virus vaccine compositions described herein may be prepared by any method known or hereafter developed in the art of pharmacology. In general, such preparatory methods include the step of bringing the active ingredient (e.g., mRNA polynucleotide) into association with an excipient and/or one or more other accessory ingredients, and then, if necessary and/or desirable, dividing, shaping and/or packaging the product into a desired single- or multi-dose unit.

[0378] Relative amounts of the active ingredient, the pharmaceutically acceptable excipient, and/or any additional ingredients in a pharmaceutical composition in accordance with the disclosure will vary, depending upon the identity, size, and/or condition of the subject treated and further depending upon the route by which the composition is to be administered. By way of example, the composition may comprise between 0.1% and 100%, e.g., between 0.5 and 50%, between 1-30%, between 5-80%, at least 80% (w/w) active ingredient.

[0379] Respiratory virus RNA (e.g., mRNA) vaccines can be formulated using one or more excipients to: (1) increase stability; (2) increase cell transfection; (3) permit the sustained or delayed release (e.g., from a depot formulation);

(4) alter the biodistribution (e.g., target to specific tissues or cell types); (5) increase the translation of encoded protein in vivo; and/or (6) alter the release profile of encoded protein (antigen) in vivo. In addition to traditional excipients such as any and all solvents, dispersion media, diluents, or other liquid vehicles, dispersion or suspension aids, surface active agents, isotonic agents, thickening or emulsifying agents, preservatives, excipients can include, without limitation, lipidoids, liposomes, lipid nanoparticles, polymers, lipoplexes, core-shell nanoparticles, peptides, proteins, cells transfected with respiratory virus RNA (e.g., mRNA) vaccines (e.g., for transplantation into a subject), hyaluronidase, nanoparticle mimics and combinations thereof.

Stabilizing Elements

[0380] Naturally-occurring eukaryotic mRNA molecules have been found to contain stabilizing elements, including, but not limited to untranslated regions (UTR) at their 5'-end (5'UTR) and/or at their 3'-end (3'UTR), in addition to other structural features, such as a 5'-cap structure or a 3'-poly(A) tail. Both the 5'UTR and the 3'UTR are typically transcribed from the genomic DNA and are elements of the premature mRNA. Characteristic structural features of mature mRNA, such as the 5'-cap and the 3'-poly(A) tail are usually added to the transcribed (premature) mRNA during mRNA processing. The 3'-poly(A) tail is typically a stretch of adenine nucleotides added to the 3'-end of the transcribed mRNA. It can comprise up to about 400 adenine nucleotides. In some embodiments the length of the 3'-poly(A) tail may be an essential element with respect to the stability of the individual mRNA.

[0381] In some embodiments the RNA (e.g., mRNA) vaccine may include one or more stabilizing elements. Stabilizing elements may include for instance a histone stem-loop. A stem-loop binding protein (SLBP), a 32 kDa protein has been identified. It is associated with the histone stem-loop at the 3'-end of the histone messages in both the nucleus and the cytoplasm. Its expression level is regulated by the cell cycle; it peaks during the S-phase, when histone mRNA levels are also elevated. The protein has been shown to be essential for efficient 3'-end processing of histone pre-mRNA by the U7 snRNP. SLBP continues to be associated with the stem-loop after processing, and then stimulates the translation of mature histone mRNAs into histone proteins in the cytoplasm. The RNA binding domain of SLBP is conserved through metazoa and protozoa; its binding to the histone stem-loop depends on the structure of the loop. The minimum binding site includes at least three nucleotides 5' and two nucleotides 3' relative to the stem-loop.

[0382] In some embodiments, the RNA (e.g., mRNA) vaccines include a coding region, at least one histone stem-loop, and optionally, a poly(A) sequence or polyadenylation signal. The poly(A) sequence or polyadenylation signal generally should enhance the expression level of the encoded protein. The encoded protein, in some embodiments, is not a histone protein, a reporter protein (e.g., Luciferase, GFP, EGFP, β -Galactosidase, EGFP), or a marker or selection protein (e.g., alpha-Globin, Galactokinase and Xanthine:guanine phosphoribosyl transferase (GPt)).

[0383] In some embodiments, the combination of a poly (A) sequence or polyadenylation signal and at least one histone stem-loop, even though both represent alternative

mechanisms in nature, acts synergistically to increase the protein expression beyond the level observed with either of the individual elements. It has been found that the synergistic effect of the combination of poly(A) and at least one histone stem-loop does not depend on the order of the elements or the length of the poly(A) sequence.

[0384] In some embodiments, the RNA (e.g., mRNA) vaccine does not comprise a histone downstream element (HDE). "Histone downstream element" (HDE) includes a purine-rich polynucleotide stretch of approximately 15 to 20 nucleotides 3' of naturally occurring stem-loops, representing the binding site for the U7 snRNA, which is involved in processing of histone pre-mRNA into mature histone mRNA. Ideally, the inventive nucleic acid does not include an intron.

[0385] In some embodiments, the RNA (e.g., mRNA) vaccine may or may not contain an enhancer and/or promoter sequence, which may be modified or unmodified or which may be activated or inactivated. In some embodiments, the histone stem-loop is generally derived from histone genes, and includes an intramolecular base pairing of two neighboring partially or entirely reverse complementary sequences separated by a spacer, including (e.g., consisting of) a short sequence, which forms the loop of the structure. The unpaired loop region is typically unable to base pair with either of the stem loop elements. It occurs more often in RNA, as is a key component of many RNA secondary structures, but may be present in single-stranded DNA as well. Stability of the stem-loop structure generally depends on the length, number of mismatches or bulges, and base composition of the paired region. In some embodiments, wobble base pairing (non-Watson-Crick base pairing) may result. In some embodiments, the at least one histone stem-loop sequence comprises a length of 15 to 45 nucleotides.

[0386] In other embodiments the RNA (e.g., mRNA) vaccine may have one or more AU-rich sequences removed. These sequences, sometimes referred to as AURES are destabilizing sequences found in the 3'UTR. The AURES may be removed from the RNA (e.g., mRNA) vaccines. Alternatively the AURES may remain in the RNA (e.g., mRNA) vaccine.

Nanoparticle Formulations In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines are formulated in a nanoparticle. In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines are formulated in a lipid nanoparticle. In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines are formulated in a lipid-polycation complex, referred to as a cationic lipid nanoparticle. As a non-limiting example, the polycation may include a cationic peptide or a polypeptide such as, but not limited to, polylysine, polyornithine and/or polyarginine. In some embodiments, respiratory virus RNA (e.g., mRNA) vaccines are formulated in a lipid nanoparticle that includes a non-cationic lipid such as, but not limited to, cholesterol or dioleoyl phosphatidylethanolamine (DOPE).

[0387] A lipid nanoparticle formulation may be influenced by, but not limited to, the selection of the cationic lipid component, the degree of cationic lipid saturation, the nature of the PEGylation, ratio of all components and biophysical parameters such as size. In one example by Semple et al. (*Nature Biotech.* 2010 28:172-176), the lipid nanoparticle formulation is composed of 57.1% cationic lipid, 7.1% dipalmitoylphosphatidylcholine, 34.3% cholesterol, and 1.4% PEG-c-DMA. As another example, changing the com-

position of the cationic lipid can more effectively deliver siRNA to various antigen presenting cells (Basha et al. *Mol Ther.* 2011 19:2186-2200).

[0388] In some embodiments, lipid nanoparticle formulations may comprise 35 to 45% cationic lipid, 40% to 50% cationic lipid, 50% to 60% cationic lipid and/or 55% to 65% cationic lipid. In some embodiments, the ratio of lipid to RNA (e.g., mRNA) in lipid nanoparticles may be 5:1 to 20:1, 10:1 to 25:1, 15:1 to 30:1 and/or at least 30:1.

[0389] In some embodiments, the ratio of PEG in the lipid nanoparticle formulations may be increased or decreased and/or the carbon chain length of the PEG lipid may be modified from C14 to C18 to alter the pharmacokinetics and/or biodistribution of the lipid nanoparticle formulations. As a non-limiting example, lipid nanoparticle formulations may contain 0.5% to 3.0%, 1.0% to 3.5%, 1.5% to 4.0%, 2.0% to 4.5%, 2.5% to 5.0% and/or 3.0% to 6.0% of the lipid molar ratio of PEG-c-DOMG (R-3-Rw-methoxy-poly(ethyleneglycol)2000carbamoyl)-1,2-dimyristyloxypropyl-3-amine) (also referred to herein as PEG-DOMG) as compared to the cationic lipid, DSPC and cholesterol. In some embodiments, the PEG-c-DOMG may be replaced with a PEG lipid such as, but not limited to, PEG-DSG (1,2-Distearoyl-sn-glycerol, methoxypolyethylene glycol), PEG-DMG (1,2-Dimyristoyl-sn-glycerol) and/or PEG-DPG (1,2-Dipalmitoyl-sn-glycerol, methoxypolyethylene glycol). The cationic lipid may be selected from any lipid known in the art such as, but not limited to, DLin-MC3-DMA, DLin-DMA, C12-200 and DLin-KC2-DMA.

[0390] In some embodiments, an respiratory virus RNA (e.g. mRNA) vaccine formulation is a nanoparticle that comprises at least one lipid. The lipid may be selected from, but is not limited to, DLin-DMA, DLin-K-DMA, 98N12-5, C12-200, DLin-MC3-DMA, DLin-KC2-DMA, DODMA, PLGA, PEG, PEG-DMG, PEGylated lipids and amino alcohol lipids. In some embodiments, the lipid may be a cationic lipid such as, but not limited to, DLin-DMA, DLin-D-DMA, DLin-MC3-DMA, DLin-KC2-DMA, DODMA and amino alcohol lipids. The amino alcohol cationic lipid may be the lipids described in and/or made by the methods described in U.S. Patent Publication No. US20130150625, herein incorporated by reference in its entirety. As a non-limiting example, the cationic lipid may be 2-amino-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-2-[[[(9Z,2Z)-octadeca-9,12-dien-1-yloxy]methyl]propan-1-ol (Compound 1 in US20130150625); 2-amino-3-[(9Z)-octadec-9-en-1-yloxy]-2-[[[(9Z)-octadec-9-en-1-yloxy]methyl]propan-1-ol (Compound 2 in US20130150625); 2-amino-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-2-[(octyloxy)methyl]propan-1-ol (Compound 3 in US20130150625); and 2-(dimethylamino)-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-2-[[[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]methyl]propan-1-ol (Compound 4 in US20130150625); or any pharmaceutically acceptable salt or stereoisomer thereof.

[0391] Lipid nanoparticle formulations typically comprise a lipid, in particular, an ionizable cationic lipid, for example, 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), or di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), and further comprise a neutral lipid, a sterol and a molecule capable of reducing particle aggregation, for example a PEG or PEG-modified lipid.

[0392] In some embodiments, a lipid nanoparticle formulation consists essentially of (i) at least one lipid selected from the group consisting of 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DL.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DL.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (1.319); (ii) a neutral lipid selected from DSPC, DPPC, POPC, DOPC and SM; (iii) a sterol, e.g., cholesterol; and (iv) a PEG-lipid, e.g., PEG-DMG or PEG-cDMA, in a molar ratio of 20-60% cationic lipid: 5-25% neutral lipid: 25-55% sterol: 0.5-15% PEG-lipid.

[0393] In some embodiments, a lipid nanoparticle formulation includes 25% to 75% on a molar basis of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DL.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DL.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (1.319), e.g., 35 to 65%, 45 to 65%, 60%, 57.5%, 50% or 40% on a molar basis.

[0394] In some embodiments, a lipid nanoparticle formulation includes 0.5% to 15% on a molar basis of the neutral lipid, e.g., 3 to 12%, 5 to 10% or 15%, 10%, or 7.5% on a molar basis. Examples of neutral lipids include, without limitation, DSPC, POPC, DPPC, DOPC and SM. In some embodiments, the formulation includes 5% to 50% on a molar basis of the sterol (e.g., 15 to 45%, 20 to 40%, 40%, 38.5%, 35%, or 31% on a molar basis. A non-limiting example of a sterol is cholesterol. In some embodiments, a lipid nanoparticle formulation includes 0.5% to 20% on a molar basis of the PEG or PEG-modified lipid (e.g., 0.5 to 10%, 0.5 to 5%, 1.5%, 0.5%, 1.5%, 3.5%, or 5% on a molar basis. In some embodiments, a PEG or PEG modified lipid comprises a PEG molecule of an average molecular weight of 2,000 Da. In some embodiments, a PEG or PEG modified lipid comprises a PEG molecule of an average molecular weight of less than 2,000, for example around 1,500 Da, around 1,000 Da, or around 500 Da. Non-limiting examples of PEG-modified lipids include PEG-distearoyl glycerol (PEG-DMG) (also referred herein as PEG-C14 or C14-PEG), PEG-cDMA (further discussed in Reyes et al. J. Controlled Release, 107, 276-287 (2005) the contents of which are herein incorporated by reference in their entirety).

[0395] In some embodiments, lipid nanoparticle formulations include 25-75% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DL.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DL.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (1.319), 0.5-15% of the neutral lipid, 5-50% of the sterol, and 0.5-20% of the PEG or PEG-modified lipid on a molar basis.

[0396] In some embodiments, lipid nanoparticle formulations include 35-65% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DL.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DL.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (1.319), 3-12% of the neutral lipid, 15-45% of the sterol, and 0.5-10% of the PEG or PEG-modified lipid on a molar basis.

[0397] In some embodiments, lipid nanoparticle formulations include 45-65% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DL.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DL.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (1.319),

5-10% of the neutral lipid, 25-40% of the sterol, and 0.5-10% of the PEG or PEG-modified lipid on a molar basis.

[0398] In some embodiments, lipid nanoparticle formulations include 60% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DL.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DL.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (1.319), 7.5% of the neutral lipid, 31% of the sterol, and 1.5% of the PEG or PEG-modified lipid on a molar basis.

[0399] In some embodiments, lipid nanoparticle formulations include 50% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DL.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DL.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (1.319), 10% of the neutral lipid, 38.5% of the sterol, and 1.5% of the PEG or PEG-modified lipid on a molar basis.

[0400] In some embodiments, lipid nanoparticle formulations include 50% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DL.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DL.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (1.319), 10% of the neutral lipid, 35% of the sterol, 4.5% or 5% of the PEG or PEG-modified lipid, and 0.5% of the targeting lipid on a molar basis.

[0401] In some embodiments, lipid nanoparticle formulations include 40% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DL.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DL.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (1.319), 15% of the neutral lipid, 40% of the sterol, and 5% of the PEG or PEG-modified lipid on a molar basis.

[0402] In some embodiments, lipid nanoparticle formulations include 57.2% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DL.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DL.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (1.319), 7.1% of the neutral lipid, 34.3% of the sterol, and 1.4% of the PEG or PEG-modified lipid on a molar basis.

[0403] In some embodiments, lipid nanoparticle formulations include 57.5% of a cationic lipid selected from the PEG lipid is PEG-cDMA (PEG-cDMA is further discussed in Reyes et al. J. Controlled Release, 107, 276-287 (2005), the contents of which are herein incorporated by reference in their entirety), 7.5% of the neutral lipid, 31.5% of the sterol, and 3.5% of the PEG or PEG-modified lipid on a molar basis.

[0404] In some embodiments, lipid nanoparticle formulations consists essentially of a lipid mixture in molar ratios of 20-70% cationic lipid: 5-45% neutral lipid: 20-55% cholesterol: 0.5-15% PEG-modified lipid. In some embodiments, lipid nanoparticle formulations consists essentially of a lipid mixture in a molar ratio of 20-60% cationic lipid: 5-25% neutral lipid: 25-55% cholesterol: 0.5-15% PEG-modified lipid.

[0405] In some embodiments, the molar lipid ratio is 50/10/38.5/1.5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG, PEG-DSPC or PEG-DPPC), 57.2/7.1/34.3/1.4 (mol % cationic lipid/neutral lipid, e.g., DPPC/Chol/PEG-modified lipid,

e.g., PE:G-cDMA), 40/15/40/5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PE:G-modified lipid, e.g., PE:G-DMG), 50/10/35/4.5/0.5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PE:G-modified lipid, e.g., PE:G-DMG), 50/10/35/5 (cationic lipid/neutral lipid, e.g., DSPC/Chol/PE:G-modified lipid, e.g., PE:G-DMG), 40/10/40/10 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PE:G-modified lipid, e.g., PE:G-DMG or PE:G-cDMA), 35/15/40/10 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PE:G-modified lipid, e.g., PE:G-DMG or PE:G-cDMA) or 52/13/30/5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PE:G-modified lipid, e.g., PE:G-DMG or PE:G-cDMA).

[0406] Non-limiting examples of lipid nanoparticle compositions and methods of making them are described, for example, in Semple et al. (2010) *Nat. Biotechnol.* 28:172-176; Jayarama et al. (2012), *Angew. Chem. Int. Ed.*, S1: 8529-8533; and Maier et al. (2013) *Molecular Therapy* 21, 1570-1578 (the contents of each of which are incorporated herein by reference in their entirety).

[0407] In some embodiments, lipid nanoparticle formulations may comprise a cationic lipid, a PE:G lipid and a structural lipid and optionally comprise a non-cationic lipid. As a non-limiting example, a lipid nanoparticle may comprise 40-60% of cationic lipid, 5-15% of a non-cationic lipid, 1-2% of a PE:G lipid and 30-50% of a structural lipid. As another non-limiting example, the lipid nanoparticle may comprise 50% cationic lipid, 10% non-cationic lipid, 1.5% PE:G lipid and 38.5% structural lipid. As yet another non-limiting example, a lipid nanoparticle may comprise 55% cationic lipid, 10% non-cationic lipid, 2.5% PE:G lipid and 32.5% structural lipid. In some embodiments, the cationic lipid may be any cationic lipid described herein such as, but not limited to, DLin-KC2-DMA, DLin-MC3-DMA and I.319.

[0408] In some embodiments, the lipid nanoparticle formulations described herein may be 4 component lipid nanoparticles. The lipid nanoparticle may comprise a cationic lipid, a non-cationic lipid, a PE:G lipid and a structural lipid. As a non-limiting example, the lipid nanoparticle may comprise 40-60% of cationic lipid, 5-15% of a non-cationic lipid, 1-2% of a PE:G lipid and 30-50% of a structural lipid. As another non-limiting example, the lipid nanoparticle may comprise 50% cationic lipid, 10% non-cationic lipid, 1.5% PE:G lipid and 38.5% structural lipid. As yet another non-limiting example, the lipid nanoparticle may comprise 55% cationic lipid, 10% non-cationic lipid, 2.5% PE:G lipid and 32.5% structural lipid. In some embodiments, the cationic lipid may be any cationic lipid described herein such as, but not limited to, DLin-KC2-DMA, DLin-MC3-DMA and I.319.

[0409] In some embodiments, the lipid nanoparticle formulations described herein may comprise a cationic lipid, a non-cationic lipid, a PE:G lipid and a structural lipid. As a non-limiting example, the lipid nanoparticle comprise 50% of the cationic lipid DLin-KC2-DMA, 10% of the non-cationic lipid DSPC, 1.5% of the PE:G lipid PE:G-DMG and 38.5% of the structural lipid cholesterol. As a non-limiting example, the lipid nanoparticle comprise 50% of the cationic lipid DLin-MC3-DMA, 10% of the non-cationic lipid DSPC, 1.5% of the PE:G lipid PE:G-DMG and 38.5% of the

structural lipid cholesterol. As yet another non-limiting example, the lipid nanoparticle comprise 55% of the cationic lipid I.319, 10% of the non-cationic lipid DSPC, 2.5% of the PE:G lipid PE:G-DMG and 32.5% of the structural lipid cholesterol.

[0410] Relative amounts of the active ingredient, the pharmaceutically acceptable excipient, and/or any additional ingredients in a vaccine composition may vary, depending upon the identity, size, and/or condition of the subject being treated and further depending upon the route by which the composition is to be administered. For example, the composition may comprise between 0.1% and 99% (w/w) of the active ingredient. By way of example, the composition may comprise between 0.1% and 100%, e.g., between 0.5 and 50%, between 1-30%, between 5-80%, at least 80% (w/w) active ingredient.

[0411] In some embodiments, the respiratory virus RNA (e.g. mRNA) vaccine composition may comprise the polynucleotide described herein, formulated in a lipid nanoparticle comprising MC3, Cholesterol, DSPC and PE:G2000-DMG, the buffer trisodium citrate, sucrose and water for injection. As a non-limiting example, the composition comprises: 2.0 mg/ml. of drug substance (e.g., polynucleotides encoding H10N8 hMPV), 21.8 mg/ml. of MC3, 10.1 mg/ml. of cholesterol, 5.4 mg/ml. of DSPC, 2.7 mg/ml. of PE:G2000-DMG, 5.16 mg/ml. of trisodium citrate, 71 mg/ml. of sucrose and 1.0 ml. of water for injection.

[0412] In some embodiments, a nanoparticle (e.g., a lipid nanoparticle) has a mean diameter of 10-500 nm, 20-400 nm, 30-300 nm, 40-200 nm. In some embodiments, a nanoparticle (e.g., a lipid nanoparticle) has a mean diameter of 50-150 nm, 50-200 nm, 80-100 nm or 80-200 nm.

Liposomes, Lipoplexes, and Lipid Nanoparticles

[0413] The RNA (e.g., mRNA) vaccines of the disclosure can be formulated using one or more liposomes, lipoplexes, or lipid nanoparticles. In some embodiments, pharmaceutical compositions of RNA (e.g., mRNA) vaccines include liposomes. Liposomes are artificially-prepared vesicles which may primarily be composed of a lipid bilayer and may be used as a delivery vehicle for the administration of nutrients and pharmaceutical formulations. Liposomes can be of different sizes such as, but not limited to, a multilamellar vesicle (MLV) which may be hundreds of nanometers in diameter and may contain a series of concentric bilayers separated by narrow aqueous compartments, a small unilamellar vesicle (SUV) which may be smaller than 50 nm in diameter, and a large unilamellar vesicle (LUV) which may be between 50 and 500 nm in diameter. Liposome design may include, but is not limited to, opsonins or ligands in order to improve the attachment of liposomes to unhealthy tissue or to activate events such as, but not limited to, endocytosis. Liposomes may contain a low or a high pH in order to improve the delivery of the pharmaceutical formulations.

[0414] The formation of liposomes may depend on the physicochemical characteristics such as, but not limited to, the pharmaceutical formulation entrapped and the liposomal ingredients, the nature of the medium in which the lipid vesicles are dispersed, the effective concentration of the entrapped substance and its potential toxicity, any additional processes involved during the application and/or delivery of the vesicles, the optimization size, polydispersity and the shelf-life of the vesicles for the intended application, and the

batch-to-batch reproducibility and possibility of large-scale production of safe and efficient liposomal products.

[0415] In some embodiments, pharmaceutical compositions described herein may include, without limitation, liposomes such as those formed from 1,2-dioleoyloxy-N,N-dimethylaminopropane (DODMA) liposomes, DL α 2 liposomes from Marina Biotech (Bothell, Wash.), 1,2-dilinoleyloxy-3-dimethylaminopropane (DLin-DMA), 2,2-dilinoleyloxy-4-(2-dimethylaminoethyl)-[1,3]-dioxolane (DLin-KC2-DMA), and MC3 (US20100324120; herein incorporated by reference in its entirety) and liposomes which may deliver small molecule drugs such as, but not limited to, DOXIL $\text{\textcircled{R}}$ from Janssen Biotech, Inc. (Horsham, Pa.).

[0416] In some embodiments, pharmaceutical compositions described herein may include, without limitation, liposomes such as those formed from the synthesis of stabilized plasmid-lipid particles (SPLP) or stabilized nucleic acid lipid particle (SNALP) that have been previously described and shown to be suitable for oligonucleotide delivery in vitro and in vivo (see Wheeler et al. *Gene Therapy*, 1999 6:271-281; Zhang et al. *Gene Therapy*, 1999 6:1438-1447; Jeffs et al. *Pharm Res*, 2005 22:362-372; Morrissey et al., *Nat Biotechnol*, 2005 2:1002-1007; Zimmermann et al., *Nature*, 2006 441:111-114; Heyes et al. *J Contr Rel*, 2005 107:276-287; Semple et al. *Nature Biotech*, 2010 28:172-176; Judge et al. *J Clin Invest*, 2009 119:661-673; deFougerolles Hum *Gene Ther*, 2008 19:125-132; U.S. Patent Publication No US20130122104; all of which are incorporated herein in their entireties). The original manufacture method by Wheeler et al. was a detergent dialysis method, which was later improved by Jeffs et al. and is referred to as the spontaneous vesicle formation method. The liposome formulations are composed of 3 to 4 lipid components in addition to the polynucleotide. As an example a liposome can contain, but is not limited to, 55% cholesterol, 20% distearylphosphatidyl choline (DSPC), 10% PEG-S-DSG, and 15% 1,2-dioleoyloxy-N,N-dimethylaminopropane (DODMA), as described by Jeffs et al. As another example, certain liposome formulations may contain, but are not limited to, 48% cholesterol, 20% DSPC, 2% PE:G-c-DMA, and 30% cationic lipid, where the cationic lipid can be 1,2-distearoyloxy-N,N-dimethylaminopropane (DSDMA), DODMA, DLin-DMA, or 1,2-dilinoleyloxy-3-dimethylaminopropane (DLinDMA), as described by Heyes et al.

[0417] In some embodiments, liposome formulations may comprise from about 25.0% cholesterol to about 40.0% cholesterol, from about 30.0% cholesterol to about 45.0% cholesterol, from about 35.0% cholesterol to about 50.0% cholesterol and/or from about 48.5% cholesterol to about 60% cholesterol. In some embodiments, formulations may comprise a percentage of cholesterol selected from the group consisting of 28.5%, 31.5%, 33.5%, 36.5%, 37.0%, 38.5%, 39.0% and 43.5%. In some embodiments, formulations may comprise from about 5.0% to about 10.0% DSPC and/or from about 7.0% to about 15.0% DSPC.

[0418] In some embodiments, the RNA (e.g., mRNA) vaccine pharmaceutical compositions may be formulated in liposomes such as, but not limited to, DL α 2 liposomes (Marina Biotech, Bothell, Wash.), SMARTICLES $\text{\textcircled{R}}$ (Marina Biotech, Bothell, Wash.), neutral DOPC (1,2-dioleoyl-sn-glycero-3-phosphocholine) based liposomes (e.g., siRNA delivery for ovarian cancer (Landen et al. *Cancer Biology &*

Therapy 2006 5(12)1708-1713); herein incorporated by reference in its entirety) and hyaluronan-coated liposomes (Quiet Therapeutics, Israel).

[0419] In some embodiments, the cationic lipid may be a low molecular weight cationic lipid such as those described in U.S. Patent Application No. 20130090372, the contents of which are herein incorporated by reference in their entirety.

[0420] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid vesicle, which may have crosslinks between functionalized lipid bilayers.

[0421] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid-polycation complex. The formation of the lipid-polycation complex may be accomplished by methods known in the art and/or as described in U.S. Pub. No. 20120178702, herein incorporated by reference in its entirety. As a non-limiting example, the polycation may include a cationic peptide or a polypeptide such as, but not limited to, polylysine, polyornithine and/or polyarginine. In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid-polycation complex, which may further include a non-cationic lipid such as, but not limited to, cholesterol or dioleoyl phosphatidylethanolamine (DOPE).

[0422] In some embodiments, the ratio of PE:G in the lipid nanoparticle (LNP) formulations may be increased or decreased and/or the carbon chain length of the PE:G lipid may be modified from C14 to C18 to alter the pharmacokinetics and/or biodistribution of the LNP formulations. As a non-limiting example, LNP formulations may contain from about 0.5% to about 3.0%, from about 1.0% to about 3.5%, from about 1.5% to about 4.0%, from about 2.0% to about 4.5%, from about 2.5% to about 5.0% and/or from about 3.0% to about 6.0% of the lipid molar ratio of PE:G-c-DOMG (R-3-[(w-methoxy-poly(ethyleneglycol)2000)carbamoyl]1,2-dimyristyloxypropyl-3-amine) (also referred to herein as PE:G-DOMG) as compared to the cationic lipid, DSPC and cholesterol. In some embodiments, the PE:G-c-DOMG may be replaced with a PE:G lipid such as, but not limited to, PE:G-DSG (1,2-Distearoyl-sn-glycerol, methoxy-polyethylene glycol), PE:G-DMG (1,2-Dimyristoyl-sn-glycerol) and/or PE:G-DPG (1,2-Dipalmitoyl-sn-glycerol, methoxypolyethylene glycol). The cationic lipid may be selected from any lipid known in the art such as, but not limited to, DLin-MC3-DMA, DLin-DMA, C12-200 and DLin-KC2-DMA.

[0423] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid nanoparticle.

[0424] In some embodiments, the RNA (e.g., mRNA) vaccine formulation comprising the polynucleotide is a nanoparticle which may comprise at least one lipid. The lipid may be selected from, but is not limited to, DLin-DMA, DLin-K-DMA, 98N12-5, C12-200, DLin-MC3-DMA, DLin-KC2-DMA, DODMA, PE:GA, PE:G, PE:G-DMG, PE:Gylated lipids and amino alcohol lipids. In another aspect, the lipid may be a cationic lipid such as, but not limited to, DLin-DMA, DLin-D-DMA, DLin-MC3-DMA, DLin-KC2-DMA, DODMA and amino alcohol lipids. The amino alcohol cationic lipid may be the lipids described in and/or made by the methods described in U.S. Patent Publication No. US20130150625, herein incorporated by reference in its entirety. As a non-limiting example, the cationic lipid may be 2-amino-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-2-[[[(9Z,2Z)-octadeca-9,12-dien-1-yloxy]methyl]propan-1-ol (Compound 1 in US20130150625);

2-amino-3-[(9Z)-octadec-9-en-1-yloxy]-2-[(9Z)-octadec-9-en-1-yloxy]methyl]propan-1-ol (Compound 2 in US20130150625); 2-amino-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-2-[(octyloxy)methyl]propan-1-ol (Compound 3 in US20130150625); and 2-(dimethylamino)-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-2-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]methyl]propan-1-ol (Compound 4 in US20130150625); or any pharmaceutically acceptable salt or stereoisomer thereof.

[0425] Lipid nanoparticle formulations typically comprise a lipid, in particular, an ionizable cationic lipid, for example, 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DI.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DI.in-MC3-DMA), or di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (I.319), and further comprise a neutral lipid, a sterol and a molecule capable of reducing particle aggregation, for example a PEG or PEG-modified lipid.

[0426] In some embodiments, the lipid nanoparticle formulation consists essentially of (i) at least one lipid selected from the group consisting of 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DI.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DI.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (I.319); (ii) a neutral lipid selected from DSPC, DPPC, POPC, DOPC, and SM; (iii) a sterol, e.g., cholesterol; and (iv) a PEG-lipid, e.g., PEG-DMG or PEG-cDMA, in a molar ratio of about 20-60% cationic lipid; 5-25% neutral lipid; 25-55% sterol; 0.5-15% PEG-lipid.

[0427] In some embodiments, the formulation includes from about 25% to about 75% on a molar basis of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DI.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DI.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (I.319), e.g., from about 35 to about 65%, from about 45 to about 65%, about 60%, about 57.5%, about 50% or about 40% on a molar basis.

[0428] In some embodiments, the formulation includes from about 0.5% to about 15% on a molar basis of the neutral lipid e.g., from about 3 to about 12%, from about 5 to about 10% or about 15%, about 10%, or about 7.5% on a molar basis. Examples of neutral lipids include, but are not limited to, DSPC, POPC, DPPC, DOPC, and SM. In some embodiments, the formulation includes from about 5% to about 50% on a molar basis of the sterol (e.g., about 15 to about 45%, about 20 to about 40%, about 40%, about 38.5%, about 35%, or about 31% on a molar basis. An exemplary sterol is cholesterol. In some embodiments, the formulation includes from about 0.5% to about 20% on a molar basis of the PEG or PEG-modified lipid (e.g., about 0.5 to about 10%, about 0.5 to about 5%, about 1.5%, about 0.5%, about 1.5%, about 3.5%, or about 5% on a molar basis. In some embodiments, the PEG or PEG modified lipid comprises a PEG molecule of an average molecular weight of 2,000 Da. In other embodiments, the PEG or PEG modified lipid comprises a PEG molecule of an average molecular weight of less than 2,000, for example around 1,500 Da, around 1,000 Da, or around 500 Da. Examples of PEG-modified lipids include, but are not limited to, PEG-distearoyl glycerol (PEG-DMG) (also referred herein as PEG-C14 or C14-PEG), PEG-cDMA (further discussed in Reyes et al. *J. Controlled Release*, 107, 276-287 (2005) the contents of which are herein incorporated by reference in their entirety)

[0429] In some embodiments, the formulations of the present disclosure include 25-75% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DI.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DI.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (I.319), 0.5-15% of the neutral lipid, 5-50% of the sterol, and 0.5-20% of the PEG or PEG-modified lipid on a molar basis.

[0430] In some embodiments, the formulations of the present disclosure include 35-65% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DI.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DI.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (I.319), 3-12% of the neutral lipid, 15-45% of the sterol, and 0.5-10% of the PEG or PEG-modified lipid on a molar basis.

[0431] In some embodiments, the formulations of the present disclosure include 45-65% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DI.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DI.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (I.319), 5-10% of the neutral lipid, 25-40% of the sterol, and 0.5-10% of the PEG or PEG-modified lipid on a molar basis.

[0432] In some embodiments, the formulations of the present disclosure include about 60% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DI.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DI.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (I.319), about 7.5% of the neutral lipid, about 31% of the sterol, and about 1.5% of the PEG or PEG-modified lipid on a molar basis. In some embodiments, the formulations of the present disclosure include about 50% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DI.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DI.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (I.319), about 10% of the neutral lipid, about 38.5% of the sterol, and about 1.5% of the PEG or PEG-modified lipid on a molar basis.

[0433] In some embodiments, the formulations of the present disclosure include about 50% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DI.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DI.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (I.319), about 10% of the neutral lipid, about 35% of the sterol, about 4.5% or about 5% of the PEG or PEG-modified lipid, and about 0.5% of the targeting lipid on a molar basis.

[0434] In some embodiments, the formulations of the present disclosure include about 40% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DI.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DI.in-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (I.319), about 15% of the neutral lipid, about 40% of the sterol, and about 5% of the PEG or PEG-modified lipid on a molar basis.

[0435] In some embodiments, the formulations of the present disclosure include about 57.2% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DI.in-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DI.in-MC3-DMA), and di((Z)-non-2-en-1-

yl) 9-((4-(dimethylamino)butanoyloxy)heptadecanediolate (I.319), about 7.1% of the neutral lipid, about 34.3% of the sterol, and about 1.4% of the PEG or PEG-modified lipid on a molar basis.

[0436] In some embodiments, the formulations of the present disclosure include about 57.5% of a cationic lipid selected from the PEG lipid is PEG-cDMA (PEG-cDMA is further discussed in Reyes et al. (*J. Controlled Release*, 107, 276-287 (2005), the contents of which are herein incorporated by reference in their entirety), about 7.5% of the neutral lipid, about 31.5% of the sterol, and about 3.5% of the PEG or PEG-modified lipid on a molar basis.

[0437] In some embodiments, lipid nanoparticle formulation consists essentially of a lipid mixture in molar ratios of about 20-70% cationic lipid: 5-45% neutral lipid: 20-55% cholesterol: 0.5-15% PEG-modified lipid: more preferably in a molar ratio of about 20-60% cationic lipid: 5-25% neutral lipid: 25-55% cholesterol: 0.5-15% PEG-modified lipid.

[0438] In some embodiments, the molar lipid ratio is approximately 50/10/38.5/1.5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG, PEG-DSG or PEG-DPG), 57.2/7.1/34.3/1.4 (mol % cationic lipid/neutral lipid, e.g., DPPC/Chol/PEG-modified lipid, e.g., PEG-cDMA), 40/15/40/5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG), 50/10/35/4.5/0.5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DSG), 50/10/35/5 (cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG), 40/10/40/10 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA), 35/15/40/10 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA) or 52/13/30/5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA).

[0439] Examples of lipid nanoparticle compositions and methods of making same are described, for example, in Semple et al. (2010) *Nat. Biotechnol.* 28:172-176; Jayarama et al. (2012), *Angew. Chem. Int. Ed.*, 51: 8529-8533; and Maier et al. (2013) *Molecular Therapy* 21, 1570-1578 (the contents of each of which are incorporated herein by reference in their entirety).

[0440] In some embodiments, the lipid nanoparticle formulations described herein may comprise a cationic lipid, a PEG lipid and a structural lipid and optionally comprise a non-cationic lipid. As a non-limiting example, the lipid nanoparticle may comprise about 40-60% of cationic lipid, about 5-15% of a non-cationic lipid, about 1-2% of a PEG lipid and about 30-50% of a structural lipid. As another non-limiting example, the lipid nanoparticle may comprise about 50% cationic lipid, about 10% non-cationic lipid, about 1.5% PEG lipid and about 38.5% structural lipid. As yet another non-limiting example, the lipid nanoparticle may comprise about 55% cationic lipid, about 10% non-cationic lipid, about 2.5% PEG lipid and about 32.5% structural lipid. In some embodiments, the cationic lipid may be any cationic lipid described herein such as, but not limited to, DLin-KC2-DMA, DLin-MC3-DMA and I.319.

[0441] In some embodiments, the lipid nanoparticle formulations described herein may be 4 component lipid nanoparticles. The lipid nanoparticle may comprise a cationic lipid, a non-cationic lipid, a PEG lipid and a structural lipid. As a non-limiting example, the lipid nanoparticle may

comprise about 40-60% of cationic lipid, about 5-15% of a non-cationic lipid, about 1-2% of a PEG lipid and about 30-50% of a structural lipid. As another non-limiting example, the lipid nanoparticle may comprise about 50% cationic lipid, about 10% non-cationic lipid, about 1.5% PEG lipid and about 38.5% structural lipid. As yet another non-limiting example, the lipid nanoparticle may comprise about 55% cationic lipid, about 10% non-cationic lipid, about 2.5% PEG lipid and about 32.5% structural lipid. In some embodiments, the cationic lipid may be any cationic lipid described herein such as, but not limited to, DLin-KC2-DMA, DLin-MC3-DMA and I.319.

[0442] In some embodiments, the lipid nanoparticle formulations described herein may comprise a cationic lipid, a non-cationic lipid, a PEG lipid and a structural lipid. As a non-limiting example, the lipid nanoparticle comprise about 50% of the cationic lipid DLin-KC2-DMA, about 10% of the non-cationic lipid DSPC, about 1.5% of the PEG lipid PEG-DMG and about 38.5% of the structural lipid cholesterol. As a non-limiting example, the lipid nanoparticle comprise about 50% of the cationic lipid DLin-MC3-DMA, about 10% of the non-cationic lipid DSPC, about 1.5% of the PEG lipid PEG-DMG and about 38.5% of the structural lipid cholesterol. As yet another non-limiting example, the lipid nanoparticle comprise about 50% of the cationic lipid DLin-MC3-DMA, about 10% of the non-cationic lipid DSPC, about 1.5% of the PEG lipid PEG-DMG and about 38.5% of the structural lipid cholesterol. As yet another non-limiting example, the lipid nanoparticle comprise about 55% of the cationic lipid I.319, about 10% of the non-cationic lipid DSPC, about 2.5% of the PEG lipid PEG-DMG and about 32.5% of the structural lipid cholesterol.

[0443] As a non-limiting example, the cationic lipid may be selected from (20Z,23Z)-N,N-dimethylnonacos-20,23-dien-10-amine, (17Z,20Z)-N,N-dimethylhexacos-17,20-dien-9-amine, (1Z,19Z)-N,N-dimethylpentacos-1 6, 19-dien-8-amine, (13Z,16Z)-N,N-dimethyldocos-13,16-dien-5-amine, (12Z,15Z)-N,N-dimethylhenicos-12,15-dien-4-amine, (14Z,17Z)-N,N-dimethyltricos-14,17-dien-6-amine, (15Z,18Z)-N,N-dimethyltetracos-15,18-dien-7-amine, (18Z,21Z)-N,N-dimethylheptacos-18,21-dien-10-amine, (15Z,18Z)-N,N-dimethyltetracos-15,18-dien-5-amine, (14Z,17Z)-N,N-dimethyltricos-14,17-dien-4-amine, (19Z,22Z)-N,N-dimethyloctacos-19,22-dien-9-amine, (18Z,21 Z)-N,N-dimethylheptacos-18,21 -dien-8-amine, (17Z,20Z)-N,N-dimethylhexacos-17,20-dien-7-amine, (16Z,19Z)-N,N-dimethylpentacos-16,19-dien-6-amine, (22Z,25Z)-N,N-dimethylhentriaconta-22,25-dien-10-amine, (21 Z,24Z)-N,N-dimethyltriaconta-21,24-dien-9-amine, (18Z)-N,N-dimethylheptacos-18-en-10-amine, (17Z)-N,N-dimethylhexacos-17-en-9-amine, (19Z,22Z)-N,N-dimethyloctacos-19,22-dien-7-amine, N,N-dimethylheptacosan-10-amine, (20Z,23Z)-N-ethyl-N-methylnonacos-20,23-dien-10-amine, 1-[(11Z,14Z)-1-nonylicos-11,14-dien-1-yl] pyrrolidine, (20Z)-N,N-dimethylheptacos-20-en-1 0-amine, (15Z)-N,N-dimethyl eptacos-15-en-1 0-amine, (14Z)-N,N-dimethylnonacos-14-en-10-amine, (17Z)-N,N-dimethylnonacos-17-en-10-amine, (24Z)-N,N-dimethyltriacont-24-en-10-amine, (20Z)-N,N-dimethylnonacos-20-en-1 0-amine, (22Z)-N,N-dimethylhentriacont-22-en-10-amine, (16Z)-N,N-dimethylpentacos-16-en-8-amine, (12Z,15Z)-N,N-dimethyl-2-nonylhenicos-12,15-dien-1-amine, (13Z,16Z)-N,N-dimethyl-3-nonyldocos-13,16-dien-1-amine, N,N-dimethyl-1-[(1S,

2R)-2-octylcyclopropyl]heptadecan-8-amine, 1-[(1S,2R)-2-hexylcyclopropyl]-N,N-dimethylnonadecan-10-amine, N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl]nonadecan-10-amine, N,N-dimethyl-21-[(1S,2R)-2-octylcyclopropyl]henicosan-10-amine, N,N-dimethyl-1-[(1S,2S)-2-[(1R,2R)-2-pentylcyclopropyl]methyl]cyclopropyl]nonadecan-10-amine, N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl]hexadecan-8-amine, N,N-dimethyl-1-(1R,2S)-2-undecylcyclopropyl]tetradecan-5-amine, N,N-dimethyl-3-{7-[(1S,2R)-2-octylcyclopropyl]heptyl}dodecan-1-amine, 1-[(1R,2S)-2-heptylcyclopropyl]-N,N-dimethyloctadecan-9-amine, 1-[(1S,2R)-2-decylcyclopropyl]-N,N-dimethylpentadecan-6-amine, N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl]pentadecan-8-amine, R,N,N-dimethyl-1-(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-3-(octyloxy)propan-2-amine, S-N,N-dimethyl-1-(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-3-(octyloxy)propan-2-amine, 1-[2-(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-1-[(octyloxy)methyl]ethyl]pyrrolidine, (2S)-N,N-dimethyl-1-(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-3-[(5Z)-oct-5-en-1-yloxy]propan-2-amine, 1-[2-(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-1-(octyloxy)methyl]ethyl]azetidine, (2S)-1-(hexyloxy)-N,N-dimethyl-3-(9Z,12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, (2S)-1-(heptyloxy)-N,N-dimethyl-3-(9Z,12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, N,N-dimethyl-1-(nonyloxy)-3-(9Z,12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, N,N-dimethyl-1-(9Z)-octadec-9-en-1-yloxy]-3-(octyloxy)propan-2-amine; (2S)-N,N-dimethyl-1-(6Z,9Z,12Z)-octadeca-6,9,12-trien-1-yloxy]-3-(octyloxy)propan-2-amine, (2S)-1-[(11Z,14Z)-icosa-11,14-dien-1-yloxy]-N,N-dimethyl-3-(pentyloxy)propan-2-amine, (2S)-1-(hexyloxy)-3-[(11Z,14Z)-icosa-11,14-dien-1-yloxy]-N,N-dimethylpropan-2-amine, 1-[(11Z,14Z)-icosa-11,14-dien-1-yloxy]-N,N-dimethyl-3-(octyloxy)propan-2-amine, 1-[(13Z,16Z)-docosa-13,16-dien-1-yloxy]-N,N-dimethyl-3-(octyloxy)propan-2-amine, (2S)-1-[(13Z,16Z)-docosa-13,16-dien-1-yloxy]-3-(hexyloxy)-N,N-dimethylpropan-2-amine, (2S)-1-[(13Z)-docos-13-en-1-yloxy]-N,N-dimethyl-3-(octyloxy)propan-2-amine, 1-[(9Z)-hexadec-9-en-1-yloxy]-N,N-dimethyl-3-(octyloxy)propan-2-amine, (2R)-N,N-dimethyl-1-(1-metoylethyl)oxy]-3-(9Z,12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, (2R)-1-[(3,7-dimethyloctyl)oxy]-N,N-dimethyl-3-(9Z,12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, N,N-dimethyl-1-(octyloxy)-3-[(8-[(1S,2S)-2-[(1R,2R)-2-pentylcyclopropyl]methyl]cyclopropyl]octyl)oxy]propan-2-amine, N,N-dimethyl-1-[[8-(2-octylcyclopropyl)octyl]oxy]-3-(octyloxy)propan-2-amine and (11Z,20Z,23Z)-N,N-dimethylnonacosan-11,20,23-trien-10-amine or a pharmaceutically acceptable salt or stereoisomer thereof.

[0444] In some embodiments, the LNP formulations of the RNA (e.g., mRNA) vaccines may contain PEG-c-DMG at 3% lipid molar ratio. In some embodiments, the LNP formulations of the RNA (e.g., mRNA) vaccines may contain PEG-c-DMG at 1.5% lipid molar ratio.

[0445] In some embodiments, the pharmaceutical compositions of the RNA (e.g., mRNA) vaccines may include at least one of the PEGylated lipids described in International Publication No. WO2012099755, the contents of which are herein incorporated by reference in their entirety.

[0446] In some embodiments, the LNP formulation may contain PEG-DMG 2000 (1,2-dimyristoyl-sn-glycero-3-

phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000]). In some embodiments, the LNP formulation may contain PEG-DMG 2000, a cationic lipid known in the art and at least one other component. In some embodiments, the LNP formulation may contain PEG-DMG 2000, a cationic lipid known in the art, DSPC and cholesterol. As a non-limiting example, the LNP formulation may contain PEG-DMG 2000, DI.in-DMA, DSPC and cholesterol. As another non-limiting example the LNP formulation may contain PEG-DMG 2000, DI.in-DMA, DSPC and cholesterol in a molar ratio of 2:40:10:48 (see e.g., Geall et al., Nonviral delivery of self-amplifying RNA (e.g., mRNA) vaccines, PNAS 2012; PMID: 22908294, the contents of each of which are herein incorporated by reference in their entirety).

[0447] The lipid nanoparticles described herein may be made in a sterile environment.

[0448] In some embodiments, the LNP formulation may be formulated in a nanoparticle such as a nucleic acid-lipid particle. As a non-limiting example, the lipid particle may comprise one or more active agents or therapeutic agents; one or more cationic lipids comprising from about 50 mol % to about 85 mol % of the total lipid present in the particle; one or more non-cationic lipids comprising from about 13 mol % to about 49.5 mol % of the total lipid present in the particle; and one or more conjugated lipids that inhibit aggregation of particles comprising from about 0.5 mol % to about 2 mol % of the total lipid present in the particle.

[0449] The nanoparticle formulations may comprise a phosphate conjugate. The phosphate conjugate may increase in vivo circulation times and/or increase the targeted delivery of the nanoparticle. As a non-limiting example, the phosphate conjugates may include a compound of any one of the formulas described in International Application No. WO2013033438, the contents of which are herein incorporated by reference in its entirety.

[0450] The nanoparticle formulation may comprise a polymer conjugate. The polymer conjugate may be a water soluble conjugate. The polymer conjugate may have a structure as described in U.S. Patent Application No. 20130059360, the contents of which are herein incorporated by reference in its entirety. In some embodiments, polymer conjugates with the polynucleotides of the present disclosure may be made using the methods and/or segmented polymeric reagents described in U.S. Patent Application No. 20130072709, the contents of which are herein incorporated by reference in its entirety. In some embodiments, the polymer conjugate may have pendant side groups comprising ring moieties such as, but not limited to, the polymer conjugates described in U.S. Patent Publication No. US20130196948, the contents which are herein incorporated by reference in its entirety.

[0451] The nanoparticle formulations may comprise a conjugate to enhance the delivery of nanoparticles of the present disclosure in a subject. Further, the conjugate may inhibit phagocytic clearance of the nanoparticles in a subject. In one aspect, the conjugate may be a "self" peptide designed from the human membrane protein CD47 (e.g., the "self" particles described by Rodriguez et al. (*Science* 2013 339, 971-975), herein incorporated by reference in its entirety). As shown by Rodriguez et al., the self peptides delayed macrophage-mediated clearance of nanoparticles which enhanced delivery of the nanoparticles. In another aspect, the conjugate may be the membrane protein CD47 (e.g., see Rodriguez et al. (*Science* 2013 339, 971-975), herein

incorporated by reference in its entirety). Rodriguez et al. showed that, similarly to "self" peptides, CD47 can increase the circulating particle ratio in a subject as compared to scrambled peptides and PEG coated nanoparticles.

[0452] In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure are formulated in nanoparticles which comprise a conjugate to enhance the delivery of the nanoparticles of the present disclosure in a subject. The conjugate may be the CD47 membrane or the conjugate may be derived from the CD47 membrane protein, such as the "self" peptide described previously. In some embodiments, the nanoparticle may comprise PEG and a conjugate of CD47 or a derivative thereof. In some embodiments, the nanoparticle may comprise both the "self" peptide described above and the membrane protein CD47.

[0453] In some embodiments, a "self" peptide and/or CD47 protein may be conjugated to a virus-like particle or pseudovirus, as described herein for delivery of the RNA (e.g., mRNA) vaccines of the present disclosure.

[0454] In some embodiments, RNA (e.g., mRNA) vaccine pharmaceutical compositions comprising the polynucleotides of the present disclosure and a conjugate that may have a degradable linkage. Non-limiting examples of conjugates include an aromatic moiety comprising an ionizable hydrogen atom, a spacer moiety, and a water-soluble polymer. As a non-limiting example, pharmaceutical compositions comprising a conjugate with a degradable linkage and methods for delivering such pharmaceutical compositions are described in U.S. Patent Publication No. US20130184443, the contents of which are herein incorporated by reference in their entirety.

[0455] The nanoparticle formulations may be a carbohydrate nanoparticle comprising a carbohydrate carrier and a RNA (e.g., mRNA) vaccine. As a non-limiting example, the carbohydrate carrier may include, but is not limited to, an anhydride-modified phytoglycogen or glycogen-type material, phytoglycogen octenyl succinate, phytoglycogen beta-dextrin, anhydride-modified phytoglycogen beta-dextrin. (See e.g., International Publication No. WO2012109121; the contents of which are herein incorporated by reference in their entirety).

[0456] Nanoparticle formulations of the present disclosure may be coated with a surfactant or polymer in order to improve the delivery of the particle. In some embodiments, the nanoparticle may be coated with a hydrophilic coating such as, but not limited to, PEG coatings and/or coatings that have a neutral surface charge. The hydrophilic coatings may help to deliver nanoparticles with larger payloads such as, but not limited to, RNA (e.g., mRNA) vaccines within the central nervous system. As a non-limiting example nanoparticles comprising a hydrophilic coating and methods of making such nanoparticles are described in U.S. Patent Publication No. US20130183244, the contents of which are herein incorporated by reference in their entirety.

[0457] In some embodiments, the lipid nanoparticles of the present disclosure may be hydrophilic polymer particles. Non-limiting examples of hydrophilic polymer particles and methods of making hydrophilic polymer particles are described in U.S. Patent Publication No. US20130210991, the contents of which are herein incorporated by reference in their entirety.

[0458] In some embodiments, the lipid nanoparticles of the present disclosure may be hydrophobic polymer particles.

[0459] Lipid nanoparticle formulations may be improved by replacing the cationic lipid with a biodegradable cationic lipid which is known as a rapidly eliminated lipid nanoparticle (rel.NP). Ionizable cationic lipids, such as, but not limited to, DLinDMA, DLin-KC2-DMA, and DLin-MC3-DMA, have been shown to accumulate in plasma and tissues over time and may be a potential source of toxicity. The rapid metabolism of the rapidly eliminated lipids can improve the tolerability and therapeutic index of the lipid nanoparticles by an order of magnitude from a 1 mg/kg dose to a 10 mg/kg dose in rat. Inclusion of an enzymatically degraded ester linkage can improve the degradation and metabolism profile of the cationic component, while still maintaining the activity of the rel.NP formulation. The ester linkage can be internally located within the lipid chain or it may be terminally located at the terminal end of the lipid chain. The internal ester linkage may replace any carbon in the lipid chain.

[0460] In some embodiments, the internal ester linkage may be located on either side of the saturated carbon.

[0461] In some embodiments, an immune response may be elicited by delivering a lipid nanoparticle which may include a nanospecies, a polymer and an immunogen. (U.S. Publication No. 20120189700 and International Publication No. WO2012099805; each of which is herein incorporated by reference in their entirety). The polymer may encapsulate the nanospecies or partially encapsulate the nanospecies. The immunogen may be a recombinant protein, a modified RNA and/or a polynucleotide described herein. In some embodiments, the lipid nanoparticle may be formulated for use in a vaccine such as, but not limited to, against a pathogen.

[0462] Lipid nanoparticles may be engineered to alter the surface properties of particles so the lipid nanoparticles may penetrate the mucosal barrier. Mucus is located on mucosal tissue such as, but not limited to, oral (e.g., the buccal and esophageal membranes and tonsil tissue), ophthalmic, gastrointestinal (e.g., stomach, small intestine, large intestine, colon, rectum), nasal, respiratory (e.g., nasal, pharyngeal, tracheal and bronchial membranes), genital (e.g., vaginal, cervical and urethral membranes). Nanoparticles larger than 10-200 nm which are preferred for higher drug encapsulation efficiency and the ability to provide the sustained delivery of a wide array of drugs have been thought to be too large to rapidly diffuse through mucosal barriers. Mucus is continuously secreted, shed, discarded or digested and recycled so most of the trapped particles may be removed from the mucosa tissue within seconds or within a few hours. Large polymeric nanoparticles (200nm -500nm in diameter) which have been coated densely with a low molecular weight polyethylene glycol (PEG) diffused through mucus only 4 to 6-fold lower than the same particles diffusing in water (Lai et al. PNAS 2007 104(5):1482-487; Lai et al. *Adv Drug Deliv Rev.* 2009 61(2): 158-171; each of which is herein incorporated by reference in their entirety). The transport of nanoparticles may be determined using rates of permeation and/or fluorescent microscopy techniques including, but not limited to, fluorescence recovery after photobleaching (FRAP) and high resolution multiple particle tracking (MPT). As a non-limiting example, compositions which can penetrate a mucosal barrier may be made as described in U.S. Pat. No. 8,241,670 or Interna-

tional Patent Publication No. WO2013110028, the contents of each of which are herein incorporated by reference in its entirety.

[0463] The lipid nanoparticle engineered to penetrate mucus may comprise a polymeric material (i.e. a polymeric core) and/or a polymer-vitamin conjugate and/or a tri-block co-polymer. The polymeric material may include, but is not limited to, polyamines, polyethers, polyamides, polyesters, polycarbamates, polyureas, polycarbonates, poly(styrenes), polyimides, polysulfones, polyurethanes, polyacetylenes, polyethylenes, polyethylenimine, polyisocyanates, polyacrylates, polymethacrylates, polyacrylonitriles, and polyarylates. The polymeric material may be biodegradable and/or biocompatible. Non-limiting examples of biocompatible polymers are described in International Patent Publication No. WO2013116804, the contents of which are herein incorporated by reference in their entirety. The polymeric material may additionally be irradiated. As a non-limiting example, the polymeric material may be gamma irradiated (see e.g., International App. No. WO201282165, herein incorporated by reference in its entirety). Non-limiting examples of specific polymers include poly(caprolactone) (PCL), ethylene vinyl acetate polymer (EVA), poly(lactic acid) (PLA), poly(L-lactic acid) (PLLA), poly(glycolic acid) (PGA), poly(lactic acid-co-glycolic acid) (PLGA), poly(L-lactic acid-co-glycolic acid) (PLLGA), poly(D,L-lactide) (PDLA), poly(L-lactide) (PLLA), poly(D,L-lactide-co-caprolactone), poly(D,L-lactide-co-caprolactone-co-glycolide), poly(D,L-lactide-co-PEO-co-D,L-lactide), poly(D,L-lactide-co-PPO-co-D,L-lactide), polyalkyl cyanoacrylate, polyurethane, poly-L-lysine (PLL), hydroxypropyl methacrylate (HPMA), polyethyleneglycol, poly-L-glutamic acid, poly(hydroxy acids), polyanhydrides, polyorthoesters, poly(ester amides), polyamides, poly(ester ethers), polycarbonates, polyalkylenes such as polyethylene and polypropylene, polyalkylene glycols such as poly(ethylene glycol) (PEG), polyalkylene oxides (PEO), polyalkylene terephthalates such as poly(ethylene terephthalate), polyvinyl alcohols (PVA), polyvinyl ethers, polyvinyl esters such as poly(vinyl acetate), polyvinyl halides such as poly(vinyl chloride) (PVC), polyvinylpyrrolidone, polysiloxanes, polystyrene (PS), polyurethanes, derivatized celluloses such as alkyl celluloses, hydroxyalkyl celluloses, cellulose ethers, cellulose esters, nitro celluloses, hydroxypropylcellulose, carboxymethylcellulose, polymers of acrylic acids, such as poly(methyl(meth)acrylate) (PMMA), poly(ethyl(meth)acrylate), poly(butyl(meth)acrylate), poly(isobutyl(meth)acrylate), poly(hexyl(meth)acrylate), poly(isodecyl(meth)acrylate), poly(lauryl(meth)acrylate), poly(phenyl(meth)acrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), poly(octadecyl acrylate) and copolymers and mixtures thereof, polydioxanone and its copolymers, polyhydroxyalkanoates, polypropylene fumarate, polyoxymethylene, poloxamers, poly(ortho)esters, poly(butyric acid), poly(valeric acid), poly(lactide-co-caprolactone), PEG-PLGA-PEG and trimethylene carbonate, polyvinylpyrrolidone. The lipid nanoparticle may be coated or associated with a co-polymer such as, but not limited to, a block co-polymer (such as a branched polyether-polyamide block copolymer described in International Patent Publication No. WO2013012476, herein incorporated by reference in its entirety), and (poly(ethylene glycol))-(poly(propylene oxide))-(poly(ethylene glycol)) triblock copolymer (see e.g., U.S. Publication 20120121718 and U.S. Publication

20100003337 and U.S. Pat. No. 8,263,665, the contents of each of which is herein incorporated by reference in their entirety). The co-polymer may be a polymer that is generally regarded as safe (GRAS) and the formation of the lipid nanoparticle may be in such a way that no new chemical entities are created. For example, the lipid nanoparticle may comprise poloxamers coating PLGA nanoparticles without forming new chemical entities which are still able to rapidly penetrate human mucus (Yang et al. *Angew. Chem. Int. Ed.* 2011 50:2597-2600; the contents of which are herein incorporated by reference in their entirety). A non-limiting scalable method to produce nanoparticles which can penetrate human mucus is described by Xu et al. (see, e.g., *J Control Release* 2013, 170(2):279-86; the contents of which are herein incorporated by reference in their entirety).

[0464] The vitamin of the polymer-vitamin conjugate may be vitamin E. The vitamin portion of the conjugate may be substituted with other suitable components such as, but not limited to, vitamin A, vitamin E, other vitamins, cholesterol, a hydrophobic moiety, or a hydrophobic component of other surfactants (e.g., sterol chains, fatty acids, hydrocarbon chains and alkylene oxide chains).

[0465] The lipid nanoparticle engineered to penetrate mucus may include surface altering agents such as, but not limited to, polynucleotides, anionic proteins (e.g., bovine serum albumin), surfactants (e.g., cationic surfactants such as for example dimethyldioctadecyl-ammonium bromide), sugars or sugar derivatives (e.g., cyclodextrin), nucleic acids, polymers (e.g., heparin, polyethylene glycol and poloxamer), mucolytic agents (e.g., N-acetylcysteine, mugwort, bromelain, papain, clerodendrum, acetylcysteine, bromhexine, carbocysteine, eprazinone, mesna, ambroxol, sobrerol, domiodol, letosteine, stepronin, tiopronin, gelsolin, thymosin β 4 domase alpha, neltexine, erdoesteine) and various DNases including rhDNase. The surface altering agent may be embedded or enmeshed in the particle's surface or disposed (e.g., by coating, adsorption, covalent linkage, or other process) on the surface of the lipid nanoparticle. (see e.g., U.S. Publication 20100215580 and U.S. Publication 20080166414 and US20130164343; the contents of each of which are herein incorporated by reference in their entirety).

[0466] In some embodiments, the mucus penetrating lipid nanoparticles may comprise at least one polynucleotide described herein. The polynucleotide may be encapsulated in the lipid nanoparticle and/or disposed on the surface of the particle. The polynucleotide may be covalently coupled to the lipid nanoparticle. Formulations of mucus penetrating lipid nanoparticles may comprise a plurality of nanoparticles. Further, the formulations may contain particles which may interact with the mucus and alter the structural and/or adhesive properties of the surrounding mucus to decrease mucoadhesion, which may increase the delivery of the mucus penetrating lipid nanoparticles to the mucosal tissue.

[0467] In some embodiments, the mucus penetrating lipid nanoparticles may be a hypotonic formulation comprising a mucosal penetration enhancing coating. The formulation may be hypotonic for the epithelium to which it is being delivered. Non-limiting examples of hypotonic formulations may be found in International Patent Publication No. WO2013110028, the contents of which are herein incorporated by reference in their entirety.

[0468] In some embodiments, in order to enhance the delivery through the mucosal barrier the RNA (e.g., mRNA) vaccine formulation may comprise or be a hypotonic solu-

tion. Hypotonic solutions were found to increase the rate at which mucin particles such as, but not limited to, mucus-penetrating particles, were able to reach the vaginal epithelial surface (see e.g., Ensign et al. *Biomaterials* 2013 34(28):6922-9, the contents of which are herein incorporated by reference in their entirety).

[0469] In some embodiments, the RNA (e.g., mRNA) vaccine is formulated as a lipoplex, such as, without limitation, the ATUPLEx™ system, the DACC system, the DIBTC system and other siRNA-lipoplex technology from Silence Therapeutics (London, United Kingdom), STEMPLECT™ from STEMGENT® (Cambridge, Mass.), and polyethylenimine (PEI) or protamine-based targeted and non-targeted delivery of nucleic acids (Aleku et al. *Cancer Res.* 2008 68:9788-9798; Strumberg et al. *Int J Clin Pharmacol Ther* 2012 50:76-78; Santel et al. *Gene Ther* 2006 13:1222-1234; Santel et al. *Gene Ther* 2006 13:1360-1370; Gutbier et al. *Pulm Pharmacol Ther.* 2010 23:334-344; Kaufmann et al. *Microvasc Res* 2010 80:286-293; Weide et al. *J Immunother.* 2009 32:498-507; Weide et al. *J Immunother.* 2008 31:180-188; Pascolo *Expert Opin Biol Ther.* 4:1285-1294; Fotin-Mleczek et al. 2011 *J Immunother.* 34:1-15; Song et al. *Nature Biotechnol.* 2005, 23:709-717; Peer et al., *Proc Natl Acad Sci U S A.* 2007 6:104:4095-4100; deFougerolles *Hum Gene Ther.* 2008 19:125-132, the contents of each of which are incorporated herein by reference in their entirety).

[0470] In some embodiments, such formulations may also be constructed or compositions altered such that they passively or actively are directed to different cell types in vivo, including but not limited to hepatocytes, immune cells, tumor cells, endothelial cells, antigen presenting cells, and leukocytes (Akinc et al. *Mol Ther.* 2010 18:1357-1364; Song et al. *Nat Biotechnol.* 2005 23:709-717; Judge et al. *J Clin Invest.* 2009 119:661-673; Kaufmann et al. *Microvasc Res* 2010 80:286-293; Santel et al. *Gene Ther* 2006 13:1222-1234; Santel et al. *Gene Ther* 2006 13:1360-1370; Gutbier et al. *Pulm Pharmacol Ther.* 2010 23:334-344; Basha et al., *Mol Ther.* 2011 19:2186-2200; Fenske and Cullis, *Expert Opin Drug Deliv.* 2008 5:25-44; Peer et al., *Science.* 2008 319:627-630; Peer and Lieberman, *Gene Ther.* 2011 18:1127-1133, the contents of each of which are incorporated herein by reference in their entirety). One example of passive targeting of formulations to liver cells includes the DLin-DMA, DLin-KC2-DMA and DLin-MC3-DMA-based lipid nanoparticle formulations, which have been shown to bind to apolipoprotein E and promote binding and uptake of these formulations into hepatocytes in vivo (Akinc et al. *Mol Ther.* 2010 18:1357-1364, the contents of which are incorporated herein by reference in their entirety). Formulations can also be selectively targeted through expression of different ligands on their surface as exemplified by, but not limited to, folate, transferrin, N-acetylgalactosamine (GalNAc), and antibody targeted approaches (Kolhatkar et al., *Curr Drug Discov Technol.* 2011 8:197-206; Musacchio and Torchilin, *Front Biosci.* 2011 16:1388-1412; Yu et al., *Mol Membr Biol.* 2010 27:286-298; Patil et al., *Crit Rev Ther Drug Carrier Syst.* 2008 25:1-61; Benoit et al., *Biomacromolecules.* 2011 12:2708-2714; Zhao et al., *Expert Opin Drug Deliv.* 2008 5:309-319; Akinc et al., *Mol Ther.* 2010 18:1357-1364; Srinivasan et al., *Methods Mol Biol.* 2012 820:105-116; Ben-Arie et al., *Methods Mol Biol.* 2012 757:497-507; Peer 2010 *J Control Release.* 20:63-68; Peer et al., *Proc Natl Acad Sci U S A.* 2007 104:4095-4100;

Kim et al., *Methods Mol Biol.* 2011 721:339-353; Subramanya et al., *Mol Ther.* 2010 18:2028-2037; Song et al., *Nat Biotechnol.* 2005 23:709-717; Peer et al., *Science.* 2008 319:627-630; Peer and Lieberman, *Gene Ther.* 2011 18:1127-1133, the contents of each of which are incorporated herein by reference in their entirety).

[0471] In some embodiments, the RNA (e.g., mRNA) vaccine is formulated as a solid lipid nanoparticle. A solid lipid nanoparticle (SLN) may be spherical with an average diameter between 10 to 1000 nm. SLN possess a solid lipid core matrix that can solubilize lipophilic molecules and may be stabilized with surfactants and/or emulsifiers. In some embodiments, the lipid nanoparticle may be a self-assembly lipid-polymer nanoparticle (see Zhang et al., *ACS Nano.* 2008, 2 (8), pp 1696-1702; the contents of which are herein incorporated by reference in their entirety). As a non-limiting example, the SLN may be the SLN described in International Patent Publication No. WO2013105101, the contents of which are herein incorporated by reference in their entirety. As another non-limiting example, the SLN may be made by the methods or processes described in International Patent Publication No. WO2013105101, the contents of which are herein incorporated by reference in their entirety.

[0472] Liposomes, lipoplexes, or lipid nanoparticles may be used to improve the efficacy of polynucleotides directed protein production as these formulations may be able to increase cell transfection by the RNA (e.g., mRNA) vaccine; and/or increase the translation of encoded protein. One such example involves the use of lipid encapsulation to enable the effective systemic delivery of polyplex plasmid DNA (Heyes et al., *Mol Ther.* 2007 15:713-720; the contents of which are incorporated herein by reference in their entirety). The liposomes, lipoplexes, or lipid nanoparticles may also be used to increase the stability of the polynucleotide.

[0473] In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure can be formulated for controlled release and/or targeted delivery. As used herein, "controlled release" refers to a pharmaceutical composition or compound release profile that conforms to a particular pattern of release to effect a therapeutic outcome. In some embodiments, the RNA (e.g., mRNA) vaccines may be encapsulated into a delivery agent described herein and/or known in the art for controlled release and/or targeted delivery. As used herein, the term "encapsulate" means to enclose, surround or encase. As it relates to the formulation of the compounds of the disclosure, encapsulation may be substantial, complete or partial. The term "substantially encapsulated" means that at least greater than 50, 60, 70, 80, 85, 90, 95, 96, 97, 98, 99, 99.9, 99.9 or greater than 99.999% of the pharmaceutical composition or compound of the disclosure may be enclosed, surrounded or encased within the delivery agent. "Partially encapsulation" means that less than 10, 10, 20, 30, 40 50 or less of the pharmaceutical composition or compound of the disclosure may be enclosed, surrounded or encased within the delivery agent. Advantageously, encapsulation may be determined by measuring the escape or the activity of the pharmaceutical composition or compound of the disclosure using fluorescence and/or electron micrograph. For example, at least 1, 5, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 95, 96, 97, 98, 99, 99.9, 99.99 or greater than 99.99% of the pharmaceutical composition or compound of the disclosure are encapsulated in the delivery agent.

[0474] In some embodiments, the controlled release formulation may include, but is not limited to, tri-block copolymers. As a non-limiting example, the formulation may include two different types of tri-block co-polymers (International Pub. No. WO2012131104 and WO2012131106, the contents of each of which are incorporated herein by reference in their entirety).

[0475] In some embodiments, the RNA (e.g., mRNA) vaccines may be encapsulated into a lipid nanoparticle or a rapidly eliminated lipid nanoparticle and the lipid nanoparticles or a rapidly eliminated lipid nanoparticle may then be encapsulated into a polymer, hydrogel and/or surgical sealant described herein and/or known in the art. As a non-limiting example, the polymer, hydrogel or surgical sealant may be PLGA, ethylene vinyl acetate (EVAc), poloxamer, GELSTIC[®] (Nanotherapeutics, Inc. Alachua, Fla.), HYLFENEX[®] (Halozyme Therapeutics, San Diego Calif.), surgical sealants such as fibrinogen polymers (Fibicon Inc. Cornelia, Ga.), TISSUE[®] (Baxter International, Inc Deerfield, Ill.), PEG-based sealants, and COSEAL[®] (Baxter International, Inc Deerfield, Ill.).

[0476] In some embodiments, the lipid nanoparticle may be encapsulated into any polymer known in the art which may form a gel when injected into a subject. As another non-limiting example, the lipid nanoparticle may be encapsulated into a polymer matrix which may be biodegradable.

[0477] In some embodiments, the RNA (e.g., mRNA) vaccine formulation for controlled release and/or targeted delivery may also include at least one controlled release coating. Controlled release coatings include, but are not limited to, OPADRY[®], polyvinylpyrrolidone/vinyl acetate copolymer, polyvinylpyrrolidone, hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxyethyl cellulose, EUDRAGIT RL[®], EUDRAGIT RS[®] and cellulose derivatives such as ethylcellulose aqueous dispersions (AQUACOAT[®] and SURELEASE[®]).

[0478] In some embodiments, the RNA (e.g., mRNA) vaccine controlled release and/or targeted delivery formulation may comprise at least one degradable polyester which may contain polycationic side chains. Degradable polyesters include, but are not limited to, poly(serine ester), poly(L-lactide-co-L-lysine), poly(4-hydroxy-L-proline ester), and combinations thereof. In some embodiments, the degradable polyesters may include a PEG conjugation to form a PEGylated polymer.

[0479] In some embodiments, the RNA (e.g., mRNA) vaccine controlled release and/or targeted delivery formulation comprising at least one polynucleotide may comprise at least one PEG and/or PEG related polymer derivatives as described in U.S. Pat. No. 8,404,222, the contents of which are incorporated herein by reference in their entirety.

[0480] In some embodiments, the RNA (e.g., mRNA) vaccine controlled release delivery formulation comprising at least one polynucleotide may be the controlled release polymer system described in US20130130348, the contents of which are incorporated herein by reference in their entirety.

[0481] In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure may be encapsulated in a therapeutic nanoparticle, referred to herein as "therapeutic nanoparticle RNA (e.g., mRNA) vaccines." Therapeutic nanoparticles may be formulated by methods described herein and known in the art such as, but not limited to, International Pub Nos. WO2010005740, WO2010030763,

WO2010005721, WO2010005723, WO2012054923, U.S. Publication Nos. US20110262491, US20100104645, US20100087337, US20100068285, US20110274759, US20100068286, US20120288541, US20130123351 and US20130230567 and U.S. Pat. Nos. 8,206,747, 8,293,276, 8,318,208 and 8,318,211; the contents of each of which are herein incorporated by reference in their entirety. In some embodiments, therapeutic polymer nanoparticles may be identified by the methods described in US Pub No. US20120140790, the contents of which are herein incorporated by reference in their entirety.

[0482] In some embodiments, the therapeutic nanoparticle RNA (e.g., mRNA) vaccine may be formulated for sustained release. As used herein, "sustained release" refers to a pharmaceutical composition or compound that conforms to a release rate over a specific period of time. The period of time may include, but is not limited to, hours, days, weeks, months and years. As a non-limiting example, the sustained release nanoparticle may comprise a polymer and a therapeutic agent such as, but not limited to, the polynucleotides of the present disclosure (see International Pub No. 2010075072 and US Pub No. US20100216804, US20110217377 and US20120201859, the contents of each of which are incorporated herein by reference in their entirety). In another non-limiting example, the sustained release formulation may comprise agents which permit persistent bioavailability such as, but not limited to, crystals, macromolecular gels and/or particulate suspensions (see U.S. Patent Publication No US20130150295, the contents of each of which are incorporated herein by reference in their entirety).

[0483] In some embodiments, the therapeutic nanoparticle RNA (e.g., mRNA) vaccines may be formulated to be target specific. As a non-limiting example, the therapeutic nanoparticles may include a corticosteroid (see International Pub. No. WO2011084518, the contents of which are incorporated herein by reference in their entirety). As a non-limiting example, the therapeutic nanoparticles may be formulated in nanoparticles described in International Pub No. WO2008121949, WO2010005726, WO2010005725, WO2011084521 and US Pub No. US20100069426, US20120004293 and US20100104655, the contents of each of which are incorporated herein by reference in their entirety.

[0484] In some embodiments, the nanoparticles of the present disclosure may comprise a polymeric matrix. As a non-limiting example, the nanoparticle may comprise two or more polymers such as, but not limited to, polyethylenes, polycarbonates, polyanhydrides, polyhydroxyacids, polypropylfumerates, polycaprolactones, polyamides, polyacetals, polyethers, polyesters, poly(orthoesters), polycyanoacrylates, polyvinyl alcohols, polyurethanes, polyphosphazenes, polyacrylates, polymethacrylates, polycyanoacrylates, polyureas, polystyrenes, polyamines, polylysine, poly(ethylene imine), poly(serine ester), poly(L-lactide-co-L-lysine), poly(4-hydroxy-L-proline ester) or combinations thereof.

[0485] In some embodiments, the therapeutic nanoparticle comprises a diblock copolymer. In some embodiments, the diblock copolymer may include PEG in combination with a polymer such as, but not limited to, polyethylenes, polycarbonates, polyanhydrides, polyhydroxyacids, polypropylfumerates, polycaprolactones, polyamides, polyacetals, polyethers, polyesters, poly(orthoesters), polycyanoacry-

lates, polyvinyl alcohols, polyurethanes, polyphosphazenes, polyacrylates, polymethacrylates, polycyanoacrylates, polyureas, polystyrenes, polyamines, polylysine, poly(ethylene imine), poly(serine ester), poly(L-lactide-co-L-lysine), poly(4-hydroxy-L-proline ester) or combinations thereof. In yet another embodiment, the diblock copolymer may be a high-X diblock copolymer such as those described in International Patent Publication No. WO2013120052, the contents of which are incorporated herein by reference in their entirety.

[0486] As a non-limiting example the therapeutic nanoparticle comprises a PLGA-PEG block copolymer (see U.S. Publication No. US20120004293 and U.S. Pat. No. 8,236,330, each of which is herein incorporated by reference in their entirety). In another non-limiting example, the therapeutic nanoparticle is a stealth nanoparticle comprising a diblock copolymer of PEG and PLA or PEG and PLGA (see U.S. Pat. No. 8,246,968 and International Publication No. WO2012166923, the contents of each of which are herein incorporated by reference in their entirety). In yet another non-limiting example, the therapeutic nanoparticle is a stealth nanoparticle or a target-specific stealth nanoparticle as described in U.S. Patent Publication No. US20130172406, the contents of which are herein incorporated by reference in their entirety.

[0487] In some embodiments, the therapeutic nanoparticle may comprise a multiblock copolymer (see e.g., U.S. Pat. Nos. 8,263,665 and 8,287,910 and U.S. Patent Pub. No. US20130195987, the contents of each of which are herein incorporated by reference in their entirety).

[0488] In yet another non-limiting example, the lipid nanoparticle comprises the block copolymer PEG-PLGA-PEG (see e.g., the thermosensitive hydrogel (PEG-PLGA-PEG) was used as a TGF- β 1 gene delivery vehicle in Lee et al. Thermosensitive Hydrogel as a Tgf- β 1 Gene Delivery Vehicle Enhances Diabetic Wound Healing, *Pharmaceutical Research*, 2003 20(12): 1995-2000; as a controlled gene delivery system in Li et al. Controlled Gene Delivery System Based on Thermosensitive Biodegradable Hydrogel, *Pharmaceutical Research* 2003 20(6):884-888; and Chang et al., Non-ionic amphiphilic biodegradable PEG-PLGA-PEG copolymer enhances gene delivery efficiency in rat skeletal muscle, *J Controlled Release*, 2007 118:245-253, the contents of each of which are herein incorporated by reference in their entirety). The RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in lipid nanoparticles comprising the PEG-PLGA-PEG block copolymer.

[0489] In some embodiments, the therapeutic nanoparticle may comprise a multiblock copolymer (see e.g., U.S. Pat. Nos. 8,263,665 and 8,287,910 and U.S. Patent Pub. No. US20130195987, the contents of each of which are herein incorporated by reference in their entirety).

[0490] In some embodiments, the block copolymers described herein may be included in a polyion complex comprising a non-polymeric micelle and the block copolymer. (see e.g., U.S. Publication No. 20120076836, the contents of which are herein incorporated by reference in their entirety).

[0491] In some embodiments, the therapeutic nanoparticle may comprise at least one acrylic polymer. Acrylic polymers include but are not limited to, acrylic acid, methacrylic acid, acrylic acid and methacrylic acid copolymers, methyl methacrylate copolymers, ethoxyethyl methacrylates, cyanoethyl

methacrylate, amino alkyl methacrylate copolymer, poly(acrylic acid), poly(methacrylic acid), polycyanoacrylates and combinations thereof.

[0492] In some embodiments, the therapeutic nanoparticles may comprise at least one poly(vinyl ester) polymer. The poly(vinyl ester) polymer may be a copolymer such as a random copolymer. As a non-limiting example, the random copolymer may have a structure such as those described in International Application No. WO2013032829 or U.S. Patent Publication No. US20130121954, the contents of each of which are herein incorporated by reference in their entirety. In some embodiments, the poly(vinyl ester) polymers may be conjugated to the polynucleotides described herein.

[0493] In some embodiments, the therapeutic nanoparticle may comprise at least one diblock copolymer. The diblock copolymer may be, but it not limited to, a poly(lactic acid)-poly(ethylene)glycol copolymer (see, e.g., International Patent Publication No. WO2013044219, the contents of which are herein incorporated by reference in their entirety). As a non-limiting example, the therapeutic nanoparticle may be used to treat cancer (see International publication No. WO2013044219, the contents of which are herein incorporated by reference in their entirety).

[0494] In some embodiments, the therapeutic nanoparticles may comprise at least one cationic polymer described herein and/or known in the art.

[0495] In some embodiments, the therapeutic nanoparticles may comprise at least one amine-containing polymer such as, but not limited to polylysine, polyethylene imine, poly(amidoamine) dendrimers, poly(beta-amino esters) (see, e.g., U.S. Pat. No. 8,287,849, the contents of which are herein incorporated by reference in their entirety) and combinations thereof.

[0496] In some embodiments, the nanoparticles described herein may comprise an amine cationic lipid such as those described in International Patent Application No. WO2013059496, the contents of which are herein incorporated by reference in their entirety. In some embodiments, the cationic lipids may have an amino-amine or an amino-amide moiety.

[0497] In some embodiments, the therapeutic nanoparticles may comprise at least one degradable polyester which may contain polycationic side chains. Degradable polyesters include, but are not limited to, poly(serine ester), poly(L-lactide-co-L-lysine), poly(4-hydroxy-L-proline ester), and combinations thereof. In some embodiments, the degradable polyesters may include a PEG conjugation to form a PEGylated polymer.

[0498] In some embodiments, the synthetic nanocarriers may contain an immunostimulatory agent to enhance the immune response from delivery of the synthetic nanocarrier. As a non-limiting example, the synthetic nanocarrier may comprise a Th1 immunostimulatory agent, which may enhance a Th1-based response of the immune system (see International Pub No. WO2010123569 and U.S. Publication No. US20110223201, the contents of each of which are herein incorporated by reference in their entirety).

[0499] In some embodiments, the synthetic nanocarriers may be formulated for targeted release. In some embodiments, the synthetic nanocarrier is formulated to release the polynucleotides at a specified pH and/or after a desired time interval. As a non-limiting example, the synthetic nanoparticle may be formulated to release the RNA (e.g., mRNA) vaccines after 24 hours and/or at a pH of 4.5 (see Interna-

tional Publication Nos. WO2010138193 and WO2010138194 and US Pub Nos. US20110020388 and US20110027217, each of which is herein incorporated by reference in their entirety).

[0500] In some embodiments, the synthetic nanocarriers may be formulated for controlled and/or sustained release of the polynucleotides described herein. As a non-limiting example, the synthetic nanocarriers for sustained release may be formulated by methods known in the art, described herein and/or as described in International Pub No. WO2010138192 and US Pub No. 20100303850, each of which is herein incorporated by reference in their entirety.

[0501] In some embodiments, the RNA (e.g., mRNA) vaccine may be formulated for controlled and/or sustained release wherein the formulation comprises at least one polymer that is a crystalline side chain (CYSC) polymer. CYSC polymers are described in U.S. Pat. No. 8,399,007, herein incorporated by reference in its entirety.

[0502] In some embodiments, the synthetic nanocarrier may be formulated for use as a vaccine. In some embodiments, the synthetic nanocarrier may encapsulate at least one polynucleotide which encode at least one antigen. As a non-limiting example, the synthetic nanocarrier may include at least one antigen and an excipient for a vaccine dosage form (see International Publication No. WO2011150264 and U.S. Publication No. US20110293723, the contents of each of which are herein incorporated by reference in their entirety). As another non-limiting example, a vaccine dosage form may include at least two synthetic nanocarriers with the same or different antigens and an excipient (see International Publication No. WO2011150249 and U.S. Publication No. US20110293701, the contents of each of which are herein incorporated by reference in their entirety). The vaccine dosage form may be selected by methods described herein, known in the art and/or described in International Publication No. WO2011150258 and U.S. Publication No. US20120027806, the contents of each of which are herein incorporated by reference in their entirety).

[0503] In some embodiments, the synthetic nanocarrier may comprise at least one polynucleotide which encodes at least one adjuvant. As non-limiting example, the adjuvant may comprise dimethyldioctadecylammonium-bromide, dimethyldioctadecylammonium-chloride, dimethyldioctadecylammonium-phosphate or dimethyldioctadecylammonium-acetate (DDA) and an apolar fraction or part of said apolar fraction of a total lipid extract of a mycobacterium (see, e.g., U.S. Pat. No. 8,241,610, the content of which is herein incorporated by reference in its entirety). In some embodiments, the synthetic nanocarrier may comprise at least one polynucleotide and an adjuvant. As a non-limiting example, the synthetic nanocarrier comprising and adjuvant may be formulated by the methods described in International Publication No. WO2011150240 and U.S. Publication No. US20110293700, the contents of each of which are herein incorporated by reference in their entirety.

[0504] In some embodiments, the synthetic nanocarrier may encapsulate at least one polynucleotide that encodes a peptide, fragment or region from a virus. As a non-limiting example, the synthetic nanocarrier may include, but is not limited to, any of the nanocarriers described in International Publication No. WO2012024621, WO201202629, WO2012024632 and U.S. Publication No. US20120064110,

US20120058153 and US20120058154, the contents of each of which are herein incorporated by reference in their entirety.

[0505] In some embodiments, the synthetic nanocarrier may be coupled to a polynucleotide which may be able to trigger a humoral and/or cytotoxic T lymphocyte (CTL) response (see, e.g., International Publication No. WO2013019669, the contents of which are herein incorporated by reference in their entirety).

[0506] In some embodiments, the RNA (e.g., mRNA) vaccine may be encapsulated in, linked to and/or associated with zwitterionic lipids. Non-limiting examples of zwitterionic lipids and methods of using zwitterionic lipids are described in U.S. Patent Publication No. US20130216607, the contents of which are herein incorporated by reference in their entirety. In some aspects, the zwitterionic lipids may be used in the liposomes and lipid nanoparticles described herein.

[0507] In some embodiments, the RNA (e.g., mRNA) vaccine may be formulated in colloid nanocarriers as described in U.S. Patent Publication No. US20130197100, the contents of which are herein incorporated by reference in their entirety.

[0508] In some embodiments, the nanoparticle may be optimized for oral administration. The nanoparticle may comprise at least one cationic biopolymer such as, but not limited to, chitosan or a derivative thereof. As a non-limiting example, the nanoparticle may be formulated by the methods described in U.S. Publication No. 20120282343, the contents of which are herein incorporated by reference in their entirety.

[0509] In some embodiments, LNPs comprise the lipid KI.52 (an amino-lipid disclosed in U.S. Application Publication No. 2012/0295832, the contents of which are herein incorporated by reference in their entirety. Activity and/or safety (as measured by examining one or more of ALT/AST, white blood cell count and cytokine induction, for example) of LNP administration may be improved by incorporation of such lipids. LNPs comprising KI.52 may be administered intravenously and/or in one or more doses. In some embodiments, administration of LNPs comprising KI.52 results in equal or improved mRNA and/or protein expression as compared to LNPs comprising MC3.

[0510] In some embodiments, RNA (e.g., mRNA) vaccine may be delivered using smaller LNPs. Such particles may comprise a diameter from below 0.1 μm up to 100 μm such as, but not limited to, less than 0.1 μm , less than 1.0 μm , less than 5 μm , less than 10 μm , less than 15 μm , less than 20 μm , less than 25 μm , less than 30 μm , less than 35 μm , less than 40 μm , less than 50 μm , less than 55 μm , less than 60 μm , less than 65 μm , less than 70 μm , less than 75 μm , less than 80 μm , less than 85 μm , less than 90 μm , less than 95 μm , less than 100 μm , less than 125 μm , less than 150 μm , less than 175 μm , less than 200 μm , less than 225 μm , less than 250 μm , less than 275 μm , less than 300 μm , less than 325 μm , less than 350 μm , less than 375 μm , less than 400 μm , less than 425 μm , less than 450 μm , less than 475 μm , less than 500 μm , less than 525 μm , less than 550 μm , less than 575 μm , less than 600 μm , less than 625 μm , less than 650 μm , less than 675 μm , less than 700 μm , less than 725 μm , less than 750 μm , less than 775 μm , less than 800 μm , less than 825 μm , less than 850 μm , less than 875 μm , less than 900 μm , less than 925 μm , less than 950 μm , less than 975 μm , or less than 1000 μm .

[0511] In some embodiments, RNA (e.g., mRNA) vaccines may be delivered using smaller LNPs, which may comprise a diameter from about 1 nm to about 100 nm, from about 1 nm to about 10 nm, about 1 nm to about 20 nm, from about 1 nm to about 30 nm, from about 1 nm to about 40 nm, from about 1 nm to about 50 nm, from about 1 nm to about 60 nm, from about 1 nm to about 70 nm, from about 1 nm to about 80 nm, from about 1 nm to about 90 nm, from about 5 nm to about 100 nm, from about 5 nm to about 10 nm, about 5 nm to about 20 nm, from about 5 nm to about 30 nm, from about 5 nm to about 40 nm, from about 5 nm to about 50 nm, from about 5 nm to about 60 nm, from about 5 nm to about 70 nm, from about 5 nm to about 80 nm, from about 5 nm to about 90 nm, about 10 to about 50 nm, from about 20 to about 50 nm, from about 30 to about 50 nm, from about 40 to about 50 nm, from about 20 to about 60 nm, from about 30 to about 60 nm, from about 40 to about 60 nm, from about 20 to about 70 nm, from about 30 to about 70 nm, from about 40 to about 70 nm, from about 50 to about 70 nm, from about 60 to about 70 nm, from about 20 to about 80 nm, from about 30 to about 80 nm, from about 40 to about 80 nm, from about 50 to about 80 nm, from about 60 to about 80 nm, from about 20 to about 90 nm, from about 30 to about 90 nm, from about 40 to about 90 nm, from about 50 to about 90 nm, from about 60 to about 90 nm and/or from about 70 to about 90 nm.

[0512] In some embodiments, such LNPs are synthesized using methods comprising microfluidic mixers. Examples of microfluidic mixers may include, but are not limited to, a slit interdigital micromixer including, but not limited to those manufactured by Microinnova (Allerheiligen bei Wildon, Austria) and/or a staggered herringbone micromixer (SHM) (Zhitgal'tsev, I.V. et al., Bottom-up design and synthesis of limit size lipid nanoparticle systems with aqueous and triglyceride cores using millisecond microfluidic mixing have been published (Langmuir, 2012, 28:3633-40; Belliveau, N. M. et al., Microfluidic synthesis of highly potent limit-size lipid nanoparticles for in vivo delivery of siRNA, Molecular Therapy-Nucleic Acids, 2012, 1:e37; Chen, D. et al., Rapid discovery of potent siRNA-containing lipid nanoparticles enabled by controlled microfluidic formulation, J Am Chem Soc, 2012, 134(16):6948-51, the contents of each of which are herein incorporated by reference in their entirety). In some embodiments, methods of LNP generation comprising SHM, further comprise the mixing of at least two input streams wherein mixing occurs by microstructure-induced chaotic advection (MICA). According to this method, fluid streams flow through channels present in a herringbone pattern causing rotational flow and folding the fluids around each other. This method may also comprise a surface for fluid mixing wherein the surface changes orientations during fluid cycling. Methods of generating LNPs using SHM include those disclosed in U.S. Application Publication Nos. 2004/0262223 and 2012/0276209, the contents of each of which are herein incorporated by reference in their entirety.

[0513] In some embodiments, the RNA (e.g., mRNA) vaccine of the present disclosure may be formulated in lipid nanoparticles created using a micromixer such as, but not limited to, a Slit Interdigital Microstructured Mixer (SIMM-V2) or a Standard Slit Interdigital Micro Mixer (SSIMM) or Caterpillar (CPMM) or Impinging-jet (IJMM) from the Institut für Mikrotechnik Mainz GmbH, Mainz (Germany).

[0514] In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in lipid nanoparticles created using microfluidic technology (see, e.g., Whitesides, George M. The Origins and the Future of Microfluidics, Nature, 2006 442: 368-373; and Abraham et al. Chaotic Mixer for Microchannels, Science, 2002 295: 647-651; each of which is herein incorporated by reference in its entirety). As a non-limiting example, controlled microfluidic formulation includes a passive method for mixing streams of steady pressure-driven flows in micro channels at a low Reynolds number (see, e.g., Abraham et al. Chaotic Mixer for Microchannels, Science, 2002 295: 647-651, the contents of which are herein incorporated by reference in their entirety).

[0515] In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in lipid nanoparticles created using a micromixer chip such as, but not limited to, those from Harvard Apparatus (Holliston, Mass.) or Dolomite Microfluidics (Royston, UK). A micromixer chip can be used for rapid mixing of two or more fluid streams with a split and recombine mechanism.

[0516] In some embodiments, the RNA (e.g., mRNA) vaccines of the disclosure may be formulated for delivery using the drug encapsulating microspheres described in International Patent Publication No. WO2013063468 or U.S. Pat. No. 8,440,614, the contents of each of which are herein incorporated by reference in their entirety. The microspheres may comprise a compound of the formula (I), (II), (III), (IV), (V) or (VI) as described in International Patent Publication No. WO2013063468, the contents of which are herein incorporated by reference in their entirety. In some embodiments, the amino acid, peptide, polypeptide, lipids (APL) are useful in delivering the RNA (e.g., mRNA) vaccines of the disclosure to cells (see International Patent Publication No. WO2013063468, the contents of which are herein incorporated by reference in their entirety).

[0517] In some embodiments, the RNA (e.g., mRNA) vaccines of the disclosure may be formulated in lipid nanoparticles having a diameter from about 10 to about 100 nm such as, but not limited to, about 10 to about 20 nm, about 10 to about 30 nm, about 10 to about 40 nm, about 10 to about 50 nm, about 10 to about 60 nm, about 10 to about 70 nm, about 10 to about 80 nm, about 10 to about 90 nm, about 20 to about 30 nm, about 20 to about 40 nm, about 20 to about 50 nm, about 20 to about 60 nm, about 20 to about 70 nm, about 20 to about 80 nm, about 20 to about 90 nm, about 30 to about 100 nm, about 30 to about 40 nm, about 30 to about 50 nm, about 30 to about 60 nm, about 30 to about 70 nm, about 30 to about 80 nm, about 30 to about 90 nm, about 40 to about 50 nm, about 40 to about 60 nm, about 40 to about 70 nm, about 40 to about 80 nm, about 40 to about 90 nm, about 40 to about 100 nm, about 50 to about 60 nm, about 50 to about 70 nm, about 50 to about 80 nm, about 50 to about 90 nm, about 50 to about 100 nm, about 60 to about 70 nm, about 60 to about 80 nm, about 60 to about 90 nm, about 60 to about 100 nm, about 70 to about 80 nm, about 70 to about 90 nm, about 70 to about 100 nm, about 80 to about 90 nm, about 80 to about 100 nm and/or about 90 to about 100 nm.

[0518] In some embodiments, the lipid nanoparticles may have a diameter from about 10 to 500 nm.

[0519] In some embodiments, the lipid nanoparticle may have a diameter greater than 100 nm, greater than 150 nm, greater than 200 nm, greater than 250 nm, greater than 300

nm, greater than 350 nm, greater than 400 nm, greater than 450 nm, greater than 500 nm, greater than 550 nm, greater than 600 nm, greater than 650 nm, greater than 700 nm, greater than 750 nm, greater than 800 nm, greater than 850 nm, greater than 900 nm, greater than 950 nm or greater than 1000 nm.

[0520] In some embodiments, the lipid nanoparticle may be a limit size lipid nanoparticle described in International Patent Publication No. WO2013059922, the contents of which are herein incorporated by reference in their entirety. The limit size lipid nanoparticle may comprise a lipid bilayer surrounding an aqueous core or a hydrophobic core; where the lipid bilayer may comprise a phospholipid such as, but not limited to, diacylphosphatidylcholine, a diacylphosphatidylethanolamine, a ceramide, a sphingomyelin, a dihydrosphingomyelin, a cephalin, a cerebroside, a C8-C20 fatty acid diacylphosphatidylcholine, and 1-palmitoyl-2-oleoyl phosphatidylcholine (POPC). In some embodiments, the limit size lipid nanoparticle may comprise a polyethylene glycol-lipid such as, but not limited to, DLPE-PEG, DMPE-PEG, DPPC-PEG and DSPC-PEG.

[0521] In some embodiments, the RNA (e.g., mRNA) vaccines may be delivered, localized and/or concentrated in a specific location using the delivery methods described in International Patent Publication No. WO2013063530, the contents of which are herein incorporated by reference in their entirety. As a non-limiting example, a subject may be administered an empty polymeric particle prior to, simultaneously with or after delivering the RNA (e.g., mRNA) vaccines to the subject. The empty polymeric particle undergoes a change in volume once in contact with the subject and becomes lodged, embedded, immobilized or entrapped at a specific location in the subject.

[0522] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in an active substance release system (see, e.g., U.S. Patent Publication No. US20130102545, the contents of which are herein incorporated by reference in their entirety). The active substance release system may comprise 1) at least one nanoparticle bonded to an oligonucleotide inhibitor strand which is hybridized with a catalytically active nucleic acid and 2) a compound bonded to at least one substrate molecule bonded to a therapeutically active substance (e.g., polynucleotides described herein), where the therapeutically active substance is released by the cleavage of the substrate molecule by the catalytically active nucleic acid.

[0523] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a nanoparticle comprising an inner core comprising a non-cellular material and an outer surface comprising a cellular membrane. The cellular membrane may be derived from a cell or a membrane derived from a virus. As a non-limiting example, the nanoparticle may be made by the methods described in International Patent Publication No. WO2013052167, the contents of which are herein incorporated by reference in their entirety. As another non-limiting example, the nanoparticle described in International Patent Publication No. WO2013052167, the contents of which are herein incorporated by reference in their entirety, may be used to deliver the RNA (e.g., mRNA) vaccines described herein.

[0524] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in porous nanoparticle-supported lipid bilayers (protocells). Protocells are described in

International Patent Publication No. WO2013056132, the contents of which are herein incorporated by reference in their entirety.

[0525] In some embodiments, the RNA (e.g., mRNA) vaccines described herein may be formulated in polymeric nanoparticles as described in or made by the methods described in U.S. Pat. Nos. 8,420,123 and 8,518,963 and European Patent No. EP2073848B1, the contents of each of which are herein incorporated by reference in their entirety. As a non-limiting example, the polymeric nanoparticle may have a high glass transition temperature such as the nanoparticles described in or nanoparticles made by the methods described in U.S. Pat. No. 8,518,963, the contents of which are herein incorporated by reference in their entirety. As another non-limiting example, the polymer nanoparticle for oral and parenteral formulations may be made by the methods described in European Patent No. EP2073848B1, the contents of which are herein incorporated by reference in their entirety.

[0526] In some embodiments, the RNA (e.g., mRNA) vaccines described herein may be formulated in nanoparticles used in imaging. The nanoparticles may be liposome nanoparticles such as those described in U.S. Patent Publication No. US20130129636, herein incorporated by reference in its entirety. As a non-limiting example, the liposome may comprise gadolinium(III)-[4,7-bis-carboxymethyl-10-[(N,N-distearylamidomethyl-N'-amido-methyl]-1,4,7,10-tetra-azaacyclododec-1-yl]-acetic acid and a neutral, fully saturated phospholipid component (see, e.g., U.S. Patent Publication No. US20130129636, the contents of which are herein incorporated by reference in their entirety).

[0527] In some embodiments, the nanoparticles which may be used in the present disclosure are formed by the methods described in U.S. Patent Application No. US20130130348, the contents of which are herein incorporated by reference in their entirety.

[0528] The nanoparticles of the present disclosure may further include nutrients such as, but not limited to, those which deficiencies can lead to health hazards from anemia to neural tube defects (see, e.g., the nanoparticles described in International Patent Publication No. WO2013072929, the contents of which are herein incorporated by reference in their entirety). As a non-limiting example, the nutrient may be iron in the form of ferrous, ferric salts or elemental iron, iodine, folic acid, vitamins or micronutrients.

[0529] In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in a swellable nanoparticle. The swellable nanoparticle may be, but is not limited to, those described in U.S. Pat. No. 8,440,231, the contents of which are herein incorporated by reference in their entirety. As a non-limiting embodiment, the swellable nanoparticle may be used for delivery of the RNA (e.g., mRNA) vaccines of the present disclosure to the pulmonary system (see, e.g., U.S. Pat. No. 8,440,231, the contents of which are herein incorporated by reference in their entirety).

[0530] The RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in polyanhydride nanoparticles such as, but not limited to, those described in U.S. Pat. No. 8,449,916, the contents of which are herein incorporated by reference in their entirety.

[0531] The nanoparticles and microparticles of the present disclosure may be geometrically engineered to modulate macrophage and/or the immune response. In some embodi-

ments, the geometrically engineered particles may have varied shapes, sizes and/or surface charges in order to incorporate the polynucleotides of the present disclosure for targeted delivery such as, but not limited to, pulmonary delivery (see, e.g., International Publication No. WO2013082111, the contents of which are herein incorporated by reference in their entirety). Other physical features the geometrically engineering particles may have include, but are not limited to, fenestrations, angled arms, asymmetry and surface roughness, charge which can alter the interactions with cells and tissues. As a non-limiting example, nanoparticles of the present disclosure may be made by the methods described in International Publication No. WO2013082111, the contents of which are herein incorporated by reference in their entirety.

[0532] In some embodiments, the nanoparticles of the present disclosure may be water soluble nanoparticles such as, but not limited to, those described in International Publication No. WO2013090601, the contents of which are herein incorporated by reference in their entirety. The nanoparticles may be inorganic nanoparticles which have a compact and zwitterionic ligand in order to exhibit good water solubility. The nanoparticles may also have small hydrodynamic diameters (HD), stability with respect to time, pH, and salinity and a low level of non-specific protein binding.

[0533] In some embodiments the nanoparticles of the present disclosure may be developed by the methods described in U.S. Patent Publication No. US20130172406, the contents of which are herein incorporated by reference in their entirety.

[0534] In some embodiments, the nanoparticles of the present disclosure are stealth nanoparticles or target-specific stealth nanoparticles such as, but not limited to, those described in U.S. Patent Publication No. US20130172406, the contents of which are herein incorporated by reference in their entirety. The nanoparticles of the present disclosure may be made by the methods described in U.S. Patent Publication No. US20130172406, the contents of which are herein incorporated by reference in their entirety.

[0535] In some embodiments, the stealth or target-specific stealth nanoparticles may comprise a polymeric matrix. The polymeric matrix may comprise two or more polymers such as, but not limited to, polyethylenes, polycarbonates, poly-anhydrides, polyhydroxyacids, polypropylfumerates, polycaprolactones, polyamides, polyacetals, polyethers, polyesters, poly(orthoesters), polycyanoacrylates, polyvinyl alcohols, polyurethanes, polyphosphazenes, polyacrylates, polymethacrylates, polycyanoacrylates, polyureas, polystyrenes, polyamines, polyesters, poly-anhydrides, polyethers, polyurethanes, polymethacrylates, polyacrylates, polycyanoacrylates or combinations thereof.

[0536] In some embodiments, the nanoparticle may be a nanoparticle-nucleic acid hybrid structure having a high density nucleic acid layer. As a non-limiting example, the nanoparticle-nucleic acid hybrid structure may be made by the methods described in U.S. Patent Publication No. US20130171646, the contents of which are herein incorporated by reference in their entirety. The nanoparticle may comprise a nucleic acid such as, but not limited to, polynucleotides described herein and/or known in the art.

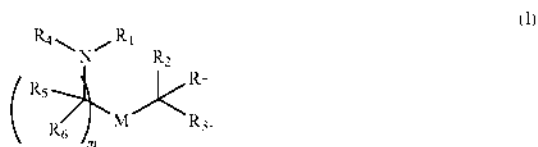
[0537] At least one of the nanoparticles of the present disclosure may be embedded in in the core nanostructure

or coated with a low density porous 3-D structure or coating which is capable of carrying or associating with at least one payload within or on the surface of the nanostructure. Non-limiting examples of the nanostructures comprising at least one nanoparticle are described in International Patent Publication No. WO2013123523, the contents of which are herein incorporated by reference in their entirety.

[0538] In some embodiments the RNA (e.g., mRNA) vaccine may be associated with a cationic or polycationic compounds, including protamine, nucleoline, spermine or spermidine, or other cationic peptides or proteins, such as poly-L-lysine (PLL), polyarginine, basic polypeptides, cell penetrating peptides (CPPs), including HIV-binding peptides, HIV-1 Tat (HIV), Tat-derived peptides, Penetratin, VP²² derived or analog peptides, Pestivirus fims, HIV, VP²² (Herpes simplex), MAP, KALA or protein transduction domains (PTDs), Pp1620, prolin-rich peptides, arginine-rich peptides, lysine-rich peptides, MPG-peptide(s), Pep-1, L-oligomers, Calcitonin peptide(s), Antennapedia-derived peptides (particularly from *Drosophila antennapedia*), pAntp, plsl, FGF, Lactoferrin, Transportan, Buforin-2, Bac715-24, SynB, SynB(1), pVEC, hCT-derived peptides, SAP, histones, cationic polysaccharides, for example chitosan, polybrene, cationic polymers, e.g. polyethylenimine (PEI), cationic lipids, e.g. DOTMA: [1-(2,3-*si*olexyloxy)propyl]-N,N,N-trimethylammonium chloride, DMRIE, di-C14-amidine, DOTIM, SAINT, DC-Chol, BGTC, CTAP, DOPC, DODAP, DOPE: Dioleoyl phosphatidylethanolamine, DOSPA, DODAB, DOIC, DMPEPC, DOGS: Dioctadecylamidoglycylspermin, DIMRI: Dimyristoxypropyl dimethyl hydroxyethyl ammonium bromide, DOTAP: dioleoyloxy-3-(trimethylammonio)propane, DC-6-14: O,O-ditetradecanoyl-N- α -trimethylammonioacetyl)diethanolamine chloride, CLIP 1: rac-[2(3-dioctadecyloxypropyl)(2-hydroxyethyl)]-dimethylammonium chloride, CLIP6: rac-[2(2,3-dihexadecyloxypropyl)oxymethoxy]ethyl]-trimethylammonium, CLIP9: rac-[2(2,3-dihexadecyloxypropyl)oxysuccinyloxy]ethyl]-trimethylammonium, oligofectamine, or cationic or polycationic polymers, e.g. modified polyaminoacids, such as beta-aminoacid-polymers or reversed polyamides, etc., modified polyethylenes, such as PVP (poly(N-ethyl-4-vinylpyridinium bromide)), etc., modified acrylates, such as pDMAEMA (poly(dimethylaminoethyl methylacrylate)), etc., modified amidoamines such as pAMAM (poly(amidoamine)), etc., modified polybetaminoester (PBAE), such as diamine end modified 1,4 butanediol diacrylate-co-5-amino-1-pentanol polymers, etc., dendrimers, such as polypropylamine dendrimers or pAMAM based dendrimers, etc., polyimine(s), such as PEI: poly(ethyleneimine), poly(propyleneimine), etc., polyallylamine, sugar backbone based polymers, such as cyclodextrin based polymers, dextran based polymers, chitosan, etc., silan backbone based polymers, such as PMOXA-PIEMS copolymers, etc., blockpolymers consisting of a combination of one or more cationic blocks (e.g. selected from a cationic polymer as mentioned above) and of one or more hydrophilic or hydrophobic blocks (e.g. polyethyleneglycole), etc.

[0539] In other embodiments the RNA (e.g., mRNA) vaccine is not associated with a cationic or polycationic compounds.

[0540] In some embodiments, a nanoparticle comprises compounds of Formula (I):



- [0541] or a salt or isomer thereof, wherein:
- [0542] R_1 is selected from the group consisting of C_{5-30} alkyl, C_{5-20} alkenyl, R^*YR'' , YR'' , and $R''MR'$;
- [0543] R_2 and R_3 are independently selected from the group consisting of H, C_{1-14} alkyl, C_{2-14} alkenyl, R^*YR'' , YR'' , and R^*OR'' , or R_2 and R_3 , together with the atom to which they are attached, form a heterocycle or carbocycle;
- [0544] R_4 is selected from the group consisting of a C_{3-6} carbocycle, $(CH_2)_nQ$, $(CH_2)_nCHQR$.
- [0545] $CHQR$, $CQ(R)_2$, and unsubstituted C_{1-6} alkyl, where Q is selected from a carbocycle, heterocycle, OR, $O(CH_2)_nN(R)_2$, $C(O)OR$, $OC(O)R$, CX_3 , CX_2H , CXH_2 , CN , $N(R)_2$, $C(O)N(R)_2$, $N(R)C(O)R$, $N(R)S(O)_2R$, $N(R)C(O)N(R)_2$, $(R)C(S)N(R)_2$, $N(R)R_8$, $O(CH_2)_nOR$, $N(R)C(NR_9)N(R)_2$, $(R)C(CHR_9)N(R)_2$, $OC(O)N(R)_2$, $N(R)C(O)OR$, $N(OR)C(O)R$, $N(OR)S(O)_2R$, $N(OR)C(O)OR$, $N(OR)C(O)N(R)_2$, $(OR)C(S)N(R)_2$, $N(OR)C(NR_9)N(R)_2$, $N(OR)C(CHR_9)N(R)_2$, $C(NR_9)N(R)_2$, $C(NR_9)R$, $C(O)N(R)OR$, and $C(R)N(R)_2C(O)OR$, and each n is independently selected from 1, 2, 3, 4, and 5;
- [0546] each R_5 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;
- [0547] each R_6 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;
- [0548] M and M' are independently selected from $C(O)$, O , $OC(O)$, $C(O)N(R')$, $N(R')C(O)$, $C(O)$, $C(S)$, $C(S)S$, $SC(S)$, $CH(OH)$, $P(O)(OR')O$, $S(O)_2$, $S-S$, an aryl group, and a heteroaryl group;
- [0549] R_7 is selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;
- [0550] R_8 is selected from the group consisting of C_{3-6} carbocycle and heterocycle;
- [0551] R_9 is selected from the group consisting of H, CN, NO_2 , C_{1-6} alkyl, OR, $S(O)_2R$, $S(O)_2N(R)_2$, C_{2-6} alkenyl, C_{3-6} carbocycle and heterocycle;
- [0552] each R is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;
- [0553] each R' is independently selected from the group consisting of C_{1-18} alkyl, C_{2-18} alkenyl, R^*YR'' , YR'' , and H;
- [0554] each R'' is independently selected from the group consisting of C_{3-14} alkyl and C_{3-14} alkenyl;
- [0555] each R^* is independently selected from the group consisting of C_{1-12} alkyl and C_{2-12} alkenyl;
- [0556] each Y is independently a C_{3-6} carbocycle;
- [0557] each X is independently selected from the group consisting of F, Cl, Br, and I; and
- [0558] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13.
- [0559] In some embodiments, a subset of compounds of Formula (I) includes those in which when R_4 is $(CH_2)_nQ$,

$(CH_2)_nCHQR$, $CHQR$, or $CQ(R)_2$, then (i) Q is not $N(R)_2$ when n is 1, 2, 3, 4 or 5, or (ii) Q is not 5, 6, or 7-membered heterocycloalkyl when n is 1 or 2.

[0560] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0561] R_1 is selected from the group consisting of C_{5-30} alkyl, C_{5-20} alkenyl, $-R^*YR''$, $-YR''$, and $R''MR'$;

[0562] R_2 and R_3 are independently selected from the group consisting of H, C_{1-14} alkyl, C_{2-14} alkenyl, R^*YR'' , YR'' , and R^*OR'' , or R_2 and R_3 , together with the atom to which they are attached, form a heterocycle or carbocycle;

[0563] R_4 is selected from the group consisting of a C_{3-6} carbocycle, $(CH_2)_nQ$, $(CH_2)_nCHQR$.

[0564] $CHQR$, $CQ(R)_2$, and unsubstituted C_{1-6} alkyl, where Q is selected from a C_{3-6} carbocycle, a 5- to 14-membered heteroaryl having one or more heteroatoms selected from N, O, and S, OR,

[0565] $O(CH_2)_nN(R)_2$, $C(O)OR$, $OC(O)R$, CX_3 , CX_2H , CXH_2 , CN , $C(O)N(R)_2$, $N(R)C(O)R$, $N(R)S(O)_2R$, $N(R)C(O)N(R)_2$, $N(R)C(S)N(R)_2$, $CRN(R)_2C(O)OR$, $N(R)R_8$, $O(CH_2)_nOR$, $N(R)C(NR_9)N(R)_2$, $N(R)C(CHR_9)N(R)_2$, $OC(O)N(R)_2$, $N(R)C(O)OR$, $N(OR)C(O)R$, $N(OR)S(O)_2R$, $N(OR)C(O)OR$, $N(OR)C(O)N(R)_2$, $(OR)C(S)N(R)_2$, $N(OR)C(NR_9)N(R)_2$, $N(OR)C(CHR_9)N(R)_2$, $C(NR_9)N(R)_2$, $C(NR_9)R$, $C(O)N(R)OR$, and a 5- to 14-membered heterocycloalkyl having one or more heteroatoms selected from N, O, and S which is substituted with one or more substituents selected from oxo (O), OH, amino, mono- or di-alkylamino, and C_{1-3} alkyl, and each n is independently selected from 1, 2, 3, 4, and 5;

[0566] each R_6 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0567] each R_6 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0568] M and M' are independently selected from $C(O)$, O , $OC(O)$, $C(O)N(R')$, $N(R')C(O)$, $C(O)$, $C(S)$, $C(S)S$, $SC(S)$, $CH(OH)$, $P(O)(OR')O$, $S(O)_2$, $S-S$, an aryl group, and a heteroaryl group;

[0569] R_7 is selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0570] R_8 is selected from the group consisting of C_{3-6} carbocycle and heterocycle;

[0571] R_9 is selected from the group consisting of H, CN, NO_2 , C_{1-6} alkyl, OR, $S(O)_2R$, $S(O)_2N(R)_2$, C_{2-6} alkenyl, C_{3-6} carbocycle and heterocycle;

[0572] each R is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0573] each R' is independently selected from the group consisting of C_{1-18} alkyl, C_{2-18} alkenyl, R^*YR'' , YR'' , and H;

[0574] each R'' is independently selected from the group consisting of C_{3-14} alkyl and C_{3-14} alkenyl;

[0575] each R^* is independently selected from the group consisting of C_{1-12} alkyl and C_{2-12} alkenyl;

[0576] each Y is independently a C_{3-6} carbocycle;

[0577] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0578] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13, or salts or isomers thereof.

[0579] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0580] R_1 is selected from the group consisting of C_{5-20} alkyl, C_{5-20} alkenyl, R^*YR'' , YR'' , and $R''MR'$;

[0581] R_2 and R_3 are independently selected from the group consisting of H, C_{1-14} alkyl, C_{2-14} alkenyl, R^*YR'' ,

YR'' , and R^*OR'' , or R_2 and R_3 , together with the atom to which they are attached, form a heterocycle or carbocycle;

[0582] R_4 is selected from the group consisting of a C_{3-6} carbocycle, $(CH_2)_nQ$, $(CH_2)_nCHQR$,

[0583] $CHQR$, $CQ(R)_2$, and unsubstituted C_{1-6} alkyl, where Q is selected from a C_{3-6} carbocycle, a 5- to 14-membered heterocycle having one or more heteroatoms selected from N, O, and S, OR,

[0584] $O(CH_2)_nN(R)_2$, $C(O)OR$, $OC(O)R$, CX_3 , CX_2H , CXH_2 , CN , $C(O)N(R)_2$, $N(R)C(O)R$, $N(R)S(O)_2R$, $N(R)C(O)N(R)_2$, $N(R)C(S)N(R)_2$, $CRN(R)_2C(O)OR$, $N(R)R_n$,

[0585] $O(CH_2)_nOR$, $N(R)C(NR_n)N(R)_2$, $N(R)C(CHIR_n)N(R)_2$, $OC(O)N(R)_2$, $N(R)C(O)OR$, $N(OR)C(O)R$, $N(OR)S(O)_2R$, $N(OR)C(O)OR$, $N(OR)C(O)N(R)_2$, $N(OR)C(S)N(R)_2$, $N(OR)C(NR_n)N(R)_2$, $N(OR)C(CHIR_n)N(R)_2$, $C(NR_n)R$,

$C(O)N(R)OR$, and $C(NR_n)N(R)_2$, and each n is independently selected from 1, 2, 3, 4, and 5; and when Q is a 5- to 14-membered heterocycle and (i) R_4 is $(CH_2)_nQ$ in which n is 1 or 2, or (ii) R_4 is $(CH_2)_nCHQR$ in which n is 1, or (iii) R_4 is $CHQR$, and $CQ(R)_2$, then Q is either a 5- to 14-membered heteroaryl or 8- to 14-membered heterocycloalkyl;

[0586] each R_5 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0587] each R_6 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0588] M and M' are independently selected from $C(O)$, O , $OC(O)$, $C(O)N(R')$, $N(R')C(O)$, $C(O)$, $C(S)$, $C(S)S$, $SC(S)$, $CH(OH)$, $P(O)(OR)O$, $S(O)_2$, $S-S$, an aryl group, and a heteroaryl group;

[0589] R_7 is selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0590] R_8 is selected from the group consisting of C_{3-6} carbocycle and heterocycle;

[0591] R_9 is selected from the group consisting of H, CN, NO_2 , C_{1-6} alkyl, OR, $S(O)_2R$, $S(O)_2N(R)_2$, C_{2-6} alkenyl, C_{3-6} carbocycle and heterocycle;

[0592] each R is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0593] each R' is independently selected from the group consisting of C_{1-18} alkyl, C_{2-18} alkenyl, R^*YR'' , YR'' , and H;

[0594] each R'' is independently selected from the group consisting of C_{3-14} alkyl and C_{3-14} alkenyl;

[0595] each R* is independently selected from the group consisting of C_{1-12} alkyl and C_{2-12} alkenyl;

[0596] each Y is independently a C_{3-6} carbocycle;

[0597] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0598] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,

[0599] or salts or isomers thereof.

[0600] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0601] R_1 is selected from the group consisting of C_{5-30} alkyl, C_{5-20} alkenyl, R^*YR'' , YR'' , and $R''MR'$;

[0602] R_2 and R_3 are independently selected from the group consisting of H, C_{1-14} alkyl, C_{2-14} alkenyl, R^*YR'' ,

YR'' , and R^*OR'' , or R_2 and R_3 , together with the atom to which they are attached, form a heterocycle or carbocycle;

[0603] R_4 is selected from the group consisting of a C_{3-6} carbocycle, $(CH_2)_nQ$, $(CH_2)_nCHQR$,

[0604] $CHQR$, $CQ(R)_2$, and unsubstituted C_{1-6} alkyl, where Q is selected from a C_{3-6} carbocycle, a 5- to 14-membered heteroaryl having one or more heteroatoms selected from N, O, and S, OR,

[0605] $O(CH_2)_nN(R)_2$, $C(O)OR$, $OC(O)R$, CX_3 , CX_2H , CXH_2 , CN , $C(O)N(R)_2$, $N(R)C(O)R$, $N(R)S(O)_2R$, $N(R)C(O)N(R)_2$, $N(R)C(S)N(R)_2$, $CRN(R)_2C(O)OR$, $N(R)R_n$, $O(CH_2)_nOR$, $N(R)C(NR_n)N(R)_2$, $N(R)C(CHIR_n)N(R)_2$, $OC(O)N(R)_2$, $N(R)C(O)OR$, $N(OR)C(O)R$, $N(OR)S(O)_2R$, $N(OR)C(O)OR$, $N(OR)C(O)N(R)_2$, $N(OR)C(S)N(R)_2$, $N(OR)C(NR_n)N(R)_2$, $N(OR)C(CHIR_n)N(R)_2$, $C(NR_n)R$, $C(O)N(R)OR$, and $C(NR_n)N(R)_2$, and each n is independently selected from 1, 2, 3, 4, and 5;

[0606] each R_5 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0607] each R_6 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0608] M and M' are independently selected from $C(O)$, O , $OC(O)$, $C(O)N(R')$, $N(R')C(O)$, $C(O)$, $C(S)$, $C(S)S$, $SC(S)$, $CH(OH)$, $P(O)(OR)O$, $S(O)_2$, $S-S$, an aryl group, and a heteroaryl group;

[0609] R_7 is selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0610] R_8 is selected from the group consisting of C_{3-6} carbocycle and heterocycle;

[0611] R_9 is selected from the group consisting of H, CN, NO_2 , C_{1-6} alkyl, OR, $S(O)_2R$, $S(O)_2N(R)_2$, C_{2-6} alkenyl, C_{3-6} carbocycle and heterocycle;

[0612] each R is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0613] each R' is independently selected from the group consisting of C_{1-18} alkyl, C_{2-18} alkenyl, R^*YR'' , YR'' , and H;

[0614] each R'' is independently selected from the group consisting of C_{3-14} alkyl and C_{3-14} alkenyl;

[0615] each R* is independently selected from the group consisting of C_{1-12} alkyl and C_{2-12} alkenyl;

[0616] each Y is independently a C_{3-6} carbocycle;

[0617] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0618] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,

[0619] or salts or isomers thereof.

[0620] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0621] R_1 is selected from the group consisting of C_{5-30} alkyl, C_{5-20} alkenyl, $-R^*YR''$, $-YR''$, and $R''MR'$;

[0622] R_2 and R_3 are independently selected from the group consisting of H, C_{2-14} alkyl, C_{2-14} alkenyl, R^*YR'' , YR'' , and R^*OR'' , or R_2 and R_3 , together with the atom to which they are attached, form a heterocycle or carbocycle;

[0623] R_4 is $(CH_2)_nQ$ or $(CH_2)_nCHQR$, where Q is $N(R)_2$, and n is selected from 3, 4, and 5;

[0624] each R_5 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0625] each R_6 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0626] M and M' are independently selected from $C(O)$, O , $OC(O)$, $C(O)N(R')$, $N(R')C(O)$,

$C(O)$, $C(S)$, $C(S)S$, $SC(S)$, $CH(OH)$, $P(O)(OR')O$, $S(O)_2$, $S-S$, an aryl group, and a heteroaryl group;

[0627] R_7 is selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0628] each R is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0629] each R' is independently selected from the group consisting of C_{1-18} alkyl, C_{2-18} alkenyl, R^*YR'' , YR'' , and H;

[0630] each R'' is independently selected from the group consisting of C_{3-14} alkyl and C_{3-14} alkenyl;

[0631] each R^* is independently selected from the group consisting of C_{1-12} alkyl and C_{1-12} alkenyl;

[0632] each Y is independently a C_{3-6} carbocycle;

[0633] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0634] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13;

[0635] or salts or isomers thereof.

[0636] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0637] R_1 is selected from the group consisting of C_{5-20} alkyl, C_{5-20} alkenyl, R^*YR'' , YR'' , and $R''MR'$;

[0638] R_2 and R_3 are independently selected from the group consisting of C_{1-14} alkyl, C_{2-14} alkenyl, R^*YR'' , YR'' , and R^*OR'' , or R_2 and R_3 , together with the atom to which they are attached, form a heterocycle or carbocycle;

[0639] R_4 is selected from the group consisting of $(CH_2)_nQ$, $(CH_2)_nCHQR$, $CHQR$, and $13CQ(R)_2$, where Q is $N(R)_2$, and n is selected from 1, 2, 3, 4, and 5;

[0640] each R_5 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H; each R_6 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0641] M and M' are independently selected from $C(O)$, O , $OC(O)$, $C(O)N(R')$, $N(R')C(O)$, $C(O)$, $C(S)$, $C(S)S$, $SC(S)$, $CH(OH)$, $P(O)(OR')O$, $S(O)_2$, $S-S$, an aryl group, and a heteroaryl group;

[0642] R_7 is selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0643] each R is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

[0644] each R' is independently selected from the group consisting of C_{1-18} alkyl, C_{2-18} alkenyl, R^*YR'' , YR'' , and H;

[0645] each R'' is independently selected from the group consisting of C_{3-14} alkyl and C_{3-14} alkenyl;

[0646] each R^* is independently selected from the group consisting of C_{1-12} alkyl and C_{1-12} alkenyl;

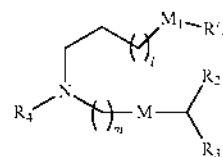
[0647] each Y is independently a C_{3-6} carbocycle;

[0648] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0649] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13;

[0650] or salts or isomers thereof.

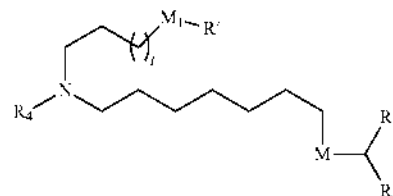
[0651] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IA):



(IA)

[0652] or a salt or isomer thereof, wherein 1 is selected from 1, 2, 3, 4, and 5; m is selected from 5, 6, 7, 8, and 9; M_1 is a bond or M' ; R_4 is unsubstituted C_{1-3} alkyl, or $(CH_2)_nQ$, in which Q is OH, $NHC(S)N(R)_2$, $NHC(O)N(R)_2$, $N(R)C(O)R$, $N(R)S(O)_2R$, $N(R)R_8$, $NHC(NR_9)N(R)_2$, $NHC(CHR_9)N(R)_2$, $OC(O)N(R)_2$, $N(R)C(O)OR$, heteroaryl or heterocycloalkyl; M and M' are independently selected from $C(O)O$, $OC(O)$, $C(O)N(R')$, $P(O)(OR')O$, $S-S$, an aryl group, and a heteroaryl group; and R_2 and R_3 are independently selected from the group consisting of H, C_{1-14} alkyl, and C_{2-14} alkenyl.

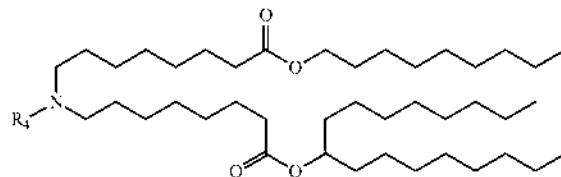
[0653] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (II):



(II)

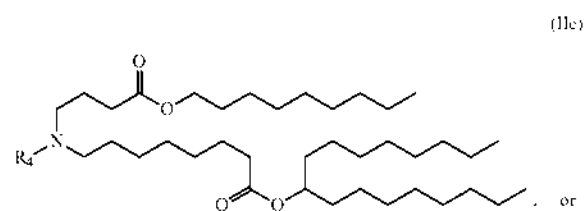
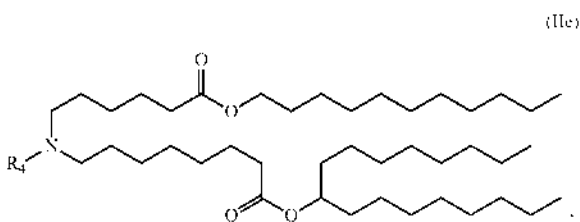
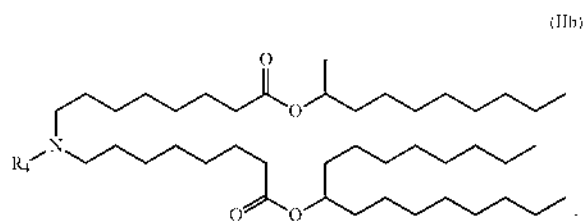
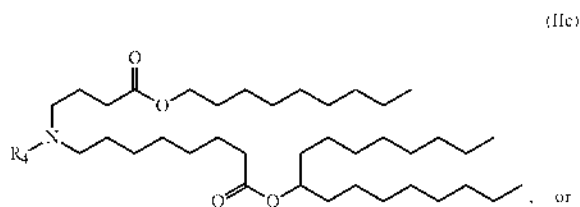
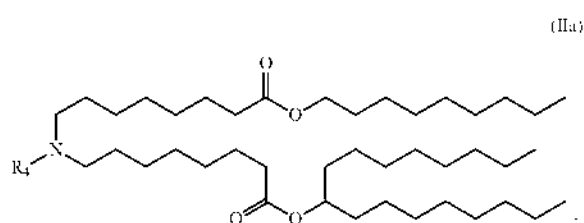
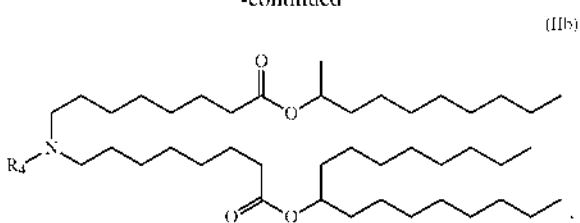
or a salt or isomer thereof, wherein 1 is selected from 1, 2, 3, 4, and 5; M_1 is a bond or M' ; R_4 is unsubstituted C_{1-3} alkyl, or $(CH_2)_nQ$, in which n is 2, 3, or 4, and Q is OH, $NHC(S)N(R)_2$, $NHC(O)N(R)_2$, $N(R)C(O)R$, $N(R)S(O)_2R$, $N(R)R_8$, $NHC(NR_9)N(R)_2$, $NHC(CHR_9)N(R)_2$, $OC(O)N(R)_2$, $N(R)C(O)OR$, heteroaryl or heterocycloalkyl; M and M' are independently selected from $C(O)O$, $OC(O)$, $C(O)N(R')$, $P(O)(OR')O$, $S-S$, an aryl group, and a heteroaryl group; and R_2 and R_3 are independently selected from the group consisting of H, C_{1-14} alkyl, and C_{2-14} alkenyl.

[0654] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IIa), (IIb), (IIc), or (Ile):



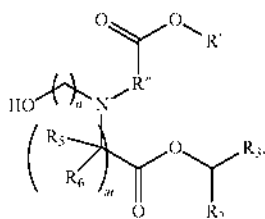
(IIa)

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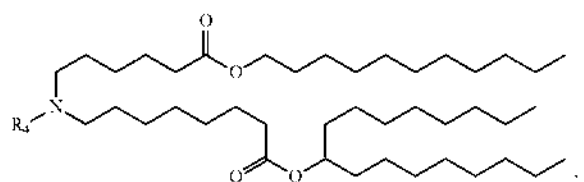
[0655] or a salt or isomer thereof, wherein R_4 is as described herein.

[0656] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IId):



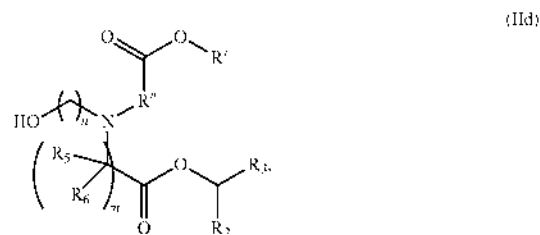
[0657] or a salt or isomer thereof, wherein n is 2, 3, or 4; and m , R' , R'' , and R_2 through R_6 are as described herein. For example, each of R_2 and R_3 may be independently selected from the group consisting of C_{5-14} alkyl and C_{5-14} alkenyl.

[0658] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IIa), (IIb), (IIc), or (IIe):



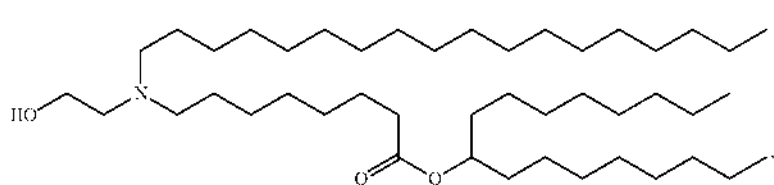
[0659] or a salt or isomer thereof, wherein R_4 is as described herein.

[0660] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IId):

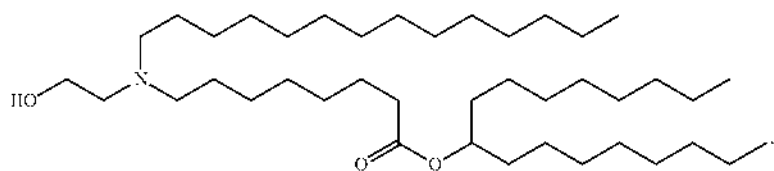


[0661] or a salt or isomer thereof, wherein n is 2, 3, or 4; and m , R' , R'' , and R_2 through R_6 are as described herein. For example, each of R_2 and R_3 may be independently selected from the group consisting of C_{5-14} alkyl and C_{5-14} alkenyl.

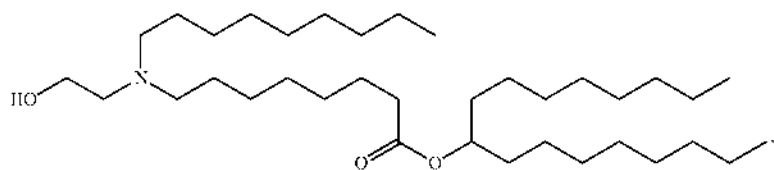
[0662] In some embodiments, the compound of Formula (I) is selected from the group consisting of:



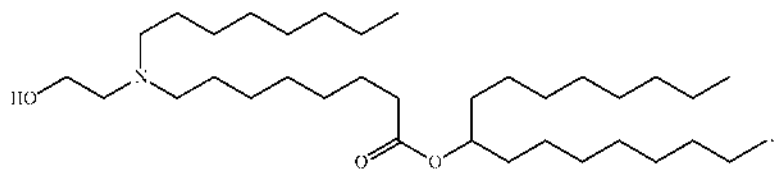
(Compound 1)



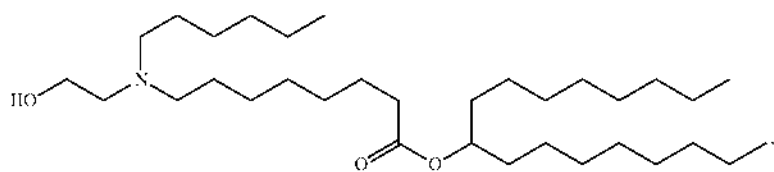
(Compound 2)



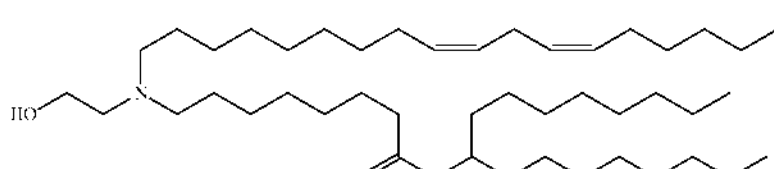
(Compound 3)



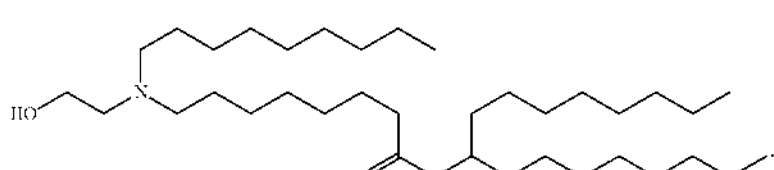
(Compound 4)



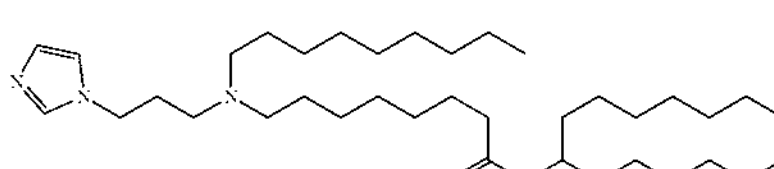
(Compound 5)



(Compound 6)

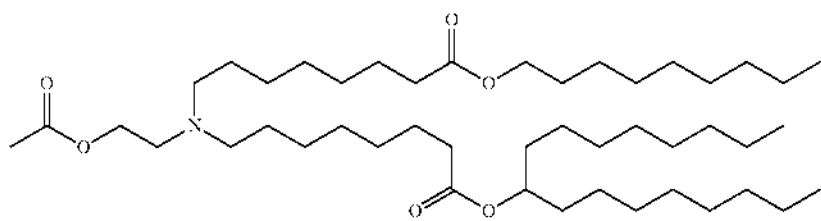


(Compound 7)

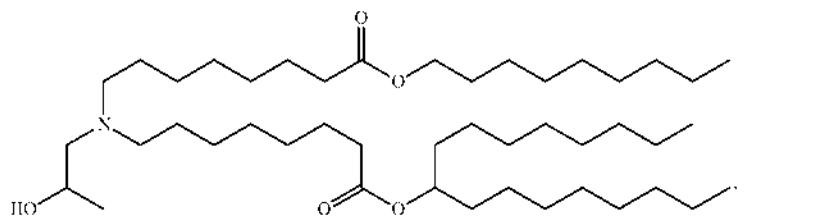


(Compound 8)

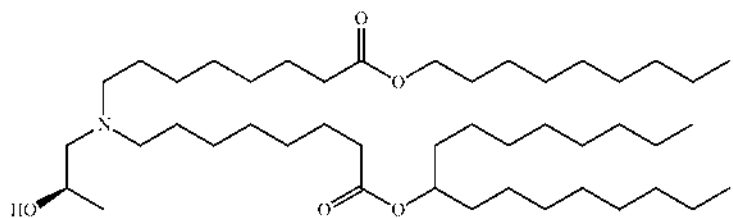
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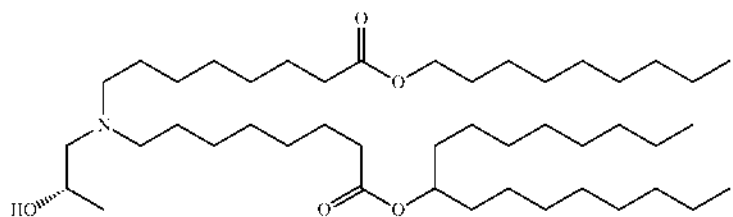
(Compound 9)



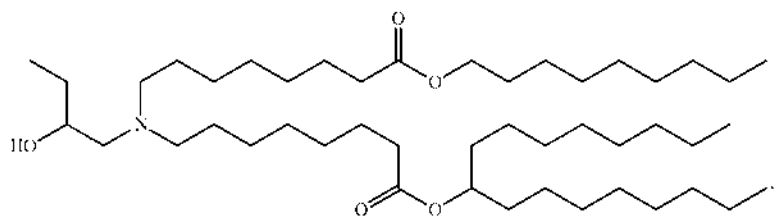
(Compound 10)



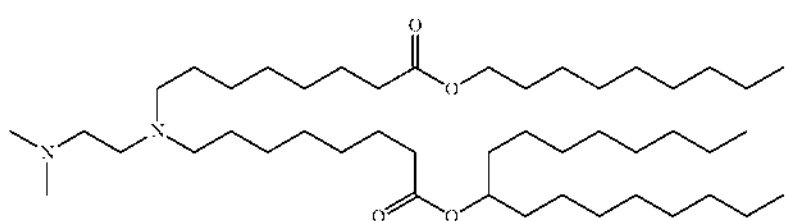
(Compound 11)



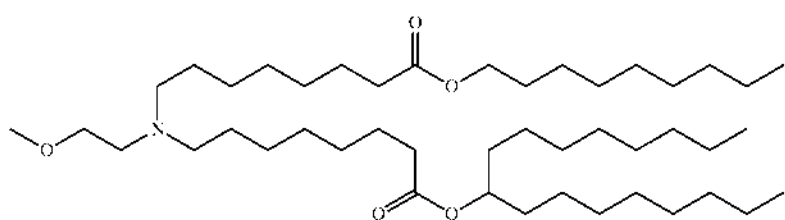
(Compound 12)



(Compound 13)

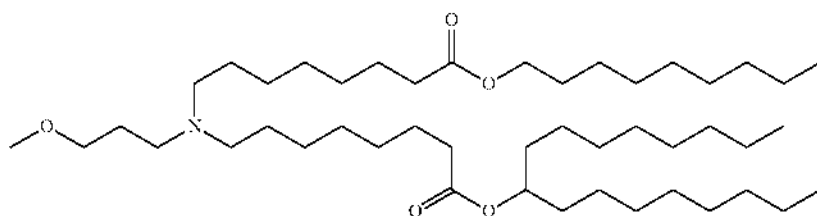


(Compound 14)

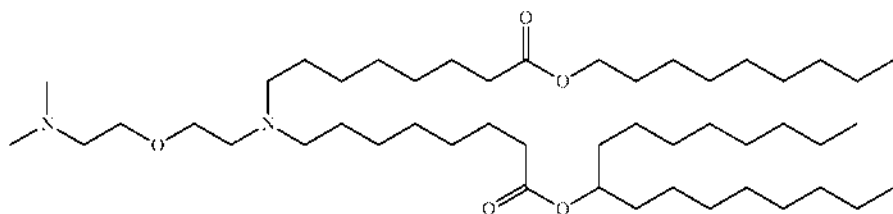


(Compound 15)

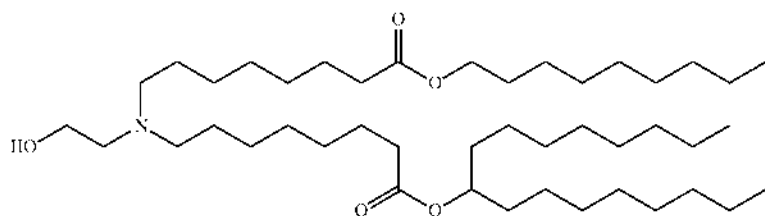
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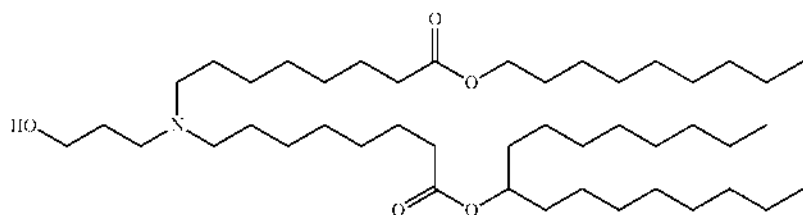
(Compound 16)



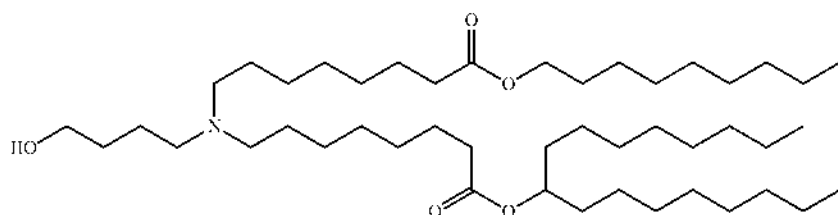
(Compound 17)



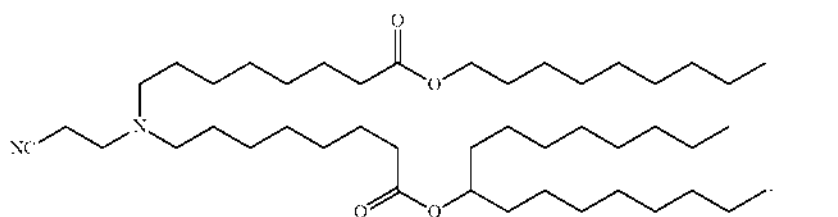
(Compound 18)



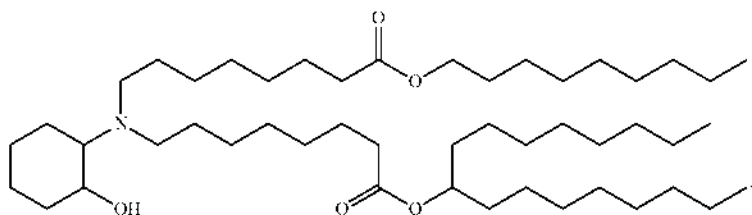
(Compound 19)



(Compound 20)

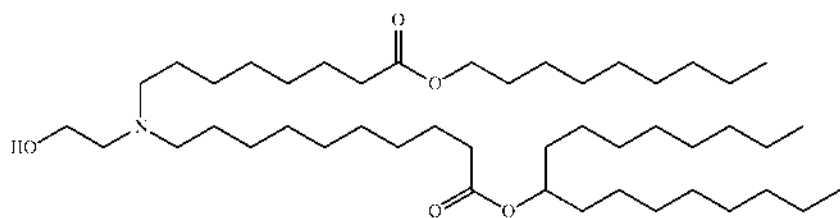


(Compound 21)

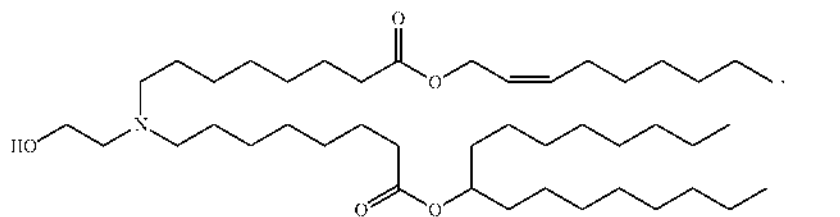


(Compound 22)

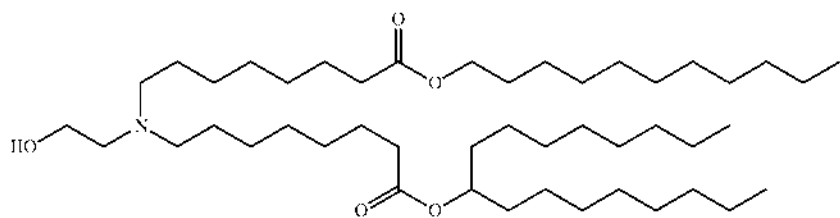
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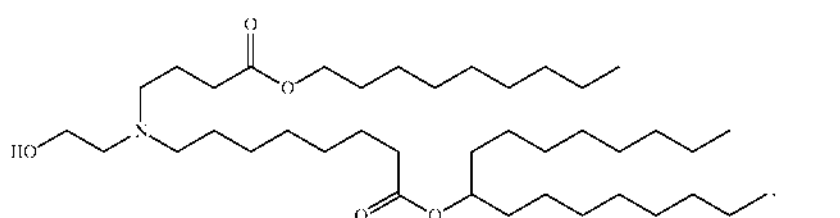
(Compound 23)



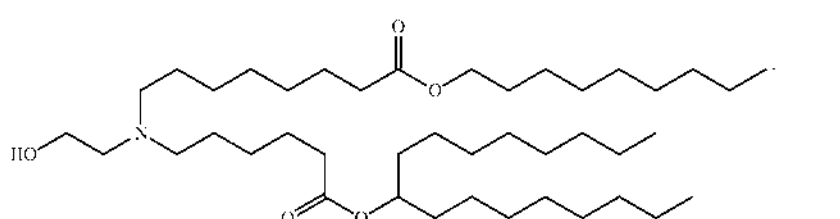
(Compound 24)



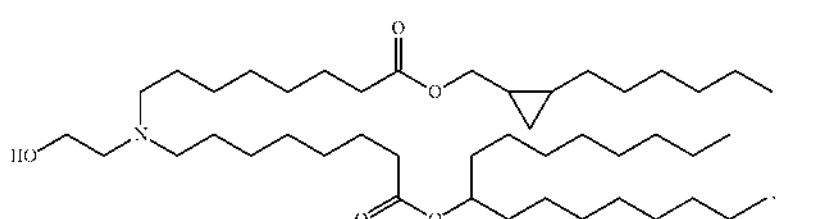
(Compound 25)



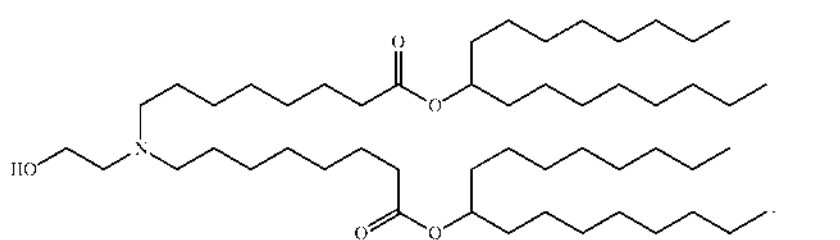
(Compound 26)



(Compound 27)

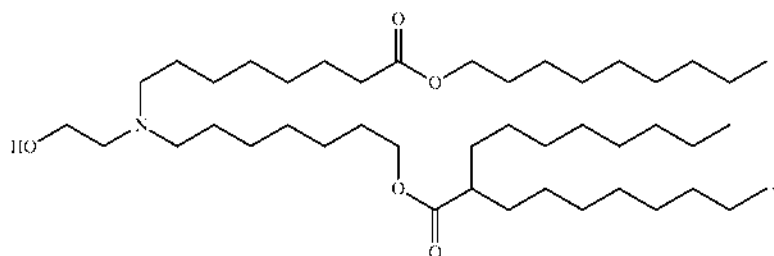


(Compound 28)

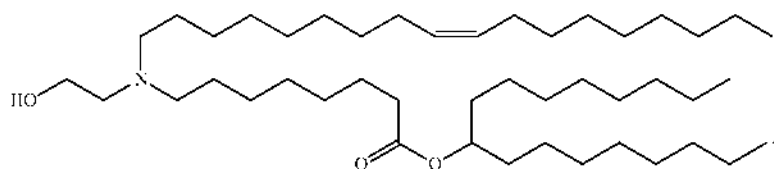


(Compound 29)

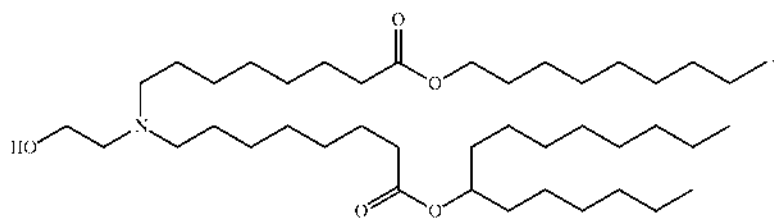
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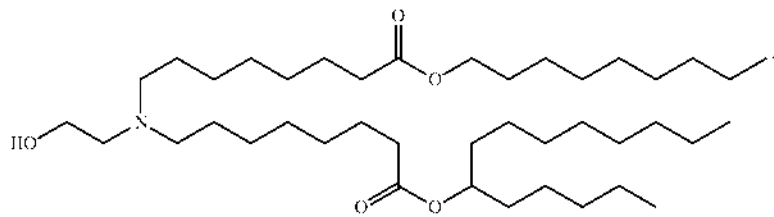
(Compound 30)



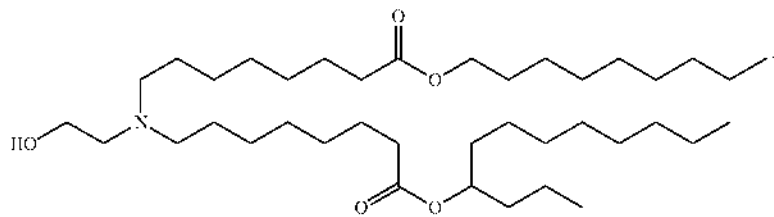
(Compound 31)



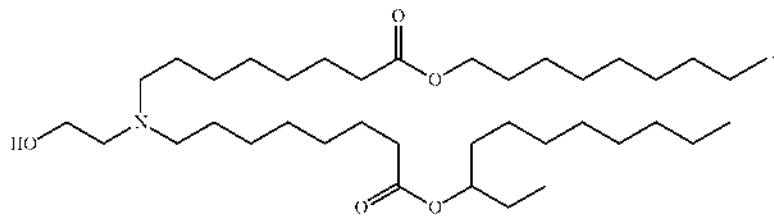
(Compound 32)



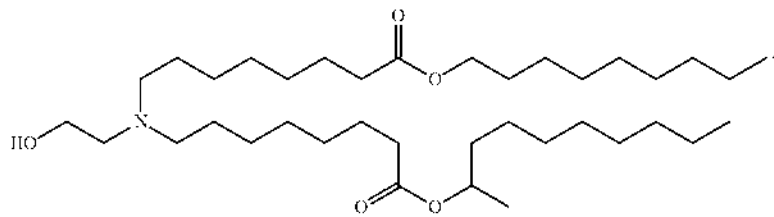
(Compound 33)



(Compound 34)

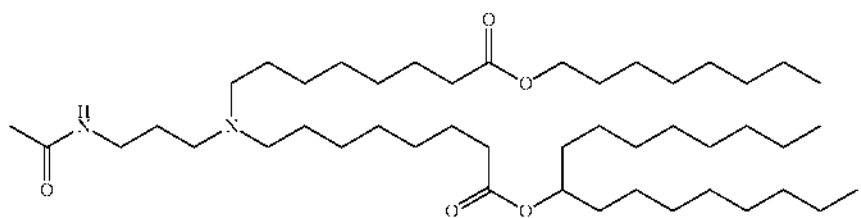


(Compound 35)

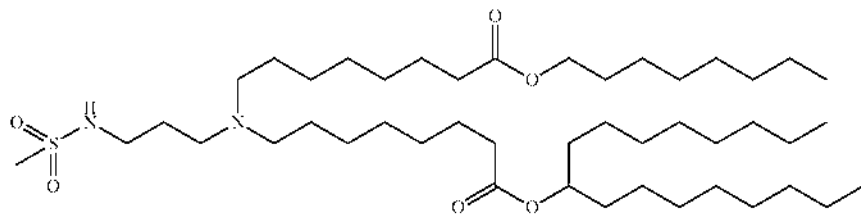


(Compound 36)

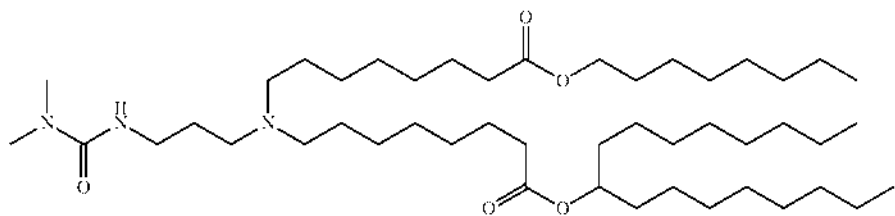
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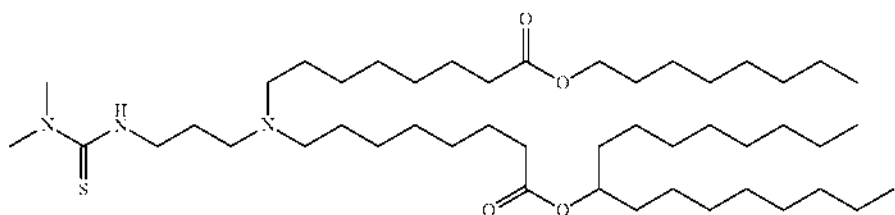
(Compound 37)



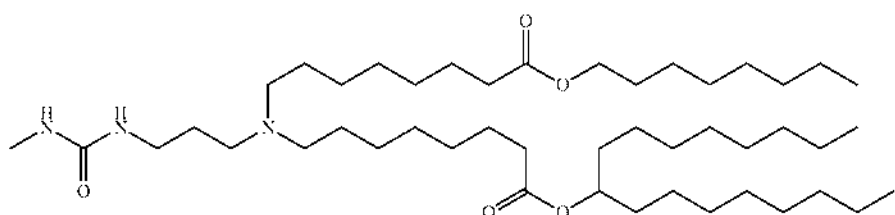
(Compound 38)



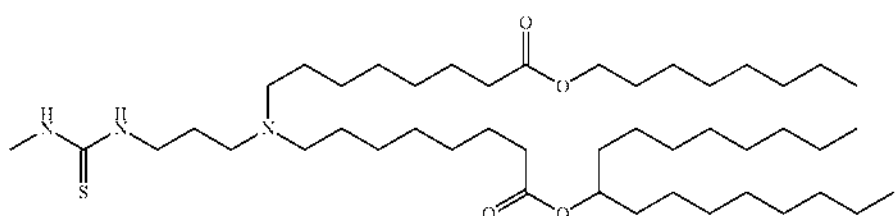
(Compound 39)



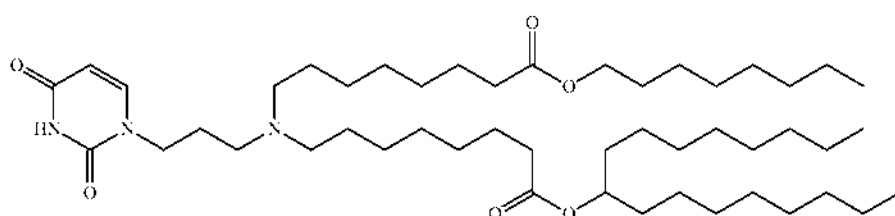
(Compound 40)



(Compound 41)

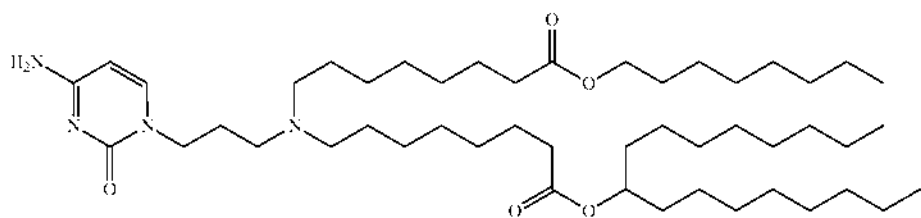


(Compound 42)

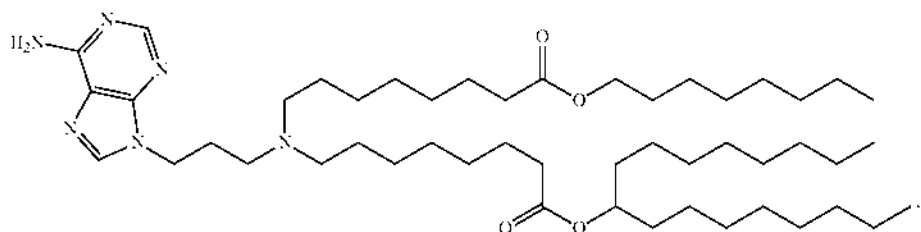


(Compound 43)

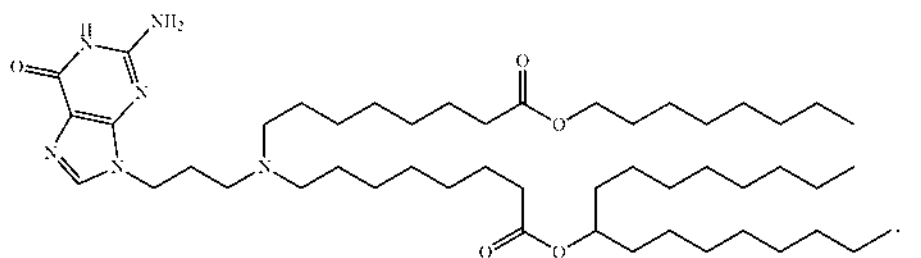
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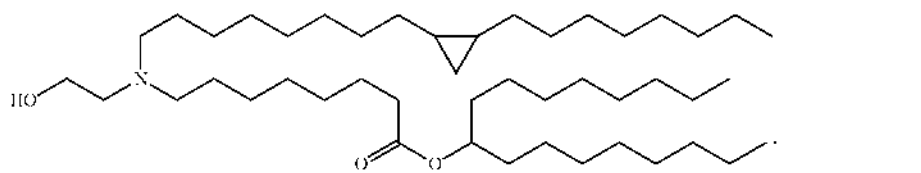
(Compound 44)



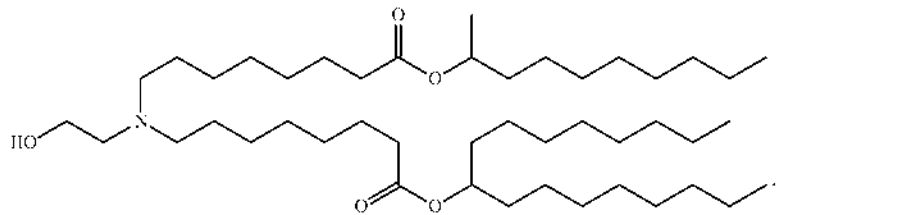
(Compound 45)



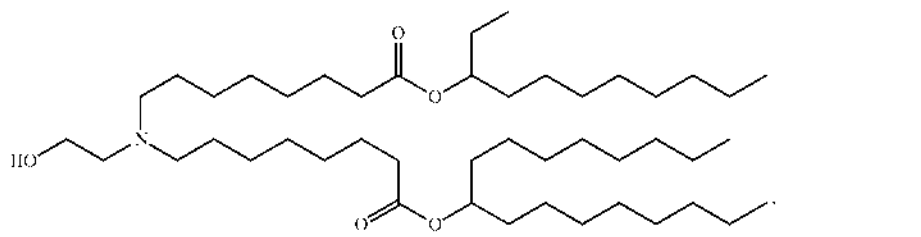
(Compound 46)



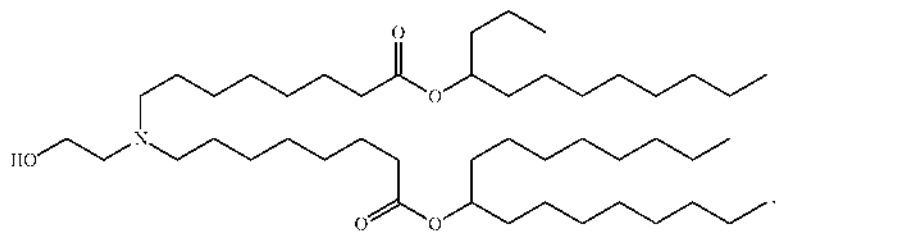
(Compound 47)



(Compound 48)

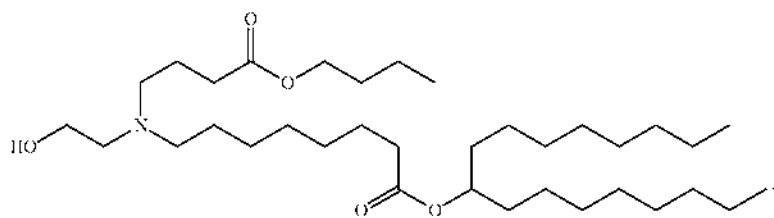


(Compound 49)

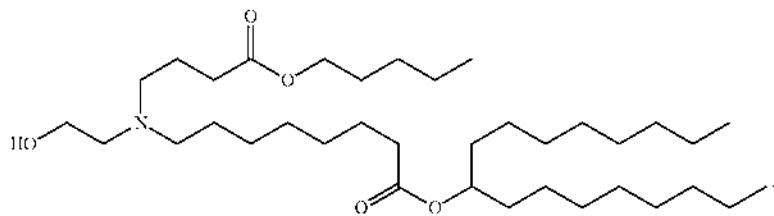


(Compound 50)

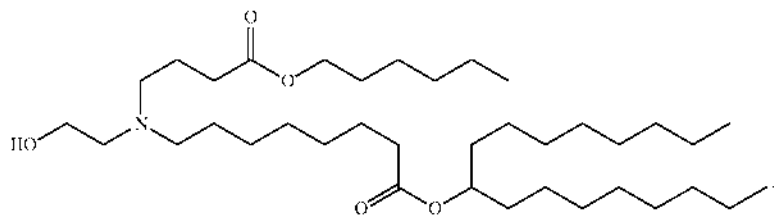
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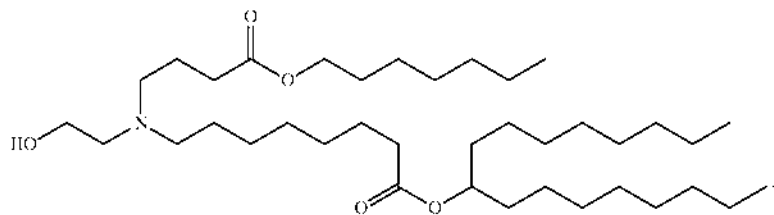
(Compound 51)



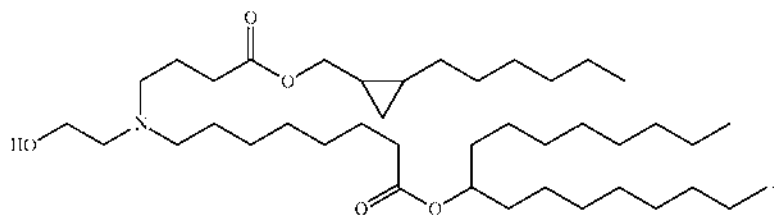
(Compound 52)



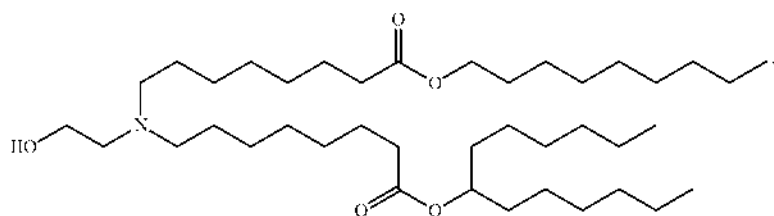
(Compound 53)



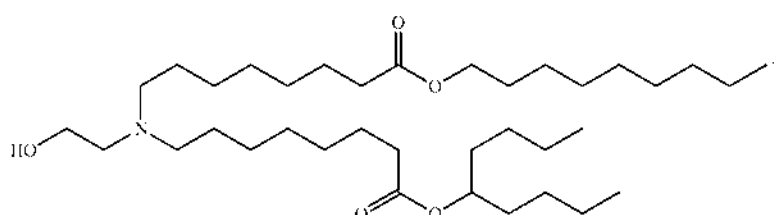
(Compound 54)



(Compound 55)

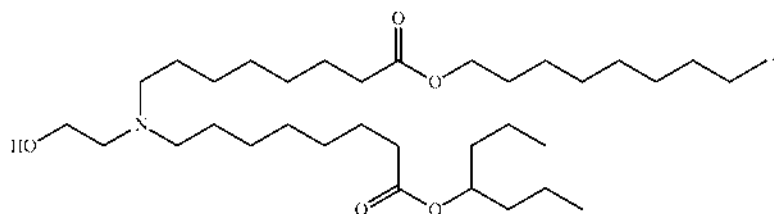


(Compound 56)

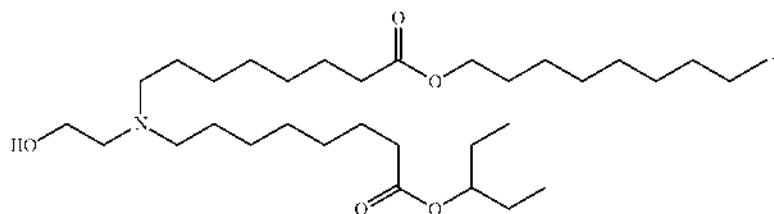


(Compound 57)

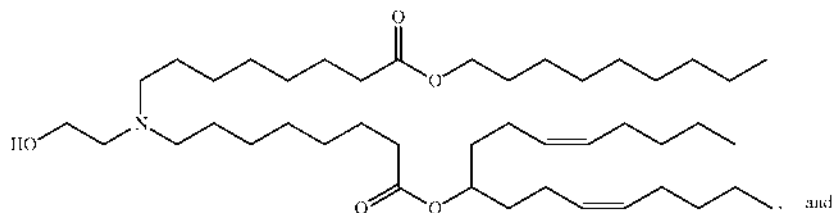
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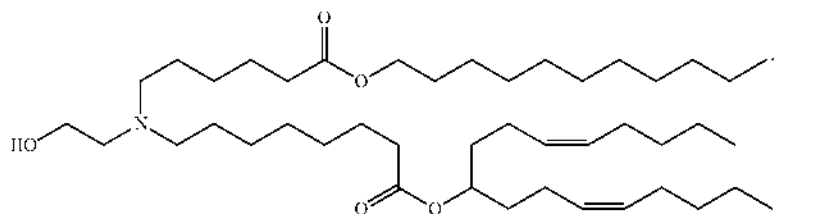
(Compound 58)



(Compound 59)



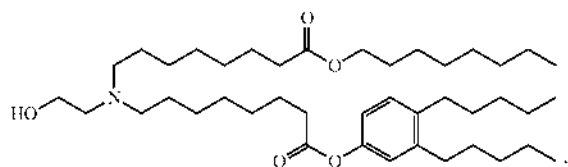
(Compound 60)



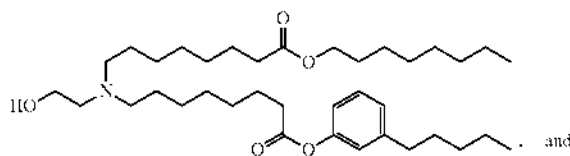
(Compound 61)

[0663] In further embodiments, the compound of Formula (I) is selected from the group consisting of:

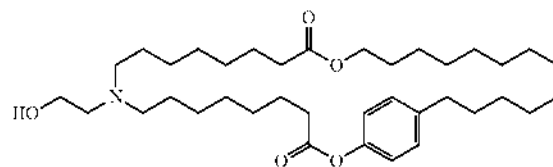
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(Compound 62)

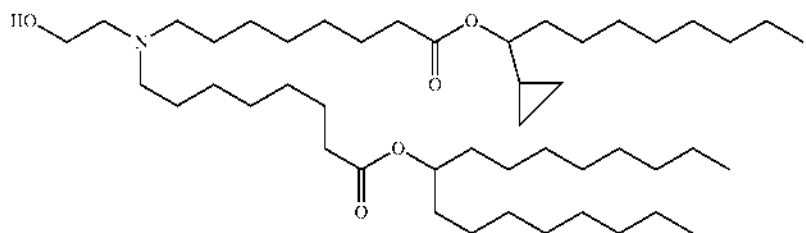


(Compound 63)

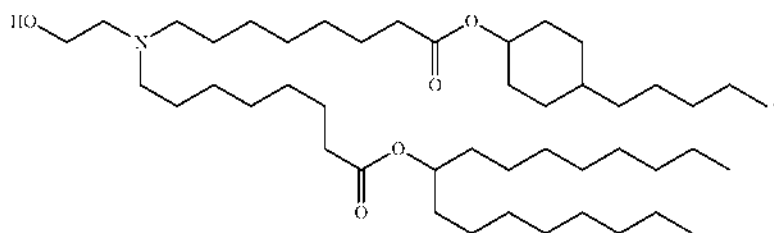


(Compound 64)

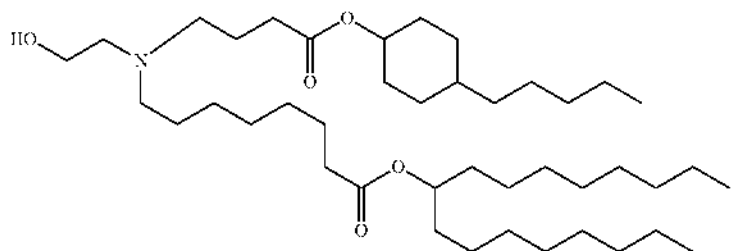
[0664] In some embodiments, the compound of Formula (I) is selected from the group consisting of:



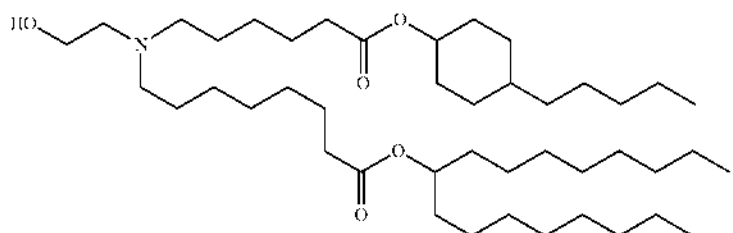
(Compound 65)



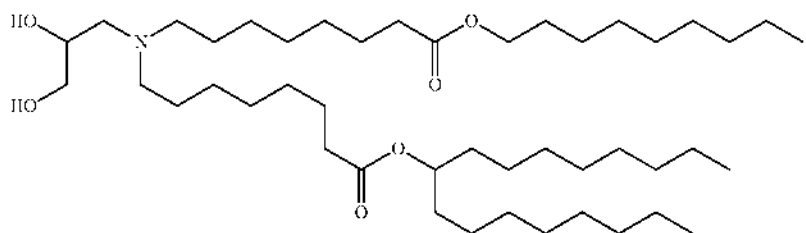
(Compound 66)



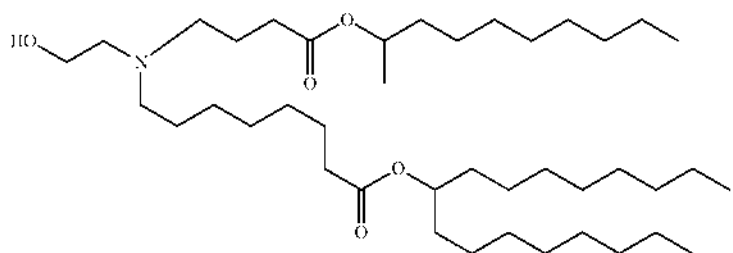
(Compound 67)



(Compound 68)

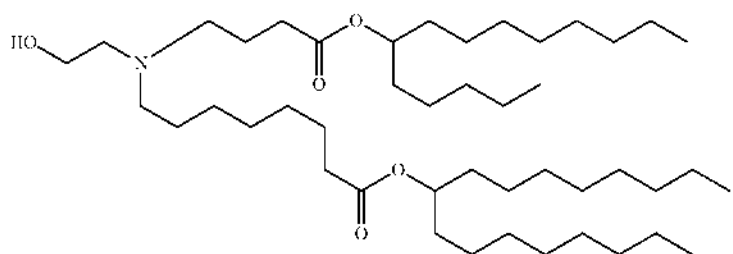


(Compound 69)

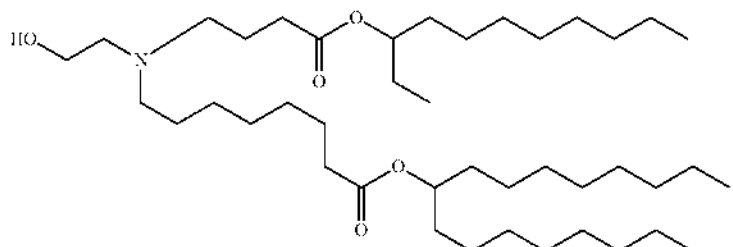


(Compound 70)

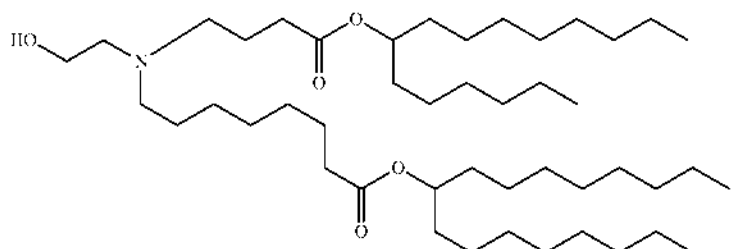
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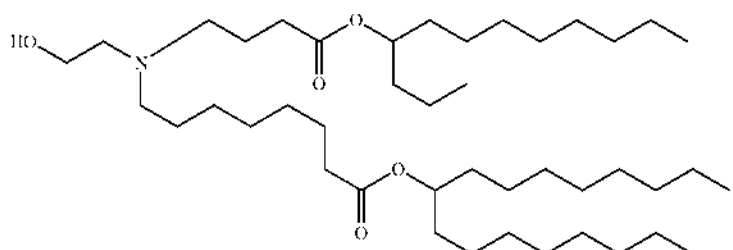
(Compound 71)



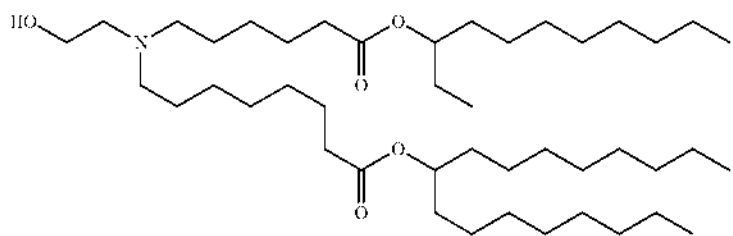
(Compound 72)



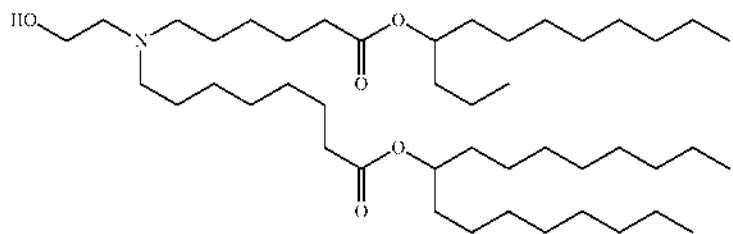
(Compound 73)



(Compound 74)

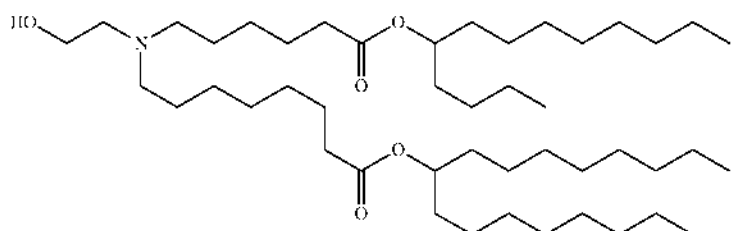


(Compound 75)

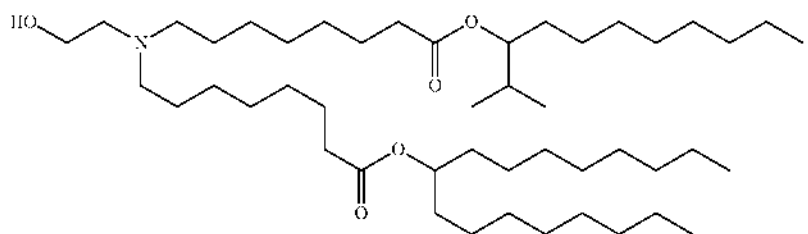


(Compound 76)

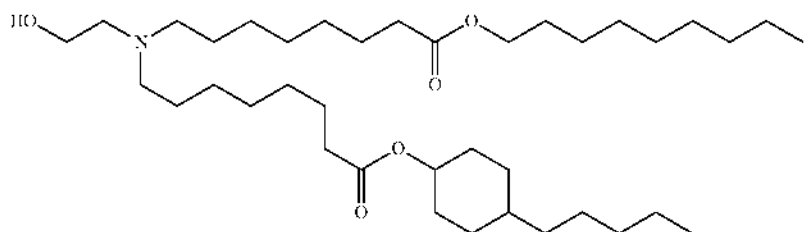
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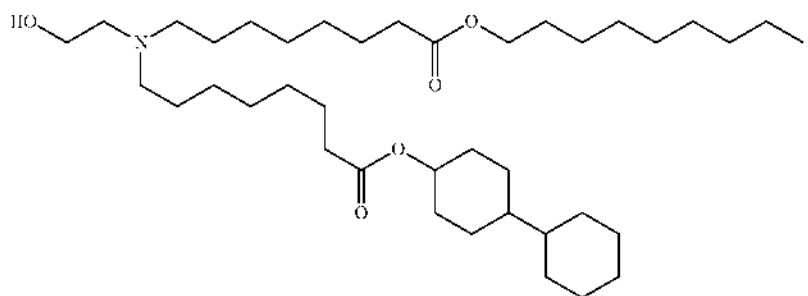
(Compound 77)



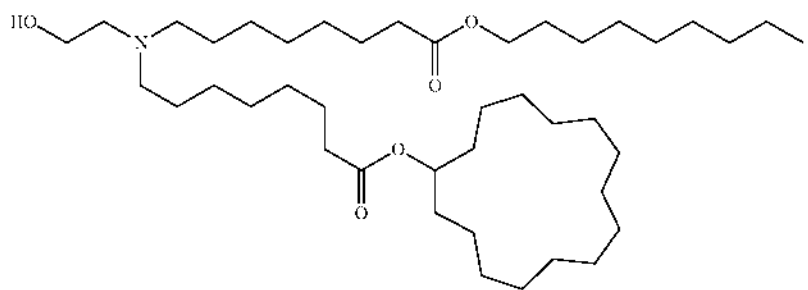
(Compound 78)



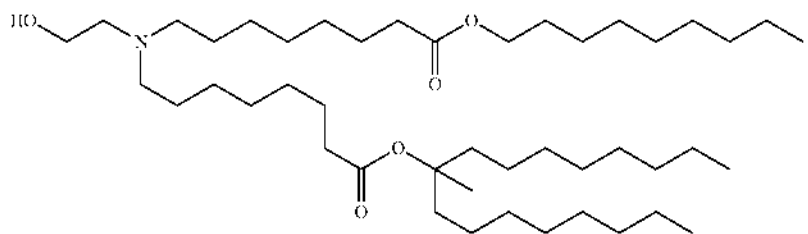
(Compound 79)



(Compound 80)

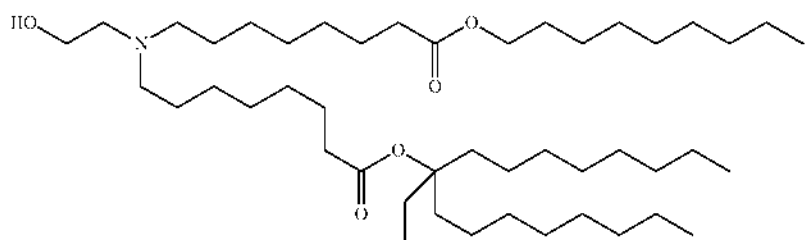


(Compound 81)

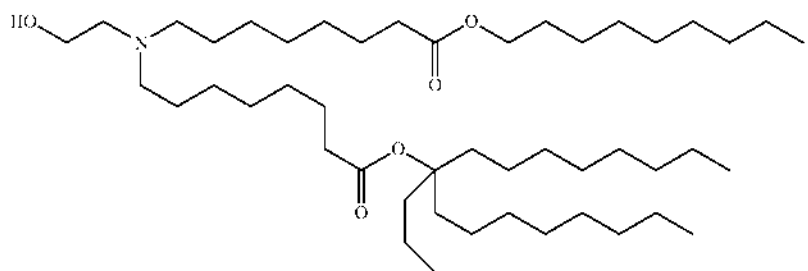


(Compound 82)

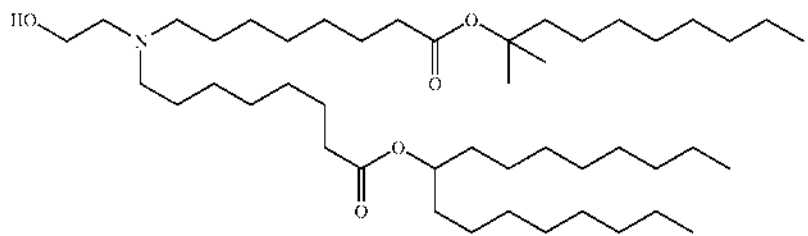
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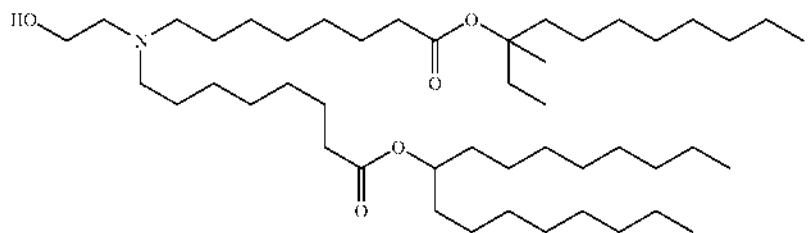
(Compound 83)



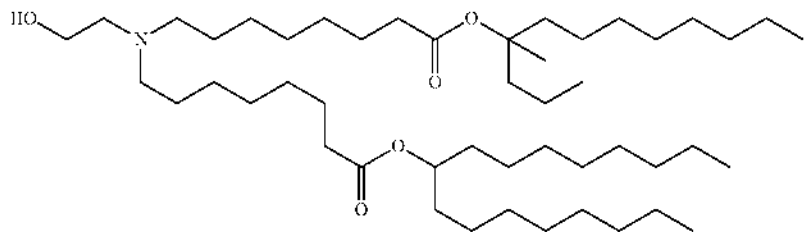
(Compound 84)



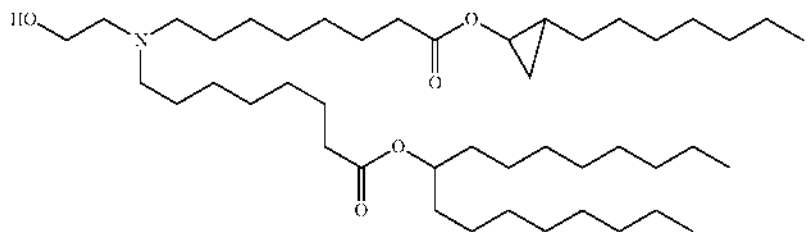
(Compound 85)



(Compound 86)

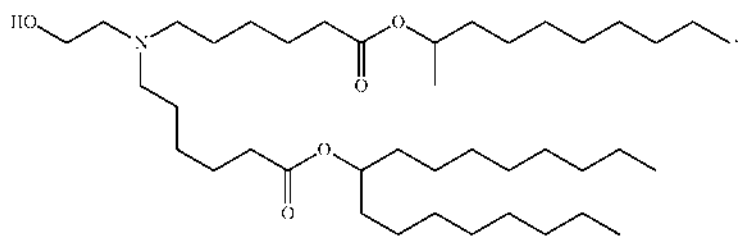


(Compound 87)

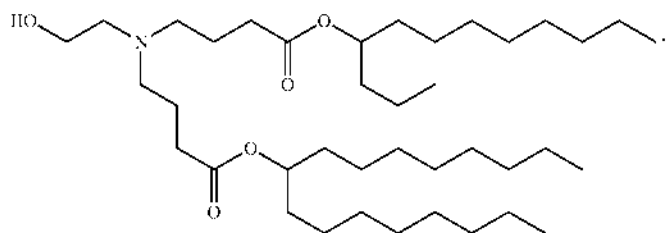


(Compound 88)

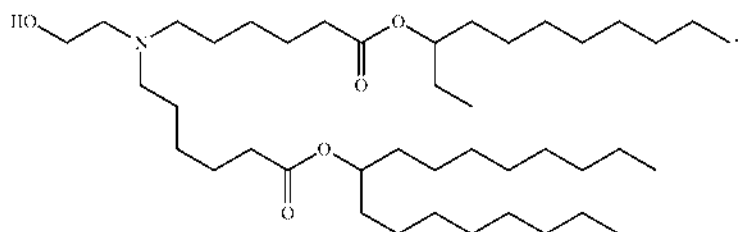
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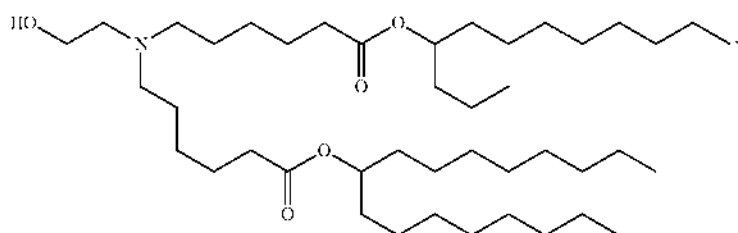
(Compound 89)



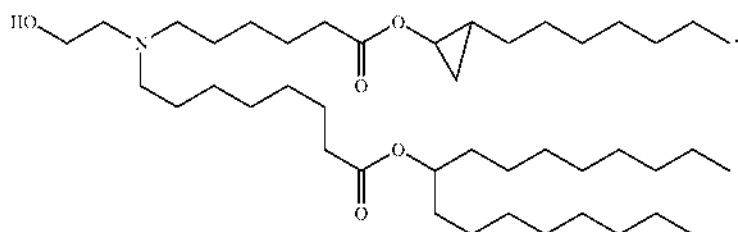
(Compound 90)



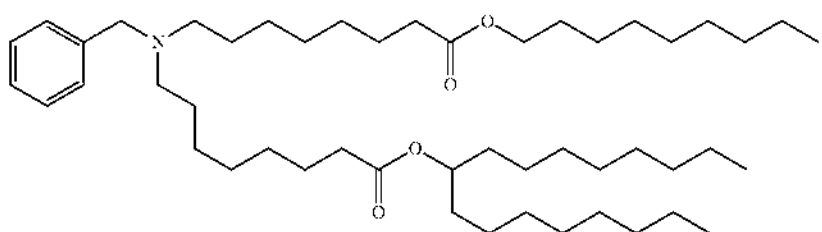
(Compound 91)



(Compound 92)

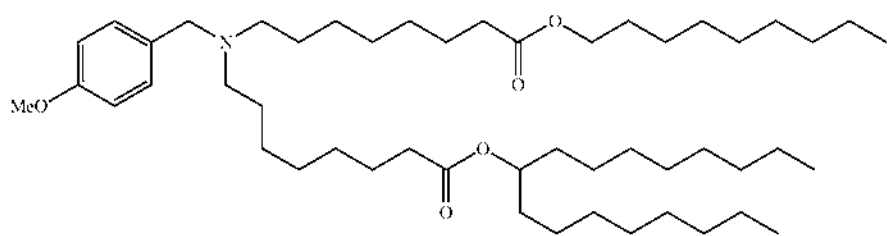


(Compound 93)

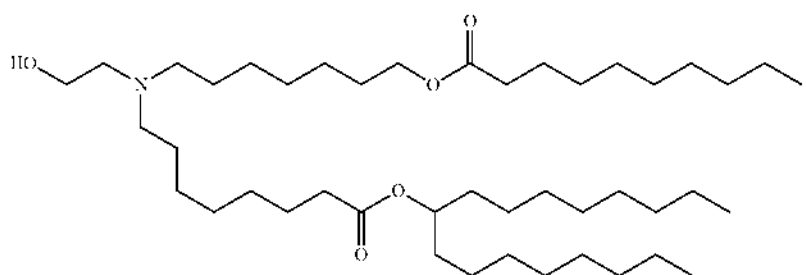


(Compound 94)

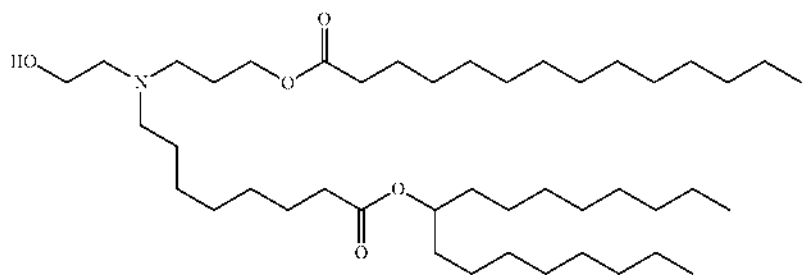
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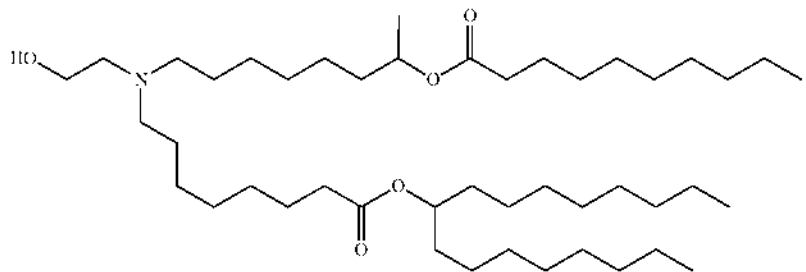
(Compound 95)



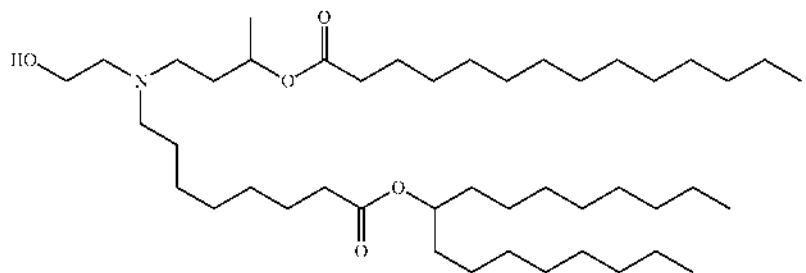
(Compound 96)



(Compound 97)

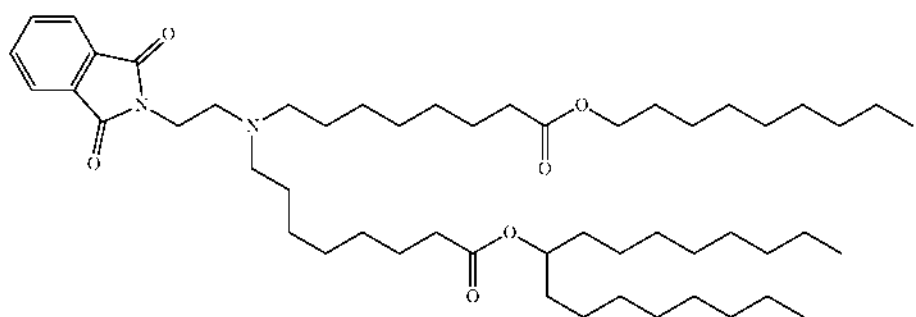


(Compound 98)

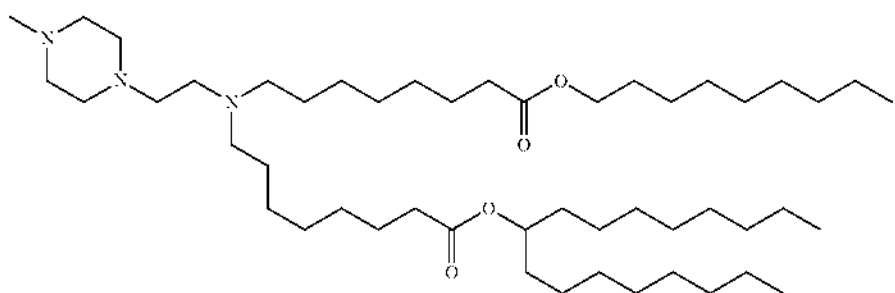


(Compound 99)

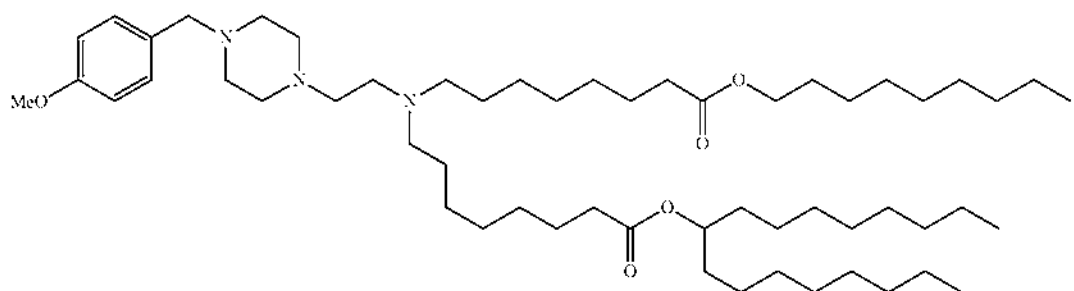
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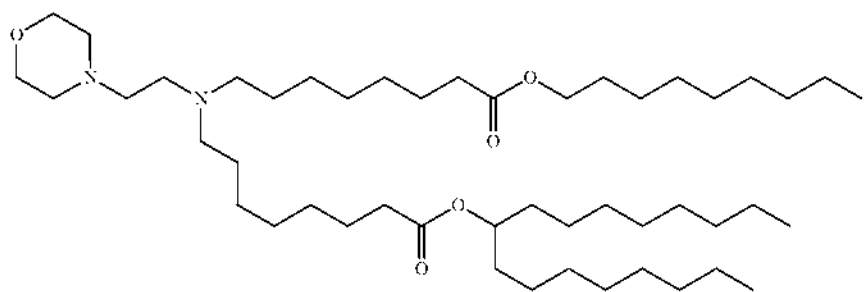
(Compound 100)



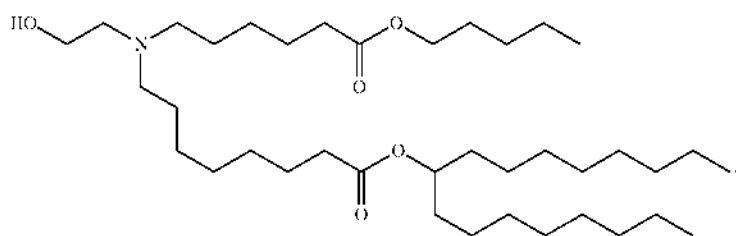
(Compound 101)



(Compound 102)

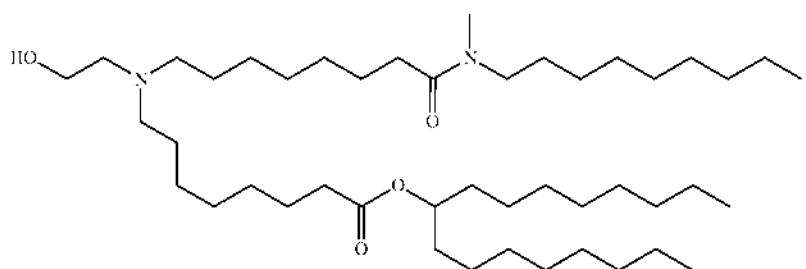


(Compound 103)

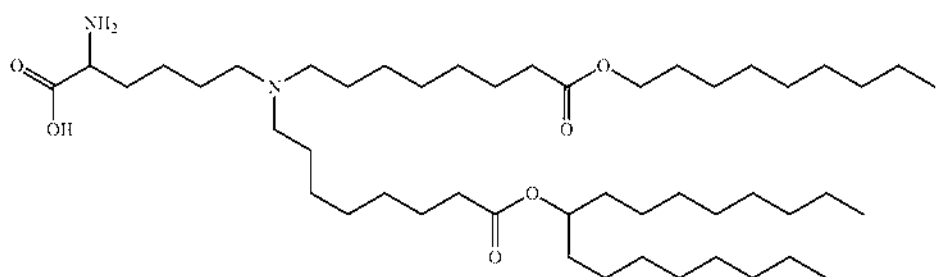


(Compound 104)

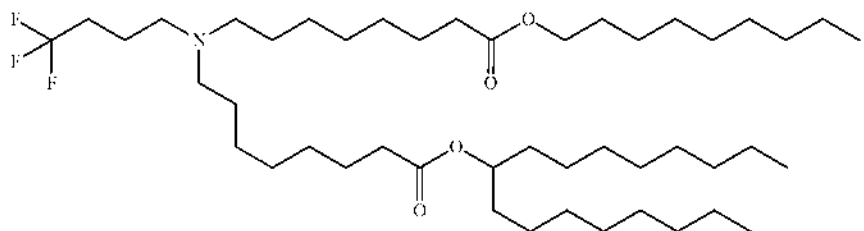
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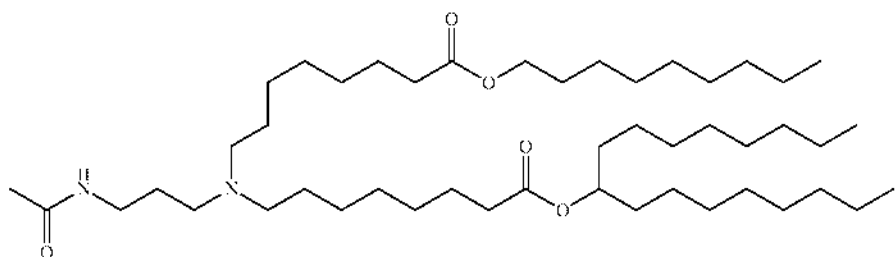
(Compound 105)



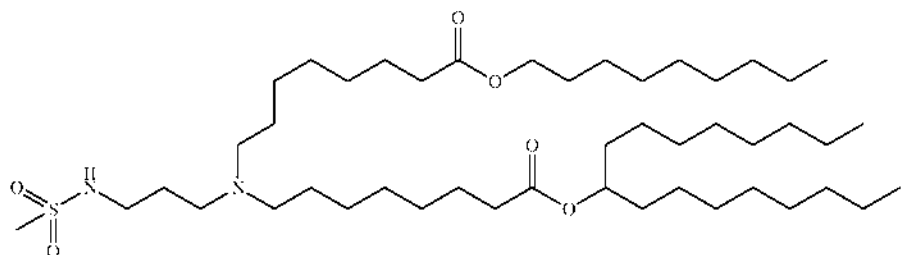
(Compound 106)



(Compound 107)



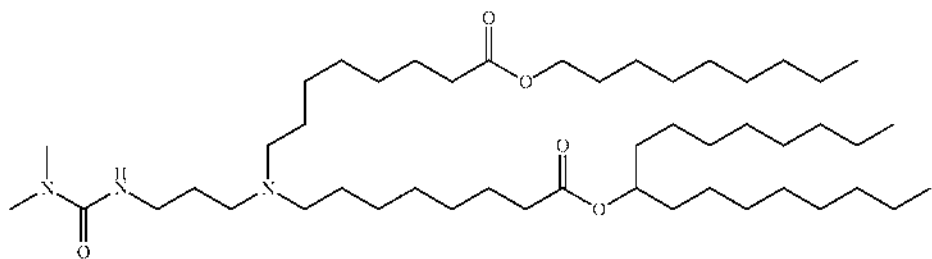
(Compound 108)



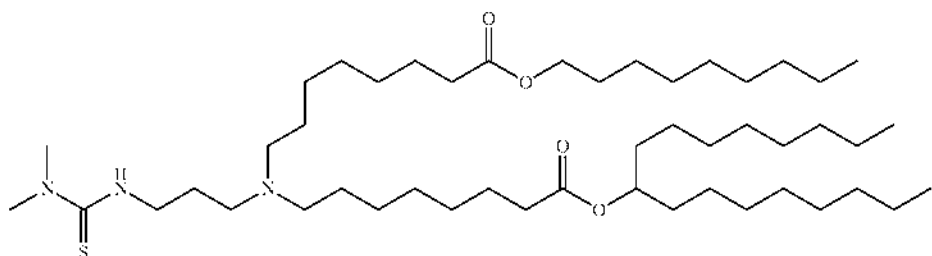
(Compound 109)

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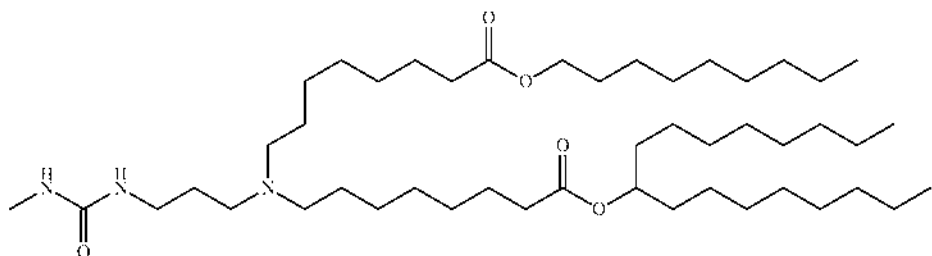
(Compound 110)



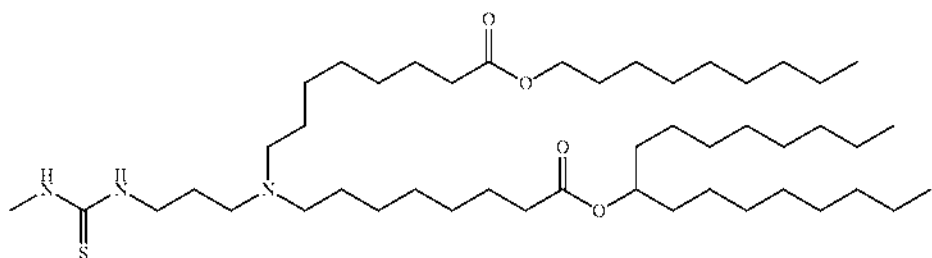
(Compound 111)



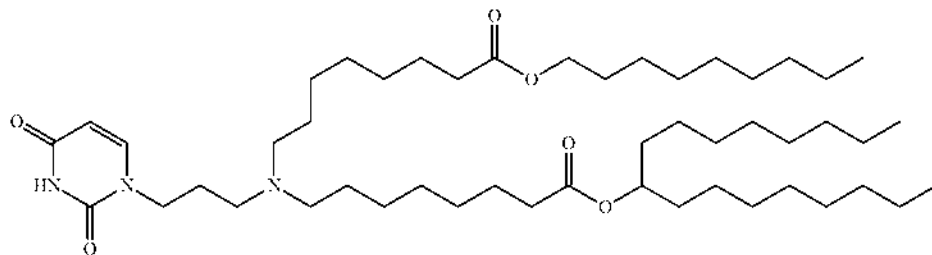
(Compound 112)



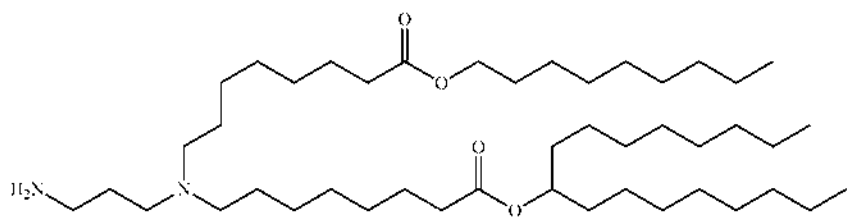
(Compound 113)



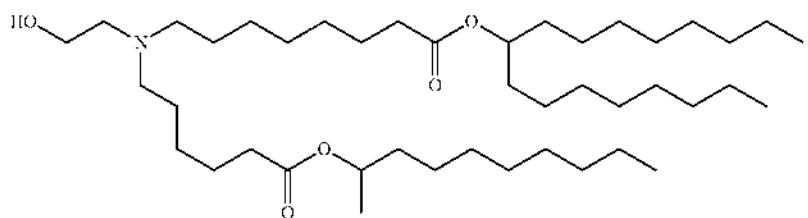
(Compound 114)



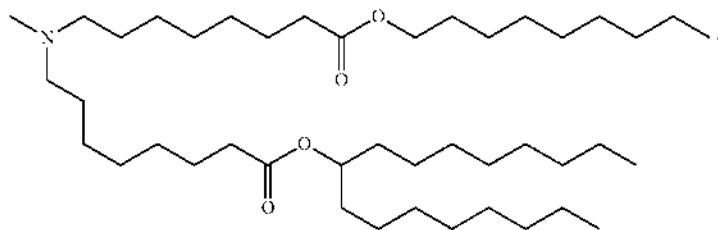
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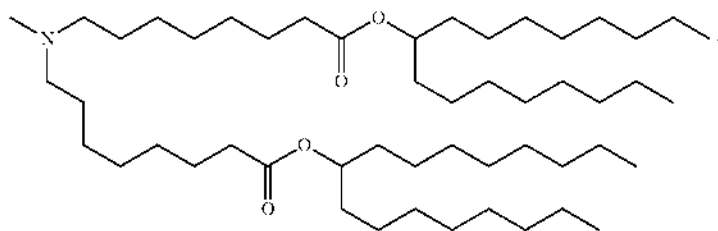
(Compound 121)



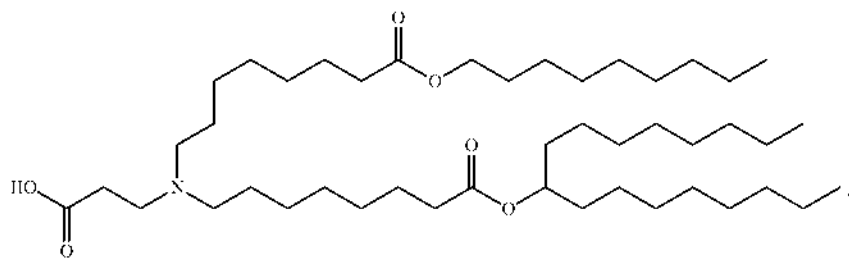
(Compound 122)



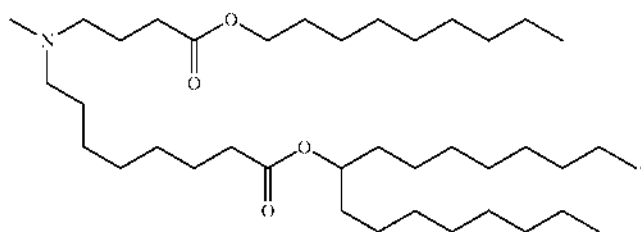
(Compound 123)



(Compound 124)

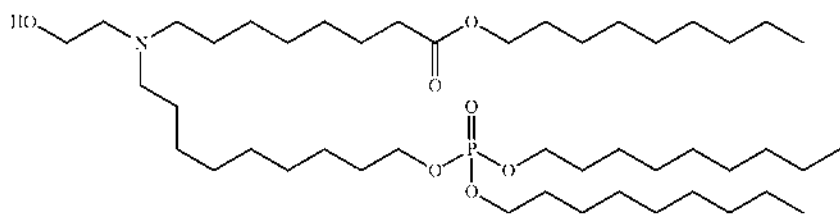


(Compound 125)

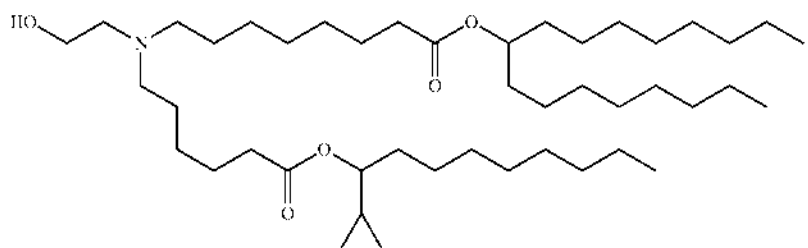


(Compound 126)

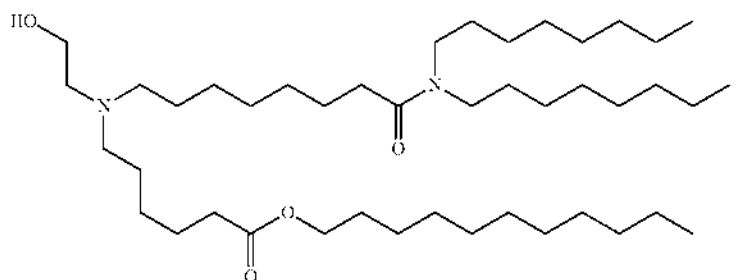
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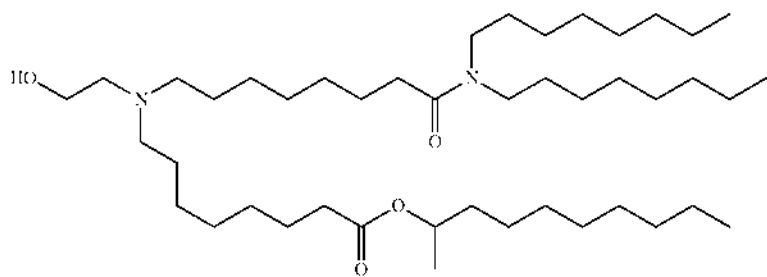
(Compound 127)



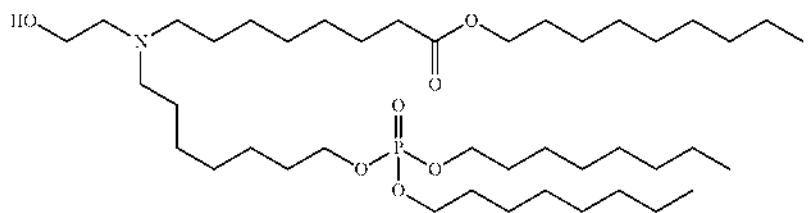
(Compound 128)



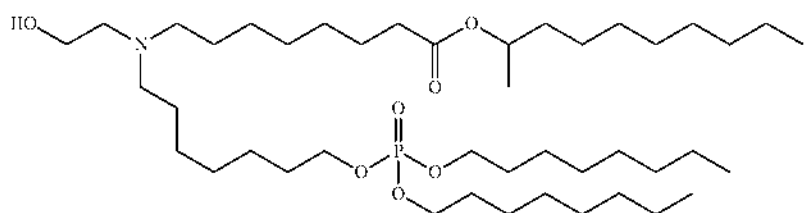
(Compound 129)



(Compound 130)

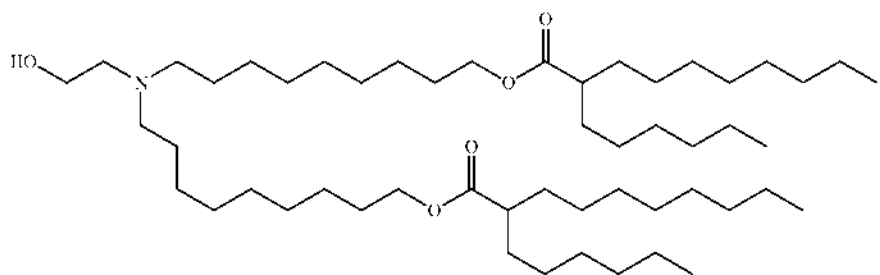


(Compound 131)

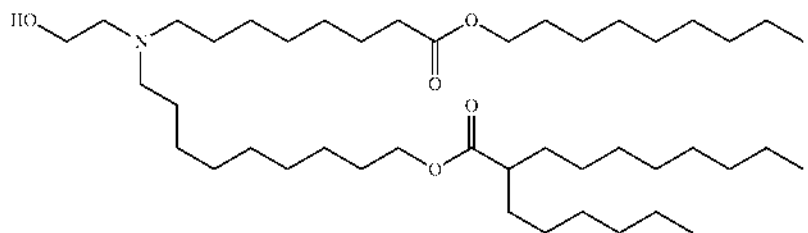


(Compound 132)

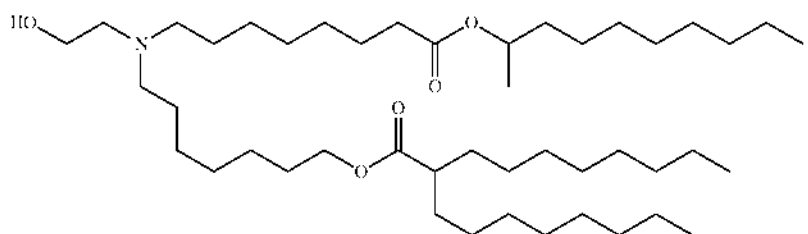
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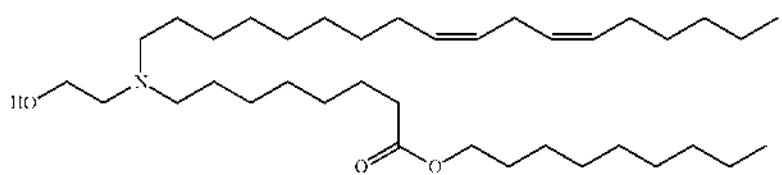
(Compound 133)



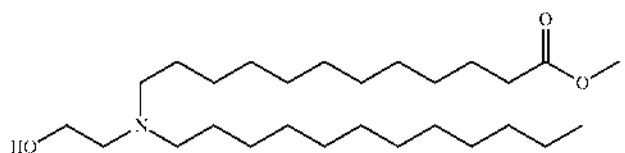
(Compound 134)



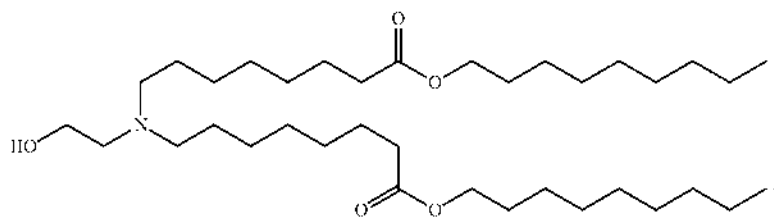
(Compound 135)



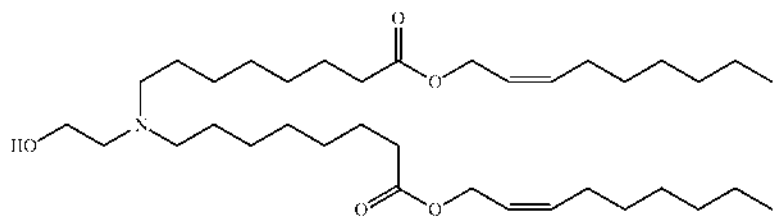
(Compound 136)



(Compound 137)

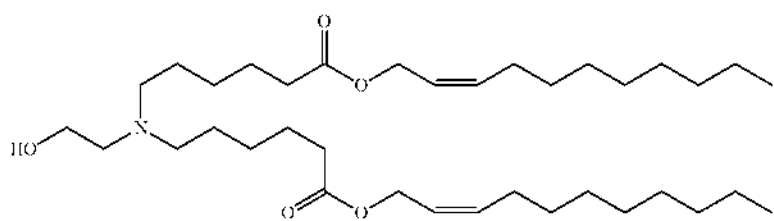


(Compound 138)

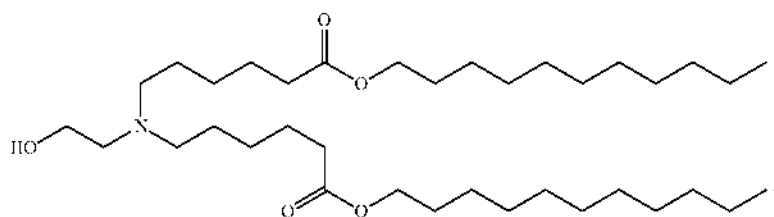


(Compound 139)

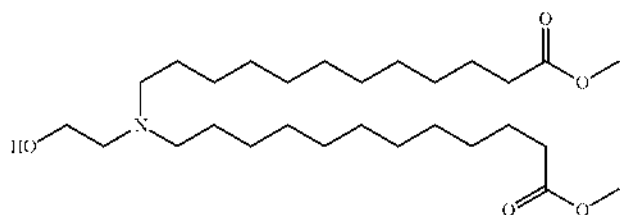
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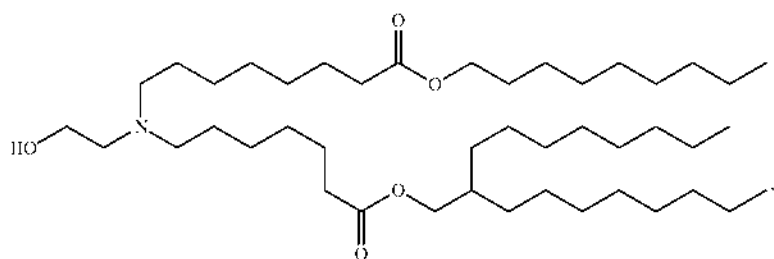
(Compound 140)



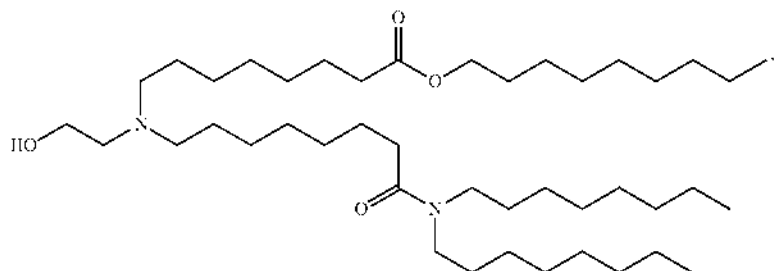
(Compound 141)



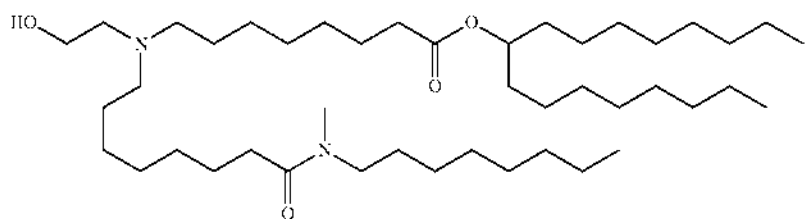
(Compound 142)



(Compound 143)

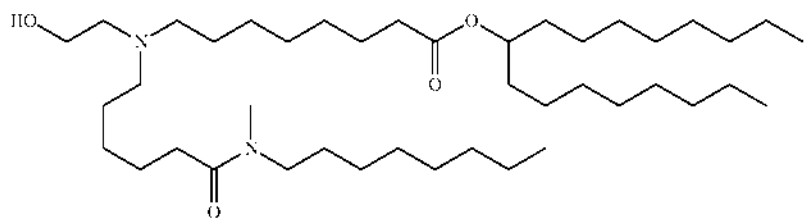


(Compound 144)

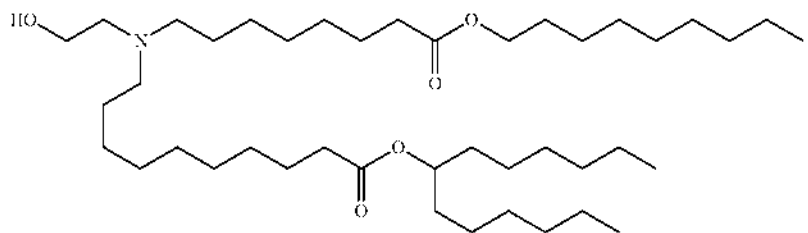


(Compound 145)

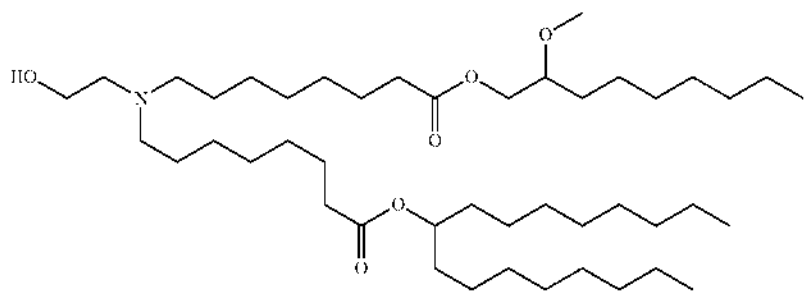
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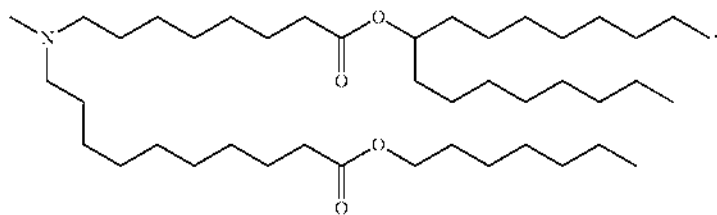
(Compound 146)



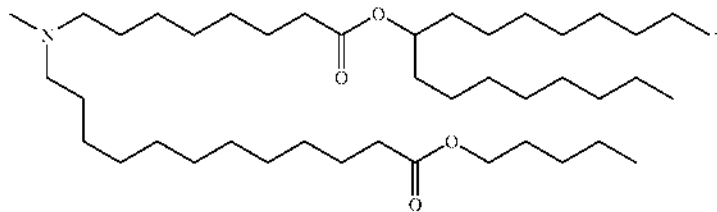
(Compound 147)



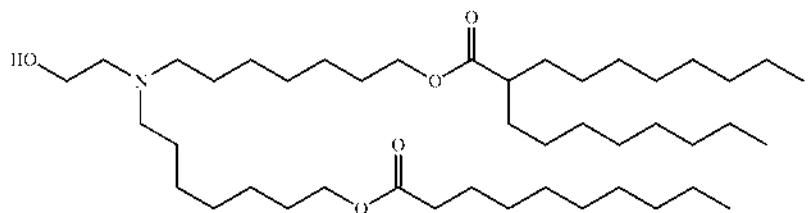
(Compound 148)



(Compound 149)



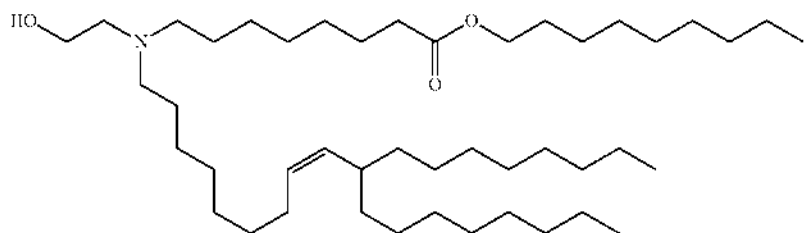
(Compound 150)



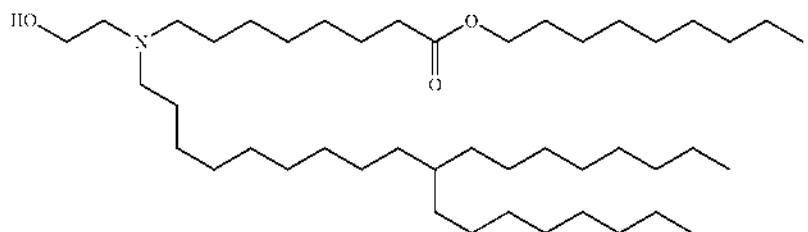
(Compound 151)

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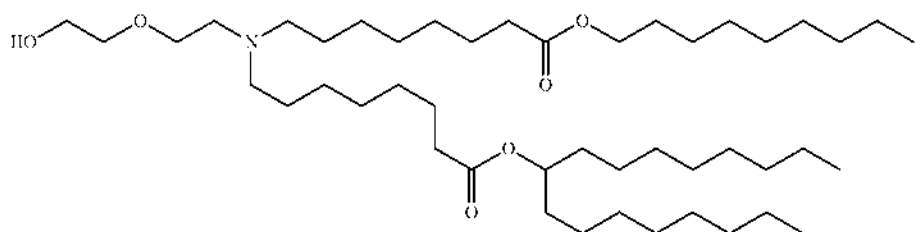
(Compound 152)



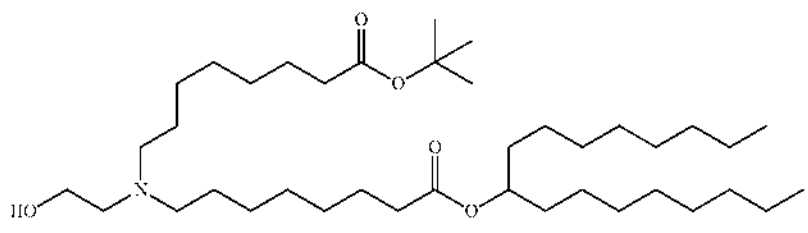
(Compound 153)



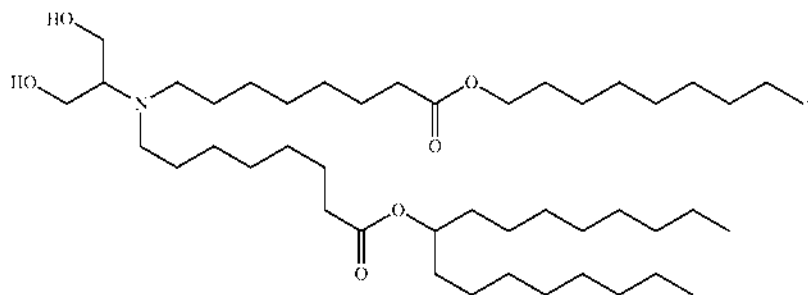
(Compound 154)



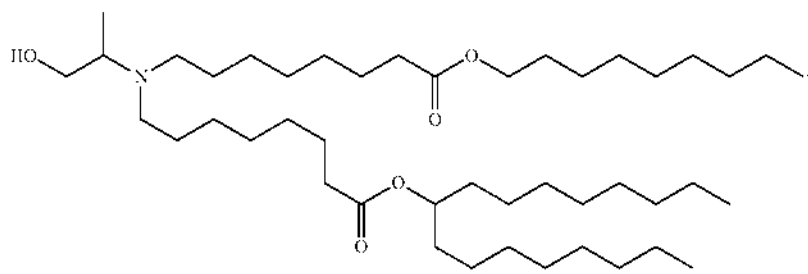
(Compound 155)



(Compound 156)

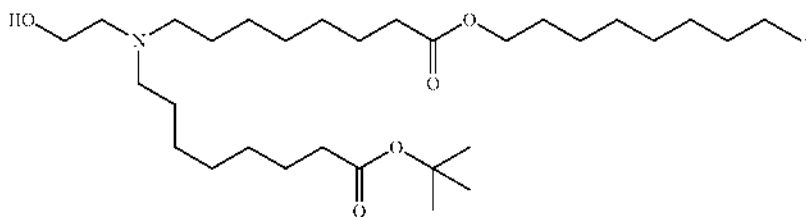


(Compound 157)

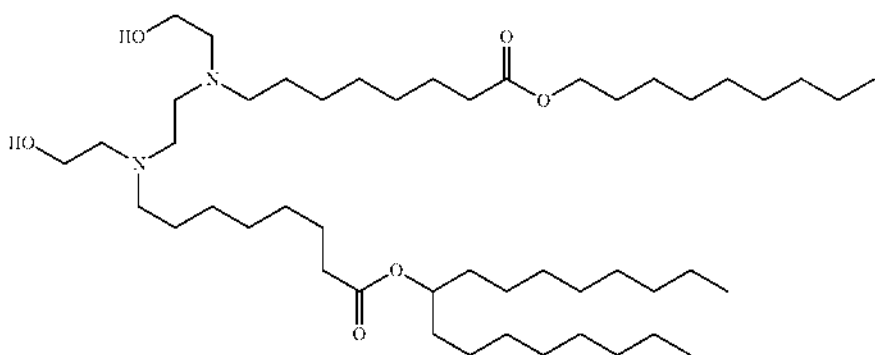


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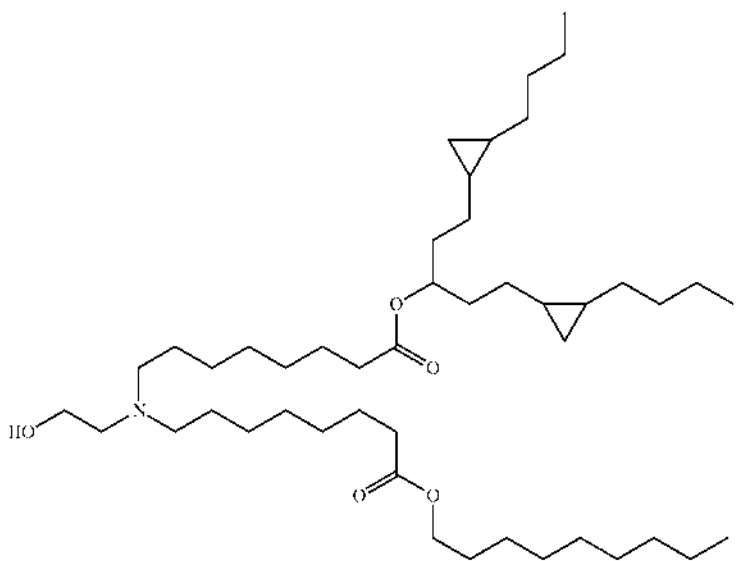
(Compound 158)



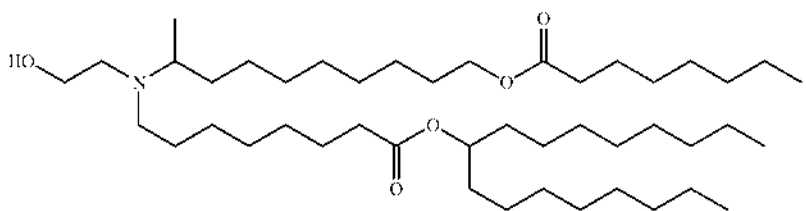
(Compound 159)



(Compound 160)

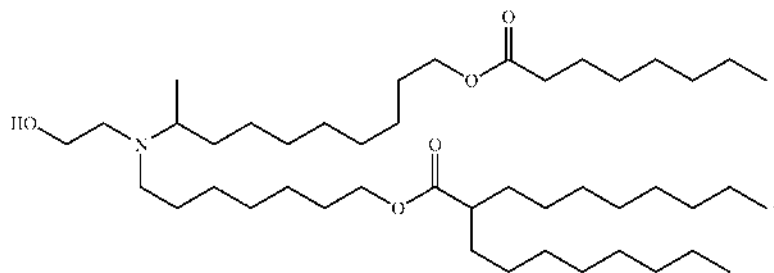


(Compound 161)

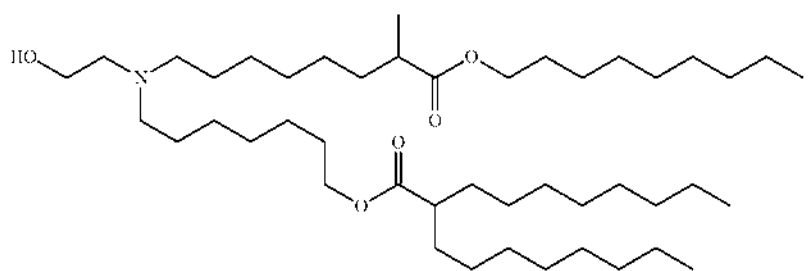


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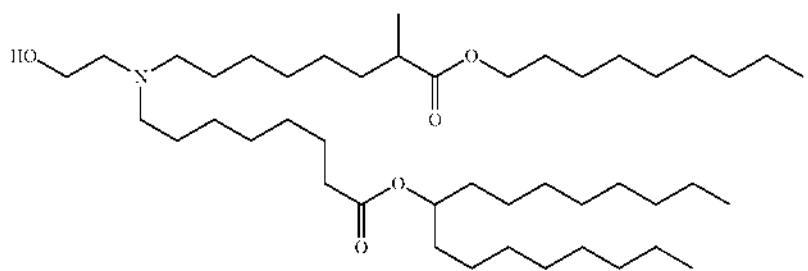
(Compound 162)



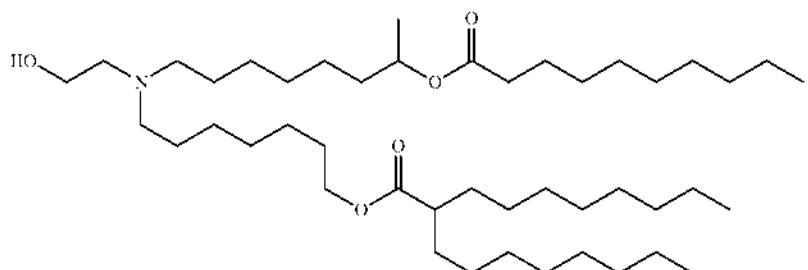
(Compound 163)



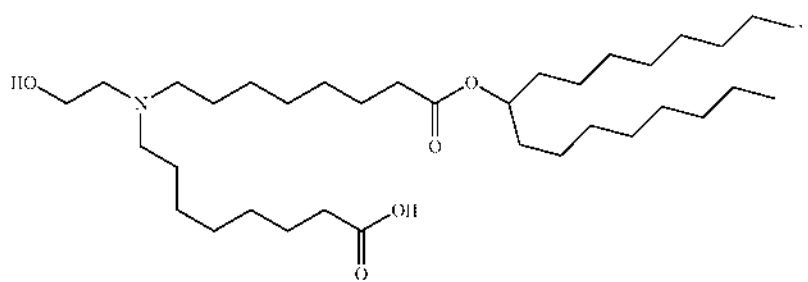
(Compound 164)



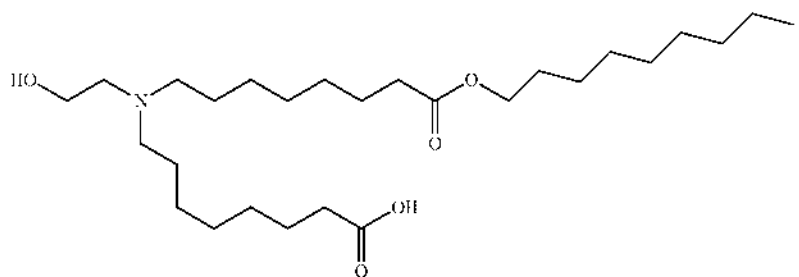
(Compound 165)



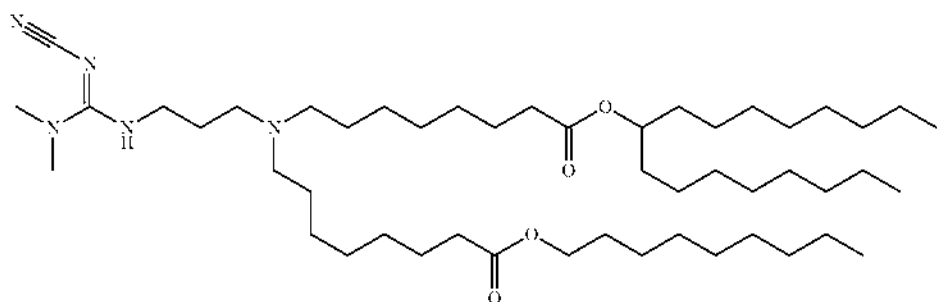
(Compound 166)



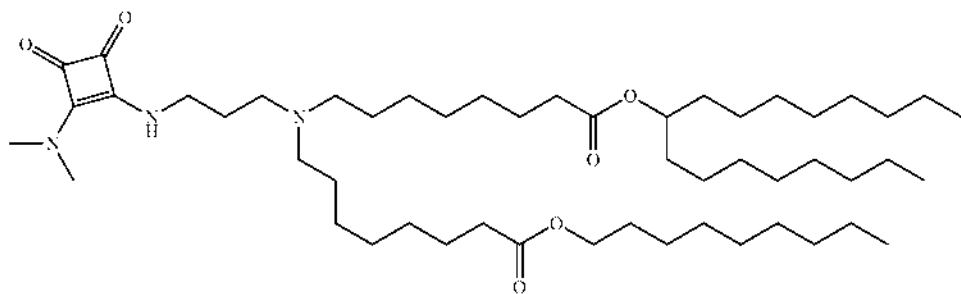
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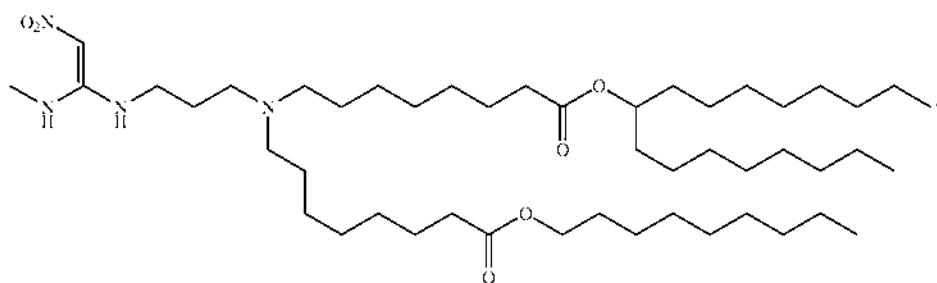
(Compound 167)



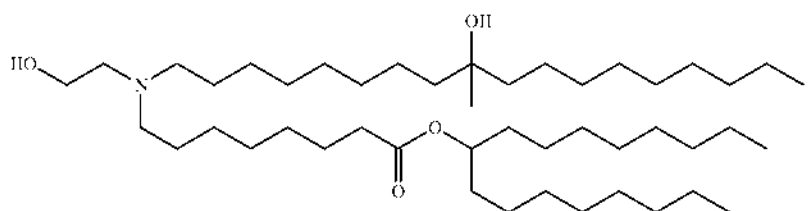
(Compound 168)



(Compound 169)

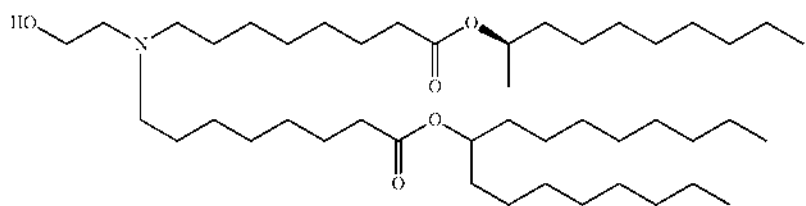


(Compound 170)

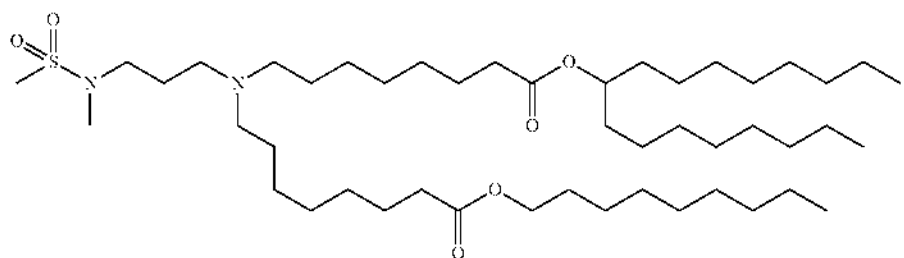


(Compound 171)

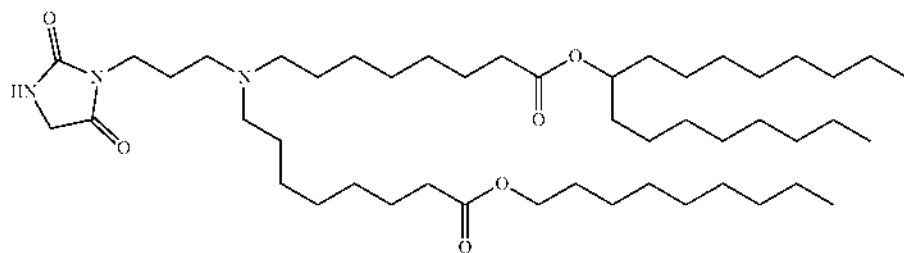
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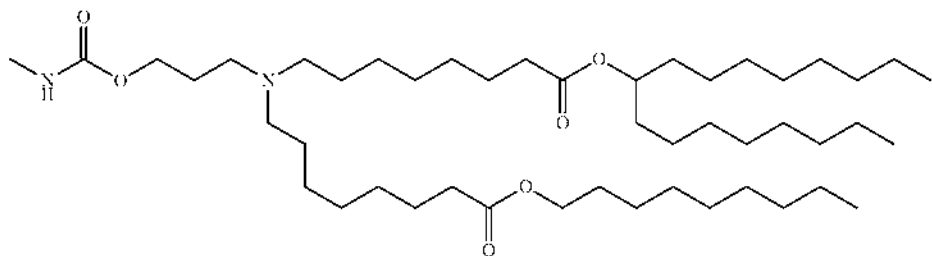
(Compound 172)



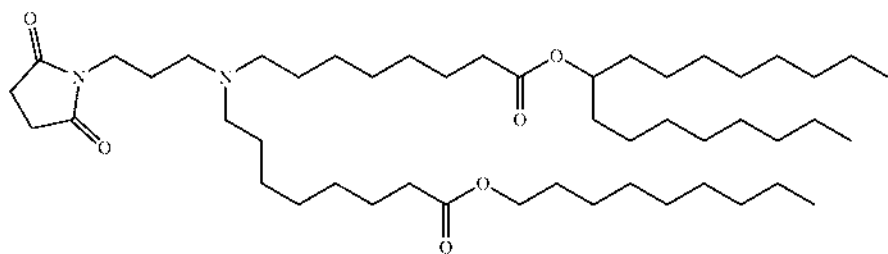
(Compound 173)



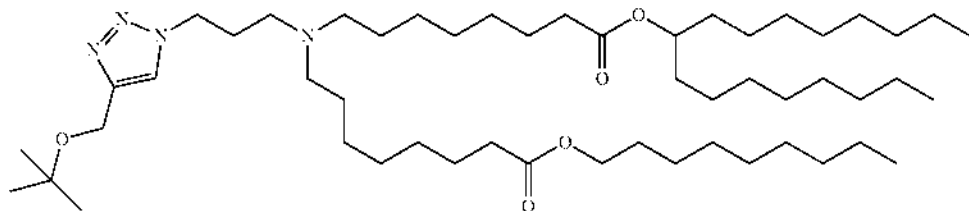
(Compound 174)



(Compound 175)



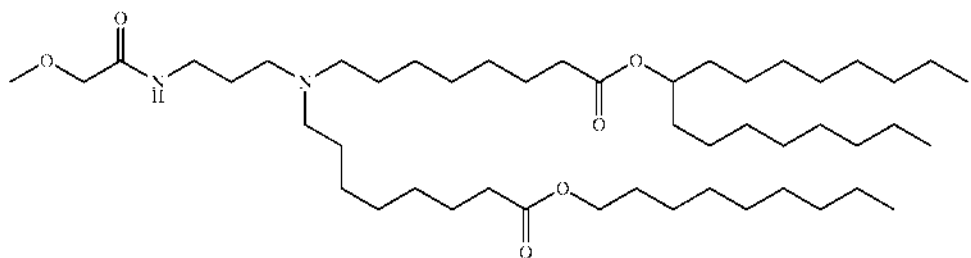
(Compound 176)



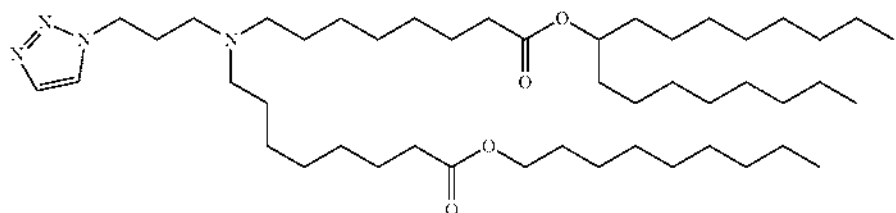
(Compound 177)

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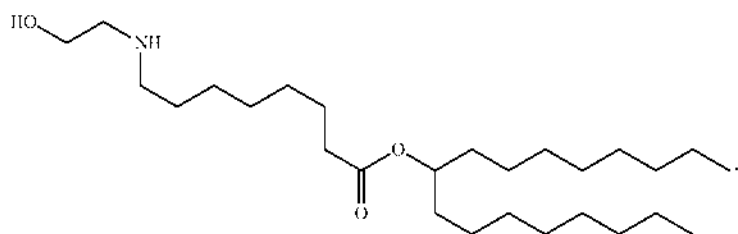
(Compound 178)



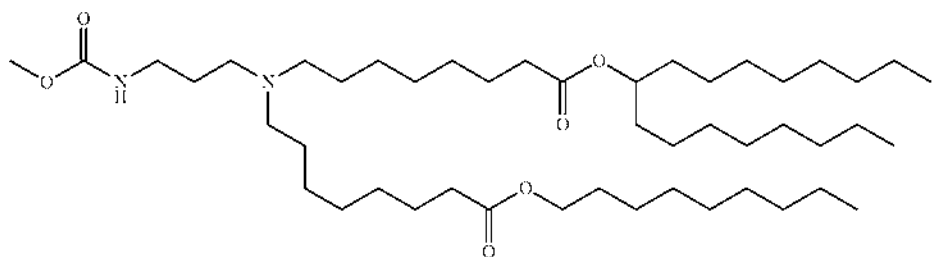
(Compound 179)



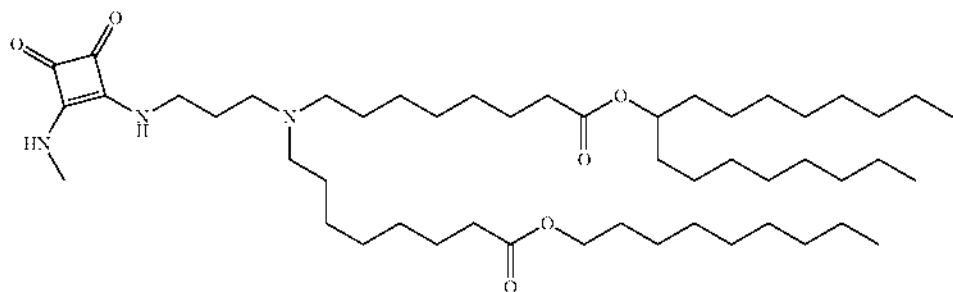
(Compound 180)



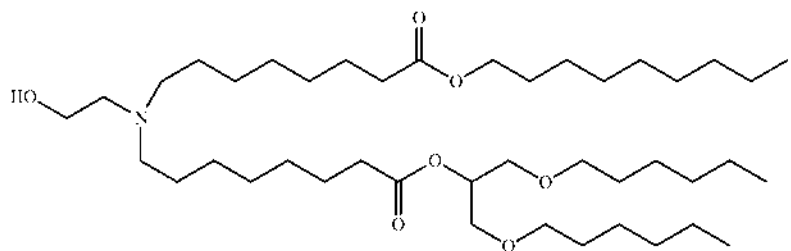
(Compound 181)



(Compound 182)

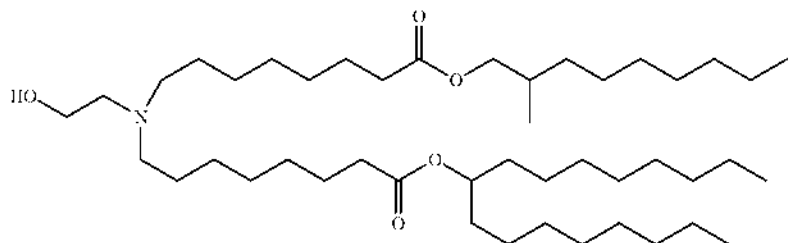


(Compound 183)

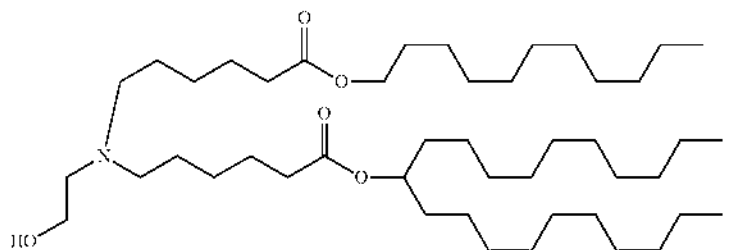


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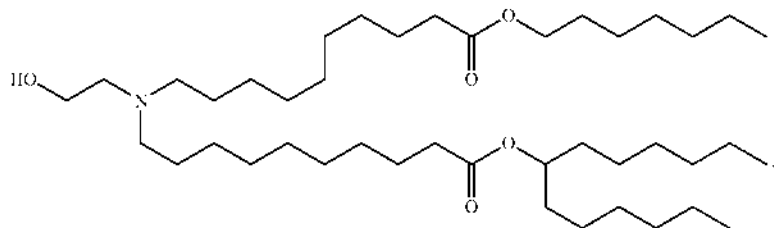
(Compound 184)



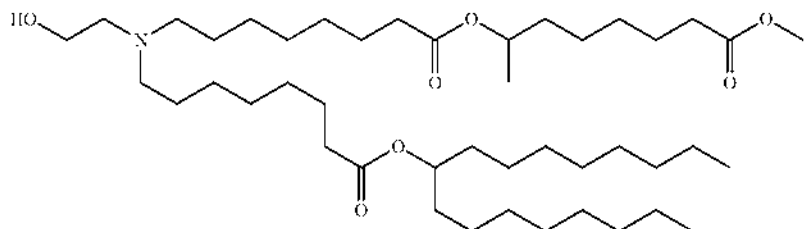
(Compound 185)



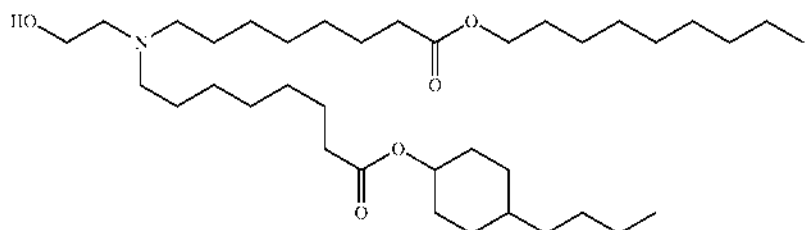
(Compound 186)



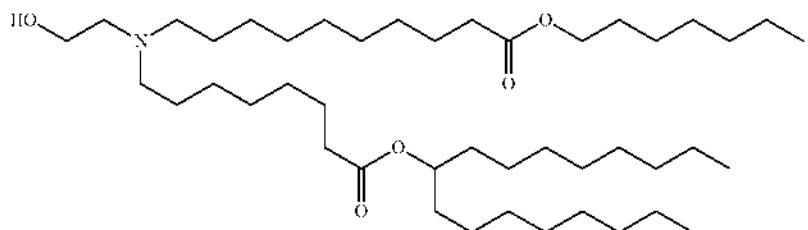
(Compound 187)



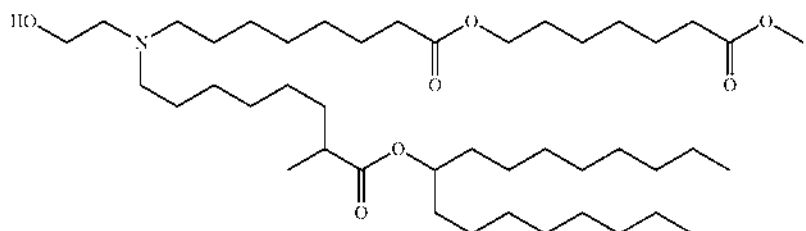
(Compound 188)



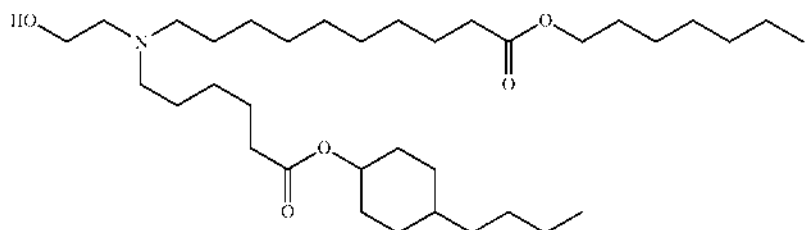
(Compound 189)



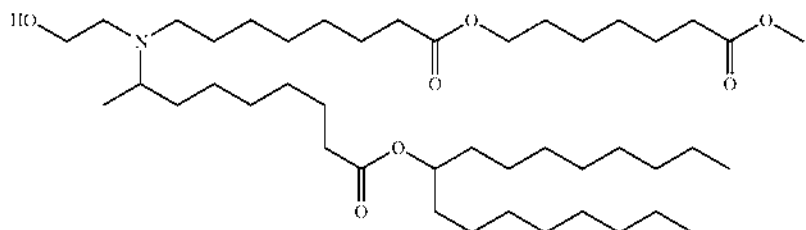
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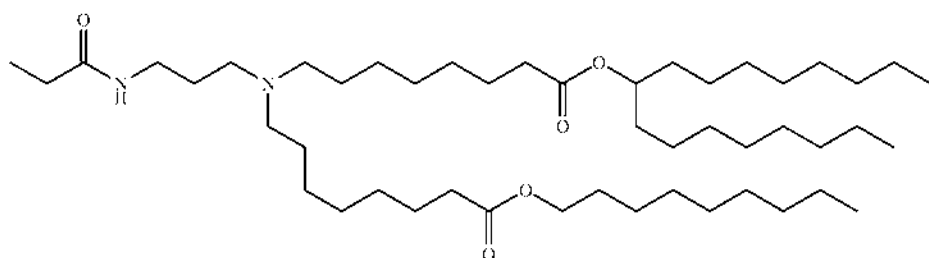
(Compound 190)



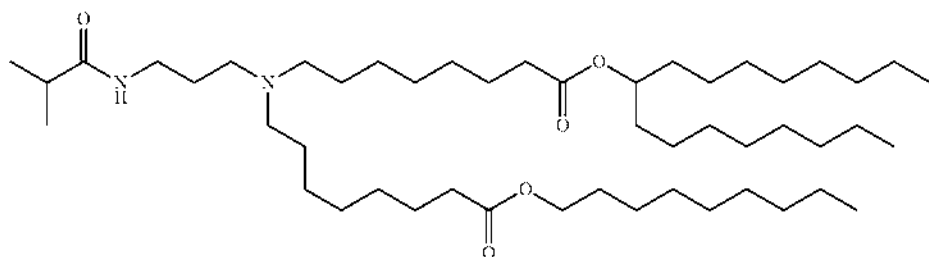
(Compound 191)



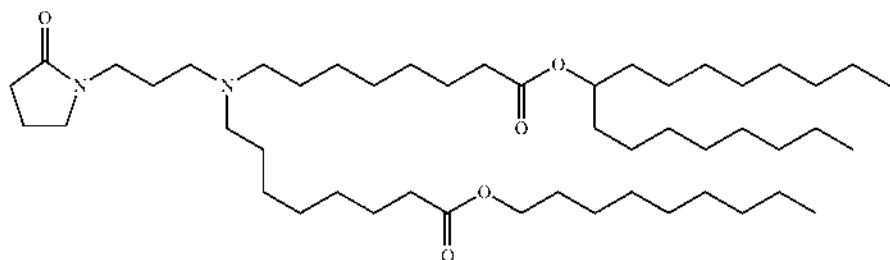
(Compound 192)



(Compound 193)



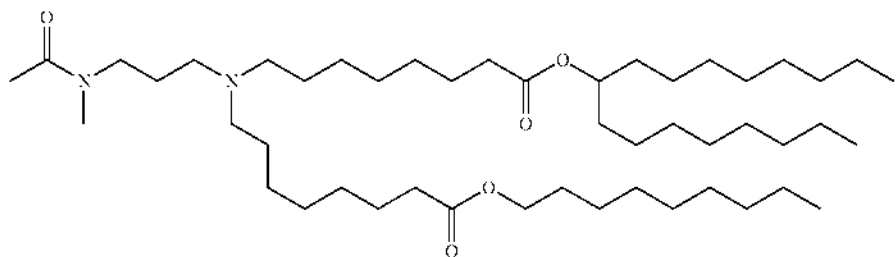
(Compound 194)



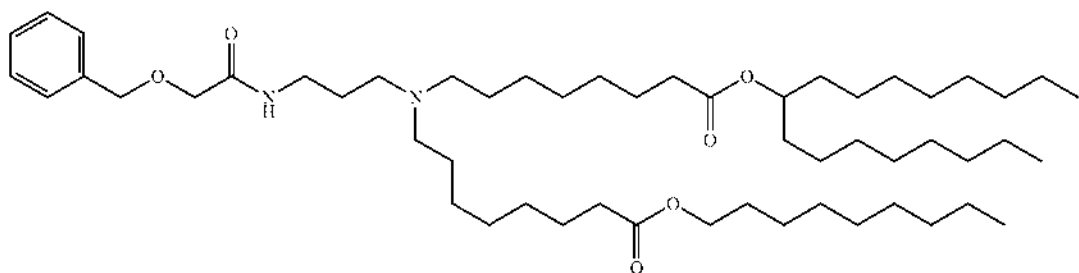
(Compound 195)

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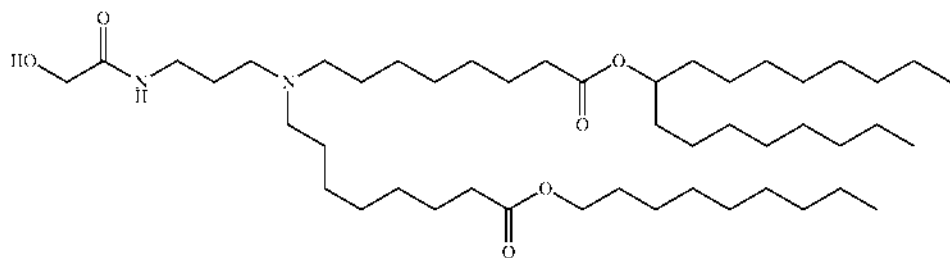
(Compound 196)



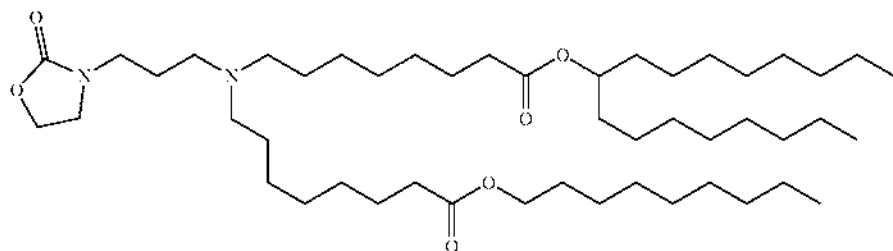
(Compound 197)



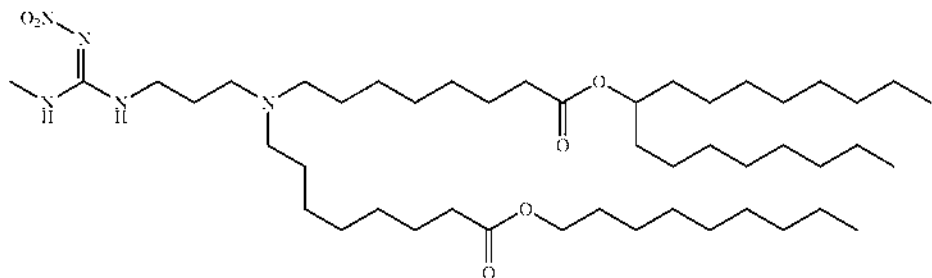
(Compound 198)



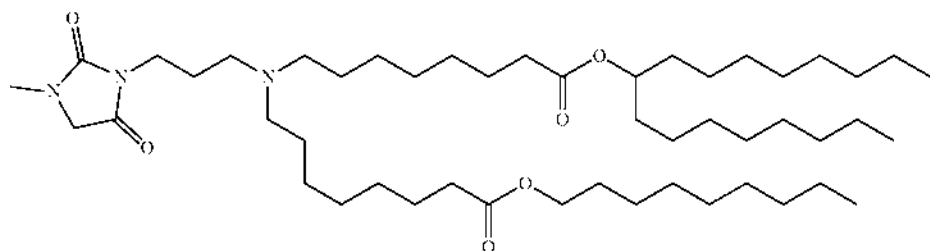
(Compound 199)



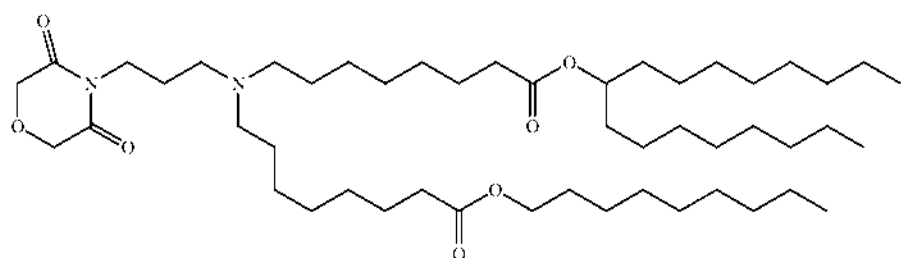
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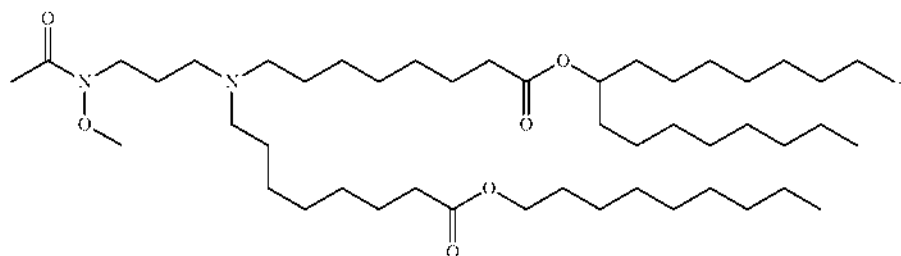
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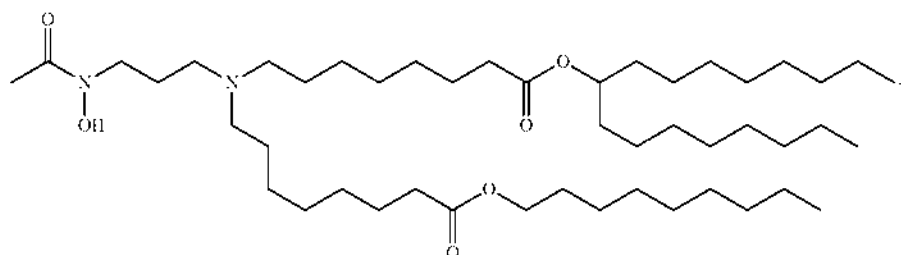
(Compound 201)



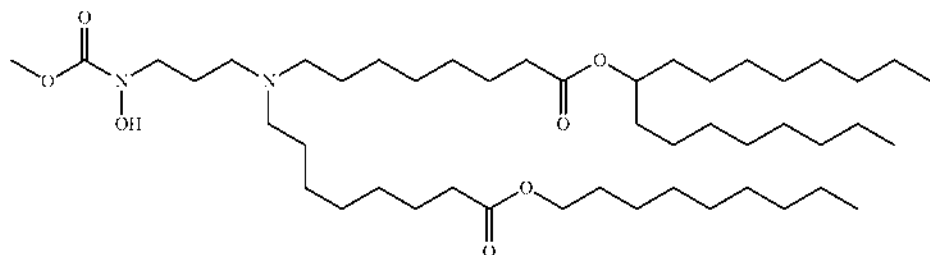
(Compound 202)



(Compound 203)

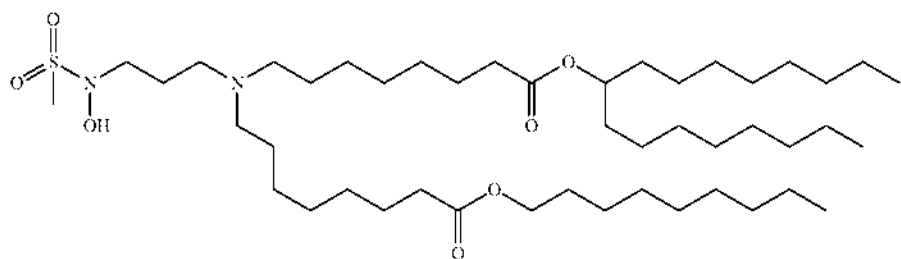


(Compound 204)

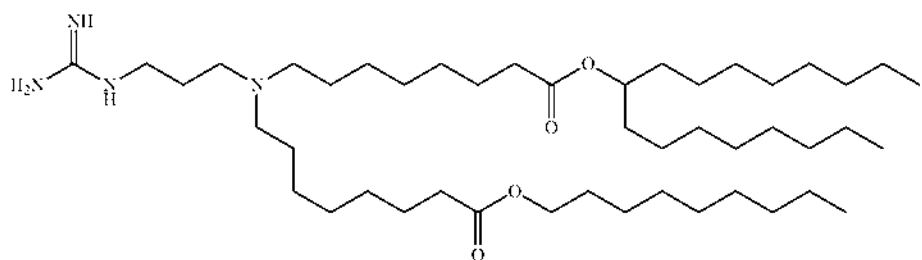


(Compound 205)

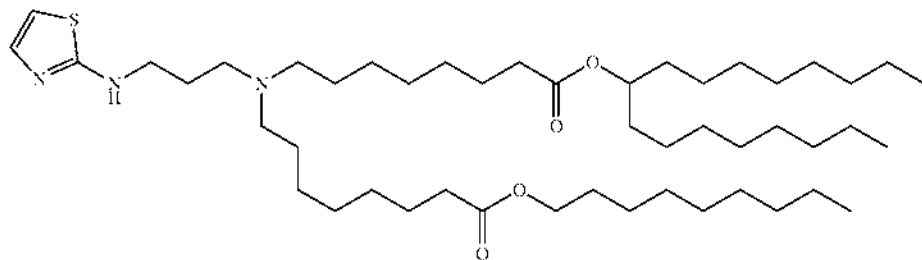
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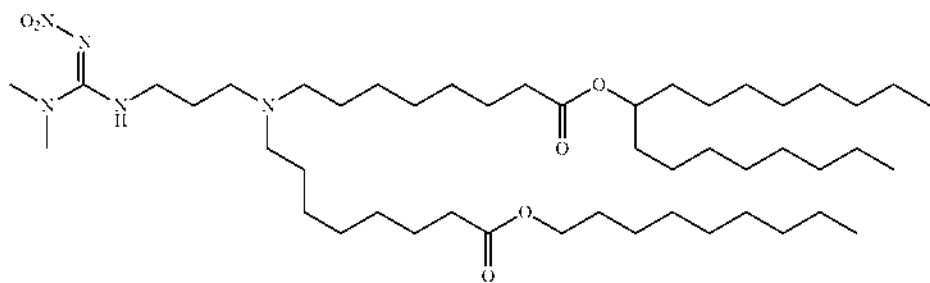
(Compound 206)



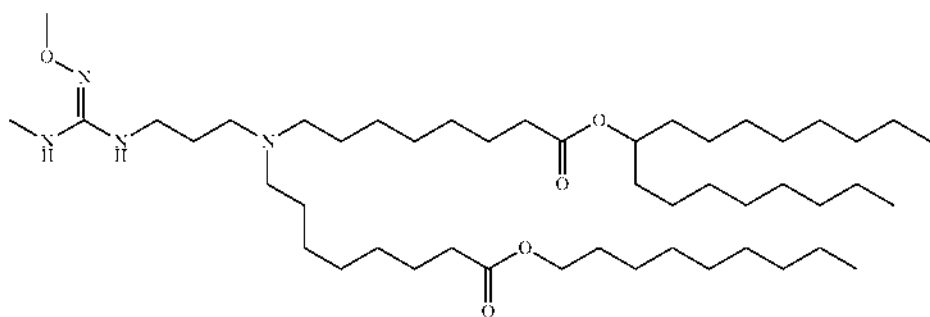
(Compound 207)



(Compound 208)



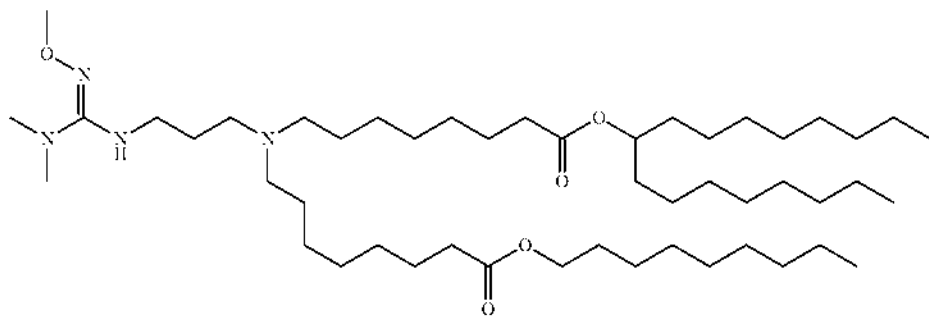
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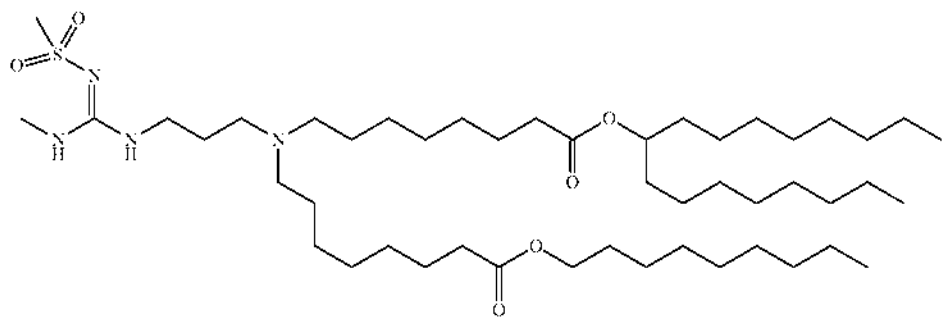
(Compound 210)

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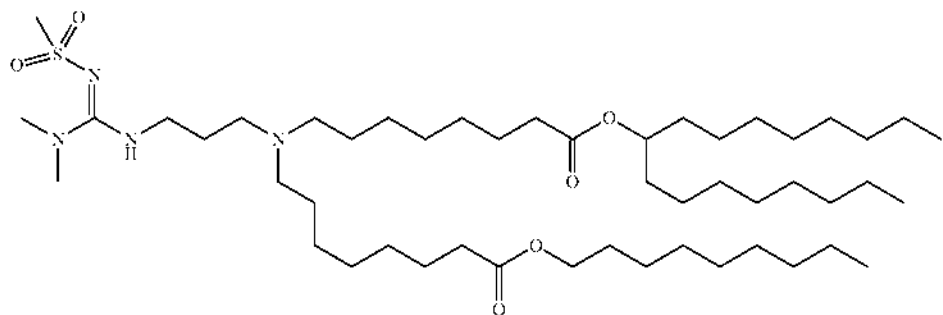
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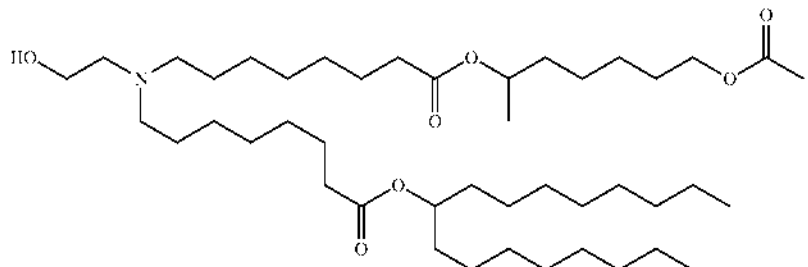
(Compound 212)



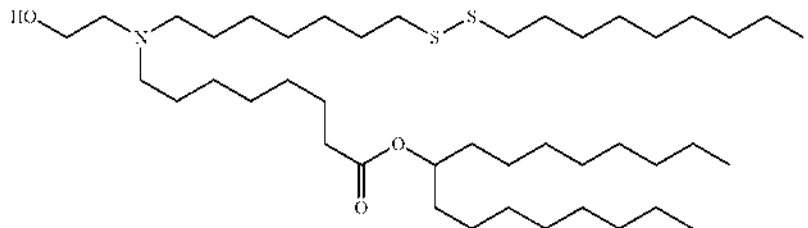
(Compound 213)



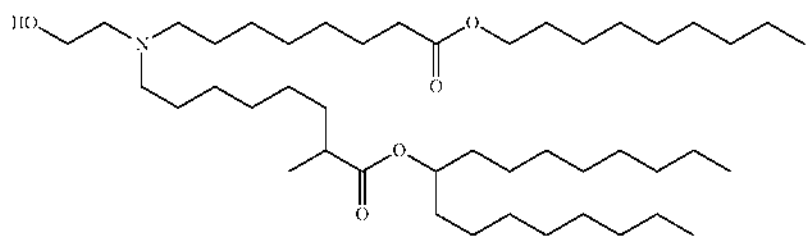
(Compound 214)



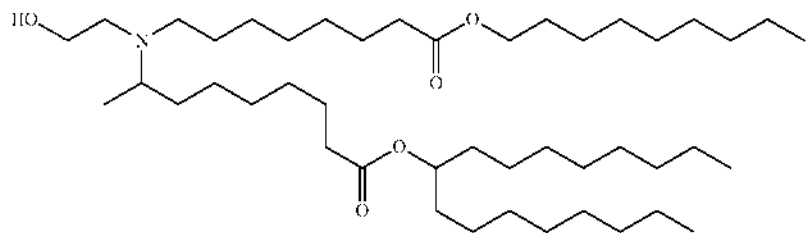
(Compound 215)



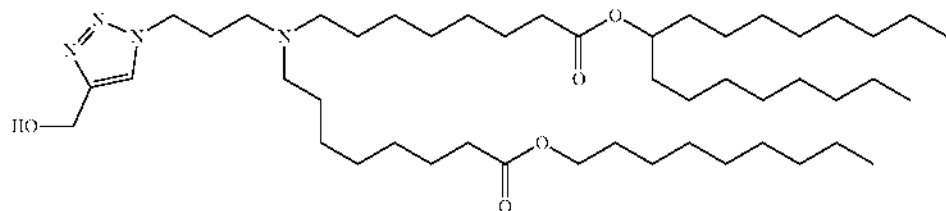
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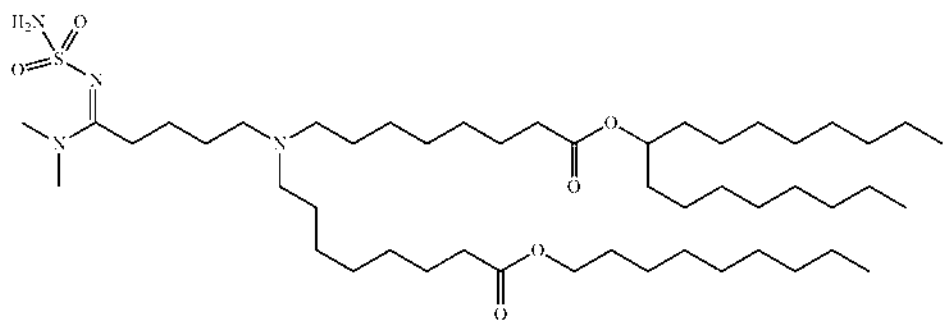
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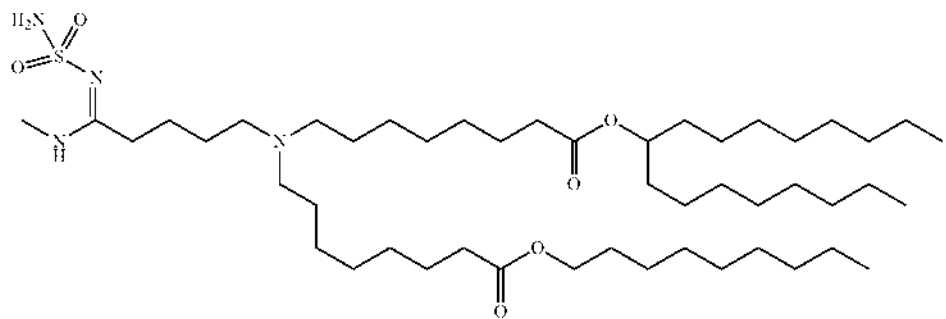
(Compound 217)



(Compound 218)

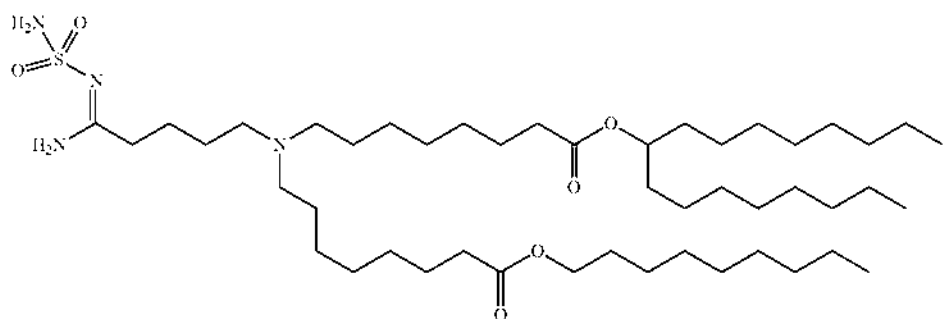


(Compound 219)

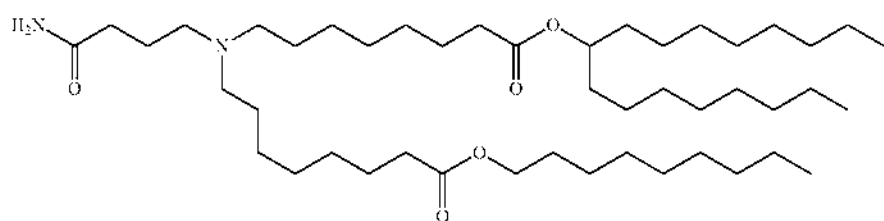


(Compound 220)

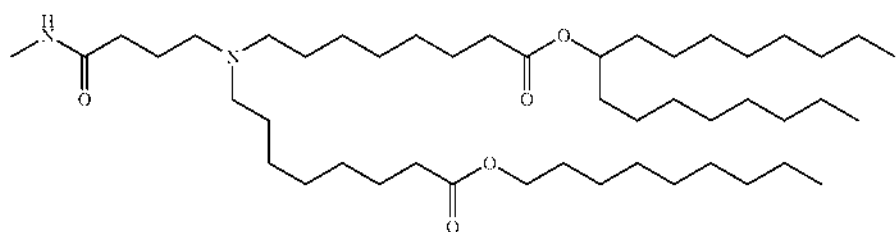
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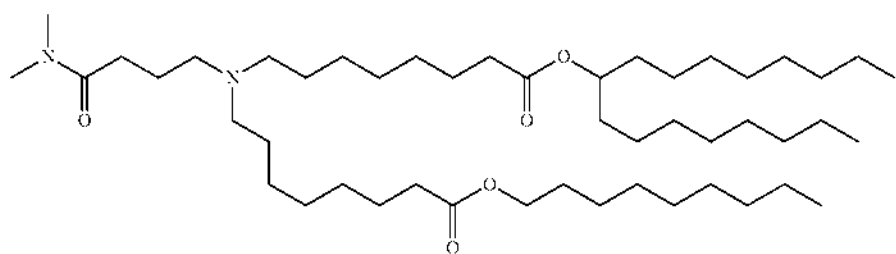
(Compound 221)



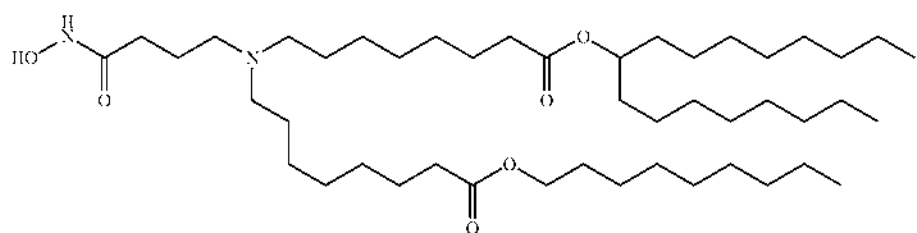
(Compound 222)



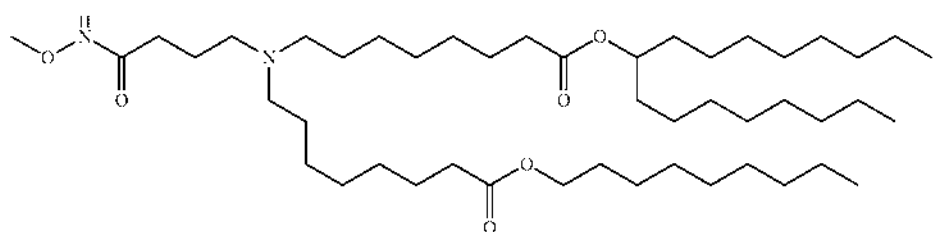
(Compound 223)



(Compound 224)

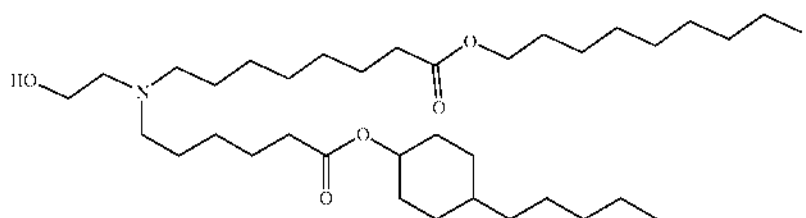
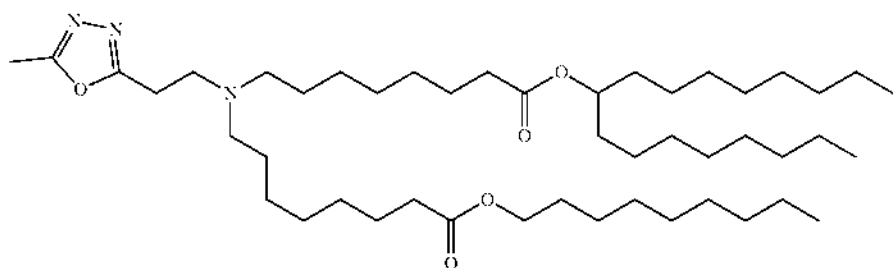
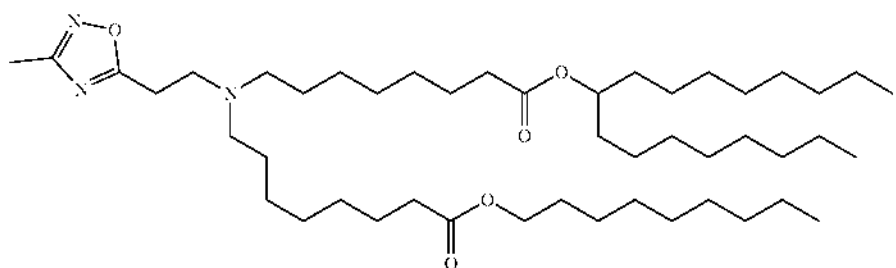
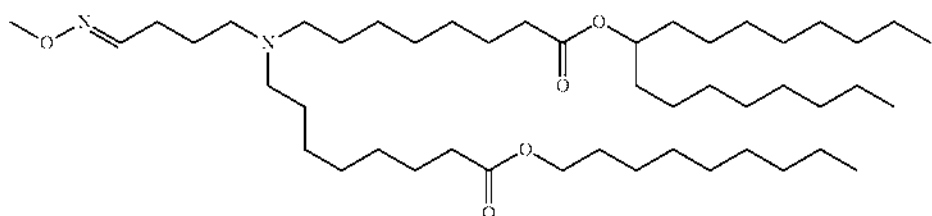
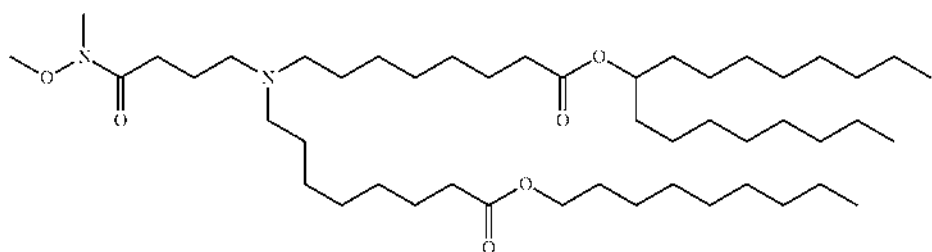
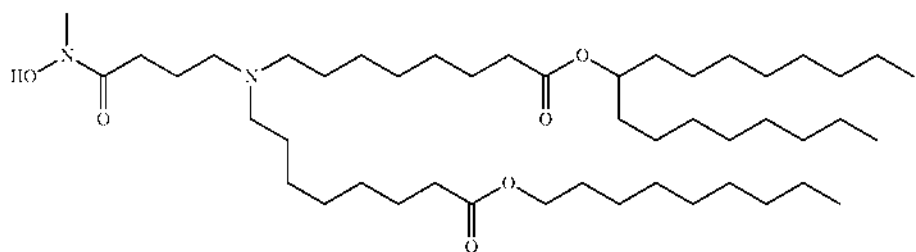


(Compound 225)



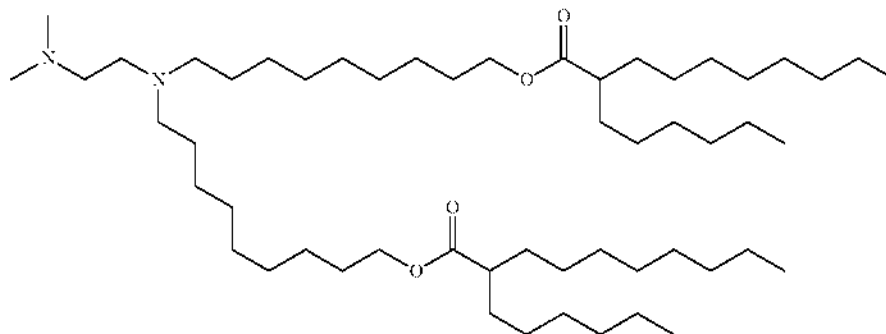
(Compound 226)

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and salts and isomers thereof.

[0665] In some embodiments, a nanoparticle comprises the following compound:



(Compound 233)

or salts and isomers thereof.

[0666] In some embodiments, the disclosure features a nanoparticle composition including a lipid component comprising a compound as described herein (e.g., a compound according to Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IID) or (Ile)).

[0667] In some embodiments, the disclosure features a pharmaceutical composition comprising a nanoparticle composition according to the preceding embodiments and a pharmaceutically acceptable carrier. For example, the pharmaceutical composition is refrigerated or frozen for storage and/or shipment (e.g., being stored at a temperature of 4° C. or lower, such as a temperature between about -150° C. and about 0° C. or between about -80° C. and about -20° C. (e.g., about -5° C., -10° C., -15° C., -20° C., -25° C., -30° C., -40° C., -50° C., -60° C., -70° C., -80° C., -90° C., -130° C. or -150° C.)). For example, the pharmaceutical composition is a solution that is refrigerated for storage and/or shipment at, for example, about -20° C., -30° C., -40° C., -50° C., -60° C., -70° C., or -80° C.

[0668] In some embodiments, the disclosure provides a method of delivering a therapeutic and/or prophylactic (e.g., RNA, such as mRNA) to a cell (e.g., a mammalian cell). This method includes the step of administering to a subject (e.g., a mammal, such as a human) a nanoparticle composition including (i) a lipid component including a phospholipid (such as a polyunsaturated lipid), a PEG lipid, a structural lipid, and a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IID) or (Ile) and (ii) a therapeutic and/or prophylactic, in which administering involves contacting the cell with the nanoparticle composition, whereby the therapeutic and/or prophylactic is delivered to the cell.

[0669] In some embodiments, the disclosure provides a method of producing a polypeptide of interest in a cell (e.g., a mammalian cell). The method includes the step of contacting the cell with a nanoparticle composition including (i) a lipid component including a phospholipid (such as a polyunsaturated lipid), a PEG lipid, a structural lipid, and a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IID) or (Ile) and (ii) an mRNA encoding the polypeptide of interest, whereby the mRNA is capable of being translated in the cell to produce the polypeptide.

[0670] In some embodiments, the disclosure provides a method of treating a disease or disorder in a mammal (e.g., a human) in need thereof. The method includes the step of

administering to the mammal a therapeutically effective amount of a nanoparticle composition including (i) a lipid component including a phospholipid (such as a polyunsaturated lipid), a PEG lipid, a structural lipid, and a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IID) or (Ile) and (ii) a therapeutic and/or prophylactic (e.g., an mRNA). In some embodiments, the disease or disorder is characterized by dysfunctional or aberrant protein or polypeptide activity. For example, the disease or disorder is selected from the group consisting of rare diseases, infectious diseases, cancer and proliferative diseases, genetic diseases (e.g., cystic fibrosis), autoimmune diseases, diabetes, neurodegenerative diseases, cardio- and reno-vascular diseases, and metabolic diseases.

[0671] In some embodiments, the disclosure provides a method of delivering (e.g., specifically delivering) a therapeutic and/or prophylactic to a mammalian organ (e.g., a liver, spleen, lung, or femur). This method includes the step of administering to a subject (e.g., a mammal) a nanoparticle composition including (i) a lipid component including a phospholipid, a PEG lipid, a structural lipid, and a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IID) or (Ile) and (ii) a therapeutic and/or prophylactic (e.g., an mRNA), in which administering involves contacting the cell with the nanoparticle composition, whereby the therapeutic and/or prophylactic is delivered to the target organ (e.g., a liver, spleen, lung, or femur).

[0672] In some embodiments, the disclosure features a method for the enhanced delivery of a therapeutic and/or prophylactic (e.g., an mRNA) to a target tissue (e.g., a liver, spleen, lung, or femur). This method includes administering to a subject (e.g., a mammal) a nanoparticle composition, the composition including (i) a lipid component including a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IID) or (Ile), a phospholipid, a structural lipid, and a PEG lipid; and (ii) a therapeutic and/or prophylactic, the administering including contacting the target tissue with the nanoparticle composition, whereby the therapeutic and/or prophylactic is delivered to the target tissue.

[0673] In some embodiments, the disclosure features a method of lowering immunogenicity comprising introducing the nanoparticle composition of the disclosure into cells, wherein the nanoparticle composition reduces the induction

of the cellular immune response of the cells to the nanoparticle composition, as compared to the induction of the cellular immune response in cells induced by a reference composition which comprises a reference lipid instead of a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IIc) or (IIc). For example, the cellular immune response is an innate immune response, an adaptive immune response, or both. The disclosure also includes methods of synthesizing a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IIc) or (IIc) and methods of making a nanoparticle composition including a lipid component comprising the compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IIc) or (IIc).

Modes of Vaccine Administration

[0674] Respiratory virus RNA (e.g., mRNA) vaccines may be administered by any route which results in a therapeutically effective outcome. These include, but are not limited, to intradermal, intramuscular, and/or subcutaneous administration. The present disclosure provides methods comprising administering RNA (e.g., mRNA) vaccines to a subject in need thereof. The exact amount required will vary from subject to subject, depending on the species, age, and general condition of the subject, the severity of the disease, the particular composition, its mode of administration, its mode of activity, and the like. Respiratory virus RNA (e.g., mRNA) vaccines compositions are typically formulated in dosage unit form for ease of administration and uniformity of dosage. It will be understood, however, that the total daily usage of RNA (e.g., mRNA) vaccine compositions may be decided by the attending physician within the scope of sound medical judgment. The specific therapeutically effective, prophylactically effective, or appropriate imaging dose level for any particular patient will depend upon a variety of factors including the disorder being treated and the severity of the disorder; the activity of the specific compound employed; the specific composition employed; the age, body weight, general health, sex and diet of the patient; the time of administration, route of administration, and rate of excretion of the specific compound employed; the duration of the treatment; drugs used in combination or coincidental with the specific compound employed; and like factors well known in the medical arts. In some embodiments, respiratory virus RNA (e.g., mRNA) vaccines compositions may be administered at dosage levels sufficient to deliver 0.0001 mg/kg to 100 mg/kg, 0.001 mg/kg to 0.05 mg/kg, 0.005 mg/kg to 0.05 mg/kg, 0.001 mg/kg to 0.005 mg/kg, 0.05 mg/kg to 0.5 mg/kg, 0.01 mg/kg to 50 mg/kg, 0.1 mg/kg to 40 mg/kg, 0.5 mg/kg to 30 mg/kg, 0.01 mg/kg to 10 mg/kg, 0.1 mg/kg to 10 mg/kg, or 1 mg/kg to 25 mg/kg, of subject body weight per day, one or more times a day, per week, per month, etc. to obtain the desired therapeutic, diagnostic, prophylactic, or imaging effect (see, e.g., the range of unit doses described in International Publication No WO2013078199, the contents of which are herein incorporated by reference in their entirety). The desired dosage may be delivered three times a day, two times a day, once a day, every other day, every third day, every week, every two weeks, every three weeks, every four weeks, every 2 months, every three months, every 6 months, etc. In some embodiments, the desired dosage may be delivered using multiple administrations (e.g., two, three, four, five, six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, or more administrations). When multiple administrations are employed, split dosing regimens such as those described

herein may be used. In exemplary embodiments, respiratory virus RNA (e.g., mRNA) vaccines compositions may be administered at dosage levels sufficient to deliver 0.0005 mg/kg to 0.01 mg/kg, e.g., about 0.0005 mg/kg to about 0.0075 mg/kg, e.g., about 0.0005 mg/kg, about 0.001 mg/kg, about 0.002 mg/kg, about 0.003 mg/kg, about 0.004 mg/kg or about 0.005 mg/kg.

[0675] In some embodiments, respiratory virus RNA (e.g., mRNA) vaccine compositions may be administered once or twice (or more) at dosage levels sufficient to deliver 0.025 mg/kg to 0.250 mg/kg, 0.025 mg/kg to 0.500 mg/kg, 0.025 mg/kg to 0.750 mg/kg, or 0.025 mg/kg to 1.0 mg/kg.

[0676] In some embodiments, respiratory virus RNA (e.g., mRNA) vaccine compositions may be administered twice (e.g., Day 0 and Day 7, Day 0 and Day 14, Day 0 and Day 21, Day 0 and Day 28, Day 0 and Day 60, Day 0 and Day 90, Day 0 and Day 120, Day 0 and Day 150, Day 0 and Day 180, Day 0 and 3 months later, Day 0 and 6 months later, Day 0 and 9 months later, Day 0 and 12 months later, Day 0 and 18 months later, Day 0 and 2 years later, Day 0 and 5 years later, or Day 0 and 10 years later) at a total dose of or at dosage levels sufficient to deliver a total dose of 0.0100 mg, 0.025 mg, 0.050 mg, 0.075 mg, 0.100 mg, 0.125 mg, 0.150 mg, 0.175 mg, 0.200 mg, 0.225 mg, 0.250 mg, 0.275 mg, 0.300 mg, 0.325 mg, 0.350 mg, 0.375 mg, 0.400 mg, 0.425 mg, 0.450 mg, 0.475 mg, 0.500 mg, 0.525 mg, 0.550 mg, 0.575 mg, 0.600 mg, 0.625 mg, 0.650 mg, 0.675 mg, 0.700 mg, 0.725 mg, 0.750 mg, 0.775 mg, 0.800 mg, 0.825 mg, 0.850 mg, 0.875 mg, 0.900 mg, 0.925 mg, 0.950 mg, 0.975 mg, or 1.0 mg. Higher and lower dosages and frequency of administration are encompassed by the present disclosure. For example, a respiratory virus RNA (e.g., mRNA) vaccine composition may be administered three or four times.

[0677] In some embodiments, respiratory virus RNA (e.g., mRNA) vaccine compositions may be administered twice (e.g., Day 0 and Day 7, Day 0 and Day 14, Day 0 and Day 21, Day 0 and Day 28, Day 0 and Day 60, Day 0 and Day 90, Day 0 and Day 120, Day 0 and Day 150, Day 0 and Day 180, Day 0 and 3 months later, Day 0 and 6 months later, Day 0 and 9 months later, Day 0 and 12 months later, Day 0 and 18 months later, Day 0 and 2 years later, Day 0 and 5 years later, or Day 0 and 10 years later) at a total dose of or at dosage levels sufficient to deliver a total dose of 0.010 mg, 0.025 mg, 0.100 mg or 0.400 mg.

[0678] In some embodiments, the respiratory virus RNA (e.g., mRNA) vaccine for use in a method of vaccinating a subject is administered to the subject as a single dosage of between 10 µg/kg and 400 µg/kg of the nucleic acid vaccine (in an effective amount to vaccinate the subject). In some embodiments the RNA (e.g., mRNA) vaccine for use in a method of vaccinating a subject is administered to the subject as a single dosage of between 10 µg and 400 µg of the nucleic acid vaccine (in an effective amount to vaccinate the subject). In some embodiments, a respiratory virus RNA (e.g., mRNA) vaccine for use in a method of vaccinating a subject is administered to the subject as a single dosage of 25-1000 µg (e.g., a single dosage of mRNA encoding hMPV, PIV3, RSV, MeV and/or BetaCoV antigen). In some embodiments, a respiratory virus RNA (e.g., mRNA) vaccine is administered to the subject as a single dosage of 25, 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 µg. For example, a respiratory virus RNA (e.g., mRNA) vaccine may be

administered to a subject as a single dose of 25-100, 25-500, 50-100, 50-500, 50-1000, 100-500, 100-1000, 250-500, 250-1000, or 500-1000 μg . In some embodiments, a respiratory virus RNA (e.g., mRNA) vaccine for use in a method of vaccinating a subject is administered to the subject as two dosages, the combination of which equals 25-1000 μg of the respiratory virus RNA (e.g., mRNA) vaccine.

[0679] A respiratory virus RNA (e.g., mRNA) vaccine pharmaceutical composition described herein can be formulated into a dosage form described herein, such as an intranasal, intratracheal, or injectable (e.g., intravenous, intraocular, intravitreal, intramuscular, intradermal, intracardiac, intraperitoneal, and subcutaneous).

Respiratory Virus RNA (e.g., mRNA) Vaccine Formulations and Methods of Use

[0680] Some aspects of the present disclosure provide formulations of the respiratory virus RNA (e.g., mRNA) vaccine, wherein the RNA (e.g., mRNA) vaccine is formulated in an effective amount to produce an antigen specific immune response in a subject (e.g., production of antibodies specific to an hMPV, PIV3, RSV, MeV and/or BetaCoV antigenic polypeptide). "An effective amount" is a dose of an RNA (e.g., mRNA) vaccine effective to produce an antigen-specific immune response. Also provided herein are methods of inducing an antigen-specific immune response in a subject.

[0681] In some embodiments, the antigen-specific immune response is characterized by measuring an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide antibody titer produced in a subject administered a respiratory virus RNA (e.g., mRNA) vaccine as provided herein. An antibody titer is a measurement of the amount of antibodies within a subject, for example, antibodies that are specific to a particular antigen (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) or epitope of an antigen. Antibody titer is typically expressed as the inverse of the greatest dilution that provides a positive result. Enzyme-linked immunosorbent assay (ELISA) is a common assay for determining antibody titers, for example.

[0682] In some embodiments, an antibody titer is used to assess whether a subject has had an infection or to determine whether immunizations are required. In some embodiments, an antibody titer is used to determine the strength of an autoimmune response, to determine whether a booster immunization is needed, to determine whether a previous vaccine was effective, and to identify any recent or prior infections. In accordance with the present disclosure, an antibody titer may be used to determine the strength of an immune response induced in a subject by the respiratory virus RNA (e.g., mRNA) vaccine.

[0683] In some embodiments, an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject is increased by at least 1 log relative to a control. For example, anti-antigenic polypeptide antibody titer produced in a subject may be increased by at least 1.5, at least 2, at least 2.5, or at least 3 log relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased by 1, 1.5, 2, 2.5 or 3 log relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased by 1-3 log relative to a control. For example, the anti-antigenic polypeptide anti-

body titer produced in a subject may be increased by 1-1.5, 1-2, 1-2.5, 1-3, 1.5-2, 1.5-2.5, 1.5-3, 2-2.5, 2-3, or 2.5-3 log relative to a control. In some embodiments, the anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject is increased at least 2 times relative to a control. For example, the anti-antigenic polypeptide antibody titer produced in a subject may be increased at least 3 times, at least 4 times, at least 5 times, at least 6 times, at least 7 times, at least 8 times, at least 9 times, or at least 10 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased 2, 3, 4, 5, 6, 7, 8, 9, or 10 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in a subject is increased 2-10 times relative to a control. For example, the anti-antigenic polypeptide antibody titer produced in a subject may be increased 2-10, 2-9, 2-8, 2-7, 2-6, 2-5, 2-4, 2-3, 3-10, 3-9, 3-8, 3-7, 3-6, 3-5, 3-4, 4-10, 4-9, 4-8, 4-7, 4-6, 4-5, 5-10, 5-9, 5-8, 5-7, 5-6, 6-10, 6-9, 6-8, 6-7, 7-10, 7-9, 7-8, 8-10, 8-9, or 9-10 times relative to a control.

[0684] A control, in some embodiments, is the anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject who has not been administered a respiratory virus RNA (e.g., mRNA) vaccine of the present disclosure. In some embodiments, a control is an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject who has been administered a live attenuated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine. An attenuated vaccine is a vaccine produced by reducing the virulence of a viable (live). An attenuated virus is altered in a manner that renders it harmless or less virulent relative to live, unmodified virus. In some embodiments, a control is an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject administered inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine. In some embodiments, a control is an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject administered a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. Recombinant protein vaccines typically include protein antigens that either have been produced in a heterologous expression system (e.g., bacteria or yeast) or purified from large amounts of the pathogenic organism. In some embodiments, a control is an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject who has been administered an hMPV, PIV3, RSV, MeV and/or BetaCoV virus-like particle (VLP) vaccine. For example, an hMPV VLP vaccine used as a control may be a hMPV VLPs, comprising (or consisting of) viral matrix (M) and fusion (F) proteins, generated by expressing viral proteins in suspension-adapted human embryonic kidney epithelial (293-F) cells (see, e.g., Cox R G et al., *J Virol.* 2014 June; 88(11): 6368-6379, the contents of which are herein incorporated by reference).

[0685] In some embodiments, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose that is reduced compared to the standard of care dose of a

90 to 1000-, 90 to 900-, 90 to 800-, 90 to 700-, 90 to 600-, 90 to 500-, 90 to 400-, 90 to 300-, 90 to 200-, 90 to 100-, 100 to 1000-, 100 to 900-, 100 to 800-, 100 to 700-, 100 to 600-, 100 to 500-, 100 to 400-, 100 to 300-, 100 to 200-, 200 to 1000-, 200 to 900-, 200 to 800-, 200 to 700-, 200 to 600-, 200 to 500-, 200 to 400-, 200 to 300-, 300 to 1000-, 300 to 900-, 300 to 800-, 300 to 700-, 300 to 600-, 300 to 500-, 300 to 400-, 400 to 1000-, 400 to 900-, 400 to 800-, 400 to 700-, 400 to 600-, 400 to 500-, 500 to 1000-, 500 to 900-, 500 to 800-, 500 to 700-, 500 to 600-, 600 to 1000-, 600 to 900-, 600 to 800-, 600 to 700-, 700 to 1000-, 700 to 900-, 700 to 800-, 800 to 1000-, 800 to 900-, or 900 to 1000-fold reduction in the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine. In some embodiments, the effective amount is a dose equivalent to (or equivalent to an at least) 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 20-, 30-, 40-, 50-, 60-, 70-, 80-, 90-, 100-, 110-, 120-, 130-, 140-, 150-, 160-, 170-, 180-, 190-, 200-, 210-, 220-, 230-, 240-, 250-, 260-, 270-, 280-, 290-, 300-, 310-, 320-, 330-, 340-, 350-, 360-, 370-, 380-, 390-, 400-, 410-, 420-, 430-, 440-, 450-, 4360-, 470-, 480-, 490-, 500-, 510-, 520-, 530-, 540-, 550-, 560-, 5760-, 580-, 590-, 600-, 610-, 620-, 630-, 640-, 650-, 660-, 670-, 680-, 690-, 700-, 710-, 720-, 730-, 740-, 750-, 760-, 770-, 780-, 790-, 800-, 810-, 820-, 830-, 840-, 850-, 860-, 870-, 880-, 890-, 900-, 910-, 920-, 930-, 940-, 950-, 960-, 970-, 980-, 990-, or 1000-fold reduction in the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some embodiments, an anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine.

[0689] In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a total dose of 50-1000 [µg]. In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a total dose of 50-1000, 50-900, 50-800, 50-700, 50-600, 50-500, 50-400, 50-300, 50-200, 50-100, 50-90, 50-80, 50-70, 50-60, 60-1000, 60-900, 60-800, 60-700, 60-600, 60-500, 60-400, 60-300, 60-200, 60-100, 60-90, 60-80, 60-70, 70-1000, 70-900, 70-800, 70-700, 70-600, 70-500, 70-400, 70-300, 70-200, 70-100, 70-90, 70-80, 80-1000, 80-900, 80-800, 80-700, 80-600, 80-500, 80-400, 80-300, 80-200, 80-100, 80-90, 90-1000, 90-900, 90-800, 90-700, 90-600, 90-500, 90-400, 90-300, 90-200, 90-100, 100-1000, 100-900, 100-800, 100-700, 100-600, 100-500, 100-400, 100-300, 100-200, 200-1000, 200-900, 200-800, 200-700, 200-600, 200-500, 200-400, 200-300, 300-1000, 300-900, 300-800, 300-700, 300-600, 300-500, 300-400, 400-1000, 400-900, 400-800, 400-700, 400-600, 400-500, 500-1000, 500-900, 500-800, 500-700, 500-600, 600-1000, 600-900, 600-800, 600-700, 700-1000, 700-900, 700-800, 800-1000, 800-900, or 900-1000 µg. In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is

a total dose of 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 µg. In some embodiments, the effective amount is a dose of 25-500 µg administered to the subject a total of two times. In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose of 25-500, 25-400, 25-300, 25-200, 25-100, 25-50, 50-500, 50-400, 50-300, 50-200, 50-100, 100-500, 100-400, 100-300, 100-200, 150-500, 150-400, 150-300, 150-200, 200-500, 200-400, 200-300, 250-500, 250-400, 250-300, 300-500, 300-400, 350-500, 350-400, 400-500 or 450-500 µg administered to the subject a total of two times. In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a total dose of 25, 50, 100, 150, 200, 250, 300, 350, 400, 450, or 500 µg administered to the subject a total of two times.

[0690] Examples of Additional Embodiments of the Disclosure

[0691] Additional embodiments of the present disclosure are encompassed by the following numbered paragraphs:

[0692] 1. A respiratory virus vaccine, comprising: at least one ribonucleic acid (RNA) polynucleotide having an open reading frame encoding at least one, at least two, at least three, at least four or at least five antigenic polypeptides selected from human metapneumovirus (hMPV) antigenic polypeptides or immunogenic fragments thereof, human parainfluenza virus type 3 (PIV3) antigenic polypeptides or immunogenic fragments thereof, respiratory syncytial virus (RSV) antigenic polypeptides or immunogenic fragments thereof, measles virus (MeV) antigenic polypeptides or immunogenic fragments thereof, and betacoronavirus (BetaCoV) antigenic polypeptides or immunogenic fragments thereof.

[0693] 2. The respiratory virus vaccine of paragraph 1, comprising:

[0694] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and a PIV3 antigenic polypeptide or an immunogenic fragment thereof; or

[0695] at least two RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof.

[0696] 3. The respiratory virus vaccine of paragraph 2, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SI:Q II NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SI:Q II NO: 5-8, and/or wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SI:Q II NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SI:Q II NO: 12-13.

[0697] 4. The respiratory virus vaccine of paragraph 1, comprising:

[0698] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and a RSV antigenic polypeptide or an immunogenic fragment thereof; or

[0699] at least two RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and one having an

- 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34.
- [0797] 54. The vaccine of any one of paragraphs 1-53, wherein at least one RNA polynucleotide has less than 80% identity to wild-type mRNA sequence.
- [0798] 55. The vaccine of any one of paragraphs 1-53, wherein at least one RNA polynucleotide has at least 80% identity to wild-type mRNA sequence, but does not include wild-type mRNA sequence.
- [0799] 56. The vaccine of any one of paragraphs 1-55, wherein at least one antigenic polypeptide has membrane fusion activity, attaches to cell receptors, causes fusion of viral and cellular membranes, and/or is responsible for binding of the virus to a cell being infected.
- [0800] 57. The vaccine of any one of paragraphs 1-56, wherein at least one RNA polynucleotide comprises at least one chemical modification.
- [0801] 58. The vaccine of paragraph 57, wherein the chemical modification is selected from pseudouridine, N1-methylpseudouridine, N1-ethylpseudouridine, 2-thiouridine, 4-thiouridine, 5-methylcytosine, 5-methyluridine, 2-thio-1-methyl-1-deaza-pseudouridine, 2-thio-1-methyl-pseudouridine, 2-thio-5-aza-uridine, 2-thio-dihydropseudouridine, 2-thio-dihydrouridine, 2-thio-pseudouridine, 4-methoxy-2-thio-pseudouridine, 4-methoxy-pseudouridine, 4-thio-1-methyl-pseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-methyluridine.
- [0802] 59. The vaccine of paragraph 57 or 58, wherein the chemical modification is in the 5-position of the uracil.
- [0803] 60. The vaccine of any one of paragraphs 57-59, wherein the chemical modification is a N1-methylpseudouridine or N1-ethylpseudouridine.
- [0804] 61. The vaccine of any one of paragraphs 57-60, wherein at least 80%, at least 90% or 100% of the uracil in the open reading frame have a chemical modification.
- [0805] 62. The vaccine of any one of paragraphs 1-61, wherein at least one RNA polynucleotide further encodes at least one 5' terminal cap, optionally wherein the 5' terminal cap is 7mG(5')ppp(5')NmpNp.
- [0806] 63. The vaccine of any one of paragraphs 1-62, wherein at least one antigenic polypeptide or immunogenic fragment thereof is fused to a signal peptide selected from: a HulgGik signal peptide (MEIQAQLLFLIIILWLPDITG; SEQ ID NO: 15); Igl1 heavy chain epsilon-1 signal peptide (MDWTWILFLVAAATRVVIS; SEQ ID NO: 16); Japanese encephalitis PRM signal sequence (MIGSNSGQRVVFTHLIIIVAPAYS; SEQ ID NO: 17); VSVg protein signal sequence (MKCLLYLAFIFIGVNCA; SEQ ID NO: 18) and Japanese encephalitis JEV signal sequence (MWLVSLAVTACAGAG; SEQ ID NO: 19).
- [0807] 64. The vaccine of paragraph 63, wherein the signal peptide is fused to the N-terminus or the C-terminus of at least one antigenic polypeptide.
- [0808] 65. The vaccine of any one of paragraphs 1-64, wherein the antigenic polypeptide or immunogenic fragment thereof comprises a mutated N-linked glycosylation site.
- [0809] 66. The vaccine of any one of paragraphs 1-65 formulated in a nanoparticle, optionally a lipid nanoparticle.
- [0810] 67. The vaccine of paragraph 66, wherein the lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid; optionally wherein the lipid nanoparticle carrier comprises a molar ratio of about 20-60% cationic lipid, 0.5-15% PEG-modified lipid, 25-55% sterol, and 25% non-cationic lipid; optionally wherein the cationic lipid is an ionizable cationic lipid and the non-cationic lipid is a neutral lipid, and the sterol is a cholesterol; and optionally wherein the cationic lipid is selected from 2,2-dilinoleyl-4-dimethylaminoethyl-1,3-dioxolane (DLin-KC2-DMA), dilinoleylmethyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (I.319). Formula (II)
- [0811] 68. The vaccine of paragraph 66 or 67, wherein the nanoparticle (e.g., lipid nanoparticle) comprises a compound of Formula (I) and/or Formula (II), optionally Compound 3, 18, 20, 25, 26, 29, 30, 60, 108-112, or 122.
- [0812] 69. The vaccine of any one of paragraphs 1-68 further comprising an adjuvant, optionally a flagellin protein or peptide that optionally comprises an amino acid sequence identified by any one of SEQ ID NO: 54-56.
- [0813] 70. The vaccine of any one of paragraphs 1-69, wherein the open reading frame is codon-optimized.
- [0814] 71. The vaccine of any one of paragraphs 1-70 formulated in an effective amount to produce an antigen-specific immune response.
- [0815] 72. A method of inducing an immune response in a subject, the method comprising administering to the subject the vaccine of any one of paragraphs 1-71 in an amount effective to produce an antigen-specific immune response in the subject.
- [0816] 73. The method of paragraph 72, wherein the subject is administered a single dose of the vaccine, or wherein the subject is administered a first dose and then a booster dose of the vaccine.
- [0817] 74. The method of paragraph 72 or 73, wherein the vaccine is administered to the subject by intradermal injection or intramuscular injection.
- [0818] 75. The method of any one of paragraphs 72-74, wherein an anti-antigenic polypeptide antibody titer produced in the subject is increased by at least 1 log relative to a control, and/or wherein the anti-antigenic polypeptide antibody titer produced in the subject is increased at least 2 times relative to a control.
- [0819] 76. The method of any one of paragraphs 72-75, wherein the control is an anti-antigenic polypeptide antibody titer produced in a subject who has not been administered a vaccine against the virus, and/or wherein the control is an anti-antigenic polypeptide antibody titer

produced in a subject who has been administered a live attenuated vaccine or an inactivated vaccine against the virus, and/or wherein the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a recombinant protein vaccine or purified protein vaccine against the virus, and/or wherein the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a VLP vaccine against the virus.

[0820] 77. The method of any one of paragraphs 72-76, wherein the effective amount is a dose equivalent to an at least 2-fold reduction in the standard of care dose of a recombinant protein vaccine or a purified protein vaccine against the virus, and wherein an anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant protein vaccine or a purified protein vaccine against the virus, respectively; and/or wherein the effective amount is a dose equivalent to an at least 2-fold reduction in the standard of care dose of a live attenuated vaccine or an inactivated vaccine against the virus, and wherein an anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a live attenuated vaccine or an inactivated vaccine against the virus, respectively; and/or wherein the effective amount is a dose equivalent to an at least 2-fold reduction in the standard of care dose of a VLP vaccine against the virus, and wherein an anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a VLP vaccine against the virus.

[0821] 78. The method of any one of paragraphs 72-77, wherein the effective amount is a total dose of 50 µg-1000 µg, optionally wherein the effective amount is a dose of 25 µg, 100 µg, 400 µg, or 500 µg administered to the subject a total of two times.

[0822] 79. The method of any one of paragraphs 72-78, wherein the efficacy of the vaccine against the virus is greater than 65%; and/or wherein the vaccine immunizes the subject against the virus for up to 2 years or wherein the vaccine immunizes the subject against the virus for more than 2 years.

[0823] 80. The method of any one of paragraphs 72-79, wherein the subject has an age of about 5 years old or younger or wherein the subject has an age of about 60 years old or older; and/or wherein the subject has a chronic pulmonary disease; and/or the subject has been exposed to the virus, wherein the subject is infected with the virus, or wherein the subject is at risk of infection by the virus; and/or wherein the subject is immunocompromised.

[0824] 81. The respiratory virus vaccine of any one of paragraphs 1-71, comprising at least one (e.g., at least two, at least three, at least four, or at least five) RNA polynucleotide having an open reading frame encoding at least one (e.g., at least two, at least three, at least four, or at least five) antigenic polypeptide selected from hMPV antigenic polypeptides (SEQ ID NO: 5-8), PIV3 antigenic polypeptides (SEQ ID NO: 12-13), RSV antigenic polypeptides, MeV antigenic polypeptides (SEQ ID NO:

47-50) and BetaCoV antigenic polypeptides (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NJ1 or HCoV-HKU1; (SEQ ID NO: 24-34)), formulated in a cationic lipid nanoparticle

[0825] (a) having a molar ratio of about 20-60% cationic lipid, about 5-25% non-cationic lipid, about 25-55% sterol, and about 0.5-15% PEG-modified lipid, and/or

[0826] (b) comprising a compound of Formula (I) and/or Formula (II).

[0827] wherein the at least one (e.g., at least two, at least three, at least four, or at least five) RNA polynucleotide comprises at least one chemical modification.

[0828] 82. The respiratory virus vaccine of any one of paragraphs 1-71, comprising at least one (e.g., at least two, at least three, at least four, or at least five) RNA polynucleotide having an open reading frame encoding at least one (e.g., at least two, at least three, at least four, or at least five) antigenic polypeptide selected from hMPV antigenic polypeptides (SEQ ID NO: 5-8), PIV3 antigenic polypeptides (SEQ ID NO: 12-13), RSV antigenic polypeptides, MeV antigenic polypeptides (SEQ ID NO: 47-50) and BetaCoV antigenic polypeptides (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NJ1 or HCoV-HKU1; (SEQ ID NO: 24-34)), formulated in a cationic lipid nanoparticle

[0829] (a) having a molar ratio of about 20-60% cationic lipid, about 5-25% non-cationic lipid, about 25-55% sterol, and about 0.5-15% PEG-modified lipid, and/or

[0830] (b) comprising at least one (e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14) Compound selected from Compounds 3, 18, 20, 25, 26, 29, 30, 60, 108-112 and 122.

[0831] 83. The respiratory virus vaccine of paragraphs 81 or 82, wherein the at least one antigenic polypeptide is selected from hMPV antigenic polypeptides (e.g., SEQ ID NO: 5-8).

[0832] 84. The respiratory virus vaccine of any one of paragraphs 81-83, wherein the at least one antigenic polypeptide is selected from PIV3 antigenic polypeptides (e.g., SEQ ID NO: 12-13).

[0833] 85. The respiratory virus vaccine of any one of paragraphs 81-84, wherein the at least one antigenic polypeptide is selected from RSV antigenic polypeptides.

[0834] 86. The respiratory virus vaccine of any one of paragraphs 81-85, wherein the at least one antigenic polypeptide is selected from MeV antigenic polypeptides (e.g., SEQ ID NO: 47-50).

[0835] 87. The respiratory virus vaccine of any one of paragraphs 81-86, wherein the at least one antigenic polypeptide is selected from BetaCoV antigenic polypeptides (e.g., SEQ ID NO: 24-34).

[0836] 88. The respiratory virus vaccine of paragraph 87, wherein the BetaCoV antigenic polypeptides are MERS antigenic polypeptides.

[0837] 89. The respiratory virus vaccine of paragraph 87, wherein the BetaCoV antigenic polypeptides are SARS antigenic polypeptides.

[0838] 90. The respiratory virus vaccine of any one of paragraphs 81-89, wherein the at least one (e.g., at least two, at least three, at least four, or at least five) RNA polynucleotide comprises at least one chemical modification (e.g., selected from pseudouridine, N1-methylpseudouridine, N1-ethylpseudouridine, 2-thiouridine, 4-thiouridine, 5-methylcytosine, 5-methyluridine, 2-thio-1-methyl-1-deaza-pseudouridine, 2-thio-1-methyl-

pseudouridine, 2-thio-5-aza-uridine, 2-thio-dihydropseudouridine, 2-thio-dihydrouridine, 2-thio-pseudouridine, 4-methoxy-2-thio-pseudouridine, 4-methoxy-pseudouridine, 4-thio-1-methyl-pseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-methyl uridine).

- [0839] 91. A respiratory virus vaccine, comprising:
- [0840] at least one messenger ribonucleic acid (mRNA) polynucleotide having a 5' terminal cap, an open reading frame encoding at least one respiratory virus antigenic polypeptide, and a 3' polyA tail.
- [0841] 92. The vaccine of paragraph 91, wherein the at least one mRNA polynucleotide comprises a sequence identified by any one of SEQ ID NO: 57-80.
- [0842] 93. The vaccine of paragraph 91 or 92, wherein the 5' terminal cap is or comprises 7mG(5')ppp(5')NmpNp.
- [0843] 94. The vaccine of any one of paragraphs 91-93, wherein 100% of the uracil in the open reading frame is modified to include N1-methyl pseudouridine at the 5-position of the uracil.
- [0844] 95. The vaccine of any one of paragraphs 91-94, wherein the vaccine is formulated in a lipid nanoparticle comprising: DLin-MC3-DMA; cholesterol; 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC); and polyethylene glycol (PEG)2000-DMG.
- [0845] 96. The vaccine of paragraph 95, wherein the lipid nanoparticle further comprises trisodium citrate buffer, sucrose and water.
- [0846] 97. A respiratory syncytial virus (RSV) vaccine, comprising:
- [0847] at least one messenger ribonucleic acid (mRNA) polynucleotide having a 5' terminal cap 7mG(5')ppp(5')NmpNp, a sequence identified by any one of SEQ ID NO: 57-80 and a 3' polyA tail, formulated in a lipid nanoparticle comprising DLin-MC3-DMA, cholesterol, 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC), and polyethylene glycol (PEG)2000-DMG, wherein the uracil nucleotides of the sequence identified by any one of SEQ ID NO: 57-80 are modified to include N1-methyl pseudouridine at the 5-position of the uracil nucleotide.
- [0848] This disclosure is not limited in its application to the details of construction and the arrangement of components set forth in the following description or illustrated in the drawings. The disclosure is capable of other embodiments and of being practiced or of being carried out in various ways. Also, the phraseology and terminology used herein is for the purpose of description and should not be regarded as limiting. The use of "including," "comprising," or "having," "containing," "involving," and variations thereof herein, is meant to encompass the items listed thereafter and equivalents thereof as well as additional items.

EXAMPLES

Example 1

Manufacture of Polynucleotides

[0849] According to the present disclosure, the manufacture of polynucleotides and/or parts or regions thereof may be accomplished utilizing the methods taught in International Publication WO2014/152027, entitled "Manufactur-

ing Methods for Production of RNA Transcripts," the contents of which is incorporated herein by reference in its entirety.

[0850] Purification methods may include those taught in International Publication WO2014/152030 and International Publication WO2014/152031, each of which is incorporated herein by reference in its entirety.

[0851] Detection and characterization methods of the polynucleotides may be performed as taught in International Publication WO2014/144039, which is incorporated herein by reference in its entirety.

[0852] Characterization of the polynucleotides of the disclosure may be accomplished using polynucleotide mapping, reverse transcriptase sequencing, charge distribution analysis, detection of RNA impurities, or any combination of two or more of the foregoing. "Characterizing" comprises determining the RNA transcript sequence, determining the purity of the RNA transcript, or determining the charge heterogeneity of the RNA transcript, for example. Such methods are taught in, for example, International Publication WO2014/144711 and International Publication WO2014/144767, the content of each of which is incorporated herein by reference in its entirety.

Example 2

Chimeric Polynucleotide Synthesis

[0853] According to the present disclosure, two regions or parts of a chimeric polynucleotide may be joined or ligated using triphosphate chemistry. A first region or part of 100 nucleotides or less is chemically synthesized with a 5' monophosphate and terminal 3'desOH or blocked OH, for example. If the region is longer than 80 nucleotides, it may be synthesized as two strands for ligation.

[0854] If the first region or part is synthesized as a non-positionally modified region or part using in vitro transcription (IVT), conversion the 5'monophosphate with subsequent capping of the 3' terminus may follow.

[0855] Monophosphate protecting groups may be selected from any of those known in the art.

[0856] The second region or part of the chimeric polynucleotide may be synthesized using either chemical synthesis or IVT methods. IVT methods may include an RNA polymerase that can utilize a primer with a modified cap. Alternatively, a cap of up to 130 nucleotides may be chemically synthesized and coupled to the IVT region or part.

[0857] For ligation methods, ligation with DNA T4 ligase, followed by treatment with DNase should readily avoid concatenation.

[0858] The entire chimeric polynucleotide need not be manufactured with a phosphate-sugar backbone. If one of the regions or parts encodes a polypeptide, then such region or part may comprise a phosphate-sugar backbone. Ligation is then performed using any known click chemistry, ortho-click chemistry, solulink, or other bioconjugate chemistries known to those in the art.

[0859] Synthetic Route

[0860] The chimeric polynucleotide may be made using a series of starting segments. Such segments include:

[0861] (a) a capped and protected 5' segment comprising a normal 3'OH (SEQ. 1)

[0862] (b) a 5' triphosphate segment, which may include the coding region of a polypeptide and a normal 3'OH (SEQ. 2)

[0863] (c) a 5' monophosphate segment for the 3' end of the chimeric polynucleotide (e.g., the tail) comprising cordycepin or no 3'OH (SEQ. 3)

[0864] After synthesis (chemical or IVT), segment 3 (SEQ. 3) may be treated with cordycepin and then with pyrophosphatase to create the 5' monophosphate.

[0865] Segment 2 (SEQ. 2) may then be ligated to SEQ. 3 using RNA ligase. The ligated polynucleotide is then purified and treated with pyrophosphatase to cleave the diphosphate. The treated SEQ.2-SEQ. 3 construct may then be purified and SEQ. 1 is ligated to the 5' terminus. A further purification step of the chimeric polynucleotide may be performed.

[0866] Where the chimeric polynucleotide encodes a polypeptide, the ligated or joined segments may be represented as: 5'UTR (SEQ. 1), open reading frame or ORF (SEQ. 2) and 3'UTR+PolyA (SEQ. 3).

[0867] The yields of each step may be as much as 90-95%.

Example 3

PCR for cDNA Production

[0868] PCR procedures for the preparation of cDNA may be performed using 2x KAPA HiFi™ HotStart ReadyMix by Kapa Biosystems (Woburn, Mass.). This system includes 2x KAPA ReadyMix 12.5 µl; Forward Primer (10 µM) 0.75 µl; Reverse Primer (10 µM) 0.75 µl; Template cDNA 100 ng; and dH₂O diluted to 25.0 µl. The reaction conditions may be at 95° C. for 5 min. The reaction may be performed for 25 cycles of 98° C. for 20 sec, then 58° C. for 15 sec, then 72° C. for 45 sec, then 72° C. for 5 min, then 4° C. to termination.

[0869] The reaction may be cleaned up using Invitrogen's PURELINK™ PCR Micro Kit (Carlsbad, Calif.) per manufacturer's instructions (up to 5 µg). Larger reactions may require a cleanup using a product with a larger capacity. Following the cleanup, the cDNA may be quantified using the NANODROP™ and analyzed by agarose gel electrophoresis to confirm that the cDNA is the expected size. The cDNA may then be submitted for sequencing analysis before proceeding to the in vitro transcription reaction.

Example 4

In Vitro Transcription (IVT)

[0870] The in vitro transcription reaction generates RNA polynucleotides. Such polynucleotides may comprise a region or part of the polynucleotides of the disclosure, including chemically modified RNA (e.g., mRNA) polynucleotides. The chemically modified RNA polynucleotides can be uniformly modified polynucleotides. The in vitro transcription reaction utilizes a custom mix of nucleotide triphosphates (NTPs). The NTPs may comprise chemically modified NTPs, or a mix of natural and chemically modified NTPs, or natural NTPs.

[0871] A typical in vitro transcription reaction includes the following:

1)	Template cDNA	1.0 µg
2)	10x transcription buffer (400 mM Tris-HCl pH 8.0, 190 mM MgCl ₂ , 50 mM DTT, 10 mM Spermidine)	2.0 µl
3)	Custom NTPs (25 mM each)	0.2 µl
4)	RNase Inhibitor	20 U
5)	T7 RNA polymerase	3000 U
6)	dH ₂ O	up to 20.0 µl, and
7)	Incubation at 37° C. for 3 hr-5 hrs.	

[0872] The crude IVT mix may be stored at 4° C. overnight for cleanup the next day. 1 U of RNase-free DNase may then be used to digest the original template. After 15 minutes of incubation at 37° C., the mRNA may be purified using Ambion's MEGACLEAR™ Kit (Austin, Tex.) following the manufacturer's instructions. This kit can purify up to 500 µg of RNA. Following the cleanup, the RNA polynucleotide may be quantified using the NanoDrop and analyzed by agarose gel electrophoresis to confirm the RNA polynucleotide is the proper size and that no degradation of the RNA has occurred.

Example 5

Enzymatic Capping

[0873] Capping of a RNA polynucleotide is performed as follows where the mixture includes: IVT RNA 60 µg-180 µg and dH₂O up to 72 µl. The mixture is incubated at 65° C. for 5 minutes to denature RNA, and then is transferred immediately to ice.

[0874] The protocol then involves the mixing of 10x Capping Buffer (0.5 M Tris-HCl (pH 8.0), 60 mM KCl, 12.5 mM MgCl₂) (10.0 µl); 20 mM GTP (5.0 µl); 20 mM S-Adenosyl Methionine (2.5 µl); RNase Inhibitor (100 U); 2' O-Methyltransferase (400 U); Vaccinia capping enzyme (Guanylyl transferase) (40 U); dH₂O (Up to 28 µl); and incubation at 37° C. for 30 minutes for 60 µg RNA or up to 2 hours for 180 µg of RNA.

[0875] The RNA polynucleotide may then be purified using Ambion's MEGACLEAR™ Kit (Austin, Tex.) following the manufacturer's instructions. Following the cleanup, the RNA may be quantified using the NANODROP™ (ThermoFisher, Waltham, Mass.) and analyzed by agarose gel electrophoresis to confirm the RNA polynucleotide is the proper size and that no degradation of the RNA has occurred. The RNA polynucleotide product may also be sequenced by running a reverse-transcription-PCR to generate the cDNA for sequencing.

Example 6

PolyA Tailing Reaction

[0876] Without a poly-T in the cDNA, a poly-A tailing reaction must be performed before cleaning the final product. This is done by mixing capped IVT RNA (100 µl); RNase Inhibitor (20 U); 10x Tailing Buffer (0.5 M Tris-HCl (pH 8.0), 2.5 M NaCl, 1100 mM MgCl₂) (12.0 µl); 20 mM ATP (6.0 µl); Poly-A Polymerase (20 U); dH₂O up to 123.5 µl and incubation at 37° C. for 30 min. If the poly-A tail is already in the transcript, then the tailing reaction may be skipped and proceed directly to cleanup with Ambion's MEGACLEAR™ kit (Austin, Tex.) (up to 500 µg). Poly-A Polymerase may be a recombinant enzyme expressed in yeast.

[0877] It should be understood that the processivity or integrity of the polyA tailing reaction may not always result in an exact size polyA tail. Hence, polyA tails of approximately between 40-200 nucleotides, e.g., about 40, 50, 60, 70, 80, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 150-165, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164 or 165 are within the scope of the present disclosure.

Example 7

Natural 5' Caps and 5' Cap Analogues

[0878] 5'-capping of polynucleotides may be completed concomitantly during the in vitro-transcription reaction using the following chemical RNA cap analogs to generate the 5'-guanosine cap structure according to manufacturer protocols: 3'-O-Me-m7G(5')ppp(5')G [the ARCA cap]; G(5')ppp(5')A; G(5')ppp(5')G; m7G(5')ppp(5')A; m7G(5')ppp(5')G (New England Biolabs, Ipswich, Mass.). 5'-capping of modified RNA may be completed post-transcriptionally using a Vaccinia Virus Capping Enzyme to generate the "Cap 0" structure: m7G(5')ppp(5')G (New England Biolabs, Ipswich, Mass.). Cap 1 structure may be generated using both Vaccinia Virus Capping Enzyme and a 2'-O methyl-transferase to generate: m7G(5')ppp(5')G-2'-O-methyl. Cap 2 structure may be generated from the Cap 1 structure followed by the 2'-O-methylation of the 5'-antepenultimate nucleotide using a 2'-O methyl-transferase. Cap 3 structure may be generated from the Cap 2 structure followed by the 2'-O-methylation of the 5'-preantepenultimate nucleotide using a 2'-O methyl-transferase. Enzymes are preferably derived from a recombinant source.

[0879] When transfected into mammalian cells, the modified mRNAs have a stability of between 12-18 hours or more than 18 hours, e.g., 24, 36, 48, 60, 72 or greater than 72 hours.

Example 8

Capping Assays

Protein Expression Assay

[0880] Polynucleotides (e.g., mRNA) encoding a polypeptide, containing any of the caps taught herein, can be transfected into cells at equal concentrations. The amount of protein secreted into the culture medium can be assayed by ELISA at 6, 12, 24 and/or 36 hours post-transfection. Synthetic polynucleotides that secrete higher levels of protein into the medium correspond to a synthetic polynucleotide with a higher translationally-competent cap structure.

Purity Analysis Synthesis

[0881] RNA (e.g., mRNA) polynucleotides encoding a polypeptide, containing any of the caps taught herein can be compared for purity using denaturing Agarose-Urea gel electrophoresis or HPLC analysis. RNA polynucleotides with a single, consolidated band by electrophoresis correspond to the higher purity product compared to polynucleotides with multiple bands or streaking bands. Chemically modified RNA polynucleotides with a single HPLC peak also correspond to a higher purity product. The capping reaction with a higher efficiency provides a more pure polynucleotide population.

Cytokine Analysis

[0882] RNA (e.g., mRNA) polynucleotides encoding a polypeptide, containing any of the caps taught herein can be transfected into cells at multiple concentrations. The amount of pro-inflammatory cytokines, such as TNF-alpha and IFN-beta, secreted into the culture medium can be assayed by ELISA at 6, 12, 24 and/or 36 hours post-transfection. RNA polynucleotides resulting in the secretion of higher levels of pro-inflammatory cytokines into the medium correspond to a polynucleotides containing an immune-activating cap structure.

Capping Reaction Efficiency

[0883] RNA (e.g., mRNA) polynucleotides encoding a polypeptide, containing any of the caps taught herein can be analyzed for capping reaction efficiency by LC-MS after nuclease treatment. Nuclease treatment of capped polynucleotides yield a mixture of free nucleotides and the capped 5'-5-triphosphate cap structure detectable by LC-MS. The amount of capped product on the LC-MS spectra can be expressed as a percent of total polynucleotide from the reaction and correspond to capping reaction efficiency. The cap structure with a higher capping reaction efficiency has a higher amount of capped product by LC-MS.

Example 9

Agarose Gel Electrophoresis of Modified RNA or RT PCR Products

[0884] Individual RNA polynucleotides (200-400 ng in a 20 µl volume) or reverse transcribed PCR products (200-400 ng) may be loaded into a well on a non-denaturing 1.2% Agarose E-Gel (Invitrogen, Carlsbad, Calif.) and run for 12-15 minutes, according to the manufacturer protocol.

Example 10

Nanodrop Modified RNA Quantification and UV Spectral Data

[0885] Chemically modified RNA polynucleotides in TE buffer (1 µl) are used for Nanodrop UV absorbance readings to quantitate the yield of each polynucleotide from an chemical synthesis or in vitro transcription reaction.

Example 11

Formulation of Modified mRNA Using Lipidoids

[0886] RNA (e.g., mRNA) polynucleotides may be formulated for in vitro experiments by mixing the polynucleotides with the lipidoid at a set ratio prior to addition to cells. In vivo formulation may require the addition of extra ingredients to facilitate circulation throughout the body. To test the ability of these lipidoids to form particles suitable for in vivo work, a standard formulation process used for siRNA-lipidoid formulations may be used as a starting point. After formation of the particle, polynucleotide is added and allowed to integrate with the complex. The encapsulation efficiency is determined using a standard dye exclusion assays.

Example 12

Immunogenicity Study

[0887] The instant study is designed to test the immunogenicity in mice of candidate hMPV vaccines comprising a mRNA polynucleotide encoding Fusion (F) glycoprotein, major surface glycoprotein G, or a combination thereof, obtained from hMPV.

[0888] Mice are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) with candidate vaccines. Candidate vaccines are chemically modified or unmodified. A total of four immunizations are given at 3-week intervals (i.e., at weeks 0, 3, 6, and 9), and sera are collected after each immunization until weeks 33-51. Serum antibody titers against Fusion (F) glycoprotein or major surface glycoprotein (G) protein are determined by ELISA. Sera collected from each mouse during weeks 10-16 are pooled, and total IgG purified. Purified antibodies are used for immunoelectron microscopy, antibody-affinity testing, and *in vitro* protection assays.

Example 13

hMPV Rodent Challenge

[0889] The instant study is designed to test the efficacy in cotton rats of candidate hMPV vaccines against a lethal challenge using an hMPV vaccine comprising mRNA encoding Fusion (F) glycoprotein, major surface glycoprotein G, or a combination of both antigens obtained from hMPV. Cotton rats are challenged with a lethal dose of the hMPV.

[0890] Animals are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) at week 0 and week 3 with candidate hMPV vaccines with and without adjuvant. Candidate vaccines are chemically modified or unmodified. The animals are then challenged with a lethal dose of hMPV on week 7 via IV, IM or ID. Endpoint is day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis are euthanized. Body temperature and weight are assessed and recorded daily.

[0891] In experiments where a lipid nanoparticle (LNP) formulation is used, the formulation may include a cationic lipid, non-cationic lipid, PEG lipid and structural lipid in the ratios 50:10:1.5:38.5. The cationic lipid is DL-in-KC2-DMA (50 mol %) or DL-in-MC3-DMA (50 mol %), the non-cationic lipid is DSPC (10 mol %), the PEG lipid is PEG-DMG (1.5 mol %) and the structural lipid is cholesterol (38.5 mol %), for example.

Example 14

Immunogenicity of hMPV mRNA Vaccine in BALB/c Mice

[0892] The instant study was designed to test the immunogenicity in BALB/c mice of hMPV vaccines comprising an mRNA polynucleotide encoding the hMPV Fusion (F) glycoprotein. The mRNA polynucleotide encodes the full-length fusion protein and comprises the wild-type nucleotide sequence obtained from the hMPV A2a strain. Mice were divided into 3 groups (n = 8 for each group) and immunized intramuscularly (IM) with PBS, a 10 µg dose of mRNA vaccines encoding hMPV fusion protein, or a 2 µg dose of

mRNA vaccines encoding hMPV fusion protein. A total of two immunizations were given at 3-week intervals (i.e., at weeks 0, and 3 weeks), and sera were collected after each immunization according to the schedule described in Table 1. Serum antibody titers against hMPV fusion glycoprotein were determined by ELISA and antibodies were detected in the sera collected on day 14 onward. Both vaccine doses tested induced comparable levels of immune response in mice (FIGS. 2A-2C).

[0893] Additionally, mice sera were used for IgG isotyping (FIGS. 3A-3C). Both hMPV fusion protein-specific IgG1 and IgG2a were detected in mice sera. hMPV fusion protein mRNA vaccine also induced Th1 and Th2 cytokine responses, with a Th1 bias.

[0894] Sera from mice immunized with either 10 µg or 2 µg doses of the hMPV fusion protein mRNA vaccine contain neutralizing antibodies. The ability of these antibodies to neutralize hMPV B2 strain was also tested. The antibody-containing sera successfully neutralized the hMPV B2 virus (FIG. 4).

Example 15

T-Cell Stimulation

[0895] The instant study was designed to test T-cell stimulation in the splenocytes of mice immunized with mRNA vaccines encoding hMPV fusion protein, as described herein. Immunization of BALB/c mice was performed as described in Example 14. The splenocytes for each group were pooled and split into two parts. One part of splenocytes from each group of mice was stimulated with hMPV-free media, Concanavalin A or a hMPV fusion protein peptide pool comprising 15-mers (15 amino acids long); while the other part of splenocytes from each group of mice was stimulated with hMPV-free media, Concanavalin A or inactivated hMPV virus. Secreted mouse cytokines were measured using the Meso Scale Discovery (MSD) assay.

[0896] Cytokines specific to Th1 or Th2 responses were measured. For Th1 response, IFN-γ, IL2 and IL12 were detected from splenocytes stimulated with the hMPV fusion protein peptide pool at a level comparable to that of Concanavalin A (FIGS. 5A-5C). For a Th2 response, the hMPV fusion protein peptide pool induced the secretion of detectable IL10, TNF-α, IL4 and IL6, but not IL5, while Concanavalin A stimulated the secretion of all the above-mentioned Th2 cytokines (FIGS. 6A-6E) at a much higher level.

[0897] In contrast, inactivated hMPV virus only induced the secretion of IL2 in the Th1 response comparable to that of Concanavalin A (FIGS. 7A-7C). For the Th2 response, the inactivated hMPV virus induced the secretion of detectable IL10, TNF-α, IL4 and IL6, but not IL5, while Concanavalin A stimulated the secretion of all the above-mentioned Th2 cytokines (FIGS. 8A-8E) at a much higher level.

Example 16

hMPV Rodent Challenge in Cotton Rats Immunized with mRNA Vaccine Encoding hMPV Fusion Protein

[0898] The instant study was designed to test the efficacy in cotton rats of hMPV vaccines against a lethal challenge. mRNA vaccines encoding hMPV fusion protein were used. The mRNA polynucleotide encodes a full-length fusion

protein and comprises the wild-type nucleotide sequence obtained from the hMPV A2a strain.

[0899] Cotton rats were immunized intramuscularly (IM) at week 0 and week 3 with the mRNA vaccines encoding hMPV fusion protein with either 2 μ g or 10 μ g doses for each immunization. The animals were then challenged with a lethal dose of hMPV in week 7 post initial immunization via IV, IM or ID. The endpoint was day 13 post infection, death or euthanasia. Viral titers in the noses and lungs of the cotton rats were measured. The results (FIGS. 9A and 9B) show that a 10 μ g dose of mRNA vaccine protected the cotton mice 100% in the lung and drastically reduced the viral titer in the nose after challenge (~2 log reduction). Moreover, a 2 μ g dose of mRNA vaccine showed a 1 log reduction in lung viral titer in the cotton mice challenged.

[0900] Further, the histopathology of the lungs of the cotton mice immunized and challenged showed no pathology associated with vaccine-enhanced disease (FIG. 10).

Example 17

Immunogenicity Study

[0901] The instant study is designed to test the immunogenicity in mice of candidate PIV3 vaccines comprising a mRNA polynucleotide encoding hemagglutinin-neuraminidase or fusion protein (F or F0) obtained from PIV3.

[0902] Mice are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) with candidate vaccines. Candidate vaccines are chemically modified or unmodified. A total of four immunizations are given at 3-week intervals (i.e., at weeks 0, 3, 6, and 9), and sera are collected after each immunization until weeks 33-51. Serum antibody titers against hemagglutinin-neuraminidase or fusion protein (F or F0) are determined by ELISA. Sera collected from each mouse during weeks 10-16 are, optionally, pooled, and total IgGs are purified. Purified antibodies are used for immunoelectron microscopy, antibody-affinity testing, and in vitro protection assays.

Example 18

PIV3 Rodent Challenge

[0903] The instant study is designed to test the efficacy in cotton rats of candidate PIV3 vaccines against a lethal challenge using a PIV3 vaccine comprising mRNA encoding hemagglutinin-neuraminidase or fusion protein (F or F0) obtained from PIV3. Cotton rats are challenged with a lethal dose of the PIV3.

[0904] Animals are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) at week 0 and week 3 with candidate PIV3 vaccines with and without adjuvant. Candidate vaccines are chemically modified or unmodified. The animals are then challenged with a lethal dose of PIV3 on week 7 via IV, IM or ID. Endpoint is day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis are euthanized. Body temperature and weight are assessed and recorded daily.

[0905] In experiments where a lipid nanoparticle (LNP) formulation is used, the formulation may include a cationic lipid, non-cationic lipid, PEG lipid and structural lipid in the ratios 50:10:1.5:38.5. The cationic lipid is DLin-KC2-DMA (50 mol %) or DLin-MC3-DMA (50 mol %), the non-cationic lipid is DSPC (10 mol %), the PEG lipid is

PEG-DOMG (1.5 mol %) and the structural lipid is cholesterol (38.5 mol %), for example.

Example 19

hMPV/PIV Cotton Rat Challenge

[0906] The instant study was designed to test the efficacy in cotton rats of candidate hMPV mRNA vaccines, PIV3 mRNA vaccines, or hMPV/PIV combination mRNA vaccines against a lethal challenge using PIV3 strain or hMPV/A2 strain. The study design is shown in Table 9.

[0907] Cotton rats of 10-12 weeks old were divided into 12 groups (n 5), and each group was vaccinated with mRNA vaccines indicated in Table 9. The PIV3 vaccine comprises mRNA encoding hemagglutinin-neuraminidase or fusion protein (F or F0) obtained from PIV3. The hMPV mRNA vaccine encodes the full-length hMPV fusion protein. The hMPV/PIV combination mRNA vaccine is a mixture of the PIV3 vaccine and hMPV vaccine at a 1:1 ratio.

[0908] Cotton rats were immunized intramuscularly (IM) at week 0 and week 3 with candidate vaccines with the doses indicated in Table 9. Cotton rats immunized with hMPV mRNA vaccines or hMPV/PIV combination mRNA vaccines were challenged with a lethal dose of hMPV/A2 strain on week 7 via IM. Cotton rats immunized with PIV mRNA vaccines or hMPV/PIV combination mRNA vaccines were challenged with a lethal dose of PIV3 strain on week 7 via IM.

[0909] The endpoint was day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis were euthanized. Body temperature and weight were assessed and recorded daily.

[0910] Lung and nose hMPV/A2 (FIG. 12) or PIV3 (FIG. 13) viral titers were assessed. Lung histopathology of the immunized and challenged cotton rat immunized and challenged were assessed to determine pathology associated with vaccine enhance disease. Neutralization antibody titers in the serum of immunized cotton rats on day 0 and 42 post immunization were assessed (FIG. 11).

[0911] hMPV/A2 (FIG. 14) or PIV3 (FIG. 15) neutralizing antibody titers in the serum samples of the immunized cotton rat 42 days post immunization were measured. All mRNA vaccines tested induced strong neutralizing antibodies cotton rats. Lung histopathology of the immunized cotton rats were also evaluated (FIG. 16). Low occurrence of alevolitis and interstitial pneumonia was observed, indicating no antibody-dependent enhancement (ADE) of hMPV or PIV associated diseases.

Example 20

Betacoronavirus Immunogenicity Study

[0912] The instant study is designed to test the immunogenicity in rabbits of candidate betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1 or a combination thereof) vaccines comprising a mRNA polynucleotide encoding the spike (S) protein, the S1 subunit (S1) of the spike protein, or the S2 subunit (S2) of the spike protein obtained from a betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1).

[0913] Rabbits are vaccinated on week 0 and 3 via intravenous (IV), intramuscular (IM), or intradermal (ID) routes. One group remains unvaccinated and one is administered inactivated betacoronavirus. Serum is collected from each rabbit on weeks 1, 3 (pre-dose) and 5. Individual bleeds are tested for anti-S, anti-S1 or anti-S2 activity via a virus neutralization assay from all three time points, and pooled samples from week 5 only are tested by Western blot using inactivated betacoronavirus (e.g., inactivated MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1).

[0914] In experiments where a lipid nanoparticle (LNP) formulation is used, the formulation may include a cationic lipid, non-cationic lipid, PEG lipid and structural lipid in the ratios 50:10:1.5:38.5. The cationic lipid is DI in-KC2-DMA (50 mol %) or DI in-MC3-DMA (50 mol %), the non-cationic lipid is DSPC (10 mol %), the PEG lipid is PEG-DOMG (1.5 mol %) and the structural lipid is cholesterol (38.5 mol %), for example.

Example 21

Betacoronavirus Challenge

[0915] The instant study is designed to test the efficacy in rabbits of candidate betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-HKU1 or a combination thereof) vaccines against a lethal challenge using a betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-HKU1 or a combination thereof) vaccine comprising mRNA encoding the spike (S) protein, the S1 subunit (S1) of the spike protein, or the S2 subunit (S2) of the spike protein obtained from betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1). Rabbits are challenged with a lethal dose (10×10^9 ; ~ 100 plaque-forming units: PFU) of betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1).

[0916] The animals used are 6-8 week old female rabbits in groups of 10. Rabbits are vaccinated on weeks 0 and 3 via an IM, ID or IV route of administration. Candidate vaccines are chemically modified or unmodified. Rabbit serum is tested for microneutralization (see Example 14). Rabbits are then challenged with $\sim 1 \times 10^9$ of betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1) on week 7 via an IN, IM, ID or IV route of administration. Endpoint is day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by $>30\%$ weight loss, extreme lethargy or paralysis are euthanized. Body temperature and weight are assessed and recorded daily.

Example 22

Microneutralization Assay

[0917] Nine serial 2-fold dilutions (1:50-1:12,800) of rabbit serum are made in 50 μ l virus growth medium (VGM) with trypsin in 96 well microtiter plates. Fifty microliters of virus containing ~ 50 pfu of betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1) is added to the serum dilutions and allowed to incubate for 60 minutes at room temperature (RT). Positive control wells of virus

without sera and negative control wells without virus or sera are included in triplicate on each plate. While the serum-virus mixtures incubate, a single cell suspension of Madin-Darby Canine-Kidney cells are prepared by trypsinizing (Gibco 0.5% bovine pancrease trypsin in EDTA) a confluent monolayer and suspended cells are transferred to a 50 ml centrifuge tube, topped with sterile PBS and gently mixed. The cells are then pelleted at 200 g for 5 minutes, supernatant aspirated and cells resuspended in PBS. This procedure is repeated once and the cells are resuspended at a concentration of 3×10^5 /ml in VGM with porcine trypsin. Then, 100 μ l cells are added to the serum-virus mixtures and the plates incubated at 35° C. in CO₂ for 5 days. The plates are fixed with 80% acetone in phosphate buffered saline (PBS) for 15 minutes at RT, air dried and then blocked for 30 minutes containing PBS with 0.5% gelatin and 2% FCS. An antibody to the S proteins, S1 protein or S2 protein is diluted in PBS with 0.5% gelatin/2% FCS/0.5% Tween 20 and incubated at RT for 2 hours. Wells are washed and horseradish peroxidase-conjugated goat anti-mouse IgG added, followed by another 2 hour incubation. After washing, O-phenylenediamine dihydrochloride is added and the neutralization titer is defined as the titer of serum that reduced color development by 50% compared to the positive control wells.

Example 23

MERS CoV Vaccine Immunogenicity Study in Mice

[0918] The instant study was designed to test the immunogenicity in mice of candidate MERS-CoV vaccines comprising a mRNA polynucleotide encoding the full-length Spike (S) protein, or the S2 subunit (S2) of the Spike protein obtained from MERS-CoV.

[0919] Mice were vaccinated with a 10 μ g dose of MERS-CoV mRNA vaccine encoding either the full-length MERS-CoV Spike (S) protein, or the S2 subunit (S2) of the Spike protein on days 0 and 21. Sera were collected from each mice on days 0, 21, 42, and 56. Individual bleeds were tested for anti-S, anti-S2 activity via a virus neutralization assay from all four time points.

[0920] As shown in FIG. 17, the MERS-CoV vaccine encoding the full-length S protein induced strong immune response after the boost dose on day 21. Further, full-length S protein vaccine generated much higher neutralizing antibody titers as compared to S2 alone (FIG. 18).

Example 24

MERS CoV Vaccine Immunogenicity Study in New Zealand White Rabbits

[0921] The instant study was designed to test the immunogenicity of candidate MERS-CoV mRNA vaccines encoding the full-length Spike (S) protein. The New Zealand white rabbits used in this study weighed about 4-5 kg. The rabbits were divided into three groups (Group 1a, Group 1b, and Group 2, n=8). Rabbits in Group 1a were immunized intramuscularly (IM) with one 20 μ g dose of the MERS-CoV mRNA vaccine encoding the full-length Spike protein on day 0. Rabbits in Group 1b were immunized intramuscularly (IM) with one 20 μ g dose of the MERS-CoV mRNA vaccine encoding the full-length Spike protein on day 0, and again on day 21 (booster dose). Group 2 received placebo (PBS). The immunized rabbits were then challenged and

samples were collected 4 days after challenge. The viral loads in the lungs, bronchoalveolar lavage (BAL), nose, and throat of the rabbits were determined, e.g., via quantitative PCR. Replicating virus in the lung tissues of the rabbits were also detected. Lung histopathology were evaluated and the neutralizing antibody titers in serum samples of the rabbits were determined.

[0922] Two 20 µg doses of MERS-CoV mRNA vaccine resulted in a 3 log reduction of viral load in the nose and led to complete protection in the throat of the New Zealand white rabbits (FIG. 19A). Two 20 µg doses of MERS-CoV mRNA vaccine also resulted in a 4 log reduction of viral load in the BAL of the New Zealand white rabbits (FIG. 19B). One 20 µg dose of MERS-CoV mRNA vaccine resulted in a 2 log reduction of viral load, while two 20 µg doses of MERS-CoV mRNA vaccine resulted in an over 4 log reduction of viral load in the lungs of the New Zealand white rabbits (FIG. 19C).

[0923] Quantitative PCR results show that two 20 µg doses of MERS-CoV mRNA vaccine reduced over 99% (2 log) of viruses in the lungs of New Zealand white rabbits (FIG. 20A). No replicating virus were detected in the lungs (FIG. 20B).

[0924] Further, as shown in FIG. 21, two 20 µg doses of MERS-CoV mRNA vaccine induced significant amount of neutralizing antibodies against MERS-CoV (I:C₅₀ between 500-1000). The MERS-CoV mRNA vaccine induced antibody titer is 3-5 fold better than any other vaccines tested in the same model.

Example 25

Immunogenicity Study

[0925] The instant study is designed to test the immunogenicity in mice of candidate MeV vaccines comprising a mRNA polynucleotide encoding MeV hemagglutinin (HA) protein, MeV Fusion (F) protein or a combination of both.

[0926] Mice are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) with candidate vaccines. Up to three immunizations are given at 3-week intervals (i.e., at weeks 0, 3, 6, and 9), and sera are collected after each

immunization until weeks 33-51. Serum antibody titers against MeV HA protein or MeV F protein are determined by ELISA.

Example 26

MeV Rodent Challenge

[0927] The instant study is designed to test the efficacy in transgenic mice of candidate MeV vaccines against a lethal challenge using a MeV vaccine comprising mRNA encoding MeV HA protein or MeV F protein. The transgenic mice express human receptor CD46 or signaling lymphocyte activation molecule (SLAM) (also referred to as CD150). Humans are the only natural host for MeV infection, thus transgenic lines are required for this study. CD46 is a complement regulatory protein that protects host tissue from complement deposition by binding to complement components C3b and C4b. Its expression on murine fibroblast and lymphoid cell lines renders these otherwise refractory cells permissive for MeV infection, and the expression of CD46 on primate cells parallels the clinical tropism of MeV infection in humans and nonhuman primates (Rall GF et al. PNAS USA 1997;94(9):4659-63). SLAM is a type I membrane glycoprotein belonging to the immunoglobulin superfamily. It is expressed on the surface of activated lymphocytes, macrophages, and dendritic cells and is thought to play an important role in lymphocyte signaling. SLAM is a receptor for both wild-type and vaccine MeV strains (Sellin CI et al. *J Virol.* 2006;80(13):6420-29).

[0928] CD46 or SLAM/CD150 transgenic mice are challenged with a lethal dose of the MeV. Animals are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) at week 0 and week 3 with candidate MeV vaccines with and without adjuvant. The animals are then challenged with a lethal dose of MeV on week 7 via IV, IM or ID. Endpoint is day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis are euthanized. Body temperature and weight are assessed and recorded daily.

[0929] In experiments where a lipid nanoparticle (LNP) formulation is used, the formulation may include a cationic lipid, non-cationic lipid, PEG lipid and structural lipid in the ratios 50:10:1.5:38.5. The cationic lipid is DLin-KC2-DMA (50 mol %), the non-cationic lipid is DSPC (10 mol %), the PEG lipid is PEG-DMG (1.5 mol %) and the structural lipid is cholesterol (38.5 mol %), for example.

TABLE 1

hMPV Immunogenicity studies bleeding schedule										
Annual groups		Day								
(n = 8)	vaccine	-2	0	7	14	21	28	35	56	
Placebo Group 1 (n = 8)	PBS (IM)	Pre-Bleed	Prime	Bleeds	Bleeds	Bleeds	Boost	Bleeds	Bleeds	Harvest Spleens Terminal Bleeds
10 µg Dose 2 (n = 8)	10 µg (IM)									
2 µg Dose 3 (n = 8)	2 µg (IM)									

Total n = 24

[0930] Each of the sequences described herein encompasses a chemically modified sequence or an unmodified sequence which includes no nucleotide modifications.

TABLE 2

hMPV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
gi 122891979 gb EF051124.1 Human metapneumovirus isolate TN/92-4 fusion protein gene, complete genome	ATGAGCTGGAAGGTGGTATTATCTTCAGCCTGCTGATTA CACCTCAACACGGCCTGAAGGAGAGCTACCTGGAAGAGA GCTGCTCCACCATCACCGAGGGCTACCTGAGCGTGTGC GGACCGGCTGGTACACCAACGTGTTCACCCCTGGAGGTGG GCGACGTGGAGAACCCTGACCTGCAGCGACGGCCCTAGCC TGATCAGACCGAGCTGGACCTGACCAAGAGCGCTCTGA GAGAGCTGAAGACCGTGTTCGCGGACAGCTGGCCAGAG AGGAACAGATCGAGAACCCTCGGCAGAGCAGATTCTGTGC TGGGCGCCATCGCTCTGGGAGTTCGCGCTGCGCGTGCAG TGACAGCTGGAGTGGCCATTGCTAAGACCATCAGACTGG AAGCGAGGTGACAGCCATCAACAATGCCCTGAAGAAG ACCAACGAGGCGGTGAGCACCCCTGGGCAATGGAGTGAGA GTGCTGGCCACAGCCGTGCGGGAGCTGAAGGACTTCGTG AGCAAGAACCTGACCAGAGCCATCAACAAGAACAAGTG CGACATCGATGACCTGAAGATGGCCGTGAGCTTCTCCCA GTTCAACAGACGGTTCCTGAACGTGGTGAGACAGTTCTC CGACAACGCTGGAATCACACCTGCCATTAGCCTGGACCT GATGACCGACCGGAGCTGGCTAGAGCCGTGCCCAACAT GCCCACAGCGCTGGCCAGATCAAGCTGATGCTGGAGAA CAGAGCCATGGTGGGAGAAAGGGCTTCGGCATCCTGAT TGGGGTGTATGGAAGCTCCGTGATCTACATGGTGCAGCT GCCCATCTTCGGCCTGATCGACACACCTGCTGGATCGTG AAGGCCGCTCCTAGCTGCTCCGAGAAGAAAGGAACTAT GCCTGTCTGCTGAGAGAGGACAGGGCTGGTACTGCCAG AACGCCGGAAGCACAGTGTACTATCCCAACGAGAAGGAC TGGGAGACCAGAGGCGACACCGTGTCTGCGACACCGCT GCCGGATCAACCTGGCCGAGCAGAGCAAGGAGTGCAA CATCAACATCAGCAACAACAACCTACCCCTGCAAGGTGAG CACCGGACGGCACCCCATCAGCATGGTGGCTCTGAGCCC TCTGGGCGCTCTGGTGGCTGCTATAAGGGCGTTCCTGT AGCATTCGGCAGCAATCGGGTGGGCATCATCAAGCAGCTG AACAAAGGATGCTCCTACATCACCAACCCAGGACGGCGAC ACCGTGACCATCGACAAACCCGTGTACAGCTGAGCAG GTGGAGGGCAGCAGCAGTGTCAAGGGCAGACCCCT GAGCTCCAGCTTCGACCCCATCAAGTTCCTGAGGACCA GTTCAACCTGGCCCTGGACAGGTGTTGAGAATCGA GAAAGCCAGGCCCTGGTGGACAGAGCAACAGAACTCT GTCCAGCGCTGAGAAGGGCAACACCGGCTTCATCATTGT GATCATTTGATCGCCCTGCTGGGCAGCTCCATGATCCTG GTGAGCATCTTATCATATATCAAGAAAGCAAGAAACCC ACCGGAGCCCTCTGAGCTGAGCGCGTGACCAACAAT GGCTTCATTCCCCAACTGA	1
gb AY525843.1 : 3065-4684 Human metapneumovirus isolate NL/1/99, complete genome	ATGTCITGGAAAGTGTATGATCATCATTTCTTACTCATAA CACCCACGACGGGCTAAAGGAGAGTATTGGAAGAA CATGTAGTACTATAACTGAGGGATACCTCAGTGTTTAAG AACAGGCTGGTACACTAATGTCTTACATTAGAAGTTGGT GATGTTGAAAATCTTACATGTAAGTGGACCTAGCTTAA TCAAAACAGAACTTGATCTAACAAAAGTGTCTTAAAGGG AACTCAAAACAGTCTCTGCTGATCAGTTGGCGAGAGAGG AGCAAAATGAAAATCCCAGACAAATCAAGATTTGTCTTAG GTGCGATAGCTCTGGAGTGTCTACAGCAGCAGCAGTCA CAGCAGGCATTGCAATAGCCAAAACCATAAGGCTTGAGA GTGAGGTGAATGCAATTAAGGTGCTCTCAAAACAAACTA ATGAAGCAGTATCCACATTAGGGAATGGTGTGCGGGTCC TAGCCACTGCAGTGAGAGAGCTAAAAGAAATTTGTGAGCA AAAACCTGACTAGTGCAATCAACAGGAACAATGTGACA TTGCTGATCTGAAGATGGCTGTGAGCTTCAATTCATTCAA CAGAAGATTTCAATGTTGTGCGGCGAGTTTTCAGACAAT GCAGGGATAACACCAGCAATATCATTGGACCTGATGACT GATGCTGAGTTGGCCAGAGCTGTATCATACATGCCAACA TCTGCAGGGCAGATAAAAAGTGTGTTGGAGAACCGCGCA ATGGTAAGGAGAAAAGGATTTGGAATCCTGATAGGGGTC TACCGAAGCTCTGTGATTTACATGGTTCAATTCGCGATCT TTGGTGTGATAGATACACCTTGTGGATCATCAAGGCAGC TCCCTCTTGTCTCAGAAAACCGGAAATTTATGCTTGCCTC CTAAGAGAGGATCAAGGTTGATTTGTAATAATGCAGGA	2

TABLE 2-continued

hMPV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	TCTACTGTTTACTACCCAAATGAAAAAGACTGCGAAACA AGAGGTGATCATGTTTTTTGTGACACAGCAGCAGGGATC AATGTTGCTGAGCAATCAAGAGAATGCACATCAACATA TCTACTACCAACTACCCATGCAAAGTCAGCACAGGAAGA CACCCATAAGCATGGTTGCACATCACCTCTCGGTGCTT TGGTGGCTTGCATAAAGGGTAAAGTCTCGATTGGCA GCAATTGGGT TGGAATCATCAAACAATTACCCAAAGGCTGCTCATAAT AACCAACCCAGGATGCAGACCTGTAAACATTTGACARTAC CGTGATCAACTAAGCAAAGTTGAAGGTGAACAGCATGT AATAAAAGGGAGACCAGTTTCAAGCAGTTTGTATCCAAT CAAGTTTCCCTGAGGATCAGTTCAATGTTGGCTTGATCAA GTCTTCGAAAGCATTGGAACAGTCAGGCACTAGTGGAC CAGTCAAACAATAATTCTAAACAGTGCAGAAAAAGGAAA CACTGGTTTTCATTATCGTAGTAATTTGGTGTGCTGTTCTG GTCTAACCATGATTTCAAGTGCATCATCATATAATCAA GAAAACAAGGAAGCCACAGGAGCACCTCCAGAGCTGA ATGTTGTCACCAACGGCGTTTCATACCACATAGTTA	
gb KJ627414.1 : 3015-4634 Human metapneumovirus strain hMPV/Homo sapiens/PER/CFI0497/ 2010/B, complete genome	ATGTCCTGGAAAGTGATGATTATCATTTCGTTACTCATAA CACCTCAGCATGGACTAAAAGAAAGTTATTTAGAAAGAAAT CATGTAGTACTATAAAGTGAAGGATATCTCAGTGTTTTAAG AACAGGTTGGTACACCAATGCTTTACATTAGAAGTTGGT GATGTTGAAAATCTTACATGTACTGTATGAGCCTAGCTTAA TCAAACAGAACTTGACCTAACCAAAAGTGTCTTAAGAG AACTCAAACAGGTTTCTGCTGATCAGTTAGCGAGAGAG AACAAATTGAAAATCCCAGCAATCAAGGTTTGTCCCTAG GTGCAATAGCTCTTGGAGTTGCCACAGCAGCAGCAGTCA CAGCAGGCATTGCAATAGCCAAAACATAAGGCTTGAGA GTGAAGTGAATGCAATCAAGGTTGCTCTCAAACAACCA ATGAGGCAGTATCAACTAGGAAATGGAGTGGCGGTTCC TAGCCACTGCAGTAAGAGAGCTGAAAAGAAATTTGTGAGCA AAAACCTGACTAGTGGATCAACAGAAACAAAGTGTGACA TTGCTGATTTGAAGATGGCTGTGAGCTTCAGTCAGTTCAA CAGAAGATTCCTAAATGTTGTGGCAGTTTTCAGACAAT GCAGGGATAACACAGCAATATCATTTGACCTGATGAAT GATGCTGAGCTGGCCAGAGCTGTATCATACATGCCAACA TCTGCAGGACAGATAAACTAATGTTAGAGAACCGTGCA ATGGTGAGGAGAAAAGGATTTGGAATCTTGATAGGGGTC TAGGAAAGCTCTGTGATTTACATGGTCCAGCTGCCGATCT TTGGTGTCAAAAACACCTTGTGGATAATCAAGGCAGC TCCCCTCTGTTTCAAAAAGATGGAATTTATGCTTGCCCTC CTAAGAGAGGATCAAGGTTGGTATTTGAAAAATGCAGGA TCCACTGTTTACTACCCAAATGAAAAAGACTGCGAAACA AGAGGTGATCATGTTTTTTGTGACACAGCAGCAGGGATC AATGTTGCTGAGCAATCAAGAGAATGCACATCAACATA TCTACCACCAACTACCCATGCAAAGTCAGCACAGGAAGA CACCCATCAGCATGGTTGCACATCACCTCTCGGTGCTT TGGTAGCTTGTACAAAGGGGTTAGCTGCTCGACTGGCA GTAATCAGGTTGGAAATAATCAAACAACCTACCTAAAGGCT GCTCATAACATAACTAACAGGACGCAGACACTGTAACAA TTGACAACACTGTGTATCAACTAAGCAAAGTTGAGGGTG AACAGCATGTAATAAAAGGGAGACCAGTTTCAAGCAGTT TTGATCCAATCAGGTTTCCCTGAGGATCAGTTCAATGTTGC GCTTGATCAAGTCTTTGAAAGCATTGAAAACAGTCAAGC ACTAGTGGACCAGTCAAACAATAATTGAAACAGTGCAGA AAAAGGAAACACTGGT TTCATTATTGTAATAATTTTGATTGCTGTTCTTGGGTTAAC CATGATTTCAAGTGCATCATCATATAATCAAACAAC AAGGAAGCCACAGGGGCACCTCCGGAGCTGAATGGTGT TACCAACGGCGGTTTCATACCCGATAGTTAG	3
gb KJ723483.1 : 5586-7310 Human respiratory syncytial virus strain RSV A/Homo sapiens/USA/841- 215A-01/1984, complete genome	ATGGAGTTGCCAATCCTCAAACAATGCAATTACCACA ATCCTTGTGTCAGTCCACTCTGTTTCGCTTCCAGTCAAA ACATCACTGAAGAATTTTATCAATCAACATGCAGTGCAG TTAGCAAAGGCTATCTTGTGCTCTAAGAAGTGGTTGGTA TACTAGTGTATAACTATAGAATTAAGTAATATCAAGGA AAATAAGTGAATGGAACAGATGCTAAGGTTAAATTTGAT AAAACAGAAATAGATAAATATAAAAATGCTGTAAACAGA ATTGCAGTTGCTCATGCAAAGCACACCAGCAGCCAAACA TCGACCCAGAAGAGAACTCAAGGTTTATGAATATATAC ACTCAATAATACCAAAAATACCAATGTAACATTAAGCAA	4

TABLE 2-continued

hMPV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	GAAAAGGAAAAGAAGATTCTTGGCTTTTGTAGGTGTT GGATCTGCAATCGCCAGTGGCATTGCTGTATCTAAGGTCC TGCACCTAGAAGGGGAGTGAACAAAATCAAAGTGTCTC TACTATCCACAAAACAGGCTGTAGTACGCTTATCAAATG GAGTTAGTGTCTTAACCAGCAAAGTGTAGACCTCAAAA ACTATATAGATAAACCGTTGTACCTATTGTGAACAAGC AAAGCTGCAGCATATCAAACATTGAAACTGTGATAGAGT TCCAACAAAAGAACAAACAGACTACTAGAGATTACCAGGG AATTTAGTGTTAATGCAGGTGTAACACCTGTARGCAC TTATATGTTAACTAATAGTGAATTATTATCATTAAATCAAT GATATGCCCTATAACAAATGATCAGAAAAGTTAATGTCC AACAAATGTTCAAATAGTTAGACAGCAAAGTTACTCTATC ATGTCCATAATAAAGGAGGAAGTCTTAGCATAATGTAGTA CAATTACCACTATATGGTGAATAGATACACCCTGTTGGA AACTGCACACATCCCTCTATGTACACCAACCAAAGG AAGGGTCCAACATCTGCTTAAACAAGAACCGACAGAGGAT OGTATTGTGACAATGCAGGATCAGTATCTTCTTCCCACA AGCTGAAACATGTAAGTTCAAATCGAATCGGGTATTTGT GACACAATGAACAGTTTAAACATTACCAAGTGAAGTAAAT CTCTGCAACATTGACATATTCACCCCAAATATGATTGCA AATTTATGACTTCAAAAACAGATGTAAAGCAGCTCCGTTA TCACATCTCTAGGAGCCATTGTGTATGCTATGGCAAAAAC TAAATGTACAGCATCCAATAAAAATCGTGGGATCATAAA GACATTTCTAACCGGTGTGATTATGTATCAATAAAGGG GGTGGATACTGTGCTGTAGGTAATACATTATATATGTGA AATAAGCAAGAAGGCCAAAAGTCTCTATGTAAGAGGTGAA CCAATAATAAATTTCTATGACCCATTAGTGTTCCTCTG ATGAATTTGATGCATCAATATCTCAAGTCAATGAGAAGA TTAACCAAGAGCCTAGCATTATTCGTAAATCCGATGAATT ATTACATAATGTAATGCTGGTAAATCCACCACAATAT CATGATAACTACTATAATTTATAGTGATTATAGTAATATTG TTATCATTAAATTCAGTTGGACTGCTCCTATACTGCAAGG CCAGAAGCACACCAGTCACTAAGTAAGGATCAACTGA GTGGTATAAATAATATTGCATTTAGTAACTGA	
hMPV mRNA Sequences		
gi 122891979 gb EF051124.1 Human metapneumo virus isolate TN/92-4 fusion protein gene, complete genome	AUGAGCUGGAAGGUGGUGAUUAUCUUCAGCCUGCUGAU UACACCUCAACACCGCCUGAAGGAGAGCUACCUGGAAG AGAGCUGCUCCACCACUACCGAGGGCUACCUGAGCGUG CUGCGGACCGGCUUGUACACCAACGUGUUCACCCUGGA GGUGGGCGAAGUGGAGAACCUGACCUGCAGCGAGCGCC CUAGCCUGAUCAGACCGAGCUGGACCUGACCAAGAGC GCUCUGAGAGAGCUGAAGACCGUUCGCCGACCAAGCU GGCCAGAGAGGAAACAGAUCCAGAACCCUGCGCAGAGCA GAUUCGUGCUGGGCGCCAUCCGUCUGGGAGUCGCCCU GCCGCUAGAGUGACAGCUGGAGUGGCCAUUGCUAAGAC CAUCAGACUGGAAGCGAGGUGACAGCCAUCAACAUAUG CCUGAAGAAGACCAACGAGGCCUGAGCACCCUGGGC ARUGGAGUGAGAGUGCUUGGCCACAGCCGUGCGGAGCU GAAGGACUUCGUGAGCAAGAACUGACCAAGACCAUCA ACAAGAACAGUGCGACAUUGAUGACCUAGAAGUGGCC GUGAGCUUCUCCAGUUCACAGACCGGUUCUGAACGU GGUGAGACAGUUCUCCGACAACCGUGGAUUCACACCCUG CCAUUAAGCCUGGACCUGAUGACCGAGCCGAGCUGGCCU AGAGCCGUGCCCAACAUCCACCAGCGCUGGCCAGAU CAAGCUGAUGCUGGAGAACAGAGCCAUUGGUGCGGAGAA AGGGCUUCGGCAUCUGAUUUGGGUGUAUGGAAGCUC GUGAUCUACAUGGUGCAGCUGCCCAUCUUCGGCGUGAU CGACACACCCUGCUGAUCGUGAAGGCCGCUCCUAGCU GCUCCGAGAAGAAAGGAAACUAUGCCUGUCUGCUGAGA GAGGACCAGGGCUGGUACUGCCAGAACCGCGAAGCAC AGUGUACUAUCCCAACGAGAAGGACUGCGAGACCAGAG GCGACCACGUGUUCUGCGACACCGCUGCCGGAUCCAC GUGGCCGAGCAGAGCAAGGAGUGCAAUCAACAACUAG CACAACCAACUACCCUGCAAGGUGAGCACCGGACGGC ACCCAUCAGCAUGGUGGCUUCUGAGCCUCUGGGCGCU CUGGUGGCCUGCUATAAGGGCGUGUCUGUAGCAUCGG CAGCAAUCCGGUGGCAUCADCAAGCAGCUGAACCAAGG GAUGCUCUACAUCACCAACCAAGGACCGACACCGUG ACCAUCGACAACACCGUGUACCAAGCUGAGCAAGGUGGA GGGCGAGCAGCACGUGAUCAGGGCAGACCGUGAGCU	57

TABLE 2-continued

hMPV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO.
	CCAGCUUCGACCCCAUCAAGUUCUCCUGAGGACCAGUUC AACGUGGCCUUGGACCAGGUGUUUGAGAACAUCGAGAA CAGCCAGGCCUUGGUGGACCAGAGCAACAGAAUCCUGU CCAGCGCUGAGAAGGGCAACACCGGCUUCAUCAUUGG AUCAUUCUGAUCGCCGUGCGGGCAGCUCCAUGAUCCU GGUGAGCAUCUUCACUUAUCAAGAGACCAGAAAC CCACCGGAGCCUUCUGAGCUGAGCGGCUGACCAAC AAUGGCUUCAUCCCCACAACUGA	
gb AY525843.1 : 3065-4684 Human metapneumovirus isolate NL/1/99, complete genome	AUGUCUUGGAAAGUGAUGAUCUCAUUUCGUUACUCAU AACACCCAGCACGGCUAAAAGGAGAGUUAUUUGGAAG AAUCAUGUAGUACUAUAACUGAGGGAUACUCAGUGUU UUAAGAACAGGCUGGUACACUAUUGUCUUCACAUUAGA AGUUUGGUGAUGUUGAAAUCUUACAUGUACUGAUGGA CCUAGCUUAUACAACAGAACUUGAUUCUAAACAAAAG UGCUUUAAGGGAAUCUAAAACAGUCUCUGUGAUCAGU UGGCAGAGAGGAGCAAAUUGAAAUCUCCAGACAAUCA AGAUUUUGUCUAGGUGCGAUAGCUCUCGGAGUUGCUAC AGCAGCAGCAGUCACAGCAGGCAUUGCAUAGCCAAA CCAUAAAGGCUUGAGAGUGAGGUGAAUGCAUUAAAGG UGCUUCUCAAACAACUAUAGUAGCAGUAUCACAUUAG GGAAUGGUGUGCGGGUCUAGCCACUGCAGUGAGAGAG CUAAAAGAAUUUGUGAGCAAAAACUUGACUAGUGCAAU CAACAGGAACAUAUUGUACAUUGCUGAUUGAAGAUGG CUGUCAGCUUCAGUCAUUCAACAGAGAUUUUAAAAD GUUGUGCGGCAGUUUUCAGACAADUGCAGGGAAUACAC AGCAAUAUCAUUGGACUGAUGACUGAUGCUGAGUUGG CCAGAGCUGUAUCAGACUAGCCAAACUUCGAGGGCAG AUAAAACUGAUGUUGGAGAACCAGCGCAUUGGUAAGGAG AAAAGGAUUUGGAUCCUGAUAGGGGUCUACGGAAAGCU CUGUGAUUDDCAUGGUUCAAUUGCCGACUUUGGUGUC AUAGAUACACCUUGUUGGAUCAUAAAGCAGCUCUCCUC UUGCUCAGAAAAAAACGGGAUUUUGCUUGCCUCAA GAGAGGAUCAAGGGUGGUUUUGUAAAUAUGCAGGAUC UAUCGUUUAUCUACCAAUUGAAAAGACUGCGAAACAA GAGGUGAUCAGUUUUUGUGACACAGCAGCAGGGAUC AAUGUUGCUGAGCAUCAGAGAAUGCAACUCAAACAU AUCUACUACCAACUACCAUGCAAGUCAGCAAGGAA GACACCUCUAAGCAUGGUUGCACUAUCACUUCUGGU GCUUUGGUGGCUUGCUAAAAGGGUAAAGCUGCUGAU UGGCAGCAAUUGGGU UGGAAUCADCAAAACAAUUAACCAAAGGCUGCUCAUACA UAACCAACAGGAUGCAGACACUGUAACAAUUGACAAU ACCGUGUAUCAACUAAGCAAAGUUGAAGGUGAACAGCA UGUAAUAAAAGGGAGACCAGUUUCAAGCAGUUUGAUC CAUACAAGUUUCCUGAGGAUCAGUUCAUUGUUGCGCUU GAUCAAGUCUUCGAAAGCAUUGAGAAAGUCAGGCACU AGUGGACCAGUCAAAACAAAUAUCUAAACAGUGCAGAAA AAGGAAACACUGGUUUCAUUUCUGUAGUAAUUUGGU UGCUGUUCUUGGUCUAAACCAUGAUUUUAGUGAGCAUCA UCAUCAAAUCAGAAAAACAGGAAGCCACAGGAGCA CCUCCAGAGCUGAAUGGUGUACCAACCGCCGUUUCAU ACCACAUAGUUAG	58
gb KJ627414.1 : 3015-4634 Human metapneumovirus strain hMPV/Homo sapiens/PER/CFI0497/ 2010/B, complete genome	AUGUCUUGGAAAGUGAUGAUUAUCAUUUCGUUACUCAU AACACCCAGCAUGGACUAAAAGAAAGUUAUUUAGAAAG AAUCAUGUAGUACUAUAACUGAGGGAUACUCAGUGUU UUAAGAACAGGUUGGUACACCAUUGUCUUAUCAUUGA AGUUUGGUGAUGUUGAAAUCUUACAUGUACUGAUGGA CCUAGCUUAUACAACAGAACUUGACCUAACCCAAAAG UGCUUUAAGGAAACUAAAACAGUUUCUGUGAUCAGU UAGCGAGAGAAGAACAAUUGAAAUCUCCAGACAAUCA AGGUUUGUCCUAGGUGCAAUAGCUCUUGGAGUUGCCAC AGCAGCAGCAGUCACAGCAGGCAUUGCAUAGCCAAA CUAUAAGGCUUGAGAGUGAAGUGAAUUGCAUCAAAGG UGCUUCUAAAACAACCAAUGAGGCAGUAUCAACACUAG GAAUUGGAGUGCGGGUCUAGCCACUGCAGUAAAGAGAG CUGAAAAGAAUUUGAGCAAAAACUUGACUAGUGCGAU CAACAAGAACAGUGUGACAUUGCUGAUUUGAAGAUUGG CUGUCAGCUUCAGUCAGUUCAAACAGAGAUUCCUAAA GUUGUGCGGCAGUUUUCAGACAADUGCAGGGAAUACACC AGCAAUAUCAUUGGACUGAUGAAUGAUGCUGAGCUGG	59

TABLE 2-continued

hMPV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	CCAGAGCUGUAUCAUACAUGCCAACAUCUGCAGGACAG AUAAAACUAAUGUUAAGAGAACCUGCAAUUGGUGAGGA GAAAAGGAAUUGGAUUCUUGAUAGGGGUUACCGAAG CUCUGUGAUUACAUUGGUCAGCUGCCGAUCUUUGGUG UCAUAAAUAACCCUUGUUGGAUAAUCAGGCAGCUCC UCUUGUUCAGAAAAGAUGGAAUUAUGCUUGCCUCCU AAGAGAGGAUCAAGGGUGGUUUGUAAAAAUGCAGGA UCCACUGUUUACUACCCAAAUGAAAAGACUGCGAAAC AAGAGGUGAUCAGUUUUUUGUGACACAGCAGCAGGGA UCBAUGUUGCUGAGCAAUCAAGAGAUAUGCAACUACAC AUAUCUACCCAAACUACCCAUUGCAAAGUCAGCACAGG AAGACCCCUAUCAGCAUGGUUGCACAUCACCUUCUG GUGCUUUGGUAGCUUGCUACAAGGGGUUAGCUGCUCG ACUGGCAGUAAUCAGGUUGGAAUAAUCAAACAACUACC UAAGGCUGCUCUACAUAACUAAACAGGACGCAGACA CUGUAAACAUUGACAACACUGUGUAUACAUAAGCAA GUUGAGGGUGAACAGCAUGUAAUAAAAGGGAGACCAG UUCACAGCAGUUUGAUCCAUCAGGUUUCUGAGGGAU CAGUUCAAUGUUGCGCUUGAUCAGUCUUGAAGCAU UGAAAACAGUCAAGCACUAGUGGACCAGUCAACAAA UUCUGAACAGUGCAGAAAAGGAAACACUGGU UUCAUUAUUGUAUUAUUUUUGAUUGCUGUUUCUUGGU UAACCAUGAUUUCAGUGAGCAUCAUCAUUAUCAA AAAACAAGGAAGCCACAGGGGCACCUCCGAGCUGAA UGGUGUUAACCAACGGCGGUUUCADACC GAUAGUUG	
gb KJ723483.1 : 5586-7310 Human respiratory syncytial virus strain RSVa/Homo sapiens/USA/84I- 215A-01/1984, complete genome	AUGGAGUUGCCAUCUCAAACAAAUGCAAUJACCAC AAUCUUGCUGCAGUCAACUCUGUUUCGCUUCCAGUC AAAACAUCACUGAAGAAUUUUAUCAUCAAUAGCAGU GCAGUAGCAAAGGCUAUCUUGAGUCUCAAGAACUGG UUGGUUAUCUAGUGUUUAACUUAUAGAAUUAAGUAAU AUCAGGAAAUAAGUGUAAUGGAACAGAUUCUAAAGG UPAAAUUGAUAAAACAGAAUUAAGUAAUUAUAAA UGCUUUAACAGAAUUGCAGUUGCUUAGCAAGCACAC CAGCAGCCAACAUCGAGCCAGAAGAGAACUACCAAGG UUUUUGAAUUUAUCACUCAUAAUACCAAAAUAACCAA UGUAAACUUAAGCARGAAAAGGAAAAGAAGAUUUCUU GGCUUUUUGUAGGGUUGGAUCUGCAUCCGCAAGUGG CAUUGCUGUAUCUAGGUCUCUGCACCUUAGAAGGGGAG UGAACAAAUCAAAAGUUCUCUACUUAUCCAAAACAAG GCUGUAGUCAGCUUAUCAAAUGGAGUUAUGUCUUAAC CAGCAAGUGUUGAGCCUCAAACUUAUUAAGAUAAAC AGUUGUUAUCUUAUUGUGAACAGCAAGCAGCAGCAUA UCBAACAUUGAAACUGUGAUAGAGUUCCAAACAAGAA CAACAGACUACUAGAGAUUACAGGGAAUUAUGUGUA AUGCAGGUGUAAUCACACUGUAAGCACUUAUUAUGUA ACUAAUAGUGAAUUAUUAUCAUUAUUAUUAUGAUUGCC UAUAACAAAUGAUCAGAAAAGUUAUUGUCCAACAAG UUCAAAUAGUUAAGCAGCAAAGUUAUCUUAUCAUGUCC AUAAUAAAGGAGGAGUCUUAAGCAUUAUGUAGUACA UAACCAUUAUUGGUGUAAUAGAUACACCCUGUUGGAAA CUGCACACAUCCUUAUGUACAACCAACAACAAGGA AGGGUCCAAACUUCUGCUUAACAAGAACCGACAGAGGAU GGUAUUGUGACAAUGCAGGAUCAGUAUCUUUCUCCCA CAAGCUGAAAACAUUAAAGUUAUUAUUGAAUUGGUAU UUGUGACACAUGAACAGUUUAACAUAUACCAAGUGAAG UAAAUCUCUGCAACAUUGACAUUUAACCCCAAUUAU GAUUGCAAAAUAUGACUUCAAAACAGAUUUAAGCAG CUCCGUUAUCAUCUCUAGGAGCCAUUGUGUCAUGCU AUGGCAAAACUAAAGUUAACAGCAUCCAAUAAAAUUCGU GGGAUCAUAAAGACAUUUUCUAAACGGGUGUAUUAUG UAUCAAUAAGGGGGUGGAUACUGUGUCUGUAGGUAA UACAUAUAUUAUCUAAAUAAGCAAGAGGCAAAAGU CUUAUGUAAAAGGGAACCAAUAAUAAUUAUUAUGA CCCAUUAGUGUUCUCCUCUGAUGAAUUAUGAUCACAA UAUCUCAAGUCAUAGAGAAGAUUAACCAAGAGCCUAGCA UUAUUAUGUAAAUCGUAUGAAUUAUUAUUAUUAUUA AUGCUGUAAAUCACCACAAUUAUCAUGAUUAACUACU	60

TABLE 2-continued

hMPV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	AUAAUUUAGUGAUUUUAGUAAUUGUUUUAUCAUUA UUGCAGUUGGACUGCUCUADACUGCAAGGCCAGAAGC ACACCAGUCACACUAAGUAGGAUCAACUGAGUGGUAD AAUAAUUAUGCAUUUAGUUAACUGA	

TABLE 3

hMPV Amino Acid Sequences		
Description	Sequence	SEQ ID NO:
gi 122891979 gb EF051124.1 Human metapneumovirus isolate TH/92-4 fusion protein gene, complete cds	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTG YTNVFTLEVGDVENLTCSDGPSLIKTELDLTKSALRELKTVS ADQLAREEQIENPRQSRFVLGAIALGVAAAAAVTAGVAIAK TIRLESEVTAIHNALKKTNEAVSTLGNQVRLATAVRELKD PVSKNLTRAIKKNKCDIDDLKMAVSPSQFNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAQGIKLMLENRA MVRKGFGLIGVYGVSSVIYMWQLPIFGVIDTPCWIKAAPCS CEKKGNYACLLREDQGWYCKNAGSTVYYPNEKDCETR DHVFCDTAAGINVAEQSKECNINISTTNYPCVKVSTGRHPISM VALSPLGALVACYKGVSCS IGSNRVGI I KQLPKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHV I KGRPVSS SFDPIKFPEDQF NVALDQVPENIENSQALVDQSNRILSSAEKNGTGFIIIVILIAV LGSSMILVSI F I I I KKT KKTGAPPEL SGVTNNGFIPHN	5
gb AY525843.1 : 3065-4684 Human metapneumovirus isolate NL/1/99, complete cds	MSWKVMIIISLLITPQHGLKESYLEESCSTITEGYLSVLRGTG YTNVFTLEVGDVENLTCSDGPSLIKTELDLTKSALRELKTVS ADQLAREEQIENPRQSRFVLGAIALGVATAAAVTAGIAIAKT IRLESEVNAIKGALKQTNEAVSTLGNQVRLATAVRELKEF VSKNLTSAINRNKCDIADLKNMAVSPSQFNRRFLNVVRQFSD NAGITPAISLDLMTDAELARAVSYMPTSAQGIKLMLENRAM VRRKGFGLIGVYGVSSVIYMWQLPIFGVIDTPCWIKAAPSCS EKNGNYACLLREDQGWYCKNAGSTVYYPNEKDCETRGDH VFCDTAAGINVAEQSRECNINISTTNYPCVKVSTGRHPISMVA LSPLGALVACYKGVSCS IGSNWVGI I KQLPKGCSYITNQDAD TVTIDNTVYQLSKVEGEQHV I KGRPVSS SFDPIKFPEDQFNV ALDQVFESIENSQALVDQSNKILNSAEKNGTGFIIIVILVAVL GLTMSVSI I I I I KKT KKTGAPPEL NGVTNNGFIPHS	6
gb KJ627414.1 : 3015-4634 Human metapneumovirus strain hMPV/ <i>Homo sapiens</i> /PER/CFI0497/ 2010/B, complete cds	MSWKVMIIISLLITPQHGLKESYLEESCSTITEGYLSVLRGTG YTNVFTLEVGDVENLTCSDGPSLIKTELDLTKSALRELKTVS ADQLAREEQIENPRQSRFVLGAIALGVATAAAVTAGIAIAKT IRLESEVNAIKGALKTNEAVSTLGNQVRLATAVRELKEF VSKNLTSAINRNKCDIADLKNMAVSPSQFNRRFLNVVRQFSD NAGITPAISLDLMTDAELARAVSYMPTSAQGIKLMLENRAM VRRKGFGLIGVYGVSSVIYMWQLPIFGVIDTPCWIKAAPSCS EKDGNACLLREDQGWYCKNAGSTVYYPNEKDCETRGDH VFCDTAAGINVAEQSRECNINISTTNYPCVKVSTGRHPISMVA LSPLGALVACYKGVSCS CTGSNQGVI I KQLPKGCSYITNQDAD TVTIDNTVYQLSKVEGEQHV I KGRPVSS SFDPIRFPEDQFNV ALDQVFESIENSQALVDQSNKILNSAEKNGTGFIIIVILIAVLG LTMISVSI I I I I KKT KKTGAPPEL NGVTNNGFIPHS	7
gb KJ723483.1 : 5586-7310 Human respiratory syncytial virus strain RSVA/ <i>Homo sapiens</i> /USA/84I- 215A-01/1984, complete cds	MELPILKTNAITTILAAVTLCFASSQNI TEEFYQSTCSAVSKG YLSALRTGWYTSVITIELSNIKENKCNKGTDAKVKLIKQELDK YKNAVTEQLQLMQSTPAAMNRRARRELPFRFMYTLNNTKNT NVTLSKKRRRFLGFLGVSASIAAGIASKVLHLEGEVNI KSALLSTNKAVVLSNGVSVLTSKVLDLKNYIDKQLLPIVN KQSCSISNIETVIEFQQKNRLLIETREFSVNAGVTPVSTYM LTNSELLSLINDMPI TNDQKKLMSNNVQIVRQQSYSIMS I I KE EVLAYVYVQLPLYGVIDTPCWLKHTSPLCTNTKEGSHICLTR TDRGWYCDNAGSVSFFPQAEETCKVQSNRVFCDTMNSLTLP SEVNLCHNIDI PNPKYDCKIMTSKTDVSSSVITSLGAVSCYGK TKCTASNKNRGI I KTFNSGCDYVSNKGVDTVSVGNTLYYVH KQEGKSLYVKGEPI INFYDPLVFPSEDFDASISQVNEKINQSL AFIRKSDLELLHMVNAGKSTTNIMITIIIVIIIVLLSLIAVGLL YKARSTPVTLTKDQLSGINNIAPSN	8

TABLE 4

hMPV NCBI Accession Numbers (Amino Acid Sequences)	
Virus	GenBank Accession
F [Human metapneumovirus] [Human metapneumovirus]	AJK26895.1
fusion glycoprotein [Human metapneumovirus]	ACJ53565.1
fusion glycoprotein [Human metapneumovirus]	ACJ53566.1
fusion glycoprotein [Human metapneumovirus]	ACJ53569.1
fusion protein [Human metapneumovirus]	AJZ52347.1
fusion glycoprotein [Human metapneumovirus]	ACJ53574.1
fusion glycoprotein [Human metapneumovirus]	AIIV79473.1
fusion glycoprotein [Human metapneumovirus]	ACJ53579.1
fusion glycoprotein [Human metapneumovirus]	ACJ53567.1
fusion protein [Human metapneumovirus]	AAS22125.1
fusion glycoprotein [Human metapneumovirus]	AIIV79795.1
fusion glycoprotein [Human metapneumovirus]	AIIV79455.1
fusion glycoprotein [Human metapneumovirus]	ACJ53568.1
fusion protein [Human metapneumovirus]	AAS22109.1
fusion glycoprotein [Human metapneumovirus]	AGL68417.1
fusion glycoprotein [Human metapneumovirus]	AGJ74228.1
fusion glycoprotein [Human metapneumovirus]	ACJ53575.1
fusion protein [Human metapneumovirus]	AAU25820.1
fusion glycoprotein [Human metapneumovirus]	AGU68377.1
fusion glycoprotein [Human metapneumovirus]	AGL68371.1
fusion glycoprotein [Human metapneumovirus]	AGJ74087.1
fusion glycoprotein [Human metapneumovirus]	ACJ53560.1
fusion glycoprotein [Human metapneumovirus]	AIIV79858.1
fusion glycoprotein [Human metapneumovirus]	ACJ53577.1
fusion protein [Human metapneumovirus]	AAS22085.1
fusion protein [Human metapneumovirus]	AJZ52348.1
fusion glycoprotein [Human metapneumovirus]	AGJ74044.1
fusion glycoprotein [Human metapneumovirus]	ACJ53563.1
fusion glycoprotein precursor [Human metapneumovirus]	YP_012608.1
fusion glycoprotein [Human metapneumovirus]	AGJ74053.1
fusion protein [Human metapneumovirus]	BAM37562.1
fusion glycoprotein [Human metapneumovirus]	ACJ53561.1
fusion glycoprotein [Human metapneumovirus]	AGL68387.1
fusion [Human metapneumovirus]	AGL74060.1
fusion glycoprotein precursor [Human metapneumovirus]	AAV88364.1
fusion protein [Human metapneumovirus]	AAN52910.1
fusion protein [Human metapneumovirus]	AAN52915.1
fusion protein [Human metapneumovirus]	BAM37564.1
fusion glycoprotein precursor [Human metapneumovirus]	BAH59618.1
fusion protein [Human metapneumovirus]	AAQ90144.1
fusion glycoprotein [Human metapneumovirus]	AIIV79446.1
fusion protein [Human metapneumovirus]	AJL87260.1
fusion glycoprotein [Human metapneumovirus]	AIIV79867.1
fusion protein [Human metapneumovirus]	ABQ66027.2
fusion glycoprotein [Human metapneumovirus]	ACJ53621.1
fusion protein [Human metapneumovirus]	AAN52911.1
fusion glycoprotein [Human metapneumovirus]	AIIV79536.1
fusion glycoprotein [Human metapneumovirus]	AGL68411.1
fusion protein [Human metapneumovirus]	AJZ52346.1
fusion protein [Human metapneumovirus]	AAN52913.1
fusion protein [Human metapneumovirus]	AAN52908.1
fusion glycoprotein [Human metapneumovirus]	ACJ53553.1
fusion glycoprotein [Human metapneumovirus]	AIY25727.1
fusion protein [Human metapneumovirus]	ABM67072.1
fusion protein [Human metapneumovirus]	AJZ52361.1
fusion protein [Human metapneumovirus]	AAN22093.1
fusion glycoprotein [Human metapneumovirus]	AGH27049.1
fusion protein [Human metapneumovirus]	AAK62968.2
fusion glycoprotein [Human metapneumovirus]	ACJ53556.1
fusion glycoprotein [Human metapneumovirus]	ACJ53620.1
fusion protein [Human metapneumovirus]	ABQ66021.1
F [Human metapneumovirus] [Human metapneumovirus]	AJK26886.1
fusion glycoprotein [Human metapneumovirus]	ACJ53619.1
fusion glycoprotein [Human metapneumovirus]	ACJ53555.1
fusion [Human metapneumovirus]	AGL74057.1
fusion protein [Human metapneumovirus]	ABD27850.1
fusion protein [Human metapneumovirus]	AJZ52349.1
fusion protein [Human metapneumovirus]	ABD27848.1
fusion protein [Human metapneumovirus]	ABD27846.1
fusion protein [Human metapneumovirus]	ABQ66021.1
fusion protein [Human metapneumovirus]	AFM57710.1
fusion protein [Human metapneumovirus]	AFM57709.1
fusion protein [Human metapneumovirus]	ABH65968.1

TABLE 4-continued

hMPV NCBI Accession Numbers (Amino Acid Sequences)	
Virus	GenBank Accession
fusion protein [Human metapneumovirus]	AJZ52350.1
fusion protein [Human metapneumovirus]	AFM57712.1
fusion protein [Human metapneumovirus]	AJZ52364.1
fusion protein [Human metapneumovirus]	AAN52912.1
fusion protein [Human metapneumovirus]	AJZ52363.1
fusion [Human metapneumovirus]	AGI_74059.1
fusion glycoprotein [Human metapneumovirus]	ACJ53583.1
fusion protein [Human metapneumovirus]	AJZ52356.1
fusion protein [Human metapneumovirus]	AJZ52353.1
fusion glycoprotein [Human metapneumovirus]	ACJ53581.1
fusion glycoprotein [Human metapneumovirus]	ACJ53578.1
fusion protein [Human metapneumovirus]	AAS22117.1
fusion protein [Human metapneumovirus]	BAN75965.1
fusion protein [Human metapneumovirus]	AGF92105.1
fusion protein [Human metapneumovirus]	AAS22077.1
fusion protein [Human metapneumovirus]	AAN52909.1
fusion glycoprotein [Human metapneumovirus]	ACJ53586.1
fusion protein [Human metapneumovirus]	AAQ90145.1
fusion glycoprotein [Human metapneumovirus]	AGI_75042.1
fusion [Human metapneumovirus]	AGI_74058.1
fusion protein [Human metapneumovirus]	AJL_87263.1
fusion glycoprotein [Human metapneumovirus]	AGH27057.1
fusion glycoprotein [Human metapneumovirus]	AJIV79491.1
F [Human metapneumovirus] [Human metapneumovirus]	AJK26906.1
fusion glycoprotein [Human metapneumovirus]	ACJ53580.1
fusion protein [Human metapneumovirus]	AJZ52354.1
fusion protein [Human metapneumovirus]	AAN52914.1
G [Human metapneumovirus] [Human metapneumovirus]	AJK26901.1
glycoprotein [Human metapneumovirus]	AFI56738.1
glycoprotein [Human metapneumovirus]	AFI56739.1
glycoprotein [Human metapneumovirus]	AFI56745.1
G protein [Human metapneumovirus]	AAQ62718.1
G protein [Human metapneumovirus]	AAQ62719.1
attachment glycoprotein G [Human metapneumovirus]	AGH27104.1
G protein [Human metapneumovirus]	AAQ62729.1
G protein [Human metapneumovirus]	AAQ62728.1
glycoprotein [Human metapneumovirus]	AFI56753.1
glycoprotein [Human metapneumovirus]	AFI56746.1
glycoprotein [Human metapneumovirus]	AFI56750.1
glycoprotein [Human metapneumovirus]	AFI56747.1
G protein [Human metapneumovirus]	AAQ62721.1
glycoprotein [Human metapneumovirus]	AAT46573.1
glycoprotein [Human metapneumovirus]	AFI56748.1
glycoprotein [Human metapneumovirus]	AFI56736.1
glycoprotein [Human metapneumovirus]	AFI56749.1
attachment glycoprotein G [Human metapneumovirus]	AGH27131.1
attachment glycoprotein G [Human metapneumovirus]	AJIV79558.1
glycoprotein [Human metapneumovirus]	AFI56740.1
glycoprotein [Human metapneumovirus]	AFI56741.1
glycoprotein [Human metapneumovirus]	AFI56744.1
attachment glycoprotein G [Human metapneumovirus]	AJIV79790.1
attachment glycoprotein G [Human metapneumovirus]	AGH27122.1
attachment glycoprotein G [Human metapneumovirus]	AJIV79763.1
attachment glycoprotein G [Human metapneumovirus]	AGZ48849.1
glycoprotein [Human metapneumovirus]	AFI56743.1
attachment glycoprotein G [Human metapneumovirus]	AJIV79450.1
glycoprotein [Human metapneumovirus]	AFI56751.1
attachment glycoprotein [Human metapneumovirus]	AAS48482.1
attachment glycoprotein G [Human metapneumovirus]	AJIV79889.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43050.1
glycoprotein [Human metapneumovirus]	AFI56754.1
attachment glycoprotein G [Human metapneumovirus]	AJIV79601.1
glycoprotein [Human metapneumovirus]	AFI56752.1
attachment glycoprotein G [Human metapneumovirus]	AJIV79871.1
G protein [Human metapneumovirus]	AJZ68099.1
attachment glycoprotein G [Human metapneumovirus]	AJIV79817.1
attachment glycoprotein G [Human metapneumovirus]	AJIV79943.1
attachment glycoprotein G [Human metapneumovirus]	BAN75968.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43045.1
attachment glycoprotein G [Human metapneumovirus]	AJIV79628.1
attachment glycoprotein [Human metapneumovirus]	AFK49783.1

TABLE 4-continued

Virus	GenBank Accession
G protein [Human metapneumovirus]	AAQ62723.1
attachment glycoprotein [Human metapneumovirus]	ABD27839.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43046.1
G protein [Human metapneumovirus]	AAQ62717.1
glycoprotein [Human metapneumovirus]	AF156742.1
attachment protein [Human metapneumovirus]	ABQ44522.1
glycoprotein [Human metapneumovirus]	AF156735.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43065.1
G protein [Human metapneumovirus]	AAQ62724.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43075.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43062.1
glycoprotein [Human metapneumovirus]	AA146579.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43064.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43054.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43042.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43078.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43067.1
G protein [Human metapneumovirus]	AAQ62722.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43063.1
glycoprotein [Human metapneumovirus]	AA146571.1
glycoprotein [Human metapneumovirus]	AA146578.1
attachment glycoprotein G [Human metapneumovirus]	AGJ74232.1
glycoprotein [Human metapneumovirus]	AA146580.1
glycoprotein [Human metapneumovirus]	AA146574.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43061.1
attachment glycoprotein [Human metapneumovirus]	AFK49791.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43047.1
glycoprotein [Human metapneumovirus]	ABC26386.1
attachment glycoprotein [Human metapneumovirus]	AAS48466.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43048.1
attachment glycoprotein G [Human metapneumovirus]	AGH27140.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43049.1
attachment glycoprotein G [Human metapneumovirus]	AGJ74082.1
attachment glycoprotein G [Human metapneumovirus]	AIIV79442.1
attachment glycoprotein G [Human metapneumovirus]	AGJ74091.1
attachment glycoprotein G [Human metapneumovirus]	AIIV79477.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43056.1
attachment protein [Human metapneumovirus]	ABQ44523.1
attachment glycoprotein G [Human metapneumovirus]	BAH59622.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43070.1
glycoprotein [Human metapneumovirus]	AA146585.1
attachment glycoprotein G [Human metapneumovirus]	AGL168409.1
attachment glycoprotein G [Human metapneumovirus]	AGJ74223.1
attachment glycoprotein [Human metapneumovirus]	AAS22129.1
attachment glycoprotein G [Human metapneumovirus]	AGJ74048.1
G protein [Human metapneumovirus]	AAQ62725.1
glycoprotein [Human metapneumovirus]	ABC26384.1
attachment protein [Human metapneumovirus]	ABQ44525.1
attachment glycoprotein G [Human metapneumovirus]	YP_012612.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43071.1
attachment glycoprotein G [Human metapneumovirus]	AGJ74162.1
attachment glycoprotein G [Human metapneumovirus]	AGH27095.1
attachment glycoprotein G [Human metapneumovirus]	AIIV79531.1
G protein [Human metapneumovirus]	AAQ62726.1
attachment glycoprotein [Human metapneumovirus]	AAS48465.1
attachment surface glycoprotein [Human metapneumovirus]	AGW43058.1
P [Human metapneumovirus] [Human metapneumovirus]	AK26894.1
phosphoprotein [Human metapneumovirus]	AIIV79631.1
phosphoprotein [Human metapneumovirus]	AIIV79901.1
phosphoprotein [Human metapneumovirus]	AIIV79570.1
phosphoprotein [Human metapneumovirus]	AGJ74076.1
phosphoprotein [Human metapneumovirus]	AAS22123.1
phosphoprotein [Human metapneumovirus]	ABB16895.1
phosphoprotein [Human metapneumovirus]	AIIV79579.1
phosphoprotein [Human metapneumovirus]	AGJ74244.1
phosphoprotein [Human metapneumovirus]	AIIV79856.1
phosphoprotein [Human metapneumovirus]	AC170113.1
phosphoprotein [Human metapneumovirus]	AGZ48843.1
phosphoprotein [Human metapneumovirus]	AIIV79498.1
phosphoprotein [Human metapneumovirus]	AIIV79480.1
phosphoprotein [Human metapneumovirus]	ABQ43382.1
phosphoprotein [Human metapneumovirus]	AAS22107.1
phosphoprotein [Human metapneumovirus]	ABB16898.1

TABLE 4-continued

hMPV NCBI Accession Numbers (Amino Acid Sequences)	
Virus	GenBank Accession
phosphoprotein [Human metapneumovirus]	AGH27134.1
phosphoprotein [Human metapneumovirus]	ABB16899.1
phosphoprotein [Human metapneumovirus]	AGH27098.1
phosphoprotein [Human metapneumovirus]	AAN52866.1
phosphoprotein [Human metapneumovirus]	AAS22083.1
phosphoprotein [Human metapneumovirus]	YP_012606.1
phosphoprotein [Human metapneumovirus]	AIIV79973.1
phosphoprotein [Human metapneumovirus]	AIIV79462.1
phosphoprotein [Human metapneumovirus]	AGJ74042.1
phosphoprotein [Human metapneumovirus]	AAV88362.1
P [Human metapneumovirus] [Human metapneumovirus]	AIJ23591.1
phosphoprotein [Human metapneumovirus]	AIIV79453.1
phosphoprotein [Human metapneumovirus]	AGJ74261.1
phosphoprotein [Human metapneumovirus]	AGH27116.1
phosphoprotein [Human metapneumovirus]	ABB16444.1
phosphoprotein [Human metapneumovirus]	ABB16445.1
phosphoprotein [Human metapneumovirus]	AIIV79507.1
phosphoprotein [Human metapneumovirus]	BAI159616.1
phosphoprotein [Human metapneumovirus]	ABB16443.1
phosphoprotein [Human metapneumovirus]	ABQ43388.1
phosphoprotein [Human metapneumovirus]	ABQ43389.1
phosphoprotein [Human metapneumovirus]	ABQ43395.1
phosphoprotein [Human metapneumovirus]	ABQ43385.1
phosphoprotein [Human metapneumovirus]	AAV884042.1
phosphoprotein [Human metapneumovirus]	AAN52868.1
phosphoprotein [Human metapneumovirus]	AAV884041.1
phosphoprotein [Human metapneumovirus]	AGH27080.1
phosphoprotein [Human metapneumovirus]	ABQ43387.1
phosphoprotein [Human metapneumovirus]	AAS22099.1
phosphoprotein [Human metapneumovirus]	ABB16896.1
phosphoprotein [Human metapneumovirus]	AGJ74094.1
phosphoprotein [Human metapneumovirus]	AEZ68089.1
phosphoprotein [Human metapneumovirus]	ABK97002.1
phosphoprotein [Human metapneumovirus]	AAV13486.1
phosphoprotein [Human metapneumovirus]	AIIV79444.1
phosphoprotein [Human metapneumovirus]	AIIV79865.1
phosphoprotein [Human metapneumovirus]	AGJ74226.1
phosphoprotein [Human metapneumovirus]	ABQ43383.1
phosphoprotein [Human metapneumovirus]	AAN52863.1
phosphoprotein [Human metapneumovirus]	AIIV79775.1
phosphoprotein [Human metapneumovirus]	AEZ68094.1
phosphoprotein [Human metapneumovirus]	AIIV79883.1
phosphoprotein [Human metapneumovirus]	AEZ68092.1
phosphoprotein [Human metapneumovirus]	ABQ43390.1
phosphoprotein [Human metapneumovirus]	ABQ43386.1
phosphoprotein [Human metapneumovirus]	ABQ43391.1
phosphoprotein [Human metapneumovirus]	ACS16062.1
phosphoprotein [Human metapneumovirus]	AEZ68090.1
phosphoprotein [Human metapneumovirus]	AAK62967.1
phosphoprotein [Human metapneumovirus]	AEZ68093.1
phosphoprotein [Human metapneumovirus]	AEZ68088.1
phosphoprotein [Human metapneumovirus]	ABQ43392.1
phosphoprotein [Human metapneumovirus]	ABQ43393.1
phosphoprotein [Human metapneumovirus]	ABQ43384.1
phosphoprotein [Human metapneumovirus]	ABQ43394.1
phosphoprotein [Human metapneumovirus]	ABK96999.1
phosphoprotein [Human metapneumovirus]	AIIV79489.1
phosphoprotein [Human metapneumovirus]	AGJ74235.1
phosphoprotein [Human metapneumovirus]	AAS22075.1
phosphoprotein [Human metapneumovirus]	AAS22115.1
phosphoprotein [Human metapneumovirus]	AIJ17601.1
phosphoprotein [Human metapneumovirus]	ABK97000.1
phosphoprotein [Human metapneumovirus]	AIIV79561.1
phosphoprotein [Human metapneumovirus]	AGT75040.1
phosphoprotein [Human metapneumovirus]	AAN52864.1
phosphoprotein [Human metapneumovirus]	ABK97001.1
phosphoprotein [Human metapneumovirus]	AGT74979.1
phosphoprotein [Human metapneumovirus]	AIIV79955.1
phosphoprotein [Human metapneumovirus]	AGH27055.1
phosphoprotein [Human metapneumovirus]	AAV88361.1
phosphoprotein [Human metapneumovirus]	ABQ43397.1
phosphoprotein [Human metapneumovirus]	AGJ74173.1

TABLE 4-continued

Virus	GenBank Accession
P [Human metapneumovirus] [Human metapneumovirus]	AJK26904.1
phosphoprotein [Human metapneumovirus]	ACJ70104.1
phosphoprotein [Human metapneumovirus]	ABK97003.1
phosphoprotein [Human metapneumovirus]	AGT74955.1
phosphoprotein [Human metapneumovirus]	AAN52856.1
phosphoprotein [Human metapneumovirus]	AAN52862.1
phosphoprotein [Human metapneumovirus]	AGJ74138.1
phosphoprotein [Human metapneumovirus]	AIIV79613.1
phosphoprotein [Human metapneumovirus]	AGJ74060.1
phosphoprotein [Human metapneumovirus]	AAQ67684.1
phosphoprotein [Human metapneumovirus]	AEA02278.1
N [Human metapneumovirus] [Human metapneumovirus]	AJK26899.1
nucleoprotein [Human metapneumovirus]	ACS16061.1
nucleoprotein [Human metapneumovirus]	AAS88425.1
nucleoprotein [Human metapneumovirus]	YP_012605.1
nucleoprotein [Human metapneumovirus]	AIIV79882.1
nucleoprotein [Human metapneumovirus]	AIIV79774.1
nucleocapsid protein [Human metapneumovirus]	AAN52886.1
nucleoprotein [Human metapneumovirus]	AAS22082.1
nucleoprotein [Human metapneumovirus]	AIIV79864.1
nucleoprotein [Human metapneumovirus]	AIIV79828.1
nucleoprotein [Human metapneumovirus]	AGJ74084.1
nucleocapsid protein [Human metapneumovirus]	AAN52888.1
N [Human metapneumovirus] [Human metapneumovirus]	AIJ23590.1
nucleoprotein [Human metapneumovirus]	AAK62966.1
nucleoprotein [Human metapneumovirus]	AIIV79972.1
nucleoprotein [Human metapneumovirus]	AIIV79470.1
nucleoprotein [Human metapneumovirus]	AIIV79452.1
nucleoprotein [Human metapneumovirus]	AGJ74243.1
nucleoprotein [Human metapneumovirus]	AIIV79533.1
nucleoprotein [Human metapneumovirus]	AGJ74181.1
nucleoprotein [Human metapneumovirus]	AIIV79497.1
nucleoprotein [Human metapneumovirus]	AIIV79702.1
nucleoprotein [Human metapneumovirus]	AIIV79648.1
nucleoprotein [Human metapneumovirus]	AIIV79435.1
putative nucleoprotein [Human metapneumovirus]	AGJ74260.1
nucleocapsid protein [Human metapneumovirus]	AAN52887.1
nucleoprotein [Human metapneumovirus]	AGL68386.1
nucleocapsid protein [Human metapneumovirus]	AAN52899.1
nucleoprotein [Human metapneumovirus]	AAR17673.1
nucleocapsid protein [Human metapneumovirus]	AAN52898.1
nucleoprotein [Human metapneumovirus]	AEA02277.1
nucleoprotein [Human metapneumovirus]	AIIV79612.1
nucleoprotein [Human metapneumovirus]	AGL68416.1
nucleoprotein [Human metapneumovirus]	AGL68408.1
nucleoprotein [Human metapneumovirus]	AGL68370.1
nucleoprotein [Human metapneumovirus]	AAQ67683.1
nucleoprotein [Human metapneumovirus]	AGJ74137.1
nucleoprotein [Human metapneumovirus]	AGL68344.1
nucleocapsid protein [Human metapneumovirus]	ABK96997.1
nucleoprotein [Human metapneumovirus]	AGL68413.1
nucleocapsid protein [Human metapneumovirus]	AAN52891.1
nucleoprotein [Human metapneumovirus]	AGL68360.1
nucleoprotein [Human metapneumovirus]	AGL68353.1
nucleocapsid protein [Human metapneumovirus]	ABK96996.1
nucleoprotein [Human metapneumovirus]	AAR17666.1
N [Human metapneumovirus] [Human metapneumovirus]	AJK26903.1
nucleoprotein [Human metapneumovirus]	AGT75039.1
nucleoprotein [Human metapneumovirus]	AGL68410.1
nucleoprotein [Human metapneumovirus]	AAS22074.1
nucleoprotein [Human metapneumovirus]	AIIV79560.1
nucleoprotein [Human metapneumovirus]	AGT74978.1
nucleoprotein [Human metapneumovirus]	AGJ74128.1
nucleoprotein [Human metapneumovirus]	AAR17663.1
nucleoprotein [Human metapneumovirus]	AAR17662.1
nucleoprotein [Human metapneumovirus]	AAR17664.1
nucleoprotein [Human metapneumovirus]	AAR17657.1
nucleoprotein [Human metapneumovirus]	AAR17659.1
nucleoprotein [Human metapneumovirus]	AAR17661.1
nucleoprotein [Human metapneumovirus]	AGL68352.1
nucleoprotein [Human metapneumovirus]	AGL68373.1
nucleoprotein [Human metapneumovirus]	AGL68376.1
nucleoprotein [Human metapneumovirus]	AGL68342.1

TABLE 4-continued

IMPV NCBI Accession Numbers (Amino Acid Sequences)	
Virus	GenBank Accession
nucleoprotein [Human metapneumovirus]	AGU68365.1
nucleoprotein [Human metapneumovirus]	AGU68363.1
nucleoprotein [Human metapneumovirus]	AGU68398.1
nucleoprotein [Human metapneumovirus]	AGU68348.1
nucleoprotein [Human metapneumovirus]	AGU68354.1
nucleoprotein [Human metapneumovirus]	AGU68391.1
nucleoprotein [Human metapneumovirus]	AGU68389.1
nucleoprotein [Human metapneumovirus]	AGU68399.1
nucleoprotein [Human metapneumovirus]	AGU68337.1
nucleoprotein [Human metapneumovirus]	AAR17660.1
nucleoprotein [Human metapneumovirus]	AAR17667.1
nucleoprotein [Human metapneumovirus]	AGU68402.1
nucleoprotein [Avian metapneumovirus type C]	CIN30025.1
nucleoprotein [Avian metapneumovirus]	AGZ87947.1
Nucleoprotein [Avian metapneumovirus type C]	CAI.25113.1
nucleocapsid protein [Avian metapneumovirus]	ABC42286.1
nucleocapsid protein [Avian metapneumovirus]	AAK38430.1
nucleocapsid protein [Avian metapneumovirus]	AAK54155.1
nucleocapsid protein [Avian metapneumovirus]	AAK38426.1
nucleocapsid protein [Avian metapneumovirus]	AAK38425.1
nucleocapsid protein [Avian metapneumovirus]	AAK38424.1
nucleocapsid protein [Avian metapneumovirus]	AAH05909.1
nucleocapsid protein [Avian metapneumovirus]	AAK38435.1
nucleocapsid protein [Avian metapneumovirus]	AAK38428.1
nucleoprotein [Human metapneumovirus]	AAR17669.1
nucleocapsid protein [Avian metapneumovirus]	AAK38429.1
nucleocapsid protein [Avian metapneumovirus]	AAK38427.1
nucleocapsid protein [Avian metapneumovirus]	AAK38423.1
nucleocapsid protein [Avian metapneumovirus]	AAK38434.1
nucleoprotein [Human metapneumovirus]	AGU68338.1
nucleoprotein [Avian metapneumovirus]	YP_443837.1
nucleoprotein [Human metapneumovirus]	AGU68384.1
nucleocapsid protein [Avian metapneumovirus]	AAK38431.1
nucleoprotein [Human metapneumovirus]	AGU68405.1
nucleoprotein [Human metapneumovirus]	AGU68382.1
nucleoprotein [Human metapneumovirus]	AGU68395.1
nucleocapsid [Human metapneumovirus]	AAI35389.3
nucleoprotein [Human metapneumovirus]	AJZ68064.1

TABLE 5

PIV3 Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO.
>gb KJ672601.1 : 4990-6609 Human parainfluenza virus 3 strain HPIV3/Homo sapiens/PER/PLA4815/ 2008 fusion glycoprotein F0	ATGCCAATTTCAACTACTGTTAATTATTACAACCATGATC ATGGCATCACACTGCCAAATAGACATCACAAAACCTACA GCATGTGGGTGTTATGGTCAACAGTCCCAAAGGGATGA AGATATCACAAAACCTCGAAACAAGATATCTAATCCTGA GTCTCATACAAAATAGAAGATTCTAACTCTGTGGTG ACCAACAGATCAAGCAATCAAGAGGTTATGGATAGA CTGATCATTCCTTTATATGATGGACTAAGATTACAGAAG GATGTGATAGTGAATAATCAAGAATCCAATGAAAACAC TGRTCCAGAACAGAACGATTCTTTGGAGGGTAAATGG AACTATTGCTCTAGGAGTAGCAACCTCAGCACAAAATTAC AGCAGCAGTGTCTCTGGTTGAAGCCAAGCAGGCAAGAT CAGACATTGAAAACCTCAGGAAGCAATCAGGGACRCA AATAAAGCAGTGCAGTCAAGTTCAGAGCTCTGTAGGAAA TTTGATAGTAGCAATTAATCAGTCCAGGATTATGTCAA CAAAGAAATCGTGCATCGATTGCGAGACTAGGTTGTG AAGCAGCAGGACTTCAGTTAGGGATTGCATTAAACACAG CATTACTCAGAATTAACAAATATATTTGGTGATAACATA GGATCGTTACAGAAAAGGAATAAAATTACAAGGTAT AGCATCATTATACCGTACAAATATCACAGAAATATTCAC AACATCAACAGTTGACAAATATGATATTTATGATCTATT ATTTACAGAAATCAATAAAGGTGAGAGTTATAGATGTTGA TTTGAATGATTACTCAATAACCCTCCAAGTCAGACTCCC TTTATTGACCAGACTGCTGAACACTCAAATCTACAAGT AGATTCATATCATACAATATCCAAAATAGAGAAATGGTA	9

TABLE 5-continued

PIV3 Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO.
	TATCCCTCTTCCCAGCCATATCATGACGAAAGGGGCATT TCTAGGTGGAGCAGATGTCAAAGAATGCATAGAAGCAT TCAGCAGTTATATATGCCCTTCTGATCCAGGATTTGTACT AAACCATGAAATGGAGAGCTGTCTATCAGGAACATAT CCCAATGTCCAAGAACCACAGTCAATCAGACATAGTTC CTAGGTATGCATTTGTCAATGGAGGAGTGGTTGCGAATT GTATAACAACACTACATGTACATGCAATGGTATCGGTAATA GAATCAACCAACCACCTGATCAAGGAGTCAAAATTTATA ACACATRAAGAATGTAATACCAATAGGTATCAACGGAAT GCTATTCAACACAAACAAAGAAGGAACCTTTCGATTCTA CACACCAGACGACATAACATTAACAATTCGTTGCACT TGATCCGATTGACATATCAATCGAGCTCAACAAGGCCAA ATCAGATCTTGAGGAATCAAAGAATGGATAAGAAGGT CAAAATCAAAGCTAGATTCTATTGGAAAGTTGGCATCAAT CTAGCACTACAATCATAGTTATTTGATATGATGATTA TATTGTTATAATTAATATAACAATAATACAATTGCAA TTAAGTATTACAGAATTCAAAAGAGAATCGAGTGGAT CAAAATGATAAGCCGTATGTATTAACAACAAG	
gi 612507167 gb AHX22430.1 hemagglutinin- neuraminidase [Human parainfluenza virus 3]	ATGGAATACTGGAAGCACACCAACCACGGAAGGATGC TGGTAAATGAGCTGGAGACATCCACAGCCACTCATGGCA ACAAGCTCACCAACAGATAACATATATATGTTGGACC ATAACCCCTGGTGTATTATCAATAGTCTTCATCATAGTG CTAACTAATTCATCAAAGTGAAAGGCCCGCGAATC ATTGCTACAAGACATAAATAATGAGTTTATGGAAGTTAC AGAAAAGATCCAAGTGGCATCGGATAATACTAATGATC TAATACAGTCAGGAGTGAATACAAGGCTTCITCAATTC AGAGTCATGTCAGAAATATATACCAATATCATTGACAC AACAAATATCGGATCTTAGGAAATTCATTAGTGAAATTA CAATTAGAAATGATAATCAAGAAGTGCCACCACAAGA ATAACACATGATGTGGGTATAAAAACCTTTAARTCCAGAT GATTTCTGGAGATGCACGTCTGGTCTTCCATCTTTGATG AAAACCTCCAAAATAAGATTAATGCCGGACCCAGGAT ATTAGCTATGCCAACGACTGTTGATGGCTGTGTGAGAAC CCCGTCCCTTAGTGATAAATGATCTGATTTATGCTTACAC CTCAAATCTAATTAATCGAGGTGCGGAGATATAGGGAA ATCATAACAAGTATTACAGATAGGGATAATAACTGTAAA CTCAGACTTGGTACTGACTTAAATCCTAGGATCTCTCA TACCTTCAACATAAATGACAAATAGAAGTCAATGTTCTCT AGCACTCCTAATACAGATGTATATCAACTGTGTTCAAC CCCAAAAGTTGATGAAAGATCAGATTATGCATCATCAG GCATAGAAGATATTGTACTTGATATTGTCAATTATGATG GCTCAATCTCGACAAACAGATTTAAGAATAAATAATATAA GTTTTGATCAACCATATGCGGCATTATACCATCTGTTG GACCAGGGATATACTACAAGGGCAAAATAATATTTCTC GGGTATGGAGTCTTGAACATCCAATAAATGAGAATGC AATCTGCAACACAACCTGGGTGTCTGGGAAAACACAGA GAGACTGTAATCAAGCATCTCATAGTCCATGGTTTTCAG ATAGAAGGATGGTCAACTCTATAATTGTTGTTGACAAGG GCTTGAACTCAGTTCCAAAATTTGAAGGTATGACGATAT CTATGAGACAAAATTAATGGGGTCAAGGAAGATTA CTTCTACTAGGTAACAAGATCTACATATACACAAGATCT ACAAGTTGGCACAGCAAGTTACAATTAGGAATAATTTGA CATTAAGTACTGACTACAGTATATAAGGATAAATGGACAT GGCATAATGTGCTATCAAGACCAGGAACAATGAATGT CCATGGGGACATTCATGTCCGGATGGATGTATAACGGG AGTATATACCGATGCATATCCACTCAATCCACAGGAAG CATTGTATCATCTGTATATTGGACTCACAAAATCGAG AGTCAACCAGTCAATACTTACTCAACAGCAACCGAAA GGGTAACAGGAGCTGGCTATCCGAAACAAAACACTCTCA GCTGGGTACACAACCAAGCTGCATTACACACTATAA CAAAGGGTATTGTTTTCATATAGTAGAATTAATCATAA AAGCTTAAACACATTTCAACCCATGTTGTTCAAACAGA GATTTCAAAGGCTGCACT	10
HPiV3_HN_Codon Optimized	ATGGAATACTGGAAGCACACCAACCACGGCAAGGACGC CGGCAACGAGCTGGAAACCAGCACAGCCACACACGGCA ACAAGCTGACCAACAAGATCACCTACATCCCTGGGACC ATCACCTGGTGTCTGCTGAGCATCGTGTTCATCATCGTG CTGACCAATAGCATCAAGAGCGGAAAGGCCAGAGAGAG CCTGCTGCAGGACATCAACAACGAGTTTCATGGAAGTGA CCGAGAAGATCCAGGTGGCCAGCGACAACCAACCGAC	11

TABLE 5-continued

PIV3 Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO.
	CTGATCCAGAGCGGGCTGAACACCCGGCTGCTGACCATC CAGAGCCACGTGCAGAACTACATCCCCATCAGCCTGACC CAGCAGATCAGCGACTCGGGAAGTTGATCAGCCAGAT CACCATCCGGAACGACAACCAGGAAGTGCCCCCAGAG GAATCACCACGACGTGGGCATCAAGCCCCGAAACCC GACGATTTCTGGCGGTACCAAGCGGCTGCCAGCCTG ATGAAGACCCCCAAGATCCGGCTGATGCCTGGCCCTGG ACTGCTGGCCATGCCCTACCACAGTGGATGGCTGTGTGCG GACCCCCAGCCTCGTGATCAACGATCTGATCTACGCCTA CACCAGCAACCTGATCACCCGGGGCTGCCAGGATATCG GCAAGAGCTACCAGGTGCTGCAGATCGGCATCATCACC GTGAACTCCGACCTGGTGCCCGACTGAACCTCGGATC AGCCACACCTTCAACATCAACGCAACAGAAAGAGCTG CAGCCTGGCTCTGCTGAACACCGAGCTGACAGCTGTG CAGCACCCCAAGGTGGACGAGAGAAGCGACTACGCCA GCAGCGCATCGAGGATATCGTCTGGACATCGTGAAC TACGACGGCAGCATCAGCACCCCGGTTCAAGAACA CACATCAGCTTCGACACGCCCTACGCCGCCCTGTACCC TTCTGTGGGCCCTGGCATCTACTACAAGGGCAGATCAT CTTCCTGGGCTACGGCGGCTGGAAACCCCATCAACGA GAACGCCATCTGCACACCCCGGCTGCCCTGGCAAGA CCCAGAGAGACTGCAATCAGGCCAGCCACAGCCCCGG TTCAGCGACCGCAGAATGGTCAACTCTATCATCGTGGTG GACAAGGGCTGAACAGCGTGCCCAAGTGAAGATGTG GACAATCAGCATGCGCCAGAACTACTGGGGCAGCGGG GCAGACTTCTGCTGCTGGGAACAAGATCTACATCTACA CCCGGTCCACCAGCTGGCACAGCAACTGCAGCTGGGA ATCATCGACATCACCGACTACAGCGACATCCGGATCAA GTGGACCTGGCACAACTGCTGAGCAGACCCGGCAACA ATGAGTGCCTTGGGGCCACAGCTGCCCGATGGATGTA TCACCGGCGTGTACACCGACGCTACCCCTGAATCCTA CCGGCTCCATCGTGTCCAGCGTATCCTGGACAGCCAGA AAAGCAGAGTGAACCCCGTGTACATACAGCACCGCC ACCGAGAGAGTGAACCAACTGGCCATCAGAAACAAGAC CCTGAGCGCCGGCTACACCAACCAAGCTGCATCACAC ACTACACAAGGGCTACTGCTTCCACATCGTGGAAATCA ACCACAAGTCCCTGAACACCTTCCAGCCCATGTCTTCA AGACCGAGATCCCCAAGAGCTGCTCC	
HPIV3, F Codon Optimized	ATGCCCATCAGCATCTGCTGATCATCACCAATGATC ATGGCCAGCCACTGCCAGATCGACATCACCAAGCTGCA GCACGTGGGGTGTCTGCTGAACAGCCCCAAGGGCATGA AGATCAGCCAGAACTTCGAGACAGCTACCTGATCCTGA GCCTGATCCCCAAGATCAGGACAGCAACAGCTGCCGC GACCAGCAGATCAAGCAGTACAAGCGGCTGCTGGACAG ACTGATCATCCCCCTGTACGACGGCCCTGGGCTGCAGAA AGACGTGATCGTGACCAACCAGGAAAGCAACGAGAACA CCGACCCCGGACCGAGAGATCTTCGGCGGCTGATCG GCACAATCGCCCTGGGAGTGGCCACAAGCGCCAGATT ACAGCCGCTGTGGCCCTGGTGGAAAGCCAAGCAGGCCAG AAGCGACATCGAGAAGCTGAAGAGGGCCATCCGGGACA CCAACAAGGCCGTGCAGAGCGTGCAGTCCAGCGTGGGC AATCTGATCGTGGCCATCAAGTCCGTGCAGGACTACGTG AACAAAGAAATCGTGCCCTCTATGCCCGGCTGGGCTGT GAAGCTGCCGACTGCAGCTGGGCATTCGCCCTGACACA GCACCTACAGCGAGCTGACCAACATCTTCGGCGACAACA TCGGCAGCCTGCAGGAAAAGGGCATTAAAGTGCAGGGA ATCGCCAGCCTGTACCCGACCAACATCACCGAGATCTTC ACCACCAGCACCGTGGATAAGTACGACATCTACGACCT GCTGTTCAACGAGAGCATCAAAGTGCAGCGTATCGACGT GGACTGAACGACTACAGCATCACCCCTGCAAGTGGCC TGCCCCGTGACAGACTGCTGAACACCCAGATCTACA AGGTGGACAGCATCTCTACAAACATCCAGAACCAGGAG TGGTACATCCCTCTGCCAGCCACATTATGACCAAGGGC GCCTTTCTGGGCGGAGCCGACGTGAAGAGTGCATCGA GGCCCTCAGCAGCTACATCTGCCCCAGCGACCCCTGGCTT CGTCTGAACCACGAGATGGAAAGCTGCCTGAGCGGCA ACATCAGCCAGTGCACCAGAACCCGTCACCTCCGAC ATCGTGCCAGATACGCCCTTCGTGAATGGCGGCTGGTG GCCAACTGCATCACCCACCTGTACCTGCACCGGCATC GGCAACCGGATCAACCAGCCTCCCGATCAGGGCGTGAA GATTATCACCCACAAGAGTGTAAACCATCGGCATCA	12

TABLE 5-continued

PIV3 Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	ACGGCATGCTGTTCATACCAACAAAGAGGGCACCCCTG GCCTTCTACACCCCGACGATATCACCTGAACAACCTCC GTGGCTCTGGACCCCATCGACATCTCCATCGAGCTGAAC AAGGCCAAGAGCGACCTGGAAGAGTCCAAAGAGTGGAT CCGGCGGAGCAACCAGAAGCTGGACTCTATCGGCAGCT GGCACCGAGCAGCACCACCATCATCGTGATCCTGATTA TGATGATTATCCTGTTCATCATCAACATTACCATCATCAC TATCGCCATTAAGTACTACCGGATCCAGAAACGGAACC GGGTGGACCAGAATGACAAAGCCCTACGTGCTGACAAAC AAG	
	PIV3 mRNA Sequences	
>gb KJ672601.1 : 4990-6609 Human parainfluenza virus 3 strain HPIV3/ <i>Homo sapiens</i> /PER/FLA4815/ 2008[fusion glycoprotein F0]	AUGCCAAUUUCAAUACUGUUAAUUUUACAACCAUGA UCAUGGCADACACUGCCCAAUAGACACACAAAACU ACAGCAUGUAGGUGUUAUUGGDUCAACAGUCCCAAAGGG AUGAAGADAUCACAAAACUUCGAAACAGAUUUCUAA UCCUGAGUCUCAUACCAAAAUAAGAAGAUUCUAACUC UUGUGUGACCAACAGAUCAAGCAAUACAGAGGUUA UUGGAUAGACUGAUCAUUCUUUAUAUGAUGGACUAA GAUUACAGAGGAUGUGAUAGUGACUAAUCAGAAUC CAUUGAAAACACUGAUCCGAGAACAGAACGAUUCUU GGAGGGUAAUUGGAACUUAUUGUCUAGGAGUAGCAA CCUCAGCACAAAUAACAGCAGCAGUUGUCUUGGUUGA AGCCAAGCAGGCAAGAUACAGACUUGAAAACUCUAG GAAGCAUACAGGGACACAAAUAAGCAGUUCAGUCAG UUCAGAGCUCUGUAGGAAAUAUGAUGUAGCAAUUA AUCAGUCCAGGAUUAUGUCAACAAGAAAUCUGGCCA UCGAUUGCGAGACUAGGUUGUGAAGCAGCAGGACUUC AGUUAAGGGAUUGCAUUAACACAGCAUUAUCAGAAUU AACAAAUAUAUUUGGUGUAACADAGGAUCGUUACAA GAAAAGGAAUAAAUAUACAAGGUUAAGCAUCAUUUA ACCGUACAAAUAUCAGAAAUAUUCACAAUCAAC AGUUGACAAAUAUGAUUUUAUGAUCUUAUUUUACA GAUCCAAUAAAGGUGAGAGUUAUAGAUGUUGAUUUGA AUGAUUACUCAAUAAACCCUCCAAGUCAGACUCCUUU AUUGACCAGACUGCUGAACACUCAAAUCUACAAGUA GAUCCAAUUAUCAUAUAUCCAAAUAAGAAAUGGU AUUCCUUCUCCAGCCAUUAUCUAGACGAAAGGGGC AUUUCUAGGUGGAGCAGAUUCAAAAGAAUGCAUAGAA GCAUUCAGCAGUUUAUUAUGCCUUCUGAUCAGGAU UUGUACUAAAACCAUGAAAUGGAGAGCUGUCUUAUAGG AAACAUAUCCCAUUGUCCAAGAACCACAGUCACAUCA GACAUAGUUCUAGGUUAUGCAUUUGUCAUUGGAGGAG UGGUUGCGAAUUGUAUAACAACUACAUGUAUGCAA UGGUUACGGUAAUAGAAUACAAACCAACCCUGAUCAA GGAGUCAAAAUAUAACACAUAAGAUAUGUAAUACAA UAGGUUAUCAACGGAAUGCUAUUCAAACAACAAAGA AGGAACUCUUGCAUUCUACACACCAGACGACUAACA UUAAACAUAUCUGUUGCAUUGAUCCGAUUGACAUAU CAUUCGAGCUCACAAGGCCAAUAUCAGAUUCUUGAGGA AUCAAAGAAUGGAUAAGAAGGUCAAAUCAAAGCUA GAUUCUAUUGGAAGUUGGCAUCAAUUAGCACUAACA UCAUAGUUAUUUGAUAAUGAUGAUUAUUGUUAU AAUUAUAUAACAUAUAUACAADUGCAUUAAGUAU UACAGAAUUCAAAAGAGAAAUCGAGUGGAUCAAUAUG AUAAGCCGUAUGUAUUAACAACAAG	61
gi 612507167 gb AHX22430.1 hemagglutinin- neuraminidase [Human parainfluenza virus 3]	AUGGAAUACUGGAAGCACCAACCAACCGAAAGGAUG CUGGUAAUAGAGCUGGAGACACCACAGCCACUCAUGG CAACAAGCUCACCACAGAUAAUUAUUAUUGUGG ACGAUAACCTUGGUGUUAUUAUUAUAGUCUUCUA UAGUGCUAACUAAUUCUACAAGGUGAAAAGGCCCG CGAAUCAUUGCUACAGACAUAAADAAUGAUUUUAUG GAAGUACAGAAAAGAUCCAAGUGGCAUCGGAUAAUA CUAAUGAUUCAAUACAGUCAGGAGUGAAUACAAGGCU UCUUAACAUCAGAGUCUUGUCCAGAAUUAUAUCCA AUAUCAUUGACACACAAAUAUCCGAUUCUAGGAAU UCAUUGGAAAUUACAUAUAGAAUGAUAAUCAA AGUGCCACCACAAGAAUAACACADGAUGUGGUAUA AAAACUUUAAAUUCAGAUUAUUUCUGGAGAUUCACGU CUGGUCUCCAUUCUUGAUGAAAACUCCAAAUAUAG	62

TABLE 5-continued

PIV3 Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO.
	AUUAAUGCCGGGACCAGGAUUUUDAGCUAUGCCAACG ACUGUUGAUGGCUGUGUCAGAACC CGUCCUUAGUGA URAAUGAUCUGAUUUUUGCUUACACCCUCAAUCUAAU UACUCGAGGUUGCCAGGAUAUAGGGAAAUCAUAUCA GUAAUACAGAUAGGGAAUUAACUGUAACUCAGACU UGGUACCUGACUUAAUCCUAGGADUCUCUAUACCUU CAACAUAUAUGACAUAUAGAAAGUCAUGUUCUCUAGCA CUCCUAAAUACAGAUUGUAUAUCAACUGGUUCAACCC CAAAAGUUGAUGAAGAUCRGAUUAUGCAUCUACAGG CAUAGAAGAUUUGUACUUGADUUGUCAUUAUGAU GGCUCADUCGACAACAAGAUUUUAGAAUUAUUAU UAGUUUUGADUCAACCAUUGCGGCAUUAUACCCAU UGUUGGACCAGGGAUUACUACAAGGCAAAUUAUUA UUUUCGGGUUUGGAGGUCUUGAACAUCCAUAUUAU AGAAUGCAAUCUGCACACAAACUGGGUGUCUGGGAA AACACAGAGAGACUGUAAUCAAGCAUCUUAUGUCCA UGGUUUUCAGAUAGAAGGAGGUCACUCUUAUUAUUG UUGUUGRCAAGGGCUGAACUCAGUCCAAAUUGAA GGUUUGGACGAUUCUUAUGGACAAAUAUCUGGGGG UCAGAAGGAAGAUUACUUCUACUAGGUAAACAGAUUC ACAUUAACACAAGAUUCUACRAGUUGGCACAGCAAGU ACAUUAAGGAUAUUGACAUUACUGACUACAGUGAU AUAAGGAUAAAUUGGACAUUGCAUAUUGUCUAUCAA GACCAGGAACAUAUGAUUGCCAGGGGACAUUC AUG UCCGGAUGGAUGUAUAACGGGAGUAUAUACCGAUGCA UAUCCAUCUCAAUCCACAGGAAGCAUUGUAUCAUCUG UCAUAUUGGACUCACAAAADUCGAGAGUCAACCCAGU CAUAACUUAUCUACAGCAACCGAAAGGUAACCGAG CUGGCUAUCCGAAACAACAACUCUCAGCUUGGUACA CAACAACAAGCUGCAUUAACACAUUAACAAGGGUA UGUUUUCUAUAGUGAGAAUAAADCAUAAAAGCUUA AACACAUUUCAACCCAUUGUUGUCAAACAGAGAUUC CAAAAGCUGCAGU	
HPiV3 HN Codon Optimized	AUGGAAUACUGGAAGCACCAACCAACCGCCAGGACG CCGGCAACGAGCUGGAAAC CAGCAAGCCACACACGGC AACAGCUGACCAACAAGAUACCUACUUCUGUGGA CCAUCACCUGGUGCUGCUGAGCAUCGUGUUAUCAUC GUGCUGACCAUAGCAUCAAGAGCGGAGAGGCCAGAG AGAGCCUGCUGCAGGACAUCAACAACGAGUUAUGGA AGUGACCGAGAAGAUCCAGGUGGCCAGCGACAACACC AACGACUUGAUCCAGAGCGGCUGAAACACC CGGUCUC GACCAUCCAGAGCCACGUGCAGAAUACAUCUCCAUCA GCCUGACCCAGCAGAUACGACCUUGCGAAUUAUCUC AGCGAGAUCAACAUCGGAAACGCAACCCAGGAAGUGC CCCCCAGAGAAUACCCACGACGUGGGCAUCAAGCC CUGAACCCCGACGAAUUCUGGCGGUGUACAAGCGGCC UGCCCAGCCUGAUGAAGACCCCAAAGAUCCGGCUGAUG CCUGGCCUGGACUGCUGGCCAUGCCUACCCAGUGGA UGGCUGUGUGCGGACCCCAAGCCUCUGAUCAACGADU UGAUCUACGCCUACACCAGCAACUUGAUCAACC GGGGC UGCCAGGAUAUCGGCAAGAGCUACCGGUGCUGCAGA UCGGCAUCAACCCGUGAACUCCGACCUUGGUGCCGAC CUGAACCCUCGGAUACAGCCACACCUUCAAACAUCAACGA CAACAGAAAGAGCUGCAGCCUGGCUCUGUGAACACC GACGUGUACCAAGCUGUGCAGCACCCCAAGGUGGACG AGAGAAGCGACUAACGCCAGCAGCGGCACGAGGAUAU CGUGCUGGACAUCCGUAACUACGACCGCAGCAUCAGC ACCACCCGGUUAAGAACAACAACAUCAUCUUCGACCA GCCUACCGCCGCCUGUACCCUUCUGUGGGCCUGGCA UCUACUACAAGGGCAGAUCAUCUUCUGGGCUACCG CGGCUGGAACACCCAUCAACGAGAACGCCAUUCUGCA ACACCAACCGGUCGCCUGGCAGACCCAGAGAGACUGC AAUCAGGCCAGCCACAGCCUUGGUCAGCGACCCGAC AAUGGUCAACTCUAUCUUGGUGGACAAAGGGCUG AACAGCGUGCCCAAGCUGAAAGUGUGGACAAUCAGCA UGCGCCAGAACUACUGGGGACGCGAGGGCAGACUUCU GCUGCUGGAAACAGAUUCACADUCUACACCCGGUCC ACCAGCUGGCACAGCAAAACUGCAGCUGGAAUCUUG ACAUACCCGACUACAGCGACAUCGGAUCAAGUGGACC UGGCACAAAGGUGCUGAGCAGACCCGGCAACAUGAGU GCCCUUGGGGCCACAGCUGCCCGAUGGAUUAUACAC	63

TABLE 5-continued

PIV3 Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	GGCGUGUACACCGACGCGCCUACCCCGUGAAUCCUACCGG CUCCAUCGUGUCCAGCGUGADCCUGGACAGCCAGAAA AGCAGAGUGAACCCCGUGAUCACAUACAGCACCAGCCAC CGAGAGAGUGAACGAACUGGCCAUCAGAAAACAGACC CUGAGCGCCGGCUACACCACCACAGCUGCAUCACACA CUCACACAGGGCUACUGCUUCCACUCUGGGAUUC AACCAAGUCCUGAACACCUCCAGCCCAUGCGUUD CAAGACCGAGAUCCECAAGAGCUGCUCC	
HPIV3, F Codon Optimized mRNA sequence	AUGCCCAUCAGCAUCCUGCGUAUCAUACCCACAAGAD CAUGGCCAGCCACUGCCAGADCCGACAUCCACCAAGCUGC AGCAGUGGGCGUGUCUGAAGCAGCCCAAGGGCAU GAAGAUCAGCCAGAACUUCGAGACAGCCUACCGUAUC CUGAGCCUGAUCCECAAGAUCCGAGGACAGCAACAGCU GCGGCGACCCAGCAGUACAGCAGUACAGCGGCGUGCU GGACAGACUGAUCUCCCGUGUACGACGGCCUGCGGC UGCAGAAAGACGUGAUCGUGACCAACCAGGAAAGCAA CGAGAACACCCGACCCCGAGCCGAGAGAUUCUUCGCG GCGUGAUCGGCACAAUCGCCUUGGGAGUGGCCACAAG CGCCAGAUUACAGCCGCGUGGGCCUUGGUGGAAGCCA AGCAGGCCAGAAAGCGACAUCCGAGAAGCUGAAGAGGC CAUCCGGGACACCAACAGGCCGUGCAGAGCGUGCAG UCCAGCGUGGGCAAUUCGAUCGUGGCCAUCAAGUCGG UGCAGGACUACGUGAACAAAGAAUUCGUGCCUCUUAU CGCCCGGCGUGGGCUGUGAAGCUGCCGGACUGCAGCUG GGCAUUGCCCGUACACAGCACUACAGCGAGCUGACCAA CAUCUUCGGCGACAAAUCCGCGAGCCUGCAGGAAAG GGCAUUAAGCUGCAGGGAUUCGCCAGCCUGUACCGCA CCAACAUCACCGAGAUUCUCCACCAGCAACCGUGGAU AAGUACGACAUUCAGCACCUGCUGUCCAGCAGAGCA UCAAGUGCGCGUGAUCGACGUGGACCUGAACGACUA CAGCAUCACCCUGCAAGUGCGGCUGCCCGUGCUGACCA GACUGCGUACACCCAGAUUCACAGGUGGACAGCAU CUCCUACAACAUCAGAACCCGAGUGGUAUCAUCCUC UGCCCGCCCAUUAUGACCAGGGCCCUUUCUGGGC GGAGCCGACGUGAAGAGUGCAUCGAGGCCUUCAGCA GCUACAUCUGCCCGCAGCACCUGGCCUUCGUGCUGAAC CACGAGAUUGAAAGCUGCCUGAGCGGCAACAUACGCC AGUGCCCGAGAACCCGUGACCCCGACAUCGUGGCC AGAUACGCCUUCGUGAAUGCGCGGUGGUGGCCAAUC GCAUCACCACCACCGUACCGCAACGCAUCGGCAAC CGGAUCAACCAGCCUCCGGAUCAGGGCGUGAAGAUUA UCACCCCAAAAGAGUGUAACACCAUCGGCAUCAACGGC AUGCUGUUAUAUACCAACAAGAGGGCACCUGGCCU UCUACACCCCGCAGUAUACCCUGAACAAUCUCCGUG GCUCUGGACCCUUCGACAUCUCCAUCCAGCUGAACAA GGCCAAGAGCCAGCCUGGAAGAGUCCAAGAGUGGAUC CGCGGAGCAACCAGAGCUGGACUCUAUCGCGAGCU GGCACCAGAGCAGCACCACCAUCAUCGUGAUCUGAUU AUGAUGAUUAUCUGUUAUCAUCAACAUAUACCAUCA UCACUAUCGCCAUUAAGUACUACCGGAUCCAGAAACG GAACCGGUGGACCGAAUGACAAGCCUACGUGCUG ACAAACAAG	64

TABLE 6

PIV3 Amino Acid Sequences		
Description	Sequence	SEQ ID NO:
>gi 612507166 gb AHK22429.1 fusion glycoprotein F0 [Human parainfluenza virus 3]	MPISILLIITTMINASHCQIDITKLQHVGLVNSPKGMKISQ NFETRYLILSLIPKIEDSNSCGDQIQKYKRLDLRLIPLYDG LRLQHDVIVTINQESNENTDPRTERFFGGVIGTIALGVATSA QITAAVALVEAKQARSDIEKLEAIRDTNKAVQSVQSSVG NLIVAIKSVQDYVNKEIVPSIARLGCBAAGLQLGIALTQHYS ELTNIFGDNIGSLQEKGIKLGQIASLYRNTNITEIFTTSTVDKY DIYDLLFTESI KVRVIDVDLNDYSITLQVRLPLLRLLNTQIY KVDSISYNIQHREWYIPLPSHIMTKGAFLLGADVKECIEAFS	13

TABLE 6-continued

PIV3 Amino Acid Sequences		
Description	Sequence	SEQ ID NO.
	SYICPSDPGPFVLNHEMESCLSGNISQCPRTTIVTSDIVPRYAF VNGGVVANCITTTCTCNGIGNRINQPPDQGVKII THKECNT I GINGMLFNTNKEGTLAFYTPDDITLNNISVALDPIDISIELNK AKSDL EESKEWIRRSNQKLD SIGSWHQSTTIIIVILIMMILFI INITIIITAIKYRILQKRNRVDQNDKPYVLTNK	
gi 612507167 gb AHX22430.1 hemagglutinin- neuraminidase [Human parainfluenza virus 3]	MEYWKHTNHGKDAGNELETSTATHGNKLTNKITYILWTIT LVLLSIVFIIIVLTNSIKSEKARESLQDINNEFMVTEKIQVA SDNTNDLIQSGVNRLLTIQSHVQNYIPISLTQQISDLRKPIS EITIRNDNQEVPPQRITHDVGIKPLNPDDPWRCTSGLPSLMK TPKIRLMPGPGLLAMPTTVDGCVRTPSLVINDLIYAYTSLI TRGCQDIGKSYQVLQIGIITVNSDLVPLNPRISHTFNINDM RKSCSLALLNTDQVQLCSTPKVDRSDYASSGIEDIVLDIV NYDGSISTTRFKNNISFDQPYAALYPSVGGPIYYKGIIFL GYGGLEHPINENAI CNTTGCPCGKTQRDCNQASHSPWFSR RMVNSIIVVDKGLNSVPLKVWTISMRQNYWGSERLLLLL GNKIYYTRSTSWHSKLQGLGIDITDYSDIRIKWTHHMLVLSR PGNNECPWGHSCPDCICTGVYTDAYPLMPTGSIVSSVILDS QKSRVHPVITYSTATERVHELAI RNKLTLSAGYTTTSCITHY NKGYCFHIVEINHKS LNTFQPMLFKTEIPKSCS	14

TABLE 7

PIV3 NCBI Accession Numbers (Nucleic Acid and Amino Acid Sequences)	
Description	GenBank Accession
Fusion glycoprotein F0 [Human parainfluenza virus 3] [PIV3/ <i>Homo sapiens</i> :PIR:FL.A4815.2008	KJ672601.1 : 4990-6609 AIX22429 (Fusion protein)
hemagglutinin-neuraminidase [Human parainfluenza virus 3] [PIV3/ <i>Homo sapiens</i> :PIR:FL.A4815.2008	KJ672601.1 : 6724-8442 AIX22430 (HN protein)
Recombinant PIV3 PIV1 virus fusion glycoprotein (F) and hemagglutinin (HN) genes, complete cds; and RNA dependent RNA polymerase (L) gene, partial cds.	AF016281 AAC25947 (hemagglutinin)
Recombinant PIV3 PIV1 virus fusion glycoprotein (F) and hemagglutinin (HN) genes, complete cds; and RNA dependent RNA polymerase (L) gene, partial cds.	AF016281 AAC25947 (fusion protein)
hemagglutinin-neuraminidase [Human parainfluenza virus 3]	BAO32044.1
hemagglutinin-neuraminidase [Human parainfluenza virus 3]	BAO32051.1
C protein [Human parainfluenza virus 3]	NP_592251.1
C protein [Human parainfluenza virus 3]	ABZ85670.1
C protein [Human parainfluenza virus 3]	AGT75164.1
C protein [Human parainfluenza virus 3]	AAI348686.1
C protein [Human parainfluenza virus 3]	AIX22115.1
C protein [Human parainfluenza virus 3]	AGW51066.1
C protein [Human parainfluenza virus 3]	AGW51162.1
C protein [Human parainfluenza virus 3]	AGT75252.1
C protein [Human parainfluenza virus 3]	AGT75188.1
C protein [Human parainfluenza virus 3]	AGW51218.1
C protein [Human parainfluenza virus 3]	AGW51074.1
C protein [Human parainfluenza virus 3]	AGT75323.1
C protein [Human parainfluenza virus 3]	AGT75307.1
C protein [Human parainfluenza virus 3]	AIX22131.1
C protein [Human parainfluenza virus 3]	AGW51243.1
C protein [Human parainfluenza virus 3]	AGT75180.1
C protein [Human parainfluenza virus 3]	AGT75212.1
C protein [Human parainfluenza virus 3]	AGW51186.1
C protein [Human parainfluenza virus 3]	AIX22075.1
C protein [Human parainfluenza virus 3]	AIX22163.1
C protein [Human parainfluenza virus 3]	AGT75196.1
C protein [Human parainfluenza virus 3]	AIX22491.1
C protein [Human parainfluenza virus 3]	AIX22139.1
C protein [Human parainfluenza virus 3]	AGW51158.1
C protein [Human parainfluenza virus 3]	AGW51114.1
C protein [Human parainfluenza virus 3]	AGT75220.1

TABLE 7-continued

Description	GenBank Accession
C protein [Human parainfluenza virus 3] RecName: Full = Protein C; AltName: Full = VP18 protein	AIX22251.1 P06165.1
C protein [Human parainfluenza virus 3]	AIX22187.1
C protein [Human parainfluenza virus 3]	AGT75228.1
C protein [Human parainfluenza virus 3]	AIX22179.1
C protein [Human parainfluenza virus 3]	AIX22427.1
C protein [Human parainfluenza virus 3]	AGW51210.1
nonstructural protein C [Human parainfluenza virus 3]	BAA00922.1
C protein [Human parainfluenza virus 3]	AIX22315.1
C protein [Human parainfluenza virus 3]	AGW51259.1
C protein [Human parainfluenza virus 3]	AIX22435.1
C protein [Human parainfluenza virus 3]	AIX22123.1
C protein [Human parainfluenza virus 3]	AIX22299.1
C protein [Human parainfluenza virus 3]	AGW51267.1
unnamed protein product [Human parainfluenza virus 3]	CAA28430.1
C protein [Human parainfluenza virus 3]	AGW51178.1
C protein [Human parainfluenza virus 3] RecName: Full = Protein C	AIX22411.1 P06164.1
phosphoprotein [Human parainfluenza virus 3]	NP_067149.1
phosphoprotein [Human parainfluenza virus 3]	AAB48685.1
phosphoprotein [Human parainfluenza virus 3]	AIX22498.1
phosphoprotein [Human parainfluenza virus 3]	AIX22490.1
phosphoprotein [Human parainfluenza virus 3]	AGT75259.1
phosphoprotein [Human parainfluenza virus 3]	AGW51157.1
phosphoprotein [Human parainfluenza virus 3]	AGW51145.1
phosphoprotein [Human parainfluenza virus 3]	AGT75298.1
phosphoprotein [Human parainfluenza virus 3]	AGW51113.1
phosphoprotein [Human parainfluenza virus 3]	AGT75203.1
phosphoprotein [Human parainfluenza virus 3]	AGT75163.1
phosphoprotein [Human parainfluenza virus 3]	AIX22506.1
phosphoprotein [Human parainfluenza virus 3]	AGW51129.1
phosphoprotein [Human parainfluenza virus 3]	AIX22194.1
phosphoprotein [Human parainfluenza virus 3]	AGT75211.1
phosphoprotein [Human parainfluenza virus 3]	AIX22258.1
phosphoprotein [Human parainfluenza virus 3]	AGW51121.1
phosphoprotein [Human parainfluenza virus 3]	AGT75282.1
phosphoprotein [Human parainfluenza virus 3]	AIX22146.1
phosphoprotein [Human parainfluenza virus 3]	AIX22138.1
phosphoprotein [Human parainfluenza virus 3]	AIX22322.1
phosphoprotein [Human parainfluenza virus 3]	AIX22370.1
phosphoprotein [Human parainfluenza virus 3]	AIX22098.1
phosphoprotein [Human parainfluenza virus 3]	AIX22130.1
phosphoprotein [Human parainfluenza virus 3]	AIX22418.1
phosphoprotein [Human parainfluenza virus 3]	AIX22114.1
phosphoprotein [Human parainfluenza virus 3]	AIX22410.1
phosphoprotein [Human parainfluenza virus 3]	AGT75306.1
phosphoprotein [Human parainfluenza virus 3]	AIX22170.1
phosphoprotein [Human parainfluenza virus 3]	AIX22266.1
phosphoprotein [Human parainfluenza virus 3]	AIX22090.1
phosphoprotein [Human parainfluenza virus 3]	AGT75195.1
phosphoprotein [Human parainfluenza virus 3]	AIX22226.1
phosphoprotein [Human parainfluenza virus 3]	AIX22178.1
phosphoprotein [Human parainfluenza virus 3]	AIX22122.1
phosphoprotein [Human parainfluenza virus 3]	AIX22186.1
phosphoprotein [Human parainfluenza virus 3]	AIX22066.1
phosphoprotein [Human parainfluenza virus 3]	AIX22522.1
phosphoprotein [Human parainfluenza virus 3]	AGW51225.1
phosphoprotein [Human parainfluenza virus 3]	BAN29032.1
phosphoprotein [Human parainfluenza virus 3]	ABZ85669.1
phosphoprotein [Human parainfluenza virus 3]	AIX22426.1
phosphoprotein [Human parainfluenza virus 3]	AIX22058.1
phosphoprotein [Simian Agent 10]	ADR00400.1
phosphoprotein [Human parainfluenza virus 3]	AIX22250.1
phosphoprotein [Human parainfluenza virus 3]	AIX22434.1
phosphoprotein [Human parainfluenza virus 3]	AIX22298.1
phosphoprotein [Human parainfluenza virus 3]	AIX22442.1
phosphoprotein [Human parainfluenza virus 3]	AIX22074.1
phosphoprotein [Human parainfluenza virus 3]	AGW51153.1
phosphoprotein [Human parainfluenza virus 3]	AGW51241.1
phosphoprotein [Human parainfluenza virus 3]	AIX22210.1
phosphoprotein [Human parainfluenza virus 3]	AGW51105.1
phosphoprotein [Human parainfluenza virus 3]	AGT75251.1
phosphoprotein [Human parainfluenza virus 3]	AIX22362.1

TABLE 7-continued

PIV3 NCBI Accession Numbers (Nucleic Acid and Amino Acid Sequences)	
Description	GenBank Accession
phosphoprotein [Human parainfluenza virus 3]	AJIX22474.1
phosphoprotein [Human parainfluenza virus 3]	AGW51217.1
phosphoprotein [Human parainfluenza virus 3]	AJG60038.1
phosphoprotein [Human parainfluenza virus 3]	AJIX22378.1
phosphoprotein [Human parainfluenza virus 3]	AGW51057.1
phosphoprotein [Human parainfluenza virus 3]	AGT75187.1
phosphoprotein [Human parainfluenza virus 3]	AGW51233.1
phosphoprotein [Human parainfluenza virus 3]	AJIX22482.1
phosphoprotein [Human parainfluenza virus 3]	AGW51161.1
phosphoprotein [Human parainfluenza virus 3]	AJIX22306.1
phosphoprotein [Human parainfluenza virus 3]	AJIX22162.1
phosphoprotein [Human parainfluenza virus 3]	ACJ70087.1
phosphoprotein [Human parainfluenza virus 3]	AJIX22466.1
phosphoprotein [Human parainfluenza virus 3]	AJIX22346.1
phosphoprotein [Human parainfluenza virus 3]	AGW51089.1
phosphoprotein [Human parainfluenza virus 3]	AGW51073.1
phosphoprotein [Human parainfluenza virus 3]	AGW51185.1
phosphoprotein [Human parainfluenza virus 3]	AGW51065.1
phosphoprotein [Human parainfluenza virus 3]	ABY47603.1
phosphoprotein [Human parainfluenza virus 3]	AGW51049.1
phosphoprotein [Human parainfluenza virus 3]	AJIX22330.1
phosphoprotein [Human parainfluenza virus 3]	AGW51250.1
phosphoprotein [Human parainfluenza virus 3]	AGT75227.1
phosphoprotein [Human parainfluenza virus 3]	AGW51282.1
phosphoprotein [Human parainfluenza virus 3]	AGW51209.1
phosphoprotein [Human parainfluenza virus 3]	AGW51193.1
phosphoprotein [Human parainfluenza virus 3]	AGT75322.1
phosphoprotein [Human parainfluenza virus 3]	AGT75219.1
phosphoprotein [Human parainfluenza virus 3]	AGW51258.1
phosphoprotein [Human parainfluenza virus 3]	AGW51041.1
phosphoprotein [Human parainfluenza virus 3]	ACJ99698.1
phosphoprotein [Human parainfluenza virus 3]	AGW51266.1
phosphoprotein [Human parainfluenza virus 3]	AGT75179.1
phosphoprotein [Human parainfluenza virus 3]	AJIX22282.1
phosphoprotein [Human parainfluenza virus 3]	AGW51169.1
phosphoprotein [Human parainfluenza virus 3]	AGW51274.1
phosphoprotein [Human parainfluenza virus 3]	AGW51201.1
phosphoprotein [Human parainfluenza virus 3]	AGW51177.1
RecName: Full = Phosphoprotein; Short = Protein P	P06162.1
P protein [Human parainfluenza virus 3]	AAA66818.1
phosphoprotein [Human parainfluenza virus 3]	AAA46866.1
phosphoprotein [Human parainfluenza virus 3]	BAA00031.1
polymerase-associated nucleocapsid phosphoprotein (version 2) - parainfluenza virus type 3	RRNZP5
[Human parainfluenza virus 3]	
phosphoprotein [Human parainfluenza virus 3]	AGT75171.1
phosphoprotein [Human parainfluenza virus 3]	BAA00921.1
D protein [Human parainfluenza virus 3]	NP_599250.1
D protein [Human parainfluenza virus 3]	AJIX22377.1
D protein [Human parainfluenza virus 3]	AJIX22121.1
D protein [Human parainfluenza virus 3]	AGT75297.1
D protein [Human parainfluenza virus 3]	AGW51136.1
D protein [Human parainfluenza virus 3]	AGW51242.1
D protein [Human parainfluenza virus 3]	AGW51112.1
D protein [Human parainfluenza virus 3]	AJIX22497.1
D protein [Human parainfluenza virus 3]	AJIX22145.1
D protein [Human parainfluenza virus 3]	AGT75202.1
D protein [Human parainfluenza virus 3]	AJIX22385.1
D protein [Human parainfluenza virus 3]	AGW51216.1
D protein [Human parainfluenza virus 3]	AGT75281.1
D protein [Human parainfluenza virus 3]	AGT75194.1
D protein [Human parainfluenza virus 3]	AJIX22521.1
D protein [Human parainfluenza virus 3]	AGW51120.1
D protein [Human parainfluenza virus 3]	AGT75315.1
D protein [Human parainfluenza virus 3]	AJIX22249.1
D protein [Human parainfluenza virus 3]	AJIX22097.1
D protein [Human parainfluenza virus 3]	AGW51144.1
D protein [Human parainfluenza virus 3]	AJIX22089.1
D protein [Human parainfluenza virus 3]	AJIX22225.1
D protein [Human parainfluenza virus 3]	AJIX22137.1
D protein [Human parainfluenza virus 3]	AJIX22065.1
D protein [Human parainfluenza virus 3]	AGW51224.1
D protein [Human parainfluenza virus 3]	AGT75210.1

TABLE 7-continued

PIV3 NCBI Accession Numbers (Nucleic Acid and Amino Acid Sequences)	
Description	GenBank Accession
D protein [Human parainfluenza virus 3]	AJIX22393.1
D protein [Human parainfluenza virus 3]	AGI75258.1
D protein [Human parainfluenza virus 3]	AJIX22345.1
D protein [Human parainfluenza virus 3]	AGI75250.1
D protein [Human parainfluenza virus 3]	AJIX22113.1
D protein [Human parainfluenza virus 3]	AGW51232.1
D protein [Human parainfluenza virus 3]	AJIX22057.1
D protein [Human parainfluenza virus 3]	AJIX22209.1
D protein [Human parainfluenza virus 3]	AGW51056.1
D protein [Human parainfluenza virus 3]	AJIX22161.1
D protein [Simian Agent 10]	ADR00402.1
D protein [Human parainfluenza virus 3]	AJIX22361.1
D protein [Human parainfluenza virus 3]	AGW51281.1
D protein [Human parainfluenza virus 3]	AGW51184.1
D protein [Human parainfluenza virus 3]	AGW51160.1
D protein [Human parainfluenza virus 3]	AJIX22465.1
D protein [Human parainfluenza virus 3]	AJIX22329.1
D protein [Human parainfluenza virus 3]	AGW51064.1
D protein [Human parainfluenza virus 3]	AGW51040.1
D protein [Human parainfluenza virus 3]	AGI75226.1
D protein [Human parainfluenza virus 3]	AJIX22425.1
D protein [Human parainfluenza virus 3]	AJIX22305.1
D protein [Human parainfluenza virus 3]	AGW51249.1
D protein [Human parainfluenza virus 3]	AJIX22481.1
D protein [Human parainfluenza virus 3]	AJIX22281.1
D protein [Human parainfluenza virus 3]	AGW51048.1
D protein [Human parainfluenza virus 3]	AJIX22297.1
D protein [Human parainfluenza virus 3]	AGW51088.1
D protein [Human parainfluenza virus 3]	AGI75305.1
D protein [Human parainfluenza virus 3]	AJIX22185.1
D protein [Human parainfluenza virus 3]	AGW51104.1
D protein [Human parainfluenza virus 3]	AJIX22081.1
D protein [Human parainfluenza virus 3]	AGW51192.1
D protein [Human parainfluenza virus 3]	AJIX22489.1
D protein [Human parainfluenza virus 3]	AJIX22441.1
D protein [Human parainfluenza virus 3]	AJIX22409.1
D protein [Human parainfluenza virus 3]	AJIX22369.1
D protein [Human parainfluenza virus 3]	AJIX22321.1
D protein [Human parainfluenza virus 3]	AJIX22073.1
D protein [Human parainfluenza virus 3]	AGW51152.1
D protein [Human parainfluenza virus 3]	AGW51072.1
D protein [Human parainfluenza virus 3]	AGI75321.1
D protein [Human parainfluenza virus 3]	AJIX22257.1
D protein [Human parainfluenza virus 3]	AJIX22129.1
D protein [Human parainfluenza virus 3]	AJIX22417.1
D protein [Human parainfluenza virus 3]	AGI75218.1
D protein [Human parainfluenza virus 3]	AJIX22265.1
D protein [Human parainfluenza virus 3]	AGI75178.1
D protein [Human parainfluenza virus 3]	AJIX22433.1
D protein [Human parainfluenza virus 3]	AGW51273.1
D protein [Human parainfluenza virus 3]	AGW51208.1
D protein [Human parainfluenza virus 3]	AGI75170.1
D protein [Human parainfluenza virus 3]	AGI75162.1
D protein [Human parainfluenza virus 3]	AGW51257.1
D protein [Human parainfluenza virus 3]	AGW51200.1
D protein [Human parainfluenza virus 3]	AGW51176.1
D protein [Human parainfluenza virus 3]	AGI75186.1
D protein [Human parainfluenza virus 3]	AGW51265.1
D protein [Human parainfluenza virus 3]	AGW51168.1

TABLE 8

Signal Peptides		
Description	Sequence	SEQ ID NO.
HuIgG ₁ signal peptide	METPAQLLFLLLLWLPDPTG	15
IgE heavy chain epsilon-1 signal peptide	MDWTWILFLVAAATRVMH	16
Japanese encephalitis PRM signal sequence	MLGSNSGQRVVFILLVAPAYS	17
VSVg protein signal sequence	MKCLLYLAFLEPIGVNCA	18
Japanese encephalitis JEV signal sequence	MWLVSIAIVTACAGA	19

TABLE 9

hMPV PIV Cotton Rat Challenge Study Design					
Group	n	Test Article	[conc] µg	Route	Challenge
1	5	Placebo	n.a	IM	hMPV A2
2	5	hMPV vaccine mRNA	30	IM	hMPV A2
3	5	hMPV vaccine mRNA	15	IM	hMPV A2
4	5	hMPV vaccine mRNA	10	IM	hMPV A2
5	5	hMPV PIV3 vaccine mRNA (15/15)	30	IM	hMPV A2
6	5	FI-hMPV	n.a	IM	hMPV A2
7	5	Placebo	n.a	IM	PIV3
8	5	PIV3 vaccine mRNA	30	IM	PIV3
9	5	PIV3 vaccine mRNA	15	IM	PIV3
10	5	PIV3 vaccine mRNA	10	IM	PIV3
11	5	hMPV PIV3 vaccine mRNA (15/15)	30	IM	PIV3
12	5	FI-PIV3	n.a	IM	PIV3
60					

TABLE 10

Betacoronavirus Nucleic Acid Sequence		
Strain	Nucleic Acid Sequence	SEQ ID NO.
gb KJ156934.1 : 21405-25466 Middle East respiratory syndrome coronavirus isolate Riyadh_14_2013, spike protein (nucleotide)	ATGATACACTCAGTGTTCCTACTGATGTTCTTGTAAACACC TACAGAAAGTTACGTTGATGTAGGGCCAGATTCTGTTAAG TCTGCTTGTATTGAGGTTGATATACAACAGACCTTCTTTGA TAAACTTGGCCTAGGCCAATTGATGTTTCTAAGGCTGAC GGTATTATATACCCCTCAAGGCCGTACATATTCTAACATAA CTATCACTTATCAAGGCTTTTTCCCTATCAGGGAGACCAT GGTGATATGATGTTTACTCTGCAGGACATGCTACAGGCA CACTCCACAAAAGTTGTTTGTAGCTAACTATTCTCAGGA CGTCAAACAGTTTGCTAATGGGTTTGTCTGCTCCGTATAGGA GCAGCTGCCAATCCACTGGCACTGTTATTATTAGCCCATC TACCAGCGCTACTATACGAAAAAATTTACCCTGCTTTTATGC TGGGTTCTTCAGTTGGTAATTTCTCAGATGGTAAAATGGG CCGCTTCTCAATCATACTCTAGTCTTTTGGCCGATGGAT GTGGCACTTACTTAGAGCTTTTATTGTATTCTAGAGCCCT CGCTCTGGAAATCATTGTCTGCTGGCAATTCCTATACTTC TTTTGCCACTTATCACACTCCTGCACAGATTGTTCTGATG GCAATTACAATCGTAATGCCAGTCTGAACTCTTTAAGGA GTATTTAATTTACGTAACCTGCACCTTTATGTACACTTATA ACATTACCGAAGATGAGATTTTAGAGTGGTTTGGCATTAC ACAACTGCTCAAGGTGTTCACTCTTCTCATCTCGGTATG TTGATTTGTACGGCGGCAATATGTTTCAATTTGCCACTTG CCTGTTTATGATACTATTAAGTATTATCTATCATTCTCTCA CAGTATTCGTTCTATCCAAAGTGATAGAAAAGCTTGGGCT GCCTTCTACGTATATAAATTTCAACCGTTAACTTTCTGTT GGATTTTCTGTTGATGGTTATATACCGCAGAGCTATAGACT GTGGTTTTAATGATTTGTCACAACTCCACTGCTCATATGAA TCCTTCGATGTTGAATCTGGAGTTTATTCAGTTTTCGCTTT CGAAGCAAAACCTTCTGGCTCAGTTGTGGAAACAGGCTGAA GGTGTGAATGTGATTTTTCACTCTTCTGCTGGCACACC TCCTCAGGTTTATAATTTCAAGCGTTTGGTTTTTACCAATT GCAATTATAATCTTACCAAATGCTTTCACCTTTTCTGTG AATGATTTTACTTTAGTCAATATCTCCAGCAGCAATTGC TAGCAACTGTTATTCTTCACTGATTTTGGATTATTTTTCAT ACCCACTTAGTATGAAATCCGATCTCAGTGTAGTTCTGCT GGTCAATATCCAGTTTAAATATAAACAGTCCCTTTCTAA TCCCACATGTTGATCTTAGCGACTGTTCCATACAACTTA CTACTATTACTAAGCCTCTAAGTACAGCTATATTAACAA GTGCTCTCGTCTTCTTCTGATGATCGTACTGAAGTACCTC AGTTAGTGAACGCTAATCAATACTCACCCCTGTGTATCCATT GTCCCATCCACTGTGTGGGAAGACGGTATTATTATAGGA AACAACTATCTCCACTTGAAGGTGGTGGCTGGCTTGTTC TAGTGGCTCAACTGTTGCCATGACTGAGCAATTAAGATG GGCTTTGGTATTACAGTTCAATATGGTACAGACACCAATA GTGTTTGGCCCAAGCTTGAATTTGCTAATGACACAAAAT	20

TABLE 10-continued

Betacoronavirus Nucleic Acid Sequence		
Strain	Nucleic Acid Sequence	SEQ ID NO:
	TGCCCTCAATTAGGCAATTGCGTGGAAATATCCCTCTATG GTGTTTCGGGCCGTGGTGTTTTTCAGAATTGCACAGCTGTA GGTGTTTCGACAGCAGCGCTTTGTTTATGATGCGTACCAGA ATTTAGTTGGCTATTATTCTGATGATGGCACTACTACTGT CTGCGTGC TTGTGTTAGTGTTCCTGTTTCTGTCATCTATGA TAAAGAACTAAAACCCACGCTACTCTATTTGGTAGTGT GCATGTGAACACATTTCTTCTACCATGTCTCAATACTCCCG TTCTACGCGATCAATGCTTAAACGGCGAGATTCTACATAT GGCCCCCTTCAGACACCTGTTGGTTGTGTCTTAGGACTTGT TAATTCCTCTTTGTTTCGTAGAGGACTGCAAGTTGCCCTCG GTCAATCTCTCTGTGCTCTTCTGACACACCTAGTACTCTC ACACCTCGCAGTGTGCGCTCTGTGCCAGGTGAAATGCGCT TGGCATCCATTGCTTTTAAATCATCCCATTGAGGTTGATCAA CTTAATAGTAGTATTTTAAATTAAGTATACCCACTAATTT TTCCCTTGGTGTGACTCAGGAGTACATTGAGCAACCAATTC AGAAAGTTACTGTTGATTGTAACAGTACGTTTGCATGG TTTCAGAAAGTGTGAGCAATTACTGCGGAGTATGGCCAG TTTTGTTCAAAATAAACAGGCTCTCCATGTTGTCATTT ACGCCAGGATGATTCTGTACGTAATTTGTTTGGGAGCGTG AAAAGCTCTCAATCATCTCTATCATAACAGGTTTGGAG GTGACTTTAATTTGACACTTC TAGAACCTGTTTCTATATCT ACTGGCAGTCGTAGTGCACGTAGTGCTATTGAGGATTTGC TATTTGACAAAGTCACTATAGCTGATCCTGGTTATATGCA ACGTTACGATGATTGTATGACGCAAGGTCAGCATCAGCT CGTGATCTTATTTGTGCTCAATATGTTGGCTGGTTATAAAGT ATTACCTCCTCTTATGGATGTTAATATGGAAGCCCGTATA CTTCATCTTTGCTTGGCAGCATAGCAGGTTTGGCTGGACT GCTGGCTTATCCTCCTTTGCTGCTATTCATTTGCACAGAG TATYTTTTATAGGTTAAACGGTGTGGCATTACTCAACAG GTCTTTTCAGAGAACC AAAAGCTTATTGCCAATAAGTTTA ATCAGGCTCTGGGAGCTATGCAACAGGCTTCACTACAAC TAATGAAGCTTTTCGGAAGGTTGAGGATGCTGTGAACAAC AATGCACAGGCTCTATCCAAATAGCTAGCAGGCTATCTA ATACTTTTGGTGTCTATTTCCGCTCTATTGGGAGACATCATA CAACGCTCTTGATGTTCTCGAACAGGACGCCAAATAGACA GACTTATTAATGGCCGTTTGACAACACTAAATGCTTTTGGT GCACAGCAGCTTGTTCGTTCCGAATCAGCTGCTCTTTCCGC TCAATTGGCTAAAGA TAAAGTCAATGAGTGTGTCAAGGCA CAATCCAGCGCTTCTGGATTTTGGCGTCAAGGCACACATA TAGTGCTCTTTGTTGTAATGCCCTTAATGGCCTTTACTTT ATGCATGTTGGTTATTAACCTAGCAACCACATTGAGGTTGT TTCTGCTTATGGTCTTTGCGATGCAGCTAACCTACTAATT GTATAGCCCTGTTAATGGCTACTTTTAAACTAATAAC ACTAGGATTTGATGAGTGGTCATATACTGGCTCGTCTCT CTATGCACCTGAGCCCATCACCTCTCTTAATACTAAGTATG TTGCACCACAGGTGACATACCAAAACATTTCTACTAACCT CCTCCTCCTCTTCTCGGCAATTCACCGGGATTGACTTCC AAGATGAGTTGGATGAGTTTTCAAAATGTTAGCACCAG TATACCTAATTTTGGTCTCTAACACAGATTAACTACTACAT TACTCGATCTTACCTACGAGATGTTGTCTCTTCAACAAGTT GTTAAAGCCCTTAATGAGTCTTACATAGACTTAAAGAGC TTGGCAATTATACTATTACAACAAATGGCCGTGGTACAT TTGGCTTGGTTTCATTGCTGGGCTTGTTCCTTAGCTCTAT GCGTCTTCTTCACTGTGCTGCACCTGGTTGTGGCACAAAC TGTATGGGAAAACCTAAGTGTAATCGTTGTTGTGATAGAT ACGAGGAATACGACCTCGAGCCGATAAGGTTTATGTTCA CTAA	
MERS S FL SPIKE 2cEMC/2012 (XbaI change(T to G)) (nucleotide)	ATGATACACTCAGTGTTC TACTGATGTTCTTGTAAACACC TACAGAAAGTTACGTTGATGTAGGGCCAGATTCTGTTAAG TCTGCTTGATTTGAGGTTGATATACAACAGACTTTCTTTGA TAAAACCTTGGCCTAGCCCAATTGATGTTCTTAAGGCTGAC GGTATTATATACCCCTCAAGGGCGTACATATTCTAACATAA CTATCACTTATCAAGGCTTTTTCCTATCAGGAGACCAT GGTGATATGTATGTTTACTCTGCAGGACATGCTACAGGCA CAACCTCCAAAAGTGTGTTGTTAGCTAATCTCTCAGGA CGTCAACAGTTTGCATAATGGGTTTGTGCTCGTATAGGA GCAGCTGCCAATTCACACTGGGCTGTTATTATTAGCCCATC TACCAGCGCTACTATACGAAAATTTACCCCTGCTTTTATGC TGGSTTCTCAGTTGGTAAATTTCTCAGATGGTAAAATGGG CCGCTTCTCAATCA TACTCTAGTTCTTTGCCCGATGGAT TGCCACTTTACTTAGAGCTTTTATTGTATTCTGGAGCCT	21

TABLE 10-continued

Betacoronavirus Nucleic Acid Sequence		
Strain	Nucleic Acid Sequence	SEQ ID NO:
	CGCTCTGGAAATCATTGTCCTGCTGGCAATTCCTATACTTC TTTTGCCACTTATCACACTCCTGCAACAGATTGTTCTGATG GCAATTACAAATCGTAATGCCAGTCTGAACTCTTTAAGGA GTATTTAATTTACGTAACGACCTTTATGTACACTTATA ACATTACCGAAGATGAGATTTTAGAGTGGTTTGGCATTAC ACAAACTGCTCAAGGTGTTACACCTTCTCATCTCGGTATG TTGATTGTACGGGGCAATATGTTCAATTTGCCACCTTG CCTGTTTATGATACTATTAAGTATTATTCTATCATTCTCA CAGTATTCGTTCTATCCAAAGTGATAGRAAAGCTTGGGCT GCCTTCTACGTATATAAATTCACCCGTTAAGTTTCTGTT GGATTTTCTGTTGATGGTTATATACGCAGAGCTATAGACT GTGGTTTTAATGATTGTGCACAACTCCACTGCTCATATGAA TCCTTCGATGTTGAACTCGGAGTTTATTGATTTCTGCTTT CGAAGCAAAACCTTCTGGCTCAGTTGTGGAACAGGCTGAA GGTTGTAATGTGATTTTACACCTTCTGTCTGGCACACC TCCTCAGGTTTATAATTCAGCGTTGGTTTTTACCAAT GCAATTATAATCTTACCAATGCTTTCACTTTTTCTGTG AATGATTTACTTGTAGTCAAATATCTCCAGCAGCAATGTC TAGCAACTGTTATTCTTCACTGATTTGGATTACTTTTCAT ACCCACTTAGTATGAAATCCGATCTCAGTGTAGTTCTGCT GGTCATATCCAGTTTAAATATAAACAGTCTTTCTAA TCCCACATGTTGATTTTAGCGACTGTTCCCTATAACCTTA CTACTATTACTAAGCCTCTTAAGTACAGCTATATTAACAA GTGCTCTCGTCTTCTTCTGATGATCGTACTGAAGTACCTC AGTTAGTGAACGCTAATCRATACTCACCTGTGTATCCATT GTCCCATCCACTGTGTGGGAAGACGGTATTATTATAGGA AACCACTATCTCCACTTGAAGGTGGTGGCTGGCTTGTGTC TAGTGGCTCACTGTTGCCATGACTGAGCAATACAGATG GGCTTTGGTATTACAGTTCAATATGGTACAGACACCAATA GTGTTGCCCCAAGCTTGAATTTGCTAATGACACAAAAT TGCTCTCAATTAGGCAATTCGCTGGAATATCCCTCTATG GTGTTTCGGGCCGTGGTGTTTTTCAGAAATGACAGCTGTA GGTTTCGACAGCAGCGCTTGTATTATGATGCGTACCAGA ATTTAGTTGGCTATTATTCTGATGATGGCACTACTACTGT TTGGCTGCTTGTGTTAGTGTCTCTGTTTCTGTCATCTATGAT AAAGAAACTAAACCACCGCTACTCTATTTGGTAGTGTG CATGTGAACACATTTCTTACCATGCTCAATACTCCCGT TCTACGCGATCAATGCTTAAACGGCGAGATTCTACATATG GCCCCCTTCAGACACTGTTGGTTGTCTTAGGACTTGT AATTCCTCTTTGTTGAGAGGACTGCAAGTTGCCCTCTTG TCAATCTCTCTGTGCTCTTCCGACACCTTAGTACTCTCA CACTCGCAGTGTGGCTCTGTTCCAGGTGAAATGCGCTT GGCATCCATTGCTTTAATCATCTTATTGAGTTGATCAAC TTAATAGTAGTTATTTTAAATTAAGTATACCCACTAATTT TCCTTTGGTGTGACTCAGGAGTACATTGAGCAACCATTC AGAAAGTTACTGTTGATGTAAACAGTACGTTTGCATGG TTTTCAGAAGTGTGAGCAATTAAGTGGGAGTATGGCCAG TTTTGTCCAAAATAAACAGGCTCTCCATGGTGCCAAAT ACGCCAGGATGATTCGTACGTAATTTGTTTGGGAGCGTG AAAAGCTCTCAATCATCTCTATCATACCAGTTTGGAG GTGACTTTAATTTGACACTTCTGGAACCTGTTCTATATCT ACTGGCAGTCTAGTGCACGTAGTGTCTATTGAGGATTTGC TATTTGACAAAGTCACTATAGCTGATCCTGGTTATATGCA AGGTTACGATGATTGCATGCAGCAAGGTCAGCATCAGCT CGTGATCTTATTTGTGCTCAATATGTGGCTGGTTACAAAGT ATTACCTCCTCTTATGGATGTTAATATGGAAGCCCGTATA CTTCACTTTGCTTGGCAGCATAGCAGGTGTTGGCTGGACT GCTGGCTTATCCTCTTTGCTGCTATTCATTGTCACAGAG TATCTTTTATAGGTTAAACGGTGTGGCATTACTCAACAGG TTCTTTCAGAGAACCAAAAGCTTATTGCAATAAGTTTAA TCAGGCTCTGGGAGCTATGCAAAACAGGCTTCACTACAACT AATGAAGCTTTTCAGAAGTTTCAAGATGCTGTGAACAACA ATGCACAGGCTCTATCCAAATAGCTAGCAGGCTATCTAA TACTTTTGGTGTCTATTCCGCTCTATTGGAGACATCATAC AACGCTCTGATGTTCTCGAACAGGACGCCAAATAGACAG ACTTATTAATGGCCGTTTGCACACACTAAATGCTTTTGTG CACAGCAGCTTGTGTTCCGAATCAGCTGCTCTTTCCGCT CAATTGGCTAAAGATAAAGTCAATGAGTGTGCAAGGCAC AATCCAAGCGTTCTGGATTTTGCGGTCAAGGCACACATAT AGTGTCTTTGTTGTAATGCCCTCAATGGCTTTACTTCA TGCATGTTGGTTATTACCCTAGCAACCAATTGAGGTTGTT CTGCTTATGGTCTTTGCGATGCAGCTAACCTACTAATTG	

TABLE 10-continued

Betacoronavirus Nucleic Acid Sequence		
Strain	Nucleic Acid Sequence	SEQ ID NO:
	TATAGCCCCTGTTAATGGCTACTTTATTA AAACTAATAACA CTAGGATTGTTGATGAGTGGTCATATACTGGCTCGTCCCTTC TATGCACCTGAGCCCATACCTCCCTTAATACTAAGTATGT TGCACCACAGGTGACATACCAAAACATTTCTACTAACCTC CCTCCTCCTCTTCTCGGCAATCCACCGGATGACTTCCA AGATGAGTTGGATGAGTTTTTCAA AATGTTAGCACCGT ATACCTAATTTTGGTTCCCTAACACAGATTAATACTACATT ACTCGATCTTACCTACGAGATGTTGTCTCTCAACAAGTTG TTAAAGCCCTTAATGAGTCTTACATAGRCCTTAAAGAGCT TGGCAATTATACTTATTACACAAAATGGCCGTGGTACATT TGGCTTGGTTTCAITGCTGGGCTTGTTCCTTAGCTCTATG CGTCTTCTTACTACTGTGCTGCACTGGTTGTGGCACAAC GTATGGGAAAACCTAAAGTGAATCGTTGTTGTGATAGATA CGAGGAATACGACCTCGAGCCGCATAAGGTTTATGTTTAC TAA	
Novel MERS_S2 subunit trimeric vaccine (nucleotide)	ATGATCCACTCCGTGTTCCCTCATGTTCTGTTGACCCC CACTGAGTCAGACTGCAAGCTCCCGCTGGGACAGTCCCTG TGTGGCTGCCGTGACACTCCTAGCACTCTGACCCCAAGCTC CGTGGGTGGTGGCTGGCGAAATGCGGCTGGCTCCATC GCCTTCAATCACCCAAATCCAGTGGATCAGCTGAATAGCT CGTATTTCAAGCTGTCCATCCCCACGAACTTCTCGTTGGG GTCACCCAGGAGTACATCCAGACCAATTCAGAAGGTCA CCGTGATGCAAGCAATACGTGTGCAACGGCTTCCAGAA GTGCGAGCAGCTGCTGAGAGAATACGGGCAGTTTTGCAGC AAGATCAACCAGGCGCTGCATGGAGCTAAGTTGCCCAAG ACGACTCCGTGCGCAACTCTTTGCCTCTGTGAAGTCATCC CAGTCTCCCAATCATCCCGGATTCGGAGGGGACTTCA ACCTGACCCTCCTGGAGCCCGTGTGATCAGCACCGGTAG CAGATCGGCGCTCAGCCATTGAAGATCTTCTGTTCGAC AAGTCCACCATCGCCGATCCGGCTACATGCGGGATACG ACGACTGTATGCAAGCAGGACAGCCTCCGCGAGGACCT CATCTGCGCGCAATACGTGGCCGGGTACAAAGTGTGCT CCTCTGATGGATGTGAACATGGAGGCCCTTATACTTCGT CCTGCTCGGCTCTATCGCCGGCTGGGTGGACCGCCGG CCTGTCTCCTTCGCGCTATCCCTTTGCACAATCCATTT TCTACCGCTCAACGGCTGGGCATTACTCAACAAGTCTT GTCGGAGAACCAGAGTTGATCGCAACAAGTTCAAATCA GGCCCTGGGGCCATGCGACATGGATTCACTACGACTAAC GARGCCTTCCAGAAGTCCAGGACGCTGTGAACAACAAC GCCAAGGCGCTCTCAAAGCTGGCTCCGAACTCAGCAACA CCTTCGGAGCCATCAGCCGATCGATCGGTGACATAATTCA GCGGCTGGACGTGCTGGAGCAGGACGCCAGATCGACCG CCTCATCAACGGACGGCTGACCACCTTGAATGCTTCTGTG GCACAACAGCTGGTCCGGAGCGAATCAGCGGCACCTTCCG CCCAACTCGCCAAAGACAAGTCAACGAATCGGTGAAGG CCCAGTCCAAAGGTTCCGTTTTCTGCGGTCAAAGCAACCA TATTTGTCTCTCGTCTGAACGCGCCCAACGGTCTGTACT TTATGCACGTGGCTACTACCCGAGCAATCATATCGAAGT GGTGTCCGCTACGCGCTGTGCGATGCCCTAACCCACT AACTGTATTGCCCTGTGAACGGATATTTATTAAGACCA ACAACACCCGCTTGTGGACGAATGGTCATACACCGGTTT GTCTTCTACGCGCCCGAGCCATCACTTCACTGAACACC AAATACGTGGCTCCGCAAGTACCTACCAAGACATCTCCA CCAATTTGCCGCGCGCTGCTCGGAACAGCACCGGAAT TGATTTCCAAAGATGAACGGACGAATTTCAAGAACGTG TCCACTTCCATCCCAACTTCGGAAGCCTGACACAGATCA ACACCACCCCTTCTCGACCTGACCTACGAGATGCTGAGCT TCAACAAGTGGTCAAGGCCCTGAACGAGAGCTACATCGAC CTGAAGGAGCTGGGCACTATACCTACTACACAAGTGGC CGGACAGATTGAGGAGATTCTGTGCAAAATCTACCACAT TGAAAACGAGATCGCCAGAATCAAGAAGCTTATCGGCGA AGCC	22
MERS_S0 Full-length Spike protein (nucleotide, codon optimized)	ATGGAAACCCCTGCCAGCTGCTGTTCTGCTGCTGCTGTG GCTGCCTGATACCACCGGCGAGCTATGTGACGTGGGCCCC GATAGCGTGAAGTCCGCTGTATCGAAGTGGACATCCAGC AGACCTTTTTGACAAAGACCTGGCCAGACCCATCGAGCT GTCCAAGGCCGACGGCATCATCTATCCCAAGGCCGGAC TACAGCAACATCACATTACCTACCGGGCTGTTCCCAT ATCAAGGCGACCAAGCGGATATGTACGTGACTCTGCGGG CCACGGCCACCGCCACACCCAGAACTGTTCTGTTGGCC	23

TABLE 10-continued

Betacoronavirus Nucleic Acid Sequence		
Strain	Nucleic Acid Sequence	SEQ ID NO:
	AACTACAGCCAGGACGTGAGCAGTTGGCCAAACGGCTTCG TCGTGGGATTGGCCCGCTGCCAATAGCACCGGCACAGT GATCATCAGCCCCAGCACAGCGCCAGCCTCCGGGAAGATC TACCCCGCCTTCATGCTGGGCAGCTCCGTGGGCAATTTCA GCGACGGCAAGATGGGCCGGTTCTTCAACACACCCCTGGT GCTGCTGCCGATGGCTGTGGCACACTGCTGAGAGCCTTC TACTGCATCCTGGAAACCGAAGCGGCAACCACTGCCCTG CCGGCAATAGCTACACCAGCTTCGCCACCTACCACACACC CGCCACCGATTGCTCCGACGGCAACTACACCGGAACGCC AGCCTGAACAGCTTCAAAGAGTACTTCAACCTGGCGAAT GCACCTTCATGTACACCTACAATATCACCGAGGACGAGAT CCTGGAATGGTTCCGGCATCACCCAGACCGCCAGGGCGTG CACCTGTTGACGAGAGATACGTGGACCTGTACGGCGGCA ACATGTTCCAGTTTCCACCCCTGCCCGTGTACGACACCATC AAGTACTACAGCATCATCCCCACAGCATCCGGTCCATCC AGAGCGACAGAAAGCCTGGGCCGCTTCTACGTGTACAA GCTGACGCCCTGACCTTCTGCTGGACTTCAGCGTGGAC GGCTACATCAGACGGGCCATCGACTGCCGCTTCAACGACC TGAGCCAGCTGCACCTGCTCCTACGAGAGCTTCGACGTGGA AAGCGCGTGTACAGCGTGTCCAGCTTCGAGGCCAAGCCT AGCGGCAGCGTGGTGGACAGGCTGAGGGCGTGGAAATGC GACTTCAGCCCTCTGCTGAGCGGCACCCCTCCCCAGTGT ACAACTTCAGCGGCTGGTGTTCACCAACTGCAATTACAA CCTGACCAAGCTGTGAGCCTGTTCGCGTGAACGACTTC ACCTGTAGCCAGATCAGCCCTGCCGCCATTCGACGCACT GCTACAGCAGCCTGATCTCGGACTACTTCAGCTACCCCT GAGCATGAAGTCCGATCTGAGCGTGTCTCCGCCGGACCC ATCAGCCAGTTCACATACAGCAGAGCTTCAGCAACCCTA CCTGCCCTGATTTGCGCCACCGTGCCTCCAACTGACCAC CATCACCAAGCCCTGAAGTACAGCTACATCAACAGTGC AGCAGACTGCTGTCCGACGACCGGACCGAAGTGCCTCCAGC TCGTGAACGCCAACAGTACAGCCCTGCGTGTCCATCGT GCCCAGCACCGTGTGGGAGGACGGCGACTACTACAGAAA GCAGCTGAGCCCTTGGAAAGCGCGGATGGCTGGTGGCT TCTGGAAGCACAGTGGCCATGACCGAGCAGCTGCAGATG GGCTTTGGCATCACCGTGCAGTACGGCACCGACACCAACA GCGTGTGCCCCAGCTGGAATTCGCCAATGACACCAAGAT CGCCAGCCAGCTGGGAAACTGCGTGGAACTACCTCCCTGTAT GCGGTGTCGGACGGGGCGTGTCCAGAATTGCACAGCAG TGGGAGTGCAGCAGCAGATTCGTGTACGATGCCCTACCA GAACCTCGTGGCTACTACAGCGACGACGGCAATTACTAC TGCTGCGGGCTGTGTGTCCGTGCCCGTGTCCGTGATCTA CGACAAGAGAGCAAGACCCACGCCACACTGTTCCGGCTCC GTGGCTTGCAGCACATCAGCTCCACCATGAGCCAGTACT CCGGCTCCACCGGTCATGCTGAAGCGGAGAGATAGCAC CTACGGCCCCCTGCAGACACCTGTGGGATGTGTCTGGGC CTCGTGAACAGCTCCCTGTTGTGGAAGATTGCAAGCTGC CCCTGGGCAGAGCCTGTGTGCCCTGCAGATAACCCCTAG CACCCTGACCCCTAGAAGCGTGCCTCTGTGCCCGGGGAA ATGCCGCTGGCTCTATCGCCTTCAATCACCCATCCAGGT GGACCAGCTGAACCTCCAGCTACTTCAAGCTGAGCATCCCC ACCAATTCAGCTTCGGCGTGACCCAGGAGTACATCCAGA CCACAAATCCAGAAAGTGACCGTGGACTGCAAGCAGTACGT GTGCAACGGCTTTCAGAAGTGCGAACAGCTGCTGCGCGAG TACGGCCAGTTCGACGCAAGATCAACCGGGCCCTGCACG GCGCCAACTGAGACAGGATGACAGCGTGGGAACTGTT CGCCAGCGTGAAGAGCAGCCAGTCCAGCCCCATCATCCCT GGCTTCGGCGGGACTTTAACTGACCCCTGCTGGAACTGT TGTCCATCAGCACCGGCTCCAGAAGCGCCAGATCCGCCAT CGAGGACCTGCTGTTCGACAAAGTGACCATGCGCAGCCCC GGCTACATGCAGGGCTACGACGATTCATGCGAGCAGGGCC CAGCCAGCCACAGGATCTGATCTGTGCCAGTATGTGGC CGGCTACAAGGTGCTGCCCCCCCTGATGGACGTGAACATG GAAGCCGCTACACCTCCAGCCTGCTGGGCTCTATTGCTG GCGTGGGATGGACAGCCCGGCTGTCTAGCTTTGCGCCAT CCCTTCGCCACAGAGCATCTTACCGGCTGAACGGCGTG GGCATCACACAACAGGTGCTGAGCGAGAACCGAAGCTG ATCGCCAAAGTTTAACCAGGCACTGGCGCCATGCGAGA CCGGCTTACACACCACCAACGAGGCTTCAGAAAGGTGCA GGAGCCGTGAACAACAACGCCCGAGGCTCTGAGCAAGCT GGCTTCGAGCTGAGCAATACCTTCGGCGCCATCAGCGCC TCCATCGGCGACATCATCCAGCGGCTGGACGTGCTGGAAC	

TABLE 10-continued

Betacoronavirus Nucleic Acid Sequence		
Strain	Nucleic Acid Sequence	SEQ ID NO:
	AGGACGCCAGATCGACCGGCTGATCAACGGCAGACTGA CCACCCGAAACGCTTCGTGGCACAGCAGCTCGTGGGAG CGAATCTGCCGCTCTGTCTGTCTGAGCTGGCCAGGACAAA GTGAACGAGTGCCTGAAGGCCAGTCCAAGCGGAGCGGC TTTTGTGGCCAGGGCACCCACATCGTGTCTTCGTCTGAA TGCCCCAACGGCTGTACTTTATGCACGTGGCTATTACC CCAGCAACACATCGAGGTGTCTCCGCTATGGCCCTGTG CGACGCCGCCAATCCTACCAACTGTATCGCCCCGTGAAC GGCTACTTCATCAAGACCACAAACCCGGATCGTGGACG AGTGGTCTACACAGGCAGCAGCTTCTACGCCCCCGAGCC CATCACCTCCCTGAACACCATAACGTGGCCCCCAAGTG ACATACCAGAACATCTCCACCACCTGCCCTCCACTGC TGGGAAATTCACCCGGCATCGACTTCCAGGACGAGCTGGA CGAGTTCTTCAAGAACGTGTCCACCTCCATCCCCAACTTCG GCAGCCTGACCCAGATCAACACCACCTCTGCTGGACTGAC CTACGAGATGCTGTCCCTGCAACAGGTCTGAAAGCCCTG AACGAGAGCTACATCGACTGAAAGAGCTGGGGAACCTAC ACCTACTACAACAAGTGGCTTGGTACATTTGGCTGGGCT TTATCGCCGGCTGGTGGCCCTGGCCCTGTGCGTGTCTTC ATCCGTGTCTGCACCGGCTGGCCACCAATGTCATGGGCA AGCTGAAATGCAACCGGTGCTGCGACAGATCGAGGAAT ACGACCTGGACCTCACAAAGTGCATGTGCAC	

Betacoronavirus mRNA Sequences

gb KJ156934.1 : 21405-25466 Middle East respiratory syndrome coronavirus isolate Riyadh 14 2013, spike protein (nucleotide)	AUGADAACACUCAGUGUUUCUACUGAUGGUUCUUGUUAAAC ACCUACAGAAAGUUACGUUGAUGUAGGGCCAGAUUCUG UUAAGUCUGCUUGUAUUGAGGUUGAUAUACACAGAGCC UUCUUUGAUAACAACUUGGCCUAGGCCAAUUGAUGUUUC UAAGGCUGACGGUAUUUAUAUACCCUACAGGCCGUAUACU AUUCUAACUAACUAUACUDAUAACAGGUUUUUUCCCU AUCAGGGAGACCAUGGUGUAUUGUAUGUUUACUCUGCA GGACAUUCUACAGGCACAACUCCACAAGUUGUUGU AGCUAACUUAUUCACGGACGUCAAACAGUUUGCUAUAUG GGUUUUGUCUCCGUUAUAGGAGCAGCUGCCAAUUCACUG GCACUGUUUAUUAUAGCCCAUCUACCGCGCUACUAUAC GAAAAUUUAACCCUGCUUUUAUGCUGGGUUCUUCAGUU GGUAUUUCUCAGAUUGGUAUUAUUGGCCUUCUUCUCAA UCAUAUCUCUAGUUUUUUUGCCCGAUGGAUGUGGCACUU UACUUAAGACUUUUUAUUGUAUUUCUAGAGCCUUCGCUUC GGAAUUCAUUGUCCUGCUGGCAAUUCCUAUAUCUUUU UGCCACUUUAUCACUCUCUGCAACAGAUUGUUUGAUGG CAUUAACAUCGUAAUGCCAGUCUGAACUCUUUAAGG AGUAUUUAUUUAACGUAAUCUGCACCUUUUAUGUACAUCU UAUAAACAUUACCGAAGAUAGAUUUUAGAGUGGUUUGG CAUUAACAACUCUGCAAGGUGUUCACUCUUCUCUACUC UCGGUAUGUUGAUUUUAUCGGCGGCAAUUUGUUUCAAU UUGCCACCUUGCCUGUUUAUGAUACUAUUUAAGUAUUUAU UCUAUCAUUCCUCACAGUAUUCGUUCUAUCCAAAGUGAU AGAAAAGCUUGGCCUGCCUUCUACGUUAUAUAAACUUC ACCGUUAACUUCCUGUUGGAUUUUUCUGUUGAUGGUU AUAUACCGCAGACUAUAGACUGUGGUUUUAUUGAUUUG UCACAAUCUCCACUGCUCUAUAGAAUCCUUCGAUGDUGAA UCUGGAGUUUAUUCAGUUUCGUCUUUCGAAGCAAACC UUCUGGCUCAGUUGGGAACAGGCUGAAGGUGUUGAAU GUGAUUUUACACCUUCUUGUCUGGCACACCCUCCAGG UUUUAUAUUUACAGCGUUUGGUUUUACCAAUUGCAAU UAUAAUCUUAACAAUUGCUUUCACUUUUUUGUGAA UGADUUUAUUUGUAGUCAAAUUCUCCAGCAGCAAUUG CUAGCAACUGUUAUUCUACUGAUUUUGGAUUUAUUUU UCAUACCCACUUAGUAUGAAUCCGUAUCUAGUUGUAG UUCUGCUGGUCCAAUAUCCAGUUUAUUUAUAAACAGU CCUUUUCAAUCCCAUGUUUGAUUUUAGCGACUGUUC CUCAUACCUUAUCUAUAUUAUUAAGCCUUCUUAAGUACA GCUAUAUUAAACAGUGUCUCUGUCUUUUUCUGADGAU CGUACUGAAGUACCUUCAGUUAGUGAACGUAUUAUUA CUCACCCUGUGUAUCCAUUGUCCAUCCACUUGUGGGGA AGACGGUGAUUUUAUAGGAAACAACUAUCUCCACUUG AAGGGGGGGCCUGGCUUGUUGCUAGUGGCUCACUGUU GCCAUGACUGAGCAAUACAGAUUGGCCUUUGGUUUUAC AGUUCAAUUGGUACAGACACCAAUAGUUUUUGCCCA AGCUUGAAUUUGCUAUAUGACACAAAUUUGCCUUCUCAA	65
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TABLE 10-continued

Betacoronavirus Nucleic Acid Sequence		
Strain	Nucleic Acid Sequence	SEQ ID NO:
	UUAGGCCAAUUGCGUGGAAUAUUBCCCUAUGGUGUUUC GGGCCGUGGUGUUUUUCAGAAUUGCACAGCUGUAGGUG UUCGACAGCAGCGCUUUGUUUUGAUGCGUACCAGAAU UUAGUUGGCUAUUAUUCUGAUGAUGGCAACUACUACUG UCUGCGUGCUGUGUUAGUUUCUGUUUCUGUCAUCU AUGAUAAAGAAACUAAACCACCGCUACUCUAUUUGGU AGUGUUGCAUGUGAACACAUUBCUUCUACCAUGUCUCA AUACUCCCGUUCUACGCGAUCAAUGCUUAAACGGCGAGA UUCUACAUAUGGCCCCUUCAGACACCGUUGUUGGUGUGU CCUAGGACUUGUUAUUCUCUUBUUGUUCGUAGAGGACU GCAAGUUGCCUCUCGGUCAUUCUCUCUGUGCUUUCUUG ACACACCUAGUACUCUCACACUCUCGAGUGUGCGUCUG UGCCAGGUGAAUUGCGCUGGGCAUCUUAUGCUUUUAAU CAUCCCAUUCAGGUUGAUCACUUAUUAUGUAGUUUUU UAAAUUAAGUAUACCCACUAUUUUUCCUUUGGUGUGA CUCAGGAGUACAUUCAGACAACCAUUCAGAAAGUUAUCU GUUGAUUGUAAACAGUACGUUUGCAAUGGUUUCAGAA GUGUGAGCAAUUACUGCGGAGUAUGGCCAGUUUUGUU CCAAAUAAACAGGCUCUCUUAUGGUGCCAAUUUACGCC AGGADGAUUCUGUACGUAAUUUGUUUGCGAGCGUGAAA AGCUCUCAAUCAUCUCUUAUCUACCAAGGUUUUGGAGGU GACUUUAAUUUGACACUUCUAGAACCGUUUUCUADAUC UACUGGCAGUCGUAGUGCACGUAGUGCUAUUGAGGAUU UGCUAUUUGACAAAGUACUAUAGCUGAUCCUGGDUAU AUGCAAGGUUACGAUUGUAUGCAGCAGGUCUACAGC AUCAGCUCUGAUCUUUUUUGUGCUCAAUAUGUGGCUG GUUUAAGAUAUACUCUCUUAUGGAGUUAUAUUG GAAGCCGCGUAUACUUCUUCUUGCUUGGCAGCAUAGCA GGUGUUUGCUGGACUGCUGGCUUUUCUCCUUUGCUGCU AUUCCAUUUGCACAGAUUUYUUUAUAGGUUAAACGG UGUUGGCAUUACUCAACAGGDUUCUUCAGAGAACCAA AGCUUAUUGCCAAUAAGUUUAAUCAGGCUCUGGGAGCU AUGCAACAGGCUCUACUACAACUAUAGUAGCUUUUCG GAAGGUUCAGGAUGCUGUGAACAAUUGCACAGGCUC UAUCCAAUUAAGCUAGCGAGCUAUCUAAUACUUUUGGU GCUAUUUCGCGUCUUAUUGGAGACUACUACACAGUCUU GAUGUUUCGAAACAGGACGCCCAAUAGACAGACUUAU UAAUGGCCUUUGACAAACAUAUAGCUUUUUGUUGCAC AGCAGCUUGUUCGUUCCGAUACAGCUGUCUUUUCGCU AAUUGGCUAAGAUAAAGUCAUAGAGUGUGUCAAGGCA CAAUCCAGCGUUCUGGAUUUUGCGGUCAAGGCACACA AUAGUGUCUUUGUUGAAUUGCCCUAAUUGGCCUUUA CUUUAUGCAUGUUGGUUAUACCCUAGCAACCAUUG AGGUUGUUUCUGCUUAGGUCUUUGCGAUGCAGCUAAC CCUACUAAUUGUAUAGCCCCUGUUAUUGGCUACUUUAU UAAAAUUAUACACUAGGAUUGUUGAUGAGUGGUCU AUACUGGCUCGUCCUUCUAGCAACCGAGCCAUACACCU CUCUUAUACUAAAGUAUGUUGCACACAGGUGACAUACC AAAACAUUUCUACUAAACUCCUCCUCCUUCUCUGGCA AUUCACCGGAAUUGACUUCUAAAGAUAGUUGGADGAG UUUUUCAAAAUUGUAGCACAGUAUACCUAAUUUGG UUCUCUAAACAGAUUAAUACUACUUAUCUGAUUCUAC CUACGAGAUUGUUCUUCUAAACAGUUUUUAAAGCCC UUAUUGAGUCUUACAUAGACUUAAAGAGCUUGGCAAU UAUACUUAUUACAAACAAUUGGCCUGGUACAUUUGGCU UGGUUUCAUUGCUGGCUUGUUGCCUAGCUUAUGCG UCUUCUUCUACUGUGCUGCACUGGUUGUGGCACAAACU GUADGGGAAACUUAAGUGUAUUGGUUGUUGADAGA UACGAGGAUACGACUUCGAGCCGAUAAGGUUCUAGU UCACUAA	
MERS S FL SPIKE 2cEMC/2012 (XBaI change (U to G)) (nucleotide)	AUGAUACACUCAGUGUUUCUACUGAUGUUCUUGUUAAC ACCUACAGAAAGUUAUCGUUGAUGUAGGGCCAGAUUCUG UUAAGUCUGCUGUUAUUGAGGUGUAGUUAACAACAGACU UUCUUUGAUAUAAACUUGGCCUAGGCCAAUUGAUGUUUC UAAGGCUGACGGUUAUUUAUACCCUCAAGGCCGUACAU AUUCUACAUAAUACUACUUAUCUUAUCAGGUCUUUUUCCCU AUACAGGAGAACCAUGGUGUAUUGUAUGUUUAUCUCUGCA GGACAUUCUACAGGCACAAUCUACAAAGUUUGUUGU AGCUAAUUAUUCUAGGACGUCAAACAGUUUGUCUAAUG GGUUUGUCGUCCGUUAAGGAGCAGCUGCCAAUUCACUUG GCACUGUUUAUUAAGCCAUUCUACAGCGCUACUUAUC	66

TABLE 10-continued

Betacoronavirus Nucleic Acid Sequence		
Strain	Nucleic Acid Sequence	SEQ ID NO:
	GAAAAUUUACCUGCUUUUUAUGCUGGGUUCUUCAGUU GGUAUUUCUCAGAUUGUAAAUGGCCGCUUCUUCAA UCAUACUCUAGUUUUUUGCCGAGUGGAGUGGCCAUU UACUAGAGCUUUUUUAUUGUAUUCUGGAGCCUCGCUCU GGAAAUCAUUGUCCUGCUGGCAAUUCCUAUACUUCUUU UGCCACUUAUCAACUCCUGCAACAGAUUUGUUCUGAUGG CAADUACAACUGUAUUGCCAGUCUGAACUUCUUUAAGG AGUAUUUUAAUUUACGUAAUGCAGACUUUAUGUACACU UAUAACAUUACCGAGAUUGAGAUUUUAGAGUGGUUUGG CAUUAACAACUGUCUACAGGUGUUACCCUUCUCUACU UCGGUAUGUUGAUUUUGUACGGCGGCAUUAUGUUCAAU UUGCCACCCUUGCCUGUUUAUGAUACUAUUUAGUAUUU UCUAUCAUUCCUCACAGUAUUCGUUCUAUCCAAAGUGAU AGAAAGCUGGGCUGCCUUCUACGUUAUUAACUUCU ACCGUUAACUUUCCUGUUGGAAUUUUCUGUUGAUGGUU AUADAACCCAGAGCUAUGACUGUGGUUUAAUGAUUUG UCACAAUCCACUGCUCUAUAGAAUCCUUCGAGUUGAA UCUGGAGUUUAUUCAGUUUCGUCUUCGAGCAAAACC UUCUGGCUAGUUGGGAACAGGCUAGAGGUUGAAU GUGAUUUUACCCUUCUUGUCUGGCAACCCUUCAGG UUUUAUAUUUACAGGUUUGGUUUUUUACCAUUGCAAU UAUAAUCUUACCAAUUGCUUUCACUUUUUUCUGUGAA UGADUUUAUUUGUAGUCAAAUUCUCCAGCAGCAAUUG CUAGCAACUGUUAUUCUACUGAUUUUGGAUUACUUU UCAUACCCACUUAGUAUGAAUCCGAUCUCAGUUGUAG UUCUGCUGGUCCAAUUAUCCAGUUUAUUUAUAAACAGU CCUUUUUUAUCCACAUGUUUGAUUUUAGCGACUGUUC CUCADRACUUACUACUUAUACUAAGCCUUAAGUACA GCUAUAUUAAACAAGUCUUCUGUUCUUUUUCGAGUAGU CGUACUGAAGUACCCUAGUUUGAAGCCUAUUAUCAAUA CUCACCCUGUGUAUCCAUUGUCCCAUCCACUGUGUGGGA AGACGGUGAUUUUAUAGGAAACAACUAUCUCCACUUG AAGGUGGUGCCUGGCUUUGUUGCUAGUGGCUCUACUGUU GCCAUGACUGAGCAAUACAGAUUGGCUUUGUUAUUAC AGUUCAAUUGGUACAGACCAAAUAGUUUUUGCCCA AGCUUGAAUUUGCUAUAUGACAAAAAUUGCCUCUCAA UUAGGCAAUUGCGUGGAUADUCCUUAUGGUGUUUC GGGCCGUGGUGUUUUUACGAAUUGCACAGCUGUAGGUG UUCGACAGCAGCCUUUGUUUAUGAUGGUACCAAGAAU UUAGUUGGCUAUUUUCUGADGAUGGCAACUACUACUG UUUUCGUGCUUGUGUUAGUUBCCUGUUUCUGUACUCU AUGADAAGAACAUAUAAACCCACGCCUACUCUAUUUGGU AGUGUUGCAUGUGAACACAUUBCUUCUACCAUGUCUCA AUACUCCGUUCUACGCAGUCAAUGCUAAAACGGCGAGA UUCUACAUAUGGCCCCUUUACAGACCCUGUUGGUUGUGU CCUAGGACUUGUUAAUUCUUCUUGUUCUGUAGAGGACU GCAAGUUGCCUUCUUGGUAADUUCUUGUGUCUUUCCUG ACACACCUAGUACUCUACACUUCGAGUGUGCGCUCUG UUCAGGUGAAUUGCGCUGGCAUCUUAUGCUUUUAU CAUCUAUUCAGGUUGAUCAACUUAUAUAGUUAUUUU UAAAUUAAGUAUACCCACUAUUUUUUCUUUGGUGUGA CUCAGGAGUACAUUCAGACAACCAUUCAGAAAGUUAUCU GUUGAUUGUAAACAGUACGUUUGCAUUGUUUCCAGAA GUGUGAGCAAUUACUGCGCAGUAUGGCCAGUUUUGUU CCAAAUAAAACAGGCUCUCCUUGGUGCCAAUUUACGCC AGGADGAUUCUGUACGUAAUUGUUUUGCAGCGUGAAA AGUCUCUCAAUCUUCUUAUCUAUACAGGUUUUGGAGGU GACUUUAUUUGACACUUCUGGAAUCUGUUUUAUAUC UACUUGGCAUGUAGUGCAUGUAGUUCUUAUGGAGU UGCUAUUUGACAAAGUACUAUAGCUGAUCUUGGUUAU AUGCAAGGUUACGAUUGGCAUGCAGCAGGUCAGC AUCAGCUCGUGAUCUUAUUUGGUCUAAUAUGUGGCUG GUUACAAGUAUUACUUCUUCUUAUGGAGUUUAUUG GAAGCCGCUUAUACUUCUUCUUGCUGGCAAGCAGCA GGUGUUGGUGGACUGCUGGCUUAUCCUCCUUUGCUGCU AUUCUAUUUGCACAGAGUAUCUUUUUAAGGUUAAACGG UGUUGGCAUUACUACACAGGUUCUUUCAGAGAACAAA AGCUUAUUCCAAUAAGUUUAUACAGGCUUCGGGAGCU AUGCAACAGGCUUCACUACAACUAUAGGAGCUUUUCA GAAGGUUCAGGAGUCUGUAGAACAAUUGCAGGCUUC UAUCCAAUUAGCUAGCGAGCUAUCUAUAUUUUUGGU GCUAUUUUCGCCUCUAUUGGAGACAUAUACACGUCUU	

TABLE 10-continued

Betacoronavirus Nucleic Acid Sequence		
Strain	Nucleic Acid Sequence	SEQ ID NO:
	GAUGUUCUGAACAGGACGCCCAAUAGACAGACUUAU UAAUGGCCGUUUGACAACACUAAAUGCUUUUGUUGCAC AGCAGCUUGUUCGUUCGGAADGAGCUGUCUUCUCCGCCU AAUUGGCUAAAGAUAAAGUCAUAGAGUGUGUCAAGGCA CAAUCCAAAGCGUUCUGGAUUUUGCGGUCAGGCACACA AUAGUGUCUUUUGUUGUAADGCCCCURAUUGGCCUUUA CUUCAUGCAUGUUGGUUAUUAUCCUAGCAACACAUUGA GGUUUUUCUGCUUAUGGUUUUGCGAUGCAGCUAACCC CUACUAAUUGUAUAGCCCGUGUUAUUGGCUACUUUAUU AAAACUAAUAACACUAGGAUUUGUAGAGUGGUCUAUA UACUGGCUCGUCUUUAUGCACCGAGCCCAUUAACUCC CCUUAAUACUAAGUAUGUUGCACCAGGUGACAUACCA AAACAUUUUCUACUAAUCCUCCUCCUUCUUCGGCAA UUCCACCGGGAUUGACUUCUCAAAGUAGUUGGAUGAGU UUUUCAAAGUUGUAGCACAGUAUACCUAAUUUUGGU UCCCUAACACAGAUUAUAUCUAUUAUCUGAUCUUAAC UACGAGAUUUGUCUUCUCAAAGUUGUUAAGCCCU UAAUGAGUCUUAACUAGACCUUAAAGAGCUUGGCAUU AUACUUAUUAACAAAUUGGCCUGGUUAUAUUGGCUU GUUUUCAUUGCUGGGCUUGUUGCCUUAAGCUCUAUGCGU CUUCUUAUAUCUGUGCUGCACUGGUUGUGGCACAAACUG UAUGGAAACUUUAUGUUAUCGUUUGUUGAUAGAU ACGAGGAUACGACCCUGAGCCGCAUAGGUUCAUGUUC ACUAA	
Novel MERS S2 subunit trimeric vaccine (nucleotide)	AUGAUCCACUCCGUGUUCUCCUCAUGUUCUGUUGACC CCCACUGAGUCAGACUGCAAGCUCCCGCUGGGACAGUCC CUGUGUGCCGUGCCUGACACUCCUAGCAUCUGACCCCA CGUCUCCGUGCCGUGCCGUGCCUGGGCAAUUGCCGUGGCC UCCAUCCGCUUCAUACCCCAAUCCAAGUGGAUCAGCUG AAUAGCUCGUUUUCAAGCUGUCCAUCCCAACGAACUUC UCGUUCGGGGUACCCAGGAGUACAUCAGACCCACAUAU CAGAAGGUCACCGUCGAUUGCAAGCAAUACGUGUGCAAC GGCUUCCAGAAGUGCGAGCAGCUGCUGAGAGAUAACGG GCAGUUUUGCAGCAGAUCAACCAGCCGUGCAUUGGAGC UAACUUGCCGACAGGACGACUCCGUGCCGCAACCUUUGC CUCUGUAGAGUCAUCCAGUCUCCCAUUAUCCCGGG AUUCGGAGGGACUUCAACUDGACCCUCCUGGAGCCCGU GUCGAUCAGCACCCGUAGCAGUUCGGCGCCUCAGCCAU UGAAGAUCUUCUGUUCAACAAGGUCACCAUCCGCAUCC GGCUCACUAGCAGGGAUACGACGACUGUAUGCAGCAGG GACCAGCCUCCGCGAGGGACCCUACUUGCGCGCAUACG UGCCCGGUACAAAGUGCUGCCUCCUUGAUGGADGUG AAACUUGGAGGCCGCUUAUAUCUUCGUCCUGCUCGGCUCU AUCGCCGGCGUGGGUGGACCGCCGGCCUGUCUUCUUC GCCGCUAUCCCUUUGCAAAUCCAUUUUUAACCGGUC AACGGCGUGGGCAUUAUCUCAAAGUCCUGUCGGAGAAC CAGAAGUUGAUCGCAACACAGUUAUAUCAGGCCUUGGG GGCCAUCCAGACUGGAUUCACUACGACUACCGAAGCGUU CCAGAAGGUCCAGGACCGUGGAACAAACCCGCCAGGC GCUCUCAAGCUGGCCUCCGAACUAGCAACACCUUCGG AGCCAUCAAGCAGUUCGAGUCGGUGACAUAAUUCAGCGGU GGACGUGCUGGAGCAGGACGCCAGAUAGCACCGCCUUAU CAACCGACGGCUGACCAUUGAAUGCCUUCUGGACACA ACAGCUGGUCGGAGCGAAUACAGGGCAUUUCCGCCCA ACUCCGCAAGGACAAAGUCAAGAAUUGGUGAAGGCCCA GUCCAAGAGGUCGGUUUCUGCGGUCAAGGAACCCAUU UGUGUCCUUCGUGGAACGCGCCCAACGGUCUGUACUU UAUGCACGUCGGCUACUACCCGAGCAUUAUUAUCGAAGU GGUGUCCGCCUACGGCCUGUGGAUGCCGCUAACCCAC UAACUGUAUUGCCUUGGAACGGAAUUUUUAUUAAGA CCAAACACACCCGCAUUGUGGACGAUUGGUCUACACCG GUUCGUCCUUCACGCGCCCGAGCCCAUACUUCACUGA ACACCAAAUACGUGGCUCGCAAGUGACCUACGAAACA UCUCCACCAAUUUGCCGCGCGCUGUCUGGAAACAGCA CCGAAUUGAUUUCCAAGAUAGACUGGACGAAUUCUUC AAGAACGUGUCCAUUCCAUUCCAAUUCGGAAAGCCUG ACACAGAUCAACACCAACCCUUCUGACCUAGCCUACGAG AUGCUGAGCCUUCAAAGUGGUCAGGCCCCUGAACGAG	67

TABLE 10-continued

Betacoronavirus Nucleic Acid Sequence		
Strain	Nucleic Acid Sequence	SEQ ID NO:
	AGCUACAUCGACCUGAAGGAGCUGGGCAACUUAUACCUAC UACAACAAGUGGCCGGACAGAUUGAGGAGAUUCUGUC GAAAACUACCAUUGAAAACGAGAUCCGCGAGAUCA AGAAGCUUAUCGGCGAAGCC	
MERS S0 Full-length Spike protein (nucleotide, codon optimized)	AUGGAAACCCCGCCAGCUGCUGUUCUGCUGCUGCUG UGGCUGCCUGAUACCCCGGCAGCUAUGGGACGUGGGC CCCGAUAGCGUGAAGUCGCGCCUGUAUCGAGUGGACAUC CAGCAGACC UUUUUCGACAGACCUGGCCAGACCCFAUC GACGUGUCCAAGGCCGACGGCAUCAUUAUCCACAAAGGC CGGACCUACAGCAACAUCACCAUUAUCCUACCGGCCUG UUCCCAUUAUCAGGGGACCCAGCGCAUAUGUAUGUGUAC UCUGCCGGCCACGCCACCGGCACACCCAGAAAACUG UUCGUGGCCAACUACAGCCAGGACGUGAAGCAGUUCGCC AACGGCUUCGUGCGGGAUUGGCCCGCUGCCAUAAGC ACCGGCACAGUGAUCUACGCCACAGCAACAGCGCCACC AUCCGGAGAUCAUCCCGCCUUCAGCUGGGCAGCUC GUGGGCAUUAUCAGCGACGGCAAGAUUGGGCCGGUUCU CAACCACACCCUGGUGCUGCUGCCGGAUGGCGUGGGAC ACUGCUGAGAGCCUUCUACUGCAUCCUGGAACCCAGAAG CGGCAACCACUGCCUGCCGGCAUAGCUACACCAGCUU CGCCACCUACACACACCCCGCACCGAUUGCUCGACGG CAACUACAACCGGAACGCCAGCCUGAACAGCUUCAAGA GUACUUAACCCUGCGGACUGCAUUCUUAUGUACACCUA CAUAUACACCGAGGACGAGAUCCUGGAUUGGUUCGGCA UCACCCAGACCGCCAGGGCGUGCACCUUUCAGCAGCA GAUACGUGGACCUGUACGGCGGCAACAUUUCAGUUU GCCACCCUGCCCGUGUACGACACCAUCAAAGUACUACAGC AUCAUCCCCACAGCAUCCGGUCCAUCCAGAGCCAGACA AAAGCCUGGGCCGCCUUCUACGUGUACAGCUGCAGCC CUGACCUCUUCUGCUGGACUUCAGCGUGGACGGCUACAU AGACGGGCCAUCGACUGCGGCUUAACAGACUAGGCCAG CUGCACUGCUCUACGAGAGCCUUCGACGUGGAAAGCGGC GUGUACAGCGUGCCAGCUUCGAGGCCAAGCCUAGCGGC AGCGUGGUGAACAGGCUGAGGGCGUGGAUUGCGACU CAGCCUCUUCUGCAGCGGCACCCUCCCGAGGUGUACAA CUUCAGCGGCUGGUGUUCACCAUCGCAAUUAACAACCU GACCAAGCUGCUGAGCCUGUUCUCCGUGAACGACUUCAC CUGUAGCCAGAUACGCCUGCCGCAUUGCCAGCAACUG CUACAGCAGCCUGAUCCUGGACUACUUCAGCUACCCCU GAGCAUGAAGUCCGAUCUGAGCGUGUCCUCCGCCGAC CAUCAGCCAGUUCACUACAAGCAGAGCUUCAGCAACCC UACCGCCUGAUUCUGGCCACCGUGCCCAACUUCUGAC CACCAUACCAAGCCUUCGAAUACAGCUACAUACAACAA GUGCAGCAGACUGCUGUCCGACGACCGGACCGAAGUGCC CCAGCUCUGAACCGCCAACAGUACAGCCUUCGCGUGUC CAUCGUGCCAGCAACCGUGUGGGAGGACGGCGACUACUA CAGAAAGCAGCUGAGCCUUCGGAAGGGCGGGGAGGGCU GGUGGCUUCUGAAGCACAGUGGCCAUGACCGAGCAGCU GCAGAUUGGCUUUGGCAUACCGUGCAGUACGGCACCGA CACCAAACAGCGUGUGCCCAAGCUGGAUUCGCCAAUGA CACCAAGAUCCGACGACCGGGAAACUCCGUGGAUA CUCCUGUAUGCCGUGUCCGGACGGGGCGUGUUCAGAA UUGCACAGCAGUGGGAGUGCGGCAGCAGAGAUUCUGU ACGAUGCCUACCAAGACCUUGGGGCUACUACAGCGACG ACGGCAAUUACUACUGCCUGCGGGCUGUGUGUCCGUGC CCGUGUCCGUGAUCUACGCAAAAGAGACAAGACCCACG CCACACUGUUCGGUCCCGUGGCCUGCGACACUACAGCU CCACCAUGAGCCAGUACUCCCGCUCACCCGGUCCAGC UGAAGCGGAGAGAUAGCACUACGGCCUCCUGCAGACAC CUGUGGGAUGUGUGCGGGCCUUGGAAACAGCUCCUGU UUGUGGAAGAUGCAAGCUGCCUUGGGCCAGAGCCUGU GUGCCUGCCAGAUACCCUAGCACCCUGACCCUAGAA GGUGGCCUUCUGUCCCGGCCAAUGGGGUGGCUCUA UCGCUCUCAAUACCCUACAGGUGGACAGCUGAACU CCAGCUACUUCAGCUGAGCAUCCCAACCAUUCAGCU UCGGCGUGACCAGGAGUACAUCAGACACCAUUCAGAA AAGUGACCGUGGACUGCAAGCAGUACGUGUGCAACGGC UUUCAGAGUGGCAACAGCUGCUGCGCAGUACGGCCAG UUCUGCAGCAAGUACACCAGGCCUUCGACGGCCCAAC CUGAGACAGGAUGACAGCGUGCGGAACCUUUCGCCAGC GUGAAAGCAGCCAGUCCAGCCCAUUAUCCUGGCUUC	68

TABLE 10-continued

Betacoronavirus Nucleic Acid Sequence		
Strain	Nucleic Acid Sequence	SEQ ID NO:
	GGCGGCGACUUUAACCCUGACCCUGCUGGAACCCUGUGUC AUCAGCACCGGCCUCCAGAAGCGCCAGAUCCGCCAUCGAG GACCCUGCGUUCGACAAAGUGACCAUUGCCGACCCCGGC UACAUGCAGGGCUACGACGAUUGCAUGCAGCAGGGCCCA GCCAGCGCCAGGGAUUCGAUCUGUGCCAGUAUGUGGC GGCUACAAGGUGUCGCCCCCUGAUGGACGUGAACAU GAAGCCGCCUACACCCAGCCUGCUGGGUCUUAUUGCU GGCGUGGGUUGGACAGCCGGCCUGUCUAGCUUUGCCGCC AUCCUUUCGCCCAGAGCAUCUUCUACCGGCUGAACGGC GUGGGCAUCACACAACAGGUGCUGAGCCGAGAACAGAA GCUGAUCGCCAACAAAGUUUAACAGGCACUGGGCCCAU GCAGACCGGCUUCACCACCACCAACAGGGCCUUCAGAAA GGUGCAGGACGCCGUGAACACAACGCCCCAGGCUCUGAG CAAGCUUGCCUCCGAGCUGAGCAUACCUUCGGCCCAU CAGCGCCUCCAUCCGCGACAUCAUCCAGCGGUCUGACGU GCUGGAACAGGACGCCAGAUCCAGCCGGCUGAUCACCG CAGACUGACCACCCUGAACGCCUUCUGGGCACAGCAGCU CGUGCGGAGCGAAUCUGCCGUCUGUCUGCUCAGCUGGC CAAGGACAAAGUGAACGAGUGCGUGAAGGCCAGUCCA AGCGGAGCGCCUUUUGGGCCAGGGCACCCACAUUGUGU CCUUCGUCGUGAUGCCCCAAACGGCCUGUACUUUUGC ACGUGGGCUAUUACCCAGCAACCACAUCCGAGGUGGUGU CCGCCUAUUGCCUGUGCCAGCCCGCAAUCCUACCAACU GUUUCGCCCCCGUAAACGGCUACUUCAUCAAGACCAACA ACACC CGGAUCGUGGACGAGUGGUCUACACAGGCAGCA GCUUCUACGCCCCCGAGCCCAUCACUCCUUGAACACCA AAUACGUGGCCCCCAAGUGACAUCCAGAACAUCCCA CCAACCCUGCCCCUCCACUGCUGGGAUUCACCCGGCA UCGACUUC CAGGACGAGCUGGACGAGUUUUCAAGAACG UGUCCACCUCUACCCCAACUUCGGCAGCCUGACCAGA UCAACACCACUCUGCUGGACCCUGACUACGAGAUCCUG CCUGCAACAGGUCUGAAGCCCGAACGAGAGCUACA UCGACCUGAAGAGCUGGGGAACUACACCUACUACAACA AGUGGCCUUGGUACAUUUGGCUGGGCUUUUACGCCGGCC UGGUGGCCUGGCCUGUGCGUGUUCUUAUCCUGUGCU GCACCGGCUGCGGCAACAAUUGCAUGGGCAAGCUGAAU GCACCGGUGCUGGACAGADACGAGGAUACGACCUGG AACCUCACAAAGUGCAUGUGCAC	

TABLE 11

Betacoronavirus Amino Acid Sequences		
Strain	Amino Acid Sequence	SEQ ID NO:
gb KJ156934.1 : 21405-25466 Middle East respiratory syndrome coronavirus isolate Riyadh 14_2013, spike protein (amino acid)	MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFDFKT WPRPIDVSKADGIIYPQGRITYSNITITYQGLFPYQGDHGDY VYSAGHATGTTpQKLFVANYSQDVKQFANGPVRIGAAANS TGTVII SPSTSATIRKIYPAFMLGSVGNFSDGKMGRFFNHTL VLLPDGCGTL LRAFYCILEPRSGNHCPAGNSYTS PATYHTPA TDCSDGNYNRNASLHSPKEYPNLRHCTFMYTYNI TEDEILEW FGLTQTAQGVHLFSSRYVDLYGGNMFQFATLPVYDTIKYYSII PHSIRSIQSDRKAWAFVYVKLQPLTFLLDPSVDGYIRRAIDC GFNDLSQLHCSYESFDVESGVYSVSSFEAKPSGGSVVEQAEV ECDPSPLLSGTPEQVYNPKRLVPTHFNLYLTKLLSLPSVNDP CSQISPAAIASNCYSLLILDYPSYPLSMKSDLVSSAGPISQFN YKQSPSNPTCLILATVPHNLTITKPLKYSYINKCRRLLSDRT EVPQLVNAHQYSPCVSI V PSTVWEDGDYRKLSPLEGGG LVASGSLVAMTEQLQMGFGITVQYGTDTNSVCPKLEFANDT KIASQLGNVCEYSLYGVSGRGVFNCTAVGVRRQRFVYDA YQNLVGYYSDDGNYCLRACVSVPSVYDKETKTHATLFG SVACEHISSTMSQYSRSTRSMLKRRDSTYGLPQTVPVGVVGL VNSSLFVEDCKLPLGQSLCALPDTPTSTLTPRSVRSVPGEMRLA SIAFNHPIQVDQLNSYFKLSIPTHFSFGVTQEIQTIIQKVTV DCKQYVCNGFQKCEQLLREYGFCSKINQALHGANLRQDDS VRNLFASVKSSQSSPIIPGFGDFNLTLLPEVSI STGSRARS EDLLFDKVTIADPGYMGGYDDCMQGGPASARDLI CAQYVA GYKVLPLPMDVNMEEAYTSSLGSIAGVGW TAGLSSFAAIPF	24

TABLE 11-continued

Betacoronavirus Amino Acid Sequences		
Strain	Amino Acid Sequence	SEQ ID NO:
	AQSI FYRLNGV GITQQV LSENQKLIANKFNQALGAMQTGFTT TNEAPF KVQDAVN NNAQALS KLA SELSNTFGAISASIGDI IQR LDVLEQDAQIDRLINGRL TTLN AFVAQQLVRS ESAALS AQLA KDKVNECVKAQSKRS GFCGQGT H I V S F V N A P N G L Y F M H V GYYP SNHIEVVSAYGLCDAANPTNC IAPVNGYFIKTNNTRIV DEW SYTGSSFYAPEPITSLNTKYVAPQV TYQNI STNLPPPLLG NSTGIDFQDELDEFFKNVST SIPNFGSLTQINTLLDLTYEMLS LQQVVKALNESYIDLKELGNYYYNKWPYIWLGF IAGLVA LALCVFFILCCTGCGTNCMGK LKCNRCDDRYEYDLEPHKV HVH	
MERS S FL SPIKE 2cEMC/2012 (XBaI change(T to G)) (amino acid)	MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQOTFFDKT WPRPIDVSKADGIIYPQGR TYSNITITTYQGLFPYQGDHGD MY VYSAGHATGTT PQLKLVANYSQDVKQFANGFVVRIGAAANS TGTV I I SPSTSATIRKI YPAFMLGSSVGNFSDGKMGRPFNHTL VLLPDGCGTLLRAF YCILEPRSGNHCPAGNSYTSFATYHTPA TDCSDGN YHRNASLNSFK EYFHLRNCTFMYTYNI TEDEILEW FGITQTAQGVHLFSSRYVDLYGGNMFQFATLPVYDTIKYYS II PHSIRSIQSDRKAWAAFVYK LQPLTFLLD FSVDGYIRRAIDC GFNDLSQLHCSYESFDVESGVYSVSFEAKPSGSSVVEQAEGV ECDFSPLLSGT PPQVY NFKRLVFTHCNYNLT KLLSLFSVNDFT CSQISPAAIASHCYSSLILDYFSYPLSMKSDLSVSSAGPISQFN YKQSF SNPTCLILATVPHNLTITKPLKYSYINKCSRLLSDDR T EVPQLVNA NQYSPCVSIVPSTVWEDGDY YRKQLS PLEGGGW LVASGSTVAMTEQLQMGPGITVQYGTDTNSVCPKLEFANDT KIASQLGNCVEYSLYGVSRGVFQNC TAVGVRQRFVYDA YQNLVGYYSDDGNYYCLRACVSVPVSVI YDKETKTHATLEF SVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCVLGL VNSSLFVEDCKLPLGQSLCALPDPSTLTPRSVRSVPGEMRLA SIAFNHPIQVDQLNSYFKLSIPTNFSFGVTQEQYIQTTIQKVTV DCKQYV CNGFPQKCEQLLREYGFQCSKINQALHGANLRQDSS VRNLPASV KSSQSSPIIPGFGDFNLTLLEPVSI STGSR S ARSAI EDLLFDKVTIADPGYMGGYDDCMQQGPASARDL ICAQYVA GYKVL PPLMDVNMEEAAYTS SLLGSIAGVGW TAGLSSFAAIPF AQSI FYRLNGV GITQQV LSENQKLIANKFNQALGAMQTGFTT TNEAPF KVQDAVN NNAQALS KLA SELSNTFGAISASIGDI IQR LDVLEQDAQIDRLINGRL TTLN AFVAQQLVRS ESAALS AQLA KDKVNECVKAQSKRS GFCGQGT H I V S F V N A P N G L Y F M H V GYYP SNHIEVVSAYGLCDAANPTNC IAPVNGYFIKTNNTRIV DEW SYTGSSFYAPEPITSLNTKYVAPQV TYQNI STNLPPPLLG NSTGIDFQDELDEFFKNVST SIPNFGSLTQINTLLDLTYEMLS LQQVVKALNESYIDLKELGNYYYNKWPYIWLGF IAGLVA LALCVFFILCCTGCGTNCMGK LKCNRCDDRYEYDLEPHKV HVH	25
Novel MERS S2 subunit trimeric vaccine (amino acid)	MIHSVFLLMFLLTPTESDCKLPLGQSLCALPDPSTLTPRSVR SVPGEMRLASIAFNHPIQVDQLNSYFKLSIPTNFSFGVTQEQYI QTTIQKVTV DCKQYV CNGFPQKCEQLLREYGFQCSKINQALH GANLRQDSSVRNLPASV KSSQSSPIIPGFGDFNLTLLEPVSI TGRSARS AI EDLLFDKVTIADPGYMGGYDDCMQQGPASAR DLICAQYVAGYKVL PPLMDVNMEEAAYTS SLLGSIAGVGWTA GLSSPAAIPFAQSI FYRLNGV GITQQV LSENQKLIANKFNQAL GAMQTGFTTNEAFKVQDAVN NNAQALS KLA SELSNTFG AISASIGDI IQR LDVLEQDAQIDRLINGRL TTLN AFVAQQLVRS ESAALS AQLAKDKVNECVKAQSKRS GFCGQGT H I V S F V N A P N G L Y F M H V G Y Y P S N H I E V V S A Y G L C D A A N P T N C I A P V N G Y F I K T N N T R I V D E W S Y T G S S F Y A P E P I T S L N T K Y V A P Q V T Y Q N I S T N L P P P L L G N S T G I D F Q D E L D E F F K N V S T S I P N F G S L T Q I N T L L L D L T Y E M L S L Q Q V V K A L N E S Y I D L K E L G N Y Y Y N K W P Y I W L G F I A G L V A E I L S K I Y H I E N E I A R I K K L I G E A	26
Isolate A1- Hasa 1 2013 (NCBI accession #AGN70962)	MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQOTFFDKT WPRPIDVSKADGIIYPQGR TYSNITITTYQGLFPYQGDHGD MY VYSAGHATGTT PQLKLVANYSQDVKQFANGFVVRIGAAANS TGTV I I SPSTSATIRKI YPAFMLGSSVGNFSDGKMGRPFNHTL VLLPDGCGTLLRAF YCILEPRSGNHCPAGNSYTSFATYHTPA TDCSDGN YHRNASLNSFK EYFHLRNCTFMYTYNI TEDEILEW FGITQTAQGVHLFSSRYVDLYGGNMFQFATLPVYDTIKYYS II PHSIRSIQSDRKAWAAFVYK LQPLTFLLD FSVDGYIRRAIDC GFNDLSQLHCSYESFDVESGVYSVSFEAKPSGSSVVEQAEGV ECDFSPLLSGT PPQVY NFKRLVFTHCNYNLT KLLSLFSVNDFT CSQISPAAIASNCYSSLILDYFSYPLSMKSDLSVSSAGPISQFN	27

TABLE 11-continued

Betacoronavirus Amino Acid Sequences		
Strain	Amino Acid Sequence	SEQ ID NO:
	YKQSPSNPTCLILATVPHNLTITKPLKYSYINKCSRLLSDORT EVPQLVNAQYSPCVSIVPSTVWEDGDYRQKLSPLEGGGW LVASGSTVAMTEQLQMGFGITVQYGTDTNSVCPKLEFANDT KIASQLGNCVEYSLYGVSGRGVFNCTAVGVRRQRFVYDA YQNLVGYYSDDGNYCLRACVSVPSVIVDKETKTHATLFG SVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCVLGL VNSSLFVEDCKLPLGQSLCALPDTPTSTLTPRSVRSVPGEMRLA SIAFNHPIQVDQLNSYFKLSIPTNFSFGVTQEIQTIIQKVTV DCKQYVCGGFQKCEQLLREYGFQFCSKINQALHGANLRQDDS VRNLPASVKSQSSPIIPGFGDFNLTLLEPVSISTGSRARSAT EDLLPDKVTIADPGYMQGYDDCMQGPASARDLICAQYVA GYKVLPLMDVHMEAAYSLLGSIAGVGTAGLSSFAIIPF AQSIFYRLNGVGTIQQVLSNQKLIANKFNQALGAMQTGFST TNEAPRKVQDAVNMNAQALSCLASELSNTFGAISASIGDIIQR LDVLEQDAQIDRLINGRLTTLNAPVAQQLVRSESAALSAQLA KDKVNECVKAQSKRSQFCGQGTHTIVSFVNAPNGLYFMHV GYYPNHIIEVVSAYGLCDAANPTNCIAPVNGYFIKTNTRIV DEWSYTGSSFYAPEPITSLNTKYVAPHVYQNIISTNLPPPLLG NSTGIDFQDELDEFFKNVSTIPNFGSLTQINTLLDLTYEMLS LQQVVKALNESYIDLKELGNYYTNKWPYIWLGFIAGLVA LALCVFFILCCTGCGTNCMGKLCNRCCDRYEYDLEPHKV HVH	
Middle East respiratory syndrome coronavirus S protein UniProtKB- R9UQ53	MIHSVFLLMPLLTPTESYVDVGPDSVKSACIEVDIQQTFDOKT WPRPIDVSKADGIIYPQGRITYSNITITYQGLFPYQGDHGMV VYSAGHATGTTPKLFLVANYSDVKQFANGFVVRIGAAANS TGTVII SPSTSATIRKIYPAPMLGSSVGNFSDGKMRFPNHTL VLLPDGCGTLGRAFYCILEPRSGNHCFAGNSYTSFATYHTPA TDCSDGNYHRNASLNSFKKEYFNLRHCTFMYTYNITTEDEILEW FGLITQTAQGVHLFSSRYVDLYGGMFQFATLPVYDTIKVYSII PHSIRSIQSDRKAWAAPVYVYKQLPLTFLDPSVDGYIRRAIDC GPNDLSQLHCSYESFDVESGVYSVSFEAKPSGSSVVEQAEGV ECDSPLLSGTTPQVYNFKRLVPTNCFNYLTKLLSLPSVNDFT CSQISPAATASHCYSLLIDYPSYPLSMKSDLSVSSAGPISQFN YKQSPSNPTCLILATVPHNLTITKPLKYSYINKCSRLLSDORT EVPQLVNAQYSPCVSIVPSTVWEDGDYRQKLSPLEGGGW LVASGSTVAMTEQLQMGFGITVQYGTDTNSVCPKLEFANDT KIASQLGNCVEYSLYGVSGRGVFNCTAVGVRRQRFVYDA YQNLVGYYSDDGNYCLRACVSVPSVIVDKETKTHATLFG SVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCVLGL VNSSLFVEDCKLPLGQSLCALPDTPTSTLTPRSVRSVPGEMRLA SIAFNHPIQVDQLNSYFKLSIPTNFSFGVTQEIQTIIQKVTV DCKQYVCGGFQKCEQLLREYGFQFCSKINQALHGANLRQDDS VRNLPASVKSQSSPIIPGFGDFNLTLLEPVSISTGSRARSAT EDLLPDKVTIADPGYMQGYDDCMQGPASARDLICAQYVA GYKVLPLMDVHMEAAYSLLGSIAGVGTAGLSSFAIIPF AQSIFYRLNGVGTIQQVLSNQKLIANKFNQALGAMQTGFST TNEAPRKVQDAVNMNAQALSCLASELSNTFGAISASIGDIIQR LDVLEQDAQIDRLINGRLTTLNAPVAQQLVRSESAALSAQLA KDKVNECVKAQSKRSQFCGQGTHTIVSFVNAPNGLYFMHV GYYPNHIIEVVSAYGLCDAANPTNCIAPVNGYFIKTNTRIV DEWSYTGSSFYAPEPITSLNTKYVAPHVYQNIISTNLPPPLLG NSTGIDFQDELDEFFKNVSTIPNFGSLTQINTLLDLTYEMLS LQQVVKALNESYIDLKELGNYYTNKWPYIWLGFIAGLVA LALCVFFILCCTGCGTNCMGKLCNRCCDRYEYDLEPHKV HVH	28
Human SARS coronavirus (SARS-CoV) (Severe acute respiratory syndrome coronavirus) Spike glycoprotein UniProtKB- P59594	MFIFLLFLTLTSGSDDLDRCTTFDDVQAPNYTQHTSSMRGVVY PDEIFRSDTLYLTDQLFLPFYSNVTGFHTINHTFGNPVIFPKDG IYFAATEKSNVVRGVRVFGSTMNKQSVIIINNSTNVVIRAC NFELCDNPFPAVSKPMCTQTHMIFDNFNCTFEYISDAPSLD VSEKSGNFKHLREFVFKNKDGLFYKGYQPIDVVRDLPSGF NTLKPIFKLPLGINITNFRAILTAFSPAQDINGTSAAYFVGYL KPTTPEMLKYDENGITDAVDCSQNLAEKCSVKSFEIDKGI YQTSNFRVVPSSGDDVRFPHNITLCPFGVEFNATKFPVYAWE RKKISNCVADYSVLYNSTFFSTFKCYGVSATKLNLCPSNVY ADSFVVKGGDDVRQIAPGQTVIADYNYKLPDDFMGCVLAW NTRNIDATSTGNYYKYRYLRHGKLRPFPERDISNVPFSPDGK PCTPPALNICYWPLNDYGFYTTTGIGYQPVVVVLSFELLNAP ATVCGPKLSTDLIKNQCVNFPNGLTGTGVLTPSSKRFQPFQ QGRDVSDFDTSVRDPKTSSELDISPCSFGGVSVITPGTNA SSE VAVLYQDVNCTDVSSTAIHADQLTPAWRIYSTGNVVFQTAG	29

TABLE 11-continued

Betacoronavirus Amino Acid Sequences		
Strain	Amino Acid Sequence	SEQ ID NO:
	CLIGAEHVDTSYECDIPIGAGICASYHTVSLRSTSQKSIVAYT MSLGADSSIAYSNNTIAIPNPSISITTEVMPVSMKTSVDCN MYTCGDSTECANLLQYGSFCTQLHRALSGIAAEQDRNTREV FAQVKQMYKPTTLKYFGGFNFSQLPDPKPKTRSFIEDLLEN KVTLDADAGFMKQYGECLGDINARDLCAQKFNGLTVLPPLL TDDMIAAYTAALVSGTATAGWTFGAGARLQIPFAMQMYR FNGIGVTVQNVLYENQKQIANQFNKAIISQIQESLTTTSTALGKL QDVVNQNAQALNLTQKLSNPGAISSVNDILSRDLKVEAE VQIDRLITGRLQSLQTYVYVQQLIRAAEIRASANLAATKMSEC VLGQSKRVDFCGKGYHLMSFPQAAPHGVVFLHVTYVPSQER NFTTAPAI CHEGKAYFPREGVVFVNGTSWFIQORNFSPQIIT DNTFVSGMCDVVIGIINNTVYDPLQPELDSRKEELDKYFKNH TSPDVLGDISGINASVVTIQKEIDRLNEVAKNLNESLIDLQE LGKYEQYIKWPYVWLGFIAGLIAIVMVTIILCCMTSCCSCL KGACSCGSCCKFDEDDSEPVKGVKLVHT	
Human coronavirus OC43 (HCoV-OC43) Spike glycoprotein UniProtKB-P36334	MFLILLISLPTAFAVIGDLKCTSDNINDKDTGPPPISTDTVOVT NGLGTYVYLDRVYLNHTTFLNGYYPSTSGSYRNMALKGSVL LSRLWPKPFLSDPFIINGIFAKVKNTKVIKDRVMYSEPPAITIGS TFVNTSYSVVQPRTLNSTQDGNLQGLLEVSVCQYNMCE YPQTI CHPNLGNHRKELWHLDTGVVYVSLYKRNFTYDVMAD YLYPHFYQEGGTFYAYPTDTGVVTKFLPNVYLGMAISHYV MPLTCNSKLTLEYVWVPLTSRQYLLAFNQDGLIFNAEDCMSD FMSEIKCKTQSIAPPTGVVELNGYVQPIADVYRRKPNLPC NIEAWLNDKSVSPPLNWERKTFNCFNFMSSLSMPIQADSP CNNIDAAKIYGMCFSSITIDKFAIPNGRKVDLQGLNGLYQSF NYRIDTTATSCQLYVNLPAANVSVSFRNPFSTWKRFGPIEDS VFKPRPAGVLTNHDVVAQHCFKAPKNCPCKLNGSCVGS PGKNNIGITCPAGTNYLTCNLTCPDPI TFGTYKCPQTKSL VGIGHCSSLAVKSDYCGGNSCTCRPQAFLGNSADSCLQGD KCNIPANFILHDVNSGLTCSTDLQKANTDIILGVCVNYDLYGI LGQGI FVEVNATYYNSWQNLLYDSNGLYGFPRDYIINRTFMI RSCYSGRVSAAFHANSSEPALFRNICKNYVFNNLSLTLQQLPI NYFDSYLGCVVMAYNSTAISVQTCOLTVGSGYCVDYSKNR SRGAI TTGYRPTNFPPTVNSVNDGLEPVGGLYEIQIPSEFTIG NMVEPIQTSSPKVTIDCAAFVCGDYAACSKQLVEYGSFCNDI NAILTEVNELDLDTQLQVANSLMNGVTLSTKLKDGVNPNVD DINFPVLGCLGSECSKASSRAIEDLLFDKVKLSDVGFVEAY NNCTGGAEIRDLCVQSYKGIKVLPLLSENQISGYTLAATSA SLFPPWTAAGVPPYLVNQYRINGLGVTMDVLSQNKLIAN AFNNALYAIQEGFDATNSALVKIQAVVHANAEBALNLLQQL SNRFGAISASLQEI LSRDLDAEAEQIDRLINGRLTALNAYVS QQLSDSTLVKFSAAQAMEKVNCEVKSQSSRINFCCGNGNHIIS LVQNAFYGLYFIHFSYVPTKYVTVARVSPGLCIAGDRGIAPKS GYFVNVNNTWMTGSGYYPPEPI TENNVVMS TCAVNYTK APYVMLNTSIPNLPDFKEELDQWFKNQTSAVDLSDYINVT FLDLQVEMNRLQEAIVLNQSYINLKDITGYEYVYKWPYV WLLICLAGVAMLVLLFFICCTPGCGTSCFKKCGGCCDDYTG YQELVIKTSRDD	30
Human coronavirus HKU1 (isolate NS) (HCoV-HKU1) Spike glycoprotein UniProtKB-Q0ZME7	MFLIFILPTTAVIGDRNCTNSFINDYNKTI PRISEDVDVSLG LGYTYVLRVYLNHTTLLFTGYPPKSGANFRDLALKGSYILST LWYKPPFLSDFNNGIFSKVNTKLYVNNLYSEFSTIVIGSYF VNTSYTIVVQPHNGILEITACQYTMCEYPHTVCKSKGSI RNES WHIDSSEPLCLFKKNFTYVNSADWLYPHFYQERGVFYAYYA DVGMPPTFLPSLYLGTILSHYVMPMLTCNAISSNTDNETLEY WVTPLSRRQYLLNPFDEHGVITNAVDCSSSFLSEIQCKTQSFAP NTGVYDLSGPTVKPVATVYRRIPNLPDCCI DNGLMNVSVSP LNWERRIFSNCFNLSTLLRLVHVDSPSCNNLDKSKIFGSCFN SITVDKFAIPNRRRDDLQGLSSGFLQSSNYKIDISSSSCQLYYS LPLVNVTIHNRNPSWRRYRGGSPNLSYDVVYSDHCFSVN SDFPCADPSVNSCAKSKPPSAICPAGTKYRHCDDLDTLYV KNWCRCSCLPDP LSTYSPNTCPQKRVVVGIGEHCPGLGINEE KCGTQLNHSSCPSPDAPLGSFSDSCISNRCNIPSNP I FNGIN SGTTCNDLLYSNTEISTGVCVNYDLYGITGQGI FKEVSAAY YNNWQNLLYDSNGLIIGFKDPLTNKTYTILPCYSGRVSAAFY QNSSSPALLYRNKCSYVLMNNSIFISQPFYFDSYLGCVLNAV LTSYVSSCDLRMGSGFCIDYALPSRRKRRGISSPYRFVTFEP FNVSFVNDSVETVGGLEFIQIPNTPIAGHEEFIQTSSPKVTIDC SAFVCSNYAACHDLLSEYGTFCNDNINSILNEVNDLLDITQLQV ANALMQGVTLSSNHLTNLHSDVDNIDFKSLGCLGSCQCGSS RSLLDLELKNVYKLSVGFVEAYNCTGGSEIRDLLCVQSFN	31

TABLE 11-continued

Betacoronavirus Amino Acid Sequences		
Strain	Amino Acid Sequence	SEQ ID NO:
	GIKVLPPIISETQISGYTTAATVAAMPFPWSAAAGVPFSLNVQ YRINGLVGVTMDVLNKNQKLIANA FNKALLSIQNGPTATNSAL AKTQSVVMAQAALNSLLQQLFNKPGAISSSLQEI LSRLDNLE AQVQIDRLINGRTALNAYVSQQLSDITLIKAGASRAIEKVNE CVKSQSPRINFCGNGMHLSLVQNAFYGLLFIHFSYKPTSFKT VLVSPGLCLSGDRGIAPKQGYRIFKQNDWMFTGSSYYYPEPIS DKNVVPMNSCSVNFTKAPFIYLNNSIPNLSDFEAELESLWPKN HTSIAPNLTFNSHINATPLDLYEMNVIQESI KSLNSSFINKKEI GTYEMVVKWPYIWLIVILFII FLMI LFFICCTGCGSACFSK CHNCCDEYGGHNDPVIKASHDD	
Novel SARS S2	MFIFLLFLTITSGSDLRALSGIAAEQDRENTREVFQVQKQMY KTPTLKYFGGFNFSQLPDPLKPTKRSFIEDLLFNKVTLADAG FMKQYGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAYT AALVSGTATAGRTFGAALQIPFAMQMAYRFNGIGVTQN VLYENQKQIANQFNKAI S QIQESLTTTSTALGKLDVVHQA QALNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITG RLQSLQTYVTQQLIRAAEIRASANLAATKMSCEVLGQSKRV DFCGKGYHLMSFPQAAPHGVVPLHVTVVPSQERNFTTAPAIC HEGKAYFPREGVVFVNGTSPFITQRNFFSPQIITDNTFVSGN CDVVIIGIINHNTVYDPLQPELDSFKEELDKYFKNHTSPDVLG DISGINASVVNIQKETDRLEVAKNLNEIDLQELGKYEQYI KWPWVWLGFIAGLIAIVMVTILLCMTSCCSCLKGACSCGS CCKFDEDDSEPVKGVKLYHT	32
Novel MERS S2	MIHSVFLMFLLTPTESDCKLPLGQSLCALPDTPTSLTPRSVR SVPGEMLASIAFNHPIQVDQLNSSFYKLSIPTNPSFGVTQEYI QTTIQKVTVDCKQYVCGFQKCEQLLREYGFQCSKINQALH GANLRQDDSVRHLFASVKSQSSPIIPGFQGFNLTLEPVVIS TGSRSARSAIEDLFDKVTIADPGYMQGYDDCMQGPASAR DLICAQYVAGYKVLPLMDVNMEEAAYTSSLGSIAGVGTWA GLSSPAAI PPAQSI FYRLNGVGI TQQVLSNQKLIANKFNQAL GANQTGFTTNEAFQKVQDAVHNNAQALS KLASLSNTFG AISASIGDIIQRLDVLEQDAQIDRLINGELTTLNFAVQQLVRS ESAALSQAQAKDKVNECVKAQSKRSFCGQGTHTIVSPVNA PNGLYFMHVGYYPSNHEVVSAYGLCDAANPTNCIAPVHGY FIKTNMTRIVDEWYSYTGSSFYAPEPITS LNTKYVAPQVTYQNI STNLFPPLGNSTGIDFQDELDFPKVSTSI PNFGLTQINTTL LDLTYEMLSLQQVVKALNESYIDLKELGNYTYYNKRP	33
Novel Trimeric SARS S2	MFIFLLFLTITSGSDLRALSGIAAEQDRENTREVFQVQKQMY KTPTLKYFGGFNFSQLPDPLKPTKRSFIEDLLFNKVTLADAG FMKQYGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAYT AALVSGTATAGRTFGAALQIPFAMQMAYRFNGIGVTQN VLYENQKQIANQFNKAI S QIQESLTTTSTALGKLDVVHQA QALNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITG RLQSLQTYVTQQLIRAAEIRASANLAATKMSCEVLGQSKRV DFCGKGYHLMSFPQAAPHGVVPLHVTVVPSQERNFTTAPAIC HEGKAYFPREGVVFVNGTSPFITQRNFFSPQIITDNTFVSGN CDVVIIGIINHNTVYDPLQPELDSFKEELDKYFKNHTSPDVLG DISGINASVVNIQKETDRLEVAKNLNEIDLQELGKYEQYI KWPWVWLGFIAGLIAIVMVTILLCMTSCCSCLKGACSCGS CCKFDEDDSEPVKGVKLYHT	34

TABLE 12

Full-length Spike Glycoprotein Amino Acid Sequences (<i>Homo sapiens</i> strains)				
GenBank Accession	Country	Collection Date	Release Date	Virus Name
AFY13307	United Kingdom	2012 Sep. 11	2012 Dec. 5	Betacoronavirus England 1, complete genome
AF588936		2012 Jun. 13	2012 Sep. 27	Human betacoronavirus 2c EMC 2012, complete genome
AGG22542	United Kingdom	2012 Sep. 19	2013 Feb. 27	Human betacoronavirus 2c England-Qatar/2012, complete genome
AHY21469	Jordan	2012	2014 May 4	Human betacoronavirus 2c Jordan-N3.2012 isolate MG167, complete genome

TABLE 12-continued

Full-length Spike Glycoprotein Amino Acid Sequences (<i>Homo sapiens</i> strains)				
GenBank Accession	Country	Collection Date	Release Date	Virus Name
AGII58717	Jordan	2012 April	2013 Mar. 25	Human betacoronavirus 2c Jordan-N3 2012, complete genome
AGV08444	Saudi Arabia	2013 May 7	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_12_2013, complete genome
AGV08546	Saudi Arabia	2013 May 11	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_15_2013, complete genome
AGV08535	Saudi Arabia	2013 May 12	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_16_2013, complete genome
AGV08558	Saudi Arabia	2013 May 15	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_17_2013, complete genome
AGV08573	Saudi Arabia	2013 May 23	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_18_2013, complete genome
AGV08480	Saudi Arabia	2013 May 23	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_19_2013, complete genome
AGN70962	Saudi Arabia	2013 May 9	2013 Jun. 10	Middle East respiratory syndrome coronavirus isolate Al-Hasa_1_2013, complete genome
AGV08492	Saudi Arabia	2013 May 30	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_21_2013, complete genome
AH148517	Saudi Arabia	2013 May 2	2014 Feb. 6	Middle East respiratory syndrome coronavirus isolate Al-Hasa_25_2013, complete genome
AGN70951	Saudi Arabia	2013 Apr. 21	2013 Jun. 10	Middle East respiratory syndrome coronavirus isolate Al-Hasa_2_2013, complete genome
AGN70973	Saudi Arabia	2013 Apr. 22	2013 Jun. 10	Middle East respiratory syndrome coronavirus isolate Al-Hasa_3_2013, complete genome
AGN70929	Saudi Arabia	2013 May 1	2013 Jun. 10	Middle East respiratory syndrome coronavirus isolate Al-Hasa_4_2013, complete genome
AGV08408	Saudi Arabia	2012 Jun. 19	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Bisha_1_2012, complete genome
AGV08467	Saudi Arabia	2013 May 13	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Buraidah_1_2013, complete genome
AH150418	United Kingdom	2013 Feb. 10	2014 Jun. 18	Middle East respiratory syndrome coronavirus isolate England 2/2013, complete genome
AH181451	United Kingdom	2013 Feb. 10	2015 Jan. 18	Middle East respiratory syndrome coronavirus isolate England 3/2013, complete genome
AH181440	United Kingdom	2013 Feb. 13	2015 Jan. 18	Middle East respiratory syndrome coronavirus isolate England 4/2013, complete genome
AH133326	France	2013 May 7	2013 Dec. 7	Middle East respiratory syndrome coronavirus isolate FRA UAE, complete genome
AH148760	USA	2014 June	2014 Dec. 14	Middle East respiratory syndrome coronavirus isolate Florida USA-2 Saudi Arabia 2014, complete genome
AGV08455	Saudi Arabia	2013 Jun. 4	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Hafr-Al-Batin_1_2013, complete genome
AH148561	Saudi Arabia	2013 Aug. 5	2014 Feb. 6	Middle East respiratory syndrome coronavirus isolate Hafr-Al-Batin_2_2013, complete genome
AH148539	Saudi Arabia	2013 Aug. 28	2014 Feb. 6	Middle East respiratory syndrome coronavirus isolate Hafr-Al-Batin_6_2013, complete genome

TABLE 12-continued

Full-length Spike Glycoprotein Amino Acid Sequences (<i>Homo sapiens</i> strains)				
GenBank Accession	Country	Collection Date	Release Date	Virus Name
AIZ74417	France	2013 Apr. 26	2015 Mar. 10	Middle East respiratory syndrome coronavirus isolate Hu-France (UAI) - FRA1_1627-2013_BAI, Sanger, complete genome
AIZ74433	France	2013 May 7	2015 Mar. 10	Middle East respiratory syndrome coronavirus isolate Hu-France - FRA2_130569-2013_JS_1115, complete genome
AIZ74439	France	2013 May 7	2015 Mar. 10	Middle East respiratory syndrome coronavirus isolate Hu-France - FRA2_130569-2013_InSpu, Sanger, complete genome
AIZ74450	France	2013 May 7	2015 Mar. 10	Middle East respiratory syndrome coronavirus isolate Hu-France - FRA2_130569-2013_Isolate, Sanger, complete genome
AKK52602	Saudi Arabia	2015 Feb. 10	2015 Jun. 8	Middle East respiratory syndrome coronavirus isolate Hu Riyadh, KSA, 2959, 2015, complete genome
AKK52612	Saudi Arabia	2015 Mar. 1	2015 Jun. 8	Middle East respiratory syndrome coronavirus isolate Hu Riyadh, KSA, 4050, 2015, complete genome
AHN10812	Saudi Arabia	2013 Nov. 6	2014 Mar. 24	Middle East respiratory syndrome coronavirus isolate Jeddah_1, 2013, complete genome
AID55071	Saudi Arabia	2014 Apr. 21	2014 Nov. 12	Middle East respiratory syndrome coronavirus isolate Jeddah_C10306, KSA, 2014-04-20, complete genome
AID55066	Saudi Arabia	2014	2014 Nov. 12	Middle East respiratory syndrome coronavirus isolate Jeddah_C7149, KSA, 2014-04-05, complete genome
AID55067	Saudi Arabia	2014	2014 Nov. 12	Middle East respiratory syndrome coronavirus isolate Jeddah_C7569, KSA, 2014-04-03, complete genome
AID55068	Saudi Arabia	2014 Apr. 7	2014 Nov. 12	Middle East respiratory syndrome coronavirus isolate Jeddah_C7770, KSA, 2014-04-07, complete genome
AID55069	Saudi Arabia	2014 Apr. 12	2014 Nov. 12	Middle East respiratory syndrome coronavirus isolate Jeddah_C8826, KSA, 2014-04-12, complete genome
AID55070	Saudi Arabia	2014 Apr. 14	2014 Nov. 12	Middle East respiratory syndrome coronavirus isolate Jeddah_C9055, KSA, 2014-04-14, complete genome
AHD78108	Saudi Arabia	2013 Nov. 5	2014 May 1	Middle East respiratory syndrome coronavirus isolate MERS-CoV-Jeddah-human-1, complete genome
AK159401	South Korea	2015 May 20	2015 Jun. 9	Middle East respiratory syndrome coronavirus isolate MERS-CoV:KOR KNH 002_05_2015, complete genome
ALD51904	Thailand	2015 Jun. 17	2015 Jul. 7	Middle East respiratory syndrome coronavirus isolate MERS-CoV:THA:CU.17_06_2015, complete genome
AID55072	Saudi Arabia	2014 Apr. 15	2014 Nov. 12	Middle East respiratory syndrome coronavirus isolate Makkah_C9355, KSA, Makkah, 2014-04-15, complete genome
AHC74088	Qatar	2013 Oct. 13	2013 Dec. 23	Middle East respiratory syndrome coronavirus isolate Quar3, complete genome

TABLE 12-continued

Full-length Spike Glycoprotein Amino Acid Sequences (<i>Homo sapiens</i> strains)				
GenBank Accession	Country	Collection Date	Release Date	Virus Name
AHC74098	Qatar	2013 Oct. 17	2013 Dec. 23	Middle East respiratory syndrome coronavirus isolate Qatar4, complete genome
AH148572	Saudi Arabia	2013 Aug. 15	2014 Feb. 6	Middle East respiratory syndrome coronavirus isolate Riyadh_14_2013, complete genome
AGV08379	Saudi Arabia	2012 Oct. 23	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Riyadh_1_2012, complete genome
AID55073	Saudi Arabia	2014 Apr. 22	2014 Nov. 12	Middle East respiratory syndrome coronavirus isolate Riyadh_2014KSA_683.KSA.2014, complete genome
AGV08584	Saudi Arabia	2012 Oct. 30	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Riyadh_2_2012, complete genome
AGV08390	Saudi Arabia	2013 Feb. 5	2013 Sep. 17	Middle East respiratory syndrome coronavirus isolate Riyadh_3_2013, complete genome
AH148605	Saudi Arabia	2013 Mar. 1	2014 Feb. 6	Middle East respiratory syndrome coronavirus isolate Riyadh_4_2013, complete genome
AH148583	Saudi Arabia	2013 Jul. 2	2014 Feb. 6	Middle East respiratory syndrome coronavirus isolate Riyadh_5_2013, complete genome
AH148528	Saudi Arabia	2013 Jul. 17	2014 Feb. 6	Middle East respiratory syndrome coronavirus isolate Riyadh_9_2013, complete genome
AH148594	Saudi Arabia	2013 Jun. 12	2014 Feb. 6	Middle East respiratory syndrome coronavirus isolate Taif_1_2013, complete genome
AH148550	Saudi Arabia	2013 Jun. 12	2014 Feb. 6	Middle East respiratory syndrome coronavirus isolate Wadi-Ad-Dawasir_1_2013, complete genome
AIY60558	United Arab Emirates	2014 Mar. 7	2014 Dec. 6	Middle East respiratory syndrome coronavirus strain Abu Dhabi UAE_2_2014, complete genome
AIY60538	United Arab Emirates	2014 Apr. 10	2014 Dec. 6	Middle East respiratory syndrome coronavirus strain Abu Dhabi UAE_16_2014, complete genome
AIY60528	United Arab Emirates	2014 Apr. 10	2014 Dec. 6	Middle East respiratory syndrome coronavirus strain Abu Dhabi UAE_18_2014, complete genome
AIY60588	United Arab Emirates	2014 Apr. 13	2014 Dec. 6	Middle East respiratory syndrome coronavirus strain Abu Dhabi UAE_26_2014, complete genome
AIY60548	United Arab Emirates	2014 Apr. 19	2014 Dec. 6	Middle East respiratory syndrome coronavirus strain Abu Dhabi UAE_30_2014, complete genome
AIY60568	United Arab Emirates	2014 Apr. 17	2014 Dec. 6	Middle East respiratory syndrome coronavirus strain Abu Dhabi UAE_33_2014, complete genome
AIY60518	United Arab Emirates	2014 Apr. 7	2014 Dec. 6	Middle East respiratory syndrome coronavirus strain Abu Dhabi UAE_8_2014, complete genome
AIY60578	United Arab Emirates	2013 Nov. 15	2014 Dec. 6	Middle East respiratory syndrome coronavirus strain Abu Dhabi UAE_9_2013, complete genome
AKJ80137	China	2015 May 27	2015 Jun. 5	Middle East respiratory syndrome coronavirus strain China/GD01, complete genome

TABLE 12-continued

Full-length Spike Glycoprotein Amino Acid Sequences (<i>Homo sapiens</i> strains)				
GenBank Accession	Country	Collection Date	Release Date	Virus Name
AHZ64057	USA	2014 May 10	2014 May 14	Middle East respiratory syndrome coronavirus strain Florida/USA-2/Saudi Arabia/2014, complete genome
AKM76229	Oman	2013 Oct. 28	2015 Jun. 23	Middle East respiratory syndrome coronavirus strain Hu/Oman_2285/2013, complete genome
AKM76239	Oman	2013 Dec. 28	2015 Jun. 23	Middle East respiratory syndrome coronavirus strain Hu/Oman_2874/2013, complete genome
AKI29284	Saudi Arabia	2015 Jan. 6	2015 May 27	Middle East respiratory syndrome coronavirus strain Hu/Riyadh-KSA-2049/2015, complete genome
AKI29265	Saudi Arabia	2015 Jan. 21	2015 May 27	Middle East respiratory syndrome coronavirus strain Hu/Riyadh-KSA-2343/2015, complete genome
AKI29255	Saudi Arabia	2015 Jan. 21	2015 May 27	Middle East respiratory syndrome coronavirus strain Hu/Riyadh-KSA-2345/2015, complete genome
AKI29275	Saudi Arabia	2015 Jan. 26	2015 May 27	Middle East respiratory syndrome coronavirus strain Hu/Riyadh-KSA-2466/2015, complete genome
AKK52582	Saudi Arabia	2015 Feb. 10	2015 Jun. 8	Middle East respiratory syndrome coronavirus strain Hu/Riyadh_KSA_2959/2015, complete genome
AKK52592	Saudi Arabia	2015 Mar. 1	2015 Jun. 8	Middle East respiratory syndrome coronavirus strain Hu/Riyadh_KSA_4050/2015, complete genome
AHZ58501	USA	2014 Apr. 30	2014 May 13	Middle East respiratory syndrome coronavirus strain Indiana/USA-1/Saudi Arabia/2014, complete genome
AGN52936	United Arab Emirates	2013	2013 Jun. 10	Middle East respiratory syndrome coronavirus, complete genome

TABLE 13

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO.
GC F MEASLES B3.1 Sequence, 5' UTR, ORF, 3' UTR) Sequence Length: 1864	TCAAGCTTTGGACCCTCGTACAGAAAGCTAATACGACT CACTATAGCGAATAAGAGAGAAAAGAGAGTAAGAA GAAATATAAGAGCCACCATGGGTCTCAAGGTGAACGTC TCTGCCGTATTTCATGGCAGTACTGTTAACTCTCCAAACA CCCGCCGGTCAAATTCATTGGGGCAATCTCTTAAGAT AGGGGTAGTAGGAATAGGAAGTGC AAGCTACAAGTT ATGACTCGTTCAGCCATCAATCATAGTCA TAA AATT AATGCCCAATATAACTCTCTCAATAACTGCACGAGGG TAGAGATTGCAGAA TACAGGAGACTACTAAGAACAGTT TTGGAACCAATTAGGGATGC ACTTAATGC AATGACCCA GAACATAAGGCCGGTTCAGAGCGTAGCTTCAAGTAGGA GACACAAGAGATTTGCGGGAGTAGTCTTGGCAGGTGCG GCCCTAGGTGTTGCCACAGCTGCTCAGATAACAGCCGG CATTGCACCTTCAACGGTCCATGCTGA ACTCTCAGGCCAT CGACAATCTGAGAGCGAGCCTGGA AACTACTAATCAGG CAATTGAGGCCAATCAGACAAGCAGGCCAGGAGATGAT ATTGGCTGTT CAGGGTTC CAAGACTACATCAATAATG AGCTGATACCGTCTATGAACAGCTATCTGTGATCTA ATCGGTCAGAAAGCTCGGGCTCA AATTGCTTAGATACTA TACAGAAATCTGT CATTATTGGCCCCAGCCTACGGG ACCCATATCTGCGGAGATATCTATCCAGGCTTTGAGTT ATGCACCTGGAGGAGATATCAATAAGGTGTTAGAAAAG	35

TABLE 13-continued

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	CTCGGATACAGTGGAGGCGATTACTAGGCATCTTAGA GAGCAGAGGAATAAAGGCTCGGATAACTCACGTCGAC ACAGAGTCCCTACTTTCATAGTCCCTCAGTATAGCCTATCCG ACGCTGTCCGAGATTAGGGGGTGATTGTCCACCGGCT AGAGGGGGTCTCGTACAAATAGGCTCTCAAGAGTGGT ATACCACGTGCCCCAAGTATGTTGCCAACCCAGGGTAC CTTATCTCGAATTTTGATGAGTCATCATGTACTTTCATG CCAGAGGGGACTGTGTGCAGCCAAAATGCCTGTACCC GATGAGTCCCTGTCTCCAAAGATGCCTCCGGGGTCCA CCAAGTCCGTGTCTCGTACACTCGTATCCGGGTCTTTG GGAACCGGTTCAATTTTATCACAAGGGAACCTAATAGCC AATTGTGCATCAATTTCTGTAGTGTAGCAACACAGGT ACGATTATTAATCAAGACCCGACAAAGATCCTAACATA CATGTCTGCCGATCGCTGCCCGTAGTCGAGGTGAACG GCGTGACCATCCAAGTCCGGAGCAGGAGGTAATCCAGA CGCTGTGTAATGACAGAAATGACCTCGGTCTCCCAT ATCATTGGAGAGGTTGGACGTAGGGACAAAATCTGGGG AATGCAATGCCCBAATGGAGGATGCCAAGGAAATGTT GGAATCATCGGACCAGATATTGAGAAGTATGAAAGGTT TATCCGAGCACTAGCATAGTCTACATCCTGATTGCAAGT TGCTTTGGAGGGTTGATAGGGATCCCACTTTAATATGT TGCTGCAGGGGGCGTTGTAACAAAAGGGAGAACAG TTGGTATGTCAGAACACAGGCTTAAAGCCTGACCTTACA GGAACATCAAAATCCTATGTAGATCGCTTTGATGATA ATAGGCTGGAGCCTCGGTGGCCAAGCTTCTTGCCCTT GGGCCTCCCCCAGCCCTCCTCCCTTCTCGACCCCGT ACCCCCGTGTCTTTGAAATAAGTCTGAGTGGGCGGC	
GC F MEASLES B3.1 ORF Sequence, NT	ATGGGTCTCAAGGTGAACGTCCTCTGCCGTATTCATGGC AGTACTGTTAACTCTCCAAACACCCCGCCGTCAAAATTC ATTGGGGCAATCTCTCTAAGATAGGGGTAGTAGGAATA GGAAGTGAAGCTACAAAGTATGACTCGTTCAGGCCA TCAATCATAGTCAATAAATTAATGCCCAATATAACTCT CCTCAATAACTGCACGAGGGTAGAGATTGCAGAATACA GGAGACTACTAAGAACAGTTTGGAAACCAATAGGGAT GCACCTAATGCAATGACCCAGAACATAAGGCCGGTCA GAGCGTAGCTTCAAGTAGGAGACACAAGAGATTGCG GGAGTAGTCTTGGCAGGTGCCGCCCTAGGTGTTGCCAC AGCTGCTCAGATAACAGCCGGCATTGCACCTCACCAGT CCATGCTGAACCTCTCAGGCCATCGACAATCTGAGAGCG AGCCTGGAACTACTAATCAGGCAATTGAGGCAATCAG ACAAGCAGGGCAGGAGATGATATTGGCTGTTGAGGGTG TCCAAGACTACATCAATAATGAGCTGATACCGTCTATG AACAGCTATCTTGTGATCTAATCGGTGAGAGCTCGG GCTCAAAATGCTTAGACTATACAGAAATCCTGTCAAT ATTTGGCCCGAGCTTACGGACCCCATATCTGCCGAGA TATCTATCCAGGCTTTGAGTATGCACTTGGAGGAGAT ATCAATAAGGTGTTAGAAAAGTCCGGTACAGTGGAG GCGATTTACTAGGCATCTTAGAGAGCAGAGGAATAAAG GCTCGGATAACTCACGTCGACACAGAGTCTTACTTCAT AGTCTCAGTATAGCCTATCCGACGCTGTCCGAGATTA AGGGGGTGATTGTCACCCGGCTAGAGGGGGTCTCGTAC AACATAGGCTCTCAAGGTGGTATACCACTGTGCCCAA GTATGTTGCAACCCCAAGGTACCTTATCTCGAATTTGA TGAGTCATCATGTACTTTTCATGCCAGAGGGGACTGTGT GCAGCCAAAATGCCCTTGTACCGATGAGTCTCTGCTC CAAGAATGCCCTCCGGGGTCCACCAAGTCCGTGTCTCG TACACTCGTATCCGGGTCTTTGGGAACCGGTTCAATTT ATCACAAGGGAACCTAATAGCCAATTTGCAATCAATTC TTTGTAAGTGTACACACAGGTACGATTATTAATCAA GACCCGACAGATCCTAACATACATTTGCTGCCGATCG CTGCCCGGTAGTCGAGGTGACGGCGTGACCATCCAAG TCGGGAGCAGGAGGTATCCAGACCGTGTGACTTGCAC AGAATTGACCTCGGTCTCCCATATCAATTGGAGAGGTT GGACGTAGGGACAAATCTGGGAATGCAATGCCAAA TTGGAGGATGCCAAGGAAATGTTGGAATCATCGGACCA GATATTGAGAAGTATGAAAGGTTTATCGAGCACTAGCA TAGTCTACATCCTGATTTGCAGTGTCTTTGGAGGGTTGA TAGGGATCCCCACTTAATATGTTGCTGCAGGGGGCGT TGTAAACAAAAGGGAGAACAAAGTTGGTATGTCAAGAC CAGGCCATAAGCCTGACCTTACAGGAACATCAAAATCC TATGTAAGATCGCTTTGA	36

TABLE 13-continued

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
GC F MEASLES B3.1 mRNA Sequence (assumes T100 tail); mRNA Sequence Length: 1925	G*GGGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAAT ATAAGAGCCACCATGGGTCTCAAGGTGAACGTCTCTGC CGTATTCATGGCAGTACTGTAACTCTCCAACACCCG CCGGTCAAATTCATTGGGGCAATCTCTAAGATAGGG GTAGTAGGARTAGGAAGTGCAAGCTACAAAGTTATGA CTCGTCCAGCCATCAATCATTAGTCATAAAATTAATGC CCAATATAACTCTCCTCAATAACTGCACGAGGGTAGAG ATTGCAGAATRCAGGAGACTACTAAGAACAGTTTGGGA ACCAATTAGGGATGCACTTAATGCAATGACCAGAACA TAAGGCCGGTTCAGAGCGTAGCTTCAAGTAGGAGACAC AAGAGATTGCGGGAGTAGTCTGGCAGGTGCGGCCCT AGGTGTTGCCACAGCTGCTCAGATAACAGCCGGCATTG CACTTCACCGGTCCATGCTGAACCTCAGGCCATCGAC AATCTGAGAGCGAGCCTGGAACTACTAATCAGGCAAT TGAGGCAATCAGACAAGCAGGCCAGGAGATGATATTG GCTGTTCAAGGTGTCCAAGACTACATCAATAATGAGCT GATACCGTCTRTGAACAGCTATCTTGTGATCTAATCG GTCAGAGCTCGGGCTCAAATTGCTTAGATACTATACA GAAATCCTGTCAATATTTGGCCCCAGCCTACGGGACCC CATATCTCGGGAGATATCTATCCAGGCTTGTAGTTATGC ACTTGGAGGAGATACTAAAGGTGTTAGAAAAGCTCG GATACAGTGGAGGCGATTACTAGGCATCTTAGAGAGC AGAGGAATAAAGGCTCGGATAACTCACGTCGACACAG AGTCCTACTTCATAGTCCCTCAGTATAGCCTATCCGACGC TGTCCGAGATTAAGGGGGTGAATTGCCACCGCTAGAG GGGGTCTCGTACAAATAGGCTCTCAAGAGTGGTATAC CACTGTGCCAAGTATGTTGCAACC AAGGGTACCTTA TCTCGAATTTGATGAGTCATCATGTAATTCATGCCAG AGGGGACTGTGTGCAGCCAAATGCCTTGTACCCGATG AGTCCCTGTGCTCCAAGAAATGCCTCCGGGGTCCACCAA GTCCGTGTGCTCGTACACTCGTATCCGGGTCTTTGGGAA CCGGTTCATTTTATCACAGGGAACTAATAGCCAAAT GTGCATCAATCTTTGTAAGTGTACACAACAGGTACG ATTATTAATCAAGACCCTGACAAGATCCTAATACATACAT TGCTGCCGATCGCTGCCCGGTAGTCGAGGTGAACGGCG TGACCATCCAAGTCCGGAGCAGGAGGTATCCAGACGCT GTGTACTTGCACAGAATTGACCTCGGTCTCCCATATCA TTGGAGAGGTTGGACGTAGGGACAAATCTGGGGAAATG CAATTGCCAAATGGAGGATGCCAAGGAATGTTGGAA TCATCGACCCAGATATTGAGAAGTATGAAAGGTTTATC GAGCACTAGCATAGTCTACATCTGATTGCAAGTGTGTC TTGGAGGGTTGATAGGGATCCCCACTTTAATATGTTGCT GCAGGGGGCGTTGTAACAAAAGGGAGAACAGTTGG TATGTCAAGACCAGGCTTAAGCCTGACCTTACAGGAA CATCAAAATCCTATGTAAGATCGCTTTGATGATAATAG GCTGGAGCCTCGGTGGCCAAAGCTTCTTGCCTTGGGC CTCCCCCAGCCCCCTCCCTCCCTTCTGCACCCGTACCC CCGTGGTCTTTGAATAAAGCTGAGTGGGGCGCAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAATCTAG	37
GC F MEASLES D8 Sequence, NT (5' UTR, ORF, 3' UTR) Sequence Length: 1864	TCAAGCTTTGGACCCTCGTACAGAAGCTAATACGACT CACTATAGGGAATAAGAGAGAAAAGAGAGTAAGAA GAAATATAAGAGCCACCATGGGTCTCAAGGTGAACGTC TCTGTCAATTCATGGCAGTACTGTAACTCTTCAACA CCCACCGTCAAATCCATTGGGGCAATCTCTAAGAT AGGGGTGGTAGGGGTAGGAAGTGCAGCTACAAAAGTT ATGACTCGTTCAGCCATCAATCATAGTCATAAAGTT AATGCCCAATATAACTCTCCTCACAAATGCGCAGGGG TAGGGATTGCAGAAATACAGGAGACTACTGAGAACAGTT CTGGAACCAATTAGAGATGCACTTAATGCAATGACCCA GAATAAAGACCAGGTTCCAGAGTGTAGCTTCAAGTAGGA GACACAAGAGATTTGCGGGAGTTGCTCTGGCAGGTGCG GCCCTAGGCGTTGCCACAGCTGCTCAATAACAGCCGG TATTGCACCTCACCCAGTCCATGCTGAACCTCAAGCCAT CGACAATCTGAGAGCGAGCCTAGAACTACTAATCAGG CAATTGAGGCAATCAGACAAGCAGGGCAGGAGATGAT ATTGGCTGTTCAAGGTGTCCAAGACTACATCAATAATG AGCTGATACCGTCTATGAATCAACTACTTGTGATTTAA TCGGCCAGAGCTAGGGCTCAAATTGCTCAGATCTAT	38

TABLE 13-continued

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	ACAGAAATCCTGTCATTATTTGGCCCCAGCTTACGGGA CCCCATATCTGCGGAGATATCTATCCAGGCTTTGAGCT ATGCCCTTGGGGGAGATATCAATRAGGTGTGGAAAG CTCGGATACAGTGGAGGTGATCTACTGGGCATCTTAGA GAGCAGAGGAATAAAGGCCCGGATAACTCAGTCGAC ACAGAGTCCCTACTTTCATTGTACTCAGTATAGCCTATCCG ACGCTATCCGAGATTAAGGGGTGATTGTCCACCGGCT AGAGGGGGTCTCGTACAAACATAGGCTCTCAAGAGTGGT ATACCACTGTGCCCAAGTATGTTGCAACCCRAGGGTAC CTTATCTCGAATTTTGTATGAGTCATCATGCACTTTCATG CCAGAGGGGACTGTGTGCGAGCCAGAATGCCTTGTACCC GATGAGTCCCTGCTCCCAAGATGCCTCCGGGGTCCA CTAAGTCCGTGCTCGTACACTCGTATCCGGGTCTTTCCG GGAACCGGTTCAATTTATCACAGGGGAACCTAATAGCC AATTGTGCATCAATCCTTTGCAAGTGTACACAACAGG AACAATCATTAAATCAAGACCCCTGACAAGATCCTAACAT ACATTGCTGCCGATCACTGCCCGGTGGTCGAGGTGAAT GGCGTGACCATCCAAAGTCGGGAGCAGGAGGTATCCGG ACGCTGTGTACTTGCACAGGATTGACCTCCGGTCCCTCC ATATCTTTGGAGAGGTGGACGTAGGGACAAATCTGGG GAATGCAATTGCTAAGTTGGAGGATGCCAAGGAATTGT TGGAGTCACTCGACAGATATTGAGGAGTATGAAAGGT TTATCGAGCACTAGTATAGTTTACATCCTGATTGCAAGT TGTCTTGGAGGATGTATAGGGATCCCGCTTTAATATGT TGCTGCAGGGGGCGTTGTAACAAGAAGGGAGAACAAAG TTGGTATGTCBAAGACAGGCTAAAGCCTGATCTTACA GGAAACATCAAATCCTATGTAAAGTCACTCTGATGATA ATAGGCTGGAGCCTCGGTGGCCAAGCTTCTTGCCCTT GGGCTCCCGCCAGCCCTCCTCCCTTCTGCAACCCGT ACCCCGTTGGTCTTTGAATAAAGTCTGAGTGGGCGGC	
GC F MEASLES D8 ORF Sequence, NT	ATGGGTCTCAAGGTGAACGTCTCTGTCAATTCATGGC AGTACTGTTAACTCTTCAAACACCCACCGGTCAAATCC ATTTGGGGCAATCTCTCTAAGATAGGGGTGGTAGGGGTA GGAAGTGCAGCTACAAGTTATGACTCGTTCAGGCCA TCAATCATTAGTCAATAAGTTAATGCCCAATATAACTCT CCTCAACAAATGACAGGGGTAGGGATTGCAGAATACA GGAGACTACTGAGAACAGTTCTGGAACCAATAGAGAT GCACCTAATGCAATGACCCAGAATATAAGACCGGTTCA GAGTGTAGCTTCAAGTAGGAGACACAAGAGATTTGCCG GAGTTGCTCTGGCAGGTGCGGCCCTAGGCGTTGCCACA GCTGCTCAAATAACAGCCGGTATTGCACTTCCACAGTC CATGCTGAACCTTCAAGCCATCGACAACTCGAGAGCGA CCTAGAACTACTAATCAGGCAATGAGGCAATCAGA CAAGCAGGGCAGGAGATGATATTGGCTGTTGAGGGTGT CCAAGACTACATCAATAATGAGCTGATACCGCTCATGA ATCAACTATCTTGTGATTAACTCGCCAGAAGCTAGGG CTCAAATGCTCAGATACTATACAGAAATCCTGTGTCATT ATTTGGCCCGAGCTTACGGGACCCCATATCTGCGGAGA TATCTATCCAGGCTTTGAGCTATGCGCTTGGAGGAGAT ATCAATAAGGTGTTGGAAAAGCTCGGATACAGTGGAG GTGATCTACTGGGCATCTTAGAGAGCAGAGGAATAAAG GCCCGGATAACTCAGTCGACACAGAGTCCACTTCAT TGTACTCAGTATAGCCTATCCGACGCTATCCGAGATTA AGGGGGTGTATGTTCCACCGGCTAGAGGGGGTCTCGTAC AACATAGGCTCTCAAGAGTGGTATACCACTGTGCCCAA GTATGTTGCAACCCCAAGGTACCTTATCTCGAATTTGA TGAGTCATCATGCACTTTCATGCCAGAGGGGACTGTGT GCAGCCAGAATGCCCTTGTACCCGATGAGTCTCTGCTC CAAGAATGCTCCGGGGTCCACTAAGTCCGTGTGCTCG TACACTCGTATCCGGGTCTTCCGGAAACCGGTTCAATTT ATCACAGGGGAACCTAATAGCCAATTTGTCATCAATCC TTTGCAAGTGTACACAACAGGAACAATCAATTAATCAA GACCTGACAAAGATCCTAACATACATTGCTGCCGATCA CTGCCCCGTTGGTCCAGGTGAATGGCGTGACCATCCAAG TCGGGAGCAGGAGGTATCCGGACGCTGTGTACTTGCAC AGGATTGACCTCGGTCCCTCCCATATCTTTGGAGAGGT GGACGTAGGGCAAAATCTGGGGAAATGCAATGCTAAGT TGGAGGATGCCAAGGAATGTTGGAGTCACTCGGACCAG ATATTGAGGAGTATGAAAGGTTTATCGAGCACTAGTAT AGTTTACATCCTGATTGCAAGTGTGCTTGGAGGATGAT AGGGATCCCGCTTTAATATGTTGCTGCAGGGGGGCTT	39

TABLE 13-continued

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	GTAACAAGAAGGGAGAACAAAGTTGGTATGTCAAGACC AGGCCTAAAGCCTGATCTTACAGGAACATCAAATCCT ATGTAAGGTCACTCTGA	
GC F MEASLES D8 mRNA Sequence (assumes T100 tail) Sequence Length: 1925	G*GGGAAATAAGAGAGAAAAGAGAGTAAGAAGAAAT ATAAGAGCCACCATGGGTCTCAAGGTGAACGTCTCTGT CATATTTCATGGCAGTACTGTAACTCTTCAAACACCCAC CGGTCAAATCCATTGGGGCAATCTCTCAAGATAGGGG TGGTAGGGTGGRAAGTGCAGCTCAAAAGTTATGACT CGTTCAGCCATCAATCATTAGTCATAAAGTTAATGCC CAATATAACTCTCTCAAACAATTGCACGAGGGTAGGGA TTGCAGATACAGGAGACTACTGGAACAGTTCTGGAA CCAAATTAGAGATGCCTTAATGCAATGACCCAGAATAT AAGACCGGTTCAAGAGTGTAGCTTCAAGTAGGAGACACA AGAGATTGCGGGAGTTGCTCTGGCAGGTGCGGCCCTA GGCGTTGCCACAGCTGCTCAAATAACAGCCGGTATTGC ACTTCAACAGTCCATGCTGAACCTCAAGCCATCGACA ATCTGAGAGCGAGCCTAGAACTACTAATCGGCCAATT GAGGCAATCAGACAAGCAGGGCAGGAGATGATATTGG CTGTTCAAGGTGTC CAAGACTACATCAATAATGAGCTG ATACCGTCTATGAATCAACTATCTTGTGATTTAATCGGC CAGAAGCTAGGGCTCAAATTTGCTCAGATACTATACAGA AATCCTGTCAATTATTGGCCCGAGCTTACGGGACCCCAT ATCTGCGGAGATATCTATCCAGGCTTTGAGCTATGCCG TTGGAGGAGATATCAATAAGGTGTTGGAAAAGCTCGGA TACAGTGGAGGTGATCTACTGGGCATCTTAGAGAGCAG AGGAATAAAGGCCCGGATCACTCAGTTCGACACAGAG TCCTACTTCATTGTACTCAGTATAGCCTATCCGACGCTA TCCAGATTAAGGGGGTATTGTCACCGGCTAGAGGG GGTCTCGTACAACATAGGCTCTCAAGAGTGGTATACCA CTGTGCCCAAGTATGTTGCAACCCAAAGGGTACCTTATC TCGAATTTGATGAGTCACTATGCACTTTCATGCCAGAG GGGACTGTGTGCAGCCAGAATGCTTGTACCCGATGAG TCCTCTGCTCCAAGAATGCCTCCGGGGTCCACTAAGT CCTGTGCTCGTACACTCGTATCCGGGCTTTTCGGGAACC GGTTCATTTTATCAGAGGGAACTAATAGCCAAATTGT GCATCAATCCTTTGCAAGTGTACACAACAGGAACAAT CATTAAATCAAGACCCTGACAAGATCCTAACATACATTG CTGCCGATCACTGCCCGGTGGTCCAGGTGAATGGCGTG ACCATCCAAAGTCGGGAGCAGGAGTATCCGGACGCTGT GTACTTGCACAGGAATTGACCTCGTCCCTCCATATCTTT GGAGAGGTTGGACGTAGGGACAATCTGGGGAAATGCA ATTGCTAAGTTGGAGGATGCCAAGGAATGTTGGAGTC ATCGGACCAGATATTGAGGAGTATGAAAGGTTTATCGA GCAC TAGTATAGTTTACATCTGATTGCAGTGTGCTTG GAGGATTTGATAGGGATCCCGCTTAAATATGTTGCTGC AGGGGGCGTTGTAA CAAGAAGGGAGAA CAAGTTGGTA TGTC AAGACCCAGGCCCTAAAGCCTGATCTTACAGGAACA TCAAATCCTATGTAAGGTCACTCTGATGATAATAGGC TGGAGCCTCGGTGGCCAAGCTTCTTGGCCCTTGGGCCTC CCCCAGCCCTCTCCCTCTCTGACCCCGTACCCCGG TGGTCTTTGAATAAAGTCTGACTGGGCGGCAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAATCTAG	40
GC H MEASLES B3 Sequence, 5' UTR, ORF, 3' UTR) Sequence Length: 2065	TCAAGCTTTGGACCCCTCGTACAGAAGCTAATACGACT CACTATAGGGAAATAAGAGAGAAAAGAGAGTAAGAA GAAATATAAGAGCCCACTGTCACCGCAACGAGACCG GATAAATGCCCTTCTACAAGATAACCCCTTATCCCAAGG GAAGTAGGATAGTTATTAACAGAGAACCTTATGATT GACAGACCTATGTTCTGCTGGCTGTTCTGTTCTGTCATG TTTCTGAGCTTGATCGGATTGCTGGCAATGTCAGGCATT AGACTTCAATCGGGCAGCCATCTACCCCGGAGATCCA TAAAAGCCTCAGTACCAATCTGGATGTGACTAACTCCA TCGAGCATCAGGTCAAGGACGTGCTGACACCCTCTTT AAATCATCGGGATGAAGTGGGCTTGAGAACACCTC AGAGATTCAGTACCTAGTGAATTCATCTCGGACAAG ATTAATTCCTTAAATCCGGATAGGAGTACGACTTCAG AGATCTCACTTGGTGCATCAACCCGCCAGAGGGATCA AACTAGATTAATGATCAATACTGTGCAGATGTGGCTGCT GAAGACCTCATGAATGCATTGGTGAACCAACTCTACT	41

TABLE 13-continued

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	GGAGACCAGAACAACCACTCAGTTCCTAGCTGTCTCAA AGGGAAACTGCTCAGGGCCACTACAATCAGAGGTCA ATTCTGAAACATGTGCTGCTTGTGGACTTGTACTT AGGTCGAGGTACAAATGTGTCATCTATAGTCACTATGA CATCCCAGGGAATGTATGGGGGAACCTACCTAGTTGAA AAGCCTAATCTGAA CAGCAAGGGT CAGAGTTGTCACA ACTGAGCATGTACCGAGTGTGAAAGTAGGTTGATCA GAAACCCGGTTTGGGGCTCCGGTGTCCATATGACA AACTATTGAGCAACAGTCAAGTAAATGGTCTCGGCAA CTGTATGGTGGCTTGGGGGAGCTCAAACCTCGCAGCCC TTTGTACCGGGGACGATTCTATCATAATCCCTATCAGG GATCAGGGAAAGGTGT CAGCTTCCAGCTCGTCAAGCTG GGTGTCTGGAATCCCCAACCGACATGCAATCCTGGGT CCCCATTATCAACGGATGATCCAGTGGTAGACAGGCTTT ACCTCTCATCTCACAGAGGTGTCTCGCTGACAAATCAA GCAAAATGGGCTGTCCGACAAACGAAACAGATGACA AGTTGCGAATGGAGACATGCTTCCAGCAGGGGTGTA GGTAAATCCRAAGCACTTCGCGAGAAATCCCGAGTGGT ACCATTGAAGGATAACAGGATTCCTTATACGGGGTCC TGTCTGTTGATCTGAGTCTGACGGTTGAGCTTAAATCA AAATGCTTCGGGATTCCGGCCATTGATCACACACGGC TCAGGGATGGACCTATACAAATCCAAC TGCAACAAATGT GTATTGGCTGACTATCCGCCAATGAGAAATCTAGCCT TAGGCGTAATCAACACATGGAGTGGATACCGAGATTC AAGGTTAGTCCCAACCTCTTCACTGTCCCAATTAAGGA AGCAGGCGAAGACTGCCATGCCCCAACATACCTACTG CGGAGGTGGAGGTGATGTCAAACCTCAGTTC CAACCTG GTGATTCACCTGGTCAAGATCTCCAATATGTTTGGCA ACCTACGATACCTCCAGGGTTGAGCATGCTGTGGTTTA TTACGTTTACAGCCCAAGCCGCTCATTTTCTTACTTTTA TCCTTTTAGGTTGCCTATAAAGGGGTCCCAATCGAAC TACAAGTGGAAATGCTTCAATGCGATCAAACCTCTGG TGCCGCTACTTCTGTGTGCTTGGGACTCAGAAATCCGGT GGACTTATCACTCACTCTGGGATGGTGGGATGGGAGT CAGCTGCACAGCTA CCGGGAGATGGAACCAATCGC AGATAATGATAATAGGCTGGAGCCTCGGTGGCCAAGCT TCTTGCCCTTGGGCTCCCCAGCCCTCTCCCTT CCTGCAACCGTACCCCGTGGTCTTTGAATAAAGTCTG AGTGGCGGC	
GC H MEASLES B3 ORF Sequence, NT	ATGTCACCCGACGAGACCGGATAAATGCCTTCTACAA AGATAACCTTATCCCAAGGGAAGTAGGATAGTTATTA ACAGAGAACATCTTATGATTGACAGACCTATGTTCTG CTGGCTGTTCGTTTGTGATGTTTCTGAGCTTGATCGGA TTGCTGGCAATGCGAGGATTAGACTTCATCGGGCAGC CATCTACACCCGGAGATCCATAAAGCCCTCAGTACCA ATCTGGATGTGACTAACTCCATCGAGCATCAGGTCAAG GACGTGCTGACACCACTCTTAAATCATCGGGATGA AGTGGGCTGAGAACCTCAGAGATTCAGTACCTAG TGAAATTCATCTCGGACAAGATTAATTCCTTAATCCG GATAGGAGTACGACTTCAGAGATCTCACTTGGTGCAT CAACCCGACAGAGAGGATCAAAC TAGATTATGATCAAT ACTGTGCAGATGTGGCTGCTGAAGGCTCATGAATGCA TTGGTGAACCTCAACTCTACTGGAGACCAGAACCAACCAC TCAGTTCCTAGCTGTCTCAAAGGGAACTGCTCAGGGC CCACTACAATCAGAGGTCAATTCCAAACATGTCGCTG TCCTTGTGGACTTGTACTTAGGTCGAGGTACAAATGTG TCATCTATAGTCACTATGACATCCAGGGAATGTATGG GGAACTTACCTAGTTGAAAAGCCTAATCTGAACAGCA AAGGGTCAGAGTTGTCAACACTGAGCATGTACCGAGTG TTTGAAGTAGGTTGATCAGAAACCCGGTTTGGGGC TCCGTTTCCATATGACAACTATTTGAGCAACCAG TCAGTAAATGGTCTCGGCAACTGTATGGTGGCTTGGGG GAGTCAAACCTCGCAGCCCTTGTACGGGGAGGATTC TATCATAATCCCTATCAGGGATCAGGGAAAGGTGTC GCTTCCAGCTCGTCAAGCTGGGTGTCTGGAATCCCCA ACCGACATGCAATCCTGGGTCCCTTATCAACGGATGA TCCAGTGGTAGACAGGCTTACCTCTCATCTCACAGAG GTGTCATCGTACCAATCAAGCAAAATGGGCTGTCCCG ACAACACGAACAGATGACAGTTGCGAATGGAGACAT GCTTCCAGCAGGCGTGAAGGTAATAATCCCAAGCACTC TCCGGAATCCGAGTGGTACCATGAAGGATAACAG	42

TABLE 13-continued

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA TAG	
GC H MEASLES D8 Sequence, NT (5' UTR, ORF, 3' UTR) Sequence Length: 2065	TCAAGCTTTGGACCTCGTACAGAAGCTAATACGACT CACTATAGGGRAATAAGAGAGARRAGAGAGTAAGAA GAAATATAAGAGCCACCATGTCAACCAACGAGACCG GATAAATGCCCTTCTACAAGACAACCCCATCCTAAGG GAAGTAGGATGTTTATTAACAGAGAACATCTTATGATT GATAGACCTTATGTTTGTGGCTGTTCTATTCCGTCATG TTTCTGAGCTTGATCGGGTTGCTAGCCATTGCAGGCATT AGACTTCATCGGGCAGCCATCTACACCGCAGAGATCCA TAAAAGCCTCAGCAACCAATCTGGATGTAACCTAACTCAA TCGAGCATCAGGTTAAGGACGTGCTGACACCACTCTTC AAGATCATCGGTGATGAAGTGGGCTTGAGGACACCTCA GAGATTCAGTACCTAGTGAAGTTCATCTCTGACAGA TTAAATTCCTTAATCCGGACAGGGAATACGACTTCAGA GATCTCACTTGGTGTATCAACCCGCCAGAGGAATCAA ATTGGATTATGATCAATACTGTGCAGATGTGGCTGCTG AAGAATCATGAATGCATTGGTGAACCAACTCTACTG GAGACCCAGGCAACCAATCAGTTCCTAGCTGTCTCAA GGGAAACTGCTCAGGGCCCACTACAATCAGAGGCCAAT TCTCAAACATGTCGCTGTCCCTGTTGGACTTGTATTTAA GTCCAGGTTACAATGTGTCTATCTATAGTCACTATGACA TCCCAGGGAATGTACGGGGGAACCTTACCTAGTGGAAAA GCCTAATCTGAGCAGCAAGGGTCAAGTGTGACAAC TGAGCATGCACCGAGTGTGAGTGGTGTATCAGA AATCCGGTTTGGGGCTCCGGTATTCATATGACAAA CTATCTTGAGCAACCAAGTCAAGTATGATTTCAAGCACT GCATGGTGGCTTGGGGGAGCTCAAGTTCGCAGCCCTC TGTCACAGGGAAGATTCTATCACAATCCCTATCAGGG ATCAGGGAAGGTGTCAAGTTCAGCTTGTCAAGCTAG GTGTCTGGAATCCCAACCGACATGCAATCCTGGGTG CCCCTATCAACGGATGATCCAGTGTAGACAGGCTTTA CCTCTCATCTCACAGAGGCGTTATCGCTGACAAATCAAG CAAAATGGGCTGTCCCGACACACGGACAGATGACAA GTTGGCAATGGAGACATGCTCCAGCAGGCGTGTAGG GTAAAATCCAAGCACTTTCGGGGAATCCCGAGTGGACA CCATGGAAGGATAACAGGATTCCTTCATACGGGGTCTT GTCTGTTGATCTGAGTCTGACAGTTGAGCTTAAAATCA AAATGTTTCAGGATTTCGGGCCATTGATCACACACGGT TCAGGGATGGACCTATACAATCCAAACCAACCAATAT GTATTGGCTGACTATCCCGCAATGAAGAACCTGGCCT TAGGTGTAATCAACACATTGGAGTGGATACCGAGATTC AAGGTTAGTCCCAACCTCTTCACTGTTCCAATTAAGGA AGCAGGCGAGGACTGCCATGCCCAACATACCTACCTG CGGAGGTGGATGGTGTATGTCAAACTCAGTTCCAATCTG GTGATTCACCTGGTCAAGATCTCCAAATATGTTCTGGCA ACCTACGATACTTCCAGAGTGAACATGCTGTAGTTTAT TACGTTTACAGCCCAAGCCGCTCATTTTCTTACTTTTAT CCTTTTAGGTGCTGTAAAGGGGGTCCCAATTGAATTA CAAGTGAATGCTTACATGGGACCAAAAACCTCTGGTG CCGTCACTTCTGTGTGCTTGGCGACTCAGAACTCGGTGG ACATATCACTCACTCTGGGATGGTGGGCATGGGAGTCA GCTGCACAGCCACTCGGGAAGTGGAAACAGCCGAG ATAGTGATAAATAGGCTGGAGCCTCGGTGGCCAAGCTTC TTGCCCTTGGGCTTCCCCCAGCCCTTCTCCCTTCC TGCACCCGTACCCCGTGGTCTTTGAATAAAGTCTGAG TGGGCGG	44
GC H MEASLES D8 ORF Sequence, NT	ATGTCCACCACACGAGACCGGATAAATGCCCTTCTACAA AGACAAACCCCATCCTAAGGGAAAGTAGGATAGTTATTA ACAGAGAACATCTTATGATTGATAGACCTTATGTTTGGC TGGCTGTTCTATTCGTCA TGTTCCTGAGCTTGATCGGGT TGCTAGCCATTGCAGGCATTAGACTTCATCGGGCAGCC ATCTACACCGCAGAGATCCATAAAGCCTCAGCACCAA TCTGGATGTAACCTCACTCAATCGAGCATCAGGTTAAGG ACGTCTGACACCACTCTTCAAGATCATCGGTGATGAA GTGGCTTGAGGACACCTCAGAGATTCCTGACCTAGT GAAGTTCATCTCTGACAAGATTAATTCCTTAATCCGG ACAGGGAATAAGACTTCAGAGATCTCACTTGGTGTATC AACCCGCCAGAGAGATCAAATTGGATTATGATCAATA	45

TABLE 13-continued

MeV Nucleic Acid Sequences		SEQ ID NO:
Description	Sequence	
	CTGTGCAGATGTGGCTGCTGAAGAAGCTCATGAATGCAT TGGTGAAGTCAACTCTACTGGAGAC CAGGGCAACCAAT CAGTTCC TAGCTGTCTCAAAGGGAAC TGCTCAGGGCC CACTACAATCAGAGGCCAATCTCAAACATGTCGCTGT CCCGTGGACTTGTATTAAAGTCGAGGTACAAATGTGT CATCTATAGTCACTATGACATCCCAGGGAATGTACGGG GGAACCTACCTAGTGGAAAAGCCTAATCTGAGCAGCAA AGGGTCAGAGTTGT CACAAC TGAGCATGCACCAGTGT TTGAAGTAGGTGTATCAGAAATCCGGGTTTGGGGCT CCGGTATTCATATGACAAAATATCTTGAGCAACCAGT CAGTAATGATTT CAGCAACTGCATGGTGGCTTTGGGG AGCTCAAGTTCGACGCCCTGTGTACAGGGAGATTCT ATCACAATTCCTATCAGGGATCAGGGAAAGGTGTCTAG CTTCCAGCTTGTCAAAGCTAGGTGTCTGGAAATCCCAA CCGACATGCATCCCTGGGTCCCTTATCAACGGATGAT CCAGTGATAGACAGGCTTTACCTCTCATCTCACAGAG CGTTATCGCTGACAAATCAAGCAAAATGGGCTGTCCGA CAACACGGACGATGACAGTTGCGAATGGGACATG CTCCAGCAGGCGTGAAGGGTAAATCCAAGCACTTT GCGAGAATCCCGAGTGGACACCATTGAAGGATAACAG GATTCCTTCATACGGGGTCTGTCTGTGTATCTGAGTCT GACAGTTGAGCTTAAAATCAAAATTTGTTTCAGGATTCG GGCCATTGATCACACACGGTTCAGGGATGGACCTATAC AAATCCAACCCACAACAATATGTATTGGCTGACTATCCC GCCAATGAAGAACCTGGCCTTAGGTGTAAATCAACACAT TGGAGTGGATACCGAGATTCAGGTTAGTCCCAACCTC TTCCTGTTCCAAATTAAGGAAGCAGGCGAGGACTGCCA TGCCCCAACATACCTACCTGCGGAGGTGGATGGTGATG TCAAACCTCAGTTCCAATCTGGTGTATCTACCTGGTCAAG ATCTCCAATATGTTCTGGCAACCTACGATACITCCAGA GTTGAACATGCTGTAGTTTATTACGTTTACAGCCCAAGC CGCTCATTTTCTTACTTTTATCCTTTTAGGTTGCCTGTAA GGGGGTCCCCATTGAATTAAGTGGAAATGCTTCACA TGGGACCAAAAACCTGCGTCCGTCACCTTCTGTGTGCTT GCGGACTCAGAACTGGTGGACATATCACTCACTCTGG GATGGTGGCATGGGAGTCAGCTGCACAGCCACTCGGG AAGATGGAACCAGCCCGAGATAG	
GC H MEASLES D8 mRNA Sequence (assumes T100 tail): Sequence Length: 2126	G*GGGAAATAAGAGAGAAAAGAGAGTAAGAGAAAT ATAAGAGCCACCATGTCAACACAACGAGACCGGATAA ATGCCTTCTACAAAGACAACCCCATCCTAAGGGAAGT AGGATAGTTATTAACAGAGAACATCTTATGATTGATAG ACCTTATGTTTTGCTGGCTGTTCTATTTCGTCAATGTTCTG AGCTTGATCGGGTTGCTAGCCATTGCAGGCATTAGACT TCATCGGGCAGCCATCTACACCGCAGAGATCCATAAAA GCCTCAGCACCAATCTGGATGTAAC TAACCTCAATCGAG CATCAGGTTAAGGACGTGCTGACACCACTCTTCAAGAT CATCGGTGATGAAGTGGGCTTGAGGACACCTCAGAGAT TCACTGACCTAGTGAAGTTCATCTCTGACAAGATTAAT TTCCTTAATCCGGACAGGGAATACGACTTCAGAGATCT CACTTGGTGTATCAACCCGCCAGAGAGAAATCAAAATGG ATTATGATCAATACTGTGCAGATGTGGCTGCTGAAGAA CTCATGAATGCATTGGTGAAGTCAACTCTACTGGAGAC CAGGGCAACCAATCAGTTCC TAGCTGTCTCAAAGGGAA ACTGCTCAGGGCCCACTACAATCAGAGGCCAATTTCTCA AACATGTCGCTGTCCCTGTTGGACTTGTATTTAAGTCGA GGTTACAATGTGTCATCTATAGTCACTATGACATCCCA GGGAAATGTACGGGGAACTTACCTAGTGGAAAAGCCT AATCTGAGCAGCAAAGGGTCAGAGTTGTCACAAC TGAG CATGCACCGAGTGTTTGAAGTAGGTGTATCAGAAATC CGGTTTGGGGCTCCGGTATTCATATGACAACTAT CTTGAGCAAC CAGTCAGTAATGATTT CAGCAACTGCAT GGTGGCTTTGGGGAGCTCAAGTTCGACGCCCTCTGTCT ACAGGGAAGATTTCTATCACAATCCCTATCAGGGATCA GGGAAAGGTGTCAGCTTCCAGCTTGTCAAGCTAGGTGT CTGGAAATCCCAACCGACATGCATCCCTGGGTCCCTC TATCAACGGATGATCCAGTGATAGACAGGCTTTACCTC TCATCTCACAGAGGCGTTATCCGTGACAAATCAAGCAA ATGGGCTGTCCGCAACACCGACAGATGACAAAGTTGC GAATGGAGACATGCTTCCAGCAGGCGTGAAGGGTAA AATCCAAGCACTTTGCGAGAATCCCGAGTGGACACCAT TGAAGGATAACAGGATTCCTTCATACGGGGTCTTGTCT	46

TABLE 13-continued

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	UCAAGACCAGGCCUAAAGCCUGACCUACAGGAACAU CAAAUCCUAUGUAAGAU CGCUUUGAUGAUAUAGG CUGGAGCCUGGGUGGCCAAGCUUCUUGCCCUUGGGC CUCCCCCAGCCCCUCCUCCUUCUUGCACCCTCGUACC CCGGUGUCUUGAAUAAAGUCUGAGUGGGCGC	
GC.F.MEASLES.B3.1 ORF Sequence, NT	AUGGGUCUCAAGGUGAACGUCUCUGCCGUUUCAUGG CAGUACUGUUAAUCUCCCAAACACCCCGCCGUCAAU UCAUUGGGGCAUCUCUCAAGAUAGGGUUGUAGG AAUAGGAAGUGCAAGCUACAAGAUUAGACUCGUUC CAGCCAUCAAUCAUUAUUAUAAAUAUAGCCCAAU AUAAUCUCUCCUCAUUAACUGCACGAGGGUAGAGAUUG CAGAAUACAGGAGACUACUAAGAACAGUUUUGGAAC CAUUUAGGGAUGCAUUAUUGCAAUGACCCAGAACAU AAGGCCGGUU CAGAGCGUAGCUUCAAGUAGGAGACAC AAGAGAUUUGCGGGAGUAGUCUUGGCAGGUGCGGCC UAGGUGUUGCCACAGCUGUCAGAUAAAGCCGGCAU UGCACUUACCCGGUCCAUGCUGAACUCUCAGGCCAUC GACAAUCUGAGAGCGAGCCUGGAAACUACUAAUCAGG CAUUUGAGGCAUUCAGACAAGCAGGCGAGGAGUA UAUUGGCUGUUCAGGGUGUCACAGACUACAUCAAUA AUGAGCUGAUACCGUCUUAAGACCAGCUAUCUUGUA UCUAUCCGGUCAGAAGCUCCGGCCUCAAUUGCUUAGA UACUUAACAGAAAUCCUGUCAUUUUUGGCCCCAGCC UACGGGACCCCAUAUCUGCGGAGAUUUAUCCAGGC UUDGAGUUAUGCAUUGGAGGAGAUUAUCAAUAAGGU GUUAGAAAAGCUCGGAUACAGUGGAGGCGAUUUACU AGGCAUCUAGAGAGCAGAGGAUUAAGGCUCGGAU AACUCACGUCGACACAGAGUCCUAUUAUAGUCCUC AGUAUAGCCUACUCCGACCGUCUCCAGAUUAAGGGG UGADUUGCCACC CGGCUAGAGGGGGUCUCGUAACAUA AGGCUCUCAAGAGUGGUUAUCCACUGGCCCAAGUUA GUUGCAACCCAGGGUACCUUAUCUCCGAUUUUGAUG AGUCAUCAUGUACUUCUUGCCAGAGGGGACUGUGU GCAGCCAAAAGCCUUGUACCCGAUGAGUCCUCUGCU CCAAGAAUGCCUCCGGGGUCACCAAGUCCUGUGCU CGUACACUCCUAUCCGGGUCUUUUGGGAACCGGUUCA UUUUAUCACAAGGGAACCUAAUAGCCAAUUGUGCAUC AAUUCUUUGUAAGUGUUAACACACAGGUACGAUUUA UAADUCAGACCCUGACAAGAUCUAAACAUACAUUGCU GCCGAUCGUCGCCCGGUAGUCGAGGUGAACGGCCUGA CCADUCCAGUCCGGGAGCAGGAGGUUUCAGACGCUUG GUACUUGCACAGAAUUGACCCUGGUCUCCCAUAUCA UUGGAGAGGUUGGACGUAGGGACAAAUUUGGGAAU GCAAUUGCCAAAUUGGAGGAGUCCAAAGGAUUUGUG GAUUCAUCCGAC CAGAUUAUGAGAGUAUGAAAGGU UUAUCGAGCACUAGCAUAGUCUACAUCCUGAUUGCAG UGDUCUUGGAGGGUUGAUAGGGAUCCCAUUAUA UADUUGCUGCAGGGGGCUUGUAACAAAAGGGAG AACAAAGUUGGUUAGUCAAGACCAGGCCUAAAGCCUGA CCUUAACAGGAACAUCAAUCCUUAUGUAAGAUCGCUU UGA	70
GC.F.MEASLES.B3.1 mRNA Sequence (assumes T100 tail) mRNA Sequence Length: 1925	G*GGGAAUAAGAGAGAAAAGAGAGUAAGAGGAAA UADAAGAGCCACCAUGGGUCUCAAGGUGAACGUCUCU GCCGUUAUUAUGGCAGUAUUGUUAACUCCCAAACAC CCGCCGGUCAAAUUCAUUGGGGCAUUCUCUAAGAU AGGGUAGUAGGAAUAGGAGUGCAAGCUACAAGU UADGACUCGUUC CAGCCAUCAAUCUUAAGUCAAAAA UUAUUGCCCAAUAUACUCUCCUCAAUAACUGCACGA GGGUAGAGAUUGCAGAAUACAGGAGACUACUAGAA CAGUUUUUGAACCAAUUAAGGAGUCACUUAUUGCAA UGACCCAGAACAUAAAGGCCGGUUCAGAGCGUAGCUUC AAGUAGGAGACACAAAGAGAUUUGCGGGAGUAGUCCU GGCAGGUGCGGCCCUAGGUGUUGCCACAGCUGUCUAG AUAAACAGCCGGCAUUGCAUUCACCAGGUCUAGUCUGA ACUCUCAGGCCAUCGACAAUCUGAGAGCGAGCCUGGA AACUAUCAAUCAGGCAAUUGAGGCAAUCAGACAAGCA GGGCAGGAGAUAGAUUUGGCUUGUUCAGGGUGUCCAA GACUACAUCAAUAUAGGUCUGAUACCGUCUAUGAAC AGCUAUCUUGUAGUUAUUCGGUCAGAAAGCUCCGGCU CAAUUGCUUAGAUACUAACAGAAUCCUGUCAUU	71

TABLE 13-continued

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	AUUUGGCCCCAGCCUACGGGACCCCAUAUCUGCGGAG AUAUCUAUCCAGGCUDUGAGUUUAGCAUCUUGGAGGA GADAUCAAUAPGGUGUUAGAAAGCUCGGAUACAGU GGAGGCGAUUACUAGGCAUCUUAAGAGAGCAGAGGA AUAAGGCUCGGAAUACUCACGUCGACACAGAGUCCU ACUDCAUAGUCCUCAGUAUAGCCUUAUCCGACGUGUC CGAGAUUAAGGGGGUGAUUUGCCACCGGCUAGAGGG GGUCUCGUACAAUAGGCUUCUAAAGAGUGGUUUAAC ACUGUGCCCAAGUUGUUGCAACCAAGGGUACCUUA UCUCGAAUUUGAUAGUCAUCUAGUACUUUAUGCC AGAGGGGACUGUGGCAGCCAAAUGCCUUGUACCCG AUGAGUCCUCUGCUCAAGAAUGCCUCGGGGGUCCA CCAAGUCCUGUGCUUGUACUCUUAUCGGGGUCUUU UGGGAACCGGUUCAUUUUUACAAGGGAACCUAAU AGCCAAUUGUGCAUCAAUUCUUUUAAGUGUUAAC AACAGGUACGAUUUAUAUCAGACCCUGACAGAUUC CUAACAUAUUGUCUGCCGACUCGUCUCCGGUAGUCG AGGUGAACGGGUGACCAUCCAGUCCGGGAGCAGGAG GUADCCAGACGCGUGUAUCUUGCACAGAAUUGACCCU GGUCUCCCAUAUCAUUGGAGAGGUUGGACGUAAGGG ACAAAUCUGGGAAUGCAAUUGCCAAAUUGGAGGAU GCCAAGGAUUUGUUGAAUUCAGGACCAAGAUUUG AGAAGUAUGAAAGGUUUUUCGAGCACUAGCAUAGUC UACAUCCUGAUUGCAGUGUGUCUGGAGGGUUGUA GGGAUCCCAUUUAUAUGUUGUCUGCAGGGGGCGUU GUAACAAAAGGGGAAACAAGUUGGUUAUGUCAAGAC CAGGCCUAAAGCCUGACCUUACAGGAAUAUCAAAAUC CUADGUAAGAUCGCUUUGAUGAAUAAGGCUGGAGC CUCGGUGGCCAAGCUUCUUGCCCUUGGCCUCCCCC CAGCCCCUCCUCCUUCUGCCACCCGUAUCCCGUGG UCDUGAAUAAAGUCUGAGUGGGCGGCAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	
GC F MEASLES D8 Sequence, NT (5' UTR, ORF, 3' UTR) Sequence Length: 1864	UCAAGCUUUUGGACCCUUGUACAGAAAGCUAAUACGAC UCACUAUAGGGAAAUAAGAGAGAAAAGAGAGUAG AAGAAUUAUAGAGCCACCAUGGGUCUAAGGUGAA CGUCUCUGUACUAUUCUAGGCAUUCUUAACUCUU CAAACACCCACCGUCAAUUCUUGGGCAAUUCU CUAAGAUAGGGUGUAGGGUAGGAAUGCAAGCU ACAAGUUAUGACUCGUUCCAGCCAUCAAUUAUAGU CADAAGUUAUUGCCCAAUAUAUCUCUCCUACAAU UGCACGAGGGUAGGGAUUGCAAAUACAGGAGACUA CUGAGAACAGUUCUGGAACCAAUUAAGAGUACAU AAUGCAAUGACCAGAAUUAAGACCCGUUCAGAGU GUAGCUUCAAUAGGAGACAAGAGAUUUGCGGGA GUDGUCCUGGACGGUGCGGCCUAGGCUGUCCACAG CUGCUCAAUUAACAGCCGGUAUUGCAUUCACCAGUC CAUGCUGAACUCUCAAGCCAUCCGAAUUCUGAGAGCG AGCCUAGAAACUACUAUCAGGCAUUGAGGCAAUCA GACAAGCAGGGCAGGAGUAGAUUUGGCUUUCAGG GUGUCCAAGACUACAUCAAUUAUAGCUGAUACCGUC UAUAGAAUCAAUAUCUUGUGAUUUAAUCGGCCAGAA GCUAGGGCUCAAUUGCUAGAUUAUUAACGAAAUC CUGUCAUUAUUGGGCCAGCUUACGGGACCCAUUAU CUGCGGAGAUUCUAUCAGGCUUUGAGCUAUGCGCU UGGAGGAGAUUCAADAAGGUGUUGGAAAAGCUCGG AUACAGUGGAGGUGAUCUACUGGCAUCUUAAGAGAG CAGAGGAUUAAGGCCCGGAUAUCUACBUCGACACA GAGUCCUACUUCUUAUGUACUCAGUAUAGCCUADCCGA CGUAUCGAGAUUAAGGGGGUGAUUGUCACCCGGCU AGAGGGGGUCUCGUACAACUAGGCUCUCAAGAGUG GUADCCACUGUGCCCAAUAUGUUGCAACCCAGGG UACCUUAUCUUGAAUUUGAUGAGUCAUCUAGCAU UCAUGCCAGAGGGGACUGUGGCGAGCCAGAUUGCCU GUACCCGAGUGUCCUCUGUCUCAAAGAAUGCCUCCGG GGGUCCAUAAGUCUUGUCUCGUACAUCGUUAUCCG GGUCUUUCGGGAACCGGUUCAUUUAUACAGGGGA ACCUAUAGCCAAUUGUGCAUCAUCCUUGCAAGUG UUAACAACAAGGAACAUAUAUAUAAGACCCUGAC AAGAUCUUAACAUAUUGCCUGCCGAUCUUGCCGG	72

TABLE 13-continued

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	UGGUCGAGGUGAAUGGGCGUGACCAUCCAGUCGGGA GCAGGAGGUAUCCGGACGCGUGUACUUGCACAGGAU UGACCUCGGUCCUCCAUAUUUUGGAGAGGUUGGAC GUAGGGACAAAUCUGGGAAUUGCAAUUGCUAAGUUG GAGGAUCCAGGAAUUGUUGGAGUCAUCGGACCAG AUADUGAGGAGUUGAAAGGUUUUUCGAGCAUAGU AUAGUUUACAUCUGAUVUGAGUGUCUUGGAGGA UUGAUAGGGAUCCCGCUUUAUUGUUGCUGCAGG GGGCGUUGUACAGAAAGGGAGAACAGUUGGUUUG UCAAGACCAGGCCUAAAGCCUGAUCUACAGGAACU CAAAUCUAUGUAAGGUCAUCUGAUGAUAUAGG CUGGAGCCUGGGUGCCAGGCUUCUUGCCCUUGGGC CUCCCCCAGCCCCUCCCCUUCUGGCACCCGUACC CCGGUGUCUUGAAUAAAGUCUGAGUGGGCGG	
GC F MEASLES D8 ORF Sequence, NT	AUGGGUCUCAAGGUGAACGUCUCUGUCAUAUUAUG GCAGUACUGUUAACUCUUAACACCCACCGGUCAAA UCCAUUGGGCAAUUCUCUAAGAUAGGGGUGGUAG GGGUAGGAAGUGCAAGCUACAAGUUAUGACUCGUU CCAGCCAUCAUCAUAGUCUAUAAAGUUAUUGCCCAA UAUAAUCUCUCUACAACAUUGCACGAGGGUAGGGAU GCAGAAUACAGGAGACUACUGAGAACAAGUUCUGGAA CCAAUUAGAGAUAGCAUUAUUGCAAUGACCCAGAAUA UAAGACCCGGUUCAGAGUGUAGCUUCAAGUAGGAGAC ACAAGAGAUUUGCGGGAGUUGUCCUGGCAGGUGCGG CCCUAGGCGUUGCCACAGCUGCCAAAUAACAGCCGG UADUGCACUUCACCAAGUCUAUGGUAUCUCUACAGCC AUCGCACAUCUGAGAGCGAGCCUAGAAACUACUAAUC AGGCAAUUGAGGCAUUCAGACAAGCAGGGCAGGAGA UGADAUUGGCGUGUUCAGGGUGUCCAAAGCAUCAUCA AUAAUAGAGCUGAUAACCGUCUAUGAAUACAUCUUCU GUGAUUUAAUCGGCCAGAAGCUAGGGCUCAAUUGC UCAGAUACUAUACAGAAUUCUGUCUAUUAUUGGCC CAGCUUACGGGACCCCAUUCUGCGGAGAUUCUUAUC CAGGCUUUGAGCUAUGCGCUUGGAGGAGAUUCAAU AAGGUGUUGGAAAGCUCGGAUACAGUGGAGGUGAU CUACUGGGCAUCUAGAGAGCAGAGGAUAAAGGCC GGAAUACUCAUGUCAGACAGAGUCCUACUUAUUGU ACUCAGUAUAGCCUUAUCGACGCUAUCGAGAUUAAG GGGUGAUUGUCCACCGGCUAGAGGGGUCUCGUACA ACAUAGGCUUCACAAGAGUGGUUAACACUGUGCCCAA GUAUGUUGCAACCCAGGGUACUUAUUCUGAAUUUU GADGAGUCAUCAUGCAUUCUUGCCAGAGGGGACUG UGUGCAGCCAGAAUGCCUUGUACCCGAGAGUCCUCU GCUCCAGAAUGCCUCCGGGGUCCACUAAGUUCUGU GCUCGUACACUCGUUUCGGGCUUUCGGGAACCGGU UCAUUAUUAUCACAGGGGAACUUAUAGCCAAUUGUGC AUCAAUCUUUGCAAGUGUUAACAACAGGAACAUC AUAAUACAAGACCCUGACAAGAUCCUAACAUACAUG CUGCCGAUCAUGCCCGGUGGUCGAGGUAUUGGCGU GACC AUCCAGUCGGGAGCAGGAGGUUCCGGACCGU GUGDAUCUUGCACAGGAUUGACCUUGGUCCUCCAUAU CUUUGGAGAGGUUGGACGUAGGACAAAUUCUGGGA AUGCAAUUGCUAAGUUGGAGGAGGCCAAGGAUUGU UGGAGUCAUCGGACCAGAUUUGAGGAGUUGAAAG GUUUUCGAGCACUAGUAUAGUUACAUCUGAUUG CAGUGUGUCUUGGAGGAUUGAUAGGGAUCCCGCUU UADAUUGUUGCUGCAGGGGGCGUUGUAACAAGAGG GAGAACAAAGUUGGUUUGUCAAGACCAGGCCUAAAGCC UGADUCUACAGGAACAUCAAAUCUUAUGUAAGGUC ACUCUGA	73
GC F MEASLES D8 mRNA Sequence (assumes T100 tail) Sequence Length: 1925	G*GGGAAUUAAGAGAGAAAAGAGAGUAGAAGAAA UADAAGAGCCACCAUGGGUCUACAGGUAGACGUCUCU GUCAUUAUCAUGGCAGUAUCUUAACUUCUCAAACAC CCACCGGUCAAAUCUUAUGGGCAUUCUCUUAAGAU AGGGGUGGUAAGGGUAGGAGUGCAAGCUACAAGU UADGACUCGUUCAGCCAUAACUUAUUGCUAUAAG UUAUUGCCAAUUAUACUCUCCUCAAACAAUUGCACGA GGGUAGGGAUUGCAGAAUACAGGAGACUACUGAGAA CAGUUCUGGAACCAAUAAGAGUUGCACUUAUUGCAA UGACCCAGAAUUAAGACCAGGUCUACAGUUGAGCUUC	74

TABLE 13-continued

MeV Nucleic Acid Sequences		SEQ ID
Description	Sequence	NO.
	AAGUAGGAGACACAAGAGAUUUGCGGGAGUUGUCCU GGCAGGUCCGGCCUAGGCGUUGCCACAGCUGUCUCAA AUAACAGCCGGUUAUUGCAUUCACAGUCCAUUGCUGA ACUCUCAAGCCAUCGACAAUCUGAGAGCGAGCCUAGA AACUACUAAUCAGGCAUUGAGGCCAUACAGACAAGCA GGGCAGGAGAUUAUUGGCUUGUUCAGGGUUGCCAA GACUACAUAUAAUAGAGCUGAUACCGUCUAUGAAUC AACUAUCUUGUUAUUAUUCGGCCAGAAGCUAGGGC UCAAAUUGCCUAGAUACUAUACAGAAAUCCUGUCAU AUUUGGCCCCAGCUUACGGGACCCCAUUCUGCGGAG AUAUCUAUCCAGGCUUUGAGCUAUGCCGUUGGAGGA GADAUCAUAUAGGUUUGGAAAGCUCGGAUACAGU GGAGGUGAUUCACUGGGCAUCUAGAGAGCAGAGGA AUAAGGCCCGGAUAACUCACGUCGACACAGAGUCCU ACUDCAUUGUACUCAGUAUAGCCUUAUCGACGCUAUC CGAGAUUAAGGGGGUGAUUUGCCACCGGCUAGAGGG GGUCUCGUACAAACAUAAGGCUUCUAGAGUUGUUAUCC ACUGUGCCCAAGUAUUGUACACCCAGGGUACCUUA UCUCGAAUUUGAUAGAGUCAUCAGCAUUCUAGGCC AGAGGGGACUGUGGCAGCCAGAAUCCUUGUACCCG AUGAGUCCUCUGCCUACAGAAUCCUCGGGGUCCA CUAAGUCCUGUCUCGUACACUCGUUUCGGGUCUUU CGGGAACCGGUUCAUUUAUACAGGGGAACCUAAUA GCCAAUUGUGCAUCAAUUCUUGCAAGUGUUAACAAA CAGGAACAUAUUAUUAUUAUUAUUAUUAUUAUUA AACAUACAUUUGCUGCCGACUCUCCGGUGGUCGAG GUGAAUUGCCUGACCAUCAGUCGGGAGCAGGAGG UAUCCGGACCGUCUGUACUUGCAGAGAUUGACCUCG GUCCUCCCAUUCUUGGAGAGGUUGGACGUAGGGAC AAUUCUGGGAAUGCAAUUGCUAAGUUGGAGGAUGC CAAGGAUUGUUGGAGUCAUCGGACCAAGUAUUGAG GAGUAUGAAAGGUUAUUCGAGCACUAGUAUAGUUUA CAUCCUGAUUGCAGUGUGUCUUGGAGGADUGAUGG GAUCCCGCCUUAAUUAUGUUGCUGAGGGGGCGUUGU AACAAAGAGGGAGAACAAUUGUUAUGUACAGACCA GGCCUAAAGCCUGAUCUACAGGAACAUAUAAUCCU AUGUAAGGUCACUCUGAUGAUUAUAGGCUUGGACCU CGGUGGCCAAGCUUCUUGCCCUUGGGCCUCCCCCA GCCCUCUCUCCUUCUGCACCCGUACCCCGUGGUC UUDGAAUAAAGUCUGAGUGGGCGCAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAUCUAG	75
GC H MEASLES B3 Sequence, NT (5' UTR, ORF, 3' UTR) Sequence Length: 2065	UCAAGCUUUGGACCCUUGUACAGAAGCUAAUACGAC UCACUUAUAGGGAAAUAAGAGAGAAAAGAGAGUAAG AAGAAAUUAUAGAGCCACCAUGUCACCCGCAACGAGAC CGGAUAAUUGCCUUCUACAAGAUAAACCUUAUCCCA AGGGAAGUAGGAUAGUUAUUAACAGAGAAACUUAU UGAUUGACAGACCCUUAUGUUCUGCUGGCUUUCUUGU CGUCAUGUUUCUGAGCUUGAUCGGAUUGCUGGCAAU UGCAGGCAUAGACUUCUACUGGGCAGCCAUUCACCC GCGGAGAUCCAUAAAGCCUUCAGUACCAUUCUGGAUG UGACUAAUCUCCAUUCGAGCAUCAGGUCAAGGACGUGCU GACACCACUCUUAAAUAUCUGGGGAUGAAGUGGGC CUGAGAACACUCUACAGAGAUUACUAGCCUAGUGAAAU UCAUCUCGGACAAGAUUAAAUUCUUAUUCGGAUAG GGAGUACGACUUCAGAGAUUCACUUGGUGCAUCAAC CCGCCAGAGAGGAUCAAUAGAUUUAUUAUUAUUAU GUGCAGAUUGGGCUGCUGAAGAGCUAUGAAUGCAU UGGUGAACUCAACUACUGGGAGCCAGAACACCAC UCAGUUCUAGCUGUCUCAAAGGGAAAUCUGCUCAGGG CCCACUACAUAUCAGAGGUCAAUUCUCAAACUUGUCG UGDCCUUGUUGGACUUGUACUUAAGGUCGAGGUACA AUGUGUACUUAUAGUCAUUAUGACAUCUCCAGGGAAU GUAUGGGGGACCUACCUAGUUGAAAGCCUAAUUCU GAACAGCAAGAGGUCAAGUUGUACAAUCUGAGCAU GUACCGAGUGUUUGAAGUAGGUGUGAUCAAGAAACC GGGUUUGGGGCUCCGGUUGUCCAUUAGACAAACUA UUUUGAGCAACAGUCAGUAUUGGUUCUGGCACUUGU AUGGUGGCUUUGGGGAGCUCAAUCUCGACAGCCUUU GUCACGGGACGAUUCUAUCAUAAUCCCUAUCAGGG	

TABLE 13-continued

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	AUCAGGGAAAGGUGUCAGCUUCCAGCUUGUCAGCUG GGUGUCUGGAAAUCCCAACCGACAUGCAUCCUGGG UCCCCUUUUCRACCGAUGAUCAGUGGUAGAAGGCU UUAACUCUCAUCACAGAGGGUGUCAUCGUCAGCAU CAAGCAAAAUGGGCUGUC CCGACAACGAAACAGAUG ACAAGUUGCGRAUGGAGACAUUGCUUCCAGCAGCGUG UAAAGGUAAAUCRACGACUCUGCGAGAAUCCCGAG UGGGUACCAUUGAAGGAUAACAGGAUCCUUCAUAC GGGGUCCUGUCUGUUGAUCUGAGUCUGACGGUUGAG CUUAAAUCAAAUGCUUCGGGAUUCGGGCCAUUG AUCACACACGGCUCAGGGAUGGACCUAUAACAAUCCA ACUGCAACAUAUGUGUAUUGGCUUGCUAUUCCGCCAAU GAGAAAUCUAGCCUUAAGGGGUAUACAACAUAUGGA GUGGAUACCGAGAUUCAAGGUUAGUCCCAACCUUUC ACUGUCCCAUUAAGGAAGCAGGCCAAGACUCCAUUG CCCAACAUACCUUACUGCGGAGGUGGACGGUGAUGU CAAACUCAGUCCCAACUGGUGAUUCUACCGGUCAA GAUCUCCAAUUGUUUUGGCACCUACGAUACCUCCA GGGUUGAGCAUGUCUGGGUUUAUACGUUAACAGCC CAAGCCGUCAUUUUCUUAUCCUUUAUCUUUUAGGUU GCCUAUAAAGGGGGUCCCAUUCGAAACACRAGUGGA UGUUUCACRUGGGAUAAAACUCUGGUGCCGUCACU UCUGUGUCUUGCGGACUCAGAAUCCGGUGGACUUAU CACUCACUCUGGGAUGGUGGGCAUGGGAGUCAGCUGC ACAGCUACCCGGGAAGAUGGAACCAUUCGCAUAUUA GADAUAUGGCGUGGACCUUGGUGGCACAGCUUCUUGC CUCUUGGGCCUCCCCAGCCUCCUCCUUCUUGC ACCCGUACCCCGUGGUCUUUGAAUAAAGUCUGAGUG GCGGGC	
GC H MEASLES B3 ORF Sequence, NT	AUGDCCCGCAACGAGACCGGAUAAAUGCCUUCACA AAGAUAAACCCUUUAUCCCAAGGGAAGUAGGAUAGUUA UUAACAGAGAACAUUUUAUGAUUGACAGCCUUAUG UUCUGCUGGCUGUUUCUGUUCGUAUGUUUCUGAGCUU GADCGGAUUGCUGGCAUUGCAGGCAUUAAGCUUCA UCGGGCAGCCAUUCACACCGCGGAGAUCCAUAAAAGC CUCAGUACCAUUCUGGAUGGACUAACUCCAUCCGAGC AUCAGGUCAAAGGACGUCUGACACACUUCUUAAAUA CAUCGGGGAUGAAGUGGGCCUGAGAACCCUCAGAGA UUCACUGACCUAGUGAAUUCAGUCUGGACAAAGAUUA AAUUCUUUAUCCCGAUAGGGAGUACGACUUCAGAG AUCUCACUUGGUGCAUCAACCCGCGAGAGGAUCAA ACUAGAUUAUGAUCRAUAUCUGUGCAGAUUGGGUCG UGAAGAGCUCAUUAUGCAUUGGUGAACUCACUCU ACUGGAGACCGAAACAACCAUCAGUUCUAGCUGUC UCAAAGGGAAACUGUCUAGGGCCACUACAACUACAGAG GUCAAUUUCRAAACADUGUCGUGUCUUUGUUGGACUU GUACUUAGGUUGAGGUUAACAUGUGUCAUUCUADAGU CACUUAUGACUCCAGGGAAUGUAUGGGGAACCUAC CUAGUUGAAAAGCCUAAUCUGAACAGCAAGGGUCA GAGUUGUCACRAACUGAGCAUGUACCGAGUUGUUGAA GUAGGUGUGAUCAGAAACCCGGUUUUGGGGUCUCCG GUGUUCCAUAUGACAAACUAUUUUGAGCAACAGUCA GUAAUUGGUUCUGGCAACUGUAUGGUGGUUUUGGGG AGCUCAAACUCGACGCCUUUUGUCAGGGGACGAUUC UAUCAUAUUCCUUAUCAGGGAUCAGGGAAGGGUGU CAGCUUCAGCUCGUAACGUGGGUGUCUGGAAAUCC CCAACCGACAUGCAUUCUGGGUCCCUUUAUCAAAGG AUGAUCCAGUGGUAAGACAGGCUUUACUCUCAUCUCA CAGAGGUGUCAUCGUGACAUAAGCAAAUUGGGCU GUCCCGACAACCGAACAGAUACAAUUGCGAAUUGG AGACAUGCUUCAGCAGGCGUGAAAGGUAAAUAUCA AGCACUCUGCGAGAAUCCGAGUGGGUACCAUUGAAG GADAACAGGAUCCUUAUACGGGUCUGUCUGUUG AUCUGAGUCUGACGGUUGAGCUUAAAUAUAAAUUG CUUCGGGAUUCGGGCCAUUGAUCACACCGGUCAGG GAUGGACCUAUAACAUCACUCGCAACAUGUGUUAU UGGCUGACUAUUCGCGCAUUGAGAAUUAAGCCUUG GCGUAAUCAACACAUUGGAGUGGAUACCGAGAUUCA AGGUUAGUCCCAACUCUUCACUGUCCCAUUAAGGA AGCAGGCGAAGACUGCCAUGCCCCAACAUACCUACCU GCGGAGGUGGACGGUGAUGUCAAAUCAGUUCCAACC	76

TABLE 13-continued

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
GC H MEASLES D8 Sequence, NT (5' UTR, ORF, 3' UTR) Sequence Length: 2065	UCAAGCUUUUGGACCCUCGUACAGAAAGCUAAUACGAC UCACUUAUAGGGAAAUAGAGAGAAAGAAAGCUAAG AAGAAAUUAAGAGCCACCAUGUCACCACAACGAGAC CGGAUAAUAGCCUUCUACAAGACAAACCCCAUCCUA AGGGAAGUAGGAUAGUUAUUAACAGAGAACAUCUUA UGAUUGAUAGACCUUADUUGUUUGCUGGCUGUUCUUA UCGUCAGUUUCUGAGCUUGAUCGGGUUGCUAGCCAU UGCAGGCAUUAAGACUUCUACGGGCAGCCAUUCACC GCAGAGAUCUAAAGCCUCAGCACCACUUCUGGAUG UAACUAAUCUAAUCGAGCAUCAGGUUAAGGACGUGCU GACACCACUCUUAAGAUCAUCGGUGAUGAUGGGC UUGAGGACACCUAGAGAUUCACUGACCUGUGAAGU UCAUCUCUGACAAGAUUAAAUUCUUAUCCGGACAG GGAAUACGACUUAAGAGAUUCACUUGGUGUADCAAC CCGCCAGAGAAUCAAUUGGAUUUAGAUCAAUAC UGUGCAGAUUGGGCUGCUGAAGAACUCAUGAAUGCA UUGGUGAACUCAACUCUACUGGAGACCAGGGCAACCA AUCAGUUCUAGCUGUCUCAAAGGGAAACUGUCAGG GCCACUACAACUAGAGGCCAAUUCUACAACAUUGCG CUGUCCUGUUGGACUUGUAUUUAAGUCGAGGUUAC AADUGUCUUAUAGUCACUAGCAUCCAGGGAA UGUACGGGGAAACUUAACUAGUGGAAAAGCCUAAUC UGAGCAGCAAGGGUCAGAGUUGUCACAAUCGAGCA UGCACCGAGUGUUUAAGUAGGUUUUAUCAGAAUUC CCGGUUUUGGGGCUCCGGUAUCCAUUAGACAACUA UCUUGAGCAACAGUCAGUAAUUAUUCAGCAACUGC AUGGUGUCUUUGGGGAGUCUAGUUCGAGCCUCUCU GUCACAGGGAAGAUUCUUAUCACAUUCCUUAUCAGGG AUCAGGGAAGGUGUCAGCUCCAGCUUGUCAGCUA GGUGUCUGGAAUCCCAACCGACAUUCAUCCUGGG UCCCCUUAUCACCGGAUGAUCCAGUGAUGACAGGCU UUACUCUCUACUCACAGAGGGUUAUCGUCACAAU CAGCAAAUUGGGCUGUCCGACAACCGGACAGAU ACAAGUUGCGAAUGGAGCAUCUUCAGCAAGCGUG UAAGGGUAAAUCCAAGCACUUUGCGAGAAUCCCGAG UGGACACCAUUGAAGGAUACAGGAUUCUUAUACG GGUCUUGUCUUGUUAUCUGAGUCUGACAGUUGAGC UUAAAUCAAAUUGUUUCAGGAUUCGGGCCAUUGA UCACACACGGUUCAGGGAUGGACCUUAACAUAUCCAA CCACAACAUAUGUADUGGCUGACUUAUCCGCCAAUG AAGAACCUGGCCUUAGGUGUAAUCAAACAUUGGAG UGGAUACCGAGAUUAAGGUUAGUCCCAACCUUUA CUGUUCAAUUAAGGAAGCAGGCGAGGACUGCCAUGC CCCAACAUAUCUACUAGCGGAGGUGGAUGGUAUGUC AAACUCAGUUCCAAUCUGGUGAUUCUACUGGUCAG AUCUCAAUAUGUUUCUGGCAACCUACGAUACUUCAG AGUUGAACAUUCUGUAGUUUAUACGUUAACAGCCC AAGCCGCUCAUUUUUUAUUUUAUCCUUUAGGUUG CCUGUAAGGGGGUCCCAUUGAAUUAUAAGUGGAA UGCUCACAUGGGACCAAAACUUCUGGUGCCGUCACU UCUGUGUCUUCGGACUCAGAAUCUGGUGGACUAU UCACUCACUCUGGGAUGGUGGCAUGGGAGUCAGCUG CAGAGCCACUCGGGAAGAUAGAACAGCCGAGAUAG UGADAUAAGGCGGAGCCUGGUGGCCAAGCUUCUG CCCCUUGGGCUCUCCCCAGCCUCCUCCCCUCCUG CACCCGUAACCCCGUGGUCUUUGAAUAAAGUCUGAGU GGGCGGC	78
GC H MEASLES D8 ORF Sequence, NT	AUGUCACCACAACGAGACCGGAUAAUAGCCUUCUACA AAGACAACCCCAUCCUAGGGGAAGUAGGAUAGUUUAU UAAACAGAGAACAUUUUAUGAUUGAUGACCUUAUGU UUUGCUGGCUGUUCUUAUUCGUCAUGUUUCUGAGCUU GADCGGGUUGCUAGCCAUUGCAGGCAUUAAGCUBCAU CGGGCAGCCAUCUACACCGCAGAGAUCAUAAAAGCC UCAGCACCAUUCUGGAGUUAACUAAUCUUAUCGAGCA UCAGGUUAAGGACGUGCUGACACCACUUCUUCAGAU AUCGGUGAUGAAGUGGGCUUGAGGACACUUCAGAGA UUCACUGACCUUAGUGAAGUUAUCUUCGACRAGAUUA AADUCCUUAUCCGGACAGGGAUACGACUUCAGAGA UCUCAUUGGUGUAUCAACCCGCCAGAGAGAUCAA UUGGAUUAUGAUCAAUACUGUCAGAUUGGCUGCU	79

TABLE 13-continued

MeV Nucleic Acid Sequences		
Description	Sequence	SEQ ID NO:
	GAAGAACUCAUGAAUGCAUUGGUGAACUCAACUCUAC UGGAGACCAGGGCAACCAACAGUUCUAGCUGUCUC AAAGGGAAACUGUCAGGGCCACUACAAUCAGAGGC CAADUCUCAACAUUGCCUGUCUCCUGUUGGACUUGU AUUUAAGUCGAGGUUACAAGUGUCAUCUAUAGUCA CUADGACAUCCAGGGAUUGUACGGGGGAACUADCCU AGUGGAAAAGCCUAADUCUGAGCAGCAAAGGGUCAGA GUUGUCACAACUGAGCAUGCACCCGAGUGUUUGAAGU AGGUGUUUUCRGAARUCCGGGUUUGGGGUCUCCGGU AUUCCAUUGACAACUAUCUUGAGCAACCAGUCAGU AAGUAUUUCAGCAACUGCAUGGUGGUUUUGGGGAG CUCAAGUUCGACGCCUCUGUCACAGGGAAGAUUCUA UCACA AUUCCUUAUCAGGGAUCAGGGAAGGUGUCAG CUUCCAGCUUGUCAAGCUAGGUGUCUGGAAUCCCA ACCGACAUUCRAUCCUGGGUCCCCUUAUACCGGAUG AUCCAGUGAUGACAGGCUUACCUUCUADUCACAG AGGCGUUAUCGUGACAUAACAGCAAAUUGGCUUGUC CCGACAAACCGGACAGAUACAGUUGGARUUGGAGA CADGCUUCAGCAGGCGUGUAGGGUAAAUCCAAGC ACUUUGCGAGAAUCCGAGUGGACACCAUUGAAGGAU AACAGGAUUCUUCAUACGGGUUUCUGUCUGUUGAUC UGAGUCUGACAGUUGAGCUAAAUAUAAAUUGUUU CAGGAUUCCGGGCCAUUGAUACACACCGGUUCAGGGAU GGACCUAUACAAAUCACACCAACAUAUUGUUAUUGG CUGACUAUCCCGCCAAUGAAGAACCUGGCCUUAGGGU UAADUCAACACAUUGGAGUGGAUACCGAGAUUAAGG UUAGUCCCAACCUUCUUCAGUUCCAUAUAGGAAGC AGGGGAGGACUGCCADGCCCAACAUAUCCUACCGCG GAGGUGGAUGGUGAUGUCAAAUCAGUUCCAAUCUG GUGAUUCUACUUGGUCAGAUUCUCAAUAUGUUCUGG CAACCUACGAUACUUCAGAGUUGAACUUGCUGUAGU UUADUACGUUUACAGCCCAAGCCGCUCAUUUUUUAUC UUUUUUCUUUUAGGUUGCCUGUAAGGGGGUCCCA UUGAAUUAACAGUGGAUUGCUACAUGGGACCAAA AACUCUGGUGCCGUCAUUCUGUGUCUUUGCGACUC AGAAUCUGGUGGACAUUACUACUCUCUGGGUUGGU GGCAUUGGGAGUCAGUCACAGCCACUCGGGAAGAU GGAACCAGCCGAGAUAG	
GC_H_MEASLES_D8 mRNA Sequence (assumes T100 tail) Sequence Length: 2126	G*GGGAAUUAAGAGAGAAAAGAGUAAGAAAGAAA UADAAGAGCCACCAUGUCACCACAACGAGACCGGAUA AADGCCUUCUACAAGACAACCCCAUCCUAAGGGAA GUAGGAUAGUUAUUAAACAGAGAACUUCUUAUGAUUG AUAGACCUUAUGUUUUGCUGGCUGUUCUAUUCGUCA UGUUUCUGAGCUUGAUCCGGGUUGCUAGCCAUUGCAG GCAUUAAGACUUCUACGGGCAGCCAUUCACACCGCAGA GADCCAUAAAAGCCUACGACCAACUUCGGAUGUAACU AACUCAAUCCGAGCAUCAGGUUAAGGACGUGCUGACAC CACUCUUCAGAUUCADCGGUGAUGAAGUGGGCUUGA GGACACCUCAAGAUUCAUGACCUAGUGAAGUUCAU CUCUGACAAGAUUAAAUCUUAUUCGGGACAGGGAA UACGACUUCAGAGAUUCUACUUGGUGUAUCAACCCGC CAGAGAGAAUCAAUUGGAUUUGAUCAAUACUGUG CAGAUUGGCGUGCUGAAGAACUCAUGAADUGCAUUGG UGAACUCAACUCUACUGGAGACCGGGCAACCAAUCA GUUCCUAGCUGUCUCAAGGGAAACUUCACGGGCCCC ACUACAUCAGAGGCAAUUCUCAAACAUUGUCGUCU CCCUGUUGGACUUGUAUUUAAGUCGAGGUUACAUAUG UGUCAUCUAUAGUCACUAUGACAUCACAGGGAAUGUA CGGGGGAACUUAUCCUAGUGGAAAAGCCUAUUCUGAGC AGCAAAGGGUCAGAGUUGUCAACAUCAGCAUUGCACC GAGUGUUUGAAGUAGGUGUUUCAGAAAUCGGGUU UGGGGGCUCGGUAUUUCAUUGACAACUAUCUUGA GCAACCAGUCAGUAUGAUAUUCAGCAAUCGCAUGGUG GCUUUUGGGGAGCUCAAUUUCGAGCCUCUGUCACA GGGAAGAUUCUAUCACAUAUCCUUAUCAGGGAUCAGG GAAAGGUGUCAGUCUCCAGCUGUCAGGCUAGGUGUC UGGAAAUCCCCAACCGACAUCGAAUCCUGGGUCCCC UADCAACGGAGUAGUCCAGUGAUGACAGGCUUUAACU CUCAUUCACAGAGGCUUUAUCGUCACAUCAGCA AAUUGGGCUGUCCCGACAACCGGACAGAUAGCAAGU UGCGAAUGGAGACAUGCUUCAGCAGGGCUGUAAGG	80

TABLE 13-continued

MeV Nucleic Acid Sequences		SEQ ID NO:
Description	Sequence	
	GUAAAAUCCAAGCACUUUGCGAGAAUCCCGAGUGGAC ACCAUUGAAGGAUAACAGGAUUCUUCAUACGGGGUC UUGUCUGUUGAUCUGAGUCUGACAGUUGAGCUAAA AUCAAAAUUGUUUCAGGAUUCGGGCCAUUGAUCACAC ACGGUUCAGGGAUGGACCUAUAACAAUCCAACCAAA CAADAUGUAUUGGCUGACUAUCCCGCCAAUGAAGAAC CUGGCCUUAGGUGUAAUCAACACAUUGGAGUGGAUA CCGAGAUUCAAGGUUAGUCCCAACCUCUUCACUGUUC CAUUUAAGGARGCRGGCGAGGACUGCCAUUGCCCCAAC AUACCUACCCUGCGGAGGUGGAUGGUGAUGUCFAACUC AGUUCCAAUCUGGUGAUUCUACCCUGGCAAGAUUCC ADAUGUUCUGGCAACCUACGAUACUUCAGAGUUGA ACAUUCUGUAGUUUADUACGUUACAGCCCCAAGCCGC UCAUUUUUUUUUUUUUUUUUUUUUUUUUUUUUUUUUU AGGGGGUCCCCAUUGAAUUAACAAGUGGAUUGCUUC ACAUGGGACCAAAAACUCUGGUGCCGUCACUUCUGUG UGCUUGCGGACUCAGAAUCUGGUGGACAUUACUCA CUCUGGGAUGGUGGGCAUGGGAGUCAGCUGCACAGCC ACUCGGGAAGAUUGGAACAGCCGACAGUAGUUA UAGGCUGGAGCCUCGGUGGCCAGCUUCUUGCCCCUU GGGCCUCCCCCAGCCUCCUCCUCCUCCUCCUCCUCCG UACCCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCGG CAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAUUAG	

TABLE 14

MeV Amino Acid Sequences		SEQ ID NO:
Description	Sequence	
GC F MEASLES B3.1 ORF Sequence, AA	MGLKVNVSVMFMAVLLTLQTPAGQIHWGNLSKIGVV GIGSASYKVMTRSSHQSLVIKLMFNITLLNNCTRVEIA EYRLLRITVLEPIRDALNAMTQNIIRPVQSVASSRRHK RFAGVVLAGAALGVATAAQITAGIALHRSMLNSQAID NLRASLETTNQAIETAIQAGQEMILAVQGVQDYINNE LIPSMNQLSCDLIGQKLGKLLRYYTEILSLFGPSLRDP ISABISIQALSYALGGDINKVLEKLGYSGGDLLGILES RGIKARITHVDTESYFIVLSIAYPTLSEIKGVIHVRLEGVS YNIGSQEWYTTVPKYVATQGYLISNFEDESSCTFMPEG TVCSQNALYPMSPLLQECLEGRSTKSCARTLVSGSFGN RFILSQGNLIANCASILCKCYTTGTIINQDPDKILTYIAA DRCPVVEVNGVTTIQVGSRRYPDAVYLHRIDLGPPIISLE RLDVGTNLGNIAKLEDAKELLESDQILRSMKGLSST SIVYILIAVCLGGLIGIPTLICCCGRGNKKGQVGMSP PGLKPDLTGTSKSYVRSI*	47
GC F MEASLES D8 ORF Sequence, AA	MGLKVNVSVMFMAVLLTLQTPGQIHWGNLSKIGVVG VGSASYKVMTRSSHQSLVIKLMFNITLLNNCTRVGIAE YRLLRITVLEPIRDALNAMTQNIIRPVQSVASSRRHKR FAGVVLAGAALGVATAAQITAGIALHQSMNSQAIDN LRSASLETTNQAIETAIQAGQEMILAVQGVQDYINNELI PSMNQLSCDLIGQKLGKLLRYYTEILSLFGPSLRDPIS AEISIQALSYALGGDINKVLEKLGYSGGDLLGILES RGIKARITHVDTESYFIVLSIAYPTLSEIKGVIHVRLEGVS YNIGSQEWYTTVPKYVATQGYLISNFEDESSCTFMPEG VCSQNALYPMSPLLQECLEGRSTKSCARTLVSGSPGNR RFILSQGNLIANCASILCKCYTTGTIINQDPDKILTYIAA HCPVVEVNGVTTIQVGSRRYPDAVYLHRIDLGPPIISLER LDVGTNLGNIAKLEDAKELLESDQILRSMKGLSSTS IYVYILIAVCLGGLIGIPALICCCGRGNKKGQVGMSP GLKPDLTGTSKSYVRSI*	48
GC H MEASLES B3 ORF Sequence, AA	MSPQRDRINAFYKDNPNYPKGSRIVINREHLMIDRPYVL LAVLFVFMFLSLIGLLAIAGIRLHRAAIYTAETHKSLSTN LDVTNSIEHQVKDVLTPLPKIGDEVGLRTPQRPTDLV KFISDKIKFLNPDREYDFRDLTWCINPPERIKLDYDQY	49

TABLE 14-continued

MeV Amino Acid Sequences		
Description	Sequence	SEQ ID NO:
	CADVAABELMNALVNSTLLETRTTTQPLAVSKGNCS GPTTIRGQFSNMSLSLDDLVLGRGYNVSSIVTMTSQG MYGGTYLVEKPNLNSKGSLSQLSMYRVFEVGVIRNP GLGAPVPHMTNYFEQPVSNGLGNCMVALGELKLAAL CHGDDSIIPYQGSKGVSFQLVKLVGWSPTDMQSW VPLSTDDPVDRLYLSHRGV IADNQAQWAVPTTRT DDKLRMETCFQACKGKI QALCENPEWVPLKDNRI PS YGVLSVDLSLTVELKIKIASGFGPLITHGSGMDLYKSN CMNVVWLTIPPMRNLALGVINTLEWIPRFKVS PNLFV PIKEAGEDCHAPTYLPAEVDGDKLSSNLVILPGQDL QYVLATYDTSRVEHAVVYVYVSPSRFSYFVPRLPK GVPIELQVECFDQKLVCRHFCVLADSESGGLITHS GMVGMGVSCTATREDGTNR*	
GC H MEASLES D8 ORF Sequence, AA	MSPQRDRINAFYKDNPHPKGSRIVINREHLMIDRPYVL LAVLFVMFLSLIGLLAIAGIRLHRAAIYTAEIHKSLSTN LDVTHSIEHQVKDVLTPLEFKIIGDEVGLRTPQRFDTLV KPI SDKI KPLNPDREYDPRDLTWCINPPERIKLDYDQY CADVAABELMNALVNSTLLETRATHQPLAVSKGNCS GPTTIRGQFSNMSLSLDDLVLGRGYNVSSIVTMTSQGM YGGTYLVEKPNLSSKGSLSQLSMHRVFEVGVIRNPG LGAPVPHMTNYLEQPVSNDFSNCMVALGELKFAALC HREDSITIPYQGSKGVSFQLVKLVGWSPTDMQSW VPLSTDDPVIDRLYLSHRGV IADNQAQWAVPTTRTD DKLRMETCFQACKGKI QALCENPEWVPLKDNRI PSY GVLSVDLSLTVELKIKIVSGFGPLITHGSGMDLYKSNH NMVWLTIPPMKNLALGVINTLEWIPRFKVS PNLFV PIKEAGEDCHAPTYLPAEVDGDKLSSNLVILPGQDL QYVLATYDTSRVEHAVVYVYVSPSRFSYFVPRLPV RGVPIELQVECFDQKLVCRHFCVLADSESGGHITH SGMVGMGVSCTATREDGTSRR*	50

TABLE 15

MeV NCBI Accession Numbers (Amino Acid Sequences)		
Type	Virus Name	GenBank Accession
hemagglutinin	hemagglutinin [Measles virus strain Moraten]	AAF85673.1
hemagglutinin	hemagglutinin [Measles virus strain Rubeovax]	AAF85689.1
hemagglutinin	hemagglutinin [Measles virus]	AAF89824.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAA91369.1
hemagglutinin	hemagglutinin [Measles virus]	BAJ23068.1
hemagglutinin	hemagglutinin protein [Measles virus]	BAJ39848.1
hemagglutinin	hemagglutinin [Measles virus]	AAA50551.1
hemagglutinin	RecName: Full = Hemagglutinin glycoprotein	P08362.1
hemagglutinin	hemagglutinin [Measles virus]	AAB63802.1
hemagglutinin	hemagglutinin [Measles virus]	AAA56650.1
hemagglutinin	hemagglutinin [Measles virus]	AAA56642.1
hemagglutinin	hemagglutinin [Measles virus]	AAA74936.1
hemagglutinin	hemagglutinin protein [Measles virus]	BAI156665.1
hemagglutinin	hemagglutinin [Measles virus]	ACC86105.1
hemagglutinin	hemagglutinin [Measles virus strain Edmonston-Zagreb]	AAF85697.1
hemagglutinin	hemagglutinin [Measles virus]	AAR89413.1
hemagglutinin	hemagglutinin [Measles virus]	AAA56653.1
hemagglutinin	RecName: Full = Hemagglutinin glycoprotein	P35971.1
hemagglutinin	Hemagglutinin [Measles virus]	CAB94916.1
hemagglutinin	hemagglutinin [Measles virus]	AAC03036.1
hemagglutinin	hemagglutinin [Measles virus]	AAF85681.1
hemagglutinin	Hemagglutinin [Measles virus]	CAB94927.1
hemagglutinin	Hemagglutinin [Measles virus]	CAB94925.1
hemagglutinin	hemagglutinin protein [Measles virus]	BAJ39835.1
hemagglutinin	Hemagglutinin [Measles virus]	CAB94931.1
hemagglutinin	hemagglutinin [Measles virus genotype A]	AF08471.2.1
hemagglutinin	hemagglutinin [Measles virus]	AAA56639.1
hemagglutinin	Hemagglutinin [Measles virus]	CAB94926.1
hemagglutinin	hemagglutinin protein [Measles virus]	BAJ39836.1
hemagglutinin	Hemagglutinin [Measles virus]	CAB94929.1
hemagglutinin	RecName: Full = Hemagglutinin glycoprotein	P06830.1

TABLE 15-continued

Type	Virus Name	GenBank Accession
hemagglutinin	Hemagglutinin [Measles virus]	CAB94928.1
hemagglutinin	hemagglutinin protein [Measles virus]	BAB39837.1
hemagglutinin	hemagglutinin [Measles virus]	AA74935.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43780.1
hemagglutinin	hemagglutinin [Measles virus]	BA06952.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43815.1
hemagglutinin	hemagglutinin [Measles virus]	AAF28390.1
hemagglutinin	Hemagglutinin [Measles virus]	CAB94923.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43785.1
hemagglutinin	hemagglutinin [Measles virus]	ABD34001.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43782.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43781.1
hemagglutinin	hemagglutinin [Measles virus]	BAI122353.1
hemagglutinin	hemagglutinin [Measles virus]	AAC35878.2
hemagglutinin	hemagglutinin protein [Measles virus]	AA186996.1
hemagglutinin	hemagglutinin [Measles virus]	CAA76066.2
hemagglutinin	hemagglutinin [Measles virus]	AAA46428.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43803.1
hemagglutinin	Hemagglutinin [Measles virus]	CAB94918.1
hemagglutinin	hemagglutinin [Measles virus]	AAF72162.1
hemagglutinin	hemagglutinin [Measles virus]	AA70154.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43776.1
hemagglutinin	hemagglutinin [Measles virus genotype D4]	AC178395.1
hemagglutinin	hemagglutinin [Measles virus genotype D7]	AA102030.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43789.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43774.1
hemagglutinin	Hemagglutinin [Measles virus]	CAB94920.1
hemagglutinin	Hemagglutinin [Measles virus]	CAB94922.1
hemagglutinin	hemagglutinin [Measles virus]	ABB59491.1
hemagglutinin	hemagglutinin protein [Measles virus]	BAB39843.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43804.1
hemagglutinin	hemagglutinin [Measles virus]	AAX52048.1
hemagglutinin	Hemagglutinin [Measles virus]	CAB94930.1
hemagglutinin	hemagglutinin [Measles virus]	AA74526.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43814.1
hemagglutinin	hemagglutinin [Measles virus]	ABB59493.1
hemagglutinin	hemagglutinin [Measles virus genotype D4]	AA102019.1
hemagglutinin	Hemagglutinin [Measles virus]	CAB94919.1
hemagglutinin	hemagglutinin protein [Measles virus]	AA186997.1
hemagglutinin	hemagglutinin [Measles virus genotype C2]	AA102017.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43769.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43808.1
hemagglutinin	hemagglutinin [Measles virus]	BA097032.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43805.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43777.1
hemagglutinin	hemagglutinin [Measles virus]	AA167793.1
hemagglutinin	hemagglutinin [Measles virus]	AAF89816.1
hemagglutinin	hemagglutinin [Measles virus genotype D4]	AA102020.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43786.1
hemagglutinin	hemagglutinin protein [Measles virus strain MVi New Jersey, USA 45.05]	AF40452.1
hemagglutinin	hemagglutinin [Measles virus]	AA74531.1
hemagglutinin	hemagglutinin [Measles virus]	AAB63800.1
hemagglutinin	hemagglutinin [Measles virus]	AA021711.1
hemagglutinin	hemagglutinin [Measles virus genotype D8]	AF27189.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43810.1
hemagglutinin	hemagglutinin [Measles virus]	AAF89817.1
hemagglutinin	hemagglutinin [Measles virus genotype D6]	AA102022.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43800.1
hemagglutinin	hemagglutinin protein [Measles virus genotype B3]	AG117219.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43770.1
hemagglutinin	hemagglutinin protein [Measles virus strain MVi Texas, USA 4.07]	AF40444.1
hemagglutinin	hemagglutinin [Measles virus]	AAX52047.1
hemagglutinin	hemagglutinin [Measles virus]	AAB63794.1
hemagglutinin	hemagglutinin [Measles virus]	AAB63796.1
hemagglutinin	hemagglutinin [Measles virus]	AA74528.1
hemagglutinin	hemagglutinin [Measles virus]	AAB63774.1
hemagglutinin	hemagglutinin [Measles virus]	AAB63795.1
hemagglutinin	hemagglutinin [Measles virus]	AA74519.1
hemagglutinin	hemagglutinin protein [Measles virus]	CAB43778.1
fusion protein	fusion protein [Measles virus strain Moraten]	AAF85672.1
fusion protein	fusion protein [Measles virus]	AAA56645.1

TABLE 15-continued

Type	Virus Name	GenBank Accession
fusion protein	fusion protein [Measles virus strain Rubecovax]	AAF85688.1
fusion protein	fusion protein [Measles virus]	AAF85680.1
fusion protein	fusion protein [Measles virus]	AIJ30359.1
fusion protein	fusion protein [Measles virus]	BAA09957.1
fusion protein	fusion protein [Measles virus]	AAV84957.1
fusion protein	fusion protein [Measles virus McV-cGFP 1xln-tag]	AIJ16636.1
fusion protein	fusion protein [Measles virus]	ABY58018.1
fusion protein	fusion protein [Measles virus]	BAA19838.1
fusion protein	fusion protein [Measles virus]	AAA56641.1
fusion protein	F protein [Measles virus]	ABK40529.1
fusion protein	fusion protein [Measles virus]	AAA56652.1
fusion protein	fusion protein [Measles virus]	ABY58017.1
fusion protein	fusion protein [Measles virus]	ABB371645.1
fusion protein	fusion protein [Measles virus]	NP_056922.1
fusion protein	fusion protein [Measles virus strain AIK-C]	AAF85664.1
fusion protein	fusion protein [Measles virus]	BAJ360865.1
fusion protein	fusion protein [Measles virus]	BAA09950.1
fusion protein	fusion protein [Measles virus strain MVi New York,USA 26.09/3]	AEP40403.1
fusion protein	fusion protein [Measles virus]	AAA74934.1
fusion protein	fusion protein [Measles virus]	CAB38075.1
fusion protein	fusion protein [Measles virus strain MVi Texas,USA 4.07]	AIJ40443.1
fusion protein	fusion protein [Measles virus]	AAF02695.1
fusion protein	fusion protein [Measles virus]	AAF02696.1
fusion protein	fusion protein [Measles virus]	AAI99301.1
fusion protein	fusion protein [Measles virus]	ABB71661.1
fusion protein	fusion protein [Measles virus]	BAK08874.1
fusion protein	fusion protein [Measles virus]	AAF02697.1
fusion protein	fusion protein [Measles virus genotype D4]	AFY12704.1
fusion protein	fusion protein [Measles virus strain MVi California,USA 16.03]	AIJ40467.1
fusion protein	fusion protein [Measles virus genotype D8]	AJN07989.1
fusion protein	fusion protein [Measles virus]	AAA46421.1
fusion protein	fusion protein [Measles virus]	AAA56638.1
fusion protein	fusion protein [Measles virus strain MVi Virginia,USA 15.09]	AEP40419.1
fusion protein	fusion protein [Measles virus genotype D8]	AJJ27200.1
fusion protein	fusion protein [Measles virus genotype D8]	AFY12695.1
fusion protein	fusion protein [Measles virus genotype D8]	AJJ27248.1
fusion protein	fusion protein [Measles virus genotype D8]	AJJ27224.1
fusion protein	fusion protein [Measles virus]	AAI99300.1
fusion protein	fusion protein [Measles virus]	BAI196592.1
fusion protein	fusion protein [Measles virus strain MVi California,USA 8.04]	AIJ40459.1
fusion protein	fusion protein [Measles virus genotype D8]	AIG94081.1
fusion protein	fusion protein [Measles virus]	BAA09951.1
fusion protein	fusion protein [Measles virus genotype D8]	AIJ27194.1
fusion protein	fusion protein [Measles virus]	BAA33871.1
fusion protein	fusion protein [Measles virus strain MVi Washington,USA 18.08/1]	AEP40427.1
fusion protein	fusion protein [Measles virus]	ABY21182.1
fusion protein	fusion protein [Measles virus genotype D8]	AJJ27284.1
fusion protein	fusion protein [Measles virus]	AC_A09725.1
fusion protein	fusion protein [Measles virus genotype D8]	AJJ27314.1
fusion protein	fusion protein [Measles virus genotype G3]	AFY12712.1
fusion protein	fusion protein [Measles virus genotype D8]	AJJ27368.1
fusion protein	RecName: Full = Fusion glycoprotein F0; Contains: RecName: Full = Fusion glycoprotein F2; Contains: RecName: Full = Fusion glycoprotein F1; Flags: Precursor	P35973.1
fusion protein	fusion protein [Measles virus genotype H1]	AIG53713.1
fusion protein	unnamed protein product [Measles virus]	CAA34588.1
fusion protein	fusion protein [Measles virus]	CAA76888.1
fusion protein	fusion protein [Measles virus genotype B3.1]	AIY55563.1
fusion protein	fusion protein [Measles virus]	ADQ17330.1
fusion protein	fusion protein [Measles virus genotype H1]	AIG53703.1
fusion protein	fusion protein [Measles virus genotype B3]	AGAI17208.1
fusion protein	fusion protein [Measles virus]	AAI29688.1
fusion protein	fusion protein [Measles virus genotype H1]	AIG53706.1
fusion protein	fusion protein [Measles virus genotype H1]	AIG53701.1
fusion protein	fusion protein [Measles virus genotype B3]	AJJ27092.1
fusion protein	fusion protein [Measles virus genotype H1]	AIG53714.1
fusion protein	fusion protein [Measles virus genotype H1]	AIG53694.1

TABLE 15-continued

MeV NCBI Accession Numbers (Amino Acid Sequences)		
Type	Virus Name	GenBank Accession
fusion protein	fusion protein [Measles virus genotype III]	AIG53668.1
fusion protein	fusion protein [Measles virus]	ACC86094.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53670.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53707.1
fusion protein	fusion protein [Measles virus genotype B3]	AGA17216.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53671.1
fusion protein	fusion protein [Measles virus strain MVi New Jersey,U.S.A 45.05]	AI:P40451.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53684.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53688.1
fusion protein	fusion protein [Measles virus genotype B3]	AGA17214.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53683.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53667.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53686.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53685.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53681.1
	unnamed protein product [Measles virus]	CAA34589.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53678.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53710.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53669.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53664.1
fusion protein	fusion protein [Measles virus]	AAA50547.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53679.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53709.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53672.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53697.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53689.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53676.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53675.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53663.1
fusion protein	fusion protein [Measles virus]	BAA19841.1
fusion protein	fusion protein [Measles virus]	AAF02701.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53680.1
fusion protein	fusion protein [Measles virus genotype III]	AIG53674.1
C protein	C protein [Measles virus strain Moraten]	AAF85670.1
C protein	RecName: Full = Protein C	P03424.1
C protein	C protein [Measles virus]	ACN54404.1
C protein	C protein [Measles virus]	ACN54412.1
C protein	RecName: Full = Protein C	P35977.1
C protein	C protein [Measles virus]	AAF85678.1
C protein	C protein [Measles virus]	ABD33998.1
C protein	unnamed protein product [Measles virus]	CAA34586.1
C protein	C protein [Measles virus]	BAJ51786.1
C protein	C protein [Measles virus]	BAA33869.1
C protein	virulence factor [Measles virus]	ABO69700.1
C protein	C protein [Measles virus]	NP_056920.1
C protein	C protein [Measles virus]	ADG17333.1
C protein	C protein [Measles virus]	ACC86082.1
C protein	C protein [Measles virus]	BAA33875.1
C protein	C protein [Measles virus]	ABY21189.1
C protein	C protein [Measles virus]	BAJ98296.1
C protein	C protein [Measles virus]	ADU17782.1
C protein	C protein [Measles virus strain MVi Virginia,U.S.A 15.09]	AEP40417.1
C protein	C protein [Measles virus]	ADU17814.1
C protein	C protein [Measles virus]	ADU17798.1
C protein	C protein [Measles virus genotype D4]	AFY12700.1
C protein	C protein [Measles virus]	ADU17784.1
C protein	C protein [Measles virus strain MVi California,U.S.A 16.03]	AEP40465.1
C protein	C protein [Measles virus]	ABB71643.1
C protein	C protein [Measles virus]	AEI91027.1
C protein	C protein [Measles virus]	ADU17874.1
C protein	C protein [Measles virus]	ADU17903.1
C protein	C protein [Measles virus]	CAA34579.1
C protein	C protein [Measles virus]	ADU17790.1
C protein	C protein [Measles virus]	ADU17800.1
C protein	C protein [Measles virus]	ABB71667.1
C protein	unnamed protein product [Measles virus]	CAA34572.1
C protein	C protein [Measles virus strain MVi Arizona,U.S.A 11.08.2]	AJ:P40433.1
C protein	C protein [Measles virus]	ADU17830.1
C protein	C protein [Measles virus]	ADU17947.1

TABLE 15-continued

Type	Virus Name	GenBank Accession
C protein	C protein [Measles virus]	ADU17818.1
C protein	C protein [Measles virus strain MVi New Jersey,USA 45.05]	AF040449.1
C protein	C protein [Measles virus strain MVi Texas,USA 4.07]	AF040441.1
C protein	C protein [Measles virus]	ADU17864.1
C protein	C protein [Measles virus]	ADU17838.1
C protein	C protein [Measles virus]	ADU17881.1
C protein	C protein [Measles virus strain MVi Washington,USA 18.08.1]	AF040425.1
C protein	C protein [Measles virus]	ADU17927.1
C protein	C protein [Measles virus]	ADU17953.1
C protein	C protein [Measles virus]	ADU17889.1
C protein	C protein [Measles virus]	ADU17963.1
C protein	C protein [Measles virus]	ADU17893.1
C protein	C protein [Measles virus]	ADU17820.1
C protein	C protein [Measles virus]	ABB71651.1
C protein	C protein [Measles virus]	ADU17786.1
C protein	C protein [Measles virus]	ADU17862.1
C protein	C protein [Measles virus]	ADU17923.1
C protein	C protein [Measles virus]	ADU17959.1
C protein	C protein [Measles virus]	ADU17951.1
C protein	C protein [Measles virus]	ADU17916.1
C protein	C protein [Measles virus]	ADU17957.1
C protein	C protein [Measles virus]	ADU17925.1
C protein	C protein [Measles virus]	ADU17901.1
C protein	C protein [Measles virus]	ADU17887.1
C protein	C protein [Measles virus]	ADU17832.1
C protein	C protein [Measles virus]	ADU17891.1
C protein	C protein [Measles virus]	ADU17961.1
C protein	C protein [Measles virus]	ADU17872.1
C protein	C protein [Measles virus]	ADU17929.1
C protein	C protein [Measles virus]	ADU17908.1
C protein	C protein [Measles virus]	ADU17910.1
C protein	C protein [Measles virus]	ADU17921.1
C protein	C protein [Measles virus]	ADU17824.1
C protein	C protein [Measles virus strain MVi Pennsylvania,USA 20.09]	AF040473.1
C protein	C protein [Measles virus]	ADU17828.1
C protein	C protein [Measles virus]	ADU17812.1
C protein	C protein [Measles virus genotype D8]	AFY12692.1
C protein	nonstructural C protein [Measles virus]	BA59559.1
C protein	RecName: Full = Protein C	Q90794.1
C protein	nonstructural C protein [Measles virus]	ADU17934.1
C protein	nonstructural C protein [Measles virus]	AC166773.1
C protein	C protein [Measles virus genotype G3]	AFY12708.1
C protein	RecName: Full = Protein C	P26035.1
C protein	C protein [Measles virus]	BAAN4128.1
nucleoprotein	RecName: Full = Nucleoprotein; AltName: Full = Nucleocapsid protein; Short = NP; Short = Protein N	Q77M43.1
nucleoprotein	nucleocapsid protein [Measles virus strain Rubcovax]	AAF85683.1
nucleoprotein	RecName: Full = Nucleoprotein; AltName: Full = Nucleocapsid protein; Short = NP; Short = Protein N	Q89933.1
nucleoprotein	nucleocapsid protein [Measles virus strain AIR-C]	AAF85659.1
nucleoprotein	nucleoprotein [Measles virus]	AB154102.1
nucleoprotein	nucleoprotein [Measles virus]	AAA56643.1
nucleoprotein	nucleoprotein [Measles virus]	AAC03050.1
nucleoprotein	nucleoprotein [Measles virus]	AA18990.1
nucleoprotein	nucleoprotein [Measles virus]	AAA56640.1
nucleoprotein	RecName: Full = Nucleoprotein; AltName: Full = Nucleocapsid protein; Short = NP; Short = Protein N	P35972.1
nucleoprotein	RecName: Full=Nucleoprotein; AltName: Full = Nucleocapsid protein; Short = NP; Short = Protein N	P10050.1
nucleoprotein	N protein [Measles virus]	BAB60956.1
nucleoprotein	RecName: Full = Nucleoprotein; AltName: Full = Nucleocapsid protein; Short = NP; Short = Protein N	BI1AAA7.1
nucleoprotein	nucleoprotein [Measles virus]	AAA18991.1
nucleoprotein	nucleoprotein [Measles virus]	CA1346894.1

TABLE 15-continued

MeV NCBI Accession Numbers (Amino Acid Sequences)		
Type	Virus Name	GenBank Accession
nucleoprotein	nucleoprotein [Measles virus]	CAB46871.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46872.1
nucleoprotein	nucleoprotein [Measles virus]	ABC49606.1
nucleoprotein	nucleocapsid protein [Measles virus]	AAA75494.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46883.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46892.1
nucleoprotein	unnamed protein product [Measles virus]	CAA34584.1
nucleoprotein	nucleoprotein [Measles virus]	AAA18997.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46863.1
nucleoprotein	nucleoprotein [Measles virus]	AF30352.1
nucleoprotein	nucleoprotein [Measles virus]	ABI54103.1
nucleoprotein	nucleocapsid protein [Measles virus]	AAA46433.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46902.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46873.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46906.1
nucleoprotein	nucleoprotein [Measles virus]	AAA74547.1
nucleoprotein	nucleoprotein [Measles virus]	AAA74537.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46862.1
nucleoprotein	nucleocapsid protein [Measles virus]	BAA09961.1
nucleoprotein	nucleoprotein [Measles virus]	AAO15875.1
nucleoprotein	nucleoprotein [Measles virus]	AAO15871.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46882.1
nucleoprotein	nucleoprotein [Measles virus]	CAB60124.1
nucleoprotein	nucleoprotein [Measles virus]	ABI54104.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46869.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46880.1
nucleoprotein	nucleoprotein [Measles virus]	AAA74541.1
nucleoprotein	nucleocapsid protein [Measles virus strain MVi New Jersey,USA 45.05]	AF40446.1
nucleoprotein	nucleoprotein [Measles virus]	ABI54110.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46903.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46899.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46901.1
nucleoprotein	nucleocapsid protein [Measles virus]	ABB71640.1
nucleoprotein	nucleoprotein [Measles virus]	CAB60113.1
nucleoprotein	nucleoprotein [Measles virus]	CAB60114.1
nucleoprotein	nucleoprotein [Measles virus]	CAB60116.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46895.1
nucleoprotein	nucleoprotein [Measles virus]	CAB60121.1
nucleoprotein	nucleoprotein [Measles virus]	ABI54111.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46889.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46898.1
nucleoprotein	nucleoprotein [Measles virus genotype B3]	ALE27083.1
nucleoprotein	nucleoprotein [Measles virus]	CAB60118.1
nucleoprotein	nucleocapsid protein [Measles virus]	CAA34570.1
nucleoprotein	nucleoprotein [Measles virus]	AAC29443.1
nucleoprotein	nucleocapsid protein [Measles virus strain MVi Washington,USA 18.08.1]	AF40422.1
nucleoprotein	nucleoprotein [Measles virus]	AAO15872.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46874.1
nucleoprotein	nucleoprotein [Measles virus]	AAA74550.1
nucleoprotein	nucleocapsid protein [Measles virus]	ABB71648.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46900.1
nucleoprotein	nucleoprotein [Measles virus]	BAI122440.1
nucleoprotein	nucleocapsid protein [Measles virus]	AAA46432.1
nucleoprotein	nucleocapsid protein [Measles virus]	BAA33867.1
nucleoprotein	nucleoprotein [Measles virus]	AAA74539.1
nucleoprotein	nucleoprotein [Measles virus]	CAB60115.1
nucleoprotein	nucleoprotein [Measles virus]	CAB60123.1
nucleoprotein	nucleocapsid protein [Measles virus]	ABB71664.1
nucleoprotein	nucleoprotein [Measles virus]	CAB60125.1
nucleoprotein	nucleoprotein [Measles virus]	AAA74546.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46886.1
nucleoprotein	nucleoprotein [Measles virus]	BAI122350.1
nucleoprotein	nucleoprotein [Measles virus]	CAB46867.1
nucleoprotein	nucleocapsid protein [Measles virus]	BAA09954.1
nucleoprotein	nucleoprotein [Measles virus]	AAO15873.1
nucleoprotein	nucleocapsid protein [Measles virus]	AF95735.1
nucleoprotein	nucleoprotein [Measles virus]	AAI37726.1
nucleoprotein	nucleoprotein [Measles virus]	AAA74549.1
nucleoprotein	RecName: Full = Nucleoprotein; AltName: Full = Nucleocapsid protein; Short = NP; Short = Protein N	P26030.1

TABLE 15-continued

Type	Virus Name	GenBank Accession
nucleoprotein	nucleoprotein [Measles virus J:J1155-99]	AAK07777.1
nucleoprotein	nucleoprotein [Measles virus genotype B3]	AGI17238.1
nucleoprotein	nucleoprotein [Measles virus]	AF130351.1
nucleoprotein	nucleoprotein [Measles virus genotype B3]	AGI17242.1
nucleoprotein	nucleoprotein [Measles virus J:J1154-98]	AAK07776.1
nucleoprotein	nucleoprotein [Measles virus]	AAA74548.1
nucleoprotein	nucleoprotein [Measles virus]	AAA19221.1
nucleoprotein	nucleoprotein [Measles virus]	AAC03039.1
nucleoprotein	nucleoprotein [Measles virus]	AAA19223.1
nucleoprotein	nucleoprotein [Measles virus genotype B3]	AGI17241.1
nucleoprotein	nucleoprotein [Measles virus]	CAB60122.1
nucleoprotein	nucleoprotein [Measles virus]	CAC34599.1
nucleoprotein	nucleoprotein [Measles virus]	AAC03042.1
nucleoprotein	nucleoprotein [Measles virus]	CAC34604.1
nucleoprotein	nucleoprotein [Measles virus]	AAA74544.1
nucleoprotein	nucleocapsid protein [Measles virus]	NP_056918.1
V Protein	RecName: Full = Non-structural protein V	Q9IC37.1
V Protein	RecName: Full = Non-structural protein V	Q9FMA9.1
V Protein	V protein [Measles virus]	ACN54411.1
V Protein	V protein [Measles virus]	ACN54403.1
V Protein	V protein [Measles virus]	AF195742.1
V Protein	V protein [Measles virus strain MVi Virginia,USA 15.09]	AF140416.1
V Protein	V protein [Measles virus]	ADU17801.1
V Protein	V protein [Measles virus]	ADU17849.1
V Protein	V protein [Measles virus]	ABB71642.1
V Protein	V protein [Measles virus genotype D8]	AFY12693.1
V Protein	V protein [Measles virus]	YP_003873249.2
V Protein	V protein [Measles virus strain MVi Arizona,USA 11.08.2]	AF140432.1
V Protein	RecName: Full = Non-structural protein V	P26036.1
V Protein	V protein [Measles virus strain MVi California,USA 16.03]	AF140464.1
V Protein	V protein [Measles virus strain MVi California,USA 8.04]	AF140456.1
V Protein	V protein [Measles virus]	ABY21188.1
V Protein	V protein [Measles virus strain MVi Washington,USA 18.08.11]	AF140424.1
V Protein	V protein [Measles virus]	BAH196581.1
V Protein	V protein [Measles virus]	ABB71666.1
V Protein	RecName: Full = Non-structural protein V	P60168.1
V Protein	V protein [Measles virus]	BAH196589.1
V Protein	V protein [Measles virus]	ADU17954.1
V Protein	V protein [Measles virus strain MVi New York,USA 26.09.3]	AF140400.1
V Protein	V protein [Measles virus]	ABY21196.1
V Protein	virulence factor [Measles virus]	ABO69701.1
V Protein	V protein [Measles virus]	ABB71650.1
V Protein	V protein [Measles virus]	ACC86086.1
V Protein	V protein [Measles virus genotype D4]	AFY12702.1
V Protein	V protein [Measles virus strain MVi New Jersey,USA 45.05]	AF140448.1
V Protein	V protein [Measles virus]	BAE98295.1
V Protein	V protein [Measles virus]	ACC86083.1
V Protein	V protein [Measles virus]	ACU5139.1
V Protein	V protein [Measles virus]	ADU17334.1
V Protein	V protein [Measles virus]	ADU17930.1
V Protein	V protein [Measles virus genotype G3]	AFY12710.1
V Protein	V protein [Measles virus strain MVi Pennsylvania,USA 20.09]	AF140472.1
V Protein	phosphoprotein [Measles virus]	ADU17839.1
V Protein	V protein [Measles virus]	ADU17894.1
V Protein	V protein [Measles virus]	ACN50010.1
V Protein	V protein [Measles virus]	ADU17892.1
V Protein	unnamed protein product [Measles virus]	CAA34585.1
V Protein	V protein [Measles virus]	ABD33997.1

TABLE 16

Name	Sequence	SEQ ID NO:
Flagellin Nucleic Acid Sequences		
NT (5' UTR, ORF, 3' UTR)	<p>TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACTCACTAT AGGGAATAAGAGAGAAAAGAAGAGTAAGAAGAAATATAAG AGCCACCATGGCACAAGTCAATTAATACAAACAGCCCTGTCCGCTG TTGACCCAGAATAACCTGAACAAATCCCAGTCCGCACTGGGCA CTGCTATCGAGCGTTTGTCTTCCGGTCTGCGTATCAACAGCGCG AAAGACGATGGCGAGGACRGGCGATTGCTAACCGTTTACCAG CGAACATCAAAGGTCAGACTCAGGCTTCCCGTAACGCTAACGA CGGTATCTCCATTGCGCAGACCCTGAAGGCGCGCTGAACGAA ATCAACAACRACCTGCAGCGTGTGCGTGAACGGGCGTTTCAAT CTGCGAATGGTACTAACTCCCAGTCTGACCTCGACTCCATCCAG GCTGAAATCACCCAGCGCCTGAACGAAATCGACCGTGTATCCG GCCAGACTCAGTTCAACGGCGTGAAGTCTTGGCGCAGGACAA CACCCTGACCATCCAGGTTGGTGGCCACGACGGTGAACATATC GATATTGATTTAAAAGAAATCAGCTCTAAAACACTGGGACTTG ATAAGCTTAATGTCCAGATGCCTACACCCCGAAGAAACTGC TGTAACCGTTGATAAAACTACCTATAAAAATGGTACAGATCCT ATTACAGCCAGAGCAATACTGATATCCAAACTGCAATTGGCG GTGGTGCAACGGGGTTACTGGGGCTGATATCAAATTTAAGA TGGTCAATACTATTTAGATGTTAAAGGCGGTCTCTGCTGGTG TTTATAAAGCCACTTATGATGAAACTACAAGAAAGTAAATAT TGATACGACTGATAAAACCTCCGTTGGCAACTGCGGARGCTACA GCTATTCCGGGAAACGGCCACTATAACCCACAACCAAATTTGCTG AAGTAACAAAAGAGGGTGTGATACGACCACAGTTGCGGCTCA ACTTGTGTCAGCAGGGTTACTGGCGCCGATAAGGACAATACT AGCCTTGTAAAACATCGTTTGGAGATAAAAACGGTAAGGTTA TTGATGGTGGCTATGCACTGAAAATGGGCGACGATTTCTATGC CGCTACATATGATGAGAAAACAGGTGCAATTAAGTCTAAAACC ACTACTTATACAGATGGTACTGGCGTTGCTCAAAC TGGAGCTGT GAAATTTGGTGGCCCAAATGGTAAATCTGAAGTTGTTACTGCT ACCGATGGTAAGACTTACTTAGCAAGCGACCTTGACAAACATA ACTTCAGAACAGGCGGTGAGCTTAAAGAGGTTAATACAGATAA GACTGAAAACCCACTGCAGAAAATGATGCTGCCTTGGCACAG GTTGATACACTTCGTTCTGACCTGGGTGCGGTTGAGAACCGTT CAACTCCGCTATCACCAACCTGGGCAATACCGTAARTAACCTG TCTTCTGCCCGTAGCCGTATCGAAGATTCGACTACGCAACCGA AGTCTCCAACATGCTCGCGCCGAGATTCTGCAGCAGGCGCGT ACCTCCGTTCTGGCGCAGGCGAACCGGTTCCGCAAAACGCTCC TCTCTTACTGCGTTGATAAATAGGCTGGAGCCTCGGTGGCCATG CTTCTTGGCCCTTGGGCTCCCCACAGCCCTCCCTCCCTTCTCTG CACCCGTACCCCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGC</p>	51
ORF Sequence, NT	<p>ATGGCACAAGTCAATTAATACAAACAGCCCTGTCCGCTTGACCC AGATAACCTGAACAAATCCCAGTCCGCACTGGGCACTGCTAT CGAGCGTTTGTCTTCCGGTCTGCGTATCAACAGCCGAAAGAC GATGGCGCAGGACAGGCGATTGCTAACCGTTTACCGCGAACA TCAAAGGCTGACTCAGGCTTCCCGTAACGCTAACGACGGTAT CTCCATTGCGCAGACCCTGAAGGCGCGCTGAACGAAATCAAC AACCACTGCAGCGTGTGCGTGAACCTGGCGGTTCAAGTCTGCGA ATGGTACTAACTCCCAGTCTGACCTCGACTCCATCCAGGCTGAA ATCACCCAGCGCTGAACGAAATCGACCGTGTATCCGGCCAGA CTCAGTCAACGGCGTGAAGTCC TGGCGCAGGACCAACCCCT GACCATCCAGGTTGGTCCACAGCGGTGAAACTATCGATATT GATTTAAAAGAAATCAGCTCTAAAACACTGGGACTTGATAAGC TTAATGTCCAAGATGCCTACACCCCGAAGAAACTGCTGTAAC CGTTGTAAAACCTACTATAAAAATGGTACAGATCCTATTACA GCCAGAGCAATACTGATATCCAAACTGCAATTGGCGGTGGTG CAACGGGGTTACTGGGGCTGATATCAAATTTAAGATGGTCA ATACTATTTAGATGTTAAAGGCGGTCTCTGCTGGTGTTTATA AAGCCCTTATGATGAAACTACAAGAAAGTAAATATTGATAC GACTGATAAAACTCCGTTGGCAACTGCGGAAGCTACAGCTATT CGGGGACGGCCACTATAACCCACAACCAAATTCCTGAAGTAA CAAAGAGGGTGTGATACGACCACAGTTGCGGCTCAACTTGC TGCAGCAGGGGTTACTGGCGCCGATAAGGACAATACTAGCCTT GTAAAACCTATCGTTTGGAGATAAAAACGGTAAGGTTATTGATG GTGGCTATGCACTGAAAATGGGCGACGATTTCTATGCCGCTAC ATATGATGAGAAAACAGGTGCAATTAAGTCTAAAACCACTACT TATACAGATGGTACTGGCGTTGCTCAAACCTGGAGCTGTGAAAT TTGGTGGCCCAAATGGTAAATCTGAAGTTGTTACTGCTACCGAT GGTAAGACTTACTTAGCAAGCGACCTTGACAAACATAACTTCA GAACAGGCGGTGAGCTTAAAGAGGTTAATACAGATAAGACTG AAAACCCACTGCAGAAAATGATGCTGCCTGGCACAGGTTGA TACACTTCGTTCTGACCTGGGTGGGTTCAAGACCGGTTTCAACT</p>	52

TABLE 16-continued

Name	Sequence	SEQ ID NO:
	CCGCTATCACCAACCTGGGCAATACCGTAAATAACCTGTCTTCT GCCCGTAGCCGTATCGAAGATTCCGACTACGCAACCGAAGTCT CCAACATGTCTCGCGCGAGATTCTGCAGCAGGCGGTACCTC CGTTCTGGCGAGGCGAACCGGTTCCGCAAAACGTCTCTCTT TACTGCGT	
mRNA	G*GGGAAUAAGAGGAAAAGAGGUAAGAAAGAAUAUAA GAGCCACCAUGGCACAAAGUCAUUAAUACAAACAGCCUGUCGC UGUUGACCAGAAUAACCGUAAACAAUCCAGUCGCGACUUGG GCACUGCUAUCGAGCGUUUGUCUUCGCGUCUGCGUAUCACACA GCAGCAAGACGAUGCGGCAGGACAGGCGAUUGCCUACCGUU UUACCGCGAACAUCAAAGGUCUGACUCAGGCUUCCCGUAAAG CUAACGACGGUAUCUCCAUUGCGCAGACCACUGAAGGCGCGC UGAAAGAAUCAAACAACACCUGCAGCGUGUGCGUAAACUGG CGGUUCAGUCUGCGAAGUGUACUAAACUCGAGUCUGACUCUG ACUCCAUCCAGGCGUAAAUCAACCAGCGCCUGAACGAAUUCG ACCGUGUAUCCCGCCAGACUCAGUUCACAGGCGUGAAAGUCC UGGCGCAGGACAAACCCUGACCAUCCAGGUUGGUGCCCAACG ACGGUGAAACUAUCGAUUAUGAUUAAAAGAAAUCAGUCUCU AAAACAUCUGGACUUGAUAAAGCUUAAUGUCCAAAGUCCUAC ACCCCGAAAGAAACUGCUGUAACCGUGUAUAAACUACCUAU AAAAAUGGUACAGAUCCUAAUACAGCCAGAGCAAUACUGAU AUCCAAACUGCAAUUGGCGGUGGUCACAGGGGGUUCUGG GGCUGAUUCAAAUUAAAAGUUGUCAAUACUUAUUAGAUG UUAAGGCGGUGUCUUCUGCUGGUGUUUAUAAAGCCACUUAD GAUGAAACUACAAAGAAAGUUAAUUAUGAUACGACUGAUAA AACUCCGUUGGCAACUGCGGAAGCUACAGCUAUUCGGGAAAC GGCCACUAUAAACCAACCAAAUUGCUGAAGUAACAAAAGA GGGUGUUGAUACGACCACAGUUGCGGCUCAACUUGCUGCAGC AGGGGUUACUGGCGCCGAUAGGACAAUACUAGCCUUGUAA AACUAUCGUUUAGGGAUAAAACCGUAAGGUUAUUGAUGGU GGCUAUUGCAGUAAAAGGGGCGACGAUUUCUAGCCGCUACA UAUGAUGAGAAAACAGGUGCAAUACUGCUAAAACCAUAC UUAUACAGAUUGUACUGGCGUUGUCUCAAACUGGAGCUGUGA AAUUUGGUGGCGCAAUUGGUAAAUUGAAGUUGUACUGCU ACCGAUGGUAAGACUUAUCUAGCAAGCGACCUGGACAAACAU AACUUCAGAACAGGCGGUGAGCUUAAAGAGGUUAUACAGA UAAGACUGAAAACCCACUGCAGAAAUAUGAUGCUGCCUUGGC ACAGGUGUAUACACUUCGUUCUGACCCUGGGUGCGGUUCAGAA CCGUUUCAAUCUCCGUUAUCACCAACUUGGGCAUAUCCGUAAA UAACCUUGUCUUCGCGGUGAGCCGUAUCGAAAGAUUCGACUA CGCAACCGAAGUCUCCAAACUUGUCUGCGCGCAGAUUCUGCA GCAGGCGGUAACCUCCGUUCUGGCGCAGGCGAACCAAGSUUC GCAAAACGUCUUCUUCUUAUCUGCGUUGAUAAAGGCGUGGAGC CUCGGUGGCCAUGCUUCUGCCUUGGCGUUCUCCCCAGCC CCUCUCCCCUUCUGCAACCCGUACCCCGUGGUCUUUGAAU AAAGUCUGAGUGGCGCGCAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAUUCUAG	53
mRNA Sequence (assumes T100 tail)		
	Flagellin mRNA Sequences	
NT (5' UTR, ORF, 3' UTR)	UCAAGCUUUUGGACCCUCGUACAGAAAGCUAAUACGACUCACU AUAGGGAAUAAGAGAGAAAAGAGAGUAAGAAGAAUUAUA AGAGCCACCAUGGCAACAAGUCAUUAAUACAAACAGCCUGUCG CUGUUGACCAGAAUAACUAGAACAAUCCAGUCGCGACUG GGCACUGCUAUCGAGCGUUUGUCUUCGCGUCUGCGUAUCAAC AGCGGAAAGACGAUGCGGCGAGGACAGGCGAUUGCUAACCGU UUUACCGGAAACAUAAAGGUUCUGACUCAGCCUUCUCCGUAA GCUAACGACGGUAUCUCCAUUGCGCAGACCACUGAAGGCGCG CUGAACGAAAUCAACAAACUUGCAGCGUGUGCGUGAACUG GCGGUUCAGUCUGCGAAUGGUACUAAUCCAGUCUGACUCUC GACUCCAUCCAGGCGUAAAUACCCAGCGCCUGAACGAAAU GACCGUGUAUCCGCGCAGACUCAGUUCAAACCGCGUGAAGGUC CUGGCGCAGGCAACACCUCAGCCAUCCAGGUUGGUGCCAAAC GACGGUGAAACUAUCGAUUAUGAUUAAAAGAAUUCAGCUC UAAAACACUGGGAUUGAUAAAGCUUAAUGUCCAAAGUAGCCU ACACCCGAAAAGAAACUGCUGUAAACCGUUGAUAAGAAACUACCU AUAAAAUUGGUACAGAUCCUAUUACAGCCAGAGCAAUACUG AUAUCCAAACUGCAAUUGCGGUGGUGCAACGGGGUUACU GGGCUGADUACAAUUAUAAAGUUGGUCAAUACUUAUUAGA UGUUAAAGGCGGUGUCUUCUGCUGGUGUUUAUAAAGCCACUU AUGAUGAAACUACAAGAAAGUUAAUUAUGAUACGACUGAU AAAACUCCGUUGGCAACUGCGGAAGCUACAGCUAUUCGGGGA ACGGCCACUUAACCCACCAACAAUUGCUGAAGUAAACAAA	81

TABLE 16-continued

Name	Sequence	SEQ ID NO:
	GAGGGUGUUGADACGACCACAGUUGCGGCUCAACUUGCUGCA GCAGGGGUUACUGGCCGCCGAUAAAGGACAAUACUAGCCUUGUA AAACUUAUCGUUUGAGGAUAAAAACGGUAAGGUUUAUUGAUGG UGUCUAUGCAGUGAATAAUGGGCGACGAUUUCUAGCCGCUAC AUUUGAUGAGAAACAGGUGCAUUAUCUGCUAAAACCAUA CUUAUACAGAUUGGUACUGGGCUUGCUCAAACUGGAGCUGUG AAAUUUGGUGGCACAAAUGGUAUAUCUGAAGUUGUUAUCUGC UACCGAUGGUAAGACUUACUUAGCAAGCGACCUUGACAAACA UAACUUACAGAACAGGGCGGUGAGCUUAAAGAGGUUAAACAG AUUAGAUCUGAAAACCCACUGCAGAAAUAUGAUGCUGCCUUGG CACAGGUUGAUACACUUCGUUCUGACCUGGGUGCGGUUCAGA ACCGUUUCAACUCGCUUACCAACCCUGGGCAUACCGUAA AUAACCUGUCUUCUGCCCGUAGCCGUUACGAAGAUAUCGACU ACACAACCGAAGUCUCCAAACUUGUCUGCGCGCAGAUUCUGC AGCAGGCCGGUACCUCCGUUCUGGCGCAGGCGAACAGGUUC CGCAAACAGUCUCUCUUUACUGCCUUGAUAAUAGGCUGGAG CCUCGUGGCCAUGCUUCUUGCCCUUGGGCCUCCCCCAGC CCUCUCUCCUUCUGCAACCGUACCCCGGUGGUUUUGAA UAAAGUCUGAGUGGGCGGC	
ORF Sequence, NT	AUGGCCAAAGUCAUUAUAACAACAGCCUGUCGUGUUGACC CAGAAUAACCGAACAATAUCCAGUCCGCACUGGGCACUGCU AUCGAGCGUUUGUCUUCGCGUCUGCGUAUCACAGCGCGAAA GACGAUGCGGCAGGACAGGGCAUUGCUAACCGUUUACCGCG AACAUCAAAGGUCUGACUCAGGCUUCCCGUAACGCUAACGAC GGUUUCUCUUAUGCGCAGACCACUGAAGGCCGCGUGAACGAA AUCAACAACAACUCGACGCGUGUGCGUGAACUGGCGGUUCAG UCUGCGAUAUGGUAUAACUCCAGUCUGACUCGACUCCAUUC CAGGCGUAAAUCACCCAGCGCCUGAACGAAAUCGACCGUGUA UCCGGCCAGACUCAGUUCACCGGCGUGAAAGUCUUGGCGCAG GACAAACACCCUGAACC AUCCAGGUUGGUGCCAAACGACGGUGAA ACUAUCGAUAUUGAUUUAAAAGAAAUCAGCUCUAAAACACU GGGACUUGAUAAGCUUAUUGUCCAAAGUAGCCUACACCCCGAA AGAAACUGCUGDAACCGUUGAUA AAAACUACCUAUA AAAAUG GUACAGAUCCUUAUACAGCCAGAGCAUAUCUGAUUUCAAA CUGCAAUUGGCGGUGUGCAACCGGGUUAUCUGGGCGUGAU AUCAAUUUUAAGAUUGUCAAUAUAUUUAGAUUUUAAGG CGGUGCUUCUGUGGUUUUAUAAAGCCACUUAUGAUGAAA CUACAAGAAAGUUAUAUUGAUACGACUGAUA AAAACUCCG UUGGCAACUGCGGAAGCUACAGCUAUUCGGGAACGGCCACU AUAAACCAACAACCAAUUGCUGAAGUAACA AAAGAGGGUGU UGAUACGACCACAGUUGCGGCCUAAAUUGCUGCAGCAGGGU UACUGGCGCCGAUAAGGACAAUACUAGCUUGUA AAAACUADU GUUUGAGGAUAAAACGGUAAGGUUAUUGAUGGUGGCUAUG CAGUGAAAUGGGCGACGAUUUCUUGCCGCUACAUUUGAU GAGAAAACAGGUGCAAUUACUGCUAAAACCAUACUUAUAAC GAUGGUACUGGCGUUGCUCAAACUGGAGCUGUGAAUUGG UGCGCAAAUGGUAUAUCUGAAGUUGUUAUCUGUAACCGAUG GUAAGACUUAUCUAGCAAGCGACCUUGACAAAACUAUAUCUA GAACAGGCGGUGAGCUUA AAAGAGGUUAUAUCAGAU AAGACU GAAAACCCACUGCAGAAAUAUGAGCUGCCUUGGCACAGGU GAUACACUUCGUUCUGACUUGGGUGCGGUUCAGAACCGUUC AACUCGCUUAUACCAACUGGGCAUACCGUAAAUAACUUG UCUCUGCCCGUAGCCGUUUGGAGAUUCCGACUAUCGCAACC GAAGUCUCCAAUAUGUCUCGCGCGAGAUUCUGCAGCAGGCC GGUACCUCCGUUCUGGCGCAGGCGAACAGGUUCCGCAAAAC GUCCUCUUAUCUGCGU	82
mRNA Sequence (assumes T100 tail)	G*GGGAAUAAGAGAGAAAAGAGAGUAAGAAAGAAUAUA GAGCCACCAUGGCACAAAGUCAUUAUAACAACAGCCUGUCGC UGUUGACCCAGAAUAACCGAACA AAUCCAGUCCGCAUUGG GCACUGCUAUCGAGCGUUUGUCUUCGCGUCUGCGUAUCACA GCGCGAAGACGAUGCGGCAGGACAGGCGAUUGCUAACCUGU UUAACCGCAACAUCAAAGGUCUGACUCAGGCUUCCGUAACG CUAAACGACGGUAUCUCCAUUGCGCAGACCAUGAAGGCGCGC UGAACGAAUUAACAACAACUUGCAGCGUGUGCGUGAACUGG CGGUUCAGUCUGCGAAUUGGUAUAACUCCAGUCUGACUUG ACUCCAUCCAGGCGUAAAUCACCCAGCGCCUGAACGAAUUCG ACCGUGUAUCCGGCCAGACUCAGUUAACCGGCGUGAAAGUCC UGCGCGAGGACAAACCCUGACCAUCCAGGUUGGUGCCAACG ACGGUGAAACUAUCGAUAUUGAUUAAAAGAAAUCAGCUUCU AAAACAUGGGACUUGAUUAGCUUAAUUGCCAAAGAUCCUAC ACCCGAAAAGAAAUCGUCUGUAACCGUUGAUA AAAACUACCUAU AAAAAUGGUACAGAUCCUAUUAACAGCCCGAGCAUAUCUGAU	83

TABLE 16-continued

Name	Sequence	SEQ ID NO:
	AUCCAAACUGCAAUUGGCGGUGGUGCAACGGGGUUAUCUGG GGCUGAUAUCAAUUUAAAAGAGUGGUCAAUACUUAUUAGAU UUAAGGGCGGUGCUUCUGCUGGUGUUAUAAAAGCCACUUAD GAUGAAACUACAAGAAGUUAAUUAUUGAUACGACUGAUAA AACUCGUGGCAACUGCGGAAGCUACAGCUAUUCGGGGAAC GGCCACUUAACCCACCAACCAAUUGCUGAAGUAAACAAAGA GGGUGUUAUACGACCACAGUUGCGGCUCAACUUGCUGCAGC AGGGUUACUGGCGCGAUAAAGGACAAUACUAGCCUUGUAA AACUUAUUGGAGGUAUAAAACGGUAAAGGUUAUUGAUGGU GGCUAUGCAGUGAAAUGGGCGACGAUUUCUUAUGCCGCUACA UAUGAUGAGAAAACAGGUGCAUUACUGCUAAAACCAUAC UUAUACAGAUUGUACUGGCGUUGCUAAAACUGGAGCUGUGA AAUUUGGUGGCGCAAUUGGUAUUAUGAAGUUGUACUGCU ACCGAUGGUAAGACUUUACUUAGCAAGCGACCUUGACAAACAU AACUUUAGAACAGGCGGUGAGCUUUAAGAGGUUUAUACAGA UAAGACUGAAAACCCACUGCAGAAAUUGAUGCUGCCUUGGC ACAGGUUGAUACAUUCGUUCUGACUGGGUGCGGUUCAGAA CCGUUUACAUCUCGCUAUACCAACCCUGGGCAAUACCGUAAA UAACUGUCUUCUGCCCGUAGCCGUAUCGAAGAUUCCGACUA CGCAACCGAAGUCUCCACAUGUCUCGCGCGCAGAUUCUGCA GCAGGCGGUACCUUCGUUCUGGCGCAGGCGAACAGGUUCC GCAAAACGUCUCUUCUUUACUGCGUUGAUUAGGCGUGGAGC CUCGUGGCGCAUGCUUCUUGCCCCUUGGGCCUCCCCAGCC CCUCCUCCCCUUCUGCACCCGUACCCCUGGUCUUUGAAB AAAGUCUGAGUGGGCGGCAAAAAAAAAAAAAAAAAAAAAAA AAA AAA AAAUCUAG	

TABLE 17

Flagellin Amino Acid Sequences

Name	Sequence	SEQ ID NO:
ORF Sequence, AA	MAQVINTNSLSLLTQNNLNKSQSALGTAIERLSSGLRINSKDDAA GQAIANRFTANI KGLTQASRNANDGIS IAQTTEGALNEINNNLQRV RELAVQSANGTNSQSDLDSIQAEITQRLNETDRVSGQTQPNGVKVL AQDNTLTIQVGANDGETIDIDLKEISSKTLGLDKLNVDAYTPKET AVTVDKTTYKNGTDPI TAQSNTDIQTAIGGGATGVTGADI KFKDG QYYLQVKGGAAGVYKATYDETTKKNVIDTDTKTPLATAEATAI RGTATI THNQIAEVTKEGVDTTTVAALAAAGVTGADKDHSTLV KLSFEDKNGKVIDGGYAVKMGDDFYAATYDEKTGAI TAKTTTYT DGTGVAQTGAVKFGGANGKSEVVATDGTKYLAGSDLKHHFRT GGELKEVHTDKTENPLQKI DAALAQVDTLRSDLGAVQNRFNSAIT NLGNTVNNLSARSRIEDSDYATEVSNMSRAQILQQAGTSVLAQA HQVPQNVLSLLR	54
Flagellin-GS linker-circumsporozoite protein (CSP)	MAQVINTNSLSLLTQNNLNKSQSALGTAIERLSSGLRINSKDDAA GQAIANRFTANI KGLTQASRNANDGIS IAQTTEGALNEINNNLQRV RELAVQSANGTNSQSDLDSIQAEITQRLNETDRVSGQTQPNGVKVL AQDNTLTIQVGANDGETIDIDLKQINSQTLGLDTLNVDQYKVS TAATVTGYADTTIALDNSTFKASATGLGGTDQKIDGDLKPDPTTG KYAKVTVTGGTGKDGYYEVSVDKTNGETVLAGGATSPFTGGLP ATATEDVKNVQVANADLTEAKAALTAAGVTGASVVKMSYTDN NGKTI DGGAVKVGDDYYSATQNKDGS ISINTTKYTADDGTSKTA LNKLGADGKTEVVSIGGKYAASKABGHNFKAQPDLEAAATT TENPLQKI DAALAQVDTLRSDLGAVQNRFNSAITNLGNTVNNLTS ARSRIEDSDYATEVSNMSRAQILQQAGTSVLAQHVPQNVLSLL RCGGGSGGGSMMAPDPNANPNANPNANPNANPNANPNANPNAN PNANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNAN ANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNAN ANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNAN NEEPSDKHIEQYLKIKNSISTEWSPCSVTCGNGIQVRIKPGSANKP KDELVDYENDIEKKICKMEKCSVFNVVNS	55
Flagellin-RPVT linker-circumsporozoite protein (CSP)	MMAPDPNANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNAN ANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNAN QGNGQGHNMPNDPNRNVDENAHANNAVKNMNEEPSDKHIEQY LKKIKNSISTEWSPCSVTCGNGIQVRIKPGSANKPKDELVDYENDIEK KICKMEKCSVFNVVNSRPVTMAQVINTNSLSLLTQNNLNKSQSAL LGTAIERLSSGLRINSKDDAAGQAIANRFTANI KGLTQASRNAND	56

TABLE 17-continued

Flagellin Amino Acid Sequences		
Name	Sequence	SEQ ID NO:
	<u>GISIAQTTEGALNEINNNLQVRRELAVQSANSTNSQSDLDLSIQAEIT</u>	
	<u>QRLNEIDRVSGQTQFNGVKVLAQDNTLTIQVGGANDGETIDIDLKQI</u>	
	<u>NSQTLGLDTLNVQOKYKVSDDTAATVTGYADTTIALDNSTFKASAT</u>	
	<u>GLGGTDQKIDGDLKFDDTTKYYAKVTVTGGTGKDGYYEVSVD</u>	
	<u>KTNGEVTLAGGATSPLTGGLPATATEDVKNVQVANADLTEAKRA</u>	
	<u>LTAAGVTGTASVVKMSYTDNNGKTIIDGLAVKVGDDYYSATQ</u>	
	<u>KDGSISINTTKYTADDGTSKTALNKLGGADGKTEVVSIGGKTYAA</u>	
	<u>SKAEGHNFKAQPDLAEEAATTENPLQKIDAALAQVDTLRSDLG</u>	
	<u>AVQNFNSAITNLGNTVMNLTARSRIEDSDYATEVSNMSRAQILQ</u>	
	<u>QAGTSLVAQANQVQNVLSLLR</u>	

TABLE 18

Human Metapneumovirus Mutant Amino Acid Sequences		
Strain	Sequence	SEQ ID NO:
HMPV_SC_DSCAV1_4MMV	MSRKVVIIIFSLLI TPQHGLKESYLEESCSTITEGYLSVLR TGWYTNVFTLEV G DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAICTIRLESEVTAINNALKKTNEAVSTLNGVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVFSQPNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLNRAMVRRKGGGIL CGVYSSVIYVQLPIFGVIDTPCWIVKAAPSCSEKKNYACLLREDQGWY QNAGSTVYYYPNEKDCETRGDHVPFCDAAGINVAEQSKECNINISTNYPC VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQ DADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKFPEDQFQVALDQVFENI ENSQLVDQSHRILSSAEKQNTGFIIVIIILIAVLGSSMILVSIPIIIKTKK TGAPPELPGVTNNGFIPHN	85
HMPV_SC_DSTRIC_4MMV	MSWKVVIIIFSLLI TPQHGLKESYLEESCSTITEGYLSVLR TGWYTNVFTLEV G DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAICTIRLESEVTAINNALKKTNEAVSTLNGVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVFSQPNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLNRAMVRRKGGGIL CGVYSSVIYVQLPIFGVIDTPCWIVKAAPSCSEKKNYACLLREDQGWY QNAGSTVYYYPNEKDCETRGDHVPFCDAAGINVAEQSKECNINISTNYPC VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQ DADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKFPEDQFQVALDQVFENI ENSQLVDQSHRILSSAEKQNTGFIIVIIILIAVLGSSMILVSIPIIIKTKK TGAPPELPGVTNNGFIPHN	86
HMPV_SC_DM_Krarup_T74LD185P	MSWKVVIIIFSLLI TPQHGLKESYLEESCSTITEGYLSVLR TGWYTNVFTLEV G DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTIIRLESEVTAINNALKKTNEAVSTLNGVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVFSQPNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLNRAMVRRKGGGIL GVYSSVIYVQLPIFGVIDTPCWIVKAAPSCSEKKNYACLLREDQGWY QNAGSTVYYYPNEKDCETRGDHVPFCDAAGINVAEQSKECNINISTNYPC VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQ ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKFPEDQFQVALDQVFENI ENSQLVDQSHRILSSAEKQNTGFIIVIIILIAVLGSSMILVSIPIIIKTKK TGAPPELPGVTNNGFIPHN	87
HMPV_SC_TM_Krarup_T74LD185PD454N	MSWKVVIIIFSLLI TPQHGLKESYLEESCSTITEGYLSVLR TGWYTNVFTLEV G DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTIIRLESEVTAINNALKKTNEAVSTLNGVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVFSQPNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLNRAMVRRKGGGIL GVYSSVIYVQLPIFGVIDTPCWIVKAAPSCSEKKNYACLLREDQGWY QNAGSTVYYYPNEKDCETRGDHVPFCDAAGINVAEQSKECNINISTNYPC VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQ ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKFPEDQFQVALDQVFENI ENSQLVDQSHRILSSAEKQNTGFIIVIIILIAVLGSSMILVSIPIIIKTKK TGAPPELPGVTNNGFIPHN	88

TABLE 18-continued

Human Metapneumovirus Mutant Amino Acid Sequences		
Strain	Sequence	SEQ ID NO:
HMPV SC 4M Krarup T74LS170LD185P	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLKLKALRELKTVSADQLAREEQIENPGSSGFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAINNALKKTNEAVSTLGNQVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMDTAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI GVYSSVIYMQQLPIFGVIDTPCWIVKAAPSCSEKKNYAACLREDDQGWYC QNAGSTVYYYPNEKDCETRGDHFVFCDTAAGINVAEQSKECNINISTTNYPC VSTGRHPISMVALSPLGALVACYKGVSCSISGNRVGIIKQLNKGCSTYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI ENQALVDQSNRILSSAEKQNTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	89
HMPV SC 5M Krarup T74LS170LD185PD454N	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLKLKALRELKTVSADQLAREEQIENPGSSGFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAINNALKKTNEAVSTLGNQVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMDTAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI GVYSSVIYMQQLPIFGVIDTPCWIVKAAPSCSEKKNYAACLREDDQGWYC QNAGSTVYYYPNEKDCETRGDHFVFCDTAAGINVAEQSKECNINISTTNYPC VSTGRHPISMVALSPLGALVACYKGVSCSISGNRVGIIKQLNKGCSTYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI ENQALVDQSNRILSSAEKQNTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	90
HMPV SC DM Krarup E51PT74L	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLKLKALRELKTVSADQLAREEQIENPGSSGFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAINNALKKTNEAVSTLGNQVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMDTAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI GVYSSVIYMQQLPIFGVIDTPCWIVKAAPSCSEKKNYAACLREDDQGWYC QNAGSTVYYYPNEKDCETRGDHFVFCDTAAGINVAEQSKECNINISTTNYPC VSTGRHPISMVALSPLGALVACYKGVSCSISGNRVGIIKQLNKGCSTYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI ENQALVDQSNRILSSAEKQNTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	91
HMPV SC TM Krarup E51PT74LD454N	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLKLKALRELKTVSADQLAREEQIENPGSSGFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAINNALKKTNEAVSTLGNQVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMDTAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI GVYSSVIYMQQLPIFGVIDTPCWIVKAAPSCSEKKNYAACLREDDQGWYC QNAGSTVYYYPNEKDCETRGDHFVFCDTAAGINVAEQSKECNINISTTNYPC VSTGRHPISMVALSPLGALVACYKGVSCSISGNRVGIIKQLNKGCSTYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI ENQALVDQSNRILSSAEKQNTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	92
HMPV SC StabilizeAlpha.T74L	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLKLKALRELKTVSADQLAREEQIENPGSSGFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAINNALKKTNEAVSTLGNQVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMDTAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI GVYSSVIYMQQLPIFGVIDTPCWIVKAAPSCSEKKNYAACLREDDQGWYC QNAGSTVYYYPNEKDCETRGDHFVFCDTAAGINVAEQSKECNINISTTNYPC VSTGRHPISMVALSPLGALVACYKGVSCSISGNRVGIIKQLNKGCSTYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI ENQALVDQSNRILSSAEKQNTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	93
HMPV SC StabilizeAlpha.V55L	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLKLKALRELKTVSADQLAREEQIENPGSSGFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAINNALKKTNEAVSTLGNQVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMDTAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI GVYSSVIYMQQLPIFGVIDTPCWIVKAAPSCSEKKNYAACLREDDQGWYC QNAGSTVYYYPNEKDCETRGDHFVFCDTAAGINVAEQSKECNINISTTNYPC VSTGRHPISMVALSPLGALVACYKGVSCSISGNRVGIIKQLNKGCSTYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI ENQALVDQSNRILSSAEKQNTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	94

TABLE 18-continued

Human Metapneumovirus Mutant Amino Acid Sequences		
Strain	Sequence	SEQ ID NO:
	ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKPPEDQFQVALDQVFENI ENSQLVDQSNRILSSAEKGTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	
HMPV SC StabilizeAlpha S170L	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSSGFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAIINNALKKTNEAVSTLNGVVRV LATAVRELKDFVSKNLTTRAIKKNKCDIDDLKMAVVSFSQPNRRFLNVVRQFS DNAGITPAISLDLMDLDAELARAVPNMPTSAGQIKLMLENRAMVRRKGGPILIG VYGVSSVIYMQQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGRDHVFCDTAAGINVAEQSKECNINI STTNYPCK VSTGRHPI SMVALSPLGALVACVYKGVSCSIGSNRVGIIKQLNKGC SYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKPPEDQFQVALDQVFENI ENSQLVDQSNRILSSAEKGTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	95
HMPV SC StabilizeAlpha T174W	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSSGFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAIINNALKKTNEAVSTLNGVVRV LATAVRELKDFVSKNLTTRAIKKNKCDIDDLKMAVVSFSQPNRRFLNVVRQFS DNAGITPAISLDLMDLDAELARAVPNMPTSAGQIKLMLENRAMVRRKGGPILIG VYGVSSVIYMQQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGRDHVFCDTAAGINVAEQSKECNINI STTNYPCK VSTGRHPI SMVALSPLGALVACVYKGVSCSIGSNRVGIIKQLNKGC SYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKPPEDQFQVALDQVFENI ENSQLVDQSNRILSSAEKGTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	96
HMPV SC 4M StabilizeAlpha V55LT74LS170LT174W	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG DLENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSSGFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAIINNALKKTNEAVSTLNGVVRV LATAVRELKDFVSKNLTTRAIKKNKCDIDDLKMAVVSFSQPNRRFLNVVRQFS DNAGITPAISLDLMDLDAELARAVPNMPTSAGQIKLMLENRAMVRRKGGPILIG VYGVSSVIYMQQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGRDHVFCDTAAGINVAEQSKECNINI STTNYPCK VSTGRHPI SMVALSPLGALVACVYKGVSCSIGSNRVGIIKQLNKGC SYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKPPEDQFQVALDQVFENI ENSQLVDQSNRILSSAEKGTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	97
HMPV ProlineStab_E51P	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSSGFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAIINNALKKTNEAVSTLNGVVRV LATAVRELKDFVSKNLTTRAIKKNKCDIDDLKMAVVSFSQPNRRFLNVVRQFS DNAGITPAISLDLMDLDAELARAVPNMPTSAGQIKLMLENRAMVRRKGGPILIG VYGVSSVIYMQQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGRDHVFCDTAAGINVAEQSKECNINI STTNYPCK VSTGRHPI SMVALSPLGALVACVYKGVSCSIGSNRVGIIKQLNKGC SYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKPPEDQFQVALDQVFENI ENSQLVDQSNRILSSAEKGTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	98
HMPV ProlineStab D185P	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSSGFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAIINNALKKTNEAVSTLNGVVRV LATAVRELKDFVSKNLTTRAIKKNKCDIDDLKMAVVSFSQPNRRFLNVVRQFS DNAGITPAISLDLMDLDAELARAVPNMPTSAGQIKLMLENRAMVRRKGGPILIG VYGVSSVIYMQQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGRDHVFCDTAAGINVAEQSKECNINI STTNYPCK VSTGRHPI SMVALSPLGALVACVYKGVSCSIGSNRVGIIKQLNKGC SYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKPPEDQFQVALDQVFENI ENSQLVDQSNRILSSAEKGTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	99
HMPV ProlineStab_D183P	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSSGFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAIINNALKKTNEAVSTLNGVVRV LATAVRELKDFVSKNLTTRAIKKNKCDIDDLKMAVVSFSQPNRRFLNVVRQFS DNAGITPAISLDLMDLDAELARAVPNMPTSAGQIKLMLENRAMVRRKGGPILIG VYGVSSVIYMQQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGRDHVFCDTAAGINVAEQSKECNINI STTNYPCK VSTGRHPI SMVALSPLGALVACVYKGVSCSIGSNRVGIIKQLNKGC SYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKPPEDQFQVALDQVFENI ENSQLVDQSNRILSSAEKGTGFIIVIIILIAVLGSSMLVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	100

TABLE 18-continued

Human Metapneumovirus Mutant Amino Acid Sequences		
Strain	Sequence	SEQ ID NO:
	VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKFPEDQPQVALDQVFENI ENSQALVDQSHRILSSAEKGTGFIIVIIILIAVLGSSMILVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	
HMPV ProlineStab E131P	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAINNALKKTNEAVSTLGNQVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSPSQPNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAQGIKLMLENRAMVRRKGFILII GVYSSSVIYMQVLPVPGVIDTPCWIVKAAPSCSEKKNYACLLREDQGGWYC QNAGSTVYYYPNEKDCETRGDHFVPCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKFPEDQPQVALDQVFENI ENSQALVDQSHRILSSAEKGTGFIIVIIILIAVLGSSMILVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	101
HMPV ProlineStab D447P	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAINNALKKTNEAVSTLGNQVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSPSQPNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAQGIKLMLENRAMVRRKGFILII GVYSSSVIYMQVLPVPGVIDTPCWIVKAAPSCSEKKNYACLLREDQGGWYC QNAGSTVYYYPNEKDCETRGDHFVPCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKFPEDQPQVALDQVFENI ENSQALVDQSHRILSSAEKGTGFIIVIIILIAVLGSSMILVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	102
HMPV TrimerRepulsionD454N	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAINNALKKTNEAVSTLGNQVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSPSQPNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAQGIKLMLENRAMVRRKGFILII GVYSSSVIYMQVLPVPGVIDTPCWIVKAAPSCSEKKNYACLLREDQGGWYC QNAGSTVYYYPNEKDCETRGDHFVPCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKFPEDQPQVALDQVFENI ENSQALVDQSHRILSSAEKGTGFIIVIIILIAVLGSSMILVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	103
HMPV TrimerRepulsionE453N	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAINNALKKTNEAVSTLGNQVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSPSQPNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAQGIKLMLENRAMVRRKGFILII GVYSSSVIYMQVLPVPGVIDTPCWIVKAAPSCSEKKNYACLLREDQGGWYC QNAGSTVYYYPNEKDCETRGDHFVPCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKFPEDQPQVALDQVFENI ENSQALVDQSHRILSSAEKGTGFIIVIIILIAVLGSSMILVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	104
HMPV StabilizeAlphaF196W	MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTRLESEVTAINNALKKTNEAVSTLGNQVVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSPSQPNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAQGIKLMLENRAMVRRKGFILII GVYSSSVIYMQVLPVPGVIDTPCWIVKAAPSCSEKKNYACLLREDQGGWYC QNAGSTVYYYPNEKDCETRGDHFVPCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKFPEDQPQVALDQVFENI ENSQALVDQSHRILSSAEKGTGFIIVIIILIAVLGSSMILVSIPIIIKTKKP TGAPPELSGVTNNGFIPHN	105

TABLE 19

Strain	Nucleic Acid Sequence	SEQ ID NO:
Human Metapneumovirus Mutant Nucleic Acid Sequences		
HMPV_SC DSCAV1.4MMV	<p>ATGAGCTGGAAGGTGGTCAATCATCTTCAGCCTGCTGATCA CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACC GGCTGGTACACCAACGTGTTACACTGGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTACAG CAGGCGTGGCCATCTGCAAGACCATCAGACTGGAAAGCG AAGTGACCGCCATCAACACGCCCCGAAAGAAGACAAACG AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGTGGC CTTTGCCGTGCGGAGCTGAAGGACTTCGTGTCCAAGAAC CTGACACGGCCCTGAACAAGAACAAGTCCGACATCGAC GACCTGAAGATGGCCGTGTCTTTAGCCAGTTCAACCGGC GGTTCTGAACCTGCTGCCGAGTTTAGCGACAACGCCGG AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT GAGCTGGCTAGAGCCGTGCCTAACATGCCCTACATCTGCCG GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG ACGGAAGGGCTTCGGCATTCTGTGTGGCGTGTACGGCAGC AGCGTGATCTATATGGTGCAGCTGCCATCTTCGGCGTGA TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG TAGCCGAGAAGAAGGGCAATTACGCCCTGCCCTGCTGAGAGA GGACCAAGGCTGGTATTGTGAGAACCAGCCGAGCACCGTG TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC CACGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG AGCAGAGCAAGAGTGCACATCAACATCAGCACACCCA ACTATCCCTGCAAGGTGTCACCGGCAGGCACCTATTTC TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT ATAAGGGCTGTCTCTGTAGCATCGGCAGCAACAGAGTGG GCATCAACAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCAGGACGCGGATACCGTGACCATCGACAAACCCGTG TATCAGCTGAGCAAGGTGGAAGGCCAACAGCACGCTGATC AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCATCAAGT TCCCTGAGGATCAGTTCAACGTGGCCCTGGACAGGTGTT CGAGAACATCGAGAATTCCAGGCTCTGGTGGACAGTCC AACAGARTCCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTTATCATCGTGATCATCTGATCGCCGCTGCTGGGAGCTC CATGATCCTGGTGTCCATCTTATCATTATCAAGAAGACC AAGAAGCCCACCGGGCTCCTCCAGAACTGAGCGGAGTG ACCAACAATGGCTTCATCCCTCACAAAC</p>	106
HMPV_SC DSTRIC.4MMV	<p>ATGAGCTGGAAGGTGGTCAATCATCTTCAGCCTGCTGATCA CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACC GGCTGGTACACCAACGTGTTACACTGGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTACAG CAGGCGTGGCCATCTGCAAGACCATCAGACTGGAAAGCG AAGTGACCGCCATCAACACGCCCCGAAAGAAGACAAACG AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGTGGC CACAGCCGTGCGGAGCTGAAGGACTTCGTGTCCAAGAAC CTGACACGGCCCTTAACAAGAACAAGTCCGACATCGAC GACCTGAAGATGGCCGTGTCTTTAGCCAGTTCAACCGGC GGTTCTGAACCTGCTGCCGAGTTTAGCGACAACGCCGG AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT GAGCTGGCTAGAGCCGTGCCTAACATGCCCTACATCTGCCG GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG ACGGAAGGGCTTCGGCATTCTGTGTGGCGTGTACGGCAGC AGCGTGATCTATATGGTGCAGCTGCCATCTTCGGCGTGA TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG TAGCCGAGAAGAAGGGCAATTACGCCCTGCCCTGCTGAGAGA GGACCAAGGCTGGTATTGTGAGAACCAGCCGAGCACCGTG TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC CACGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG AGCAGAGCAAGAGTGCACATCAACATCAGCACACCCA ACTATCCCTGCAAGGTGTCACCGGCAGGCACCTATTTC TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT ATAAGGGCTGTCTCTGTAGCATCGGCAGCAACAGAGTGG</p>	107

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID No:
HMPV SC DM Krarup T74LD185P	<p>GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCAGGACGCCGATACCGTGACCATCGACACACCCGTG TATCAGCTGAGCAAGGTGGAGGCCAACAGCAACGTGATC AAGGGCAGACCTGTGTCCAGCAGCTTCGACCTATCAAGT TCCTGAGCACAGTGGCAATGTGGCCCTGGACAGGTGTT CGAGAATCGAGAATTCACAGGCTCTGGTGGACAGTCC AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTCATCATCGTGATCATCTGATCGCCGTGTGGCAGCTC CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC AAGAAGCCACCGCGCTCCTCCAGAACTGAGCGGAGTG ACCAACAATGGCTTCATCCCTCACAAC</p> <p>ATGAGCTGGAAGGTGGTCAATCTTCAGCCTGCTGATCA CACCTCAGCACGGCTGAAGAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACCGCTGGTACACCAACGTGTTCACTGGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCGGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGGACGCTTTGTGCTGGGAG CCATTGCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGC AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAACGA AGTGACCGCCATCAACAACGCCCTGAAGAAGCAAAACGA GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGTGGCC ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC TGACACGGGCCATTAACAAGAACAGTGGGACATCCCTGA CCTGAAGATGGCCGTGCTCTTTAGCCAGTTCACCCGGCGG TTTCTGAACGTCGTGGCGAGTTTAGCGACAAACCGCGGAA TCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTGA GCTGGCTAGAGCCGTGCCAATGCCTACATCTGCCCGC CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC GGAAAGGCTTCGGCATTCTGATTTGGCGGTACGGCAGCAG CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG CGAGAAGAGGGCAATTACGCCCTGCCGTGCTGAGAGAGGA CCAAGGCTGGTATTGTCAAGACCGCCGCGACCCGCTGATC TACCTTAACGAGAAGGACTCGGAGACAAAGAGCGACCCAC GTGTTCTGTGATACCCCGCTGGAATCAATGTGGCCGAGC AGAGCAAGAGTGCACATCAACATCAGCACCACCAACT ATCCCTGCAGGTGTCCACCGGACGACCCCTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAC CAGGACCGCGATACCGTGACCATCGACAAACCCGTGATC AGCTGAGCAAGGTGGAAGGCGAAGCAGCACGTGATCAAGG GCAGACCTGTGTCAGCAGCTTCGACCTATCAAGTTCCT TGAGGATCAGTTCAGGTGGCCCTGGACAGGTGTTCCGAG AACATCGAGATTCACAGGCTCTGGTGGACAGTCCAACA GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT CATCGTGATCATCTGATCGCCGTGTGGCAGCTCCATG ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA AGCCCAACCGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC</p>	108
HMPV SC TM Krarup T74LD185PD454N	<p>ATGAGCTGGAAGGTGGTCAATCTTCAGCCTGCTGATCA CACCTCAGCACGGCTGAAGAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACCGCTGGTACACCAACGTGTTCACTGGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCGGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGGACGCTTTGTGCTGGGAG CCATTGCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGC AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAACGA AGTGACCGCCATCAACAACGCCCTGAAGAAGCAAAACGA GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGTGGCC ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC TGACACGGGCCATTAACAAGAACAGTGGGACATCCCTGA CCTGAAGATGGCCGTGCTCTTTAGCCAGTTCACCCGGCGG TTTCTGAACGTCGTGGCGAGTTTAGCGACAAACCGCGGAA TCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTGA GCTGGCTAGAGCCGTGCCAATGCCTACATCTGCCCGC CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC GGAAAGGCTTCGGCATTCTGATTTGGCGGTACGGCAGCAG</p>	109

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID No:
HMPV SC 4M Krarup T74LS170LD185P	CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG CGAGAAGAAGGGCAATTACGCCCTGCCTGCTGAGAGAGGA CCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGATC TACCTTAACGAGAAGGACTGCGAGACAGAGGCGACCAC GTGTTCTGTGATAACGCCCTGGAATCAATGTGGCCGAGC AGAGCAAAGAGTGCAACATCAACATCAGCACCCCAACT ATCCCTGC AAGGTGTCCACCGGCAGGACCCCTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCARGCAGTGAACAAGGGCTGCAGCTACATCACCAC CAGGACGCCGATACCGTGAACATCGACAACACCGTGTATC AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG GCAGACCTGTGTCCAGCAGCTTCGACCCCTATCAAGTTCC TGAGAACCAAGTTCAGGTGGCCCTGGACCAGGTGTTCCGAG AACATCGAGAATCCAGGCTCTGGTGGACCAGTCCAAACA GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA AGCCCAACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAA	110
HMPV SC 5M Krarup T74LS170LD185PD454N	ATGAGCTGGAAGGTGGTCAATCATCTTCAGCCTGCTGATCA CACCTCAGCACCGCCGTAAGAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTACACTGGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGCTCAAGAGCCCTGAGAGA ACTCARGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCCGAGCTTTGTCTGGGAG CCATTGCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGC AGCGGTGGCCATCGCTAAGACCATCAGACTGGAAGCGA AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC ACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTTAAGAACC TGACACGGGCCATTAACAAGAACAAGTGGACATCCCTGA CCTGAAGATGGCCGTGCTTTAGCCAGTTCAACCGCGG TTTCTGAACCTCGTGGCCAGTTTAGCGACAACCGCGGAA TCACACAGCCATCAGCCTGGACCTGATGACAGATGCTGA GCTGGCTAGAGCCGTGCCTAACATGCTACATCTGCCGCG CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC GGAAGGCTTCGGCATTCTGATTGGCGGTGACGGCAGCAG CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG CGAGAAGAAGGGCAATTACGCCCTGCCTGCTGAGAGAGGA CCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGATC TACCTTAACGAGAAGGACTGCGAGACAGAGGCGACCAC GTGTTCTGTGATAACGCCCTGGAATCAATGTGGCCGAGC AGAGCAAAGAGTGCAACATCAACATCAGCACCCCAACT ATCCCTGC AAGGTGTCCACCGGCAGGACCCCTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCARGCAGTGAACAAGGGCTGCAGCTACATCACCAC CAGGACGCCGATACCGTGAACATCGACAACACCGTGTATC AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG GCAGACCTGTGTCCAGCAGCTTCGACCCCTATCAAGTTCC TGAGGATCAAGTTCAGGTGGCCCTGGACCAGGTGTTCCGAG AACATCGAGAATCCAGGCTCTGGTGGACCAGTCCAAACA GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA AGCCCAACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAA	111

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
	AGTGACCGCCATCAACAACGCCCTGAAGAAGCAAACGA GGCCGTGAGCAGCTCGGCATGGCGTTAGAGTGCTGGCC ACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTTAAGAACC TGACACGGGCCATTAAACAGAACAAGTGCACATCCCTGA CCTGAAGATGCGCGTCTCTTAGCCAGTTCAACCGCGG TTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGAA TCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTGA GCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGGC CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC GGAAAGGCTTCGGCATTCGATTGGCGGTACGGCAGCAG CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG ACACACCCTGCTGGATTGTGAAGGCCCGCTCCTAGCTGTAG CGAGAAGAAGGGCAATTACGCCCTGCCCTGCTGAGAGAGGA CCAAGGCTGGTATTGTGAGAAGCGCGGCGACCCGTGTAC TACCCTAACGAGAAGGACTGCGGAGACAAGAGGCGACCAC GTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAGC AGAGCAAAGAGTGCAACATCAACATCAGCACCACTCAACT ATCCCTGCAAGGTGTCCACCGGCAGGCACCTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA AGGGCGTGTCTGTAGCATCGGCAGCAACAGGTGGGCAT CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAC CAGGACCCGATACCGTGACCATCGACAACACCGTGTATC AGCTGAGCAAGGTGGAAAGGCGAACAGCACGTGATCAAGG GCAGACCTGTGTCAGCAGCTTCGACCCTATCAAGTTCCC TGAGAACCAGTTCCAGGTGGCCCTGGACCAGGTGTTCCGAG AACATCGAGAATCCAGGCTCTGGTGGACAGTCCCAACA GAATCCTGTCTAGCCCGGAGAAGGGAACACCGGCTTCAT CATCGTGATCATCTGATCGCCGTGCTGGGACGCTCCATG ATCCTGGTGTCCATCTCAATATCAAGAGACCAAGA AGCCACCCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC	
HMPV SC DM Krarup E51PT74L	ATGAGCTGGAAGGTGGTCAATCCTTCAGCCTGCTGATCA CACCTCAGCACCGCCCTGAAGAAGAGAGTCACTGGAAGAGT CCTGCAGCACCATCAGAGGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTACACTGCCTGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCGGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGCAGCTTTGTGCTGGGAG CCATGCTCTTGGAGTGGCTGCTGCTGCAGCTGTACAGC AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA AGTGACCGCCATCAACAACGCCCTGAAGAAGCAAACGA GGCCGTGAGCAGCTCGGCATGGCGTTAGAGTGCTGGCC ACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTCAAGAACC TGACACGGGCCATTAAACAGAACAAGTGCACATCGACG ACCTGAAGATGGCCGTCTCTTAGCCAGTTCAACCGGGG GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACCGCCGA ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA CGAAAGGCTTCGGCATTCGATTGGCGGTACGGCAGCA GCCTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC GACACACCCCTGCTGGATTGTGAAGGCCCTCCTAGCTGTA GCGAGAAGAAGGGCAATTACGCCCTGCCCTGCTGAGAGAGG ACCAAGGCTGGTATTGTGAGAAGCGCGGACGACCCGTGTA CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA CGTGTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG CAGAGCAAAGAGTGCAACATCAACATCAGCACCACTCAAC TATCCCTGCAAGGTGTCCACCGGCAGGCACCTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA AGGGCGTGTCTGTAGCATCGGCAGCAACAGGTGGGCAT CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAC CAGGACCCGATACCGTGACCATCGACAACACCGTGTATC AGCTGAGCAAGGTGGAAAGGCGAACAGCACGTGATCAAGG GCAGACCTGTGTCAGCAGCTTCGACCCTATCAAGTTCCC TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCCGAG AACATCGAGAATCCAGGCTCTGGTGGACAGTCCCAACA GAATCCTGTCTAGCCCGGAGAAGGGAACACCGGCTTCAT CATCGTGATCATCTGATCGCCGTGCTGGGACGCTCCATG ATCCTGGTGTCCATCTCAATATCAAGAGACCAAGA AGCCACCCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC	112

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID No:
HMPV SC TM Krarup E51PT74LD454N	ATGAGCTGGAAGGTGGTCAATCATT CAGCCTGCTGATCA CACCTCAGCACGGCC TGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGCTGTGTGCTGAG AACCGCTGGTACACCAACGTGTTCACTGCTGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGGAGCTTTGTGCTGGGAG CCATTGCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGC AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA AGTGACCGCCATCAACAACGCCCTGAAGAGACAAACGA GGCCGTGAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTTCAAGAACC TGACACGGGCCATTAAACAAGAACAGTGGACATCGAGC ACCTGAAGATGGCCGTGCTTTAGCCAGTTCACCGGGC GTTCTGAAACGTGCTGCCGAGTTAGCCACAACCGCCGA ATCACACCGCCATCGCCCTGGACCTGATGACAGATGCTG AGCTGGCTAGAGCCGTGCC TAACATGCC TACATCTGCCGG CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA CGAAAGGCTTCGGCATTCGATTGGCGTGTACGGCAGCA GCGTGATCTATATGGTGCAGCTGCCATCTTCGGCGTGATC GACACACCTGCTGGATTGTGAAGGCCGCTCC TAGCTGTA GCGAGAGAAAGGGCAATTAACGCTGCCCTGCTGAGAGAGG ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA CTACCC TAACGAGAAGGACTGCGAGACAAGAGCCGACCA CGTGTCTCTGTATACCGCCGCTGGAATCAATGTGGCCGAG CAGAGCAAAGAGTGCAACATCAACATCAGCACCAAC TATCCCTGCAAGGTGTCCACCGCAGGCCATTTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCAAGCAGCTGAAACAAGGGCTGCAGCTACATCACCAC CAGGACCGCGATACCGTGACCATCGACAACACCGTGATC AGCTGAGCAAGGTGGAAGGGCAACAGCACCGTGATCAAGG GCAGACCTGTGTCCAGCAGCTTCGACCCATCAAGTTCCC TGAGAACAGTTCAGGTGGCCCTGGACAGGTGTTTCGAG AACATCGAGAATCCCAGGCTCTGGTGGACAGTCCAACA GAATCCTGTCTAGCCCGAGAGGGAAACACCGGCTTCAT CATCGTGATCATCTGATCGCCGCTGGGCGCTCCATG ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA AGCCCAACCGCGCTCCTCCAGAATGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAA	113
HMPV SC StabilizeAlpha T74L	ATGAGCTGGAAGGTGGTCAATCATT CAGCCTGCTGATCA CACCTCAGCACGGCC TGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGCTGTGTGCTGAG AACCGCTGGTACACCAACGTGTTCACTGGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGGAGCTTTGTGCTGGGAG CCATTGCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGC AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA AGTGACCGCCATCAACAACGCCCTGAAGAGACAAACGA GGCCGTGAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTTCAAGAACC TGACACGGGCCATTAAACAAGAACAGTGGACATCGAGC ACCTGAAGATGGCCGTGCTTTAGCCAGTTCACCGGGC GTTCTGAAACGTGCTGCCGAGTTAGCCACAACCGCCGA ATCACACCGCCATCGCCCTGGACCTGATGACAGATGCTG AGCTGGCTAGAGCCGTGCC TAACATGCC TACATCTGCCGG CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA CGAAAGGCTTCGGCATTCGATTGGCGTGTACGGCAGCA GCGTGATCTATATGGTGCAGCTGCCATCTTCGGCGTGATC GACACACCTGCTGGATTGTGAAGGCCGCTCC TAGCTGTA GCGAGAAAGGGCAATTAACGCTGCCCTGCTGAGAGAGG ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA CTACCC TAACGAGAAGGACTGCGAGACAAGAGCCGACCA CGTGTCTCTGTATACCGCCGCTGGAATCAATGTGGCCGAG CAGAGCAAAGAGTGCAACATCAACATCAGCACCAAC TATCCCTGCAAGGTGTCCACCGCAGGCCATTTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCAAGCAGCTGAAACAAGGGCTGCAGCTACATCACCAC CAGGACCGCGATACCGTGACCATCGACAACACCGTGATC	114

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
HMPV SC StabilizeAlpha V55L	<p>AGCTGAGCAAGGTGGAGGCGAACAGCACGTGATCAAGG GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCCGAG AACATCGAGAATTCCAGGCTCTGGTGGACCAAGTCCAACA GAATCCTGTCTAGCCCGGAGAGGGAAACACCCGGCTTCAT CATCGTGATCATCTGATCGCCGTGCTGGGCAGCTCCATG ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA AGCCCAACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAAC</p> <p>ATGAGCTGGAAGGTGGTCAATCATCTTCAGCCTGCTGATCA CACCTCAGCACCGCCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC GACCTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG AAGTGACCGCCATCAACAAACCGCCCTGAGAAGACAAACG AGGCCGTACGCACACTCCGGCAATGGCGT TAGAGTGTGGC CACAGCCGTGCCGAGCTGAGGACTTCCTGTCCAAAGAAC CTGACACGGGCCATTAAACAAGAACAAAGTGGCAGATCGAC GACCTGAAGATGGCCGTGCTCTTAGCCAGTTCAACCGGC GGTTCTGAACGTCTGTCGGCAGTTTAGCGACAAACCGCG AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG ACGGAAGGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA TCGACACACCCTGCTGGATTGTGAAGCCGCTCCTAGCTG TAGCGAGAAGAAGGGCAATTACGCCCTGCCCTGCTGAGAGA GGACCAAGGCTGGTATTGTGAGAACCGCCGACGACCCGTG TACTACCCCTAACGAGAAGGACTGCCAGACAAGAGGCGAC CACGTGTTCTGTGATACCGCCGCTGGAAATCAATGTGGCCG AGCAGAGCAAGAGTGCACATCAACATCAGCACCACCA ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCTATTTCT TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT ATAAGGCGGTGCTCTGTAGCATCGGCAGCAACAGAGTGG GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCAGGACCGGATACCGTGACCATCGACAAACCCGTG TATCAGCTGAGCAAGGTGGAGGCGAACAGCAAGTGTGATC AAGGGCAGACCTGTGTCAGCAGCTTCGACCCCTATCAAGT TCCTGAGGATCAGTTCAGGTGGCCCTGGACCAGGTGTT CGAGAATCAGAGAATCCAGGCTCTGGTGGACAGTCC AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTCATCATCGTGATCATCTGATCGCCGTGCTGGGCAGCTC CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC ARGAAGCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG ACCAACAATGGCTTCATCCCTCACAAAC</p>	115
HMPV SC StabilizeAlpha S170L	<p>ATGAGCTGGAAGGTGGTCAATCATCTTCAGCCTGCTGATCA CACCTCAGCACCGCCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC GACCTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG AAGTGACCGCCATCAACAAACCGCCCTGAGAAGACAAACG AGGCCGTACGCACACTCCGGCAATGGCGT TAGAGTGTGGC CACAGCCGTGCCGAGCTGAGGACTTCCTGTCTAAGAAC CTGACACGGGCCATTAAACAAGAACAAAGTGGCAGATCGAC GACCTGAAGATGGCCGTGCTCTTAGCCAGTTCAACCGGC GGTTCTGAACGTCTGTCGGCAGTTTAGCGACAAACCGCG AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG ACGGAAGGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA TCGACACACCCTGCTGGATTGTGAAGCCGCTCCTAGCTG</p>	116

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID No:
HMPV SC StabilizeAlpha T174W	<p>TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA GGACCRAAGGCTGGTATTGTGAGAACCGCCGCGCAGCACCGTG TACTACCTAACGAGAAGGACTGCGAGACAAGAGGGCGAC CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG AGCAGAGCAAGAGTGCACATCAACATCAGCACCCACA ACTATCCCTGCAAGGTGTCACCGGCAGGCACCTATTTTC TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCAGGACGCCGATACCGTGACCATCGACAAACCCGTG TATCAGCTGAGCAAGGTGGAGGGCAACAGCAGTGTATC AAGGGCAGACCTGTGTCACGACGCTTCGACCCATCAAGT TCCCTGAGGATCAGTTCAGGTGGCCCTGGACAGGTGTT CGAGAACATCGAGAAATCCAGGCTCTGGTGGACAGTCC AACAGAACTCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTCATCATCGTGATCATCTGATCGCCGTGCTGGGCAGCTC CATGATCCTGGTGTCCATCTTCATCATTATCAGAAGACC AAGAAGCCACCGCCGCTCTCCAGAACTGAGCGGAGTG ACCAACAATGGCTTCATCCCTCACAAC</p>	117
HMPV SC 4M StabilizeAlpha V55LT74LS170LT174W	<p>ATGAGCTGGAGGTGGTCAATCATCTTCAGCCTGCTGATCA CACCTCAGCACCGCCCTGAAGAGAGACTACTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCAACTGGAAGTGGGC GACCTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGCTCAAGAGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGCAGCTTGTGCTGGGA GCCATTGCTCTGGAGTGGCTGCTGCTGCAGCTGTACAG CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG AAGTGACCCGCCATCAACAACCGCCCTGAAGAAGACAAACG AGGCCGTGACACACTCGGCATGGCCGTAGAGTGTGCGC CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC CTGTGGCCGGCCATTAAACAAGAACAAGTCCGACATCGAC GACCTGAAGATGGCCGTGTCTTTAGCCAGTTCAACCGGC GGTTCTGAACGTGCTGGCCAGTTTAGCGACAAACCGCG AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT GAGCTGGCTAGAGCCCTGCCTAACATGCCATACATCTGCCG GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG ACGGAAGAGGCTTCGGCATTCTGATGGCCGTGTACGGCAGC AGCGTGATCTATATGGTGCAGCTGCCATATCTTCGGCGTGA TCGACACACCCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA GGACCRAAGGCTGGTATTGTGAGAACCGCCGCGCAGCACCGTG TACTACCTAACGAGAAGGACTGCGAGACAAGAGGGCGAC CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG AGCAGAGCAAGAGTGCACATCAACATCAGCACCCACA ACTATCCCTGCAAGGTGTCACCGGCAGGCACCTATTTTC TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCAGGACGCCGATACCGTGACCATCGACAAACCCGTG TATCAGCTGAGCAAGGTGGAGGGCAACAGCAGTGTATC AAGGGCAGACCTGTGTCACGACGCTTCGACCCATCAAGT TCCCTGAGGATCAGTTCAGGTGGCCCTGGACAGGTGTT CGAGAACATCGAGAAATCCAGGCTCTGGTGGACAGTCC AACAGAACTCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTCATCATCGTGATCATCTGATCGCCGTGCTGGGCAGCTC CATGATCCTGGTGTCCATCTTCATCATTATCAGAAGACC AAGAAGCCACCGCCGCTCTCCAGAACTGAGCGGAGTG ACCAACAATGGCTTCATCCCTCACAAC</p>	118

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
	ACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTTAAGAACC TGTTGGCGGGCCATTAAACAGAACCAAGTGGGACATCGACG ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGGC GTTTCTGAACGTCGTGCGGCAGTTTAGCGACACCGCCGA ATCAGACCAGCCATCAGCCCTGGACCTGTGACAGATGCTG AGCTGGCTAGAGCCGTGCTTAACATGCTTACATCTGCCGG CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA CGGAAAGGCTTCGGCATTCGATTGGCGTGTACGGCAGCA GGGTGATCTATATGGTGCAGCTGCCATCTTCGGCGTGATC GACACACCCTGCTGGATTGTGAAGCCGCTCCTAGCTGTA GCGAGAGAAGGGCAATTCGCTGCTGCTGTGAGAGAGG ACCAAGGCTGGTATTGTGAGAACCGCCGGCAGCACCGTGTA CTACCTTAACGAGAAGGACTGCGAGACAAGAGGCGACCA CGTGTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG CAGAGCAAGAGTGAACATCAACATCAGCACCCACCAAC TATCCCTGCAAGGTGTCCACCGGCAGGCCATTTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAACCAAC CAGGACGCCGATACCGTGCATCGACACACCGTGTATC AGCTGAGCAAGGTGGAGGGCAACAGCACCGTGTCAAGG GCAGACCTGTGTCAGCAGCTTCGACCCATCAAGTTCC TGAGGATCAGTTCAGGTGGCCCTGGACCAAGTGTTCGAG AACATCGAAGTTCACAGGCTCTGGTGGACCAAGTCAACAA GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCA CATCGTATCATCTGATCGCCGTGCTGGGCAGCTCCATG ATCCTGGTGTCCATCTTCATCATTATCAGAGACCAAGA AGCCCCACCGGCGCTCCTCCAGAAGTGAAGGGAGTGACCAA CAATGGCTTCATCCCTCAACAAC	
HMPV ProlineStab E51P	ATGAGCTGGAAGGTGGTCAATCTTCAGCCCTGCTGATCA CACCTCAGCACGGCCGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAAGTGTTCACACTGCCTGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCTGGCAGCGGCAGCTTTGTGCTGGGA GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG AGGCGTGCAGCACACTGGCAATGGCGTTAGRGTGCTGGC CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC CTGACACGGGCATTAACAAGAACAAGTGGCAGATCGAC GACCTGAAGATGGCCGTGCTCTTAGCCAGTTCAACCGGC GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAAACCGCG AATCACCACAGCCATCAGCCTGACCTGATGACAGATGCT GAGCTGGCTAGAGCCGTGCCTAACATGCCATACATCTGCCG GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC AGCGTGATCTATATGGTGCAGCTGCCATCTTCGGCGTGA TCGACACACCCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG TAGCGAGAAGAAGGGCAATTACGCTGCTGCTGAGAGA GGACCAAGGCTGGTATTGTGAGAACGCCCGCAGCACCGTG TACTACCTAACGAGAAGGACTGCGAGACAAGAGGCGAC CACGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG AGCAGAGCAAGAGTGCACATCAACATCAGCACCCACCA ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCTATTTT TATGGTGGCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCAGGACGCCGATACCGTGACCTGACACACCGTGT TATCAGCTGAGCAAGGTGGAAGGCAGACAGCAGTGTATC AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCATCAAGT TCCTGAGGATCAGTTCAGGTGGCCCTGGACAGGTGT CGAGAATCGAGAATTCAGGCTCTGGTGGACAGTCC AACAGAACTCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTCATCATCGTGTATCTTCATCATTATCAAGAAGACC AAGAAGCCACCGGCGCTCCTCCAGAAGTGAAGGGAGTG ACCACAAATGGCTTCATCCCTCAACAAC	119

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID No:
HMPV ProlineStab D185P	ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA CACCTCAGCACGGCCGTAAGAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCACTCGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGACGCTTGTGCTGGGA GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG CAGGCGTGGCCATCGCTARGACCATCAGACTGGAAAGCG AAGTGACCGCCATCAACAAAGCCCTGAAGAAGACAAACG AGGCCGTAGCACACTCGGCAATGGCGTTAGAGTGTGGC CACAGCCGTGCCGAGCTGAAGGACTTCGTGTCCAAGAAC CTGACACGGGCCATTAAACAAGAACAAGTGGCAGATCCCTG ACCTGAAGATGGCCGTGTCTTTAGCCAGTTCAACCGGCG GTTCTGAACGTCGTGCGGCAGTTAGCGACACGCGCGGA ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG AGCTGGCTAGAGCCGTGCCAATGCTTACATCTGCCCG CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTATC GACACACCTGTCTGGATTGTGAAGGCCGCTCCTAGCTGTA GCGAGAAGAAGGGCAATTACGCTGCCTGCTGAGAGAGG ACCAAGCTGATTTGTGAGAACGCGCGCAGCACCGTGT CTACCTTAACGAGAAGGACTGCGAGACAGAGGCGACCA CGTGTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG CAGAGCAAGAGTGCACAACAACATCAGCACCAACCAAC TATCCC TGCAAGGTGTCCACCGGCAGGCACCC TATTTCTAT GGTGGCTCTGTCTCTCTGGGAGCCCTGGTGGCTTGTATATA AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC CAGGACGCGGATACCGTGACCATCGACACACCGTGTATC AGCTGAGCAAGGTGGAAAGGCGAACAGCACTGTGATCAAG GCAGACCTGTGTCCAGCAGCTTCGACCCATCAAGTTCCC TGAGGATCAGTTCCAGGTGGCCCTGGACCCAGTGTTCGAG AACATCGAGAATTCACAGGCTCTGGTGGACAGTCCAAACA GAATCTGTCTAGCGCCGAGAGGGAAACACCGGCTTCAT CATCGTATCATCTGATCGCCGTGCTGGGCAGCTCCATG ATCTTGTGTCCATCTTCACTATTATCAAGAAGACCAAGA AGCCACCGGCGCTCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAA	120
HMPV ProlineStab D183P	ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA CACCTCAGCACGGCCGTAAGAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCACTCGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGACGCTTGTGCTGGGA GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG CAGGCGTGGCCATCGCTARGACCATCAGACTGGAAAGCG AAGTGACCGCCATCAACAAAGCCCTGAAGAAGACAAACG AGGCCGTAGCACACTCGGCAATGGCGTTAGAGTGTGGC CACAGCCGTGCCGAGCTGAAGGACTTCGTGTCCAAGAAC CTGACACGGGCCATTAAACAAGAACAAGTGGCCCTATCGAGC ACCTGAAGATGGCCGTGTCTTTAGCCAGTTCAACCGGCG GTTCTGAACGTCGTGCGGCAGTTAGCGACACGCGCGGA ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG AGCTGGCTAGAGCCGTGCCAATGCTTACATCTGCCCG CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTATC GACACACCTGTCTGGATTGTGAAGGCCGCTCCTAGCTGTA GCGAGAAGAAGGGCAATTACGCTGCCTGCTGAGAGAGG ACCAAGCTGATTTGTGAGAACGCGCGCAGCACCGTGT CTACCTTAACGAGAAGGACTGCGAGACAGAGGCGACCA CGTGTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG CAGAGCAAGAGTGCACAACAACATCAGCACCAACCAAC TATCCC TGCAAGGTGTCCACCGGCAGGCACCC TATTTCTAT GGTGGCTCTGTCTCTCTGGGAGCCCTGGTGGCTTGTATATA AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC	121

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID No:
HMPV_ProlineStab_E131P	<p>CAGGACGCCGATACCGTGACCATCGACAACCCGTGTATC AGCTGAGCAAGGTGGAGGGCGAACAGCAGCTGATCAAGG GCAGACCTGTGTCCAGCAGCTTCCAGCCCTATCAAGTTCCC TGAGGATCAGTTCAGGTGGCCCTGGACCAGGTGTTTCGAG AACATCGAGAATCCAGGCTCTGGTGGACAGTCCAACA GAATCCTGTCTAGCCCGGAGAAGGGAAACCCGGCTTCAT CATCGTGATCATCTGATCGCCGTGCTGGCAGCTCCATG ATCCTGGTGTCCATCTTCATCATTATCARGARGACCAAGA AGCCCACCCGGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAAC</p>	122
HMPV_ProlineStab_D447P	<p>ATGAGCTGGAGGTGGTCAATCCTTCAGCCCTGCTGATCA CACCTCAGCACCGCCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCAAGAGGGCTACCTGTCTGTGCTGAG AACCCGGCTGGTACACCAACGTGTTCCACTGGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCCCTCGAGAG AACTCAAGACCCGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGCAGCTTGTGCTGGGA GCCATGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG CAGCCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG AGTGACCCGCATCAACAACGCCCTGAAGAAGACAAACG AGCCCGTCAGCACACTCGGCAATGGCGTTAGAGTGTGGC CACAGCCGTGCCGAGCTGAAAGGACTTCGTGTCCAAGAAC CTGACACCGGCCATTAACAAGAACAAGTGGCAGATCGAC GACCTGAAGATGGCCGTGCTCTTAGCCAGTTCAACCCGGC GTTTTGAAACGTCGTGCCGAGTTTAGCGACACCCCGGA ATCACACCAGCCATCAGCCCTGGACCTGATGACAGATGCTG AGCTGGCTAGAGCCGTGCCCTAACATGCCATCTGCCC CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA GCGTGATCTATATGGTGCAGCTGCCATCTTCGGCGTGATC GACACACCCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG ACCAAGGCTGGTATTGTGAGAACCGCCGAGCACCGTGTA CTACCCTAACGAGAGGACTGCGAGACAAGAGGCGACCA CGTGTTCTGTGATACCCCGCTGGAATCAATGTGGCCGAG CAGAGCAAGAGTGCACATCAACATCAGCACCAAC TATCCCTGCAGGTGTCCACCCGGCAGGCACCCATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAACCAAC CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC AGCTGAGCAAGGTGGAGGGCGAACAGCAGCTGATCAAGG GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC TGAGGATCAGTTCAGGTGGCCCTGGACCAGGTGTTTCGAG AACATCGAGAATCCAGGCTCTGGTGGACAGTCCAACA GAATCCTGTCTAGCCCGGAGAAGGGAAACCCGGCTTCAT CATCGTGATCATCTGATCGCCGTGCTGGCAGCTCCATG ATCCTGGTGTCCATCTTCATCATTATCARGARGACCAAGA AGCCCACCCGGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAAC</p>	123

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID No:
	<p>TCGACACACCCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG TAGCCGAGAGAAGGGCAATTACGCCCTGCCCTGCTGAGAGA GGACCAAGGCTGGTATTGTGAGAACCGCCGCGACACCGTG TACTACCCTAACGAGAAGGACTGCCGAGACAAGAGGCGAC CAGTGTTCCTGTGATACCGCCGCTGGAAATCAATGTGGCCG AGCAGAGCAAGAGTGAACATCAACATCAGCACCCACCA ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCATTTTC TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG GCATCAACAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCGGACCGCGATACCGTGACCATCGACRACACCGTG TATCAGCTGAGCAAGGTGGAGGCCAACAGCAAGTGTATC AAGGGCAGACCTGTGTCCAGCAGCTTCCACCTATCAAGT TCCCTGAGGATCAGTTCCAGGTGGCCCTGGACAGGTGT CGAACAATCGAGAATTCCAGGCTCTGGTGGACAGTCC AACAGAATCCTGTCTAGCCCGGAGAAGGGAAACACCGGC TTCATCATCGTGTATCCTGTATCGCCGTGTGGGCGAGT CATGATCCTGGTGTCCATCTTCATCATTATCAGAAGACC AAGAAGCCACCGCCGCTCCTCCAGAACTGAGCGGAGTG ACCAACATGGCTTCATCCCTCACAAC</p>	
HMPV TrimerRepulsionD454N	<p>ATGAGCTGGAAGGTGGTCAATCTTCAGCCTGCTGATCA CACCTCAGCACCGCCTGAAAGAGAGCTACCTGGAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACC GGCTGGTACACCAACGTGTTCAACTGGAAGTGGGC GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGCAGCTTGTGTCTGGGA GCCATTGCTCTTGGAGTGGTGTCTGCTGCAGCTGTTACAG CAGGCCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG AAGTGACCGCCATCAACAACCGCCCTGAGAAGACAACCG AGGCCGTGACACACTCGGCAATGGCGTTAGAGTGTCTGGC CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC CTGACACGGGCCATTAACAAGAACAGTGCACATCGAC GACCTGAAGATGGCCGTGTCTTTAGCCAGTTCAACCGGC GGTTTCTGAACCGTGTGCGCGAGTTTAGCCACACCGCCG AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT GAGCTGGCTAGAGCCGTGCTAACATGCTACATCTGCCG GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG ACGGAAGGCTTCGGCATTCTGATGGCGTGTACGGCAGC AGCGTGATCTATATGGTGCAGCTGCCATCTTCGGCGTGA TCGACACACCCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG TAGCCGAGAGAAGGGCAATTACGCCCTGCCCTGCTGAGAGA GGACCAAGGCTGGTATTGTGAGAACCGCCGCGCACCCGTT TACTACCCTAACGAGAAGGACTGCCGAGACAAGAGGCGAC CAGTGTTCCTGTGATACCGCCGCTGGAAATCAATGTGGCCG AGCAGAGCAAGAGTGAACATCAACATCAGCACCCACCA ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCATTTTC TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG GCATCAACAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCGGACCGCGATACCGTGACCATCGACRACACCGTG TATCAGCTGAGCAAGGTGGAGGCCAACAGCAAGTGTATC AAGGGCAGACCTGTGTCCAGCAGCTTCCACCTATCAAGT TCCCTGAGAACAGTTCCAGGTGGCCCTGGACAGGTGT CGAACAATCGAGAATTCCAGGCTCTGGTGGACAGTCC AACAGAATCCTGTCTAGCCCGGAGAAGGGAAACACCGGC TTCATCATCGTGTATCCTGTATCGCCGTGTGGGCGAGT CATGATCCTGGTGTCCATCTTCATCATTATCAGAAGACC AAGAAGCCACCGCCGCTCCTCCAGAACTGAGCGGAGTG ACCAACATGGCTTCATCCCTCACAAC</p>	124
HMPV TrimerRepulsionE453N	<p>ATGAGCTGGAAGGTGGTCAATCTTCAGCCTGCTGATCA CACCTCAGCACCGCCTGAAAGAGAGCTACCTGGAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACC GGCTGGTACACCAACGTGTTCAACTGGAAGTGGGC GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGCAGCTTGTGTCTGGGA GCCATTGCTCTTGGAGTGGTGTCTGCTGCAGCTGTTACAG CAGGCCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG AAGTGACCGCCATCAACAACCGCCCTGAGAAGACAACCG AAGTGACCGCCATCAACAACCGCCCTGAGAAGACAACCG</p>	125

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
HMPV StabilizeAlphaFl196W	<p>AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGTGGC CACAGCCGTGCCGAGCTGAAGGACTTCGTGTCCAAGAAC CTGACACGGGCCATTAAACAAGAACAAGTGGCAGATCGAC GACCTGAAGATGGCCGTGTCTTTAGCCAGTTCAACCGGC GGTTCGAAAGCTCGTGGCGAGTTTAGCGACAGCCCGG AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT GAGCTGGCTAGAGCCGTGCCTAACATGCCATACATCTGCCG GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC AGCGTGATCTATATGGTGCAGCTGCCATCTTCGGCGTGA TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG TAGCGAGAAGAAGGGCAATTACGCCCTGCCCTGCTGAGAGA GGACCAAGGCTGGTATTGTGAGAAGCCGGCAGCACCGTG TACTACCTTAACGAGAAGGACTGCGAGCAAGAGGCGAC CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG AGCAGAGCAAGAGTGCACATCAACATCAGCACCCCA ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCTATTTT TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCAGGACGCCGATACCGTGACCATCGACCAACCCGTG TATCAGCTGAGCAAGGTGGAAGGCCAACAGCACGTGATC AAGGGCAGACCTGTGTCCAGCAGCTTCGACCTTATCAAGT TCCTCAGGATCAGTTCAGGTGGCCCTGGACAGGTGTT CGAGAATCGAGAATTCCAGGCTCTGGTGGACAGTCC AACAGAACTCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTCATCATCGTGATCATCTGATCGCCGTGCTGGGAGCTC CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC AAGAAGCCACCGGCTCCTCCAGAAGTGAAGCGGAGTG ACCAACATGGCTTCATCCCTCACAAC</p> <p>ATGAGCTGGAAGGTGGTCAATCATCTTCAGCCCTGCTGATCA CACCTCAGCACCGCCGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCAAGAGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCAACTGGAAGTGGGC GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCTGGCAGCGCAGCTTGTGTGGGA GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG AAGTGACCCCATCAACAACGCCCTGAAGAAGACAAACG AGGCCGTGAGCACACTCGGCAATGGCGTTAGAGTGTGGC CACAGCCGTGCCGAGCTGAAGGACTTCGTGTCCAAGAAC CTGACACGGGCCATTAAACAAGAACAAGTGGCAGATCGAC GACCTGAAGATGGCCGTGTCTTTAGCCAGTGAACCGGC GGTTCGAAAGCTCGTGGCGAGTTAGCGACAGCCCGG AATCACACCAGCCATCAGCCTGACCTGATGACAGATGCT GAGCTGGCTAGAGCCGTGCCTAACATGCCATACATCTGCCG GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC AGCGTGATCTATATGGTGCAGCTGCCATCTTCGGCGTGA TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG TAGCGAGAAGAAGGGCAATTACGCCCTGCCCTGCTGAGAGA GGACCAAGGCTGGTATTGTGAGAAGCCGGCAGCACCGTG TACTACCTTAACGAGAAGGACTGCGAGCAAGAGGCGAC CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG AGCAGAGCAAGAGTGCACATCAACATCAGCACCCCA ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCTATTTT TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCAGGACGCCGATACCGTGACCATCGACCAACCCGTG TATCAGCTGAGCAAGGTGGAAGGCCAACAGCACGTGATC AAGGGCAGACCTGTGTCCAGCAGCTTCGACCTTATCAAGT TCCTCAGGATCAGTTCAGGTGGCCCTGGACAGGTGTT CGAGAATCGAGAATTCCAGGCTCTGGTGGACAGTCC AACAGAACTCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTCATCATCGTGATCATCTGATCGCCGTGCTGGGAGCTC CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC AAGAAGCCACCGGCTCCTCCAGAAGTGAAGCGGAGTG ACCAACATGGCTTCATCCCTCACAAC</p>	126

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID No:
Human Metapneumovirus mRNA Sequences		
HMPV_SC.DSCAV1.4MMV	<p>AUGAGCUGGAAGGUGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAGAGCUACCUUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUUGUCUGUGCU GAGAACCAGGUGUACACCAACGUGUUCACACUGGAAGU GGGCGACGUCGAGAAUCUGACAUGUCUGAUGGCCCUAG CCUGAUCAGACCCGAGCUGGAUCUGACCRAGRGCCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCCGAGAUCUUGGCAGCGGCAGCUUUG UGCUUGGAGCCAUUGUCUUGGAGUGGCCUGCUGCA GCUGUACAGCAGGCGUGGCCAUCUGCAAGACCAUCAGA CUGGAAGCGAAGUGACCGCCAUAACAACGCCUUGAAG AAGACAACGAGGCCGUCAGCACACUCCGCAUUGCGUU AGAGUGCUGGCCUUUGCCGUGCCGAGCUGAAGGACUUC GUGUCCAAGAACCUGACACGGGCCUGAACAAGAACAG UGCGACAUCCGACCCUGAAGAUUGGCCGUGUCUUUAGC CAGUUCACCGCGGCUUCUGAACGUCGUGCCGAGUUU AGCGACAACCGCGGAUACACACAGCCAUACAGCCUGGAC CUGAUGACAGAUCCUGAGCUGGCUGAGCCGUGCCUAAC AUGCCUACAUCUGCCGGCCAGAUAAGCUGAUGCUCGAG AAUAGAGCCAUUGGUCGACGGAAGGCCUUCGGCAUUCU GUGUGCGUGUACCGCAGCAGCGUGAUCUAUUGGGCC AGCUGCCUAUCUUGCGGUGAUCGACACACCCUUGCUGGA UUGUGAAGGCCCGUCUAGCUGUAGCGAGAAGAGGGC AAUUACGCCUGCCUGCUGAGAGAGGACCAGGCUUGGUA UUGUCAGAACCGCGCAGCACCGUGUACUACCUAACGA GAAGGACUGCCGAGACAAAGAGGCGACCAGUUGUUCUGG AUACCGCCGUGGAUCARUGGGCCGAGCAGAGCAAAG AGUGCAACAUACAUCAGCACCAACCAUUCUUGCA AGGUGUCCACCGGCAGGCACCUUAUUUCUAUGGUGGCUC UGUCUCUCUGGGAGCCUGGUGGCCUUGUUUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAAAGGCCUGCAGCUACAUCACCAACAG GACGCCGAUACCGUGACCUCGACACACCGUGUAUCAG CUGAGCAAGGUGGAAAGGCAACAGCAGCUGAUCAAGGG CAGACCUGUCCAGCAGCUUCGACCUAUCAAGUUCUCC UGAGGAUCAGUUCACGUGGCCUGGACAGGUGUUCG AGAACAUCCAGAAUUCACAGGCCUGGUGGACAGUCCA ACAGAAUCUGUCUAGCGCCGAGAAGGGAAACACCGGCU UCACUUCUGUAUCAUCUGAUCGCCGUGCUGGGCAGCU CCAUGAUCCUGGUGUCCAUUCUACAUAUCAAGAAGA CCAAGAAGCCACCGGCUCUCCUCCAGAACUGAGCGGAG UGACCAACAAGGCCUUCAUCCUCACAAAC</p>	127
HMPV_SC.DSURI1.4MMV	<p>AUGAGCUGGAAGGUGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAGAGCUACCUUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUUGUCUGUGCU GAGAACCAGGUGUACACCAACGUGUUCACACUGGAAGU GGGCGACGUCGAGAAUCUGACAUGUCUGAUGGCCCUAG CCUGAUCAGACCCGAGCUGGAUCUGACCAAGAGCCGCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCCGAGAUCUUGGCAGCGGCAGCUUUG UGCUUGGAGCCAUUGUCUUGGAGUGGCCUGCUGCA GCUGUACAGCAGGCGUGGCCAUCUGCAAGACCAUCAGA CUGGAAGCGAAGUGACCGCCAUAACAACCGCCUUGAAG AAGACAACGAGGCCGUCAGCACACUCCGCAUUGCGUU AGAGUGCUGGCCACAGCCGUGCCGAGCUGAAGGACUUC GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAG UGCGACAUCGACGACUGAAGAUGGCCGUGUCUUUAGC CAGUUCACCGCGGCUUCUGAACGUCGUGCCGAGUUU AGCGACAACCGCGGAUACACACAGCCAUACAGCCUGGAC CUGAUGACAGAUCCUGAGCUGGCUGAGCCGUGCCUAAC AUGCCUACAUCUGCCGGCCAGAUAAGCUGAUGCUCGAG AAUAGAGCCAUUGGUCGACGGAAGGCCUUCGGCAUUCU GUGUGCGUGUACCGCAGCAGCGUGAUCUAUUGGUGC AGCUGCCUAUCUUGCGGUGAUCGACACACCCUUGCUGGA UUGUGAAGGCCCGUCUAGCUGUAGCGAGAAGAGGGC AAUUACGCCUGCCUGCUGAGAGAGGACCAGGCUUGGUA UUGUCAGAACCGCGCAGCACCGUGUACUACCUAACGA GAAGGACUGCGAGACAAAGAGGCGACCAGUUGUUCUGG AUACCGCCGUGGAUCAAUUGGGCCGAGCAGAGCAAAG AGUGCAACAUACAUCAGCACCAACCAUUCUUGCA AGGUGUCCACCGGCAGGCACCUUAUUUCUAUGGUGGCUC</p>	128

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
HMPV SC DM Krarup U74LD185P	UGUCUCCUCUGGGAGCCUGGUGGCUUGUUUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAGGGGUGCAGCUACAUACCAACCAG GACGCCGAUACCGUGACCACUACGACAACACCGUGUAUCAG CUGAGCAAGGUGGAAGGGCAACAGCAACGUGAUCAGGG CAGACCUGUGUCAGCAGCUUCGACCUCUAAGUUCUCC UGAGCAACAGUGGCAUGUGGCCUGGACCAGGUGUUCGA GAACAUCCGAAUUCACAGGUCUGGUGGACCAGUCCAA CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU CAUCAUCGUGAUCAUCCUGAUCGCGUGCUGGGCAGCUC CAUGAUCUGGUGUCUUCUUCAUCAUUAUCRAGAAGAC CAGAAGCCACCGGCGCUCCUCCAGAACUGAGCGGAGU GACCAACAAGGCUUCAUCCUCACAAAC	129
HMPV SC UM Krarup U74LD185PD454N	AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAGAGCUACCUUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUUGUCUGUGCU GAGAACCAGGUGUACACCAACGUGUUCACACUGGAAGU GGGCGACGUCGAGAUCUGACAUGCUCUGAUGGCCUAG CCUGAUCAGACCCGAGCUGAUCUGCUCRAGRGCGCCU GAGAGAACUCAAGACCGUGUCUGCCGUAUCAGCUGGCCAG AGAGGAACAGAUCCGAGAUCUUGGCAGCGGCAGCUUUG UGCUUGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA GCUGUUCAGCAGGGGUGGCCAUCCGUAAGACCAUCAGA CUGGAAGCGAAGUGACCGCCAUAACAACGCCUUGAAG AAGACAACGAGGCCUACGCAACUUGGCCAUGGCGUU AGAGUGCUGGCCACAGCCGUGCCGAGCUGAAGGACUUC GUGUCCAGAACCUGACACGGGCCAUUAACAAGAAACAG UGCGACAUCCUGACCUAGAGAUGGCCGUGUCUUAUAGC CAGUUCACCGCGGUUCUGAACGUCUGCGGCAGUUU AGCGACAACCGCGGAUCAACACAGCUCUAGCCUUGGAC CUGAUGACAGAUCCUGAGCUGGCUAGAGCCUGGCCUAC AUGCCUACAUCCUGCCGCGAGUAACAGCUGAUGCUCGAG AAUAGAGCCAUUGGUCGACGGAAGGCUUCGCAUUCU GAUUGCGUGUACGGCAGCAGCGUGAUCUAUUGGUGC AGCUGCCUAUCUUCGGCGUAUCGACACACCCUGCUGGA UUGUGAAGGCCCGUCCUAGCUGUAGCGAGAAGAGGGC AAUUAACGCCUGCCUGCUGAGAGAGGCCAAGCUGGUA UUGUCAGAAGCCGCGCAGCACCGUGUACUACCUAACCA GAAGGACUGCGAGACAGAGGGGACCAAGUUCUUGUG AUACCGCCGUGGAAUCAUUGGCCGAGCAGAGCAAAG AGUGCAACAUACAUCAGCACCAACAUCUCCUGCA AGGUGUCCACCGGCAGGCACCUAUUUUCUAUGGUGCUC UGUCUCCUCUGGAGCCUGGUGGCCUUGUUUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAGGGCUGCAGCUACAUCACCAACCAG GACGCCGAUACCGUGACCACUACGACAACAACCGUGUAUCAG CUGAGCAAGGUGGAAGGGCAACAGCAGGUAUCAAGGG CAGACCUGUGUCCAGCAGCUUCGACCUCUAACAGUUCUCC UGAGGAUCAGUUCACAGGUGGCCUGGACCAGGUGUUCG AGAACAUCCGAGAAUUCACAGGCUUCUGGUGGACCAGUCCA ACAGAAUCUGUCUAAGCCGAGAAGGGAAACACCGGCU UCAUCAUCGUGAUCAUCCUGAUCGCGUGCUGGGCAGCU CCAUGAUCUGGUGUCCAUUCUUAUCUAUUAUCAGAAGA CCAAGAAAGCCACCGCGCUCUCCAGAACUGAGCGGAG UGACCAACAAGGCUUCAUCCUCACAAAC	130

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
	CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC AUGCCUACAUCUGCCGGCCAGAUCAGCCUGAUGCUCGAG AAUAGAGCCAUUGGUCGACGGAAAGGCUUCGGCAUUCU GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUUGGUGC AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA UUGUGAAGGCCGUCUUCAGCUGUAGCGAGAAGAGGGC AAUUACGCCUGCCUGCUGAGAGAGGCCAAGGCUUGUA UUGUCAGAACGCGCGGACAGCCGUGUACUACCCUAACGA GAAGGACUGCGAGACAAGAGGCGACACGUGUUCUGUG AUACCGCCGCGUGGAUUCARUGGGCCGAGCAGAGCAAAG AGUGCACAUAACAUCAGCACCACCAACUUAUCCUGCA AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC UGUCUCCUCUGGGAGCCUGGUGGCUUGUUAUAGGGC GUGUCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCABC AAGCAGCUGAACAGGGCUGCAGCUACAUCACCAACCAG GACGCCGAUACCGUGACCAUCGACAACCCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG CAGACCUGUGCCAGCAGCUUCGACCUCUAAGUUCUCC UGAGAACAGUUCAGGUGGCCUGGACCAAGGUGUUCGA GAACAUCGAGAUAUCCAGGUCUGGUGGACCAUCCAA CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACAACCGGCU CAUCAUCGUGAUCUCCUGAUCGCGUGCUGGGCAGCUC CAUGAUCUGGUGUCUUCUACAUCUUAUCRAGAAGAC CAAGAAGCCACCGGCGCUCUCCAGAACUGAGCGGAGU GACCAACAAGGGCUCAUCCUCACAAAC	
HMPV SC 4M Krarup U74LS170LD185P	AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAGAGAGCCUACUUGGAAGA GUCCUGCAGCACCACACAGAGGGCUACCUUGUCUGUGCU GAGAACCAGGCGGUACACCAACGUGUUCACACUGGAAGU GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCUAG CCUGAUCAGACCGAGCUGAUCUGUCUAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGACUAGCUGGCCAG AGAGGAACAGAUCAAGAAUCCUGGACGCGGACGCUUG UGUCGGGAGCCAUUGCUCUUGGAGUGGCCUGCUGUGCA GCUGUACAGCAGGCGUGGCCUACGCUAAGACCACUAGA CUGGAAGCGAAGUGACCGCCAUAACAACCGCCUGAAG AAGACAAACGAGGCCUGACGACACUCCGCAUUGGCGUU AGAGUGCUGGCCACAGCCGUGCCGAGCUGAAGGACUUC GUGCUUAAGAACCUGACACGGGCCAUUAACAAGAAACA GUGCGACAUCCUGACCUGAAGUUGGCCUGUCCUUDAG CCAGUUCACCGGCGGUUUCUGAACGUCUGCGGCAGUU UAGCGACAACGCGGAAUCACACCAGCCAUACGCCUGGA CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA GAADAGAGCCAUUGGUCGACGGAAGGCUUCGGCAUUC UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUUGGUG CAGCUGCCUAUCUUCGGCGUGAUCGACACCCUGCUGG AUUGUGAAGGCCGCUCCUAGCUGAUCGAGAAAGGGG CRAUUAACGCGUGCCUGUGAGAGAGGACCAAGGCUGGUA UUGUCAGAACGCGCGCAGCACCUGUACUACCCUAACGA GAAGGACUGCGAGACAAGAGGGGACCAAGGUCUCUGUG AUACCGCCGCGUGGAUUCARUGGGCCGAGCAGAGCAAAG AGUGCAACAUAACAUCAGCACCACCAACUUAUCCUGCA AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGCUC UGUCUCCUCUGGGAGCCUGGUGGCUUGUUAUAGGGC GUGUCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCABC AAGCAGCUGAACAGGGCUGCAGCUACAUCACCAACCAG GACGCGAUACCGUGACCAUCGACAACAACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCAGGUAUCAAGGG CAGACCUGUGCCAGCAGCUUCGACCUCUAUCAGUUCUCC UGAGGAUCAGUUCAGGUGGCCUGGACCAAGGUGUUCG AGAACAUCGAGAAUUCACGGCCUGGUGGACCAUCCAA ACAGAAUCUGUCUAGCGCCGAGAAGGGAAACACCGGCU UCUAUCUGUGAUCUCCUGAUCGCGUGGUGGGCAGCU CCAUGAUCUGGUGUCCAUUCUACAUCUAUCRAGAAGA CCAAGAAGCCACCGGCGCUCUCCAGAACUGAGCGGAG UGACCAACAAGGGCUCAUCCUCACAAAC	131
HMPV SC 5M Krarup U74LS170LD185PD454N	AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAGAGAGCCUACUUGGAAGA GUCCUGCAGCACCACACAGAGGGCUACCUUGUCUGUGCU GAGAACCAGGCGGUACACCAACGUGUUCACUUGGAAGU GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCUAG CCUGAUCAGACCGAGCUGAUCUGUCUAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGACUAGCUGGCCAG AGAGGAACAGAUCAAGAAUCCUGGACGCGGACGCUUG UGUCGGGAGCCAUUGCUCUUGGAGUGGCCUGCUGUGCA GCUGUACAGCAGGCGUGGCCUACGCUAAGACCACUAGA CUGGAAGCGAAGUGACCGCCAUAACAACCGCCUGAAG AAGACAAACGAGGCCUGACGACACUCCGCAUUGGCGUU AGAGUGCUGGCCACAGCCGUGCCGAGCUGAAGGACUUC GUGCUUAAGAACCUGACACGGGCCAUUAACAAGAAACA GUGCGACAUCCUGACCUGAAGUUGGCCUGUCCUUDAG CCAGUUCACCGGCGGUUUCUGAACGUCUGCGGCAGUU UAGCGACAACGCGGAAUCACACCAGCCAUACGCCUGGA CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA GAADAGAGCCAUUGGUCGACGGAAGGCUUCGGCAUUC UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUUGGUG CAGCUGCCUAUCUUCGGCGUGAUCGACACCCUGCUGG AUUGUGAAGGCCGCUCCUAGCUGAUCGAGAAAGGGG CRAUUAACGCGUGCCUGUGAGAGAGGACCAAGGCUGGUA UUGUCAGAACGCGCGCAGCACCUGUACUACCCUAACGA GAAGGACUGCGAGACAAGAGGGGACCAAGGUCUCUGUG AUACCGCCGCGUGGAUUCARUGGGCCGAGCAGAGCAAAG AGUGCAACAUAACAUCAGCACCACCAACUUAUCCUGCA AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGCUC UGUCUCCUCUGGGAGCCUGGUGGCUUGUUAUAGGGC GUGUCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCABC AAGCAGCUGAACAGGGCUGCAGCUACAUCACCAACCAG GACGCGAUACCGUGACCAUCGACAACAACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCAGGUAUCAAGGG CAGACCUGUGCCAGCAGCUUCGACCUCUAUCAGUUCUCC UGAGGAUCAGUUCAGGUGGCCUGGACCAAGGUGUUCG AGAACAUCGAGAAUUCACGGCCUGGUGGACCAUCCAA ACAGAAUCUGUCUAGCGCCGAGAAGGGAAACACCGGCU UCUAUCUGUGAUCUCCUGAUCGCGUGGUGGGCAGCU CCAUGAUCUGGUGUCCAUUCUACAUCUAUCRAGAAGA CCAAGAAGCCACCGGCGCUCUCCAGAACUGAGCGGAG UGACCAACAAGGGCUCAUCCUCACAAAC	132

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
	CCUGAUC AAGACCGAGCUGGAUCUGUCAAGAGCGCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCCGAGAAUCCUGGCAGCGGCAGCUCUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCA GCUGUACAGCAGCGUGGCCAUCGCUAGACCAUCAGA CUGGAAGCGAAGUGACCGCCAUCACACAGCCUUGAAG AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU AGAGUGCUGGCCACAGCCGUGCGGAGCUGAGGACUUC GUGCUUAAGAACCUGACACGGGCCAUUAACAAGAACAA GUGCGACAUCUCCUGACCUGAAGAUUGGCCGUGUCCUUDAG CCAGUUAACCCGGCGGUUUCUGAACGUCGUGCGGAGUU UAGCGACAACCGCGGAUACACACAGCCAUACGCCUGGA CCUGAUGACAGAUUGCUGAGCUGGCUAGAGCCGUGCCUAA CAUGCCUACAUUCGCGGCAGAUCAAGCUGAUGCUGCA GAADAGAGCCAUUGGCCGACGGAAAGGCUUCGGCAUUC UGAUUGGCUGUACCGCAGCAGCGUGAUCUAUAUGGUG CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG AUUGUGAAGGCCGCUUCUAGCUGUAGCGAGAAGAAGGG CAUUUAACCGCCUGCUGCUGAGAGAGGACCAAGGCUGGUA UUGUCGAAACCGCGCAGCACCGUGUACUACCUAACGA GAAGGACUGCGAGACAAAGAGCGGACACGUGUUCUGDG AUACCGCCCGUGGAUCAAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUACAUCAGCACCAACAUUCCUGCA AGGUGUCCACCGCAGGCACCUUAUUUCUAGGUGGCUC UGUCUCCUCUGGGAGCCUGGUGGCUUGUUUAAGGGC GUGUCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAAAGGGCUGCAGCUACUACCAACCAG GACGCGGAUACCGUGACCAUCGACAAACCCUGUAUCAG CUGAGCAAGGUGGAAGCGACAGCACGUGAUCAGGG CAGACUUGUGCCAGCAGCUUCGACCCUAUCAAGUUCUCC UGAGAACCAAGUUCAGAGUGGCCUGGACCAAGGUGUUCGA GAACAUCCGAGAUCUCCAGGCUCUGGUGGACAGUCCAA CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACAACCGGCU CAUCAUCGUGAUCAUCCUGAUCGCGUGCUGGGCAGCUC CAUGAUCUGGUGUCUUCUUCUUCUUAUCAAGAAAGAC CAAGAAGCCACCGCGGCUCCUCCAGAACUGAGCGGAGU GACCAACAAGGCUUCAUCCUCACAAAC	
HMPV SC DM Krarup E51PU74L	AUGAGCUGGAAGGUGGUAUCAUCUUCAGCCUGCUGAU CACACUCAGCACCGCCUGAAAGAGAGCUACCCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACUUGUCUGUGCU GAGAACCAGCUGGUAACCAACGUGUUCACACUGCCUGU GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCUAG CCUGAUCAGACCCAGCUGAUCUGCUCAGAGCGCCCU GAGAGAACUCAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCCGAGAAUCCUGGCAGCGGCAGCUCUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCA GCUGUACAGCAGGCGUGCCAUCCGUAAGACCAUCAGA CUGGAAGCGAAGUGACCGCCAUCACACCGCCUUGAAG AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU AGAGUGCUGGCCACAGCCGUGCCGAGCUGAAGGACUUC GUGUCCAGAAACCUGACACGGCCAUUAACAAGAAACAAG UGCAGCAUCGACGACCUAGAGAUGGCCGUGUCCUUAAGC CAGUUCACCGCGGUUUCUGAACGUCGUGCCGAGUU AGCGACAACCGCGGAUACACACAGCAUCAGCCUGGAC CUGAUGACAGAUUGCUGAGCUGGCUAGAGCCGUGCCUAA AUGCCUACAUUCGCGCCGAGAUCAAGCUGAUGCUCGAG AAUAGAGCCUAGGUCGACCGAAAGGCUUCGGCAUUCU GAUUGGCGUGUACCGCAGCAGCGUGAUCUAUAUGGUGC AGCUGCCUAUCUUCGGCGUAUCGACACACCCUGCUGGA UUGUGAAGGCCCGUCCUAGCUGUAGCGAGAAGAGGGC AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA UUGUCAGAACCGCCGACCCGUGUACUACCUAACCGA GAAGGACUUGCAGACAAAGAGCGACCAAGUGUUCUGUG AUACCGCCGUGGAAUCAUUGGCGGAGCAGAGCAAAG AGUGCAACAUACAUCAGCACCAACAUUCCUGCA AGGUGUCCACCGCAGGCACCUUAUUUCUAGGUGGCUC UGUCUCCUCUGGGAGCCUGGUGGCUUGUUUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAAAGGGCUGCAGCUACUACCAACCAG GACGCCGAUACCGUGACCAUCGACAAACCCUGUAUCAG CUGAGCAAGGUGGAAGGGCAACAGCACCGUGAUCAGGG CAGACCUGUGUCCAGCAGCUCGACCCUAUCAAGUUCUCC UGAGGAUCAGUUCAGGUGGCCUGGACCAAGGUGUUCG	133

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID No:
HMPV_SC_UM_Krarup_E51PU74LD454N	AGAACAUCCGAGAAUCCAGGCUCUGGUGGACCAGUCCA ACAGAAUCCUGUCUAGCGCCGAGAAGGGAACACCGGCU UCADCAUCUGUAUCAUCUGAUCCGCCUGGUGGCGAGCU CCAUGAUCUGGUGUCCAUUCUCAUCAUAUCAAGAAGA CCAAGAAGCCACCGGCGUCCUCCAGAACUGAGCGGAG UGACCACAAUGGCUUCAUCCUCACAAC	134
HMPV_SC_SUabilizeAlpha_U74L	AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU GAGAACCAGGUGGUAACCAACGUGUUCACACUGGAAGU GGGCGACGUCGAGAAUCUGACUUGCUCUGAUGGCCUAG CCUGAUCAGACCGAGCUGGUCUGCUCAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCCAGAAUCCUGGACGGCGAGCUUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUUGCUGUCA GCUGUACAGCAGGCGUGCCAUCCGUAAGACCAUCAGA CUGGAAGCGAAGUGACCGCAUCAACAACGCCUUGAAG AAGACAAACGAGGCGGUCAGCACACUCGGCAUUGGCGUU AGAGUGCUGGCCACAGCCGUGCCGAGCUGAAGGACUUC GUGUCCAGAAACUGACACGGCCAUUAACAAGAAACAG UGCGACAUCCAGACCUGAAGAUGGCGGUGUCUUAUAGC CAGUUCACCGGCGUUUCUGAACGUCUGGCGGAGUUU AGCGACAACGCCGGAUAACAACAGCCAUACAGCCUGGAC CUGAUGACAGAUUCUGAGCUGGCUAGAGCCGUGCCUAAC AUGCCUACAUCUGCCGGCCGAUCAAGCUGAUGCUCGAG AAUAGAGCCUAGGUCGACGGAAGGCUUCCGCAUUCU GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAGGUGC AGCUGCCUAUCUCCGGCGUADCGACACCCUUGCUGGA UUGUGAAGGCCCGUCCUAGCUGUAGCGAGAAGAAGGC AAUUAACGCCUGCCUGCUGAGAGAGGACCAAGGCUUGUA UUGUCAGAACGCCGCGAGCACCGUGUACUACCUAACGA GAAGGACUGCGAGACAAAGAGGCGACCACGUGUUCUGDG AUACCGCCGUGGAAUCAUUGUGGCCGAGCAGAGCAAAG AGUGCAACAUACAUCAGCACCAACCUAUCCUGCA AGGUGUCCACCGGCGAGCACCCUAUUUCUAUGGUGGUC UGUCUCUCUGGGAGCCUGGUGGCUUGUUUAAGGCG GUGUCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCABC AAGCAGCUGAACAGGGCGCAGCUACAUACCAACCAG GACGCCGAUACCGUGACCAUCGACACAACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAGGG CAGACCUGUGUCAGCAGCUUCGACCUAUCAAGUUC UGAGAACCAAGUCCAGGUGGCCUGGACCAAGGUGUUCGA GAACAUCCGAGAAUUCAGGCUUCUGGUGGACAGUCCAA CAGAAUCCUGUCUAGCGCCGAGAGGGAAACACCGGCUU CAUCAUCGUGAUCUCCUGAUCGCGUGCUGGGCAGCUC CAUGAUCUGGUGUCUUCUUCUUCUUAUCAAGAAAGAC CAAGAAACCCACCGGCGUCCUCCAGAACUGAGCGGAGU GACCAACAAGGCUUCAUCCUCACAAC	135

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
HMPV SC SUabilizeAlpha V55L	<p>UUGUCAGAACGCCGGCAGCACCCGUGUACUACCCUAACGA GAAGGACUGCGAGACAAAGAGGCCGACCAGUGUUCUGUG AUACCCGCCGUGGAUACAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUCAACAUCAGCACCACCAACUUAUCCUGCA AGGUGUCCACCGGCAGGCACCCUAUUUUAUGGUGGCUC UGUUCUCUCUGGGAGCCUCGGUGGCUGUUAUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAAAGGCGUCAGCUAUCUACCAACCAG GACGCCGAUACCGUGACCUCGACAACACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAAGG CAGACCUGUGUCCAGCAGCUUCGACCUCUACRAGUUC UGAGGAUCAGUUCAGGUGGCCUGGACCAGGUGUUCG AGAACAUCCAGAAUUC CAGGCCUCUGGUGGACCAGUCCA ACAGAAUCCUGUCUAGCGCCGAGAGAGGGAACACCGGCU UCADAUCCUGUAUCAUCUGAUCGCGGUGGUGGGCAGCU CC AUGAUCCUGGUGUCCAUUCUCAUAUUAUCAGAAGA CCAAGAAGCCACCGGCGUCUCCAGAACUGAGCGGAG UGACCAACAAGGCUUCAUCCUCACAAC</p>	136
HMPV SC SUabilizeAlpha S170L	<p>AUGAGCUGGAAGGUGGUCUACAUCUUCAGCCUGCUGAU CACACCUCAGCACCGCCUGAAAGAGAGCUACCCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUUGUCUGUGCU GAGAACCGGUGGUAACCAACGUGUUCACACUGGAAGU GGGCGACUCGAGAAUCUGACAUGCUCUGAUGGCCUAG CCUGAUCAGACCGAGCUGAUCUGACCAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCCAGAAUCCUGGCAGCGGCGAGCUUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCA GCUGUACAGCAGGCGUGGCCAUCGCUAAGACCUCAGAA CUGGAAGCGAAGUGACCGCCAUACAACAACCGCCUGAAG AAGACAACGAGGCCGUCAGCACACUCGGCAUUGGCGUU CACACCUCAGCACCGCCUGAAAGAGAGCUACCCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUUGUCUGUGCU GAGAACCGGUGGUAACCAACGUGUUCACACUGGAAGU GGGCGACUCGAGAAUCUGACAUGCUCUGAUGGCCUAG CCUGAUCAGACCGAGCUGAUCUGACCAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCCAGAAUCCUGGCAGCGGCGAGCUUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCA GCUGUACAGCAGGCGUGGCCAUCGCUAAGACCUCAGAA CUGGAAGCGAAGUGACCGCCAUACAACAACCGCCUGAAG AAGACAACGAGGCCGUCAGCACACUCGGCAUUGGCGUU</p>	137

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
HMPV SC SUabilizeAlpha U174W	<p>AGAGUGCUGGCCACAGCCGUGCGGAGCUGAAGGACUUC GUGCUUAGAACCCUGACACGGGCCAUUAGAGAACAA GUGCGACAUCGACGACCCUGAAGAUAGCCGUGUCCUUDAG CCAGUUCAACCGCGGCUUUCUGAACGUCGUGCGGCAGUU UAGCGACAACCGCGAAUCACACCAGCCUUCAGCCUGGA CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA CAUGCCUACAUUCGCGGCCAGAUCAAGCUGAUGCUCGA GAUAGAGCCAUUGGUCGACGGAAGGCCUUCGGCAUUC UGAUUGCCGUGUACGGCAGCAGCGUGAUUAUUGGGU CAGCUGCCUAUCUUCGGCGUGAUCGACACACCUGCUGG AUUGUGAAGGCCGUCUCCUGCUGUAGCGRAGGAAGGG CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGCCUGGUA UUGUCAGAACCGCGGAGCACCUGUACUACCUAACGA GAAGGACUGCGAGACAGAGGCCGACCCGUGUUCUGUG AUACCGCCGUGGAAUCAAUGGGCCGAGCAGAGCAAAG AGUGCAACAUACAUCAGCACCACCAACUUAUCCUGCA AGGUGUCCACCGGCAGGCACCUAUUUCUUAUGGUGCUC UGUCUCUCUGGGAGCCUGGUGGCUGUUUAUAGGGC GUGUCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAGGGCUGCAGCUACUCCCAACCAG GACGCCGAUACCGUGACCAUCGACAACCCUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG CAGACCUGUGUCCAGCAGCUUCGACCUAUCRAGUCC UGAGGAUCAGUUCAGGUGGCCUGGACCCAGGUGUUCG AGAACAUCGAGAAUUCACGGCUCUGGUGGACAGUCCA ACAGAAUCUGUCUAGCGCCGAGAAGGGAACACCGGCU UCAUCAUCGUGAUCUCCUGAUCGCCGUGCUGGGCAGCU CCAUGAUCUGGUGUCCAUUCUUAUCAUUAUCAGAAGA CCAAGAGCCACCGGCUCUCCAGAACUGAGCGGAG UGACCAACAAGGCUUCAUCCUCACAAC</p>	138

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID No:
HMPV SC 4M SUabilizeAlpha V55LU74LS170LU174W	<p>AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAGAGCUACCUUGGAAGA GUCCUCGAGCACCAUCACAGAGGGCUACCUUGUCUGUGCU GAGAACC GGCGUGUACACCAACGUGUUCACACUGGAAGU GGGCGACCGUGAGAUCUGACAUCCUGAUGGCCCUAG CCUGAUCAGACCGAGCUGGAUCUGUCUAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCCGAGAUCUUGGCCAGCGGCGCUUUG UGCUGGGAGCCAUUGUCUUGGAGUGGCCUGCUGCUGCA GCUGUACAGCAGGCGUGGCCAUCGCUAAGACCACUAGAGA CUGGAAGCGAAGUGACCGCCAUCAACACAGCCCUUGAAG AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU AGAGUGCUGGCCACAGCCUGGCGGAGCUGAAGGACUUC GUGCUUAGAACCUUGGGCGGGCCAUUUAACAGAACAA GUGCGACAUCCGACGACCUUGAAGAUUGGCCUGUCUUDAG CCAGUUCACCCGGCGUUUCUGAACGUCUGCGGCGAGUU UAGCGACAACCGCCGGAUCACACCAGCCUUCRGCUGGA CCUGAUGACAGAUCCUGAGCUGGCCUAGAGCCUGGCCUAA CAUGCCUACAUUCUGCCGGCCAGAUCAAGCUGAUGCUCGA GAUAGAGCCAUUGGUCGACGGAAGGCCUUCGGCAUUC UGAUUGGGGUGUACGGCAGCAGCGUGAUCUAUUGGGG CAGCUGCCUAUCUUCGGCGUGAUCGACACACCUGCUGG AUUGUGAAGGCCGUCUCCUAGCUGUAGCGAGAGGAGGG CAUUAACGCGUGCCUGCUGAGAGAGGACCAAGGCUGGUA UUGUCAGAACCGCCGGCAGCACCGUGUACUACCUAACGA GAAGGACUGCGAGACAGAGGCCGACACCGUUCUGUG AUACCGCCGUGGAUCAAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUCAACAUACAGCACCAACUAUCCUGCA AGGUGUCCACCGGCAGGCAUCCUAUUCUUGGUGGCUC UGUCUCUCUGGGAGCCUGGUGGCUUGUUAUAGGGC GUGUCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAGGGCUGCAGCUACAUCCACCAACAG GACGCGAUACCGUGACCAUCGACAACCCUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG CAGACCUGUGUCCAGCAGCUUCGACCUCUACAGUUCUCC UGAGGAUCAGUUCAGGUGGCCUGGACCGGUGUUCG AGAACUCGAGAAUUCAGGCUUGGUGGACAGUCCA ACAGAAUCUGUCUAGCGCCGAGAGGGAAACACCGGCU UC AUCAUCGUGAUCUUCUGAUCGCCGUGCUGGGCAGCU CCADGAUCUGGUGUCCAUUCUACAUUAUCAAGAAGA CCAGAAAGCCACCGGCGUCUCCAGAAUCUGAGCGGAG UGACCAACAAGGCUUCAUCCUCCACAC</p>	139
HMPV_ProlineSUab_E51P	<p>AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAGAGCUACCUUGGAAGA GUCCUCGAGCACCAUCACAGAGGGCUACCUUGUCUGUGCU GAGAACC GGCGUGUACACCAACGUGUUCACACUGCCUGU GGGCGACCGUGAGAUCUGACAUCCUGAUGGCCCUAG CCUGAUCAGACCGAGCUGGAUCUGAUCAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCCGAGAUCUUGGCCAGCGGCGCUUUG UGCUGGGAGCCAUUGUCUUGGAGUGGCCUGCUGCUGCA GCUGUACAGCAGGCGUGGCCAUCGCUAAGACCACUAGAGA CUGGAAGCGAAGUGACCGCCAUCAACACAGCCCUUGAAG AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU AGAGUGCUGGCCACAGCCGUGCGGAGCUGAAGGACUUC GUGUCCAGAACCUAGACACGGCCAUUAACAAGAACAAG UGCGACAUCCAGCACCUAGAGAUGGCCGUGUCUUAAGC CAGUUCACCCGGCGUUUCUGAACGUCUGCGGCGAGUUU AGCGACAACCGCGGAUCAACACAGCCAUACAGCCUGGAC CUGAUGACAGAUCCUGAGCUGGCCUAGAGCCUGCCUAA AUGCCUACAUUCGCCGCCAGAUCAAGCUGAUGCUCGAG AAUAGAGCCAUUGUCCGACGGAAGGCUUCGGCAUUCU GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUUGGGC AGCUGCCUUCUUCGGCGUGAUCGACACACCCUGCUGGA UUGUGAAGGCCGUCUCUAGCUGUAGCGAGAAGAGGGC AAUUAACCCUGCCUGCUGAGAGAGGACCAAGGCUUGUA UUGUCAGAACCGCCGGCAGCACCGUGUACUACCUAACGA GAAGGACUGCGAGACAGAGGGCGACACCGUGUUCUGUG AUACCGCCGUGGAUCAAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUCAACAUACAGCACCAACUAUCCUGCA AGGUGUCCACCGGCAGGCAUCCUAUUCUUGGUGGCUC UGUCUCUCUGGGAGCCUGGUGGCUUGUUAUAGGGC GUGUCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC</p>	140

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
HMPV ProlineSUab D185P	<p>AAGCAGCUGAACAAAGGGCUGCAGCUACAUCACCAACCAG GACGCCGAUACCGUGACCAUCGACACACCCGUGUAUCAG CUGAGCAAGGUGGAAAGGCGACAGCAGCUGAUCAGGG CAGACCUGUGUCCAGCAGCUUCGACC UAUCAAGUUC UGAGGAUCAGUUC CAGGUGGCCUGGACAGGUGUUCG AGAACAUCGAGAAUCC CAGGCCUGGUGGAC CAGUCCA ACAGAAUCUGUCUAGCGCCGAGAAGGGAACACCGGCU UCAUCAUCGUGAUCUCCUGAUCGCGGUGGUGGACAGCU CCAUGAUCCUGGUGUCCAUCUUCACAUUAUCAGAAGA CCAAGAAGCCACCGGCGCUCUCCAGAACUGAGCGGAG UGACCAACAAGGCUUCAUCCUCAC AAC</p> <p>AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAGAGCUACCCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUAC CUGU CUGUGCU GAGAACC GGCUGGUA CACC AACGUGUUCACACUGGAAGU GGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCUAG CCUGAUCAGACCCGAGCUGAUCUGACCAAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGACAGAUCCGAGAAUCCUGGCAGCGGCGUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA GCUGUACAGCAGGCGUGGCCAUCCGUAAGACCAUCAGA CUGGAAGCGAAGUGACCGCCAUCAACACCGCCUGAAG AAGACAACGAGGCGGUCAGCACACUCGGCAUUGGCGUU AGAGUGCUGGCCACAGCCGUGCGGAGCUGAAGGACUUC GUGUCCAGAAACUGACACGGGCCAUUAACAGAAACAG UGCGACAUCCUGACUGAAGAUUGGCUGUGUCUUAAGC CAGUUCACCGGGCGUUUCUGAACGUCUGCGGAGUUC AGCGACACCGCGGAUCCACACAGCAUCAGCCUGGAC CUGAUGACAGAUCCUGAGCUGGCCUAGAGCCUGGCCUAAC AUGCCUACAUUCGCGGCCAGAUCAAGCUGAUCUCGAG AAUAGAGCCAUUGGUCGACGGAAGGCUUCGGCAUUCU GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUUGGUGC AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA UUGUGAAGGCCGCUUCUAGCUGUAGCGAGAAGAGGGC AAUUCAGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA UUUGUCAGACCGCCGCGAGCACCGUGUACUACCUAACGA GAGGACUGCGAGACAAAGGGCGACACCGUUCUGUG AUACCGCCGUGGAUCAAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUCAACAUACAGCACCAACAUUCCUGCA AGGUGUCCACCGGCGAGCACCUAUUUCUAGGUGGCU UGUCUCUCUGGGAGCCUGGUGGCUUGUUAUAGGGC GUGUCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAAAGGCGUGCAGCUACACCAACAG GACGCGGAUACCGUGACCAUCGACAACACCGUUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAGGG CAGACCUGUGUCCAGCAGCUUCGACC UAUCAAGUUC UGAGGAUCAGUUC CAGGUGGCCUGGAC CAGGUGUUCG AGAACAUCGAGAAUCC CAGGCCUGGUGGAC CAGUCCA ACAGAAUCUGUCUAGCGCCGAGAAGGGAACACCGGCU UCAUCAUCGUGAUCUCCUGAUCGCGGUGGUGGACAGCU CCAUGAUCCUGGUGUCCAUCUUCACAUUAUCAGAAGA CCAAGAAGCCACCGGCGCUCUCCAGAACUGAGCGGAG UGACCAACAAGGCUUCAUCCUCAC AAC</p>	141
HMPV ProlineSUab D183P	<p>AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAGAGCUACCCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUAC CUGU CUGUGCU GAGAACC GGCUGGUA CACC AACGUGUUCACACUGGAAGU GGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCUAG CCUGAUCAGACCCGAGCUGAUCUGACCAAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGACAGAUCCGAGAAUCCUGGCAGCGGACGCUUDG UGCUGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA GCUGUACAGCAGGCGUGGCCAUCCGUAAGACCAUCAGA CUGGAAGCGAAGUGACCGCCAUCAACACCGCCUGAAG AAGACAACGAGGCGGUCAGCACACUCGGCAUUGGCGUU AGAGUGCUGGCCACAGCCGUGCGGAGCUGAAGGACUUC GUGUCCAGAAACUGACACGGGCCAUUAACAGAAACAG UGCCUUAUCGACGACUGAAGAUGGCCGUGUCUUAAGC CAGUUCACCGGCGGUUUCUGAACGUCUGCGGAGUUC AGCGACACCGCGGAUCAACACAGCAUCAGCCUGGAC CUGAUGACAGAUCCGAGCUGGCUAGAGCCGUGCCUAAC AUGCCUACAUUCGCGGCCAGAUCAAGCUGAUCUCGAG</p>	142

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
HMPV ProlineSUb E131P	AAUAGGCCAUGGUCCGACGGAAGGCCUUCGGCAUUCU GAUUGGCGUACGGCAGCAGCGUGAUCUAUUGGUGC AGCUGCCUAUCUUCGGCGUADCGACACCCUUGCUGGA UUGUGAAGGCCCGCUUCUAGCUGUAGCGAGAAGAAGGC AAUUACGCCUGCCUGCUGAGAGAGGCCAAGCUGGUA UUGUCAGAAGCCGGCAGCACCGUGUACUACCUAACGA GAAGGACUGCGAGACAGAGGCCACCAGUUCUGUG AUACCGCCGUGGAUCUAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUCACAUCAGCACCCACUAUCCUGCA AGGUGUCCACCGGCAGGCACCUAUUUCUAUGGUGGCUC UGUCUCCUGGGAGCCUGGUGGCUGUUUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAC AAGCAGCUGAACAGGGCUGCAGCUACUACCAACCAG GACGCCGAUACCGUGACCAUCGACACACCGUGUAUCAG CUGAGCAAGGUGGAGGGCAACAGCAGUGAUCAAGGG CAGACCUGUGCCAGCAGCUUCGACCUAUCAAGUCCC UGAGGAUCAGUCCAGGUGGCCUGGACAGGUGUUCG AGAACAUCCAGAAUCCAGGCUCUGGUGGACAGUCCA ACAGAAUCUGUCUAGCGCCGAGAAGGGAACACCGGCU UCAUCUCUGUAUCAUCUGAUCGCGUGGUGGGCAGCU CCAUGAUCUGGUGUCCAUCUUCACUAUUAUCAAGAAGA CCAAGAAGCCACCAGCGCUCUCCAGAACUGAGCGGAG UGACCAACAUGGCCUUCAUCCUCCACAC	143
HMPV ProlineSUb D447P	AUGAGCUGGAAGGUGGUCUAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU GAGAACCAGCGUGGUACACCACCGUUCACACUGGAAGU GGGCGACGUCGAGAUCUGACAUUCUGAUGGCCUAG CCUGAUCAGACCAGCUGAUCUGACCAGAGCGCCCU GAGAGAACUCAAGACCUGUCUGCCGUAUCAGCUGGCCAG AGAGGAACAGAUCCGAGAUCUUGGCCAGCGGCAGCUUG UGCUGGAGCCAUUGCUCUUGGAGUGGCCUGCUGCUGCA GCUGUACAGCAGCGGUGGCCAUCCGUAAGACCAUCAGA CUGCCUAGCGAAGUGACCGCCAUCAACAAGCCUUGAAG AAGACAACAGAGCCGUCAGCACACUCGGCAUUGGCGUU AGAGUGCUGGCCACAGCCUGCGCAGCUGAAGGACUUC GUGUCCAGAACCCUGACACGGGCCAUUAGCAAGAACAG UGCAGCAUCGACGACUGAAGAUGGCCUGUCUUUAGC CAGUUCACCGGGCGUUUCUGAACGUCUGCGCGAGUU AGCGACAACCCGGAUUCACACAGCCAUCCAGCCUGGAC CUGAUGACAGAUCCUGAGCUGGCCUAGAGCCUGCCUAAC AUGCCUACAUUCGCGGCCAGAUCAAGCUGAUGCUCGAG AAUAGAGCCAUUGGUCGACGGAAAGGCCUUCGGCAUUCU GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUUGGUGC AGCUGCCUAUCUUCGGCGUAUCGACACACCUGCUGGA UUGUGAAGGCCCGUCUAGCUGUAGCGAGAAGAGGGC AAUUACGCCUGCCUGCUGAGAGAGGCCAAGGCUGGUA UUGUCAGAACGCGCGCAGCACCGUGUACUACCUAACGA GAAGGACUGCGAGACAGAGGGCAGCACCGUGUUCUGDG AUACCGCCGUGGAUCUAUGUGGCCGAGCAGAGCAAAG AGUGCAACAACAUCAGCACCAACCAUAUCCUGCA AGGUGUCCACCGGCAGGCACCUAUUUCUAUGGUGGCUC UGUCUCCUGGGAGCCUGGUGGCCUGUUUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAGGGCUGCAGCUACAUCCACCAACCAG GACGCCGAUACCGUGACCAUCGACAACCCUGUAUCAG CUGAGCAAGGUGGAAGGCCAACAGCACCGUAUCAAGGG CAGACCUGUGUCCAGCAGCUUCGACCUAUCAAGUCCC UGAGGAUCAGUCCAGGUGGCCUGGACAGGUGUUCG AGAACUCCAGAAUCCAGGCUCUGGUGGACAGUCCA ACAGAAUCUGUCUAGCGCCGAGAAGGGAACACCGGCU UCAUCAUCUGUAUCAUCUGAUCGCGCUGGUGGGCAGCU CCAUGAUCUGGUGUCCAUCUUCACUAUUAUCAAGAAGA CCAAGAAGCCACCAGCGCUCUCCAGAACUGAGCGGAG UGACCAACAUGGCCUUCAUCCUCCACAC	144

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
	AGAGGAACAGAUCCGAGAUCUUGGCAGCGGCAGCUUUG UGCUUGGAGCCAUUGCUUUGGAGUGGCUGCUGUGCA GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA CUGGAAGCGAAGUGACCGCCAUCAACAACGCCUGAAG AAGACAAACGAGGCCGUCAGCACACUCCGGCAUUGCGUU AGAGUGCUGGCCACAGCCGUGCGGAGCUGAAGGACUUC GUGUCCAGAACCCUGACACGGGCCAUUAAACAAGAACAG UGCGACAUCCGACCCUGRAGAUGGCCGUGUCCUUUAGC CAGUUCACCGGGCGUUUCUGAACGUCGUGCGGCAGUUU AGCGACAACCGCGGAUACACACCAGCAUCAGCCUGGAC CUGAUGACAGAUUCUGAGCUGGCUAGAGCCGUGCCUAA AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG AAUAGAGCCAUUGGUCCGACGGAAGGCCUUCGGCAUUCU GAUUGCGUGUACGGCAGCAGCGUGAUCUUAUUGGUGC AGCUGCCUAUCUUGCGCGAUCGACACACCCUGCUGGA UUGUGAAGGCCCGUCCUAGCUGUAGCGAGAAGAGGGC AAUUACGCCUGCCUGUGAGAGAGGCCAAGGCGUGUA UUGUCAGAACCGCGCAGCACCGUGUACUACCUAACGA GAAGGACUGCGAGACAGAGGGCGACCAGUUGUUCUGG AUACCGCCGUGGAUCARUUGGGCCGAGCAGAGCAAAG AGUGCAACAUCACUACAGCACCCACACUUAUCCUGCA AGGUGUCCACCGGCAGGCACCCUAAUUCUUAUGGUGCUC UGUCUCUCUGGGAGCCUGGUGGCUGUUUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAC AAGCAGCUGAACAGGGCCUGCAGCUACAUCACCAACCAG GACGCCAUACCGUGACCUCGACACACCCGUGUAUCAG CUGAGCAAGGUGGAGGGCAACAGCACCGUUAUAGGG CAGACCUGUGUCCAGCAGCUUCCACCUAUCAGUUCUCC UGAGGAUCAGUCCAGGUGGCCUGGACCAGGUGUUCG AGAACAUCCGAGAUCUCCAGGCUCUGGUGGAC CAGUCCA ACAGAAUCUGUCUAGCGCCGAGAAGGGAAACACCGGCU UCACUCCUGUAUCAUCUGAUCGCCGUGCUGGGCAGCU CCAUGAUCCUGGUGUCCAUUCUUAUCUUAUCAGAGA CCAAGAAAGCCACCGGCUCUCCAGAACUGAGCGGAG UGACCAACAAGGCUUCAUCCUCACAAC	
HMPV UrimerRepulsionD454N	AUGAGCUGGAAGGUGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAGAGCUACCCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCCUGUCUGUGCU GAGAACCAGCGUGGUAACCAACGUGUUCACACUGGAAGU GGGCGACGUCGAGAUCUGACAUGCUCUGAUGGCCUAG CCUGAUCAGACCGAGCUGAUCUGACCAGAGCCGCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCCGAGAUCUUGGCAGCGCCAGCUUUG UGCUUGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA CUGGAAGCGAAGUGACCGCCAUCAACAACGCCUUGAAG AAGACAAACGAGGCCUCAGCACACUCCGGCAUUGCGUU AGAGUGCUGGCCACAGCCGUGCGGAGCUGAAGGACUUC GUGUCCAGAACCCUGACACGGGCCAUUAAACAAGAACAG UGCGACAUCCGACCCUGAAGAUGGCCGUGUCUUUAGC CAGUUCACCGCGGCUUCUGAACCGUGCCGCGAGUUU AGCGACAACCGCGGAUACACACCAGCAUCAGCCUGGAC CUGAUGACAGAUUCUGAGCUGGCUAGAGCCUGCCUAAC AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG AAUAGAGCCAUUGGUCGACGGAAGGCCUUCGGCAUUCU GAUUGCGUGUACGGCAGCAGCGUGAUCUUAUUGGUGC AGCUGCCUAUCUUGCGCGAUCGACACACCCUGCUGGA UUGUGAAGGCCCGUCCUAGCUGUAGCGAGAAGAGGGC AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUUGUA UUGUCAGAACCGCGCAGCACCGUGUACUACCUAACGA GAAGGACUGCGAGACAGAGGGCGACCAGUUGUUCUGG AUACCGCCGUGGAUCUUAUGGGCCGAGCAGAGCAAAG AGUGCAACAUCACAUCAGCACCAACAUCUUAUCCUGCA AGGUGUCCACCGGCAGGCACCCUAAUUCUUAUGGUGCUC UGUCUCUCUGGGAGCCUGGUGGCUGUUUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAC AAGCAGCUGAACAGGGCCUGCAGCUACAUCACCAACCAG GACGCCAUACCGUGACCAUCGACAAACCCGUGUAUCAG CUGAGCAAGGUGGAGGGCAACAGCACCGUUAUAGGG CAGACCUGUGUCCAGCAGCUUCGACCUCUACAAGUUCUCC USAGAACCAAGUUCAGGUGGCCUGGACCAAGGUGUUCGA GAACAUCAGAAUUCACAGGCUUGGUGGACCAAGUCCAA CAGAAUCCUGUCUAGCCCGAGAGGGAAACACCGGCUU	145

TABLE 19-continued

Strain	Nucleic Acid Sequence	SEQ ID NO:
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Equivalents

[0931] Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the disclosure

described herein. Such equivalents are intended to be encompassed by the following claims.

[0932] All references, including patent documents, disclosed herein are incorporated by reference in their entirety.

SEQUENCE LISTING

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<210> SEQ ID NO 1

<211> LENGTH: 1620

<212> TYPE: DNA

<213> ORGANISM: Human metapneumovirus

<400> SEQUENCE: 1

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<212> TYPE: DNA

<213> ORGANISM: Human metapneumovirus

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actgatggac ctactttaat caaacagaa ctgatctaa caaaaagtgc ttaagggaa	240
ctcaaacag tctctgtga tcagttggcg agagaggagc aaattgaaa tccagacaa	300
tcaagatttg tcttaggtgc gatagctctc ggagttgcta cagcagcagc agtcacagca	360
ggcattgcaa tagccaaaac cataaggctt gagagtgagg tgaatgcaat taaagtgct	420
ctcaaacaaa ctaatgaagc agtatccaca ttagggaatg gtgtgagggt cctagccact	480
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gatcaagtct tcgaaagcat tgagaacagt caggcactag tggaccagtc aaacaaaatt	1440
ctaaacagtg cagaaaaagg aaacactggt ttcattatcg tagtaatttt ggttgcctgt	1500

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cttggcttaa ccatgatttc agtgagcacc atcatcataa tcaagaaaac aaggaagccc 1560
acaggagcac ctccagagct gaatgggtgc accaacggcg gtttcatacc acatagttag 1620

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<210> SEQ ID NO 3
<211> LENGTH: 1620
<212> TYPE: DNA
<213> ORGANISM: Human metapneumovirus

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<400> SEQUENCE: 3

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atgtcttggg aagtgatgat taccatttcg ttactcataa cacctcagca tggactaaaa 60
gaaagtattt tagaagaatc atgtagtact ataactgaag gatattctcag tgttttaaga 120
acaggttggt acaccaatgt ctttacatta gaagttggty atgttgaaa tcttaccatgt 180
actgatggac ctagcttaat caaaacagaa cttgacctaa ccaaaagtgc ttttaagagaa 240
ctcaaaacag tttctgctga tcagttagcg agayaagaac aaattgaaa tcccagacaa 300
tcaaggtttg tcttaggtgc aatagctctt ggagttgcca cagcagcagc agtcacagca 360
ggcattgcaa tagccaaaac tataaggctt gagagtgaag tgaatgcaat caaaggtgct 420
ctcaaaacaa ccaatgaggc agtatcaaca ctaggaaatg gagtgcgggt cctagccact 480
gcagtaagag agctgaaaga atttgtgagc aaaaacctga ctagtgcgat caacaagaac 540
aagtgtgaca ttgctgattt gaagatggct gtcagcttca gtcagttcaa cagaagattc 600
ctaaatggtt tgcggcagtt ttcagacaat gcagggataa caccagcaat atcattggac 660
ctgatgaatg atgctgagct ggcagagct gtatcataca tgccaacatc tgcaggacag 720
ataaaactaa tgttagagaa ccgtgcaatg gtgaggagaa aaggatttgg aatcttgata 780
ggggtctacg gaagctctgt gatttacatg gtcagctgc cgatctttgg tgcataaat 840
acacctgtt ggataatcaa ggcagctccc tcttgttcag aaaaagatgg aaattatgct 900
tgctctctaa gagaggatca aggggtggtat tgtaaaaaty caggatccac tgtttactac 960
ccaaatgaaa aagactgcga aacaagaggt gatcatgttt tttgtgacac agcagcaggg 1020
atcaatggtt ctgagcaatc aagagaatgc aacatcaaca tatctaccac caactacca 1080
tgcaaaagtc gcacaggaag acaccctatc agcatggtty cactatcacc tctcgggtgct 1140
ttggtagctt gotacaaaag ggttagctgc tgcactggca gtaatcaggt tggaaataac 1200
aaacaactac ctaaaagctg ctcatacata actaaccagg acgcagacac tgtaaacaat 1260
gacaacactg tgtatcaact aagcaaaagt gaggggtgaa agcatgtaat aaaagggaga 1320
ccagtttcaa gcagttttga tccaatcagg tttcctgagg atcagttcaa tgttgcgctt 1380
gatcaagtct ttgaaagcat tgaaaaacgt caagcactag tggaccagtc aaacaaaatt 1440
ctgaacagtg cagaaaaagg aaacactggt ttcattatgt taataatatt gattgctggt 1500
cttggggtta ccatgatttc agtgagcacc atcatcataa tcaaaaaaac aaggaagccc 1560
acaggggac ctccggagct gaatgggtgt accaacggcg gtttcatacc gcatagttag 1620

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<210> SEQ ID NO 4
<211> LENGTH: 1725
<212> TYPE: DNA
<213> ORGANISM: Human respiratory syncytial virus

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<400> SEQUENCE: 4

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atggagttgc caatctctaa aacaaatgca attaccacaa tcttctgtgc agtcacactc 60

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tgtttcgctt ccagtcacaaa catcactgaa gaattttatc aatcaacatg cagtgcagtt 120
agcaaaggct atcttagtgc tctaagaact ggttggtata ctagtgttat aactatagaa 180
ttaagtaata tcaaggaaaa taagtgtaat ggaacagatg ctaaggtaaa attgataaaa 240
caagaattag ataaatataa aaatgctgta acagaattgc agttgctcat gcaaagcaca 300
ccagcagcca acaatcgagc cagaagagaa ctaccaaggt ttatgaatta tacactcaat 360
aatacacaaa ataccaatgt aacattaagc aagaaaagga aaagaagatt tcttggttt 420
ttgttaggtg ttggatctgc aatcgccagt ggcattgctg tatctaaggt cctgcaccta 480
gaaggggaag tgaacaaaat caaaagtgtc ctactatcca caaacaaggc tgtagtcagc 540
ttatcaaatg gagttagtgt cttaccagc aaagtgttag acctcaaaaa ctatatagat 600
aaacagttgt tacctattgt gaacaagca agctgcagca tatcaaacat tgaactgtg 660
atagagttcc aacaaaagaa caacagacta ctayagatta ccagggaatt tagtgtaaat 720
gcaggtgtaa ctacacctgt aagcacttat atgttaacta atagtgaatt attatcatta 780
atcaatgata tgcctataac aaatgatcag aaaaagttaa tgtccaacaa tgttcaata 840
gttagacagc aaagttactc tatcatgtcc ataataaagg aggaagtctt agcatatgta 900
gtacaattac cactatatgg tghtaatagat acacctgtt ggaaactgca cacateccct 960
ctatgtacaa ccaacacaaa ggaaggttcc aacatctgtc taacaagaac cgacagagga 1020
tggattgtg acaatgcagg atcagtatct ttcttccac aagctgaaac atgtaaagtt 1080
caatcgaatc gggttatttg tgacacaatg aacagtttaa cattaccaag tgaagtaaat 1140
ctctgcaaca ttgacatatt caaccccaaa tatgattgca aaattatgac ttcaaaaaca 1200
gatgtaagca gctccgttat cacatctcta ggagccattg tgtcatgcta tggcaaaact 1260
aaatgtacag catccaataa aaatcgtggg atcataaaga cattttctaa cgggtgtgat 1320
tatgtatcaa ataagggggg ggatactgtg tctgtaggta atacattata ttatgtaaat 1380
aagcaagaag gcaaaagtct ctatgtaaaa ggtgaaccaa taataaattt ctatgacca 1440
ttagtgttcc cctctgatga atttgatgca tcaatatctc aagtcaatga gaagattaac 1500
cagagcctag catttattcg taaatccgat gaattattac ataatgtaaa tgcctggtaaa 1560
tccaccacaa atatcatgat aactactata attatagtga ttatagtaat attgttatca 1620
ttaattgcag ttggactgct cctatactgc aagycagaa gcacaccagt cacactaagt 1680
aaggatcaac tgagtggat aaataatatt gcatttagta actga 1725

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<210> SEQ ID NO 5
<211> LENGTH: 539
<212> TYPE: PRT
<213> ORGANISM: Human metapneumovirus isolate

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<400> SEQUENCE: 5

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Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1           5           10          15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
                20                25                30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
                35                40                45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
50                55                60

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Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80
 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95
 Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110
 Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125
 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140
 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160
 Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
 165 170 175
 Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
 180 185 190
 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205
 Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220
 Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240
 Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
 245 250 255
 Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
 260 265 270
 Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285
 Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300
 Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320
 Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335
 Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350
 Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365
 Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380
 Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400
 Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415
 Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430
 Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445
 Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
 450 455 460

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Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                               470                               475                               480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
                               485                               490                               495

Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
                               500                               505                               510

Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
                               515                               520                               525

Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
   530                               535

<210> SEQ ID NO 6
<211> LENGTH: 539
<212> TYPE: PRT
<213> ORGANISM: Human metapneumovirus

<400> SEQUENCE: 6

Met Ser Trp Lys Val Met Ile Ile Ile Ser Leu Leu Ile Thr Pro Gln
1      5      10      15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
   20      25      30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
   35      40      45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Thr Asp Gly Pro
   50      55      60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
   65      70      75      80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
   85      90      95

Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
  100     105     110

Ala Thr Ala Ala Ala Val Thr Ala Gly Ile Ala Ile Ala Lys Thr Ile
  115     120     125

Arg Leu Glu Ser Glu Val Asn Ala Ile Lys Gly Ala Leu Lys Gln Thr
  130     135     140

Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
  145     150     155     160

Ala Val Arg Glu Leu Lys Glu Phe Val Ser Lys Asn Leu Thr Ser Ala
  165     170     175

Ile Asn Arg Asn Lys Cys Asp Ile Ala Asp Leu Lys Met Ala Val Ser
  180     185     190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
  195     200     205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
  210     215     220

Ala Glu Leu Ala Arg Ala Val Ser Tyr Met Pro Thr Ser Ala Gly Gln
  225     230     235     240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
  245     250     255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
  260     265     270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala
  275     280     285

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Ala Pro Ser Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300

Glu Asp Gln Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile
 340 345 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Trp Val Gly Ile Ile
 385 390 395 400

Lys Gln Leu Pro Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445

Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
 450 455 460

Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Lys Ile
 465 470 475 480

Leu Asn Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Val Ile
 485 490 495

Leu Val Ala Val Leu Gly Leu Thr Met Ile Ser Val Ser Ile Ile Ile
 500 505 510

Ile Ile Lys Lys Thr Arg Lys Pro Thr Gly Ala Pro Pro Glu Leu Asn
 515 520 525

Gly Val Thr Asn Gly Gly Phe Ile Pro His Ser
 530 535

<210> SEQ ID NO 7

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Human metapneumovirus

<400> SEQUENCE: 7

Met Ser Trp Lys Val Met Ile Ile Ile Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
 35 40 45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Thr Asp Gly Pro
 50 55 60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95

Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val

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100					105					110					
Ala	Thr	Ala	Ala	Ala	Val	Thr	Ala	Gly	Ile	Ala	Ile	Ala	Lys	Thr	Ile
		115					120					125			
Arg	Leu	Glu	Ser	Glu	Val	Asn	Ala	Ile	Lys	Gly	Ala	Leu	Lys	Thr	Thr
	130					135					140				
Asn	Glu	Ala	Val	Ser	Thr	Leu	Gly	Asn	Gly	Val	Arg	Val	Leu	Ala	Thr
145						150					155				160
Ala	Val	Arg	Glu	Leu	Lys	Glu	Phe	Val	Ser	Lys	Asn	Leu	Thr	Ser	Ala
				165							170				175
Ile	Asn	Lys	Asn	Lys	Cys	Asp	Ile	Ala	Asp	Leu	Lys	Met	Ala	Val	Ser
			180					185					190		
Phe	Ser	Gln	Phe	Asn	Arg	Arg	Phe	Leu	Asn	Val	Val	Arg	Gln	Phe	Ser
		195					200						205		
Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Asn	Asp
	210					215					220				
Ala	Glu	Leu	Ala	Arg	Ala	Val	Ser	Tyr	Met	Pro	Thr	Ser	Ala	Gly	Gln
225						230					235				240
Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe
				245					250					255	
Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln
		260						265					270		
Leu	Pro	Ile	Phe	Gly	Val	Ile	Asn	Thr	Pro	Cys	Trp	Ile	Ile	Lys	Ala
		275					280						285		
Ala	Pro	Ser	Cys	Ser	Glu	Lys	Asp	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
	290					295					300				
Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Lys	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
305						310					315				320
Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp
				325					330					335	
Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Arg	Glu	Cys	Asn	Ile
			340					345						350	
Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
		355					360						365		
Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
	370					375					380				
Tyr	Lys	Gly	Val	Ser	Cys	Ser	Thr	Gly	Ser	Asn	Gln	Val	Gly	Ile	Ile
385						390					395				400
Lys	Gln	Leu	Pro	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
				405					410					415	
Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
			420					425						430	
Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
		435					440						445		
Ile	Arg	Phe	Pro	Glu	Asp	Gln	Phe	Asn	Val	Ala	Leu	Asp	Gln	Val	Phe
	450					455					460				
Glu	Ser	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Lys	Ile
465						470					475				480
Leu	Asn	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile
				485					490					495	
Leu	Ile	Ala	Val	Leu	Gly	Leu	Thr	Met	Ile	Ser	Val	Ser	Ile	Ile	Ile
			500					505						510	

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Ile Ile Lys Lys Thr Arg Lys Pro Thr Gly Ala Pro Pro Glu Leu Asn
515 520 525

Gly Val Thr Asn Gly Gly Phe Ile Pro His Ser
530 535

<210> SEQ ID NO 8

<211> LENGTH: 574

<212> TYPE: PRT

<213> ORGANISM: Human respiratory syncytial virus

<400> SEQUENCE: 8

Met Glu Leu Pro Ile Leu Lys Thr Asn Ala Ile Thr Thr Ile Leu Ala
1 5 10 15

Ala Val Thr Leu Cys Phe Ala Ser Ser Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
85 90 95

Met Gln Ser Thr Pro Ala Ala Asn Asn Arg Ala Arg Arg Glu Leu Pro
100 105 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Thr Lys Asn Thr Asn Val Thr
115 120 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
130 135 140

Gly Ser Ala Ile Ala Ser Gly Ile Ala Val Ser Lys Val Leu His Leu
145 150 155 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
165 170 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
180 185 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Val Asn
195 200 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
210 215 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225 230 235 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
245 250 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
260 265 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
275 280 285

Met Ser Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
290 295 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305 310 315 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg

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	325		330		335										
Thr	Asp	Arg	Gly	Trp	Tyr	Cys	Asp	Asn	Ala	Gly	Ser	Val	Ser	Phe	Phe
			340					345						350	
Pro	Gln	Ala	Glu	Thr	Cys	Lys	Val	Gln	Ser	Asn	Arg	Val	Phe	Cys	Asp
			355					360					365		
Thr	Met	Asn	Ser	Leu	Thr	Leu	Pro	Ser	Glu	Val	Asn	Leu	Cys	Asn	Ile
			370					375					380		
Asp	Ile	Phe	Asn	Pro	Lys	Tyr	Asp	Cys	Lys	Ile	Met	Thr	Ser	Lys	Thr
			385			390				395					400
Asp	Val	Ser	Ser	Ser	Val	Ile	Thr	Ser	Leu	Gly	Ala	Ile	Val	Ser	Cys
				405					410						415
Tyr	Gly	Lys	Thr	Lys	Cys	Thr	Ala	Ser	Asn	Lys	Asn	Arg	Gly	Ile	Ile
			420					425						430	
Lys	Thr	Phe	Ser	Asn	Gly	Cys	Asp	Tyr	Val	Ser	Asn	Lys	Gly	Val	Asp
			435				440						445		
Thr	Val	Ser	Val	Gly	Asn	Thr	Leu	Tyr	Tyr	Val	Asn	Lys	Gln	Glu	Gly
	450					455					460				
Lys	Ser	Leu	Tyr	Val	Lys	Gly	Glu	Pro	Ile	Ile	Asn	Phe	Tyr	Asp	Pro
			465		470					475					480
Leu	Val	Phe	Pro	Ser	Asp	Glu	Phe	Asp	Ala	Ser	Ile	Ser	Gln	Val	Asn
				485					490						495
Glu	Lys	Ile	Asn	Gln	Ser	Leu	Ala	Phe	Ile	Arg	Lys	Ser	Asp	Glu	Leu
			500						505					510	
Leu	His	Asn	Val	Asn	Ala	Gly	Lys	Ser	Thr	Thr	Asn	Ile	Met	Ile	Thr
		515					520						525		
Thr	Ile	Ile	Ile	Val	Ile	Ile	Val	Ile	Leu	Leu	Ser	Leu	Ile	Ala	Val
	530					535						540			
Gly	Leu	Leu	Leu	Tyr	Cys	Lys	Ala	Arg	Ser	Thr	Pro	Val	Thr	Leu	Ser
	545				550					555					560
Lys	Asp	Gln	Leu	Ser	Gly	Ile	Asn	Asn	Ile	Ala	Phe	Ser	Asn		
			565						570						

<210> SEQ ID NO 9
 <211> LENGTH: 1617
 <212> TYPE: DNA
 <213> ORGANISM: Human parainfluenza virus 3
 <400> SEQUENCE: 9

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atgccaatTT caatactgtt aattattaca accatgatca tggcatcaca ctgccaaata    60
gacatcacia aactacagca tgtagggtga ttggtcaaca gtcccaaagg gatgaagata    120
tcacaaaact tcgaacaag atacttaate ctgagtctca taccaaaaat agaagattct    180
aactcttgtg gtgaccaaca gatcaagcaa tacaagaggt tattggatag actgatcatt    240
cctttatatg atggactaag attacagaag gatgtgatag tgactaatca agaatccaat    300
gaaaacactg atcccagaac agaacgatc tttggagggg taattggaac tattgctcta    360
ggagttagca cctcagcaca aattacagca gcagttgctc tggttgaagc caagcaggca    420
agatcagaca ttgaaaaact caaggaagca atcagggaca caaataaagc agtgcagtca    480
gttcagagct ctgtaggaaa tttgatagta gcaattaat cagtccagga ttatgtcaac    540
aaagaaatcy tgccatgat tgcgagacta ggttgtgaag cagcaggact tcagttaggg    600
attgcattaa cacagcatta ctcagaatta acaaatatat ttggtgataa cataggatcy    660
    
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ttacaagaaa aaggaataaa attacaaggt atagcatcat tataccgtac aaatatcaca 720
gaaatattca caacatcaac agttgacaaa tatgatattt atgatctatt atttacagaa 780
tcaataaagg tgagagttat agatgttgat ttgaatgatt actcaataac cctccaagtc 840
agactccett tattgaccag actgctgaac actcaaatct acaaagtaga ttccatatca 900
tacaatatcc aaaatagaga atggtatate cctcttccca gccatatcat gacgaaaggg 960
gcatttctag gtggagcaga tgtcaaaaga tgcataagaag cattcagcag ttatatatgc 1020
ccttctgac caggatttgt actaaaacct gaaatggaga gctgtctate aggaaacata 1080
tcccaatgtc caagaaccac agtcacatca gacatagttc ctaggtatgc atttgtcaat 1140
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<210> SEQ ID NO 10

<211> LENGTH: 1716

<212> TYPE: DNA

<213> ORGANISM: Human parainfluenza virus 3

<400> SEQUENCE: 10

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ctggtgttat tatcaatagt cttcatcata gtgctaacta attccatcaa aagtgaaaag 180
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caagtggcat cggataatac taatgatcta atacagtcag gagtgaatac aaggcttctt 300
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aaagggtatt gttttcatat agtagaata aatcataaaa gcttaaacac atttcaacc 1680
atggtgttca aaacagagat tccaaaaagc tgcagt 1716

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<210> SEQ ID NO 11

<211> LENGTH: 1716

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 11

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atcagaaaca agaccctgag cgcggctac accaccacaa gctgcatcac acactacaac	1620
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<210> SEQ ID NO 12

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 12

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aaacagctcg cgaaccagca gatcaagcag tacaagcggc tgctggacag actgatcacc	240
ccctgtacg accgctcg cctgcagaaa gacgtgatcg tgaccaacca ggaagcaac	300
gagaacaccg acccccggac cgagagattc ttccggcgcg tgatcggcac aatcccccctg	360
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<210> SEQ ID NO 13

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Human parainfluenza virus 3

<400> SEQUENCE: 13

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His Cys Gln Ile Asp Ile Thr Lys Leu Gln His Val Gly Val Leu Val
 20 25 30

Asn Ser Pro Lys Gly Met Lys Ile Ser Gln Asn Phe Glu Thr Arg Tyr
 35 40 45

Leu Ile Leu Ser Leu Ile Pro Lys Ile Glu Asp Ser Asn Ser Cys Gly
 50 55 60

Asp Gln Gln Ile Lys Gln Tyr Lys Arg Leu Leu Asp Arg Leu Ile Ile
 65 70 75 80

Pro Leu Tyr Asp Gly Leu Arg Leu Gln Lys Asp Val Ile Val Thr Asn
 85 90 95

Gln Glu Ser Asn Glu Asn Thr Asp Pro Arg Thr Glu Arg Phe Phe Gly
 100 105 110

Gly Val Ile Gly Thr Ile Ala Leu Gly Val Ala Thr Ser Ala Gln Ile
 115 120 125

Thr Ala Ala Val Ala Leu Val Glu Ala Lys Gln Ala Arg Ser Asp Ile
 130 135 140

Glu Lys Leu Lys Glu Ala Ile Arg Asp Thr Asn Lys Ala Val Gln Ser
 145 150 155 160

Val Gln Ser Ser Val Gly Asn Leu Ile Val Ala Ile Lys Ser Val Gln
 165 170 175

Asp Tyr Val Asn Lys Glu Ile Val Pro Ser Ile Ala Arg Leu Gly Cys
 180 185 190

Glu Ala Ala Gly Leu Gln Leu Gly Ile Ala Leu Thr Gln His Tyr Ser
 195 200 205

Glu Leu Thr Asn Ile Phe Gly Asp Asn Ile Gly Ser Leu Gln Glu Lys
 210 215 220

Gly Ile Lys Leu Gln Gly Ile Ala Ser Leu Tyr Arg Thr Asn Ile Thr
 225 230 235 240

Glu Ile Phe Thr Thr Ser Thr Val Asp Lys Tyr Asp Ile Tyr Asp Leu
 245 250 255

Leu Phe Thr Glu Ser Ile Lys Val Arg Val Ile Asp Val Asp Leu Asn
 260 265 270

Asp Tyr Ser Ile Thr Leu Gln Val Arg Leu Pro Leu Leu Thr Arg Leu
 275 280 285

Leu Asn Thr Gln Ile Tyr Lys Val Asp Ser Ile Ser Tyr Asn Ile Gln
 290 295 300

Asn Arg Glu Trp Tyr Ile Pro Leu Pro Ser His Ile Met Thr Lys Gly
 305 310 315 320

Ala Phe Leu Gly Gly Ala Asp Val Lys Glu Cys Ile Glu Ala Phe Ser
 325 330 335

Ser Tyr Ile Cys Pro Ser Asp Pro Gly Phe Val Leu Asn His Glu Met
 340 345 350

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<210> SEQ ID NO 15
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 15
Met Glu Thr Pro Ala Gln Leu Leu Phe Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly
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<210> SEQ ID NO 16
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 16
Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1 5 10 15

His Ser

<210> SEQ ID NO 17
<211> LENGTH: 24
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 17
Met Leu Gly Ser Asn Ser Gly Gln Arg Val Val Phe Thr Ile Leu Leu
1 5 10 15

Leu Leu Val Ala Pro Ala Tyr Ser
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<210> SEQ ID NO 18
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 18
Met Lys Cys Leu Leu Tyr Leu Ala Phe Leu Phe Ile Gly Val Asn Cys
1 5 10 15

Ala

<210> SEQ ID NO 19
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 19
Met Trp Leu Val Ser Leu Ala Ile Val Thr Ala Cys Ala Gly Ala
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<210> SEQ ID NO 20
<211> LENGTH: 4062
<212> TYPE: DNA
<213> ORGANISM: Middle East respiratory syndrome coronavirus
<400> SEQUENCE: 20

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cgtaatgcca gtctgaactc ttttaaggag tattttaatt taogtaactg cacctttatg 720
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<210> SEQ ID NO 21

<211> LENGTH: 4062

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

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<400> SEQUENCE: 21

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tattattctg atgatggcaa ctactactgt ttgcgtgctt gctttagtyt tctgtttct    1980
gtcatctatg ataaagaaac taaaaccac gctactctat ttggtagtgt tgcagtgtgaa    2040
cacatttctt ctaccatgct tcaatactcc cgttctacgc gatcaatgct taaacggcga    2100
gattctacat atggccccct tcagacacct gttggttgtg tcttaggact tgttaattcc    2160
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acacctagta ctctcacacc tgcagtggtg cgcctctgttc caggtgaaat gcgcttgcca 2280
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gatcttacct acgagatgtt gctcttcaa caagttgta aagcccttaa tgagctttac 3840
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cttggtttca ttgctgggct tgttgctta gctctatgcy tcttctctat actgtgctgc 3960
actggttgtg gcacaaaactg tatgggaaaa cttaagtgt atcgttggty tgatagatac 4020
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<210> SEQ ID NO 22

<211> LENGTH: 1845

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 22

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atgatccact cagtgcttct cctcatgttc ctggtgacct ccaactgagtc agactgcaag 60
ctcccgtggy gacagtcctt gtgtgcgctg cctgacactc ctgacactct gacccccagc 120

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tcogtgoggt cgggtgectgg cgaaatgegg ctggectcca tegeettcaa teaccaate	180
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ggggtcacc caggatcacat ccagaccaca attcagaagg tcaccgtcga ttgcaagcaa	300
taogtgtgca aoggcttcca gaagtgcgag cagetgctga gagaatacgg gcagttttgc	360
agcaagatca accaggcgct gcattggagct aacttgccgc aggacgactc cgtgcgcaac	420
ctctttgect ctgtgaagtc atcccagtc tccccaatca tccccggatt cggaggggac	480
ttcaacctga cctctctgga gccogtctcg atcagcaccg gtagecagtc ggcgcgctca	540
gccattgaag atcttctggt cgaacaaggtc accatgcgag atccgggcta catgcagggc	600
taagcagact gtatgcagca gggaccagcc tcgcgaggg accctatctg cgcgcaatac	660
gtggcoggg acaaatgtgt gctctctctg atggatgtga acatggaggc cgtttatact	720
tcgtccctgc tcggctctat cgcggcgctg ggggtggacc cgggcctgct ctccttgcgc	780
gctatccctc ttgcacaatc cttttctac cggctcaacg gcgtgggcat tactcaacaa	840
gtcctgtcgg agaaccagaa gttgatcgca aacaagttca atcaggccct gggggccatg	900
cagactggat tcactacgac taacgaagcg ttccagaagg tccaggacgc tgtgaacaac	960
aacgcccagg cgtctctaaa gctggcctcc gaactcagca acaccttgg agccatcagc	1020
gcctcagtc gtgacataat tcagcggctg gacgtgctgg agcaggaagc ccagatcgac	1080
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cttcaacaag tggtaaggc cctgaacgag agctacatcg acctgaagga gctgggcaac	1740
tatacctact acaacaagtg gccggacaag attgaggaga ttctgtcgaa aatctaccac	1800
attgaaaacg agatgccag aatcaagaag cttatcggcg aagcc	1845

<210> SEQ ID NO 23

<211> LENGTH: 4071

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 23

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agctatgtgg acgtgggccc cgatagegty aagtcgcct gtatcgaagt ggacatccag	120
cagacctttt togacaagac ctggcccaga cccatcgacg tgtccaaggc cgacggcatc	180
atctatccac aaggccggac ctacagcaac atcaccatta cctaccaggy cctgttccca	240

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tatcaaggcg	accacggcga	tatgtacgtg	tactctgccg	gccacgccac	cgcaaccaca	300
ccccagaaac	tggtcgtggc	caactacagc	caggacgtga	agcagttcgc	caacggcttc	360
gtcgtgcgga	ttggcgccgc	tgccaatagc	accggcacag	tgatcatcag	ccccagcacc	420
agcgccacca	tccggaagat	ctaaccggcc	ttcatgctgg	gcagctccgt	gggcaatttc	480
agcgacggca	agatgggccc	gttcttcaac	cacaccctgg	tgctgctgcc	cgatggctgt	540
ggcacactgc	tgagagcctt	ctactgcate	ctggaacca	gaagcggcaa	ccactgccct	600
gcggcaata	gotadaccag	cttggccacc	taccacacac	ccgcccacga	ttgctccgac	660
ggcaactaca	accggaacgc	cagcctgaac	agcttcaaac	agtacttcaa	cctgcgggac	720
tgacacctta	tgtaacacta	caatataacc	gaggacgaga	tcctggaatg	gttcggcacc	780
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<210> SEQ ID NO 24

<211> LENGTH: 1353

<212> TYPE: PRT

<213> ORGANISM: Middle East respiratory syndrome coronavirus

<400> SEQUENCE: 24

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Met Ile His Ser Val Phe Leu Leu Met Phe Leu Leu Thr Pro Thr Glu
1             5             10             15

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Ser Tyr Val Asp Val Gly Pro Asp Ser Val Lys Ser Ala Cys Ile Glu
20             25             30

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Val Asp Ile Gln Gln Thr Phe Phe Asp Lys Thr Trp Pro Arg Pro Ile
35             40             45

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Asp Val Ser Lys Ala Asp Gly Ile Ile Tyr Pro Gln Gly Arg Thr Tyr
50             55             60

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Ser Asn Ile Thr Ile Thr Tyr Gln Gly Leu Phe Pro Tyr Gln Gly Asp
65             70             75             80

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His Gly Asp Met Tyr Val Tyr Ser Ala Gly His Ala Thr Gly Thr Thr

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85					90					95					
Pro	Gln	Lys	Leu	Phe	Val	Ala	Asn	Tyr	Ser	Gln	Asp	Val	Lys	Gln	Phe
			100					105					110		
Ala	Asn	Gly	Phe	Val	Val	Arg	Ile	Gly	Ala	Ala	Ala	Asn	Ser	Thr	Gly
		115					120					125			
Thr	Val	Ile	Ile	Ser	Pro	Ser	Thr	Ser	Ala	Thr	Ile	Arg	Lys	Ile	Tyr
	130					135					140				
Pro	Ala	Phe	Met	Leu	Gly	Ser	Ser	Val	Gly	Asn	Phe	Ser	Asp	Gly	Lys
145					150					155					160
Met	Gly	Arg	Phe	Phe	Asn	His	Thr	Leu	Val	Leu	Leu	Pro	Asp	Gly	Cys
			165					170						175	
Gly	Thr	Leu	Leu	Arg	Ala	Phe	Tyr	Cys	Ile	Leu	Glu	Pro	Arg	Ser	Gly
		180						185					190		
Asn	His	Cys	Pro	Ala	Gly	Asn	Ser	Tyr	Thr	Ser	Phe	Ala	Thr	Tyr	His
		195					200					205			
Thr	Pro	Ala	Thr	Asp	Cys	Ser	Asp	Gly	Asn	Tyr	Asn	Arg	Asn	Ala	Ser
	210					215					220				
Leu	Asn	Ser	Phe	Lys	Glu	Tyr	Phe	Asn	Leu	Arg	Asn	Cys	Thr	Phe	Met
225					230					235					240
Tyr	Thr	Tyr	Asn	Ile	Thr	Glu	Asp	Glu	Ile	Leu	Glu	Trp	Phe	Gly	Ile
			245						250					255	
Thr	Gln	Thr	Ala	Gln	Gly	Val	His	Leu	Phe	Ser	Ser	Arg	Tyr	Val	Asp
			260					265						270	
Leu	Tyr	Gly	Gly	Asn	Met	Phe	Gln	Phe	Ala	Thr	Leu	Pro	Val	Tyr	Asp
		275					280					285			
Thr	Ile	Lys	Tyr	Tyr	Ser	Ile	Ile	Pro	His	Ser	Ile	Arg	Ser	Ile	Gln
	290					295					300				
Ser	Asp	Arg	Lys	Ala	Trp	Ala	Ala	Phe	Tyr	Val	Tyr	Lys	Leu	Gln	Pro
305					310					315					320
Leu	Thr	Phe	Leu	Leu	Asp	Phe	Ser	Val	Asp	Gly	Tyr	Ile	Arg	Arg	Ala
			325						330					335	
Ile	Asp	Cys	Gly	Phe	Asn	Asp	Leu	Ser	Gln	Leu	His	Cys	Ser	Tyr	Glu
			340					345					350		
Ser	Phe	Asp	Val	Glu	Ser	Gly	Val	Tyr	Ser	Val	Ser	Ser	Phe	Glu	Ala
		355					360						365		
Lys	Pro	Ser	Gly	Ser	Val	Val	Glu	Gln	Ala	Glu	Gly	Val	Glu	Cys	Asp
	370					375					380				
Phe	Ser	Pro	Leu	Leu	Ser	Gly	Thr	Pro	Pro	Gln	Val	Tyr	Asn	Phe	Lys
385					390					395					400
Arg	Leu	Val	Phe	Thr	Asn	Cys	Asn	Tyr	Asn	Leu	Thr	Lys	Leu	Leu	Ser
			405						410					415	
Leu	Phe	Ser	Val	Asn	Asp	Phe	Thr	Cys	Ser	Gln	Ile	Ser	Pro	Ala	Ala
			420					425					430		
Ile	Ala	Ser	Asn	Cys	Tyr	Ser	Ser	Leu	Ile	Leu	Asp	Tyr	Phe	Ser	Tyr
	435							440					445		
Pro	Leu	Ser	Met	Lys	Ser	Asp	Leu	Ser	Val	Ser	Ser	Ala	Gly	Pro	Ile
	450					455						460			
Ser	Gln	Phe	Asn	Tyr	Lys	Gln	Ser	Phe	Ser	Asn	Pro	Thr	Cys	Leu	Ile
465					470					475					480
Leu	Ala	Thr	Val	Pro	His	Asn	Leu	Thr	Thr	Ile	Thr	Lys	Pro	Leu	Lys
				485					490						495

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Lys Val Thr Ile Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys
 900 905 910

Met Gln Gln Gly Pro Ala Ser Ala Arg Asp Leu Ile Cys Ala Gln Tyr
 915 920 925

Val Ala Gly Tyr Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu
 930 935 940

Ala Ala Tyr Thr Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp
 945 950 955 960

Thr Ala Gly Leu Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile
 965 970 975

Phe Tyr Arg Leu Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu
 980 985 990

Asn Gln Lys Leu Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met
 995 1000 1005

Gln Thr Gly Phe Thr Thr Thr Asn Glu Ala Phe Arg Lys Val Gln
 1010 1015 1020

Asp Ala Val Asn Asn Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser
 1025 1030 1035

Glu Leu Ser Asn Thr Phe Gly Ala Ile Ser Ala Ser Ile Gly Asp
 1040 1045 1050

Ile Ile Gln Arg Leu Asp Val Leu Glu Gln Asp Ala Gln Ile Asp
 1055 1060 1065

Arg Leu Ile Asn Gly Arg Leu Thr Thr Leu Asn Ala Phe Val Ala
 1070 1075 1080

Gln Gln Leu Val Arg Ser Glu Ser Ala Ala Leu Ser Ala Gln Leu
 1085 1090 1095

Ala Lys Asp Lys Val Asn Glu Cys Val Lys Ala Gln Ser Lys Arg
 1100 1105 1110

Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val Ser Phe Val Val
 1115 1120 1125

Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly Tyr Tyr Pro
 1130 1135 1140

Ser Asn His Ile Glu Val Val Ser Ala Tyr Gly Leu Cys Asp Ala
 1145 1150 1155

Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe Ile
 1160 1165 1170

Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly
 1175 1180 1185

Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys
 1190 1195 1200

Tyr Val Ala Pro Gln Val Thr Tyr Gln Asn Ile Ser Thr Asn Leu
 1205 1210 1215

Pro Pro Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp
 1220 1225 1230

Glu Leu Asp Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn
 1235 1240 1245

Phe Gly Ser Leu Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr
 1250 1255 1260

Tyr Glu Met Leu Ser Leu Gln Gln Val Val Lys Ala Leu Asn Glu
 1265 1270 1275

Ser Tyr Ile Asp Leu Lys Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn

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1280	1285	1290
Lys Trp Pro Trp Tyr Ile	Trp Leu Gly Phe Ile Ala	Gly Leu Val
1295	1300	1305
Ala Leu Ala Leu Cys Val	Phe Phe Ile Leu Cys Cys	Thr Gly Cys
1310	1315	1320
Gly Thr Asn Cys Met Gly	Lys Leu Lys Cys Asn Arg	Cys Cys Asp
1325	1330	1335
Arg Tyr Glu Glu Tyr Asp	Leu Glu Pro His Lys Val	His Val His
1340	1345	1350

<210> SEQ ID NO 25

<211> LENGTH: 1353

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 25

Met Ile His Ser Val Phe Leu Leu Met Phe Leu Leu Thr Pro Thr Glu		
1	5	10 15
Ser Tyr Val Asp Val Gly Pro Asp Ser Val Lys Ser Ala Cys Ile Glu		
	20	25 30
Val Asp Ile Gln Gln Thr Phe Phe Asp Lys Thr Trp Pro Arg Pro Ile		
	35	40 45
Asp Val Ser Lys Ala Asp Gly Ile Ile Tyr Pro Gln Gly Arg Thr Tyr		
50	55	60
Ser Asn Ile Thr Ile Thr Tyr Gln Gly Leu Phe Pro Tyr Gln Gly Asp		
65	70	75 80
His Gly Asp Met Tyr Val Tyr Ser Ala Gly His Ala Thr Gly Thr Thr		
	85	90 95
Pro Gln Lys Leu Phe Val Ala Asn Tyr Ser Gln Asp Val Lys Gln Phe		
	100	105 110
Ala Asn Gly Phe Val Val Arg Ile Gly Ala Ala Ala Asn Ser Thr Gly		
	115	120 125
Thr Val Ile Ile Ser Pro Ser Thr Ser Ala Thr Ile Arg Lys Ile Tyr		
	130	135 140
Pro Ala Phe Met Leu Gly Ser Ser Val Gly Asn Phe Ser Asp Gly Lys		
145	150	155 160
Met Gly Arg Phe Phe Asn His Thr Leu Val Leu Leu Pro Asp Gly Cys		
	165	170 175
Gly Thr Leu Leu Arg Ala Phe Tyr Cys Ile Leu Glu Pro Arg Ser Gly		
	180	185 190
Asn His Cys Pro Ala Gly Asn Ser Tyr Thr Ser Phe Ala Thr Tyr His		
	195	200 205
Thr Pro Ala Thr Asp Cys Ser Asp Gly Asn Tyr Asn Arg Asn Ala Ser		
	210	215 220
Leu Asn Ser Phe Lys Glu Tyr Phe Asn Leu Arg Asn Cys Thr Phe Met		
225	230	235 240
Tyr Thr Tyr Asn Ile Thr Glu Asp Glu Ile Leu Glu Trp Phe Gly Ile		
	245	250 255
Thr Gln Thr Ala Gln Gly Val His Leu Phe Ser Ser Arg Tyr Val Asp		
	260	265 270
Leu Tyr Gly Gly Asn Met Phe Gln Phe Ala Thr Leu Pro Val Tyr Asp		

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275				280				285							
Thr	Ile	Lys	Tyr	Tyr	Ser	Ile	Ile	Pro	His	Ser	Ile	Arg	Ser	Ile	Gln
290						295						300			
Ser	Asp	Arg	Lys	Ala	Trp	Ala	Ala	Phe	Tyr	Val	Tyr	Lys	Leu	Gln	Pro
305					310						315				320
Leu	Thr	Phe	Leu	Leu	Asp	Phe	Ser	Val	Asp	Gly	Tyr	Ile	Arg	Arg	Ala
			325						330						335
Ile	Asp	Cys	Gly	Phe	Asn	Asp	Leu	Ser	Gln	Leu	His	Cys	Ser	Tyr	Glu
			340						345						350
Ser	Phe	Asp	Val	Glu	Ser	Gly	Val	Tyr	Ser	Val	Ser	Ser	Phe	Glu	Ala
		355					360								365
Lys	Pro	Ser	Gly	Ser	Val	Val	Glu	Gln	Ala	Glu	Gly	Val	Glu	Cys	Asp
		370				375									380
Phe	Ser	Pro	Leu	Leu	Ser	Gly	Thr	Pro	Pro	Gln	Val	Tyr	Asn	Phe	Lys
385					390						395				400
Arg	Leu	Val	Phe	Thr	Asn	Cys	Asn	Tyr	Asn	Leu	Thr	Lys	Leu	Leu	Ser
			405							410					415
Leu	Phe	Ser	Val	Asn	Asp	Phe	Thr	Cys	Ser	Gln	Ile	Ser	Pro	Ala	Ala
			420							425					430
Ile	Ala	Ser	Asn	Cys	Tyr	Ser	Ser	Leu	Ile	Leu	Asp	Tyr	Phe	Ser	Tyr
			435								440				445
Pro	Leu	Ser	Met	Lys	Ser	Asp	Leu	Ser	Val	Ser	Ser	Ala	Gly	Pro	Ile
			450			455									460
Ser	Gln	Phe	Asn	Tyr	Lys	Gln	Ser	Phe	Ser	Asn	Pro	Thr	Cys	Leu	Ile
465					470						475				480
Leu	Ala	Thr	Val	Pro	His	Asn	Leu	Thr	Thr	Ile	Thr	Lys	Pro	Leu	Lys
			485							490					495
Tyr	Ser	Tyr	Ile	Asn	Lys	Cys	Ser	Arg	Leu	Leu	Ser	Asp	Asp	Arg	Thr
			500							505					510
Glu	Val	Pro	Gln	Leu	Val	Asn	Ala	Asn	Gln	Tyr	Ser	Pro	Cys	Val	Ser
			515				520								525
Ile	Val	Pro	Ser	Thr	Val	Trp	Glu	Asp	Gly	Asp	Tyr	Tyr	Arg	Lys	Gln
			530			535									540
Leu	Ser	Pro	Leu	Glu	Gly	Gly	Gly	Trp	Leu	Val	Ala	Ser	Gly	Ser	Thr
545					550						555				560
Val	Ala	Met	Thr	Glu	Gln	Leu	Gln	Met	Gly	Phe	Gly	Ile	Thr	Val	Gln
			565								570				575
Tyr	Gly	Thr	Asp	Thr	Asn	Ser	Val	Cys	Pro	Lys	Leu	Glu	Phe	Ala	Asn
			580							585					590
Asp	Thr	Lys	Ile	Ala	Ser	Gln	Leu	Gly	Asn	Cys	Val	Glu	Tyr	Ser	Leu
			595				600								605
Tyr	Gly	Val	Ser	Gly	Arg	Gly	Val	Phe	Gln	Asn	Cys	Thr	Ala	Val	Gly
			610				615								620
Val	Arg	Gln	Gln	Arg	Phe	Val	Tyr	Asp	Ala	Tyr	Gln	Asn	Leu	Val	Gly
625					630						635				640
Tyr	Tyr	Ser	Asp	Asp	Gly	Asn	Tyr	Tyr	Cys	Leu	Arg	Ala	Cys	Val	Ser
			645							650					655
Val	Pro	Val	Ser	Val	Ile	Tyr	Asp	Lys	Glu	Thr	Lys	Thr	His	Ala	Thr
			660							665					670
Leu	Phe	Gly	Ser	Val	Ala	Cys	Glu	His	Ile	Ser	Ser	Thr	Met	Ser	Gln
			675				680								685

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Tyr Ser Arg Ser Thr Arg Ser Met Leu Lys Arg Arg Asp Ser Thr Tyr
 690 695 700
 Gly Pro Leu Gln Thr Pro Val Gly Cys Val Leu Gly Leu Val Asn Ser
 705 710 715 720
 Ser Leu Phe Val Glu Asp Cys Lys Leu Pro Leu Gly Gln Ser Leu Cys
 725 730 735
 Ala Leu Pro Asp Thr Pro Ser Thr Leu Thr Pro Arg Ser Val Arg Ser
 740 745 750
 Val Pro Gly Glu Met Arg Leu Ala Ser Ile Ala Phe Asn His Pro Ile
 755 760 765
 Gln Val Asp Gln Leu Asn Ser Ser Tyr Phe Lys Leu Ser Ile Pro Thr
 770 775 780
 Asn Phe Ser Phe Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln
 785 790 795 800
 Lys Val Thr Val Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys
 805 810 815
 Cys Glu Gln Leu Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn
 820 825 830
 Gln Ala Leu His Gly Ala Asn Leu Arg Gln Asp Asp Ser Val Arg Asn
 835 840 845
 Leu Phe Ala Ser Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly
 850 855 860
 Phe Gly Gly Asp Phe Asn Leu Thr Leu Leu Glu Pro Val Ser Ile Ser
 865 870 875 880
 Thr Gly Ser Arg Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp
 885 890 895
 Lys Val Thr Ile Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys
 900 905 910
 Met Gln Gln Gly Pro Ala Ser Ala Arg Asp Leu Ile Cys Ala Gln Tyr
 915 920 925
 Val Ala Gly Tyr Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu
 930 935 940
 Ala Ala Tyr Thr Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp
 945 950 955 960
 Thr Ala Gly Leu Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile
 965 970 975
 Phe Tyr Arg Leu Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu
 980 985 990
 Asn Gln Lys Leu Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met
 995 1000 1005
 Gln Thr Gly Phe Thr Thr Thr Asn Glu Ala Phe Gln Lys Val Gln
 1010 1015 1020
 Asp Ala Val Asn Asn Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser
 1025 1030 1035
 Glu Leu Ser Asn Thr Phe Gly Ala Ile Ser Ala Ser Ile Gly Asp
 1040 1045 1050
 Ile Ile Gln Arg Leu Asp Val Leu Glu Gln Asp Ala Gln Ile Asp
 1055 1060 1065
 Arg Leu Ile Asn Gly Arg Leu Thr Thr Leu Asn Ala Phe Val Ala
 1070 1075 1080

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Leu Asn Ser Ser Tyr Phe Lys Leu Ser Ile Pro Thr Asn Phe Ser Phe
 65 70 75 80
 Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln Lys Val Thr Val
 85 90 95
 Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys Cys Glu Gln Leu
 100 105 110
 Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn Gln Ala Leu His
 115 120 125
 Gly Ala Asn Leu Arg Gln Asp Asp Ser Val Arg Asn Leu Phe Ala Ser
 130 135 140
 Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly Phe Gly Gly Asp
 145 150 155 160
 Phe Asn Leu Thr Leu Leu Glu Pro Val Ser Ile Ser Thr Gly Ser Arg
 165 170 175
 Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp Lys Val Thr Ile
 180 185 190
 Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys Met Gln Gln Gly
 195 200 205
 Pro Ala Ser Ala Arg Asp Leu Ile Cys Ala Gln Tyr Val Ala Gly Tyr
 210 215 220
 Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu Ala Ala Tyr Thr
 225 230 235 240
 Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp Thr Ala Gly Leu
 245 250 255
 Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile Phe Tyr Arg Leu
 260 265 270
 Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu Asn Gln Lys Leu
 275 280 285
 Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met Gln Thr Gly Phe
 290 295 300
 Thr Thr Thr Asn Glu Ala Phe Gln Lys Val Gln Asp Ala Val Asn Asn
 305 310 315 320
 Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser Glu Leu Ser Asn Thr Phe
 325 330 335
 Gly Ala Ile Ser Ala Ser Ile Gly Asp Ile Ile Gln Arg Leu Asp Val
 340 345 350
 Leu Glu Gln Asp Ala Gln Ile Asp Arg Leu Ile Asn Gly Arg Leu Thr
 355 360 365
 Thr Leu Asn Ala Phe Val Ala Gln Gln Leu Val Arg Ser Glu Ser Ala
 370 375 380
 Ala Leu Ser Ala Gln Leu Ala Lys Asp Lys Val Asn Glu Cys Val Lys
 385 390 395 400
 Ala Gln Ser Lys Arg Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val
 405 410 415
 Ser Phe Val Val Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly
 420 425 430
 Tyr Tyr Pro Ser Asn His Ile Glu Val Val Ser Ala Tyr Gly Leu Cys
 435 440 445
 Asp Ala Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe
 450 455 460
 Ile Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly

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465              470              475              480
Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys Tyr
              485              490              495
Val Ala Pro Gln Val Thr Tyr Gln Asn Ile Ser Thr Asn Leu Pro Pro
              500              505              510
Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp Glu Leu Asp
              515              520              525
Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn Phe Gly Ser Leu
              530              535              540
Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr Tyr Glu Met Leu Ser
545              550              555              560
Leu Gln Gln Val Val Lys Ala Leu Asn Glu Ser Tyr Ile Asp Leu Lys
              565              570              575
Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn Lys Trp Pro Asp Lys Ile Glu
              580              585              590
Glu Ile Leu Ser Lys Ile Tyr His Ile Glu Asn Glu Ile Ala Arg Ile
              595              600              605
Lys Lys Leu Ile Gly Glu Ala
              610              615

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<210> SEQ ID NO 27

<211> LENGTH: 1353

<212> TYPE: PRT

<213> ORGANISM: Middle East respiratory syndrome coronavirus

<400> SEQUENCE: 27

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Met Ile His Ser Val Phe Leu Leu Met Phe Leu Leu Thr Pro Thr Glu
1              5              10              15
Ser Tyr Val Asp Val Gly Pro Asp Ser Val Lys Ser Ala Cys Ile Glu
              20              25              30
Val Asp Ile Gln Gln Thr Phe Phe Asp Lys Thr Trp Pro Arg Pro Ile
              35              40              45
Asp Val Ser Lys Ala Asp Gly Ile Ile Tyr Pro Gln Gly Arg Thr Tyr
50              55              60
Ser Asn Ile Thr Ile Thr Tyr Gln Gly Leu Phe Pro Tyr Gln Gly Asp
65              70              75              80
His Gly Asp Met Tyr Val Tyr Ser Ala Gly His Ala Thr Gly Thr Thr
              85              90              95
Pro Gln Lys Leu Phe Val Ala Asn Tyr Ser Gln Asp Val Lys Gln Phe
              100              105              110
Ala Asn Gly Phe Val Val Arg Ile Gly Ala Ala Ala Asn Ser Thr Gly
              115              120              125
Thr Val Ile Ile Ser Pro Ser Thr Ser Ala Thr Ile Arg Lys Ile Tyr
              130              135              140
Pro Ala Phe Met Leu Gly Ser Ser Val Gly Asn Phe Ser Asp Gly Lys
145              150              155              160
Met Gly Arg Phe Phe Asn His Thr Leu Val Leu Leu Pro Asp Gly Cys
              165              170              175
Gly Thr Leu Leu Arg Ala Phe Tyr Cys Ile Leu Glu Pro Arg Ser Gly
              180              185              190
Asn His Cys Pro Ala Gly Asn Ser Tyr Thr Ser Phe Ala Thr Tyr His
              195              200              205

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Thr	Pro	Ala	Thr	Asp	Cys	Ser	Asp	Gly	Asn	Tyr	Asn	Arg	Asn	Ala	Ser
	210					215					220				
Leu	Asn	Ser	Phe	Lys	Glu	Tyr	Phe	Asn	Leu	Arg	Asn	Cys	Thr	Phe	Met
225				230						235					240
Tyr	Thr	Tyr	Asn	Ile	Thr	Glu	Asp	Glu	Ile	Leu	Glu	Trp	Phe	Gly	Ile
			245						250					255	
Thr	Gln	Thr	Ala	Gln	Gly	Val	His	Leu	Phe	Ser	Ser	Arg	Tyr	Val	Asp
			260					265					270		
Leu	Tyr	Gly	Gly	Asn	Met	Phe	Gln	Phe	Ala	Thr	Leu	Pro	Val	Tyr	Asp
		275					280					285			
Thr	Ile	Lys	Tyr	Tyr	Ser	Ile	Ile	Pro	His	Ser	Ile	Arg	Ser	Ile	Gln
	290					295					300				
Ser	Asp	Arg	Lys	Ala	Trp	Ala	Ala	Phe	Tyr	Val	Tyr	Lys	Leu	Gln	Pro
305				310						315					320
Leu	Thr	Phe	Leu	Leu	Asp	Phe	Ser	Val	Asp	Gly	Tyr	Ile	Arg	Arg	Ala
			325						330					335	
Ile	Asp	Cys	Gly	Phe	Asn	Asp	Leu	Ser	Gln	Leu	His	Cys	Ser	Tyr	Glu
			340					345					350		
Ser	Phe	Asp	Val	Glu	Ser	Gly	Val	Tyr	Ser	Val	Ser	Ser	Phe	Glu	Ala
		355					360					365			
Lys	Pro	Ser	Gly	Ser	Val	Val	Glu	Gln	Ala	Glu	Gly	Val	Glu	Cys	Asp
	370					375					380				
Phe	Ser	Pro	Leu	Leu	Ser	Gly	Thr	Pro	Pro	Gln	Val	Tyr	Asn	Phe	Lys
385					390					395					400
Arg	Leu	Val	Phe	Thr	Asn	Cys	Asn	Tyr	Asn	Leu	Thr	Lys	Leu	Leu	Ser
			405						410						415
Leu	Phe	Ser	Val	Asn	Asp	Phe	Thr	Cys	Ser	Gln	Ile	Ser	Pro	Ala	Ala
			420					425					430		
Ile	Ala	Ser	Asn	Cys	Tyr	Ser	Ser	Leu	Ile	Leu	Asp	Tyr	Phe	Ser	Tyr
		435					440					445			
Pro	Leu	Ser	Met	Lys	Ser	Asp	Leu	Ser	Val	Ser	Ser	Ala	Gly	Pro	Ile
	450					455					460				
Ser	Gln	Phe	Asn	Tyr	Lys	Gln	Ser	Phe	Ser	Asn	Pro	Thr	Cys	Leu	Ile
465					470					475					480
Leu	Ala	Thr	Val	Pro	His	Asn	Leu	Thr	Thr	Ile	Thr	Lys	Pro	Leu	Lys
			485						490						495
Tyr	Ser	Tyr	Ile	Asn	Lys	Cys	Ser	Arg	Leu	Leu	Ser	Asp	Asp	Arg	Thr
			500					505					510		
Glu	Val	Pro	Gln	Leu	Val	Asn	Ala	Asn	Gln	Tyr	Ser	Pro	Cys	Val	Ser
		515					520					525			
Ile	Val	Pro	Ser	Thr	Val	Trp	Glu	Asp	Gly	Asp	Tyr	Tyr	Arg	Lys	Gln
	530					535					540				
Leu	Ser	Pro	Leu	Glu	Gly	Gly	Gly	Trp	Leu	Val	Ala	Ser	Gly	Ser	Thr
545					550					555					560
Val	Ala	Met	Thr	Glu	Gln	Leu	Gln	Met	Gly	Phe	Gly	Ile	Thr	Val	Gln
			565						570					575	
Tyr	Gly	Thr	Asp	Thr	Asn	Ser	Val	Cys	Pro	Lys	Leu	Glu	Phe	Ala	Asn
			580					585					590		
Asp	Thr	Lys	Ile	Ala	Ser	Gln	Leu	Gly	Asn	Cys	Val	Glu	Tyr	Ser	Leu
		595					600					605			
Tyr	Gly	Val	Ser	Gly	Arg	Gly	Val	Phe	Gln	Asn	Cys	Thr	Ala	Val	Gly

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610				615				620							
Val	Arg	Gln	Gln	Arg	Phe	Val	Tyr	Asp	Ala	Tyr	Gln	Asn	Leu	Val	Gly
625					630						635				640
Tyr	Tyr	Ser	Asp	Asp	Gly	Asn	Tyr	Tyr	Cys	Leu	Arg	Ala	Cys	Val	Ser
			645						650					655	
Val	Pro	Val	Ser	Val	Ile	Tyr	Asp	Lys	Glu	Thr	Lys	Thr	His	Ala	Thr
			660					665						670	
Leu	Phe	Gly	Ser	Val	Ala	Cys	Glu	His	Ile	Ser	Ser	Thr	Met	Ser	Gln
		675						680						685	
Tyr	Ser	Arg	Ser	Thr	Arg	Ser	Met	Leu	Lys	Arg	Arg	Asp	Ser	Thr	Tyr
	690						695				700				
Gly	Pro	Leu	Gln	Thr	Pro	Val	Gly	Cys	Val	Leu	Gly	Leu	Val	Asn	Ser
705					710						715				720
Ser	Leu	Phe	Val	Glu	Asp	Cys	Lys	Leu	Pro	Leu	Gly	Gln	Ser	Leu	Cys
				725					730						735
Ala	Leu	Pro	Asp	Thr	Pro	Ser	Thr	Leu	Thr	Pro	Arg	Ser	Val	Arg	Ser
			740					745						750	
Val	Pro	Gly	Glu	Met	Arg	Leu	Ala	Ser	Ile	Ala	Phe	Asn	His	Pro	Ile
		755						760						765	
Gln	Val	Asp	Gln	Leu	Asn	Ser	Ser	Tyr	Phe	Lys	Leu	Ser	Ile	Pro	Thr
	770							775						780	
Asn	Phe	Ser	Phe	Gly	Val	Thr	Gln	Glu	Tyr	Ile	Gln	Thr	Thr	Ile	Gln
785					790					795					800
Lys	Val	Thr	Val	Asp	Cys	Lys	Gln	Tyr	Val	Cys	Asn	Gly	Phe	Gln	Lys
				805					810						815
Cys	Glu	Gln	Leu	Leu	Arg	Glu	Tyr	Gly	Gln	Phe	Cys	Ser	Lys	Ile	Asn
			820					825						830	
Gln	Ala	Leu	His	Gly	Ala	Asn	Leu	Arg	Gln	Asp	Asp	Ser	Val	Arg	Asn
		835						840						845	
Leu	Phe	Ala	Ser	Val	Lys	Ser	Ser	Gln	Ser	Ser	Pro	Ile	Ile	Pro	Gly
	850							855						860	
Phe	Gly	Gly	Asp	Phe	Asn	Leu	Thr	Leu	Leu	Glu	Pro	Val	Ser	Ile	Ser
865					870					875					880
Thr	Gly	Ser	Arg	Ser	Ala	Arg	Ser	Ala	Ile	Glu	Asp	Leu	Leu	Phe	Asp
				885					890						895
Lys	Val	Thr	Ile	Ala	Asp	Pro	Gly	Tyr	Met	Gln	Gly	Tyr	Asp	Asp	Cys
			900					905						910	
Met	Gln	Gln	Gly	Pro	Ala	Ser	Ala	Arg	Asp	Leu	Ile	Cys	Ala	Gln	Tyr
		915						920						925	
Val	Ala	Gly	Tyr	Lys	Val	Leu	Pro	Pro	Leu	Met	Asp	Val	Asn	Met	Glu
	930							935						940	
Ala	Ala	Tyr	Thr	Ser	Ser	Leu	Leu	Gly	Ser	Ile	Ala	Gly	Val	Gly	Trp
945					950						955				960
Thr	Ala	Gly	Leu	Ser	Ser	Phe	Ala	Ala	Ile	Pro	Phe	Ala	Gln	Ser	Ile
				965						970					975
Phe	Tyr	Arg	Leu	Asn	Gly	Val	Gly	Ile	Thr	Gln	Gln	Val	Leu	Ser	Glu
			980						985					990	
Asn	Gln	Lys	Leu	Ile	Ala	Asn	Lys	Phe	Asn	Gln	Ala	Leu	Gly	Ala	Met
		995						1000						1005	
Gln	Thr	Gly	Phe	Thr	Thr	Thr	Asn	Glu	Ala	Phe	Arg	Lys	Val	Gln	
	1010							1015						1020	

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Asp Ala Val Asn Asn Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser
 1025 1030 1035
 Glu Leu Ser Asn Thr Phe Gly Ala Ile Ser Ala Ser Ile Gly Asp
 1040 1045 1050
 Ile Ile Gln Arg Leu Asp Val Leu Glu Gln Asp Ala Gln Ile Asp
 1055 1060 1065
 Arg Leu Ile Asn Gly Arg Leu Thr Thr Leu Asn Ala Phe Val Ala
 1070 1075 1080
 Gln Gln Leu Val Arg Ser Glu Ser Ala Ala Leu Ser Ala Gln Leu
 1085 1090 1095
 Ala Lys Asp Lys Val Asn Glu Cys Val Lys Ala Gln Ser Lys Arg
 1100 1105 1110
 Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val Ser Phe Val Val
 1115 1120 1125
 Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly Tyr Tyr Pro
 1130 1135 1140
 Ser Asn His Ile Glu Val Val Ser Ala Tyr Gly Leu Cys Asp Ala
 1145 1150 1155
 Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe Ile
 1160 1165 1170
 Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly
 1175 1180 1185
 Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys
 1190 1195 1200
 Tyr Val Ala Pro His Val Thr Tyr Gln Asn Ile Ser Thr Asn Leu
 1205 1210 1215
 Pro Pro Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp
 1220 1225 1230
 Glu Leu Asp Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn
 1235 1240 1245
 Phe Gly Ser Leu Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr
 1250 1255 1260
 Tyr Glu Met Leu Ser Leu Gln Gln Val Val Lys Ala Leu Asn Glu
 1265 1270 1275
 Ser Tyr Ile Asp Leu Lys Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn
 1280 1285 1290
 Lys Trp Pro Trp Tyr Ile Trp Leu Gly Phe Ile Ala Gly Leu Val
 1295 1300 1305
 Ala Leu Ala Leu Cys Val Phe Phe Ile Leu Cys Cys Thr Gly Cys
 1310 1315 1320
 Gly Thr Asn Cys Met Gly Lys Leu Lys Cys Asn Arg Cys Cys Asp
 1325 1330 1335
 Arg Tyr Glu Glu Tyr Asp Leu Glu Pro His Lys Val His Val His
 1340 1345 1350

<210> SEQ ID NO 28

<211> LENGTH: 1353

<212> TYPE: PRT

<213> ORGANISM: Middle East respiratory syndrome coronavirus

<400> SEQUENCE: 28

Met Ile His Ser Val Phe Leu Leu Met Phe Leu Leu Thr Pro Thr Glu

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1	5	10	15
Ser Tyr Val Asp Val Gly Pro Asp Ser Val Lys Ser Ala Cys Ile Glu	20	25	30
Val Asp Ile Gln Gln Thr Phe Phe Asp Lys Thr Trp Pro Arg Pro Ile	35	40	45
Asp Val Ser Lys Ala Asp Gly Ile Ile Tyr Pro Gln Gly Arg Thr Tyr	50	55	60
Ser Asn Ile Thr Ile Thr Tyr Gln Gly Leu Phe Pro Tyr Gln Gly Asp	65	70	80
His Gly Asp Met Tyr Val Tyr Ser Ala Gly His Ala Thr Gly Thr Thr	85	90	95
Pro Gln Lys Leu Phe Val Ala Asn Tyr Ser Gln Asp Val Lys Gln Phe	100	105	110
Ala Asn Gly Phe Val Val Arg Ile Gly Ala Ala Ala Asn Ser Thr Gly	115	120	125
Thr Val Ile Ile Ser Pro Ser Thr Ser Ala Thr Ile Arg Lys Ile Tyr	130	135	140
Pro Ala Phe Met Leu Gly Ser Ser Val Gly Asn Phe Ser Asp Gly Lys	145	150	155
Met Gly Arg Phe Phe Asn His Thr Leu Val Leu Leu Pro Asp Gly Cys	165	170	175
Gly Thr Leu Leu Arg Ala Phe Tyr Cys Ile Leu Glu Pro Arg Ser Gly	180	185	190
Asn His Cys Pro Ala Gly Asn Ser Tyr Thr Ser Phe Ala Thr Tyr His	195	200	205
Thr Pro Ala Thr Asp Cys Ser Asp Gly Asn Tyr Asn Arg Asn Ala Ser	210	215	220
Leu Asn Ser Phe Lys Glu Tyr Phe Asn Leu Arg Asn Cys Thr Phe Met	225	230	235
Tyr Thr Tyr Asn Ile Thr Glu Asp Glu Ile Leu Glu Trp Phe Gly Ile	245	250	255
Thr Gln Thr Ala Gln Gly Val His Leu Phe Ser Ser Arg Tyr Val Asp	260	265	270
Leu Tyr Gly Gly Asn Met Phe Gln Phe Ala Thr Leu Pro Val Tyr Asp	275	280	285
Thr Ile Lys Tyr Tyr Ser Ile Ile Pro His Ser Ile Arg Ser Ile Gln	290	295	300
Ser Asp Arg Lys Ala Trp Ala Ala Phe Tyr Val Tyr Lys Leu Gln Pro	305	310	315
Leu Thr Phe Leu Leu Asp Phe Ser Val Asp Gly Tyr Ile Arg Arg Ala	325	330	335
Ile Asp Cys Gly Phe Asn Asp Leu Ser Gln Leu His Cys Ser Tyr Glu	340	345	350
Ser Phe Asp Val Glu Ser Gly Val Tyr Ser Val Ser Ser Phe Glu Ala	355	360	365
Lys Pro Ser Gly Ser Val Val Glu Gln Ala Glu Gly Val Glu Cys Asp	370	375	380
Phe Ser Pro Leu Leu Ser Gly Thr Pro Pro Gln Val Tyr Asn Phe Lys	385	390	395
Arg Leu Val Phe Thr Asn Cys Asn Tyr Asn Leu Thr Lys Leu Leu Ser	405	410	415

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1205	1210	1215
Pro Pro Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp		
1220	1225	1230
Glu Leu Asp Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn		
1235	1240	1245
Phe Gly Ser Leu Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr		
1250	1255	1260
Tyr Glu Met Leu Ser Leu Gln Gln Val Val Lys Ala Leu Asn Glu		
1265	1270	1275
Ser Tyr Ile Asp Leu Lys Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn		
1280	1285	1290
Lys Trp Pro Trp Tyr Ile Trp Leu Gly Phe Ile Ala Gly Leu Val		
1295	1300	1305
Ala Leu Ala Leu Cys Val Phe Phe Ile Leu Cys Cys Thr Gly Cys		
1310	1315	1320
Gly Thr Asn Cys Met Gly Lys Leu Lys Cys Asn Arg Cys Cys Asp		
1325	1330	1335
Arg Tyr Glu Glu Tyr Asp Leu Glu Pro His Lys Val His Val His		
1340	1345	1350

<210> SEQ ID NO 29

<211> LENGTH: 1255

<212> TYPE: PRT

<213> ORGANISM: Human SARS coronavirus

<400> SEQUENCE: 29

Met Phe Ile Phe Leu Leu Phe Leu Thr Leu Thr Ser Gly Ser Asp Leu		
1	5	10 15
Asp Arg Cys Thr Thr Phe Asp Asp Val Gln Ala Pro Asn Tyr Thr Gln		
	20	25 30
His Thr Ser Ser Met Arg Gly Val Tyr Tyr Pro Asp Glu Ile Phe Arg		
	35	40 45
Ser Asp Thr Leu Tyr Leu Thr Gln Asp Leu Phe Leu Pro Phe Tyr Ser		
	50	55 60
Asn Val Thr Gly Phe His Thr Ile Asn His Thr Phe Gly Asn Pro Val		
65	70	75 80
Ile Pro Phe Lys Asp Gly Ile Tyr Phe Ala Ala Thr Glu Lys Ser Asn		
	85	90 95
Val Val Arg Gly Trp Val Phe Gly Ser Thr Met Asn Asn Lys Ser Gln		
	100	105 110
Ser Val Ile Ile Ile Asn Asn Ser Thr Asn Val Val Ile Arg Ala Cys		
	115	120 125
Asn Phe Glu Leu Cys Asp Asn Pro Phe Phe Ala Val Ser Lys Pro Met		
	130	135 140
Gly Thr Gln Thr His Thr Met Ile Phe Asp Asn Ala Phe Asn Cys Thr		
145	150	155 160
Phe Glu Tyr Ile Ser Asp Ala Phe Ser Leu Asp Val Ser Glu Lys Ser		
	165	170 175
Gly Asn Phe Lys His Leu Arg Glu Phe Val Phe Lys Asn Lys Asp Gly		
	180	185 190
Phe Leu Tyr Val Tyr Lys Gly Tyr Gln Pro Ile Asp Val Val Arg Asp		
	195	200 205

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Leu Pro Ser Gly Phe Asn Thr Leu Lys Pro Ile Phe Lys Leu Pro Leu
 210 215 220

Gly Ile Asn Ile Thr Asn Phe Arg Ala Ile Leu Thr Ala Phe Ser Pro
 225 230 235 240

Ala Gln Asp Ile Trp Gly Thr Ser Ala Ala Ala Tyr Phe Val Gly Tyr
 245 250 255

Leu Lys Pro Thr Thr Phe Met Leu Lys Tyr Asp Glu Asn Gly Thr Ile
 260 265 270

Thr Asp Ala Val Asp Cys Ser Gln Asn Pro Leu Ala Glu Leu Lys Cys
 275 280 285

Ser Val Lys Ser Phe Glu Ile Asp Lys Gly Ile Tyr Gln Thr Ser Asn
 290 295 300

Phe Arg Val Val Pro Ser Gly Asp Val Val Arg Phe Pro Asn Ile Thr
 305 310 315 320

Asn Leu Cys Pro Phe Gly Glu Val Phe Asn Ala Thr Lys Phe Pro Ser
 325 330 335

Val Tyr Ala Trp Glu Arg Lys Lys Ile Ser Asn Cys Val Ala Asp Tyr
 340 345 350

Ser Val Leu Tyr Asn Ser Thr Phe Phe Ser Thr Phe Lys Cys Tyr Gly
 355 360 365

Val Ser Ala Thr Lys Leu Asn Asp Leu Cys Phe Ser Asn Val Tyr Ala
 370 375 380

Asp Ser Phe Val Val Lys Gly Asp Asp Val Arg Gln Ile Ala Pro Gly
 385 390 395 400

Gln Thr Gly Val Ile Ala Asp Tyr Asn Tyr Lys Leu Pro Asp Asp Phe
 405 410 415

Met Gly Cys Val Leu Ala Trp Asn Thr Arg Asn Ile Asp Ala Thr Ser
 420 425 430

Thr Gly Asn Tyr Asn Tyr Lys Tyr Arg Tyr Leu Arg His Gly Lys Leu
 435 440 445

Arg Pro Phe Glu Arg Asp Ile Ser Asn Val Pro Phe Ser Pro Asp Gly
 450 455 460

Lys Pro Cys Thr Pro Pro Ala Leu Asn Cys Tyr Trp Pro Leu Asn Asp
 465 470 475 480

Tyr Gly Phe Tyr Thr Thr Thr Gly Ile Gly Tyr Gln Pro Tyr Arg Val
 485 490 495

Val Val Leu Ser Phe Glu Leu Leu Asn Ala Pro Ala Thr Val Cys Gly
 500 505 510

Pro Lys Leu Ser Thr Asp Leu Ile Lys Asn Gln Cys Val Asn Phe Asn
 515 520 525

Phe Asn Gly Leu Thr Gly Thr Gly Val Leu Thr Pro Ser Ser Lys Arg
 530 535 540

Phe Gln Pro Phe Gln Gln Phe Gly Arg Asp Val Ser Asp Phe Thr Asp
 545 550 555 560

Ser Val Arg Asp Pro Lys Thr Ser Glu Ile Leu Asp Ile Ser Pro Cys
 565 570 575

Ser Phe Gly Gly Val Ser Val Ile Thr Pro Gly Thr Asn Ala Ser Ser
 580 585 590

Glu Val Ala Val Leu Tyr Gln Asp Val Asn Cys Thr Asp Val Ser Thr
 595 600 605

Ala Ile His Ala Asp Gln Leu Thr Pro Ala Trp Arg Ile Tyr Ser Thr

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610			615			620									
Gly	Asn	Asn	Val	Phe	Gln	Thr	Gln	Ala	Gly	Cys	Leu	Ile	Gly	Ala	Glu
625					630					635					640
His	Val	Asp	Thr	Ser	Tyr	Glu	Cys	Asp	Ile	Pro	Ile	Gly	Ala	Gly	Ile
				645					650						655
Cys	Ala	Ser	Tyr	His	Thr	Val	Ser	Leu	Leu	Arg	Ser	Thr	Ser	Gln	Lys
			660					665						670	
Ser	Ile	Val	Ala	Tyr	Thr	Met	Ser	Leu	Gly	Ala	Asp	Ser	Ser	Ile	Ala
		675					680					685			
Tyr	Ser	Asn	Asn	Thr	Ile	Ala	Ile	Pro	Thr	Asn	Phe	Ser	Ile	Ser	Ile
	690						695				700				
Thr	Thr	Glu	Val	Met	Pro	Val	Ser	Met	Ala	Lys	Thr	Ser	Val	Asp	Cys
705					710					715					720
Asn	Met	Tyr	Ile	Cys	Gly	Asp	Ser	Thr	Glu	Cys	Ala	Asn	Leu	Leu	Leu
				725						730					735
Gln	Tyr	Gly	Ser	Phe	Cys	Thr	Gln	Leu	Asn	Arg	Ala	Leu	Ser	Gly	Ile
			740					745						750	
Ala	Ala	Glu	Gln	Asp	Arg	Asn	Thr	Arg	Glu	Val	Phe	Ala	Gln	Val	Lys
		755						760						765	
Gln	Met	Tyr	Lys	Thr	Pro	Thr	Leu	Lys	Tyr	Phe	Gly	Gly	Phe	Asn	Phe
	770						775				780				
Ser	Gln	Ile	Leu	Pro	Asp	Pro	Leu	Lys	Pro	Thr	Lys	Arg	Ser	Phe	Ile
785					790						795				800
Glu	Asp	Leu	Leu	Phe	Asn	Lys	Val	Thr	Leu	Ala	Asp	Ala	Gly	Phe	Met
				805						810					815
Lys	Gln	Tyr	Gly	Glu	Cys	Leu	Gly	Asp	Ile	Asn	Ala	Arg	Asp	Leu	Ile
			820					825						830	
Cys	Ala	Gln	Lys	Phe	Asn	Gly	Leu	Thr	Val	Leu	Pro	Pro	Leu	Leu	Thr
		835					840							845	
Asp	Asp	Met	Ile	Ala	Ala	Tyr	Thr	Ala	Ala	Leu	Val	Ser	Gly	Thr	Ala
	850						855				860				
Thr	Ala	Gly	Trp	Thr	Phe	Gly	Ala	Gly	Ala	Ala	Leu	Val	Gln	Ile	Pro
865					870						875				880
Ala	Met	Gln	Met	Ala	Tyr	Arg	Phe	Asn	Gly	Ile	Gly	Val	Thr	Gln	Asn
				885						890					895
Val	Leu	Tyr	Glu	Asn	Gln	Lys	Gln	Ile	Ala	Asn	Gln	Phe	Asn	Lys	Ala
			900					905						910	
Ile	Ser	Gln	Ile	Gln	Glu	Ser	Leu	Thr	Thr	Thr	Ser	Thr	Ala	Leu	Gly
		915						920						925	
Lys	Leu	Gln	Asp	Val	Val	Asn	Gln	Asn	Ala	Gln	Ala	Leu	Asn	Thr	Leu
	930							935			940				
Val	Lys	Gln	Leu	Ser	Ser	Asn	Phe	Gly	Ala	Ile	Ser	Ser	Val	Leu	Asn
					945			950			955				960
Asp	Ile	Leu	Ser	Arg	Leu	Asp	Lys	Val	Glu	Ala	Glu	Val	Gln	Ile	Asp
				965						970					975
Arg	Leu	Ile	Thr	Gly	Arg	Leu	Gln	Ser	Leu	Gln	Thr	Tyr	Val	Thr	Gln
				980				985							990
Gln	Leu	Ile	Arg	Ala	Ala	Glu	Ile	Arg	Ala	Ser	Ala	Asn	Leu	Ala	Ala
								1000						1005	
Thr	Lys	Met	Ser	Glu	Cys	Val	Leu	Gly	Gln	Ser	Lys	Arg	Val	Asp	
		1010						1015						1020	

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Phe Cys Gly Lys Gly Tyr His Leu Met Ser Phe Pro Gln Ala Ala
 1025 1030 1035
 Pro His Gly Val Val Phe Leu His Val Thr Tyr Val Pro Ser Gln
 1040 1045 1050
 Glu Arg Asn Phe Thr Thr Ala Pro Ala Ile Cys His Glu Gly Lys
 1055 1060 1065
 Ala Tyr Phe Pro Arg Glu Gly Val Phe Val Phe Asn Gly Thr Ser
 1070 1075 1080
 Trp Phe Ile Thr Gln Arg Asn Phe Phe Ser Pro Gln Ile Ile Thr
 1085 1090 1095
 Thr Asp Asn Thr Phe Val Ser Gly Asn Cys Asp Val Val Ile Gly
 1100 1105 1110
 Ile Ile Asn Asn Thr Val Tyr Asp Pro Leu Gln Pro Glu Leu Asp
 1115 1120 1125
 Ser Phe Lys Glu Glu Leu Asp Lys Tyr Phe Lys Asn His Thr Ser
 1130 1135 1140
 Pro Asp Val Asp Leu Gly Asp Ile Ser Gly Ile Asn Ala Ser Val
 1145 1150 1155
 Val Asn Ile Gln Lys Glu Ile Asp Arg Leu Asn Glu Val Ala Lys
 1160 1165 1170
 Asn Leu Asn Glu Ser Leu Ile Asp Leu Gln Glu Leu Gly Lys Tyr
 1175 1180 1185
 Glu Gln Tyr Ile Lys Trp Pro Trp Tyr Val Trp Leu Gly Phe Ile
 1190 1195 1200
 Ala Gly Leu Ile Ala Ile Val Met Val Thr Ile Leu Leu Cys Cys
 1205 1210 1215
 Met Thr Ser Cys Cys Ser Cys Leu Lys Gly Ala Cys Ser Cys Gly
 1220 1225 1230
 Ser Cys Cys Lys Phe Asp Glu Asp Asp Ser Glu Pro Val Leu Lys
 1235 1240 1245
 Gly Val Lys Leu His Tyr Thr
 1250 1255

<210> SEQ ID NO 30

<211> LENGTH: 1353

<212> TYPE: PRT

<213> ORGANISM: Human coronavirus

<400> SEQUENCE: 30

Met Phe Leu Ile Leu Leu Ile Ser Leu Pro Thr Ala Phe Ala Val Ile
 1 5 10 15
 Gly Asp Leu Lys Cys Thr Ser Asp Asn Ile Asn Asp Lys Asp Thr Gly
 20 25 30
 Pro Pro Pro Ile Ser Thr Asp Thr Val Asp Val Thr Asn Gly Leu Gly
 35 40 45
 Thr Tyr Tyr Val Leu Asp Arg Val Tyr Leu Asn Thr Thr Leu Phe Leu
 50 55 60
 Asn Gly Tyr Tyr Pro Thr Ser Gly Ser Thr Tyr Arg Asn Met Ala Leu
 65 70 75 80
 Lys Gly Ser Val Leu Leu Ser Arg Leu Trp Phe Lys Pro Pro Phe Leu
 85 90 95
 Ser Asp Phe Ile Asn Gly Ile Phe Ala Lys Val Lys Asn Thr Lys Val

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100					105					110					
Ile	Lys	Asp	Arg	Val	Met	Tyr	Ser	Glu	Phe	Pro	Ala	Ile	Thr	Ile	Gly
	115						120					125			
Ser	Thr	Phe	Val	Asn	Thr	Ser	Tyr	Ser	Val	Val	Val	Gln	Pro	Arg	Thr
	130					135					140				
Ile	Asn	Ser	Thr	Gln	Asp	Gly	Asp	Asn	Lys	Leu	Gln	Gly	Leu	Leu	Glu
145				150					155						160
Val	Ser	Val	Cys	Gln	Tyr	Asn	Met	Cys	Glu	Tyr	Pro	Gln	Thr	Ile	Cys
			165						170						175
His	Pro	Asn	Leu	Gly	Asn	His	Arg	Lys	Glu	Leu	Trp	His	Leu	Asp	Thr
		180						185					190		
Gly	Val	Val	Ser	Cys	Leu	Tyr	Lys	Arg	Asn	Phe	Thr	Tyr	Asp	Val	Asn
	195						200					205			
Ala	Asp	Tyr	Leu	Tyr	Phe	His	Phe	Tyr	Gln	Glu	Gly	Gly	Thr	Phe	Tyr
	210					215					220				
Ala	Tyr	Phe	Thr	Asp	Thr	Gly	Val	Val	Thr	Lys	Phe	Leu	Phe	Asn	Val
225					230					235					240
Tyr	Leu	Gly	Met	Ala	Leu	Ser	His	Tyr	Tyr	Val	Met	Pro	Leu	Thr	Cys
			245						250						255
Asn	Ser	Lys	Leu	Thr	Leu	Glu	Tyr	Trp	Val	Thr	Pro	Leu	Thr	Ser	Arg
		260						265					270		
Gln	Tyr	Leu	Leu	Ala	Phe	Asn	Gln	Asp	Gly	Ile	Ile	Phe	Asn	Ala	Glu
		275					280					285			
Asp	Cys	Met	Ser	Asp	Phe	Met	Ser	Glu	Ile	Lys	Cys	Lys	Thr	Gln	Ser
	290					295					300				
Ile	Ala	Pro	Pro	Thr	Gly	Val	Tyr	Glu	Leu	Asn	Gly	Tyr	Thr	Val	Gln
305					310						315				320
Pro	Ile	Ala	Asp	Val	Tyr	Arg	Arg	Lys	Pro	Asn	Leu	Pro	Asn	Cys	Asn
			325						330						335
Ile	Glu	Ala	Trp	Leu	Asn	Asp	Lys	Ser	Val	Pro	Ser	Pro	Leu	Asn	Trp
		340							345						350
Glu	Arg	Lys	Thr	Phe	Ser	Asn	Cys	Asn	Phe	Asn	Met	Ser	Ser	Leu	Met
		355					360					365			
Ser	Phe	Ile	Gln	Ala	Asp	Ser	Phe	Thr	Cys	Asn	Asn	Ile	Asp	Ala	Ala
	370					375					380				
Lys	Ile	Tyr	Gly	Met	Cys	Phe	Ser	Ser	Ile	Thr	Ile	Asp	Lys	Phe	Ala
385					390					395					400
Ile	Pro	Asn	Gly	Arg	Lys	Val	Asp	Leu	Gln	Leu	Gly	Asn	Leu	Gly	Tyr
			405						410						415
Leu	Gln	Ser	Phe	Asn	Tyr	Arg	Ile	Asp	Thr	Thr	Ala	Thr	Ser	Cys	Gln
		420						425						430	
Leu	Tyr	Tyr	Asn	Leu	Pro	Ala	Ala	Asn	Val	Ser	Val	Ser	Arg	Phe	Asn
		435					440						445		
Pro	Ser	Thr	Trp	Asn	Lys	Arg	Phe	Gly	Phe	Ile	Glu	Asp	Ser	Val	Phe
	450					455					460				
Lys	Pro	Arg	Pro	Ala	Gly	Val	Leu	Thr	Asn	His	Asp	Val	Val	Tyr	Ala
465					470					475					480
Gln	His	Cys	Phe	Lys	Ala	Pro	Lys	Asn	Phe	Cys	Pro	Cys	Lys	Leu	Asn
			485						490						495
Gly	Ser	Cys	Val	Gly	Ser	Gly	Pro	Gly	Lys	Asn	Asn	Gly	Ile	Gly	Thr
			500					505							510

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Cys Pro Ala Gly Thr Asn Tyr Leu Thr Cys Asp Asn Leu Cys Thr Pro
 515 520 525
 Asp Pro Ile Thr Phe Thr Gly Thr Tyr Lys Cys Pro Gln Thr Lys Ser
 530 535 540
 Leu Val Gly Ile Gly Glu His Cys Ser Gly Leu Ala Val Lys Ser Asp
 545 550 555 560
 Tyr Cys Gly Gly Asn Ser Cys Thr Cys Arg Pro Gln Ala Phe Leu Gly
 565 570 575
 Trp Ser Ala Asp Ser Cys Leu Gln Gly Asp Lys Cys Asn Ile Phe Ala
 580 585 590
 Asn Phe Ile Leu His Asp Val Asn Ser Gly Leu Thr Cys Ser Thr Asp
 595 600 605
 Leu Gln Lys Ala Asn Thr Asp Ile Ile Leu Gly Val Cys Val Asn Tyr
 610 615 620
 Asp Leu Tyr Gly Ile Leu Gly Gln Gly Ile Phe Val Glu Val Asn Ala
 625 630 635 640
 Thr Tyr Tyr Asn Ser Trp Gln Asn Leu Leu Tyr Asp Ser Asn Gly Asn
 645 650 655
 Leu Tyr Gly Phe Arg Asp Tyr Ile Ile Asn Arg Thr Phe Met Ile Arg
 660 665 670
 Ser Cys Tyr Ser Gly Arg Val Ser Ala Ala Phe His Ala Asn Ser Ser
 675 680 685
 Glu Pro Ala Leu Leu Phe Arg Asn Ile Lys Cys Asn Tyr Val Phe Asn
 690 695 700
 Asn Ser Leu Thr Arg Gln Leu Gln Pro Ile Asn Tyr Phe Asp Ser Tyr
 705 710 715 720
 Leu Gly Cys Val Val Asn Ala Tyr Asn Ser Thr Ala Ile Ser Val Gln
 725 730 735
 Thr Cys Asp Leu Thr Val Gly Ser Gly Tyr Cys Val Asp Tyr Ser Lys
 740 745 750
 Asn Arg Arg Ser Arg Gly Ala Ile Thr Thr Gly Tyr Arg Phe Thr Asn
 755 760 765
 Phe Glu Pro Phe Thr Val Asn Ser Val Asn Asp Ser Leu Glu Pro Val
 770 775 780
 Gly Gly Leu Tyr Glu Ile Gln Ile Pro Ser Glu Phe Thr Ile Gly Asn
 785 790 795 800
 Met Val Glu Phe Ile Gln Thr Ser Ser Pro Lys Val Thr Ile Asp Cys
 805 810 815
 Ala Ala Phe Val Cys Gly Asp Tyr Ala Ala Cys Lys Ser Gln Leu Val
 820 825 830
 Glu Tyr Gly Ser Phe Cys Asp Asn Ile Asn Ala Ile Leu Thr Glu Val
 835 840 845
 Asn Glu Leu Leu Asp Thr Thr Gln Leu Gln Val Ala Asn Ser Leu Met
 850 855 860
 Asn Gly Val Thr Leu Ser Thr Lys Leu Lys Asp Gly Val Asn Phe Asn
 865 870 875 880
 Val Asp Asp Ile Asn Phe Ser Pro Val Leu Gly Cys Leu Gly Ser Glu
 885 890 895
 Cys Ser Lys Ala Ser Ser Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp
 900 905 910

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Lys Val Lys Leu Ser Asp Val Gly Phe Val Glu Ala Tyr Asn Asn Cys
 915 920 925

Thr Gly Gly Ala Glu Ile Arg Asp Leu Ile Cys Val Gln Ser Tyr Lys
 930 935 940

Gly Ile Lys Val Leu Pro Pro Leu Leu Ser Glu Asn Gln Ile Ser Gly
 945 950 955 960

Tyr Thr Leu Ala Ala Thr Ser Ala Ser Leu Phe Pro Pro Trp Thr Ala
 965 970 975

Ala Ala Gly Val Pro Phe Tyr Leu Asn Val Gln Tyr Arg Ile Asn Gly
 980 985 990

Leu Gly Val Thr Met Asp Val Leu Ser Gln Asn Gln Lys Leu Ile Ala
 995 1000 1005

Asn Ala Phe Asn Asn Ala Leu Tyr Ala Ile Gln Glu Gly Phe Asp
 1010 1015 1020

Ala Thr Asn Ser Ala Leu Val Lys Ile Gln Ala Val Val Asn Ala
 1025 1030 1035

Asn Ala Glu Ala Leu Asn Asn Leu Leu Gln Gln Leu Ser Asn Arg
 1040 1045 1050

Phe Gly Ala Ile Ser Ala Ser Leu Gln Glu Ile Leu Ser Arg Leu
 1055 1060 1065

Asp Ala Leu Glu Ala Glu Ala Gln Ile Asp Arg Leu Ile Asn Gly
 1070 1075 1080

Arg Leu Thr Ala Leu Asn Ala Tyr Val Ser Gln Gln Leu Ser Asp
 1085 1090 1095

Ser Thr Leu Val Lys Phe Ser Ala Ala Gln Ala Met Glu Lys Val
 1100 1105 1110

Asn Glu Cys Val Lys Ser Gln Ser Ser Arg Ile Asn Phe Cys Gly
 1115 1120 1125

Asn Gly Asn His Ile Ile Ser Leu Val Gln Asn Ala Pro Tyr Gly
 1130 1135 1140

Leu Tyr Phe Ile His Phe Ser Tyr Val Pro Thr Lys Tyr Val Thr
 1145 1150 1155

Ala Arg Val Ser Pro Gly Leu Cys Ile Ala Gly Asp Arg Gly Ile
 1160 1165 1170

Ala Pro Lys Ser Gly Tyr Phe Val Asn Val Asn Asn Thr Trp Met
 1175 1180 1185

Tyr Thr Gly Ser Gly Tyr Tyr Tyr Pro Glu Pro Ile Thr Glu Asn
 1190 1195 1200

Asn Val Val Val Met Ser Thr Cys Ala Val Asn Tyr Thr Lys Ala
 1205 1210 1215

Pro Tyr Val Met Leu Asn Thr Ser Ile Pro Asn Leu Pro Asp Phe
 1220 1225 1230

Lys Glu Glu Leu Asp Gln Trp Phe Lys Asn Gln Thr Ser Val Ala
 1235 1240 1245

Pro Asp Leu Ser Leu Asp Tyr Ile Asn Val Thr Phe Leu Asp Leu
 1250 1255 1260

Gln Val Glu Met Asn Arg Leu Gln Glu Ala Ile Lys Val Leu Asn
 1265 1270 1275

Gln Ser Tyr Ile Asn Leu Lys Asp Ile Gly Thr Tyr Glu Tyr Tyr
 1280 1285 1290

Val Lys Trp Pro Trp Tyr Val Trp Leu Leu Ile Cys Leu Ala Gly

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1295	1300	1305
Val Ala Met Leu Val Leu Leu Phe Phe Ile Cys Cys Cys Thr Gly		
1310	1315	1320
Cys Gly Thr Ser Cys Phe Lys Lys Cys Gly Gly Cys Cys Asp Asp		
1325	1330	1335
Tyr Thr Gly Tyr Gln Glu Leu Val Ile Lys Thr Ser His Asp Asp		
1340	1345	1350

<210> SEQ ID NO 31

<211> LENGTH: 1351

<212> TYPE: PRT

<213> ORGANISM: Human coronavirus

<400> SEQUENCE: 31

Met Phe Leu Ile Ile Phe Ile Leu Pro Thr Thr Leu Ala Val Ile Gly		
1	5	10 15
Asp Phe Asn Cys Thr Asn Ser Phe Ile Asn Asp Tyr Asn Lys Thr Ile		
	20	25 30
Pro Arg Ile Ser Glu Asp Val Val Asp Val Ser Leu Gly Leu Gly Thr		
	35	40 45
Tyr Tyr Val Leu Asn Arg Val Tyr Leu Asn Thr Thr Leu Leu Phe Thr		
	50	55 60
Gly Tyr Phe Pro Lys Ser Gly Ala Asn Phe Arg Asp Leu Ala Leu Lys		
65	70	75 80
Gly Ser Ile Tyr Leu Ser Thr Leu Trp Tyr Lys Pro Pro Phe Leu Ser		
	85	90 95
Asp Phe Asn Asn Gly Ile Phe Ser Lys Val Lys Asn Thr Lys Leu Tyr		
	100	105 110
Val Asn Asn Thr Leu Tyr Ser Glu Phe Ser Thr Ile Val Ile Gly Ser		
	115	120 125
Val Phe Val Asn Thr Ser Tyr Thr Ile Val Val Gln Pro His Asn Gly		
	130	135 140
Ile Leu Glu Ile Thr Ala Cys Gln Tyr Thr Met Cys Glu Tyr Pro His		
145	150	155 160
Thr Val Cys Lys Ser Lys Gly Ser Ile Arg Asn Glu Ser Trp His Ile		
	165	170 175
Asp Ser Ser Glu Pro Leu Cys Leu Phe Lys Lys Asn Phe Thr Tyr Asn		
	180	185 190
Val Ser Ala Asp Trp Leu Tyr Phe His Phe Tyr Gln Glu Arg Gly Val		
	195	200 205
Phe Tyr Ala Tyr Tyr Ala Asp Val Gly Met Pro Thr Thr Phe Leu Phe		
	210	215 220
Ser Leu Tyr Leu Gly Thr Ile Leu Ser His Tyr Tyr Val Met Pro Leu		
225	230	235 240
Thr Cys Asn Ala Ile Ser Ser Asn Thr Asp Asn Glu Thr Leu Glu Tyr		
	245	250 255
Trp Val Thr Pro Leu Ser Arg Arg Gln Tyr Leu Leu Asn Phe Asp Glu		
	260	265 270
His Gly Val Ile Thr Asn Ala Val Asp Cys Ser Ser Ser Phe Leu Ser		
	275	280 285
Glu Ile Gln Cys Lys Thr Gln Ser Phe Ala Pro Asn Thr Gly Val Tyr		
	290	295 300

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Asp	Leu	Ser	Gly	Phe	Thr	Val	Lys	Pro	Val	Ala	Thr	Val	Tyr	Arg	Arg	320
305					310					315						
Ile	Pro	Asn	Leu	Pro	Asp	Cys	Asp	Ile	Asp	Asn	Trp	Leu	Asn	Asn	Val	
			325						330					335		
Ser	Val	Pro	Ser	Pro	Leu	Asn	Trp	Glu	Arg	Arg	Ile	Phe	Ser	Asn	Cys	
			340					345					350			
Asn	Phe	Asn	Leu	Ser	Thr	Leu	Leu	Arg	Leu	Val	His	Val	Asp	Ser	Phe	
		355					360					365				
Ser	Cys	Asn	Asn	Leu	Asp	Lys	Ser	Lys	Ile	Phe	Gly	Ser	Cys	Phe	Asn	
	370					375					380					
Ser	Ile	Thr	Val	Asp	Lys	Phe	Ala	Ile	Pro	Asn	Arg	Arg	Arg	Asp	Asp	
385					390					395					400	
Leu	Gln	Leu	Gly	Ser	Ser	Gly	Phe	Leu	Gln	Ser	Ser	Asn	Tyr	Lys	Ile	
			405						410					415		
Asp	Ile	Ser	Ser	Ser	Ser	Cys	Gln	Leu	Tyr	Tyr	Ser	Leu	Pro	Leu	Val	
			420					425					430			
Asn	Val	Thr	Ile	Asn	Asn	Phe	Asn	Pro	Ser	Ser	Trp	Asn	Arg	Arg	Tyr	
		435					440					445				
Gly	Phe	Gly	Ser	Phe	Asn	Leu	Ser	Ser	Tyr	Asp	Val	Val	Tyr	Ser	Asp	
	450					455					460					
His	Cys	Phe	Ser	Val	Asn	Ser	Asp	Phe	Cys	Pro	Cys	Ala	Asp	Pro	Ser	
465					470					475					480	
Val	Val	Asn	Ser	Cys	Ala	Lys	Ser	Lys	Pro	Pro	Ser	Ala	Ile	Cys	Pro	
				485					490					495		
Ala	Gly	Thr	Lys	Tyr	Arg	His	Cys	Asp	Leu	Asp	Thr	Thr	Leu	Tyr	Val	
			500					505					510			
Lys	Asn	Trp	Cys	Arg	Cys	Ser	Cys	Leu	Pro	Asp	Pro	Ile	Ser	Thr	Tyr	
		515					520					525				
Ser	Pro	Asn	Thr	Cys	Pro	Gln	Lys	Lys	Val	Val	Val	Gly	Ile	Gly	Glu	
	530					535						540				
His	Cys	Pro	Gly	Leu	Gly	Ile	Asn	Glu	Glu	Lys	Cys	Gly	Thr	Gln	Leu	
545					550					555					560	
Asn	His	Ser	Ser	Cys	Phe	Cys	Ser	Pro	Asp	Ala	Phe	Leu	Gly	Trp	Ser	
				565					570					575		
Phe	Asp	Ser	Cys	Ile	Ser	Asn	Asn	Arg	Cys	Asn	Ile	Phe	Ser	Asn	Phe	
			580					585					590			
Ile	Phe	Asn	Gly	Ile	Asn	Ser	Gly	Thr	Thr	Cys	Ser	Asn	Asp	Leu	Leu	
		595					600					605				
Tyr	Ser	Asn	Thr	Glu	Ile	Ser	Thr	Gly	Val	Cys	Val	Asn	Tyr	Asp	Leu	
	610					615						620				
Tyr	Gly	Ile	Thr	Gly	Gln	Gly	Ile	Phe	Lys	Glu	Val	Ser	Ala	Ala	Tyr	
625					630					635					640	
Tyr	Asn	Asn	Trp	Gln	Asn	Leu	Leu	Tyr	Asp	Ser	Asn	Gly	Asn	Ile	Ile	
				645					650					655		
Gly	Phe	Lys	Asp	Phe	Leu	Thr	Asn	Lys	Thr	Tyr	Thr	Ile	Leu	Pro	Cys	
			660					665					670			
Tyr	Ser	Gly	Arg	Val	Ser	Ala	Ala	Phe	Tyr	Gln	Asn	Ser	Ser	Ser	Pro	
		675					680					685				
Ala	Leu	Leu	Tyr	Arg	Asn	Leu	Lys	Cys	Ser	Tyr	Val	Leu	Asn	Asn	Ile	
	690					695					700					
Ser	Phe	Ile	Ser	Gln	Pro	Phe	Tyr	Phe	Asp	Ser	Tyr	Leu	Gly	Cys	Val	

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705	710	715	720
Leu Asn Ala Val Asn Leu Thr Ser Tyr Ser Val Ser Ser Cys Asp Leu	725	730	735
Arg Met Gly Ser Gly Phe Cys Ile Asp Tyr Ala Leu Pro Ser Ser Arg	740	745	750
Arg Lys Arg Arg Gly Ile Ser Ser Pro Tyr Arg Phe Val Thr Phe Glu	755	760	765
Pro Phe Asn Val Ser Phe Val Asn Asp Ser Val Glu Thr Val Gly Gly	770	775	780
Leu Phe Glu Ile Gln Ile Pro Thr Asn Phe Thr Ile Ala Gly His Glu	785	790	800
Glu Phe Ile Gln Thr Ser Ser Pro Lys Val Thr Ile Asp Cys Ser Ala	805	810	815
Phe Val Cys Ser Asn Tyr Ala Ala Cys His Asp Leu Leu Ser Glu Tyr	820	825	830
Gly Thr Phe Cys Asp Asn Ile Asn Ser Ile Leu Asn Glu Val Asn Asp	835	840	845
Leu Leu Asp Ile Thr Gln Leu Gln Val Ala Asn Ala Leu Met Gln Gly	850	855	860
Val Thr Leu Ser Ser Asn Leu Asn Thr Asn Leu His Ser Asp Val Asp	865	870	875
Asn Ile Asp Phe Lys Ser Leu Leu Gly Cys Leu Gly Ser Gln Cys Gly	885	890	895
Ser Ser Ser Arg Ser Leu Leu Glu Asp Leu Leu Phe Asn Lys Val Lys	900	905	910
Leu Ser Asp Val Gly Phe Val Glu Ala Tyr Asn Asn Cys Thr Gly Gly	915	920	925
Ser Glu Ile Arg Asp Leu Leu Cys Val Gln Ser Phe Asn Gly Ile Lys	930	935	940
Val Leu Pro Pro Ile Leu Ser Glu Thr Gln Ile Ser Gly Tyr Thr Thr	945	950	955
Ala Ala Thr Val Ala Ala Met Phe Pro Pro Trp Ser Ala Ala Ala Gly	965	970	975
Val Pro Phe Ser Leu Asn Val Gln Tyr Arg Ile Asn Gly Leu Gly Val	980	985	990
Thr Met Asp Val Leu Asn Lys Asn Gln Lys Leu Ile Ala Asn Ala Phe	995	1000	1005
Asn Lys Ala Leu Leu Ser Ile Gln Asn Gly Phe Thr Ala Thr Asn	1010	1015	1020
Ser Ala Leu Ala Lys Ile Gln Ser Val Val Asn Ala Asn Ala Gln	1025	1030	1035
Ala Leu Asn Ser Leu Leu Gln Gln Leu Phe Asn Lys Phe Gly Ala	1040	1045	1050
Ile Ser Ser Ser Leu Gln Glu Ile Leu Ser Arg Leu Asp Asn Leu	1055	1060	1065
Glu Ala Gln Val Gln Ile Asp Arg Leu Ile Asn Gly Arg Leu Thr	1070	1075	1080
Ala Leu Asn Ala Tyr Val Ser Gln Gln Leu Ser Asp Ile Thr Leu	1085	1090	1095
Ile Lys Ala Gly Ala Ser Arg Ala Ile Glu Lys Val Asn Glu Cys	1100	1105	1110

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Val Lys Ser Gln Ser Pro Arg Ile Asn Phe Cys Gly Asn Gly Asn
 1115                1120                1125

His Ile Leu Ser Leu Val Gln Asn Ala Pro Tyr Gly Leu Leu Phe
 1130                1135                1140

Ile His Phe Ser Tyr Lys Pro Thr Ser Phe Lys Thr Val Leu Val
 1145                1150                1155

Ser Pro Gly Leu Cys Leu Ser Gly Asp Arg Gly Ile Ala Pro Lys
 1160                1165                1170

Gln Gly Tyr Phe Ile Lys Gln Asn Asp Ser Trp Met Phe Thr Gly
 1175                1180                1185

Ser Ser Tyr Tyr Tyr Pro Glu Pro Ile Ser Asp Lys Asn Val Val
 1190                1195                1200

Phe Met Asn Ser Cys Ser Val Asn Phe Thr Lys Ala Pro Phe Ile
 1205                1210                1215

Tyr Leu Asn Asn Ser Ile Pro Asn Leu Ser Asp Phe Glu Ala Glu
 1220                1225                1230

Leu Ser Leu Trp Phe Lys Asn His Thr Ser Ile Ala Pro Asn Leu
 1235                1240                1245

Thr Phe Asn Ser His Ile Asn Ala Thr Phe Leu Asp Leu Tyr Tyr
 1250                1255                1260

Glu Met Asn Val Ile Gln Glu Ser Ile Lys Ser Leu Asn Ser Ser
 1265                1270                1275

Phe Ile Asn Leu Lys Glu Ile Gly Thr Tyr Glu Met Tyr Val Lys
 1280                1285                1290

Trp Pro Trp Tyr Ile Trp Leu Leu Ile Val Ile Leu Phe Ile Ile
 1295                1300                1305

Phe Leu Met Ile Leu Phe Phe Ile Cys Cys Cys Thr Gly Cys Gly
 1310                1315                1320

Ser Ala Cys Phe Ser Lys Cys His Asn Cys Cys Asp Glu Tyr Gly
 1325                1330                1335

Gly His Asn Asp Phe Val Ile Lys Ala Ser His Asp Asp
 1340                1345                1350

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<210> SEQ ID NO 32

<211> LENGTH: 526

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 32

```

Met Phe Ile Phe Leu Leu Phe Leu Thr Leu Thr Ser Gly Ser Asp Leu
 1           5           10          15

Asp Arg Ala Leu Ser Gly Ile Ala Ala Glu Gln Asp Arg Asn Thr Arg
 20          25          30

Glu Val Phe Ala Gln Val Lys Gln Met Tyr Lys Thr Pro Thr Leu Lys
 35          40          45

Tyr Phe Gly Gly Phe Asn Phe Ser Gln Ile Leu Pro Asp Pro Leu Lys
 50          55          60

Pro Thr Lys Arg Ser Phe Ile Glu Asp Leu Leu Phe Asn Lys Val Thr
 65          70          75          80

Leu Ala Asp Ala Gly Phe Met Lys Gln Tyr Gly Glu Cys Leu Gly Asp
 85          90          95

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Ile Asn Ala Arg Asp Leu Ile Cys Ala Gln Lys Phe Asn Gly Leu Thr
 100 105 110
 Val Leu Pro Pro Leu Leu Thr Asp Asp Met Ile Ala Ala Tyr Thr Ala
 115 120 125
 Ala Leu Val Ser Gly Thr Ala Thr Ala Gly Trp Thr Phe Gly Ala Gly
 130 135 140
 Ala Ala Leu Gln Ile Pro Phe Ala Met Gln Met Ala Tyr Arg Phe Asn
 145 150 155 160
 Gly Ile Gly Val Thr Gln Asn Val Leu Tyr Glu Asn Gln Lys Gln Ile
 165 170 175
 Ala Asn Gln Phe Asn Lys Ala Ile Ser Gln Ile Gln Glu Ser Leu Thr
 180 185 190
 Thr Thr Ser Thr Ala Leu Gly Lys Leu Gln Asp Val Val Asn Gln Asn
 195 200 205
 Ala Gln Ala Leu Asn Thr Leu Val Lys Gln Leu Ser Ser Asn Phe Gly
 210 215 220
 Ala Ile Ser Ser Val Leu Asn Asp Ile Leu Ser Arg Leu Asp Lys Val
 225 230 235 240
 Glu Ala Glu Val Gln Ile Asp Arg Leu Ile Thr Gly Arg Leu Gln Ser
 245 250 255
 Leu Gln Thr Tyr Val Thr Gln Gln Leu Ile Arg Ala Ala Glu Ile Arg
 260 265 270
 Ala Ser Ala Asn Leu Ala Ala Thr Lys Met Ser Glu Cys Val Leu Gly
 275 280 285
 Gln Ser Lys Arg Val Asp Phe Cys Gly Lys Gly Tyr His Leu Met Ser
 290 295 300
 Phe Pro Gln Ala Ala Pro His Gly Val Val Phe Leu His Val Thr Tyr
 305 310 315 320
 Val Pro Ser Gln Glu Arg Asn Phe Thr Thr Ala Pro Ala Ile Cys His
 325 330 335
 Glu Gly Lys Ala Tyr Phe Pro Arg Glu Gly Val Phe Val Phe Asn Gly
 340 345 350
 Thr Ser Trp Phe Ile Thr Gln Arg Asn Phe Phe Ser Pro Gln Ile Ile
 355 360 365
 Thr Thr Asp Asn Thr Phe Val Ser Gly Asn Cys Asp Val Val Ile Gly
 370 375 380
 Ile Ile Asn Asn Thr Val Tyr Asp Pro Leu Gln Pro Glu Leu Asp Ser
 385 390 395 400
 Phe Lys Glu Glu Leu Asp Lys Tyr Phe Lys Asn His Thr Ser Pro Asp
 405 410 415
 Val Asp Leu Gly Asp Ile Ser Gly Ile Asn Ala Ser Val Val Asn Ile
 420 425 430
 Gln Lys Glu Ile Asp Arg Leu Asn Glu Val Ala Lys Asn Leu Asn Glu
 435 440 445
 Ser Leu Ile Asp Leu Gln Glu Leu Gly Lys Tyr Glu Gln Tyr Ile Lys
 450 455 460
 Trp Pro Trp Tyr Val Trp Leu Gly Phe Ile Ala Gly Leu Ile Ala Ile
 465 470 475 480
 Val Met Val Thr Ile Leu Leu Cys Cys Met Thr Ser Cys Cys Ser Cys
 485 490 495

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Leu Lys Gly Ala Cys Ser Cys Gly Ser Cys Cys Lys Phe Asp Glu Asp
500 505 510

Asp Ser Glu Pro Val Leu Lys Gly Val Lys Leu His Tyr Thr
515 520 525

<210> SEQ ID NO 33

<211> LENGTH: 588

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 33

Met Ile His Ser Val Phe Leu Leu Met Phe Leu Leu Thr Pro Thr Glu
1 5 10 15

Ser Asp Cys Lys Leu Pro Leu Gly Gln Ser Leu Cys Ala Leu Pro Asp
20 25 30

Thr Pro Ser Thr Leu Thr Pro Arg Ser Val Arg Ser Val Pro Gly Glu
35 40 45

Met Arg Leu Ala Ser Ile Ala Phe Asn His Pro Ile Gln Val Asp Gln
50 55 60

Leu Asn Ser Ser Tyr Phe Lys Leu Ser Ile Pro Thr Asn Phe Ser Phe
65 70 75 80

Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln Lys Val Thr Val
85 90 95

Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys Cys Glu Gln Leu
100 105 110

Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn Gln Ala Leu His
115 120 125

Gly Ala Asn Leu Arg Gln Asp Asp Ser Val Arg Asn Leu Phe Ala Ser
130 135 140

Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly Phe Gly Gly Asp
145 150 155 160

Phe Asn Leu Thr Leu Leu Glu Pro Val Ser Ile Ser Thr Gly Ser Arg
165 170 175

Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp Lys Val Thr Ile
180 185 190

Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys Met Gln Gln Gly
195 200 205

Pro Ala Ser Ala Arg Asp Leu Ile Cys Ala Gln Tyr Val Ala Gly Tyr
210 215 220

Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu Ala Ala Tyr Thr
225 230 235 240

Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp Thr Ala Gly Leu
245 250 255

Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile Phe Tyr Arg Leu
260 265 270

Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu Asn Gln Lys Leu
275 280 285

Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met Gln Thr Gly Phe
290 295 300

Thr Thr Thr Asn Glu Ala Phe Gln Lys Val Gln Asp Ala Val Asn Asn
305 310 315 320

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tttgatgata ataggetgga gctcgggtgg ccaagcttct tgccccttgg gctccccccc 1800
agccccctct ccccttctctg caccogtacc ccogtggctt ttgaataaag tctgagtggt 1860
cggc 1864

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<210> SEQ ID NO 36
<211> LENGTH: 1653
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

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<400> SEQUENCE: 36

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```

atgggtctca aggtgaaagt ctctgcgta ttcattggcag tactgttaac tctccaaaca 60
cccgccggtc aaattcattg gggcaatctc tctaagatag gggtagtagg aataggaagt 120
gcaagctaca aagttatgac tcgttccagc catcaatcat tagtcataaa attaattgcc 180
aatataacte tctcaataa ctgcacgagg gtagagattg cagaatacag gagactacta 240
agaacagttt tggaaccaat tagggatgca cttaatgcaa tgaccagaa cataaggccg 300
gttcagagcg tagcttcaag taggagacac aagagatttg cgggagtagt cctggcaggt 360
ggggccctag gtgttgccac agctgtctag ataacagccg gcattgcact taccgggtcc 420
atgtgaaact ctcaggccat cgacaatctg agagcgagcc tggaaactac taatcaggca 480
attgaggcaa tcagacaagc agggcaggag atgatattgg ctgttcaggg tgtccaagac 540
tacatcaata atgagctgat accgtctatg aaccagctat cttgtgatct aatcggctag 600
aagctcgggc tcaaatgtct tagatactat acagaaatcc tgtcattatt tggccccagc 660
ctacgggacc ccatactctg ggagatatct atccaggctt tgagttatgc acttgaggga 720
gatatcaata aggtgttaga aaagctcggg tacagtgagc gcgatttact aggcattctt 780
gagagcagag gaataaaggc tcggataact cacgtcgaca cagagtccta cttcatagtc 840
ctcagtatag cctatccgac gctgtccgag attaaggggg tgattgtcca ccggttagag 900
ggggctctct acaacatagg ctctcaagag tggatataca ctgtgccccaa gtatgttgca 960
acccaagggt acctatctct gaattttgat gagtcatcat gtactttcat gccagagggg 1020
actgtgtgca gccaaaatgc cttgtaccgg atgagtcctc tgctccaaga atgcctccgg 1080
gggtccacca agtctctgtc tegtacactc gtatccgggt cttttgggaa ccggttcatt 1140
ttatcacaag ggaacctaat agccaattgt gcatcaattc tttgtaagt ttacacaaca 1200
ggtacgatta ttaatcaaga cctgacaag atcctaact acattgtctc cgatcgtctc 1260
ccggtagtct aggtgaaagg cgtgaccatc caagtccggg gcaggaggta tccagacgct 1320
gtgtactctc acagaattga cctcggctct cccatcatct tggagaggtt ggacgtaggg 1380
acaaatctgg ggaatgcaat tgccaaattg gaggatgcca aggaattgtt ggaatcatcg 1440
gaccagatat tgagaagtat gaaaggttta tcgagcacta gcattgtcta catcctgatt 1500
gcagtgctgc ttggagggtt gatagggatc cccactttaa tatgttgctg cagggggcgt 1560
tgtaacaaaa agggagaaca agttgggtatg tcaagaccag gcctaaagcc tgacctaca 1620
ggaacatcaa aatcctatgt aagatcgtct tga 1653

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<210> SEQ ID NO 37
<211> LENGTH: 1925
<212> TYPE: DNA

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-continued

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 37

```

ggggaataa gagagaaaag aagagtaaga agaaatataa gagccacccat gggctctcaag    60
gtgaacgtct ctgccgtatt catggcagta ctgttaactc tccaaacacc cgcgggtcaa    120
attcattggg gcaatctctc taagataggg gtagtaggaa taggaagtgc aagctacaaa    180
gttatgactc gttccagcca tcaatcatta gtcataaaat taatgccaa tataactctc    240
ctcaataact gcacgagggg agagattgca gaatacagga gactactaag aacagttttg    300
gaaccaatta gggatgcact taatgcaatg acccagaaca taaggccggg tcagagcgta    360
gcttcaagta ggagacacaa gagatttggg ggagtagtcc tggcaggtgc ggccttaggt    420
gttgccacag ctgctcagat aacagccggc attgcacttc accgggccat gctgaactct    480
caggccatcg acaatctgag agcagagcctg gaaactacta atcaggcaat tgaggcaatc    540
agacaagcag ggcaggagat gatattggct gttcaggggtg tccaagacta catcaataat    600
gagctgatac cgtctatgaa ccagctatct tgtgatctaa tcggtcagaa gctcgggctc    660
aaattgctta gatactatac agaaatcctg tcattatttg gccccagcct acgggacccc    720
atatctggg agatatctat ccaggctttg agttatgcac ttggaggaga tatcaataag    780
gtgtagaaaa agctcggata cagtggaggc gatttactag gcatcttaga gagcagagga    840
ataaaggctc ggataactca cgtcgcacaca gactcctact tcatagtcct cagtatagcc    900
tatecgacgc tgtccgagat taaggggggtg attgtccacc ggctagaggg ggtctcgtac    960
aacataggct ctcaagagtg gtataccact gtgcccaagt atgttgcaac ccaagggtac    1020
cttatctcga attttgatga gtcacatgt actttcctgc cagagggggac tgtgtgcagc    1080
caaaatgctt tgtacccgat gagtctcttg ctccaagaat gcctccgggg gtcccacaag    1140
tctgtgctc gtacactcgt atccgggtct tttgggaacc ggttcatttt atcacaaggg    1200
aacctaatag ccaattgtgc atcaattcct tgtaagtgtt acacaacagg tacgattatt    1260
aatcaagacc ctgacaagat cctaacatac attgctgccc atcgtgccc ggtagtcgag    1320
gtgaacggcg tgaccatcca agtcygggagc aggaggatc cagacgctgt gtacttgac    1380
agaattgacc tcggctctcc catatcattg gagaggttgg acgtagggac aaatctgggg    1440
aatgcaattg ccaaattgga ggatgccaaag gaattgttgg aatcatcgga ccagatattg    1500
agaagtatga aaggtttata gagcactagc atagtctaca tcttgattgc agtgtgtctt    1560
ggaggggttg tagggatccc cactttaata tgttctgca gggggcgttg taacaaaaag    1620
ggagaacaag ttggtatgtc aagaccaggc ctaaagcctg acctacagg aacatcaaaa    1680
tctatgtaa gatcgctttg atgataatag gctggagcct cggtaggcaa gcttcttgcc    1740
ccttgggctt cccccagcc cctcctcccc ttctgcaacc cgtacccccg tggctcttga    1800
ataaagtctg agtggcgggc aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa    1860
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa    1920
tctag                                          1925

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<210> SEQ ID NO 38

<211> LENGTH: 1864

<212> TYPE: DNA

-continued

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 38

```

tcaagctttt ggaccctcgt acagaagcta atacgactca ctatagggaa ataagagaga    60
aaagaagagt aagaagaaat ataagagcca ccatgggtct caaggtgaac gtctctgtca    120
tattcatggc agtactgtta actcttcaaa caccaccggg tcaaatccat tggggcaatc    180
tctetaagat aggggtggta ggggtaggaa gtgcaagcta caaagttatg actcgttcca    240
gccaatcaatc attagtata aagttaatgc ccaatataac tctcctcaac aattgcacga    300
gggtagggat tgcagaatac aggagactac tgagaacagt tctggaacca attagagatg    360
cacttaatgc aatgaccagc aatataagac cggttcagag tgtagcttca agtaggagac    420
acaagagatt tgcgggagtt gtctcggcag gtgcggccct aggcggtgcc acagctgctc    480
aaataacagc cggttattgca ctccaccagt ccatgctgaa ctctcaagcc atcgacaatc    540
tgagagcgag cctagaaact actaatcagg caattgaggc aatcagacaa gcagggcagg    600
agatgatatt ggctgttcag ggtgtccaag actacatcaa taatgagctg ataccgtcta    660
tgaatcaact atcttgtgat ttaatcggcc agaagctagg gctcaaatg ctcagatact    720
atacagaaat cctgtcatta tttggcccca gcttaacggga ccccatatct gcggagatat    780
ctatccaggc tttgagctat gcgcttgagg gagatatcaa taagggtgtg gaaaagctcg    840
gatacagtggt aggtgatcta ctgggcatct tagagagcag aggaataaag gcccgataa    900
ctcacgtcga cacagagtec tacttcattg tactcagtat agcctatccg acgctatccg    960
agattaaggg ggtgattgtc caccggctag aggggggtctc gtacaacata ggctctcaag   1020
agtgggtatac cactgtgccc aagtatgttg caacccaagg gtacccttate tcgaattttg   1080
atgagtcatc atgcactttc atgccagagg ggaactgtgtg cagccagaat gccttgtacc   1140
cgatgagtcc tctgtcctca gaatgcctcc ggggggtccac taagtccgtg gctcgtacac   1200
tcgtatccgg gtctttcggg aaccgggttca ttttatcaca ggggaaccta atagccaatt   1260
gtgcatcaat cctttgcaag tgttacacaa caggaacaat cattaatcaa gaccctgaca   1320
agatcctaac atacattgct gccgatcact gcccggtggt cgagggtgaat ggcgtgacca   1380
tccaagtcgg gagcaggagg tatccggagc ctgtgtactt gcacaggatt gacctcggtc   1440
ctcccatac tttggagagg ttggacgtag ggacaaatct ggggaatgca attgctaagt   1500
tggaggatgc caaggaattg ttggagtcac cggaccagat attgaggagt atgaaaggtt   1560
tatcgagcac tagtatagtt tacatcctga ttgcagtgtg tcttggagga ttgataggg   1620
tccccgcttt aatatgttgc tgcagggggc gttgtaacaa gaaggagaa caagttggt   1680
tgtcaagacc aggcctaaag cctgatctta caggaacatc aaaatcctat gtaaggtcac   1740
tctgatgata ataggctgga geectcggtag ccaagcttct tgccccttgg geectcccc   1800
agccccctct ccccttctg caccctgacc cccgtggtct ttgaataaag tctgagtggt   1860
cggc

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<210> SEQ ID NO 39

<211> LENGTH: 1653

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 39

```

atgggtctca aggtgaacgt ctctgtcata ttcattggcag tactgttaac tcttcaaaca    60
cccaccggtc aatccattg gggcaatctc tctaagatag gggtagtagg ggttaggaagt    120
gcaagctaca aagttatgac tcgttccagc catcaatcat tagtcataaa gttaatgccc    180
aatataacte tctcaacaaa ttgcacgagg gtagggattg cagaatacag gagactactg    240
agaacagttc tggaaaccaat tagagatgca cttaatgcaa tgaccocaga tataagaccg    300
gttcagagtg tagcttcaag taggagacac aagagatttg cgggagttgt cctggcaggt    360
ggggccctag gcggttgcac agctgctcaa ataacagccg gtattgcaact tcaccagtcc    420
atgctgaact ctcaagccat cgacaatctg agagcgagcc tagaaactac taatcaggca    480
attgaggcaa tcagacaagc agggcaggag atgatattgg ctgttcaggg tgtccaagac    540
tacatcaata atgagctgat accgtctatg aatcaactat cttgtgattt aatcgccag    600
aagctagggc tcaaatgtct cagatactat acagaatcc tgctattatt tggcccagc    660
ttacgggacc ccatactctg ggagatatct atccaggctt tgagctatgc gcttgaggga    720
gatatcaata aggtgttggg aaagctggga tacagtggag gtgatctact gggcatetta    780
gagagcagag gaataaaggc ccggataact cacgtcgaca cagagtctca cttcattgta    840
ctcagtatag cctatccgac gctatccgag attaaggggg tgattgtcca ccggctagag    900
ggggtctctg acaacatagg ctctcaagag tggatataca ctgtgcccga gtatgttgca    960
acccaagggt acctatctc gaattttgat gagtcatcat gcactttcat gccagagggg    1020
actgtgtgca gccagaatgc cttgtaccgg atgagtcctc tgctccaaga atgcctccgg    1080
gggtccacta agtctctgtc tcgtacactc gtatccgggt ctttcgggaa ccggttcatt    1140
ttatcacagg ggaacctaat agccaattgt gcatcaatcc tttgcaagtg ttacacaaca    1200
ggaacaatca ttaatcaaga ccttgacaag atcctaactc acattgctgc cgatcactgc    1260
ccggtygtcg aggtgaatgg cgtgaccate caagtgggga gcaggaggta tccggacgct    1320
gtgtacttgc acaggattga cctcggtcct cccatattct tggagagggt ggaogtaggg    1380
acaaatctgg ggaatgcaat tgctaagttg gaggatgcca aggaattgtt ggagtcactg    1440
gaccagatat tgaggagtat gaaaggttta tcgagcacta gtatagttta catcctgatt    1500
gcagtgtgtc ttggaggatt gatagggatc cccgctttaa tatgttctg cagggggcgt    1560
tgtaacaaga agggagaaca agttggtatg tcaagaccag gcctaaagcc tgatcttaca    1620
ggaacatcaa aatctctatg aaggctactc tga    1653

```

<210> SEQ ID NO 40

<211> LENGTH: 1925

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 40

```

ggggaaataa gagagaaaag aagagtaaga agaaatataa gagccaccat gggctctcaag    60
gtgaacgtct ctgtcatatt catggcagta ctgttaactc ttcaaacacc cacoggtcaa    120
atccattggg gcaatctctc taagataggg gtggtagggg taggaagtgc aagctacaaa    180

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gttatgactc gttccagcca tcaatcatta gtcataaagt taatgcccac tataactctc 240
ctcaacaatt gcacgagggg agggattgca gaatacagga gactactgag aacagttctg 300
gaaccaatta gagatgcact taatgcaatg acccagaata taagaccggg tcagagtgtg 360
gottcaagta ggagacacaa gagatttgcg ggagttgtcc tggcaggtgc ggccctaggg 420
gttgccacag ctgctcaaat aacagccggg attgcacttc accagtccat gctgaactct 480
caagccatcg acaatctgag agcagagccta gaaactacta atcaggcaat tgaggcaatc 540
agacaagcag ggcaggagat gatattggct gttcaggggtg tccaagacta catcaataat 600
gagctgatac cgtctatgaa tcaactatct tgtgatttaa tgggccagaa gctagggctc 660
aaattgctca gatactatac agaaatctctg tcattatttg gcccagctt acgggacccc 720
atatctgcgg agatatctat ccaggctttg agctatgcgc ttggaggaga tatcaataag 780
gtgttggaag agctcggata cagtggaggt gatctactgg gcatcttaga gagcagagga 840
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aacctaatag ccaattgtgc atcaatcctt tgcaagtgtt acacaacagg aacaatcatt 1260
aatcaagacc ctgacaagat cctaacatac attgctgccg atcactgccc ggtggtcgag 1320
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aatgcaattg ctaagttgga ggatgccaaag gaattgttg agtcatcgga ccagatattg 1500
aggagtatga aaggtttatc gagcactagt atagtttaca tctgattgc agtgtgtctt 1560
ggaggattga tagggatccc cgttttaata tgttctgca gggggcgttg taacaagaag 1620
ggagaacaag ttggtatgtc aagaccaggc ctaaagcctg atcttacagg aacatcaaaa 1680
tctatgtaa ggtcactctg atgataatag gctggagcct cggtgggcaa gcttcttgcc 1740
ccttgggccc cccccagcc cctctctccc tctctgacc cgtacccccg tggctcttga 1800
ataaagtctg agtggggcgc aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1860
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1920
tctag 1925

```

<210> SEQ ID NO 41

<211> LENGTH: 2065

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 41

```

tcaagctttt ggaccctcgt acagaagcta atacgactca ctatagggaa ataagagaga 60
aaagaagagt aagaagaaat ataagagcca ccatgtcacc gcaacgagac cggataaatg 120
ccttctacaa agataaccct tatccaagg gaagtaggat agttattaac agagaacatc 180

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ttatgattga cagacctat gttctgctgg ctggtctggt cgteatgttt ctgagcttga	240
toggattgct ggcaattgca ggcattagac ttcctcgggc agccatctac accgaggaga	300
tccataaaag cctcagtacc aatctggatg tgactaactc catcgagcat caggtaaagg	360
acgtgctgac accactcttt aaaatcatcg gggatgaagt gggcctgaga acacctcaga	420
gattcactga cctagtghaa ttcctctcgg acaagattaa attccttaat ccggataggg	480
agtacgactt cagagatctc acttgggtgca tcaaccgcc agagaggate aaactagatt	540
atgatcaata ctgtgcagat gtggctgctg aagagctcat gaatgcattg gtgaactcaa	600
ctctactgga gaccagaaca accactcagt tcttagctgt ctcaaaggga aactgctcag	660
ggcccactac aatecagaggt caattctcaa acatgctcgt gtccttgttg gacttgtact	720
taggtcaggg ttacaatgtg tcatctatag tcaactatgac atcccaggga atgtatgggg	780
gaacctacct agttgaaaag cctaactctga acagcaaagg gtcagagttg tcacaactga	840
gcatgtaccg agtgtttgaa gtaggtgtga tcagaaacc gggtttgggg gctccggtgt	900
tccatagac aaactatctt gagcaaccag tcagtatgg tctcggcaac tgtatgggtg	960
ctttggggga gctcaaacct gcagcccttt gtcacgggga cgattctatc ataattccct	1020
atcagggatc agggaaaagg gtcagcttcc agctcgtcaa gctgggtgct tggaaatccc	1080
caaccgacat gcaatcctgg gtcaccttat caacggatga tccagtggta gacagcttt	1140
acctctctc tcacagaggt gtcctcctg acaatcaagc aaaatgggct gtcaccgaca	1200
cacgaacaga tgacaagtg cgaatggaga catgcttcca gcaggcgtgt aaaggtaaaa	1260
tccaagcact ctgcgagaat cccgagtggg taccattgaa ggataacagg attccttcat	1320
acggggtcct gctctgtgat ctgagctgca cgggtgagct taaaatcaaa attgcttcgg	1380
gattcgggac attgatcaca cccgctcag ggatggacct atacaaatcc aactgcaaca	1440
atgtgtattg gctgactatt ccgccaatga gaaatctagc cttaggcgta atcaacacat	1500
tggagtggat accgagatcc aagggttagc ccaacctctt caetgtccca attaagggaag	1560
caggcgaaga ctgccatgcc ccaacatacc tacctcggga ggtggacggt gatgtcaaac	1620
tcagttccaa cctgggtgatt ctacctggtc aagatctcca atatgttttg gcaacctacg	1680
atacctccag ggttgagcat gctgtggttt attacgttta cagcccaagc cgtctatctt	1740
cttactttta tcttttttagg ttgctataa aggggggtccc aatcgaacta caagtggaa	1800
gcttcacatg ggatcaaaaa ctctgggtgc gtcactctctg tgtgcttgcg gactcagaat	1860
ccgggtgact tctcactcac tctgggatgy tgggcatggg agtcagctgc acagctacce	1920
gggaagatgg aaccaatcgc agataatgat aataggtggy agcctcgggtg gccaagcttc	1980
ttgccccttg ggcctcccc cagcccctcc tccccttctt gcacccgtac ccccggtgct	2040
tttgaataaa gctctgagtgg ggggc	2065

<210> SEQ ID NO 42

<211> LENGTH: 1954

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 42

atgtcaccgc aacgagaccg gataaatgcc ttctacaaag ataaccctta tcccaaggga 60

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agtaggatag ttattaacag agaacatett atgattgaca gacctatgt tetgetgget 120
gttctgttcc tcatgtttct gagcttgatc ggattgctgg caattgcagg cattagactt 180
catcgggcag ccctctacac cgcggagatc cataaaagcc tcagtaccaa tctggatgtg 240
actaactcca togagcatca ggtcaaggac gtgetgacac cactotttaa aatcatcggg 300
gatgaagtgg gcctgagaac acctcagaga ttcactgacc tagtgaaatt catctcggac 360
aagattaat tccttaatcc ggatagggag tacgacttca gagatctcac ttgggtgcac 420
aaccgccag agaggatcaa actagattat gatcaact gtgcagatgt ggctgctgaa 480
gagctcatga atgcattggt gaactcaact ctactggaga ccagaacaac cactcagttc 540
ctagetgtct caaagggaaa ctgctcaggg cccactacaa tcagaggtea attctcaaac 600
atgtcgtgt cctgttgga cttgtactta ggtcaggtt acaatgtgtc atctatagtc 660
actatgacat cccagggaaat gtatggggga acctacctag ttgaaaagcc taatctgaa 720
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cacggggaag attctatcat aatccctat cagggatcag ggaagggtgt cagcttccag 960
ctcgtcaagc tgggtgtctg gaaatcccca accgacatgc aatcctgggt ccccttaca 1020
acggatgac cagtggtaga caggctttac ctctcatctc acagaggtgt catcgtgac 1080
aatcaagcaa aatgggctgt cccgacaaca cgaacagatg acaagttgcg aatggagaca 1140
tgcttccagc aggcgtgtaa aggtaaaatc caagcactct gcgagaatcc cgagtgggta 1200
ccattgaagg ataacaggat tcttcatac ggggtcctgt ctgttgatct gactctgacg 1260
gttgagctta aaatcaaaaat tgettcggga ttcgggccat tgatcacaca cggctcaggg 1320
atggacctat acaaatccaa ctgcaacaat gtgtattggc tgactattcc gccaatgaga 1380
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aacctcttca ctgtcccaat taaggaagca ggcgaagact gccatgccc aacataccta 1500
cctgcggagg tggacggtga tgtcaaaact agttccaacc tggtgattct acctggtcaa 1560
gatctccaat atgttttggc aacctcagat acctccaggg ttgagcatgc tgtggtttat 1620
tacgtttaca gcccagcgc ctcatcttct tacttttacc cttttagggt gctataaag 1680
ggggtcccaa tcgaactaca agtggaatgc ttcacatggg atcaaaaact ctggtgccgt 1740
cacttctgtg tgcttgcgga ctcagaatcc ggtggactta tcaactcctc tgggatggtg 1800
ggcatgggag tcagctgcac agctaccggg gaagatggaa ccaatcgcag ataa 1854

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<210> SEQ ID NO 43

<211> LENGTH: 2126

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 43

```

ggggaataa gagagaaaag aagagtaaga agaaatataa gagccaccat gtcaccgcaa 60
cgagaccgga taaatgcott ctcaaaagat aacccttacc ccaagggaaag taggatagtt 120
attaacagag aacatcttat gattgacaga ccctatgttc tgctggctgt tctgttctg 180

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atgtttctga gcttgatcgg attgctggca attgcaggca ttagacttca tgggceagcc 240
atctacaccg cggagatcca taaaagcctc agtaccacac tggatgtgac taactccatc 300
gagcatcagg tcaaggacgt gctgacacca ctcttataaa tcatcgggga tgaagtgggc 360
ctgagaacac ctcagagatt cactgaccta gtgaaattca tctcggacaa gattaaattc 420
cttaatcccg ataggagta cyacttcaga gatctcactt ggtgcatcaa cccgccagag 480
aggatcaaac tagattatga tcaatactgt gcagatgtgg ctgctgaaga gctcatgaat 540
gcattggtga actcaactct actggagacc agaacaacca ctcaagttct agctgtctca 600
aagggaaact gctcagggcc cactacaatc agaggtcaat tctcaaacat gtctgtgtcc 660
ttggtggact tgaacttagg tggaggttac aatgtgtcat ctatagtca tatgacatcc 720
cagggaatgt atgggggaac ctacctagt taaaagccta atctgaacag caaagggta 780
gagttgtcac aactgagcat gtaccgagtg ttgaaagtag gtgtgatcag aaaccgggt 840
ttgggggctc cgggtgtcca tatgacaaac tattttgagc aaccagtcag taatggtctc 900
ggcaactgta tgggtggctt gggggagctc aaactcgcag cctttgtca cggggacgat 960
tctatcataa tccctatca gggatcaggg aaaggtgtca gcttcagct cgtcaagctg 1020
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gtggtagaca ggctttacct ctcactcac agaggtgtca tgcctgacaa tcaagcaaaa 1140
tgggtgtgac cgacaacacg aacagatgac aagttgcgaa tggagacatg cttccagcag 1200
gogtgtaaa gtaaaatcca agcaactctc gagaatccc agtgggtacc attgaaggat 1260
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gacggtyatg tcaaaactcag tccaaactg gtgattctac ctggtcaaga tctccaatat 1620
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ccaagccgct cattttctta cttttatcct tttagggtgc ctataaaggg ggtcccaatc 1740
gaactacaag tggaatgctt cacatgggat caaaaactct ggtgcctca cttctgtgtg 1800
cttgcggact cagaatccgg tggacttatc actcaactct ggatggtggg catgggagtc 1860
agctgcacag ctaccocgga agatggaacc aatcgcagat aatgataata ggtcggagcc 1920
tgggtggcca agcttcttgc ccttggggcc tccccccagc cctctctccc ctctctgac 1980
ccgtaccccc gtggtctttg aataaagtct gagtgggctg caaaaaaaaa aaaaaaaaaa 2040
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2100
aaaaaaaaa aaaaaaaaaa atctag 2126

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<210> SEQ ID NO 44

<211> LENGTH: 2065

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 44

-continued

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teaagctttt ggaccctcgt acagaageta atacgactca ctatagggaa ataagagaga    60
aaagaagagt aagaagaat ataagagcca ccatgtcacc acaacgagac cggataaatg    120
cctttcacia agacaacccc cctcctaagg gaagtaggat agttattaac agagaacatc    180
ttatgattga tagaccttat gttttgctgg ctgtttctatt cgtcatgttt ctgagcttga    240
tcgggttgct agccattgca ggcattagac ttcacgggc agccatctac accgcagaga    300
tccataaaag cctcagcacc aatctggatg taactaactc aatcgagcat caggtaaagg    360
acgtgctgac accactcttc aagatcatcg gtgatgaagt gggcttgagg acaccctcaga    420
gattcactga cctagtgaag ttcactctcty acaagattaa attccttaac ccggacaggg    480
aatacgactt cagagatctc acttgggtga tcaacccgcc agagagaatc aaattggatt    540
atgatcaata ctgtgcagat gtggtgctgt aagaactcat gaatgcattg gtgaactcaa    600
ctctactgga gaccagggca accaatcagt tcttagctgt ctcaaaggga aactgctcag    660
ggcccactac aatcagaggc caattctcaa acatgtcgtc gtccctggtg gacttgtatt    720
taagtcgagg ttacaatgtg tcactctatag tcaactatgac atcccaggga atgtacgggg    780
gaacttacct agtggaaaag cctaactctga gcagcaaagg gtcagagtgg tcacaactga    840
gcatgcaccg agtgtttgaa gtaggtggtta tcagaaatcc gggtttgggg gctccgggat    900
tccatgatgc aaactatctt gagcaaccag tcagttaatga ttccagcaac tgcattggtgg    960
ctttggggga gctcaagttc gcagccctct gtcacagggg agattctatc acaattccct    1020
atcagggatc agggaaaagg gtcagcttcc agcttgtaaa gctaggtgct tggaaatccc    1080
caaccgacat gcaatctctg gtcacctat caacggatga tccagtata gacaggcttt    1140
acctctcacc tcacagaggc gttatcgtg acaatcaagc aaaaatgggct gtcccgacaa    1200
cacggacaga tgacaagtgg cgaatggaga catgcttcca gcaggcgtgt aagggtaaaa    1260
tccaagcact ttgcgagaat cccgagtggg caccattgaa ggataacagg attccttcat    1320
acggggctct gtctgttgat ctgagtctga cagttgagct taaaatcaaa attgtttcag    1380
gattcggggc attgatcaca cacggttcag ggatggacct atacaaatcc aaccacaaca    1440
atatgtattg gotgactatc ccgcaatga agaacctggc cttaggtgta atcaacacat    1500
tggagtggat accgagatcc aaggttagtc ccaacctctt cactgttcca attaagggaag    1560
caggcgagga ctgccatgcc ccaacatacc tacctcgga ggtggatggt gatgtcaaac    1620
tcagttccaa tctggtgatt ctacctggtc aagatctcca atatgttctg gcaacctacg    1680
atacttccag agttgaacat gctgtagttt attacgttta cagcccaagc cgtctatctt    1740
cttactttta tcttttagg ttgctgtgaa ggggggtccc cattgaatta caagtggaa    1800
gcttcacatg ggaccaaaaa ctctggtgoc gtcacttctg tgtgcttgcg gactcagaat    1860
ctggtggaca taccactcac tctgggatgg tgggcattgg agtcagctgc acagccactc    1920
gggaagatgg aaccagccgc agatagtgat aataggctgg agcctcggtg gccaaagctc    1980
ttgccccttg ggcctcccc cagcccctcc tccccttctt gcaccctgac ccccgtggtc    2040
tttgaataaa gctctgagtgg gcggc                                     2065

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<210> SEQ ID NO 45

<211> LENGTH: 1854

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 45

```

atgtcaccac aacgagaccg gataaatgcc ttctacaaag acaaccccca tectaaggga    60
agtaggatag ttattaacag agaacatctt atgattgata gaccttatgt ttgctggct    120
gttctattcg tcattgttct gagcttgatc gggttgctag ccattgcagg cattagactt    180
catcggggcag ccatctacac cgcagagatc cataaaagcc tcagcaccaa tctggatgta    240
actaactcaa tcgagcatca ggtaaggac gtgctgacac cactcttcaa gatcatcggt    300
gatgaagtgg gcttgaggac acctcagaga ttcactgacc tagtgaagtt catctctgac    360
aagattaatc tccttaatcc ggacagggaa tacgacttea gagatctcac ttgggtgatac    420
aaccgcgacg agagaatcaa attggattat gatcaatact gtgcagatgt ggctgctgaa    480
gaactcatga atgcattggg gaactcaact ctactggaga ccagggcaac caatcagttc    540
ctagctgtct caaagggaaa ctgctcaggg cccactacaa tcagaggcca attctcaaac    600
atgtcgtctg ccctgttggg cttgtattta agtcgaggtt acaatgtgtc atctatagtc    660
actatgacat cccaggyaat gtacggggga acttacctag tggaaaagcc taatctgagc    720
agcaaaaggt cagagttgtc acaactgagc atgcaccgag tgtttgaagt aggtgttate    780
agaaatccgg gtttgggggc tccggtatcc catatgacaa actatcttga gcaaccagtc    840
agtaatgatt tcagcaactg catggtggct ttgggggagc tcaagttcgc agccctctgt    900
cacagggaaq attctatcac aattccctat cagggatcag ggaaaggtgt cagcttccag    960
cttgtcaagc taggtgtctg gaaatcccca accgacatgc aatcctgggt cccctatca   1020
acggatgac cagtgataga caggctttac ctctcatctc acagaggcgt tatoctgac   1080
aatcaagcaa aatgggctgt cccgacaaca cggacagatg acaagttgcy aatggagaca   1140
tgcttccagc aggcgtgtaa gggtaaaatc caagcacttt gcgagaatcc cagtgagaca   1200
ccattgaagg ataacaggat tccttcatac ggggtcttgt ctgttgatct gagtctgaca   1260
gttgagctta aaatacaaat tgtttcagga ttccggccat tgateacaca cggttcaggg   1320
atggacctat acaaatccaa ccacaacaat atgtattggc tgactatccc gccaatgaag   1380
aacctggcct taggtgtaat caacacattg gaggggatc cgagattcaa ggttagtccc   1440
aacctcttca ctgttccaat taaggaagca ggcgaggact gccatgcccc aacataccta   1500
cctgcggagg tggatgggta tgcaaaactc agttccaatc tggtgattct acctgggtaa   1560
gatctccaat atgttcttgc aacctacgat acttccagag ttgaacatgc tgtagtttat   1620
tacgtttaca gcccagccg ctcattttct tacttttate cttttagggt gcctgtaagg   1680
ggggtcccca ttgaattaca agtggaatgc ttcacatggg accaaaaact ctggtgccgt   1740
cacttctgtg tgcttgcgga ctcagaatct ggtggacata tcactcactc tgggatgggt   1800
ggcatgggag tcagctgcac agccactcgg gaagatggaa ccagccgcag atag       1854

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<210> SEQ ID NO 46

<211> LENGTH: 2126

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 46

-continued

ggggaataa gagagaaaag aagagtaaga agaaatataa gagccaccat gtcaccacaa	60
cgagaccgga taaatgcctt ctacaaagac aacccccatc ctaagggaaag taggatagtt	120
attaacagag aacatcttat gattgataga ctttatgttt tgetggctgt tetattcgtc	180
atgtttctga gottgatcgg gttgetagcc attgcaggca ttagacttca tcgggcagcc	240
atctacaccg cagagatcca taaaagcctc agcaccaatc tggatgtaac taactcaatc	300
gagcatcagg ttaaggacgt gctgacacca ctctcaaga tcatcggtga tgaagtgggc	360
ttgaggacac ctcaagagatt cactgacctc gtgaagttca tctctgacaa gattaaatc	420
cttaatccgg acaggggaata cgaactcaga gatctcactt ggtgtatcaa cccgccagag	480
agaatcaaat tggattatga tcaatactgt gcagatgtgg ctgctgaaga actcatgaat	540
gcattggtga actcaactct actggagacc agggcaacca atcagttcct agctgtctca	600
aagggaaact gctcagggcc cactacaatc agaggccaat tctcaaacat gtcgctgtcc	660
ctgttggaact tgtatttaag tcgaggttac aatgtgtcat ctatagtcac tatgacatcc	720
cagggaatgt acgggggaac ttacctagtg gaaaagccta atctgagcag caaagggcca	780
gagttgtcac aactgagcat gcaccgagtg tttgaagtag gtgttatcag aaatccgggt	840
ttgggggctc cgggtattcca tatgacaaac tatcttgagc aaccagtcag taatgattc	900
agcaactgca tggtygcttt gggggagctc aagttcgcag cctctgtca cagggagat	960
tctatcacia ttcctatca gggatcaggg aaaggtgtca gcttcagct tgtcaagcta	1020
ggtgtctgga aatccccaac cgaatgcaa tctcgggtcc cctatcaac ggatgatcca	1080
gtgatagaca ggctttacct ctcatctcac agaggcgtta tcgctgacaa tcaagcaaaa	1140
tgggtctgcc cgacaacacg gacagatgac aagttgcgaa tggagacatg cttccagcag	1200
gcgtgtaagy gtaaaatcca agcactttgc gagaatcccg agtggacacc attgaaggat	1260
aacaggattc cttcatacgg ggtcttctct gttgatctga gtctgacagt tgagcttaa	1320
atcaaaatg tttcaggatt cggggcattg atcacacacg gttcagggat ggacctatac	1380
aaatccaaac acaacaatat gtattggctg actatcccgc caatgaagaa cctggcetta	1440
ggtgtaatca acacattgga gtggataccg agattcaagg ttagtcccaa cctcttcaact	1500
gttccaatta aggaagcagg cgaaggactgc catgccccaa catacctacc tcgaggggtg	1560
gatggtgatg tcaaaactcag ttccaactg gtgattctac ctggtcaaga tctccaatat	1620
gttctggcaa cctaogatac ttcagagtt gaacatgctg tagtttatta cgtttacagc	1680
ccaagccgct cttttctta cttttatcct tttaggttgc ctgtaagggg ggtcccatt	1740
gaattacaag tggaatgctt cacatgggac caaaaactct ggtgcogtca cttctgtgtg	1800
cttgggact cagaatctgg tggacatctc actcaactctg ggatgggtggg catgggagtc	1860
agctgcacag ccactcggga agatggaacc agccgcagat agtgataata ggctggagcc	1920
tcggtggcca agcttcttgc ccttgggccc tccccccagc cctctctccc ctctctgca	1980
ccgtaccccc gtygtctttg aataaagtct gagtgggctg caaaaaaaaa aaaaaaaaa	2040
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaa	2100
aaaaaaaaaa aaaaaaaaaa atctag	2126

<210> SEQ ID NO 47

<211> LENGTH: 550

<212> TYPE: PRT

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<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 47

Met Gly Leu Lys Val Asn Val Ser Ala Val Phe Met Ala Val Leu Leu
 1 5 10 15

Thr Leu Gln Thr Pro Ala Gly Gln Ile His Trp Gly Asn Leu Ser Lys
 20 25 30

Ile Gly Val Val Gly Ile Gly Ser Ala Ser Tyr Lys Val Met Thr Arg
 35 40 45

Ser Ser His Gln Ser Leu Val Ile Lys Leu Met Pro Asn Ile Thr Leu
 50 55 60

Leu Asn Asn Cys Thr Arg Val Glu Ile Ala Glu Tyr Arg Arg Leu Leu
 65 70 75 80

Arg Thr Val Leu Glu Pro Ile Arg Asp Ala Leu Asn Ala Met Thr Gln
 85 90 95

Asn Ile Arg Pro Val Gln Ser Val Ala Ser Ser Arg Arg His Lys Arg
 100 105 110

Phe Ala Gly Val Val Leu Ala Gly Ala Ala Leu Gly Val Ala Thr Ala
 115 120 125

Ala Gln Ile Thr Ala Gly Ile Ala Leu His Arg Ser Met Leu Asn Ser
 130 135 140

Gln Ala Ile Asp Asn Leu Arg Ala Ser Leu Glu Thr Thr Asn Gln Ala
 145 150 155 160

Ile Glu Ala Ile Arg Gln Ala Gly Gln Glu Met Ile Leu Ala Val Gln
 165 170 175

Gly Val Gln Asp Tyr Ile Asn Asn Glu Leu Ile Pro Ser Met Asn Gln
 180 185 190

Leu Ser Cys Asp Leu Ile Gly Gln Lys Leu Gly Leu Lys Leu Leu Arg
 195 200 205

Tyr Tyr Thr Glu Ile Leu Ser Leu Phe Gly Pro Ser Leu Arg Asp Pro
 210 215 220

Ile Ser Ala Glu Ile Ser Ile Gln Ala Leu Ser Tyr Ala Leu Gly Gly
 225 230 235 240

Asp Ile Asn Lys Val Leu Glu Lys Leu Gly Tyr Ser Gly Gly Asp Leu
 245 250 255

Leu Gly Ile Leu Glu Ser Arg Gly Ile Lys Ala Arg Ile Thr His Val
 260 265 270

Asp Thr Glu Ser Tyr Phe Ile Val Leu Ser Ile Ala Tyr Pro Thr Leu
 275 280 285

Ser Glu Ile Lys Gly Val Ile Val His Arg Leu Glu Gly Val Ser Tyr
 290 295 300

Asn Ile Gly Ser Gln Glu Trp Tyr Thr Thr Val Pro Lys Tyr Val Ala
 305 310 315 320

Thr Gln Gly Tyr Leu Ile Ser Asn Phe Asp Glu Ser Ser Cys Thr Phe
 325 330 335

Met Pro Glu Gly Thr Val Cys Ser Gln Asn Ala Leu Tyr Pro Met Ser
 340 345 350

Pro Leu Leu Gln Glu Cys Leu Arg Gly Ser Thr Lys Ser Cys Ala Arg
 355 360 365

Thr Leu Val Ser Gly Ser Phe Gly Asn Arg Phe Ile Leu Ser Gln Gly

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370			375			380									
Asn	Leu	Ile	Ala	Asn	Cys	Ala	Ser	Ile	Leu	Cys	Lys	Cys	Tyr	Thr	Thr
385				390						395					400
Gly	Thr	Ile	Ile	Asn	Gln	Asp	Pro	Asp	Lys	Ile	Leu	Thr	Tyr	Ile	Ala
			405						410					415	
Ala	Asp	Arg	Cys	Pro	Val	Val	Glu	Val	Asn	Gly	Val	Thr	Ile	Gln	Val
			420				425						430		
Gly	Ser	Arg	Arg	Tyr	Pro	Asp	Ala	Val	Tyr	Leu	His	Arg	Ile	Asp	Leu
	435					440						445			
Gly	Pro	Pro	Ile	Ser	Leu	Glu	Arg	Leu	Asp	Val	Gly	Thr	Asn	Leu	Gly
	450					455					460				
Asn	Ala	Ile	Ala	Lys	Leu	Glu	Asp	Ala	Lys	Glu	Leu	Leu	Glu	Ser	Ser
465				470						475					480
Asp	Gln	Ile	Leu	Arg	Ser	Met	Lys	Gly	Leu	Ser	Ser	Thr	Ser	Ile	Val
			485						490					495	
Tyr	Ile	Leu	Ile	Ala	Val	Cys	Leu	Gly	Gly	Leu	Ile	Gly	Ile	Pro	Thr
			500					505					510		
Leu	Ile	Cys	Cys	Cys	Arg	Gly	Arg	Cys	Asn	Lys	Lys	Gly	Glu	Gln	Val
		515					520					525			
Gly	Met	Ser	Arg	Pro	Gly	Leu	Lys	Pro	Asp	Leu	Thr	Gly	Thr	Ser	Lys
	530					535					540				
Ser	Tyr	Val	Arg	Ser	Leu										
545				550											

<210> SEQ ID NO 48

<211> LENGTH: 550

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 48

Met	Gly	Leu	Lys	Val	Asn	Val	Ser	Val	Ile	Phe	Met	Ala	Val	Leu	Leu
1				5					10					15	
Thr	Leu	Gln	Thr	Pro	Thr	Gly	Gln	Ile	His	Trp	Gly	Asn	Leu	Ser	Lys
			20					25					30		
Ile	Gly	Val	Val	Gly	Val	Gly	Ser	Ala	Ser	Tyr	Lys	Val	Met	Thr	Arg
		35					40					45			
Ser	Ser	His	Gln	Ser	Leu	Val	Ile	Lys	Leu	Met	Pro	Asn	Ile	Thr	Leu
	50					55					60				
Leu	Asn	Asn	Cys	Thr	Arg	Val	Gly	Ile	Ala	Glu	Tyr	Arg	Arg	Leu	Leu
65					70					75					80
Arg	Thr	Val	Leu	Glu	Pro	Ile	Arg	Asp	Ala	Leu	Asn	Ala	Met	Thr	Gln
				85					90					95	
Asn	Ile	Arg	Pro	Val	Gln	Ser	Val	Ala	Ser	Ser	Arg	Arg	His	Lys	Arg
			100					105						110	
Phe	Ala	Gly	Val	Val	Leu	Ala	Gly	Ala	Ala	Leu	Gly	Val	Ala	Thr	Ala
		115					120					125			
Ala	Gln	Ile	Thr	Ala	Gly	Ile	Ala	Leu	His	Gln	Ser	Met	Leu	Asn	Ser
	130					135					140				
Gln	Ala	Ile	Asp	Asn	Leu	Arg	Ala	Ser	Leu	Glu	Thr	Thr	Asn	Gln	Ala
145				150						155					160
Ile	Glu	Ala	Ile	Arg	Gln	Ala	Gly	Gln	Glu	Met	Ile	Leu	Ala	Val	Gln

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165					170					175					
Gly	Val	Gln	Asp	Tyr	Ile	Asn	Asn	Glu	Leu	Ile	Pro	Ser	Met	Asn	Gln
			180					185					190		
Leu	Ser	Cys	Asp	Leu	Ile	Gly	Gln	Lys	Leu	Gly	Leu	Lys	Leu	Leu	Arg
		195					200					205			
Tyr	Tyr	Thr	Glu	Ile	Leu	Ser	Leu	Phe	Gly	Pro	Ser	Leu	Arg	Asp	Pro
	210					215					220				
Ile	Ser	Ala	Glu	Ile	Ser	Ile	Gln	Ala	Leu	Ser	Tyr	Ala	Leu	Gly	Gly
225						230					235				240
Asp	Ile	Asn	Lys	Val	Leu	Glu	Lys	Leu	Gly	Tyr	Ser	Gly	Gly	Asp	Leu
			245						250					255	
Leu	Gly	Ile	Leu	Glu	Ser	Arg	Gly	Ile	Lys	Ala	Arg	Ile	Thr	His	Val
		260					265						270		
Asp	Thr	Glu	Ser	Tyr	Phe	Ile	Val	Leu	Ser	Ile	Ala	Tyr	Pro	Thr	Leu
		275					280					285			
Ser	Glu	Ile	Lys	Gly	Val	Ile	Val	His	Arg	Leu	Glu	Gly	Val	Ser	Tyr
	290					295					300				
Asn	Ile	Gly	Ser	Gln	Glu	Trp	Tyr	Thr	Thr	Val	Pro	Lys	Tyr	Val	Ala
305				310							315				320
Thr	Gln	Gly	Tyr	Leu	Ile	Ser	Asn	Phe	Asp	Glu	Ser	Ser	Cys	Thr	Phe
			325						330					335	
Met	Pro	Glu	Gly	Thr	Val	Cys	Ser	Gln	Asn	Ala	Leu	Tyr	Pro	Met	Ser
		340						345					350		
Pro	Leu	Leu	Gln	Glu	Cys	Leu	Arg	Gly	Ser	Thr	Lys	Ser	Cys	Ala	Arg
		355					360					365			
Thr	Leu	Val	Ser	Gly	Ser	Phe	Gly	Asn	Arg	Phe	Ile	Leu	Ser	Gln	Gly
	370					375					380				
Asn	Leu	Ile	Ala	Asn	Cys	Ala	Ser	Ile	Leu	Cys	Lys	Cys	Tyr	Thr	Thr
385				390							395				400
Gly	Thr	Ile	Ile	Asn	Gln	Asp	Pro	Asp	Lys	Ile	Leu	Thr	Tyr	Ile	Ala
				405					410					415	
Ala	Asp	His	Cys	Pro	Val	Val	Glu	Val	Asn	Gly	Val	Thr	Ile	Gln	Val
		420					425						430		
Gly	Ser	Arg	Arg	Tyr	Pro	Asp	Ala	Val	Tyr	Leu	His	Arg	Ile	Asp	Leu
		435					440					445			
Gly	Pro	Pro	Ile	Ser	Leu	Glu	Arg	Leu	Asp	Val	Gly	Thr	Asn	Leu	Gly
	450					455					460				
Asn	Ala	Ile	Ala	Lys	Leu	Glu	Asp	Ala	Lys	Glu	Leu	Leu	Glu	Ser	Ser
465				470					475					480	
Asp	Gln	Ile	Leu	Arg	Ser	Met	Lys	Gly	Leu	Ser	Ser	Thr	Ser	Ile	Val
			485						490					495	
Tyr	Ile	Leu	Ile	Ala	Val	Cys	Leu	Gly	Gly	Leu	Ile	Gly	Ile	Pro	Ala
		500						505					510		
Leu	Ile	Cys	Cys	Cys	Arg	Gly	Arg	Cys	Asn	Lys	Lys	Gly	Glu	Gln	Val
		515					520					525			
Gly	Met	Ser	Arg	Pro	Gly	Leu	Lys	Pro	Asp	Leu	Thr	Gly	Thr	Ser	Lys
	530					535					540				
Ser	Tyr	Val	Arg	Ser	Leu										
545				550											

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<211> LENGTH: 617
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 49
Met Ser Pro Gln Arg Asp Arg Ile Asn Ala Phe Tyr Lys Asp Asn Pro
1          5          10          15
Tyr Pro Lys Gly Ser Arg Ile Val Ile Asn Arg Glu His Leu Met Ile
20          25          30
Asp Arg Pro Tyr Val Leu Leu Ala Val Leu Phe Val Met Phe Leu Ser
35          40          45
Leu Ile Gly Leu Leu Ala Ile Ala Gly Ile Arg Leu His Arg Ala Ala
50          55          60
Ile Tyr Thr Ala Glu Ile His Lys Ser Leu Ser Thr Asn Leu Asp Val
65          70          75          80
Thr Asn Ser Ile Glu His Gln Val Lys Asp Val Leu Thr Pro Leu Phe
85          90          95
Lys Ile Ile Gly Asp Glu Val Gly Leu Arg Thr Pro Gln Arg Phe Thr
100         105         110
Asp Leu Val Lys Phe Ile Ser Asp Lys Ile Lys Phe Leu Asn Pro Asp
115         120         125
Arg Glu Tyr Asp Phe Arg Asp Leu Thr Trp Cys Ile Asn Pro Pro Glu
130         135         140
Arg Ile Lys Leu Asp Tyr Asp Gln Tyr Cys Ala Asp Val Ala Ala Glu
145         150         155         160
Glu Leu Met Asn Ala Leu Val Asn Ser Thr Leu Leu Glu Thr Arg Thr
165         170         175
Thr Thr Gln Phe Leu Ala Val Ser Lys Gly Asn Cys Ser Gly Pro Thr
180         185         190
Thr Ile Arg Gly Gln Phe Ser Asn Met Ser Leu Ser Leu Leu Asp Leu
195         200         205
Tyr Leu Gly Arg Gly Tyr Asn Val Ser Ser Ile Val Thr Met Thr Ser
210         215         220
Gln Gly Met Tyr Gly Gly Thr Tyr Leu Val Glu Lys Pro Asn Leu Asn
225         230         235         240
Ser Lys Gly Ser Glu Leu Ser Gln Leu Ser Met Tyr Arg Val Phe Glu
245         250         255
Val Gly Val Ile Arg Asn Pro Gly Leu Gly Ala Pro Val Phe His Met
260         265         270
Thr Asn Tyr Phe Glu Gln Pro Val Ser Asn Gly Leu Gly Asn Cys Met
275         280         285
Val Ala Leu Gly Glu Leu Lys Leu Ala Ala Leu Cys His Gly Asp Asp
290         295         300
Ser Ile Ile Ile Pro Tyr Gln Gly Ser Gly Lys Gly Val Ser Phe Gln
305         310         315         320
Leu Val Lys Leu Gly Val Trp Lys Ser Pro Thr Asp Met Gln Ser Trp
325         330         335
Val Pro Leu Ser Thr Asp Asp Pro Val Val Asp Arg Leu Tyr Leu Ser
340         345         350
Ser His Arg Gly Val Ile Ala Asp Asn Gln Ala Lys Trp Ala Val Pro
355         360         365

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Lys Ile Ile Gly Asp Glu Val Gly Leu Arg Thr Pro Gln Arg Phe Thr
 100 105 110
 Asp Leu Val Lys Phe Ile Ser Asp Lys Ile Lys Phe Leu Asn Pro Asp
 115 120 125
 Arg Glu Tyr Asp Phe Arg Asp Leu Thr Trp Cys Ile Asn Pro Pro Glu
 130 135 140
 Arg Ile Lys Leu Asp Tyr Asp Gln Tyr Cys Ala Asp Val Ala Ala Glu
 145 150 155 160
 Glu Leu Met Asn Ala Leu Val Asn Ser Thr Leu Leu Glu Thr Arg Ala
 165 170 175
 Thr Asn Gln Phe Leu Ala Val Ser Lys Gly Asn Cys Ser Gly Pro Thr
 180 185 190
 Thr Ile Arg Gly Gln Phe Ser Asn Met Ser Leu Ser Leu Leu Asp Leu
 195 200 205
 Tyr Leu Ser Arg Gly Tyr Asn Val Ser Ser Ile Val Thr Met Thr Ser
 210 215 220
 Gln Gly Met Tyr Gly Gly Thr Tyr Leu Val Glu Lys Pro Asn Leu Ser
 225 230 235 240
 Ser Lys Gly Ser Glu Leu Ser Gln Leu Ser Met His Arg Val Phe Glu
 245 250 255
 Val Gly Val Ile Arg Asn Pro Gly Leu Gly Ala Pro Val Phe His Met
 260 265 270
 Thr Asn Tyr Leu Glu Gln Pro Val Ser Asn Asp Phe Ser Asn Cys Met
 275 280 285
 Val Ala Leu Gly Glu Leu Lys Phe Ala Ala Leu Cys His Arg Glu Asp
 290 295 300
 Ser Ile Thr Ile Pro Tyr Gln Gly Ser Gly Lys Gly Val Ser Phe Gln
 305 310 315 320
 Leu Val Lys Leu Gly Val Trp Lys Ser Pro Thr Asp Met Gln Ser Trp
 325 330 335
 Val Pro Leu Ser Thr Asp Asp Pro Val Ile Asp Arg Leu Tyr Leu Ser
 340 345 350
 Ser His Arg Gly Val Ile Ala Asp Asn Gln Ala Lys Trp Ala Val Pro
 355 360 365
 Thr Thr Arg Thr Asp Asp Lys Leu Arg Met Glu Thr Cys Phe Gln Gln
 370 375 380
 Ala Cys Lys Gly Lys Ile Gln Ala Leu Cys Glu Asn Pro Glu Trp Thr
 385 390 395 400
 Pro Leu Lys Asp Asn Arg Ile Pro Ser Tyr Gly Val Leu Ser Val Asp
 405 410 415
 Leu Ser Leu Thr Val Glu Leu Lys Ile Lys Ile Val Ser Gly Phe Gly
 420 425 430
 Pro Leu Ile Thr His Gly Ser Gly Met Asp Leu Tyr Lys Ser Asn His
 435 440 445
 Asn Asn Met Tyr Trp Leu Thr Ile Pro Pro Met Lys Asn Leu Ala Leu
 450 455 460
 Gly Val Ile Asn Thr Leu Glu Trp Ile Pro Arg Phe Lys Val Ser Pro
 465 470 475 480
 Asn Leu Phe Thr Val Pro Ile Lys Glu Ala Gly Glu Asp Cys His Ala
 485 490 495

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Pro	Thr	Tyr	Leu	Pro	Ala	Glu	Val	Asp	Gly	Asp	Val	Lys	Leu	Ser	Ser
			500					505					510		
Asn	Leu	Val	Ile	Leu	Pro	Gly	Gln	Asp	Leu	Gln	Tyr	Val	Leu	Ala	Thr
		515					520					525			
Tyr	Asp	Thr	Ser	Arg	Val	Glu	His	Ala	Val	Val	Tyr	Tyr	Val	Tyr	Ser
	530					535					540				
Pro	Ser	Arg	Ser	Phe	Ser	Tyr	Phe	Tyr	Pro	Phe	Arg	Leu	Pro	Val	Arg
545					550					555					560
Gly	Val	Pro	Ile	Glu	Leu	Gln	Val	Glu	Cys	Phe	Thr	Trp	Asp	Gln	Lys
				565					570					575	
Leu	Trp	Cys	Arg	His	Phe	Cys	Val	Leu	Ala	Asp	Ser	Glu	Ser	Gly	Gly
			580					585					590		
His	Ile	Thr	His	Ser	Gly	Met	Val	Gly	Met	Gly	Val	Ser	Cys	Thr	Ala
		595					600					605			
Thr	Arg	Glu	Asp	Gly	Thr	Ser	Arg	Arg							
		610				615									

<210> SEQ ID NO 51

<211> LENGTH: 1729

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 51

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tcaagctttt ggaccctcgt acagaagcta atacgactca ctatagggaa ataagagaga    60
aaagaagagt aagaagaat ataagagcca ccatggcaca agtcattaat acaaacagcc    120
tgtcgtctgt gaccagaat aacctgaaca aatcccagtc cgcactgggc actgctatcg    180
agcgtttgtc ttccggctct cgtatcaaca gcgcgaaaga cgatgcggca ggacaggcga    240
ttgctaaccg ttttaccgcy aacatcaaag gtctgactca ggcttcccg aacgctaacg    300
acggtatctc cattgcgcag accactgaag gcgcgctgaa cgaatcaac aacaacctgc    360
agcgtgtgcy tgaactggcg gtctcgtcty cgaatggtac taactccag tctgaacctg    420
actccatcca ggctgaaatc acccagcgcc tgaacgaaat cgaccgtgta tccggccaga    480
ctcagttcaa cggcgtgaaa gtccctggcgc aggacaacac cctgaccatc caggttgggtg    540
ccaacgacgg tgaactatc gatattgatt taaaagaat cagctctaaa aactggggac    600
ttgataagct taatgtccaa gatgcctaca ccccgaaaga aactgctgta accgttgata    660
aaactaccta taaaaatggt acagatccta ttacagccca gagcaatact gatatccaaa    720
ctgcaattgg cgggtggtgca accgggggta ctggggctga tacaatattt aaagatggtc    780
aatactatth agatgttaaa ggccgtgctt ctgctgggtg ttataaagcc acttatgatg    840
aaactacaaa gaaagttaat attgatacga ctgataaac tccggtggca actgcggaag    900
ctacagctat tgggggaacy gccactataa cccacaacca aattgctgaa gtaacaaaag    960
aggggtgtga tacgaccaca gttgcggctc aacttgcctc agcaggggtt actggcgccg    1020
ataaggacaa tactagecct gtaaaactat cgtttgagga taaaacggg aaggttattg    1080
atggtggcta tgcagtgaaa atgggcgacg atttctatgc cgtacatat gatgagaaaa    1140
caggtgcaat tactgctaaa accactactt atacagatgg tactggcggtt gctcaactg    1200
gagctgtgaa atttgggtggc gcaaatggta aatctgaagt tgttactgct accgatggta    1260

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agacttactt agcaagcgac cttgacaaac ataacttcag aacaggcggt gagcttaaag 1320
aggttaatac agataagact gaaaacccac tgcagaaaat tgatgctgcc ttggcacagg 1380
ttgatacact tcgttctgac ctgggtgctg ttcagaaccg tttcaactcc getatcacca 1440
acctgggcaa taccgtaaat aacctgtctt ctgccgtag ccgtatcgaa gattccgact 1500
acgcaaccga agtctccaac atgtctcgcg cgcagattct gcagcaggcc ggtacctccg 1560
ttctggcgca ggcgaaccag gttccgcaaa acgtcctctc tttactgcgt tgataatagg 1620
ctggagcctc ggtggccatg cttcttgcct cttgggcctc cccccagccc ctctccct 1680
tcctgcaccc gtaccccctt ggtctttgaa taaagtctga gtgggcggc 1729

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<210> SEQ ID NO 52

<211> LENGTH: 1518

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 52

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atggcacaag tcattaatac aaacagcctg tcgctgttga cccagaataa cctgaacaaa 60
tcccagtcag cactgggcaac tgetatogag cgtttgtctt ccggtctgcg tatcaacagc 120
gcgaaagacg atgcggcagg acaggcgatt gctaacctgt ttaccggcaa catcaaaagg 180
ctgaetcagg cttcccgtaa cgttaacgac ggtatctcca ttgcgcagac caetgaaggc 240
gcgctgaacg aaatcaacaa caacctgcag cgtgtgcgtg aactggcggt tcagtctgcg 300
aatggtacta actcccagtc tgacctgac tccatccagg ctgaaatcac ccagcgcctg 360
aacgaaatcg accgtgtatc cggccagact cagttcaacg gcgtgaaagt cctggcgagc 420
gacaacaccc tgaccatcca ggttgggtgc aacgaoggtg aaactatcga tattgattta 480
aaagaatca gctctaaac actgggactt gataagctta atgtccaaga tgcctacacc 540
ccgaaagaaa ctgctgtaac cgttgataaa actacctata aaaatggtac agatcctatt 600
acagcccaga gcaatactga tatccaaact gcaattggcg gtggtgcaac gggggttact 660
ggggctgata tcaaatltaa agatggtaa tactatlttag atgttaaagg cgggtgcttct 720
gctggtgttt ataagccac ttatgatgaa actacaaaga aagttaatat tgatacgact 780
gataaaaactc cgttggcaac tgcggaagct acagctatcc ggggaacggc cactataacc 840
cacaacccaa ttgctgaagt aacaaaagag ggtgttgata cgaccacagt tgcggctcaa 900
cttctgcagc caggggttac tggcgcgat aaggacaata ctagccttgt aaaaactatcg 960
tttgaggata aaaacggtaa ggttattgat ggtggctatg cagtgaaaat gggcgacgat 1020
ttctatgccc ctacatatga tgagaaaaca ggtgcaatta ctgctaaaac cactacttat 1080
acagatggta ctggcgttgc tcaaacgga gctgtgaaat ttggtggcgc aaatggtaaa 1140
tctgaagttg ttactgtac cgatggtaag acttacttag caagcgacct tgacaaacat 1200
aaacttcagaa caggcgggtg gcttaagag gttataacag ataagactga aaaccactg 1260
cagaaaattg atgctgcctt ggcacaggtt gatacacttc gttctgacct gggctcggtt 1320
cagaaccgtt tcaactccgc taccaccaac ctgggcaata ccgtaataaa cctgtcttct 1380
gcccgtagcc gtatcgaaaga ttcogactac gcaaccgaag tctccaacat gtctcgcgcg 1440
cagattctgc agcagggcgg tacctccgtt ctggcgcagg cgaaccaggt tccgcaaac 1500

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-continued

 gtctctctctt tactgctt 1518

<210> SEQ ID NO 53

<211> LENGTH: 1790

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 53

ggggaaauaa gagagaaaag aagaguaaga agaaauuaa gagccaccu ggcacaaguc 60
 auuaauacaa acagccuguc gcuguugacc cagaauaac ugaacaauc ccaguccgca 120
 cugggcacug cuaucgagcg uuugucucc ggucugcgua ucaacagcgc gaaagacgau 180
 ggggcaggac agggcauugc uaaccguuuu accgcgaaca ucaaggguu gacucaggcu 240
 ucccguaacg cuaacgacgg uaucuccauu gcgcagacca cugaaggcgc gcugaacgaa 300
 aucaacaaca accugcagcg ugugcgugaa cuggcgguuc agucugcgaa ugguacuaac 360
 ucccagucug accucgacuc cauccaggcu gaaauacccc agcgcugaa cgaauucgac 420
 cguguaucgg gccagacuca guucaacggc gugaagucc uggcgcagga caacaccucg 480
 accauccagg uuggugccaa cgcgcgugaa acuaucgaa uugauuaaa agaaucagc 540
 ucuaaaacac ugggacuuga uaagcuuaau guccaagau ccaaccccc gaaagaaacu 600
 gcuguaaccg uugauaaaac uaccuaaaa aaugguacag auccuauuac agcccagagc 660
 aaucugaua uccaaacugc aaugggggu ggugcaaccg ggguuacugg ggcugauauc 720
 aaaaaaaag auggucaaua cuuuuagau guuaaaggcg gugcuucugc ugguguuuu 780
 aaagccacu augaugaac uacaaagaaa guuaauuug auacgacuga uaaaacuccg 840
 uggcaacug cggagcuaac agcuauucgg ggaacggcca cuuaaccca caaccuuuu 900
 gcugaaguaa caaaagaggg uguugauacg accacaguug cggcucaacu ugcugcagca 960
 gggguuacug gcgcccguua ggacaauacu agccuuguaa aacuaucguu ugaggauaaa 1020
 aacgguaag uuuuugaugg uggcuauagc gugaauaugg gcgacgauu cuaugccgcu 1080
 acuaugaug agaaaacagg ugcauuuacu gcuaaaacca cuacuuauc agaugguacu 1140
 ggcguugcuc aaacugcagc ugugaauuu gguggcgcaa augguaauc ugaaguuuu 1200
 acugcuaccg augguagac uuacuuagca agcgaaccuug acaaaauaa cuucagaaca 1260
 ggcggugagc uuaaagaggu uaauacagau aagacugaaa acccacugca gaaaauugau 1320
 gcugccuugg cacaggguua uacacuucgu ucugaccugg gucggguuca gaaccguuu 1380
 aacuccgcu uacccaaccu gggcaauacc guaaaaaac ugcuuucugc ccguagccgu 1440
 aucgaagauu ccgacuacgc aaccgaaguc uccaacauu cucgcgcgca gauucugcag 1500
 caggccggua ccuccguucu ggcgcaggcg aaccaggguu cgcaaaacgu ccucucuuu 1560
 cugcgugau aauaggcugg agccucggug gccaugcuu uugcccuug ggcuccccc 1620
 cagccccucc uccccuuccu gcacccguac ccccggguc uuugaauaaa gucugagugg 1680
 gcggcaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1740
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaucua 1790

<210> SEQ ID NO 54

<211> LENGTH: 506

<212> TYPE: PRT

-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 54

Met Ala Gln Val Ile Asn Thr Asn Ser Leu Ser Leu Leu Thr Gln Asn
 1 5 10 15

Asn Leu Asn Lys Ser Gln Ser Ala Leu Gly Thr Ala Ile Glu Arg Leu
 20 25 30

Ser Ser Gly Leu Arg Ile Asn Ser Ala Lys Asp Asp Ala Ala Gly Gln
 35 40 45

Ala Ile Ala Asn Arg Phe Thr Ala Asn Ile Lys Gly Leu Thr Gln Ala
 50 55 60

Ser Arg Asn Ala Asn Asp Gly Ile Ser Ile Ala Gln Thr Thr Glu Gly
 65 70 75 80

Ala Leu Asn Glu Ile Asn Asn Asn Leu Gln Arg Val Arg Glu Leu Ala
 85 90 95

Val Gln Ser Ala Asn Gly Thr Asn Ser Gln Ser Asp Leu Asp Ser Ile
 100 105 110

Gln Ala Glu Ile Thr Gln Arg Leu Asn Glu Ile Asp Arg Val Ser Gly
 115 120 125

Gln Thr Gln Phe Asn Gly Val Lys Val Leu Ala Gln Asp Asn Thr Leu
 130 135 140

Thr Ile Gln Val Gly Ala Asn Asp Gly Glu Thr Ile Asp Ile Asp Leu
 145 150 155 160

Lys Glu Ile Ser Ser Lys Thr Leu Gly Leu Asp Lys Leu Asn Val Gln
 165 170 175

Asp Ala Tyr Thr Pro Lys Glu Thr Ala Val Thr Val Asp Lys Thr Thr
 180 185 190

Tyr Lys Asn Gly Thr Asp Pro Ile Thr Ala Gln Ser Asn Thr Asp Ile
 195 200 205

Gln Thr Ala Ile Gly Gly Gly Ala Thr Gly Val Thr Gly Ala Asp Ile
 210 215 220

Lys Phe Lys Asp Gly Gln Tyr Tyr Leu Asp Val Lys Gly Gly Ala Ser
 225 230 235 240

Ala Gly Val Tyr Lys Ala Thr Tyr Asp Glu Thr Thr Lys Lys Val Asn
 245 250 255

Ile Asp Thr Thr Asp Lys Thr Pro Leu Ala Thr Ala Glu Ala Thr Ala
 260 265 270

Ile Arg Gly Thr Ala Thr Ile Thr His Asn Gln Ile Ala Glu Val Thr
 275 280 285

Lys Glu Gly Val Asp Thr Thr Thr Val Ala Ala Gln Leu Ala Ala Ala
 290 295 300

Gly Val Thr Gly Ala Asp Lys Asp Asn Thr Ser Leu Val Lys Leu Ser
 305 310 315 320

Phe Glu Asp Lys Asn Gly Lys Val Ile Asp Gly Gly Tyr Ala Val Lys
 325 330 335

Met Gly Asp Asp Phe Tyr Ala Ala Thr Tyr Asp Glu Lys Thr Gly Ala
 340 345 350

Ile Thr Ala Lys Thr Thr Thr Tyr Thr Asp Gly Thr Gly Val Ala Gln
 355 360 365

Thr Gly Ala Val Lys Phe Gly Gly Ala Asn Gly Lys Ser Glu Val Val

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Gln Thr Thr Glu Gly Ala Leu Asn Glu Ile Asn Asn Asn Leu Gln Arg
 275 280 285
 Val Arg Glu Leu Ala Val Gln Ser Ala Asn Ser Thr Asn Ser Gln Ser
 290 295 300
 Asp Leu Asp Ser Ile Gln Ala Glu Ile Thr Gln Arg Leu Asn Glu Ile
 305 310 315 320
 Asp Arg Val Ser Gly Gln Thr Gln Phe Asn Gly Val Lys Val Leu Ala
 325 330 335
 Gln Asp Asn Thr Leu Thr Ile Gln Val Gly Ala Asn Asp Gly Glu Thr
 340 345 350
 Ile Asp Ile Asp Leu Lys Gln Ile Asn Ser Gln Thr Leu Gly Leu Asp
 355 360 365
 Thr Leu Asn Val Gln Gln Lys Tyr Lys Val Ser Asp Thr Ala Ala Thr
 370 375 380
 Val Thr Gly Tyr Ala Asp Thr Thr Ile Ala Leu Asp Asn Ser Thr Phe
 385 390 395 400
 Lys Ala Ser Ala Thr Gly Leu Gly Gly Thr Asp Gln Lys Ile Asp Gly
 405 410 415
 Asp Leu Lys Phe Asp Asp Thr Thr Gly Lys Tyr Tyr Ala Lys Val Thr
 420 425 430
 Val Thr Gly Gly Thr Gly Lys Asp Gly Tyr Tyr Glu Val Ser Val Asp
 435 440 445
 Lys Thr Asn Gly Glu Val Thr Leu Ala Gly Gly Ala Thr Ser Pro Leu
 450 455 460
 Thr Gly Gly Leu Pro Ala Thr Ala Thr Glu Asp Val Lys Asn Val Gln
 465 470 475 480
 Val Ala Asn Ala Asp Leu Thr Glu Ala Lys Ala Ala Leu Thr Ala Ala
 485 490 495
 Gly Val Thr Gly Thr Ala Ser Val Val Lys Met Ser Tyr Thr Asp Asn
 500 505 510
 Asn Gly Lys Thr Ile Asp Gly Gly Leu Ala Val Lys Val Gly Asp Asp
 515 520 525
 Tyr Tyr Ser Ala Thr Gln Asn Lys Asp Gly Ser Ile Ser Ile Asn Thr
 530 535 540
 Thr Lys Tyr Thr Ala Asp Asp Gly Thr Ser Lys Thr Ala Leu Asn Lys
 545 550 555 560
 Leu Gly Gly Ala Asp Gly Lys Thr Glu Val Val Ser Ile Gly Gly Lys
 565 570 575
 Thr Tyr Ala Ala Ser Lys Ala Glu Gly His Asn Phe Lys Ala Gln Pro
 580 585 590
 Asp Leu Ala Glu Ala Ala Ala Thr Thr Thr Glu Asn Pro Leu Gln Lys
 595 600 605
 Ile Asp Ala Ala Leu Ala Gln Val Asp Thr Leu Arg Ser Asp Leu Gly
 610 615 620
 Ala Val Gln Asn Arg Phe Asn Ser Ala Ile Thr Asn Leu Gly Asn Thr
 625 630 635 640
 Val Asn Asn Leu Thr Ser Ala Arg Ser Arg Ile Glu Asp Ser Asp Tyr
 645 650 655
 Ala Thr Glu Val Ser Asn Met Ser Arg Ala Gln Ile Leu Gln Gln Ala
 660 665 670

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Gly	Thr	Ser	Val	Leu	Ala	Gln	Ala	Asn	Gln	Val	Pro	Gln	Asn	Val	Leu
		675					680					685			
Ser	Leu	Leu	Arg												
		690													

<210> SEQ ID NO 57
 <211> LENGTH: 1620
 <212> TYPE: RNA
 <213> ORGANISM: Human metapneumovirus

<400> SEQUENCE: 57

augagcugga aggguggugau uaucuucagc cugcugauua caccucaaca cggccugaag	60
gagagcuacc uggaagagag cugcuuccacc aucaccgagg gcuaaccugag cgugcugcgg	120
accggcuggu acaccaacgu guucacccug gagguggggcg acguggagaa ccugaccugc	180
agcgacggcc cuagccugau caagaccgag cuggaccuga ccaagagcgc ucugagagag	240
cugaagaccg uguccgcga ccagcuggcc agagaggaac agaucgagaa ccucggcag	300
agcagauucg ugcuggggcg caucgcucug ggagucggcg cugccgcugc agugacagcu	360
ggaguggcca uugcuaagac caucagacug gaaagcgagg ugacagccau caacaaugcc	420
cugaagaaga ccaacgaggc cgugagcacc cugggcaaug gagugagagu gcuggccaca	480
gcccugcggg agcugaagga cuucgugagc aagaaccuga ccagagccau caacaagaa	540
aagugcgaca ucgauaccu gaagauggcc gugagcuuc cccaguucac cagacgguuc	600
cugaacgugg ugagacaguu cuccgacaac gcuggaauca caccugccau uagccuggac	660
cugaugaccg accccgagcu ggcuaagacc guggccaaca ugcccaccag cgcuggccag	720
aucaagcuga ugcuggagaa cagagccaug guggggagaa agggcuucgg cauccugauu	780
gggguguaug gaagcuccgu gaucuacaug gugcagcugc ccaucucygy cuguaucyag	840
acaccucgcu ggauccugaa ggcgcucuu agcugcuccg agaagaaagg aaacuaugcc	900
ugucugcuga gagaggacca gggcugguac ugccagaacg ccggaagcac aguguaucuu	960
ccccaacgaga aggacugcga gaccagaggc gaccaagugu ucugcgacac cgcugccgga	1020
aucaacgugg ccgagcagag caaggagugc aacaucaca ucagcacac caacuacccc	1080
ugcaagguga gcaccgagc gcaccccac agcauggugg cucugagccc ucuggggcgu	1140
cugguggccu gcuaaaaggg cguguccgu agcaucggca gcaaucgggu gggcaucauc	1200
aagcagcuga acaagggau gcucaacauc accaacagc acgcccagac cgugaccauc	1260
gacaacaccg uguaccagcu gagcaaggug gaggggcagc agcacgugau caagggcaga	1320
cccugagcgu ccagcuucga ccccaucaag ucccugagg accaguucaa cguggcccug	1380
gaccaggugu uugagaacau cgagaacagc caggcccugg uggaccagag caacagaau	1440
cuguccagcg cugagaaggg caacaccggc uucaucauug ugaucuuuc gaucgccgug	1500
cugggcagcu ccaugauccu ggugagcauc uucaucaua ucaagaagac caagaaacc	1560
accggagccc cuccugagcu gagcggcgug accaacaau gcuucauucc ccacaacuga	1620

<210> SEQ ID NO 58
 <211> LENGTH: 1620
 <212> TYPE: RNA
 <213> ORGANISM: Human metapneumovirus

<400> SEQUENCE: 58

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augucuuugga aagugaugau caucuuuucg uuacucauaa caccuccagca cgggcuaaaag 60
gagaguuuuuu uggaagaauuc auguaguacu auaacugagg gauaccucag uguuuuaaga 120
acaggcuggu acacuaaangu cuucacauua gaaguuggug auguugaaaa ucuuacaugu 180
acugauggac cuagcuuaau caaaacagaa cuugaucuaa caaaaagugc uuuuagggaa 240
cucaaaacag ucucugcuga ucaguuggcg agagaggagc aaauugaaaa ucccagacaa 300
ucaagauuug ucuuaggugc gauagcucuc ggaguugcua cagcagcagc agucacagca 360
ggcauugcaa uagccaaaac cauaggcuu gagagugagg ugaauucau uaaaggugcu 420
cucaaacaaa cuaauagauc aguauccaca uuagggaug gugugcgggu ccuagccacu 480
gcagugagag agcuaaaaga auuugugagc aaaaaccuga cuagugcau caacaggaac 540
aaauugaca uugcugaucu gaagauggcu gucagcuuca gucauuuca cagaagauuu 600
cuaaaugug ugcggcaguu uucagacaau gcagggaaua caccagcau aucuuggac 660
cugaugacug augcugaguu ggcagagcu guaucuaca ugccaacauc ugcaggcag 720
auaaaacuga uguuggagaa ccgcccuaug guaaaggagaa aaggauuugg aaucugaua 780
ggggucucag gaagcucugu gauuuacau gguaauugc cgauuuuug ugucauagau 840
acaccuuguu ggaucauca ggcagucucc ucuugcucag aaaaaaacgg gaauuauugc 900
ugccuccuaa gagaggauca agggugguau uguaaaaaug caggaucuac uguuuacuac 960
ccaaaugaaa aagacucgca aacaagaggu gaucauguuu uuugugacac agcagcaggg 1020
aucaauugug cugagcauuc aagagaauuc aacaucaaca uaucuacuac caacuacca 1080
ugcaauuga gcacaggaag acaccuuaa agcaugguug cacuauacc ucucggugcu 1140
uugguggcuu gcuuaaaagg gguuagcuc ucgaauuggca gcaauugggu uggaucauc 1200
aaacaauuac ccaaaaggcug cucauacua accaacagg augcagacac uguuacaauu 1260
gacauuaccg uguaucaacu aagcaaguu gaaggugaac agcauguaa aaaagggaga 1320
ccaguuucaa gcaguuuuga uccaaucaag uuuccugagg aucaguucua uguugcgcuu 1380
gaucaaugcu ucgaaagcau ugagaacagu caggcacuag uggaccaguc aaacaaaauu 1440
cuaaacagug cagaaaaagg aaacacuggu uucauuuucg uaguauuuuu gguugcuguu 1500
cuuggucuaa ccaugauuuc agugagcauc aucaucaua ucaagaaaac aaggaagccc 1560
acaggagcac cuccagagcu gaauuggugc accaacggcg guuucuuacc acauaguua 1620

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<210> SEQ ID NO 59

<211> LENGTH: 1620

<212> TYPE: RNA

<213> ORGANISM: Human metapneumovirus

<400> SEQUENCE: 59

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augucuuugga aagugaugau uaucuuuucg uuacucauaa caccucagca uggacuaaaa 60
gaaaguuuuuu uagaagaauuc auguaguacu auaacugaag gauaucucag uguuuuaaga 120
acaggauuggu acccaangu cuuucacaua gaaguuggug auguugaaaa ucuuacaugu 180
acugauggac cuagcuuaau caaaacagaa cuugaccuaa ccaaaaagugc uuuuagagaa 240
cucaaaacag uuucugcuga ucaguuagcg agagaagaac aaauugaaaa ucccagacaa 300
ucaagguuug uccuaggugc auuagcucuu ggaguugcca cagcagcagc agucacagca 360
ggcauugcaa uagccaaaac uauaggcuu gagagugaag ugaauucau caaaggugcu 420

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cucaaaacaa ccaaugagge aguaucaaca cuaggaaaug gagugcgggu ccuagccacu	480
gcaguaagag agcugaaaga auuugugagc aaaaaccuga cuagugcgau caacaagaac	540
aagugugaca uugcugauuu gaagauggcu gucagcuca gucaguuca cagaagaau	600
cuaaauguug ugcggcaguu uucagacaau gcagggaua caccagcau aucauuggac	660
cugaugaau augcugagcu ggcagagcu guaucuaca ugccaacac ucagagacag	720
auaaaacuaa uguuagagaa ccgugcaaug gugaggagaa aaggauuugg aaucugaua	780
gggugucacg gaagcucugu gauuuacaug guccagcugc cgauuuuugg ugucauaaa	840
acaccuuguu ggauaaucua ggcagcuccc ucuuguucag aaaaagaugg aaauuugcu	900
ugccuccuaa gagaggauca agggugguau uguaaaaaug caggauccac uguuuacua	960
ccaaaugaaa aagacugcga aacaaagaggu gaucauguuu uuugugacac agcagcagg	1020
aucaauguug cugagcauc aagagaaugc aacaucaca uaucuaccac caacuacca	1080
ugcaauguca gcacaggaag acaccuauc agcaugguug cacuaucac ucucggugcu	1140
uugguagcuu gcuacaaagg gguuagcugc ucgacuggca guauucaggu uggaauaau	1200
aaacaacua cuaaaggcug cucauacua acuaaccagg acgcagacac uguacaauu	1260
gacaacacug uguaucaacu aagcaaugu gagggugaac agcauguaua aaaagggaga	1320
ccaguuucaa gcaguuuuga uccaaucagg uuucugagg aucaguucua uguugcguu	1380
gaucaagucu uugaaagcau ugaaaacagu caagcacuag uggaccaguc aaacaaaau	1440
cugaacagug cagaaaaagg aaacacuggu uucauuuug uaauuuuuu gauugcuguu	1500
cuuggguuaa ccaugauuuc agugagcauc aucaucaua ucaaaaaac aaggaagccc	1560
acaggggac cuccggagcu gaauugguu accaacggcg guuucuauc gcauaguua	1620

<210> SEQ ID NO 60

<211> LENGTH: 1725

<212> TYPE: RNA

<213> ORGANISM: Human respiratory syncytial virus

<400> SEQUENCE: 60

auggaguugc caauccuaa aacaaugca auuaccaca uccuugcugc agucacacuc	60
uguuucgcuu ccagucaaaa caucacugaa gaauuuuauc aaucacaug cagugcaguu	120
agcaaaaggcu aucuuaguc ucuaagaacu gguugguaua cuaguguuuu aacuaagaa	180
uuaguuaua ucaaggaaaa uaaguguauu ggaacagau cuaagguaaa auugauaaaa	240
caagaauuag auaaaauaa aaauugcugua acagaauugc aguugcucua gcaaaagcaca	300
ccagcagcca acaaucgagc cagaagagaa cuaccaaggu uuugaauua uacacuaau	360
aaucacaaa auaccuauu aacauuaagc aagaaaagga aaagaagau ucuugcuuu	420
uuguuaggug uuggaucugc aaucgccagu ggcuuugcug uaucuaaggu ccugcaccua	480
gaaggggaag ugaacaaaau caaaagugcu cuacuaucca caaacaaaggc uguagucagc	540
uuaucaauug gaguuagugu cuuaaccagc aaaguguuag accucaaaaa cuauauagau	600
aaacaguugu uaccuauuug gaacaagcaa agcugcagca uaucaacau ugaaacugug	660
auagaguucc aacaaaagaa caacagacua cuagagauua ccagggaauu uaguguuau	720
gcagguguaa cuacaccugu aagcacuuu auguuacua auagugaauu auuacauua	780
aucaauguaa ugccuauaac aaauagucag aaaaaguuaa uguccaaca uguucaaua	840

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guuagacagc	aaaguacuc	uaucaugucc	auaauaaagg	aggaagucuu	agcauaugua	900
guacaauuac	cacuauaugg	uguauuagau	acaccucguu	ggaacucgca	cacauccccu	960
cuauguacaa	ccaacacaaa	ggaagggucc	aacaucugcu	uaacaagaac	cgacagagga	1020
ugguauugug	acaauagcagg	aucaguaucu	uucuucccac	aagcugaaac	auguaaaguu	1080
caaucgauc	ggguuuuuug	ugacacaaug	aacaguuuaa	cauuaccaag	ugaaguaaa	1140
cucugcaaca	uugacauuu	caaccccaaa	uaugauugca	aaauuugac	uucaaaaaca	1200
gauguaagca	gcuccguuau	cacaucucua	ggagccauug	ugucaugcua	uggcaaaacu	1260
aaauguacag	cauccaauaa	aaaucguggg	aucauaaaga	cauuuucuaa	cgggugugau	1320
uauguaucaa	auaagggggg	ggauacugug	ucuguaggua	auacauuaa	uuauguaaa	1380
aagcaagaag	gcaaaagucu	cuauguaaaa	ggugaaccaa	uaauaaaauu	cuauagacca	1440
uuaguguucc	ccucugauga	auuugaugca	ucauuauuc	aagucaauga	gaaguuuac	1500
cagagccuag	cauuuuuucg	uaauucogau	gaauuuuac	auaauguaaa	ugcugguaaa	1560
uccaccacaa	auaucaugau	aacuacuua	auuuuaguga	uuauaguau	auuguuuaca	1620
uuauuugcag	uuggacugcu	ccuauacugc	aaggccagaa	gcacaccagu	cacacuaagu	1680
aaggaucaac	ugagugguau	aaauuuuuu	gcauuuagua	acuga		1725

<210> SEQ ID NO 61

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Human parainfluenza virus

<400> SEQUENCE: 61

augccaauuu	cauacuguu	auuuuuaca	accaugauca	uggcaucaca	cugccaaaua	60
gacaucacaa	aacuacagca	uguaggugua	uuggucaaca	gucccaaaag	gaugaagaua	120
ucacaaaaacu	ucgaaacaag	auaucuaauc	cugagucuca	uaccaaaaa	agaagauucu	180
aacucuuug	gugaccaaca	gaucaagcaa	uacaagaggu	uuuuggauag	acugaucauu	240
ccuuuuauug	auggacuaag	auuacagaag	gaugugauag	ugacuaauca	agaauccaau	300
gaaaacacug	aucccagaac	agaacgauuc	uuuggagggg	uuuuggaac	uuugcucua	360
ggaguagcaa	ccucagcaca	auuacagca	gcaguugcuc	ugguuugaagc	caagcaggca	420
agaucagaca	uugaaaaacu	caagggaagca	aucagggaca	caauuuuagc	agugcaguca	480
guucagagcu	cuguaggaaa	uuugauagua	gcauuuuuu	caguccagga	uuauucaac	540
aaagaaauug	ugccaucgau	ugcgagacua	gguuugaaag	cagcaggacu	ucaguuaagg	600
auugcauuua	cacagcauu	cucagaauua	acaaauuuu	uuggugauaa	cauaggauug	660
uuacaagaaa	aaggaaauaa	auuacaaggu	auagcaucau	uuuaccguac	aaauaucaca	720
gaaauuuuca	caacaucaac	aguugacaaa	uauuuuuuu	augaucuuuu	auuuacagaa	780
ucauuuuagg	ugagaguuuu	agauguugau	uugaauugau	acucauuuac	ccuccaaguc	840
agacucccuu	uuuugaccag	acugcugaac	acucauuuu	acaaaguaga	uuccauuca	900
uacaauuucc	aaaauagaga	augguauuuc	ccucuuucca	gccauuucuu	gacgaaagg	960
gcauuuucua	guggagcaga	ugucaaagaa	ugcauagaag	cauucagcag	uuuuuuuugc	1020
ccuucugauc	caggauuuug	acuuuacuu	gaaauuggaga	gcugucuauc	aggaaacaua	1080
ucccaauguc	caagaaccac	agucacauca	gacauuuguc	cuagguaugc	uuuuuucuuu	1140

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auccgaaaca aaacacucuc agcuggguac acaacaacaa gcugcauuac acacuauaac 1620
aaaggguauu guuuucuuu aguagaaaua aaucuaaaa gcuuaaacac auuucaaccc 1680
auguuguuca aaacagagau uccaaaaagc ugcagu 1716

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<210> SEQ ID NO 63
<211> LENGTH: 1716
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

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<400> SEQUENCE: 63

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auggaauacu ggaagcacac caaccacggc aaggacgccc gcaacgagcu ggaaccagc 60
acagccacac acggcaacaa gcugaccaac aagaucaccu acauccugug gaccuaccc 120
cuggugcugc ugagcaucgu guucaucauc gugcugacca auagcauca gagcgagaag 180
gccagagaga gccugcugca ggacaucac aacgaguuca uggaagugac cgagaagau 240
cagguggcca gcgacaacac caacgaccug auccagagcg gcgugaacac ccggcugcug 300
accauccaga gccacgugca gaacuacac cccaucagcc ugacccagca gaucagcgac 360
cugcggaagu ucaucagcga gaucaccauc cggaaacgaca accaggaagu gccccccag 420
agaauacccc acgacguggg caucaagccc cugaaacccc acgauuuucg gcgguguaca 480
agcggccugc ccagccugau gaagaccccc aagaucggc ugauccugg ccucggacug 540
cuggccaucg cuaccacagu ggauuggcugu guggggccc ccagccucgu gaurcaagau 600
cugaucuacg ccuacaccag caaccugauc acccggggcu gccaggauau cggcaagagc 660
uaccaggugc ugcagaucgg caucaucacc gugaacuccg accuggugcc cgaccugaac 720
ccucggauca gccacaccuu caacaucaac gacaacagaa agagcugcag ccuggcucug 780
cugaacaccg acguguaacca gcugugcagc acccccagg uggaacgagag aagcgacua 840
gccagcagcg gcaucgagga uaucgugcug gacaucguga acuaacgagg cagcaucagc 900
accaccccgu ucaagaacaa caacaucagc uucgaaccag ccuacgccc ccuguaaccu 960
ucugugggcc cuggcaucua cuacaagggc aagaucucu uccugggcu cggcgccug 1020
gaacacccc ucaacgagaa cgcacucugc aacaccaccg gcugcccug caagaccag 1080
agagacugca aucaggccag ccacagcccc ugguucagcg accgcagaau ggucaacucu 1140
aucaucuggg uggacaaggc ccugaacagc guggccaagc ugaagugug gacaaucagc 1200
augcgcaga acuaucgggg cagcgagggc agacuucugc ugucgggaaa caagaucua 1260
aucuacaccc gguccaccag cuggcacagc aaacugcagc ugggaaucua cgacaucac 1320
gacuacagcg acaucggau caaguggacc uggacaacg ucugagcag acccgcaac 1380
aaugagugcc cuuggggcca cagcugcccc gauggaugua ucaccggcgu guacaccgac 1440
gccuaccccc ugaauccuac cggcuccauc guggccagcg ugaucugga cagccagaaa 1500
agcagaguga accccugau cacauacagc accgccaccg agagagugaa cgaacuggcc 1560
aucagaaaca agaccucgag cgcgggcuac accaccacaa gcugcaucac acacuacaac 1620
aaggguacu gcuuccacau cguggaaauc aaccacaagu ccugaacac cuuccagccc 1680
augcuguuca agaccagau ccccaagagc ugcucc 1716

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<210> SEQ ID NO 64

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<211> LENGTH: 1617
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 64
augcccauca gcauccugcu gaucaucacc acaaugauca uggccagcca cugccagauc    60
gacaucacca agcugcagca cgugggcgug cucgugaaca gcccgaagg caugaagauc    120
agccagaacu ucgagacacg cuaccugauc cugagccuga ucccgaagau cgaggacagc    180
aacagcugcg gcgaccagca gaucaagcag uacaagcggc ugcuggacag acugaucauc    240
ccccguacg acggccugcg gcugcagaaa gacgugaucg ugaccaacca ggaagcaac    300
gagaacaccg acccccggac cgagagauuc uucggcggcg ugaucggcac aaucgcccug    360
ggaguggcca caagcggcca gauuacagcc gcuguggccc ugguggaagc caagcaggcc    420
agaagcgaca ucgagaagcu gaaagaggcc auccgggaca ccaacaagge cgugcagagc    480
gugcagucca gcgugggcaa ucugaucgug gccaucaagu ccgugcagga cuacgugaac    540
aaagaaaucg ugcccucua ugcggcgug ggcugugaag cugccggacu gcagcugggc    600
auugcccuga cacagcaua cagcgagcug accaacaucu ucggcgaca caucggcagc    660
cugcaggaaa agggcauuua gcugcagggc aucgcccggc uguaccgac caacaucacc    720
gagaucuuca ccaccagcac cguggauaag uacgacaucu acgaccugcu guuaccggag    780
agcaucaaa agcgcgugau cgauguggac cugaacgacu acagcauac ccugcaagug    840
cggcugcccc ugcugaccag acugcugaac acccagaucu acaaggugga cagcaucucc    900
uacaacauc agaacccga gugguacauc ccucugccc gccacauuu gaccaagggc    960
gccuuucug gcgagccga cgugaagag ugcaucgagg ccuucagcag cuacaucugc    1020
cccagcgacc cuggcuucgu gcugaaccac gagauggaaa gcugccugag cggcaacauc    1080
agccagugcc ccagaaccac cgugaccucc gacaucgugc ccagauacgc cuucgugaau    1140
ggcggcgugg uggccaacug caucaccacc acccuguaccu gcaacggcau cggcaaccgg    1200
aucaaccagc cucccgauca gggcgugaag auuauacccc acaagagug uaacaccauc    1260
ggcaucaacg gcaugcuguu caauaccaac aaagagggca ccugggccuu cuacccccc    1320
gacgauauca ccugaacaa cuccguggcu cuggacccca ucgacaucuc caucgagcug    1380
aacaaggcca agagcgaccu ggaagagucc aaagagugga uccggcggag caaccagaag    1440
cuggacucua ucggcagcug gcaccagagc agcaccacca ucaucgugau ccugauuau    1500
augauuuacc uguucaucau caacaauacc aucaucacua ucgccauuaa guacuaccgg    1560
auccagaaac ggaaccgggu ggaccagaau gacaagcccu acgugcugac aaacaag    1617

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<210> SEQ ID NO 65
<211> LENGTH: 4062
<212> TYPE: RNA
<213> ORGANISM: Middle East respiratory syndrome coronavirus

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<400> SEQUENCE: 65
augauacacu caguguuucu acugauguuc uuguuaacac cuacagaaag uuacguugau    60
guagggccag auucuguuua gucugcuugu auugagguug auauacaaca gaccuucuuu    120
gauaaaaacu ggccuaggcc aaauauguu ucuaaggcug acggauuuau auaccucaa    180

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ggccguacau auucuaacau aacuaucacu uaucaagguc uuuuucccua ucagggagac	240
cauggugaua uguauguuua cucugcagga caugcuacag gcacaacucc aaaaaaguug	300
uuuguagcua acuaaucuca ggacgucaaa caguuuagcua auggguuugu cguccguaua	360
ggagcagcug ccaauuccac uggeacuguu auuuuuagcc caucuccag cgcuacuua	420
cgaaaauuu acccugcuuu uaugcugggu ucuucaguug guaaaaucuc agaugguaaa	480
augggccgcu ucuucaauca uacucuaguu cuuuugcccg auggaugugg cacuuuacuu	540
agagcuuuuu auuguauucu agagccucgc ucuggaauc auuguccugc uggeaauc	600
uauacuucu uugccacuua ucacacuccu gcaacagauu guucugaugg caauuacau	660
cgaaaugcca gucugaacuc uuuuaaggag uauuuuaau uacguaacug caccuuuau	720
uacacuuua acauuaccga agaugagauu uuagaguggu uuggcauuc acaaacugcu	780
caagguguuc acccuucuc aucucggau guuguuuugu acggcggcaa uauguucaa	840
uuugccaccu ugccuguuua ugaucuaau aaguauuuu cuaucuucc ucacaguau	900
cguuacuucc aaagugauag aaaagcuugg gcugccuucu acguauuaa acuucaaccg	960
uuacuuucc uguuggauu uucuguugau gguuuauac gcagagcuau agacuguggu	1020
uuuaugauu ugucaacu ccacugcuca uaugaauccu ucgauguuga aucuggaguu	1080
uauucaguuu cgucuuucga agcaaaaccu ucuggcucag uuguggaaca ggcugaaggu	1140
guugaaugug auuuuucc ucuuucugcu ggcacaccuc cucagguua uauuucaag	1200
cguuugguuu uuaccaauug cauuuaauu cuuaccuuu ugcuuucacu uuuuucugug	1260
aaugauuuu cuuguaguca aaauucucca gcagcaauug cuagcaacug uauuucua	1320
cugauuuugg auuuuuuuc auaccacuu aguaugaaau ccgaucucag uguuaguucu	1380
gcugguccaa uauccaguu uauuuuaaaa caguccuuu cuauuccac auguuugau	1440
uuagcgacug uuccucauaa ccuucucu auuacuaagc cucuuuagua cagcuauuu	1500
aaacaugucu cucgcuucu uucugaugau cguacugaag uaccucaguu agugaacgc	1560
aaucuuuuc caccucugug auccauuguc ccuuccacug ugugggaaga cggugauuu	1620
uauuggaac aacuaucucc acuuagaaggu gguggcuggc uuguugcuag ugucuaacu	1680
guugccauga cugagcauu acagaugggc uuuguaaua caguucaua uggucagac	1740
accaauagug uuugcccau gcuuagaauu gcuauagaca caaaaauugc cucucaaau	1800
ggcaauugcg uggaauuuc ccuuauggu guuucgggc gugguuuuu ucagaauugc	1860
acagcugug guguucgaca gcagcgcuuu guuuuagug cguaccagaa uuuaugugc	1920
uauuuucug augauggca cuacuacug ucugcugcuu guguuagugu uccuguuuc	1980
gucacuauug auaaagaac uaaaaccac gcuaucuuu uugguagugu ugcauguga	2040
cacauuucu cuaccauguc ucaauacucc cguucucgc gaucuuugcu uaaacggcg	2100
gaucucacu auggccccu ucagacaccu guugguugug uccuaggacu uguuaauuc	2160
ucuuugucg uagaggacug caaguugcu cucggucuu cucucuguc ucuuccugac	2220
acaccuagua cucucacacc ucgcagugug cgcucuguc caggugaaa gcgcuuggca	2280
uccauugcu uuaaucauc cauucagguu gaucacuua auaguauua uuuuaauua	2340
aguauacca cuuuuuuuc cuuuggugug acucaggagu acuuucagac aaccuuucag	2400
aaaguuacug uugauugua acagucguu ugcaauggu uccagaagug ugagcauuu	2460

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cugcgcgagu auggccaguu uuguuccaaa auaaacccagg cucuccaugg ugccaauuuu 2520
cgccaggauug auucuguacg uauuuuguuu gcgagcguga aaagcucuca aucaucuccu 2580
aucauaccag guuuuggagg ugacuuuuau uugacacuc uagaaccugu uucuauaucu 2640
acuggcgaguc guagugcagc uagugcuauu gaggauuugc uauuugacaa agucacuuaa 2700
gcugauccug guuauaugca agguuacgau gauuguaugc agcaaggucc agcaucagcu 2760
cgugaucuaa uuugugcuca auauguggcu gguuauaaag uauuaccucc ucuuuggau 2820
guuauauugg aagcccgua uacuucacuu uugcuuggca gcuaagcagg uguuggcugg 2880
acugcuggcu uauccuccuu ugucugcuuu ccuuuugcac agaguauyu uauaggguu 2940
aacggugugug gcauuacuca acagguuuuu ucagagaacc aaaagcuuuu ugccaauaag 3000
uuuauucagg cucugggagc uaugcaaca gccuucacua caacuauga agcuuuucgg 3060
aagguucagg augcugugaa caacaugca caggcucuu ccaauuagc uagcgagcu 3120
ucuaauacuu uuggugcuau uuccgccucu auuggagaca ucauacaacg ucuugauguu 3180
cucgaacagg acgccc aaau agacagacuu auuauuggcc guuugacaac acuaaaugcu 3240
uuuugucac agcagcuugu ucguuccgaa ucagcugcuc uuuccgcuca auuggcuaaa 3300
gauaaaguca augagugugu caaggcaca uccaagcguu cuggauuuug cggucaaggc 3360
acacauauag uguccuuugu uguaaaugcc ccuaauuggcc uuuacuuuuu gcauguuugu 3420
uauuaccua gcaaccacau ugagguuguu ucugcuuau gucuuuugca ugcaucuaac 3480
ccuacuaauu guauagcccc uguuuauuggc uacuuuuuuu aaacuaauaa cacuaggauu 3540
guugaugagu ggucuuuac uggcucguc uucuauugc cugagccau caccucucuu 3600
aaucuaaagu auguugcacc acaggugaca uaccaaaaca uuucuaaua ccuccuccu 3660
ccucuuucug gcaauuccac cgggauugac uuccaagaug aguuggauga guuuuucaaa 3720
aauuuuagca ccaguauacc uauuuuuggu ucucuaacac agauuuauac uacauuacuc 3780
gacuuuaccu acgagauguu gucucuucaa caaguuguuu aagccuuua ugagucuuac 3840
auagaccuaa aagagcuugg cauuuauacu uauuacaaca aauggccgug guacauuugg 3900
cuugguuuca uugcugggcu uguugccuaa gcucuauugc ucuucuucau acugugcugc 3960
acugguugug gcacaaaacug uaugggaaa cuuaagugua aucguugug ugauagauac 4020
gaggauuacg accucgagcc gcuaaagguu cauguucacu aa 4062

```

<210> SEQ ID NO 66

<211> LENGTH: 4062

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 66

```

augauacacu caguguuuu acugauguuc uuguuaacac cuacagaaaag uuacguugau 60
guagggccag auucuguuua gucugcuugu auugagguug auuacaaca gacuuucuuu 120
gauaaaacuu ggccuaggcc auuugauguu ucuuaggcug acgguuuuu auaccucaa 180
ggccguacau auucuaacau aacuaucacu uaucaagguc uuuuuuccua ucagggagac 240
cauggugaua uguauguuu cucugcagga caugcuacag gcacaacucc acaaaaguu 300
uuuguagcua acuaucuca ggacgucaaa caguuuucua auggguuugu cguccguaua 360

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ggagcagcug	ccaauccac	uggeacuguu	auuuuagcc	caucuaaccag	cgcuaacuua	420
cgaaaaauu	accucgcuuu	uagcugggu	ucucaguu	guaauucuc	agaugguaaa	480
augggccgc	ucuucaauca	uacucuaguu	uuuugccc	auggauggg	cacuuuacu	540
agagcuuuu	auuguauuc	ggagccucg	ucuggaauc	auuguccgc	uggeaaucc	600
uauacuuc	uugccacuua	ucacacucc	gcaacagau	guucugaug	cauuuacaau	660
cguaaugcc	gucugaacuc	uuuuaggag	uuuuuuuu	uacguaacg	cacuuuau	720
uacacuuua	acauuaccga	agaugagau	uuagagugg	uuggcauuc	acaaucgcu	780
caaggugu	accucucuc	aucucggau	guugauuu	acggcggca	uanguucaa	840
uuugccacc	ugccuguuu	ugauacuau	aaguauuu	cuaucauuc	ucacaguau	900
cguucuauc	aaagugauag	aaaagcuug	gcugccuuc	acguauuaa	acuucaacc	960
uuacuucc	uguuggauu	uucuguug	gguuuuac	gcagagcuu	agacugugg	1020
uuuaugau	ugucacaac	ccacugcu	uauuauuc	ucgauguu	aucuggagu	1080
uauucaguu	cgucuuucg	agcaaac	ucuggcuc	uuguggaac	ggcugaagg	1140
guugaaug	auuuucacc	ucucugcu	ggcacacc	cucagguuu	uaauucaa	1200
cguugguu	uuaccaau	cauuuuuu	uuuaccuu	ugcuuuc	uuuuucug	1260
augauuuu	cuuguaguc	aaauuc	gcagcau	cuagcauc	uuuuuuc	1320
cugauuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	1380
gcuggucc	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	1440
uuagcgac	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	1500
aaacaugc	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	1560
aucauuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	1620
uuaggaa	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	1680
guugccau	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	1740
accaauag	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	1800
ggcauuug	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	1860
acagcugu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	1920
uuuuuuuc	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	1980
gucuuuuc	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	2040
cacuuuuc	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	2100
gauuuuuc	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	2160
ucuuuuuc	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	2220
acaccuag	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	2280
uccuuuuc	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	2340
aguuuuuc	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	2400
aaaguuc	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	2460
cugcggag	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	2520
cgccagg	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	2580
aucauacc	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	uuuuuuu	2640

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acuggcaguc guagugcacg uagugcuauu gaggauuugc uauuugacaa agucacuaaa 2700
gcugauccug guuauaugca agguuacgau gauugcaugc agcaaggucc agcaucagcu 2760
cgugaucuaa uuugugcuca auauguggcu gguuacaaag uauuaccucc ucuauggau 2820
guuaauaugg aagccgcgua uacuucacuc uugcuuggca gcuaagcagg uguuggcugg 2880
acugcuggcu uauccuccuu ugcugcuauu ccuuuugcac agaguauuuu uuauagguaa 2940
aacggugugug gcauuacuca acagguucuu ucagagaacc aaaagcuuuu ugccaauaag 3000
uuuaaucagg cucugggagc uaugcaaaaca ggcuucacua caacuaauga agcuuuucag 3060
aagguucagg augcugugaa caacaauugca caggcucuaa ccaauuagc uagcagcua 3120
ucuaauacuu uuggugcuau uuccgcccuc auuggagaca ucauacaacg ucuaugauu 3180
cucgaacagg acgcccacuu agacagacuu auuaauggcc guuugacaa acuaaaugcu 3240
uuuguugcac agcagcuugu ucguuucgaa ucagcugcuc uuuccgcuca auuggcuaaa 3300
gaaauaugca augagugugu caaggcaca uccaagcguu cuggauuuug cggucaaggc 3360
acacauauag uguccuuugu uguaaaugcc ccuaauggcc uuuaucuaa gcauguuugu 3420
uauuaccua gcaaccacau ugagguuguu ucugcuuug gucuuugcga ucagcuaac 3480
ccuacuaauu guauagcccc uguuaauggc uacuuuaua aaacuaaua cacuaggauu 3540
guugaugagu ggucuuuac uggcucguc uucuaugcac cugagccau uaccuccuu 3600
aaucuaagu auguugcacc acaggugaca uaccacaa uucuaucua ccuccuccu 3660
ccucuuucug gcaauuccac cggguugac uuccaagaug aguuggauga guuuuucaaa 3720
aauguuagca ccaguauacc uauuuuuggu uccuaacac agauuaauac uacuuuacuc 3780
gaucuuaccu acgagauguu gucuuucaa caaguugua aagccuuua ugagcuuac 3840
auagaccuaa aagagcuugg cauuuauacu uauuacaa caauggccgug guacuuuug 3900
cuugguuuca uugcugggcu uguugccua gcucuaugcg ucuuucua acugugcugc 3960
acugguugug gcacaaacug uaugggaaa cuuaagugua aucguugug ugauagauac 4020
gaggaaucg accucgagcc gcauaagguu cauguucacu aa 4062

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<210> SEQ ID NO 67

<211> LENGTH: 1845

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 67

```

augauccacu ccguguuccu ccucauguuc cugugacccc ccacugaguc agacugcaag 60
cucccgucug gacaguccu guugcgcug ccugacacuc cuagcacuc gaccccacgc 120
uccgugcggg cggugccugg cgaauugcgg cuggccuca ucgccuua ucacccaauc 180
caaguggauc agcugaauag cucguuuuc aagcugucca ucccacgaa cuucucguuc 240
gggguacccc aggaguacau ccagaccaca auucagaagg ucaccgucga uugcaagcaa 300
uacgugugca accgcuucca gaagugcgag cagcugcuga gagaauacgg gcaguuuugc 360
agcaagauca accagcgcuc gcauggagcu aacuugcgc aggaacacuc cgugcgcac 420
cucuugccu cugugaaguc aucccagucc ucccacua ucccgggguu cggaggggac 480
uucaaccuga cccuccgga gcccgugcg aucagcaccg guagcagauc ggcgcgcuca 540

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gccauugaag aucuucuguu cgacaagguc accaucgccc auccgggcua caugcagggg 600
uacgacgacu guaugcagca gggaccagcc uccgcgaggg accucaucug cgcgcaauac 660
guggccgggu acaaagugcu gccuccucug auggauguga acauggaggc cgcuuauacu 720
ucguccucg uoggcucuau cgcggcgug ggguggaccg ccggccuguc cuccuucgcc 780
gcuauccccc uugcacaauc cauuuucua cggcucaacg gcgugggcau uacucaaaaa 840
guccugucgg agaaccagaa guugaucgca aacaaguua aucaggcccu gggggccaug 900
cagacuggau ucacuacgac uaacgaagcg uuccagaagg uccaggagcg ugugaadaac 960
aacgcccagc cgcucuaaaa gcuggccucc gaacucagca acaccuucgg agccaucagc 1020
gcaucgaucg gugacauau ucagcggcug gacgugcugg agcaggagcg ccagaucgac 1080
cgccucauca acggacggcu gaccaccuug aaugccuucg uggcacaaca gcugguocgg 1140
agcgaucag cggcacuuuc cgcacaacuc gccaaaggca aagucaacga augcgugaag 1200
gccagucca agaggucggg uuucugcggu caaggaaacc auauuguguc cuucgucgug 1260
aacgcccga acgguucgua cuuuuugcag gucggcuacu acccgagcaa ucauaucgaa 1320
gugguguccg ccuacggccu gugcgauccg gcuaacccca cuaacugua ugcuccugug 1380
aacggauau uuauuaagac caacaacacc cgcuuugugg acgaaugguc auacaccggu 1440
ucguccuuc acgcgcccga gcccaucacu ucacugaaca ccaauaagcu ggcuccgcaa 1500
gugaccuacc agaacaucuc caaccauuug ccgcccggc ugcucggaa cagcaaccgga 1560
auugauuucc aagaugaacu ggacgaauc uucaagaacg uguccacuuc cauucccaac 1620
uucggaagcc ugacacagau caacaccacc cuucugacc ugaccuacga gaugcugagc 1680
cuucaacaag uggucaaggc ccugaacgag agcuacaucg accugaagga gcugggcaac 1740
uauaccuacu acaacaagug gccggacaag auugaggaga uucugucgaa aaucuaacc 1800
auugaaaacg agaucgcccag aaucagaag cuuauccggc aagcc 1845

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<210> SEQ ID NO 68

<211> LENGTH: 4071

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 68

```

auggaaacc cugcccagcu gcuguuccug cugcugcugu ggcugccuga uaccaccggc 60
agcuauuggg acgugggccc cgauagcgug aaguccgcu guaucgaagu ggacauccag 120
cagaccuuuu ucgacaagac cuggcccaga ccaucgacg uguccaaggc cgaaggcauc 180
aucuauccac aaggccggac cuacagcaac aucaccaua ccuaccaggg ccuguuucca 240
uaucaaggcg accacggcga uauguacgug uacucugccg gccacgccac cggcaccaca 300
ccccagaaac uguucguggc caacuacagc caggacguga agcaguucgc caacggcuuc 360
gucgugcgga uugggcccgc ugccaauagc accggcacag ugaucaucag ccccagcacc 420
agcggccacca uccggaagau cuaccccggc uucaugcugg gcagcuccgu gggcauuuc 480
agcgaccgca agaugggccc guucuucaac cacaccucgg ugcugcugcc cgauggcugu 540
ggcacacugc ugagagccuu cuacugcauc cuggaaccca gaagcggcaa ccacugcccu 600
gccggcaaua gcuaaccag cuucgccacc uaccacacac ccgccaccga ugcuccgac 660

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ggcaacuaca accggaacgc cagccugaac agcuucaaag aguacuuaa ccugcggaac	720
ugcaccuuca uguacaccua caauaucacc gaggacgaga uccuggaug guucggcauc	780
accagaccg cccagggcgu gcaccuguuc agcagcagau acguggaccu guacggcggc	840
aaauuguucc aguuugccac ccugcccgug uacgacacca ucaaguacua cagcaucauc	900
ccccacagca uccgguccau ccagagcgcac agaaaagccu gggccgccuu cuaccgugac	960
aagcugcagc cccugaccuu ccugcuggac uucagcggug acggcuacau cagacgggcc	1020
aucgacugcg gcuucaacga ccugagccag cugcaucugc ccuacgagag cuucgacgug	1080
gaaagcggcg uguacagcgu guccagcuuc gaggccaagc cuagcggcag cuggguggaa	1140
caggcugagg gcguggaaug cgaucuacgc ccucugcuga gcgccacccc uccccaggug	1200
uacaacuuca agcggcuggu guuacccaac ugcauuaca accugaccaa gcugcugagc	1260
cuguucuccg ugaacgacuu caccuguagc cagaucagcc cugccgcca ugcacgcaac	1320
ugcuacagca gccugauccu ggaucuauuc agcuaccccc ugagcaugaa guccgaucug	1380
agcguguccu cgcgggacc caucagccag uucaacuaca agcagagccu cagcaacccu	1440
accugccuga uucggccac cgugccccc aaucugacca ccuacacca gccccugaag	1500
uacagcuaca ucaacaagug cagcagacug cuguccgacg accggaccga agugcccccag	1560
cucgugaacg ccaaccagua cagcccccgc guguccaucg ugcccagcac cgugugggag	1620
gacggcgacu acuacagaaa gcagcugagc ccccuggaag gcggcggaug gcugguggcu	1680
ucuggaagca caguggccau gaccgagcag cugcagauug gcuuuggcau caccgugcag	1740
uacggcaccg acaccaacag cgugugcccc aagcuggaau ucgccaauga caccaagauc	1800
gccagccagc ugggaaacug cguggaauc ucccugaug gcguguccgg acggggcgug	1860
uuccagaauu gcacagcagu gggagugcgg cagcagagau ucguguaacy ugccuaccag	1920
aaaccugugg gcuacuacag cgaacagcgc aauuacuacu gccugcgggc cugugugucc	1980
gugcccgugu ccgugaucua cgacaaagag acaaagacc accccacacu guucggcuuc	2040
guggccugcg agcacaucag cuccaccaug agccaguacu cccgcuccc ccgguccaug	2100
cugaagcggg gagauagcac cuaccgcccc cugcagacac cugugggaur ugugcugggc	2160
cucgugaaca gcucccuguu uguggaagau ugcaagcugc cccugggcca gagccugugu	2220
gcccugccag auaccccuag caccucgacc ccuagaagcg uggcucucgu gcccgcgaa	2280
augcggcugg ccucuauccg cuucaaucc cccauccagg uggaccagcu gaacuccagc	2340
uacuuaagc ugagcauccc caaccaauuc agcuucggcg ugaccagga guacauccag	2400
accacaaucc agaaagugac cguggacugc aagcaguacg ugugcaacgg cuuucagaag	2460
ugogaacagc ugucgcgca guacggccag uucugcagca agaucaacca gggccugcac	2520
ggcgccaaac ugagacagga ugacagcug cggaaccugu ucgcccagcu gaaaagcagc	2580
caguccagcc ccuacauccc uggcuucggc ggcgacuua accugaccuu gcuggaaccu	2640
guguccauca gcaccggcuc cagaagcgc accuaccgca ucgaggaccu gcuguuagc	2700
aaagugacca uugccgaccc cggcuacaug cagggcuacg accgauugcau gcagcagggc	2760
ccagccagcg ccagggaucc gauucugucc caguaugug cggcuacaa ggugcugccc	2820
ccccugaugg acugaaacau ggaagccgcc uacaccucca gccugcuggg cuuauugcu	2880
ggcgugggau ggacagccgg ccugucagc uuugccgca uccuuucgc ccagagcauc	2940

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uucuaccggc ugaacggcgu gggcaucaca caacaggugc ugagcgagaa ccagaagcug 3000
aucgccaaca aguuuaacca ggcacugggc gccaugcaga cggguucac caccaccaac 3060
gaggccuua gaaaggugca ggcgcggug aacaacaacg cccaggcucu gagcaagcug 3120
gccuccgagc ugagcaauac cuucggcgcc aucagcgccu ccuocggcga caucauccag 3180
cggcuggagc ugcuggaaca ggcgcccag aucgaccggc ugaucacgg cagacugacc 3240
accugaaag ccuucguggc acagcagcuc gugcggagcg aaucgcccgc ucugucugcu 3300
cagcuggcca aggacaaagu gaacgagugc gugaaggccc aguccaagcg gagcggcuuu 3360
uguggccagc gcaccaccac cgugucuuuc gucgugaaug ccccaacgg ccuguacuuu 3420
augcacgugg gcuuuuacc cagcaaccac aucgaggugg uguccgccua ugccucuguc 3480
gacgcgccca aucuaccaa cuguuocgcc cccgugaacg gcuacuucau caagaccac 3540
aacaccggga ucguggagca gugguccuac acaggcagca gcuucucgc ccccgagccc 3600
aucaccuccc ugaacaccaa auacguggcc cccaaguga cauaccagaa cauccacc 3660
aaccugcccc cuccacugcu gggaaauuc accggcaucg acuuccagga cagcuggac 3720
gaguucuuca agaacguguc caccuccauc cccaacuucg gcagccugac ccagaucaac 3780
accacucugc uggaccugac cuacgagauy cugucccugc aacaggucgu gaaagcccug 3840
aacgagagcu acaucgaccu gaaagagcug gggaaucuaa ccuacuaaa caaguggccu 3900
ugguacauuu ggcugggcuu uaucgcccgc cugguggccc uggcccugug cguguucuu 3960
auccugugcu gcaccggcug cggcaccacu ugcaugggca agcugaaaug caaccggugc 4020
ugcgacagau acgaggaaau cgaccuggaa ccucacaaag ugcaugugca c 4071

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<210> SEQ ID NO 69

<211> LENGTH: 1864

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 69

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ucaagcuuuu ggaccucugc acagaagcua auacgacuca cuauagggaa auagagaga 60
aaagaagagu aagaagaaau auagagcca ccaugggucu caaggugaac gucucugccg 120
uaucauggc aguacugua acucuccaaa ccccggcgg ucaaaaucau uggggcaauc 180
ucucuaagau agggguagua ggaauaggaa gugcaagcua caaaguuauy acucguucca 240
gccaucaauc auuagucuaa aaauuaaugc ccaauuaaac ucuccucaa aacugcacga 300
ggguagagau ugcagaauac aggagacuac uaagaacagu uuuggaacca auuagggauy 360
cacuuauugc aaugaccag aacauaaggc cgguucagag cguagcuuca aguaggagac 420
acaagagauu ugcgggagua guccuggcag gugcggcccu agguuuugcc acagcugcuc 480
agauaacagc cggcauugca cuucaccggu ccuagcugaa cucucaggcc aucgacaauc 540
ugagagcgag ccuggaaacu acuaaucagg caauugaggc aaucagacaa gcagggcagg 600
agaugauuuu ggcuguucag gguguccaag acuacaucau uauagagcug auaccgucua 660
ugaaccagcu aucuugugau cuauucgguc agaagcucgg gcucaaaauy cuuagauacu 720
auacagaaau ccugucuuua uuuggcccca gccuacggga ccccauucu gggagauau 780
cuauccaggc uuugauuuu gcacuuggag gagauucaa uaaggguua gaaaagcucg 840

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gauacagugg	aggcgauuuu	cuaggcaucu	uagagagcag	aggaauaaag	gcucggauaa	900
cucacgucga	cacagagucc	uacuucauag	uccucaguau	agccuauccg	acgcuguccg	960
agauuaaggg	ggugauuguc	caccggcuag	agggggucuc	guacaacaua	ggcucucaag	1020
agugguauac	cacugugccc	aaguauguug	caaccaaggg	guaccuuuac	ucgaauuuug	1080
augagucauc	auguacuuc	augccagagg	ggacugugug	cagccaaaa	gccuuguacc	1140
cgauagagucc	ucugcuccaa	gaaugccucc	ggggguccac	caaguccugu	gcucguacac	1200
ucguauccgg	gucuuuuggg	aaccgguuca	uuuuuacaca	agggaaaccua	auagccaauu	1260
gugcaucaau	ucuuuguuag	uguuacacaa	cagguaccgau	uuuuuucaa	gaccucgaca	1320
agauccuaac	aucauuugcu	gcccgaucgu	gcccggagu	cgaggugaac	ggcgugacca	1380
uccaagucgg	gagcaggagg	uauccagacg	cuguguacuu	gcacagaauu	gaccucgguc	1440
cucccauauc	auuggagagg	uuggacguag	ggacaaaucu	ggggaauuca	auugccaaa	1500
uggaggaugc	caaggaauug	uuggaaucau	cggaccagau	auugagaagu	augaaagguu	1560
uaucgagcac	uagcauaguc	uacaucucga	uugcagugug	ucuuaggagg	uugauaggga	1620
uccccacuuu	aaauugugc	ugcagggggc	guuguacaa	aaagggagaa	caaguuggua	1680
ugucaagacc	aggccuaaag	ccugaccuua	caggaacauc	aaaauccuau	guaagaucgc	1740
uuugaugaua	auaggcugga	gccucggugg	ccaagcuucu	ugcccuugg	gccucccccc	1800
agccccuccu	ccccuuccug	cacccguacc	cccggugucu	uugaauaaag	ucugaguggg	1860
cggc						1864

<210> SEQ ID NO 70

<211> LENGTH: 1653

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 70

auugguucua	aggugaacgu	cucugccgua	uucauggcag	uacuguuuac	ucuccaaaca	60
cccgccgguc	aaauucauug	ggcacaucuc	ucuaagauag	ggguaguagg	aaauaggaagu	120
gcaagcuaca	aaguuaugac	ucguuccagc	caucaaucau	uagucuuaaa	auuaaugccc	180
aaauuaacuc	uccucaauaa	cugcacgagg	guagagaauug	cagaauacag	gagacuacua	240
agaacaguuu	uggaacccau	uagggauuca	cuuaaugcaa	ugaccacagaa	cauaaggccg	300
guucagagcg	uagcuucaag	uaggagacac	aagagauuug	cgaggaguagu	ccuggcagggu	360
ggggcccuag	guguugccac	agcugcucag	auaacagccg	gcauugcacu	ucaccggucc	420
augcugaacu	cucagggccau	cgacaauucg	agagcagacc	uggaaacuac	uaaucaggca	480
auugaggcaa	ucagacaagc	agggcaggag	augauuuugg	cuguucagggg	uguccaagac	540
uacaucaaua	augagcugau	accgucuaug	aaccagcuau	cuugugaucu	aaucggucag	600
aaucucgggc	uccaaauugcu	uagauacuau	acagaaaucc	ugucauuuuu	uggccccagc	660
cuaccgggacc	ccauaucugc	ggagauaucu	auccaggcuu	ugaguuaugc	acuuaggagga	720
gauaucaaua	agguguuaga	aaagcucgga	uacaguggag	gcauuuuacu	aggcaucuuu	780
gagagcagag	gaauaaaggc	ucggauaacu	cacgucgaca	cagaguccua	cuucauaguc	840
cucaguuuag	ccuauccgac	gcuguccgag	auuaaggggg	ugauuugucca	ccggcuagag	900

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ggggucucgu acaacauagg cucucaagag uggauuacca cugugcccaa guauguugca 960
acccaagggg accuauucuc gaauuuugau gagucaucau guacuuucau gccagagggg 1020
acugugugca gccaaaaugc cuuguacccg augaguccuc ugcuccaaga augccuccgg 1080
ggguccacca aguccugugc ucuacacuc guaucogggg cuuuugggaa ccgguucauu 1140
uuaucaacaag ggaaccuaau agccaauugu gcaucaauuc uuuguaagug uuacacaaca 1200
gguacgauua uuaaucaaga ccugacaag auccuaacau acauugcugc cgaucgcugc 1260
ccgguauguc aggugaacgg cgugaccauc caaguogggg gcaggaggua uccagacgcu 1320
guguacuugc acagaauuga ccucgguccu cccauaucau uggagagguu ggacguaggg 1380
acaaaucugg ggaauugcau ugccaaaauug gaggaugcc aagaaauugu ggaaucaucg 1440
gaccagauau ugagaaguau gaaagguua ucgagcacia gcuaugucua cauccugauu 1500
gcaguguguc uuggaggggu gauagggauc cccacuuuaa uauguugcug cagggggcgu 1560
uguaacaaaa agggagaaca aguugguaug ucaagaccag gccuaaagcc ugaccuaca 1620
ggaacaucaa aauccuaugu aagaucgcuu uga 1653

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<210> SEQ ID NO 71

<211> LENGTH: 1925

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 71

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ggggaauuaa gagagaaaag aagaguaaga agaaauuaa gagccaccau gggucuaag 60
gugaacgucu cugccguauu cauggcagua cuguuaacuc uccaaacacc cgccggucua 120
auucauuggg gcaaucucuc uaagauaggg guaguaggaa uaggaauguc aagcuacaaa 180
guuugacuc guuccagcca ucaucauaa gucauaaaau uaaugcccaa uauaacucuc 240
cucauaaacu gcacgagggg agagauugca gaauacagga gacuacuaag aacaguuuug 300
gaaccuuuaa gggaugcacu uaaugcaauug acccagaaca uaaggccggg ucagagcgua 360
gcuucaagua ggagacacaa gagauuugcg ggaguagucc uggcaggugc ggccuaggu 420
guugccacag cugcucagau aacagccgjc auugcacuuc accgguccau gcugaacucu 480
caggccaucg acaaucugag agcagaccug gaaacuacua aucaggcaau ugaggcaauc 540
agacaagcag ggcaggagau gauauuggcu guucagggug uccaagacua caucauaau 600
gagcugauac cgucuaugaa ccagcuauuc uugauucuaa ucggucagaa gcucggguc 660
aaaugcuua gauacuauac agaaaucug ucauuuuuug gcccagccu acgggacccc 720
auaucugcgg agauaucuau ccaggcuuug aguuaugcac uuggaggaga uaucauaag 780
guguuagaaa agcucggaua caguggagjc gauuuacuag gcaucuaaga gagcagagga 840
auaaaggcuc gguaaacuca cguogacaca gaguccuacu ucauaguccu caguauagcc 900
uauccgacgc ugucagagau uaagggggug auuguccacc ggcuaagagg gguucguac 960
aacauaggcu cucaagagug guauaccacu gugcccaagu auguugcaac ccaaggguac 1020
cuuauucoga auuuugauga gucaucaugu acuuucaugc cagaggggac ugugugcagc 1080
caaaaugccu uguaccggau gaguccucug cuccaagaau gccuccgggg guccaccaag 1140
uccugugcuc guacacucgu auccgggucu uuugggaacc gguucauuuu aucacaaggg 1200

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aaccuaauag ccaauugugc aucaaauucuu uguaauguuu acacaacagg uacgauuuuu	1260
aaucaagacc cugacaagau ccuaacauac auugcugccg aucgcugccc gguagucgag	1320
gugaacggcg ugaccaucca agucgggagc aggagguauc cagacgcugu guacuugcac	1380
agaaugacc uogguccucc cauaucuuug gagagguugg acguagggac aaauucgggg	1440
aaugcaauug ccaaaauugga ggauGCCaag gaauguuugg aaucaucgga ccagauuuug	1500
agaaguaua aagguuuuac gaggacuagc auagucuaca uccugauugc agugugucuu	1560
ggaggguuuga uagggauccc cacuuuaaua uguugcugca gggggcguug uaacaaaaag	1620
ggagaacaag uugguauugc aagaccaggc cuaaagccug accuuacagg aacaucaaaa	1680
uccuauguaa gauccguuug augauuuuag gcugggccu cgguggccaa gcuuuuugcc	1740
ccuugggccu cccccagcc ccuuccccc uuccugcacc cguacccccg uggucuuuga	1800
auaaagucug aguggggcgc aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa	1860
aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa	1920
ucuag	1925

<210> SEQ ID NO 72

<211> LENGTH: 1864

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 72

ucaagcuuuu ggaccucgu acagaagcua auacgacuca cuauaggga auaagagaga	60
aaagaagagu aagaagaaau auaagagcca ccaugggucu caaggugaac gucucuguca	120
uaucuauggc aguacuguaa acucuucaaa caccaccgg ucaaauccau uggggcaauc	180
ucucuaagau agggguggua gggguaggaa gugcaagcua caaaguuaug acucguucca	240
gccaucaauc auuagucua aaguuaaagc ccaauuaaac ucuccucaac aaauugcacga	300
ggguagggau ugcagaauac aggagacuac ugagaacagu ucuggaacca auuagagauG	360
cacuuuaugc aaugaccagc aaauuaagac cgguuacagag uguagcuuca aguaggagac	420
acaagagauu ugcgggaguu guccuggcag gugcggccu aggcguugcc acagcugcuc	480
aaauaacagc cgguaauuca cuucaccagu ccaugcugaa cucucaagcc aucgacaauc	540
ugagagcgag ccuagaaacu acuaaucagg caauugaggc aaucagacaa gcagggcagg	600
agaugauuuu ggcugucag gguguccaag acuaacuaa uaaugagcug auaccgucua	660
ugaaucaacu aucuugugau uuaauaggcc agaagcuagg gcuccaaaug cucagauacu	720
auacagaaau ccugucuuu uuuuggcccc gcuaacggga ccccauauu cgggagauu	780
cuauccaggc uuugagcuu ggcguuggag gagauucaa uaaggguuug gaaaagcucg	840
gauacagugg aggugaucua cugggcaucu uagagagcag aggaauaaag gcccgauaa	900
cucacgucga cacagagucc uacuucuuug uacucaguau agccuauccg acgcuauccg	960
agauuaaggg ggugauugc caccggcuag agggggucuc guacaacuaa ggcucuaaag	1020
agugguauac cacugugccc aaguauguug caaccacagg guaccuuuac ucgaauuuug	1080
augagucauc augcacuuuc augccagagg ggacugugug cagccagaau gccuuquacc	1140
cgaugagucc ucugucucca gaaugccucc ggggguccac uaaguccugu gcucguacac	1200

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ucguauccgg gucuuucggg aaccgguuca uuuuaucaca ggggaaccua auagccaauu	1260
gugcaucaau ccuugcaag uguuacacaa caggaacaau cauuauca gaccucgaca	1320
agauccuaac auacaauugc gccgaucacu gcccguggu cgaggugaau ggcgugacca	1380
uccaagucgg gagcaggagg uauccggacg cuguguacuu gcacaggauu gaccucgguc	1440
cucccauauc uuuggagagg uggacguag ggacaaauc ggggaauuca auugcuuagu	1500
uggaggaucc caaggauug uggagucuu cggaccagau auugaggagu augaaagguu	1560
uaucgagcac uaguauaguu uacaucuga uugcagugug ucuuggagga uugauagga	1620
ucuccgcuu aauauguugc ugcagggggc guuguacaa gaaggagaa caaguugua	1680
uguaagacc aggccuaag ccugaucua caggaacac aaaauccuu guaaagucac	1740
ucugaugau auaggucgga gccucggug ccaagcuuc ugccccuug gccuccccc	1800
agccccucc cccuuccug cccccuacc cccgugucu ugaauaaag ucugaguggg	1860
cggc	1864

<210> SEQ ID NO 73

<211> LENGTH: 1653

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 73

augggucua aggugaacgu cucugucua uucauggcag uacuguaac ucuucaaca	60
cccaccgguc aaauccauug gggcaucuc ucaagauag gggugguagg gguaggaagu	120
gcaagcuaca aaguuaugac ucuuccagc caucaaucau uagucauaa guuaaugccc	180
aaauaacuc uccucaaca uugcaccagg guagggaug cagaauacag gagacuacug	240
agaacaguuc uggaaccau uagagaugca cuuaaugca ugacccagaa uauaagaccg	300
guucagagug uagcucaag uaggagacac aagagauug cgggaguugu ccuggcagg	360
ggggccuag gccguuccac agcugcuaa auaacagccg guauugcacu ucaccagucc	420
augcugaacu cucaagccau cgacaucug agagcgagcc uagaaacuac uaaucaggca	480
auugaggcaa ucagacaagc agggcaggag augauauugg cuguucaggg uguccaagc	540
uacaucaua augagcugau accgucuaug aaucaacuau cuugugauuu aaucggccag	600
aagcuagggc ucaauugcu cagauacuau acagaaaucc ugucuuuuu ugccccagc	660
uuaccggacc ccuaucugc ggagauauc uaccaggcuu ugagcuuagc gcuuggagg	720
gaulucaua agguguugga aaagcucgga uacaguggag gugaucua cuugcaucua	780
gagagcagag gaauaaaggc ccggauaac cacgucgaca cagagucca cuucauugua	840
cucaguauag ccuauccgac gcuaucgag auuaaggggg ugauugucca ccggcuagag	900
ggggucucgu acaacauagg cucucaagag ugguaaucca cugugccca guauguugca	960
acccaagggu accuuauuc gaauuuugau gagucauau gcacuuucau gccagagggg	1020
acugugugca gccagaaucc cuugucucc augaguccuc ugcuccaaga augccuccg	1080
gggucccaua aguccuguc ucguacacuc guaucoggu cuuucggga ccgguucau	1140
uuacacagg ggaaccuau agccaauug gcaucaaucc uuugcaagug uuacacaaca	1200
ggaacauca uuaaucaaga ccugacaag auccuaacu acuuugcuc gaucacugc	1260

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cggguggucg	aggugaauagg	cgugaccauc	caagucggga	gcaggaggua	uccggacgcu	1320
guguacuugc	acaggauuga	ccucgguccu	cccuaucuu	uggagagguu	ggacguaggg	1380
acaaaucugg	ggaaucaau	ugcuaaguug	gaggauGCCA	aggaauuguu	ggagucaucg	1440
gaccagauau	ugaggaguau	gaaagguuuu	ucgagcacua	guauaguuuu	cauccugauu	1500
gcaguguguc	uuggaggauu	gauagggauc	cccgcuuuuu	uauguugcug	cagggggcgu	1560
uguaacaaga	agggagaaca	aguugguaug	ucaagaccag	gccuaaagcc	ugaucuuaca	1620
ggaacaucaa	aauccuangu	aaggucacuc	uga			1653

<210> SEQ ID NO 74

<211> LENGTH: 1925

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 74

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gugaacgucu	cugucuuuu	cauggcagua	cuguuuacuc	uucaaacacc	caccggucaa	120
auccauuggg	gcaaucucuc	uaagauaggg	gugguagggg	uaggaagugc	aagcuacaaa	180
guuauagacuc	guuccagcca	ucaaucuuu	gucuuuuuu	uaaugcccaa	uauaacucuc	240
cucaacaauu	gcacgagggg	agggauugca	gaaucagga	gacuacugag	aacaguucug	300
gaaccauuu	gagaugcacu	uaaugcaaug	accagaauu	uaagaccggg	ucagagugua	360
gcuucaagua	ggagacacaa	gagauuugc	ggaguuugc	uggcaggugc	ggcccuaggc	420
guugccacag	cugcucauuu	aacagccggg	auugcacuuc	accaguccau	gcugaacucu	480
caagccaucg	acaauugag	agcagaccua	gaaacuacua	aucaggcauu	ugaggcaauc	540
agacaagcag	ggcaggagau	gauuuugcuc	guucagggug	uccaagacua	caucauuuu	600
gagcugauac	cgucuaugaa	ucaacuauuc	uguguuuuu	ucggccagaa	gcuaagggcuc	660
aaauugcuca	gauacuauac	agaaauuccg	ucauuuuuu	gcccagcguu	acgggacccc	720
auaucugcgg	agauaucuau	ccaggcuuu	agcuauugc	uuggaggaga	uaucauuuag	780
guguuggaaa	agcucygaau	caguygaggu	gaucuaucg	gcaucuuaga	gagcagaggga	840
auaaaggccc	ggauaacuca	cgucgacaca	gaguccuacu	ucauuugacu	caguauagcc	900
uauccgacgc	uauccgagau	uaagggggug	auuguccacc	ggcuagaggg	ggucucguac	960
aacauaggcu	cucaagagug	guauaccacu	gugcccaguu	auguuycaac	ccaaggguae	1020
cuuauucgca	uuuuugauga	gucaucaugc	acuuucaugc	cagaggggac	ugugugcagc	1080
cagaauccu	uguaaccgau	gaguccucug	cuccaagaau	gccuccgggg	guccacuaag	1140
uccugugcuc	guacacucgu	aucggggucu	uucgggaacc	gguucauuuu	aucacagggg	1200
aaccuaauag	ccaaauuguc	aucaauccuu	ugcaaguguu	acacaacagg	aacaaucauu	1260
aaucaagacc	cugacaagau	ccuaacauac	auugcugccg	aucacugccc	gguggucgag	1320
gugaauuggc	ugaccaucca	agucgggagc	aggagguauc	cggacgcugu	guacuugcac	1380
aggauugacc	ucggucucuc	cauauuuuu	gagagguugg	acguagggac	aaauucgggg	1440
aaugcaauug	cuaaguugga	ggaugccaag	gaaauugugg	agucaucgga	ccagauuuug	1500
aggaguuuga	aagguuuuac	gagcacuagu	auaguuuaca	uccugauugc	agugugucuu	1560

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ggaggauuga uagggauccc cgcuuuaaua uguugcugca gggggcgguug uaacaagaag	1620
ggagaacaag uugguauguc aagaccaggc cuaaagccug aucuuacagg aacaucaaaa	1680
uccuauguaa ggucacucug augauaaauag gcuggagccu cgguggccaa gcuuuugcc	1740
ccuugggccu cccccagcc ccuuccccc uuccugcacc cguacccccg uggucuuga	1800
auaaagucug agugggcggc aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa	1860
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa	1920
ucuag	1925

<210> SEQ ID NO 75

<211> LENGTH: 2065

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 75

ucaagcuuuu ggaccucug acagaagcua auacgacuca cuauagggaa auagagaga	60
aaagaagagu aagaagaaau auagagcca ccaugucacc gcaacgagac cggauaaau	120
ccuucuaaa agauaacccu uaucccaag gaaguaggau aguuuuuac agagaacau	180
uuugauuga cagaccuau guucugcug cuguucuguu cgucauguu cugagcuuga	240
ucggauugcu ggcaauugca ggcauuagac ucaucgggc agccaucua acgcggaga	300
uccauaaaag ccucaguacc aaucuggaug ugacuaacuc caucgagcau cagguaagg	360
acgugcugac accacucuuu aaaaucucg gggauagaau gggccugaga acaccucaga	420
gaucacuga ccuagugaaa ucaucucgg acaagauua auccuuuuu ccggauagg	480
aguacgacuu cagagaucuc acuuugguca ucaaccgcc agagaggauc aaacuaguu	540
augaucaua cugugcagau guggcugcug aagagcucau gaugcauug gugaacuaa	600
cucucugga gaccagaaca accacucagu uccuagcugu cucaaggga aacugcucag	660
ggcccacua acacagaggu caauucuaa caaugcgcg guccuugug gacuuuacu	720
uaggucgagg uuacaauug ucaucuaug ucacuaugac auccaggga auguagggg	780
gaaccuaccu aguugaaaag ccuaaucuga acagcaagg gucagaguug ucacaacuga	840
gcauguaccg aguguugaa guagguguga ucagaaacc ggguuugggg gcuccggugu	900
uccauaugac aaacuauuu gagcaaccag ucaguauug ucucggcaac uguaugggg	960
cuuuggggga gcuaaacuc gcagccuuu gucacgggga cgauucuauc auuuuuccu	1020
aucagggauc agggaaaaggu gucagcuucc agcucugua gcuggguguc uggaaaacc	1080
caaccgacau gcaaucugg guccccuuu caacggaua uccaguggua gacagcuuu	1140
accucuauc ucacagaggu gucaucguc acaaucaagc aaaaugggcu gucccgaaa	1200
cacgaacaga ugacaaguug cgaauaggga caugcuuca gcaggcgugu aaaguuuuu	1260
uccaagcacu cugcgagaau cccgaguggg uaccuuugaa ggauaacagg auccuuuau	1320
acgggguccu gucuguugau cugagucuga cgguugagcu uaaaaucaa auugcuucg	1380
gauucgggc auugaucaca cacggcucag ggauggaccu auacaaaucc aacugcaaca	1440
auguguauug gcugacuauu ccgccaauga gaaaucaagc cuuaggcgua aucaacacu	1500
uggaguggau accgagauuc aagguuaguc ccaaccucu cacugucca auuaaggaa	1560

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caggcgaaga	cugccaugcc	ccaacauacc	uaccugcgga	gguggacggu	gaugcaaac	1620
ucaguuccaa	ccuggugauu	cuaccugguc	aagaucucca	auauguuuug	gcaaccuacg	1680
auaccuccag	ggugagcau	gcugugguuu	auuacguua	cagcccaagc	cgcuauuuu	1740
cuuacuuuuu	uccuuuagg	uugccuauaa	aggggguccc	aaucgaacua	caaguggaau	1800
gcuucacaug	ggaucaaaaa	cucuggugcc	gucacuucug	ugugcuugcg	gacucagaau	1860
ccgguggacu	uaucacucac	ucugggaugg	ugggcauggg	agucagcugc	acagcuacc	1920
gggaagaugg	aaccaaucgc	agauauggau	aauggcugg	agccucggug	gccaaagcuu	1980
uugcccuug	ggccuccccc	cagcccccuc	uccccuuccu	gcaccguac	ccccgugguc	2040
uuugaauaaa	gucugagugg	gcggc				2065

<210> SEQ ID NO 76

<211> LENGTH: 1854

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 76

augucaccgc	aacgagaccg	gauaaaugcc	uucuacaaag	auaacccuua	ucccaagggg	60
aguaggauag	uuuuuacag	agaacauuu	augauugaca	gaccuauuu	ucugcuggcu	120
guucguuucg	ucauguuuu	gagcuugauc	ggauugcugg	caauugcagg	cauuagacuu	180
caucgggacg	ccaucucac	cgcgagagau	cauaaaagcc	ucaguaccua	ucuggaugug	240
acuaacucca	ucgagcauca	ggucaaggac	gugcugacac	cacucuuuu	aaucaucggg	300
gaugaagugg	gccugagaac	accucagaga	uucacugacc	uagugaaau	caucucggac	360
aagauuuuuu	uccuuuuu	ggauaggagg	uacgacuuca	gagaucucac	uuggugcauc	420
aaaccgccc	agaggaucaa	acuagauuu	gaucaauacu	gugcagaugu	ggcugcugaa	480
gagcucauga	augcauuggu	gaacucaacu	cuacuggaga	ccagaacaac	cacucaguu	540
cuagcugucu	caaagggaaa	cugcucaggg	cccacuaaca	ucagaggua	auucuaaac	600
augucgcugu	ccuuguugga	cuuguaacua	ggucgagguu	acaauguguc	aucuauaguc	660
acuauagacau	cccagggaau	guauggggga	accuaccuag	uugaaaagcc	uaaucugaac	720
agcaaaaggu	cagaguuguc	acaacugagc	auguaccgag	uguuugaagu	aggugugauc	780
agaaaccgg	guuugggggc	uccgguguu	cauauagaca	acuauuuuga	gcaaccaguc	840
aguuauuguc	ucggcaacug	uauugggcu	uugggggagc	ucaaacucgc	agcccuuugu	900
cacggggacg	auucuaucuu	aaucuccuau	cagggauacg	ggaaaggugu	cagcuuccag	960
cucgucacgc	ugggugucug	gaaauccca	accgacaugc	aaucucgggu	ccccuauca	1020
acggauaguc	cagugguaga	caggcuuuac	cucucaucuc	acagaggugu	caucgcugac	1080
aaucaagcaa	aaugggcugu	cccgacaaca	cgaacagaug	acaaguugcg	aauggagaca	1140
ugcuuccagc	aggcguguaa	agguaaaauc	caagcacucu	gcyagaaucc	cyagugggua	1200
ccauugaagg	auaacaggau	uccuucuuac	gggguccugu	cuguuagacu	gagucugacg	1260
guugagcuua	aaaucaaaa	ugcuucggga	uucgggccau	ugaucacaca	cggcucaggg	1320
auggaccuau	acaaauccaa	cugcaacaau	guguauuggc	ugacuauucc	gccaauagaga	1380
aaucuaagccu	uagggcuuuu	caacacauug	gaguggauac	cgagauucaa	gguuaguccc	1440

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aaccucuuca	cugucccaau	uaaggaagca	ggcgaagacu	gccaugcccc	aacauaccua	1500
ccugcggagg	uggacgguga	ugucaaacuc	aguuccaacc	uggugauucu	accuggucaa	1560
gaucuccaau	auguuuuggc	aaccuacgau	accuccaggg	uugagcaugc	ugugguuuuu	1620
uacguuuaca	goccaagccg	cucuuuuucu	uacuuuuuac	cuuuuagguu	gccuauaaag	1680
ggggucccaa	ucgaacuaca	aguggaauuc	uucacauggg	aucaaaaaac	cugggucggc	1740
cacuucugug	ugcuugcgga	cucagaaucc	gguggacuaa	ucacucacuc	ugggauuggg	1800
ggcauggggag	ucagcugcac	agcuaccggg	gaagauggaa	ccaauccgag	auaa	1854

<210> SEQ ID NO 77

<211> LENGTH: 2126

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 77

ggggaaauaa	gagagaaaag	aagaguaaga	agaaauuaa	gagccaccau	gucaccgcaa	60
cgagaccgga	uaaaugccuu	cucaaaagau	aaccuuuac	ccaagggag	uaggauaguu	120
auuaacagag	aacauuuau	gauugacaga	ccuauuguu	ugcuggcugu	ucuguucguc	180
auguuucuga	gcuugaucgg	auugcuggca	auugcaggca	uuagacuua	ucgggcagcc	240
aucuacaccg	cgagaucca	uaaaagccuc	aguaccaauc	uggaugugac	uaacuccauc	300
gagcaucagg	ucaaggacgu	gcugacacca	cucuuaaaaa	ucaucgggga	ugaagugggc	360
cugagaacac	cucagagauu	cacugaccua	gugaaauca	ucucggacaa	gauuaaauc	420
cuuaauccgg	auaggggua	cgacuucaga	gaucucacuu	ggugcaucaa	cccggcagag	480
aggaucaaac	uagauuauga	ucaauacugu	gcagaugugg	cugcugaaga	gcucaugaau	540
gcauugguga	acucaacucu	acuggagacc	agaacaacca	cucaguuccu	agcugucuca	600
aagggaaacu	gcucagggcc	cacuacaauc	agaggucaau	ucucaaaau	gucgcugucc	660
uuuguugacu	uguacuuaag	ucgagguuac	aaugugucuu	cuauagucac	uauagcaucc	720
cagggaaugu	augggggaac	cuaccuaguu	gaaaagccua	aucugaacag	caaaggguca	780
gaguuuguc	aacugagcau	guaccgagug	uuugaaguag	gugugaucag	aaaccggggu	840
uuuggggguc	cgguuuucca	uauagacaa	uauuuuagc	aaccagucag	uauuggucuc	900
ggcaacugua	ugguggcuuu	gggggagcuc	aaacucgag	ccuuuugua	cggggacgau	960
ucuaucuaaa	uucccuauca	gggaucaggg	aaaggugua	gcuuccagcu	cgucaagcug	1020
ggugucugga	aaucuccaac	cgacaugcaa	uocugggucc	ccuuaucaac	ggauagacca	1080
gugguagaca	ggcuuuaccu	cucaucucac	agaggugua	ucgcugacaa	ucaagcaaaa	1140
ugggcugucc	cgacaacacg	aacagaugac	aaguugcgaa	uggagacaug	cuuccagcag	1200
gcguguaaag	guaaaauucca	agcacucugc	gagaaucccg	aguggguacc	auugaaggau	1260
aacaggauuc	cuucuuacgg	gguccugucu	guugaucuga	gucugacggg	ugagcuuaaa	1320
aucaaaaauug	cuucggggaau	cgggccauug	aucacacacg	gcucagggga	ggaccuauac	1380
aaauccaacu	gcaacaauug	guauuggcug	acuuuuccgc	caaugagaaa	ucuaagccua	1440
ggcguaauca	acacauugga	guggauaccg	agauucaagg	uuagucccaa	ccucuucacu	1500
gucccaauua	aggagcagg	cgaagacugc	caugcccaaa	cauaccuacc	ucgggaggug	1560

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gacggugaug ucaaacucag uccaaccug gugauucua cuggucaaga ucuccaaau	1620
guuuuggcaa ccuacgauac cuccaggguu gagcaugcug ugguuuaua cguuuacagc	1680
ccaagccgcu cauuuucuaa cuuuuauccu uuugguugc cuauaaaggg ggucccauc	1740
gaacuacaag uggaaugcuu cacaugggau caaaaacucu ggugccguca cuucugugug	1800
cuugcggacu cagaauccgg uggacuuauc acucacucug ggaugguggg caugggaguc	1860
agcugcacag cuaccggga agauggaacc aaucgcagau aaugauaaua ggcuggagcc	1920
ucgguggcca aguuucuuug cccuugggoc uccccccagc cccuucccc cuuccugca	1980
ccguacccc guggucuuug auaaaagucu gagugggagg caaaaaaaaa aaaaaaaaa	2040
aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa	2100
aaaaaaaaa aaaaaaaaa aucuag	2126

<210> SEQ ID NO 78

<211> LENGTH: 2065

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 78

ucaagcuuuu ggaccucug acagaagcua auacgacua cuauagggaa auagagaga	60
aaagaagagu aagaagaaau auagagcca ccaugcacc acaacgagc cggauaaau	120
ccuucacaa agacaacccc cauccuagg gaaguaggau aguuuuuac agagaacuc	180
uuauauuga uagaccuuau guuuugcugg cuguucuuu cgucauguuu cugagcuuga	240
ucggguugcu agccauugca ggcuuuagac uucaucgggc agccaucuac accgcagaga	300
uccauaaaag ccucagcacc aaucuggaug uaacuaacuc aaucgagcau cagguaagg	360
acgugcugac accacucuc aagaucucg gugaugaagu gggcuaggg acaccucaga	420
gauucacuga ccuagugaag uucaucucug acaaguuua auuccuuau cgggacagg	480
aaucgacuu cagagaucuc acuuugggua ucaacccgcc agagagaauc aaauuggauu	540
augaucaua cugugcagau guggucugc aagaacucau gaaugcauu gugaacuaa	600
cucuacugga gaccagggca accaaucagu uccuagcugu cucaaaggga aacugcucag	660
ggcccacuaa aaucagaggc caauucuaa acaugcgcg gucccugug gacuuguuu	720
uaagucgagg uuacaauug ucaucuaug ucaucaugac aucccaggga auguacggg	780
gaacuuaccu aguggaaaag ccuaaucuga gcagcaagg gucagaguug ucacaacuga	840
gcaugcaccg aguguuugaa guagguguua ucagaaaucc ggguuugggg gcuccgguu	900
uccauaugac aaacuucuu gagcaaccag ucaguauga uuucagcaac ugcauggug	960
cuuuggggga gcucaaguuc gcagcccucu gucacaggga agauucuauc acauucccu	1020
aucagggauc agggaaaaggu gucagcuucc agcuuguca gcuagguguc uggaaaucc	1080
caaccgacau gcaaucugg guccccuau caacggaga uccagugua gacaggcuuu	1140
accucucuc ucacagagc guuaucgug acaaucaagc aaaaugggcu gucccgaca	1200
caaggacaga ugacaaguug cgaugggaga caugcuucca gcaggcgugu aaggguaaa	1260
uccaagcacu uugcgagaau cccgagugga caccuugaa ggauaacagg auuccuuc	1320
acggggucuu gucugugau cugagucuga caguugagcu uaaaaucaaa auuguuucag	1380

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gauucggggcc auugaucaca cacgguucag ggauggaccu auacaaaacc aaccacaaca	1440
auauguaauug gcugacuauc ccgccaauga agaaccuggc cuuaggugua aucaacacau	1500
uggaguggau accgagauuc aagguuaguc ccaaccucu cacugucca auuaaggaag	1560
caggcgagga cugccaugcc ccaacauacc uaccugcgga gguggauggu gaugucaaac	1620
ucaguuccaa ucuggugauu cuaccugguc aagaucucca auauguucug gcaaccuacg	1680
auacuuccag aguugaacau gcuguaguuu auuacguua cagcccaagc cgcucuuuu	1740
cuuacuuuuu uccuuuuagg uugccuguaa ggggggucce cauugaauua caaguggaau	1800
gcuucacauug ggacaaaaa cucuggugcc gucacuucug ugugcuugcg gacucagaau	1860
cugguggaca uaucacucac ucugggaugg ugggcauggg agucagcugc acagccacuc	1920
gggaagauug aaccagccgc agauagugau auuagggcug agccucggug gccaaagcuc	1980
uugcccccug ggccuccccc cagcccuccc ucccccuccc gcacccgua ccccgugguc	2040
uuugaauaaa gucugagugg ggggc	2065

<210> SEQ ID NO 79

<211> LENGTH: 1854

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 79

augucaccac aacgagaccg gauaaaugcc uucuacaaag acaaccccc auccaagggg	60
aguaggaug uuuuuacag agaacaucuu augauugaua gaccuuauu uuugcuggcu	120
guucuaauug ucauguuucu gagcuugauc gggguugcuag ccuuugcagg cauuagacuu	180
caucgggcag ccacucacac cgcagagauc cauaaaagcc ucagcacc aa ucuggaugua	240
acuaacuc aa ucgagcauca gguuaaggac gugcugacac cacucuuca gaucaucggg	300
gaugaagugg gcuugaggac accucagaga uucacugacc uagugaaguu caucucugac	360
aagauuuuuu uccuuuuacc ggcaggggaa uacgaucuca gagaucucac uugguguauc	420
aaccgcacc agagaaucaa auuggauuuu gaucaauacu gugcagaugu ggcugcugaa	480
gaacucauga augcauuggu gaacucaacu cuacuggaga ccagggcaac caaucaguuc	540
cuagcugucu caaagggaaa cugcucaggg cccacuacaa ucagaggcca auucuaaac	600
augucgcugu cccuguugga cuuguauuu agucgagguu acaauguguc aucuauaguc	660
acuaugacau cccagggaa guacggggga acuuaccuag uggaaaagcc uaaucugagc	720
agcaaaaggu cagaguuguc acaacugagc augcacagag uguuuagaagu agguguuau	780
agaaauccgg guuuuggggc uccgguaauc cauaugacaa acuaucuuuga gcaaccaguc	840
aguaaaguu ucagcaacug caugguggcu uugggggagc ucaaguucgc agcccucugu	900
cacaggggag auucuaucac aaaucccuau cagggauacg ggaaaggugu cagcuuccag	960
cuugucaagc uaggugucug gaaaucucca accgacaugc aaucugggu ccccuauca	1020
acggauauc cagugauaga caggcuuuac cucucaucuc acagaggcgu uaucgcugac	1080
aaucaagcaa auugggcugu cccgacaaca cggacagaug acaaguugcg auuggagaca	1140
ugcuuccagc aggcguguaa ggguaaaauc caagcucu ugcgagaaucc cgaguggaca	1200
ccauugaagg auaacaggau uccuucuauc ggggucuuu cuguugaucu gagucugaca	1260

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guugagcuua aaaucaaaa uguuucagga uuogggccau ugaucaacac cgguucaggg	1320
auggaccuau acaaaucaca ccacaacaau auguauuggc ugacuauccc gccaaugaag	1380
aaccuggccu uagguguaau caacacauug gaguggauac cgagauucaa gguuaguccc	1440
aaccucuua cuguuccaau uaaggaagca ggcgaggacu gccaugcccc aacauaccua	1500
ccugcggagg uggauugga ugucaaacuc aguuccaac uggugauucu accuggucaa	1560
gaucuccaau auguucuggc aaccuacgau acuuccagag uugaacaugc uguaguuuau	1620
uacguuuaca gcccaagccg cucuuuuuu uacuuuuuac cuuuuagguu gccuguaagg	1680
ggggucccca uugaauuaca aguggaauug uucacauggg accaaaaacu cuggugccgu	1740
cacuucugug ugcuugcgga cucagaauuc gguggacaua ucacucacuc ugggauggug	1800
ggcaugggag ucagcugcac agccacucgg gaagauggaa ccagccgcag auag	1854

<210> SEQ ID NO 80

<211> LENGTH: 2126

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 80

gggaaauaa gagagaaaag aagaguaaga agaaauuaa gagccaccu gucaccacaa	60
cgagaccgga uaaaugccu cuacaagac aacccccauc cuaagggag uaggauaguu	120
auaaacagag aacauuuau gauugauaga ccuuauuuu ugcuugcugu ucuaucguc	180
auguuucuga gcuugaucgg guugcuagcc auugcaggca uuagacuua ucgggcagcc	240
aucuacaccg cagagaucca uaaaagccuc agcaccaac uggauguaac uaacucauc	300
gagcaucagg uuaagagcgu gcugacacca cucuuaaga ucaucgguga ugaagugggc	360
uugaggcac cucagagau cacugaccua gugaaguua ucucugacaa gauuaaauc	420
cuuaauccgg acagggaaau cgacuucaga gaucucacuu gguguaucua cccgccagag	480
agaaucaaa uggauuauga ucaauacgu gcagaugugg cugcugaaga acucaugaau	540
gcauugguga acucaacuc acuggagacc agggcaacca aucaguuccu agcugucua	600
aagggaacu gcucagggcc cacuacauc agaggccaau ucuaaaacu gucgucugcc	660
cuguuggacu uguauuaag ucgagguuac aaugugucuu cuauagucac uaugacauc	720
cagggaaugu acgggggaac uuaccuagug gaaaagccua aucugagcag caaagggua	780
gaguuugcac aacugagcau gcaccgagug uuugaaguag guuuuauca gaaucgggu	840
uuggggguc cgguaaucca uaugacaaac uaucuugagc aaccagucag uaaugauuc	900
agcaacugca uggugguuuu gggggagcuc aaguucgcag ccucucuga cagggagau	960
ucuaucacaa uucccuauca gggauacagg aaaggguca gcuuccagcu ugucaagcu	1020
ggugucugga aaucaccaac cgacaugca uccugggucc ccuaucacac ggaugauca	1080
gugauagaca ggcuuuaccu cucaucucac agaggcgua ucgucugacaa ucaagcaaaa	1140
ugggcugucc cgacaacacg gacagauagc aaguugcgaa uggagacaug cuuccagcag	1200
gcguguaagg guaaaaucca agcacuuugc gagaaucccg aguggacacc auugaaggau	1260
aacaggauuc cuucauacgg ggcuuugcu guugaucuga gucugacagu ugagcuuaaa	1320
aucaaaaauug uuucaggaau cgggccauug aucacacacg guucagggau ggaccuauac	1380

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aaauccaacc	acaacaauau	guauuggcug	acuauccegc	caaugaagaa	ccuggccuaa	1440
gguguauuca	acacauugga	guggauaccg	agauucaagg	uuaguccaa	ccucucacu	1500
guuccaaaua	aggaagcagg	cgaggacugc	caugcccaa	cauaccuacc	ugcggaggug	1560
gauggugaug	ucaaacucag	uuccaaucug	gugauucua	cuggucaaga	ucuccaaau	1620
guucuggcaa	ccuacgauac	uuccagaguu	gaacaugcug	uaguuuaua	cguuuacagc	1680
ccaagccgcu	cauuuucua	cuuuuauccu	uuuaggguug	cuguaagggg	gguccccauu	1740
gaauuacaag	uggaaugcuu	cacauuggac	caaaaacucu	ggugccguca	cuucugugug	1800
cuugcggacu	cagaauucgg	uggacauauc	acucacucug	ggaugguggg	caugggaguc	1860
agcugcacag	ccacucggga	agauuggaac	agccgcagau	agugauaua	ggcuggagcc	1920
ucgguggcca	agcuucugc	ccuuggggcc	uccccccagc	ccuuccuccc	cuuccugcac	1980
ccguaccccc	guggucuuug	auaaaagucu	gaguggggcg	caaaaaaaaa	aaaaaaaaaa	2040
aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	2100
aaaaaaaaaa	aaaaaaaaaa	aucuag				2126

<210> SEQ ID NO 81

<211> LENGTH: 1729

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 81

ucaagcuuuu	ggacccucgu	acagaagcua	auacgacuca	cuauagggaa	auaagagaga	60
aaagaagagu	aagaagaaau	auaagagcca	ccauggcaca	agucuuuuu	acaaacagcc	120
ugucgcuguu	gaccccaauu	aaccugaaca	auucccaguc	cgcacugggc	acugcuaucg	180
agcguuuguc	uuccggucug	cguaucaaca	gcgcgaaaga	cgauccggca	ggacagggca	240
uugcuaccgg	uuuuaccggc	aacaucaaa	gucugacuca	ggcuucccgu	aacgcuaacg	300
acgguaucuc	cauugcgcag	accacugaag	ggcgcugaa	cgaaaaaac	aacaaccugc	360
agcugugcgc	ugaacuggcg	guucagucug	cgaauggua	uaacucccag	ucugaccucg	420
acuccaucca	ggcugaaau	accacagcgc	ugaacgaaau	cgaccgugua	uccggccaga	480
cucaguucua	cgccgugaaa	guccuggcgc	aggacaacac	ccugaccauc	cagguuggug	540
ccaacgacgg	ugaaacuauc	gauauugauu	uaaaagaaau	cagcucuaaa	acacugggac	600
uugauaagcu	uaauguccaa	gaugccuaca	ccccgaaaga	aacugcugua	accguugaua	660
aaacuaccua	uaaaaauggu	acagaucua	uuacagccca	gagcauuacu	gauauccaaa	720
cugcaauugg	cgguugggca	acggggguua	cuggggcuga	uaucauuuu	aaagaugguc	780
aaacuauuuu	agauguuuuu	ggcggugcuu	cugcuggugu	uuuuuuagcc	acuuuugaug	840
aaacuacaaa	gaaaguuuuu	auugauacga	cugauuuuac	uccguuggca	acugcgggag	900
cuacagcuau	ucgggggaa	gccacuauaa	cccacaacca	aaaugcugaa	guaacaaaag	960
aggguguuua	uacgaccaca	guugcggcuc	aacuuugcuc	agcagggguu	acuggcggcc	1020
auaaggacaa	uacuagccuu	guuuuacuu	cguuuaggga	uaaaacgggu	aagguuuuug	1080
augguggcua	ugcagugaaa	augggcgagc	auuuuauugc	cgcuacuuuu	gaugagaaaa	1140
caggugcauu	uacugcuuuu	accacuacuu	auacagaugg	uacuggcguu	gcucuaaacug	1200

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gagcugugaa auuugguggc gcaaauggua aaucugaagu uguuacugcu accgauggua	1260
agacuuaacu agcaagcgac cuugacaaac auaacuucag aacagggcgu gagcuuaag	1320
agguuaauac agauaagacu gaaaaccac ugcagaaaau ugaugcugcc uggcacagg	1380
uugauacacu uoguucugac cugggugcgg uucagaaccg uuucaacucc gcuaucacca	1440
accugggcaa uaccguaaa aaccugucuu cugcccguag ccguaucgaa gauuccgacu	1500
acgcaaccga agucuccaac augucucgcg cgcagauucu gcagcaggcc gguaccuccg	1560
uucuggcgca gggaaccag guuocgcaa acgucucuc uuuaucugcu ugauauagg	1620
cuggagccuc gguggccaug cuucucgccc cuugggccuc ccccagccc cuccucccu	1680
uucugcacc cguaccccg ugcuuugaa uaaagucuga guggggcgc	1729

<210> SEQ ID NO 82

<211> LENGTH: 1518

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 82

auggcacaag ucauuauac aaacagccug ugcuguuuga cccagaauaa ccugaacaaa	60
ucccaguccg cacugggcac ugcuaucgag cguuugucuu ccgucucgcu uaucaacagc	120
gcgaaagac augcggcagg acagggcgaau gcuaaccguu uuaccgcgaa caucaaaaggu	180
cugacucagg cuuuccguaa cgcuaacgac gguaucucca uugcgcagac cacugaaggc	240
gcgcugaacg aaaucaacaa caaccugcag cguugcgcug aacuggcggc ucagucucg	300
aaugguacua acucccaguc ugaccucgac uccauccagg cugaaaucac ccagcgcucg	360
aacgaaaucg accguguauc cggccagacu caguucaacg gcgugaaagu ccuggcgcag	420
gaccaacccc ugaccuucca gguuggugcc aacgacggug aaacuaucga uauugauua	480
aaagaaauca gcucuaaaac acugggacuu gaaagcuua auguccaaga ugccuacacc	540
ccgaaagaaa cugcuguaac cguugauaaa acuaaccuaa aaaaugguac agauccuauu	600
acagcccaga gcaauacuga uauccaaacu gcaauuggcg guggugcaac gggguuacu	660
ggggcugaua ucaaauuuaa agauggucaa uacuauuug auguuuaagg cggugcuucu	720
gcugguguuu auaaagccac uuauaugaa acuaacaaga aaguuauuu ugauacgacu	780
gaaaaaacuc cguuggcaac ugcggaagcu acagcuauuc ggggaacggc cacuaaacc	840
cacaacccaa uugcugaagu aacaaaagag gguguugaua cgaccacagu ugcggcucaa	900
cuugcugcag cagggguuac uggcgcggau aaggacaaua cuagccuugu aaaaauaucg	960
uuugaggaua aaaaagguaa gguuuuugau gguggcuau cagugaaaau gggcgcagau	1020
uucuaugccg cuacauauga ugagaaaaca ggugcaaua cugcuaaaac cacuacuauu	1080
acagauggua cuggcguugc ucaaacugga gcugugaaau ugguggcgc aaauguaaa	1140
ucugaaguug uuacugcuac cgaugguaag acuuacuua cgaagcaccu ugacaaacau	1200
aacuucagaa cagggcguga gcuaaaagag guuaauacag auuagacuga aaaccacug	1260
cagaaaauug augcugccuu ggcacagguu gauacacuuc guucugaacc gggugcgguu	1320
cagaaccguu ucaacucgcg uacaccaac cugggcaua ccguaaaaua ccugcuucu	1380
gcccguagcc guaucgaaga uuccgacuac gcaaccgaag ucuccaaau gucucgcgcg	1440

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cagauucugc agcagggccgg uaccuccguu cuggcgcagg cgaaccaggu uccgcaaac 1500
guccucucu uacugcgu 1518

<210> SEQ ID NO 83
<211> LENGTH: 1790
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 83
ggggaaauaa gagagaaaag aagaguaaga agaaaauaaa gagccaccau ggcacaaguc 60
auuaauacaa acagccuguc gcuguugacc cagaauaac ugaacaaauc ccaguccgca 120
cugggcacug cuaucgagcg uuugucuucc ggucugcgua ucaacagcgc gaaagagau 180
gcggcaggac aggcgauugc uaaccguuuu acccgcaaca ucaaaggucu gacucaggcu 240
ucccguaacg cuaacgacgg uaucuccauu gcgcagacca cugaaggcgc gcugaacgaa 300
aucaacaaca accugcagcg ugugcgugaa cuggcgguuc agucugcgaa ugnuacuaac 360
ucccagucug accucgacuc cauccaggcu gaaucacccc agcgcugaa cgaauccgac 420
cguguaucgg gccagacuca guucaacggc gugaagucc uggcgcagga caacaccucg 480
accauccagg uuggugccaa cgaocggugaa acuaucgaua uugauuuaaa agaaucagc 540
ucuaaaacac ugggacuuga uaagcuuaau guccaagau ccaacacccc gaaagaaacu 600
gcuguaaccg uugauaaaac uaccuauaaa aaugguacag auccuauuac agcccagagc 660
aaucugaua uccaaacugc aauggcgggu ggugcaacgg ggguuacugg ggcugauauc 720
aaauuuuaag auggucauaa cuuuuugau guuaaaggcg gugcuucugc ugguguuuau 780
aaagccacu uauguaaac uacaaagaaa guuaauuug auacgacuga uaaaacuccg 840
uuggcaacug cggaaagcuac agcuuuucgg ggaacggcca cuuaaccca caaccaaau 900
gcugaaguaa caaaagaggg uguugauacg accacaguu gggcucaacu ucugcagca 960
gggguuacug gcgocgauaa ggaacaauacu agccuuguaa aacuaucguu ugaggauaaa 1020
aacguaagg uuauugaugg uggcuaugca gugaauaugg gcgacgauuu cuaugccgcu 1080
acauaugaug agaaacagg ucuaauuacu gcuaaaacca cuacuuauc agaugguacu 1140
ggcguugcuc aaacuggagc ugugaaauuu gguggcgcga augguaauc ugaaguuguu 1200
acugcuaccg augguaagac uuacuuagca agcgaaccuug acaaacuaa cuucagaaca 1260
ggcggugagc uuaaagaggu uaauacagau aagacugaaa acccaccgca gaaaauugau 1320
gcugccuugg cacagguuga uacacuucgu ucugaccugg gugcgguuca gaaccguuuc 1380
aacuccgcu uacccaaccu gggcaauacc guaaaauacc ugucuuucgc ccguagccgu 1440
aucgaagauu ccgacuacgc aaccgaaguc uccaacaugu cucgcgcgca gauucugcag 1500
caggccggua ccuccguucu ggcgcaggcg aaccaggguu cgcaaacgcu ccucucuuu 1560
cugcguugau aaauaggcug agccucggug gccaugcuuc uugccccuug ggcucccccc 1620
cagcccccuc uccccuuccu gcaaccguac ccccgugguc uuugaauaaa gucugagugg 1680
gcggcaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1740
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaucua 1790

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<210> SEQ ID NO 84

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Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320
 Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335
 Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350
 Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365
 Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380
 Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400
 Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415
 Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430
 Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445
 Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
 450 455 460
 Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480
 Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495
 Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510
 Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525
 Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
 530 535

<210> SEQ ID NO 86

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 86

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15
 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30
 Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
 35 40 45
 Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50 55 60
 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80
 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95
 Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110

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Ala	Ala	Ala	Ala	Ala	Val	Thr	Ala	Gly	Val	Ala	Ile	Cys	Lys	Thr	Ile
		115					120					125			
Arg	Leu	Glu	Ser	Glu	Val	Thr	Ala	Ile	Asn	Asn	Ala	Leu	Lys	Lys	Thr
	130					135					140				
Asn	Glu	Ala	Val	Ser	Thr	Leu	Gly	Asn	Gly	Val	Arg	Val	Leu	Ala	Thr
145					150					155					160
Ala	Val	Arg	Glu	Leu	Lys	Asp	Phe	Val	Ser	Lys	Asn	Leu	Thr	Arg	Ala
				165					170					175	
Ile	Asn	Lys	Asn	Lys	Cys	Asp	Ile	Asp	Asp	Leu	Lys	Met	Ala	Val	Ser
			180					185					190		
Phe	Ser	Gln	Phe	Asn	Arg	Arg	Phe	Leu	Asn	Val	Val	Arg	Gln	Phe	Ser
		195					200					205			
Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Thr	Asp
	210					215					220				
Ala	Glu	Leu	Ala	Arg	Ala	Val	Pro	Asn	Met	Pro	Thr	Ser	Ala	Gly	Gln
225					230					235					240
Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe
				245					250					255	
Gly	Ile	Leu	Cys	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln
			260					265					270		
Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala
		275					280					285			
Ala	Pro	Ser	Cys	Ser	Glu	Lys	Lys	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
	290					295					300				
Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Gln	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
305					310					315					320
Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp
				325					330					335	
Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Lys	Glu	Cys	Asn	Ile
			340					345					350		
Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
		355					360					365			
Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
	370					375					380				
Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile
385					390					395					400
Lys	Gln	Leu	Asn	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
				405					410					415	
Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
			420					425					430		
Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
		435					440						445		
Ile	Lys	Phe	Pro	Glu	His	Gln	Trp	His	Val	Ala	Leu	Asp	Gln	Val	Phe
	450					455					460				
Glu	Asn	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Arg	Ile
465					470					475					480
Leu	Ser	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile
				485					490					495	
Leu	Ile	Ala	Val	Leu	Gly	Ser	Ser	Met	Ile	Leu	Val	Ser	Ile	Phe	Ile
			500					505					510		
Ile	Ile	Lys	Lys	Thr	Lys	Lys	Pro	Thr	Gly	Ala	Pro	Pro	Glu	Leu	Ser

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325					330					335					
Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Lys	Glu	Cys	Asn	Ile
			340						345					350	
Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
		355					360					365			
Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
		370				375					380				
Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile
385						390					395				400
Lys	Gln	Leu	Asn	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
				405					410					415	
Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
			420					425						430	
Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
		435					440						445		
Ile	Lys	Phe	Pro	Glu	Asp	Gln	Phe	Gln	Val	Ala	Leu	Asp	Gln	Val	Phe
	450					455					460				
Glu	Asn	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Arg	Ile
465				470							475				480
Leu	Ser	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile
				485					490					495	
Leu	Ile	Ala	Val	Leu	Gly	Ser	Ser	Met	Ile	Leu	Val	Ser	Ile	Phe	Ile
			500					505						510	
Ile	Ile	Lys	Lys	Thr	Lys	Lys	Pro	Thr	Gly	Ala	Pro	Pro	Glu	Leu	Ser
		515					520						525		
Gly	Val	Thr	Asn	Asn	Gly	Phe	Ile	Pro	His	Asn					
	530					535									

<210> SEQ ID NO 88

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 88

Met	Ser	Trp	Lys	Val	Val	Ile	Ile	Phe	Ser	Leu	Leu	Ile	Thr	Pro	Gln
1				5						10				15	
His	Gly	Leu	Lys	Glu	Ser	Tyr	Leu	Glu	Glu	Ser	Cys	Ser	Thr	Ile	Thr
			20					25					30		
Glu	Gly	Tyr	Leu	Ser	Val	Leu	Arg	Thr	Gly	Trp	Tyr	Thr	Asn	Val	Phe
		35						40					45		
Thr	Leu	Glu	Val	Gly	Asp	Val	Glu	Asn	Leu	Thr	Cys	Ser	Asp	Gly	Pro
		50					55					60			
Ser	Leu	Ile	Lys	Thr	Glu	Leu	Asp	Leu	Leu	Lys	Ser	Ala	Leu	Arg	Glu
65					70					75				80	
Leu	Lys	Thr	Val	Ser	Ala	Asp	Gln	Leu	Ala	Arg	Glu	Glu	Gln	Ile	Glu
				85					90					95	
Asn	Pro	Gly	Ser	Gly	Ser	Phe	Val	Leu	Gly	Ala	Ile	Ala	Leu	Gly	Val
				100					105					110	
Ala	Ala	Ala	Ala	Ala	Val	Thr	Ala	Gly	Val	Ala	Ile	Ala	Lys	Thr	Ile
				115				120					125		
Arg	Leu	Glu	Ser	Glu	Val	Thr	Ala	Ile	Asn	Asn	Ala	Leu	Lys	Lys	Thr

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130				135				140							
Asn	Glu	Ala	Val	Ser	Thr	Leu	Gly	Asn	Gly	Val	Arg	Val	Leu	Ala	Thr
145					150				155						160
Ala	Val	Arg	Glu	Leu	Lys	Asp	Phe	Val	Ser	Lys	Asn	Leu	Thr	Arg	Ala
			165						170					175	
Ile	Asn	Lys	Asn	Lys	Cys	Asp	Ile	Pro	Asp	Leu	Lys	Met	Ala	Val	Ser
			180						185				190		
Phe	Ser	Gln	Phe	Asn	Arg	Arg	Phe	Leu	Asn	Val	Val	Arg	Gln	Phe	Ser
		195					200						205		
Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Thr	Asp
	210					215					220				
Ala	Glu	Leu	Ala	Arg	Ala	Val	Pro	Asn	Met	Pro	Thr	Ser	Ala	Gly	Gln
225					230					235					240
Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe
			245						250					255	
Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln
		260					265						270		
Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala
		275					280						285		
Ala	Pro	Ser	Cys	Ser	Glu	Lys	Lys	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
	290					295					300				
Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Gln	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
305					310					315					320
Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp
			325						330					335	
Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Lys	Glu	Cys	Asn	Ile
			340						345				350		
Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
		355					360						365		
Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
	370					375					380				
Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile
385					390					395					400
Lys	Gln	Leu	Asn	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
			405						410					415	
Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
			420						425				430		
Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
		435					440						445		
Ile	Lys	Phe	Pro	Glu	Asn	Gln	Phe	Gln	Val	Ala	Leu	Asp	Gln	Val	Phe
	450				455						460				
Glu	Asn	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Arg	Ile
465					470					475					480
Leu	Ser	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile
			485						490					495	
Leu	Ile	Ala	Val	Leu	Gly	Ser	Ser	Met	Ile	Leu	Val	Ser	Ile	Phe	Ile
			500						505				510		
Ile	Ile	Lys	Lys	Thr	Lys	Lys	Pro	Thr	Gly	Ala	Pro	Pro	Glu	Leu	Ser
		515					520						525		
Gly	Val	Thr	Asn	Asn	Gly	Phe	Ile	Pro	His	Asn					
	530					535									

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<210> SEQ ID NO 89
<211> LENGTH: 539
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 89
Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1          5          10          15
His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
20          25          30
Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35          40          45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
50          55          60
Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu
65          70          75          80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
85          90          95
Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100         105         110
Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
115         120         125
Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
130         135         140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145         150         155         160
Ala Val Arg Glu Leu Lys Asp Phe Val Leu Lys Asn Leu Thr Arg Ala
165         170         175
Ile Asn Lys Asn Lys Cys Asp Ile Pro Asp Leu Lys Met Ala Val Ser
180         185         190
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
195         200         205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
210         215         220
Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
225         230         235         240
Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
245         250         255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
260         265         270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
275         280         285
Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
290         295         300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305         310         315         320
Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
325         330         335
Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
340         345         350

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Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
  355                               360                               365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
  370                               375                               380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
  385                               390                               395                               400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                               405                               410                               415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
  420                               425                               430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
  435                               440                               445

Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe
  450                               455                               460

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
  465                               470                               475                               480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
                               485                               490                               495

Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
  500                               505                               510

Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
  515                               520                               525

Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
  530                               535

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<210> SEQ ID NO 90

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 90

```

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
  1           5           10           15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
  20           25           30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
  35           40           45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
  50           55           60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu
  65           70           75           80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
  85           90           95

Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
  100          105          110

Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
  115          120          125

Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
  130          135          140

Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
  145          150          155          160

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Ala Val Arg Glu Leu Lys Asp Phe Val Leu Lys Asn Leu Thr Arg Ala
165 170 175

Ile Asn Lys Asn Lys Cys Asp Ile Pro Asp Leu Lys Met Ala Val Ser
180 185 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
195 200 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
210 215 220

Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
225 230 235 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
245 250 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
260 265 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
275 280 285

Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
290 295 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305 310 315 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
325 330 335

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
340 345 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
355 360 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
370 375 380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385 390 395 400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
405 410 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
420 425 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
435 440 445

Ile Lys Phe Pro Glu Asn Gln Phe Gln Val Ala Leu Asp Gln Val Phe
450 455 460

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465 470 475 480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
485 490 495

Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
500 505 510

Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
515 520 525

Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
530 535

<210> SEQ ID NO 91

<211> LENGTH: 539

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 91

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1           5           10           15
His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
           20           25           30
Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
           35           40           45
Thr Leu Pro Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50           55           60
Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu
 65           70           75           80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
           85           90           95
Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
          100          105          110
Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
          115          120          125
Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
          130          135          140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
          145          150          155          160
Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
          165          170          175
Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
          180          185          190
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
          195          200          205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
          210          215          220
Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
          225          230          235          240
Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
          245          250          255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
          260          265          270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
          275          280          285
Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
          290          295          300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
          305          310          315          320
Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
          325          330          335
Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
          340          345          350
Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
          355          360          365

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Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
      180      185      190
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
      195      200      205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
      210      215      220
Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
      225      230      235
Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
      245      250      255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
      260      265      270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
      275      280      285
Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
      290      295      300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
      305      310      315
Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
      325      330      335
Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
      340      345      350
Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
      355      360      365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
      370      375      380
Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
      385      390      395
Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
      405      410      415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
      420      425      430
Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
      435      440      445
Ile Lys Phe Pro Glu Asn Gln Phe Gln Val Ala Leu Asp Gln Val Phe
      450      455      460
Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
      465      470      475
Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
      485      490      495
Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
      500      505      510
Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
      515      520      525
Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
      530      535

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<210> SEQ ID NO 93

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

-continued

<400> SEQUENCE: 93

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15
 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30
 Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
 35 40 45
 Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50 55 60
 Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu
 65 70 75 80
 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95
 Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110
 Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125
 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140
 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160
 Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
 165 170 175
 Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
 180 185 190
 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205
 Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220
 Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240
 Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
 245 250 255
 Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
 260 265 270
 Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285
 Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300
 Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320
 Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335
 Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350
 Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365
 Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380
 Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile

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385                390                395                400
Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                410                415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
                420                425                430
Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
                435                440                445
Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe
                450                455                460
Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
                465                470                475                480
Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
                485                490                495
Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
                500                505                510
Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
                515                520                525
Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
                530                535

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<210> SEQ ID NO 94

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 94

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Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1                5                10                15
His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
                20                25                30
Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
                35                40                45
Thr Leu Glu Val Gly Asp Leu Glu Asn Leu Thr Cys Ser Asp Gly Pro
50                55                60
Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                70                75                80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                90                95
Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100                105                110
Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
115                120                125
Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
130                135                140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145                150                155                160
Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
165                170                175
Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
180                185                190
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser

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195					200					205					
Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Thr	Asp
210						215					220				
Ala	Glu	Leu	Ala	Arg	Ala	Val	Pro	Asn	Met	Pro	Thr	Ser	Ala	Gly	Gln
225					230					235					240
Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe
				245					250					255	
Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln
		260						265					270		
Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala
		275					280						285		
Ala	Pro	Ser	Cys	Ser	Glu	Lys	Lys	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
	290					295					300				
Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Gln	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
305					310					315					320
Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp
				325					330					335	
Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Lys	Glu	Cys	Asn	Ile
			340					345					350		
Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
		355					360						365		
Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
	370					375					380				
Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile
385					390					395					400
Lys	Gln	Leu	Asn	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
				405					410					415	
Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
			420					425					430		
Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
		435					440						445		
Ile	Lys	Phe	Pro	Glu	Asp	Gln	Phe	Gln	Val	Ala	Leu	Asp	Gln	Val	Phe
	450				455						460				
Glu	Asn	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Arg	Ile
465					470					475					480
Leu	Ser	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile
				485					490					495	
Leu	Ile	Ala	Val	Leu	Gly	Ser	Ser	Met	Ile	Leu	Val	Ser	Ile	Phe	Ile
		500						505					510		
Ile	Ile	Lys	Lys	Thr	Lys	Lys	Pro	Thr	Gly	Ala	Pro	Pro	Glu	Leu	Ser
		515					520						525		
Gly	Val	Thr	Asn	Asn	Gly	Phe	Ile	Pro	His	Asn					
	530					535									

<210> SEQ ID NO 95

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 95

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln

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1	5	10	15
His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr	20	25	30
Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe	35	40	45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro	50	55	60
Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu	65	70	75
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu	85	90	95
Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val	100	105	110
Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile	115	120	125
Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr	130	135	140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr	145	150	155
Ala Val Arg Glu Leu Lys Asp Phe Val Leu Lys Asn Leu Thr Arg Ala	165	170	175
Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser	180	185	190
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser	195	200	205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp	210	215	220
Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln	225	230	235
Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe	245	250	255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln	260	265	270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala	275	280	285
Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg	290	295	300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr	305	310	315
Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp	325	330	335
Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile	340	345	350
Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His	355	360	365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys	370	375	380
Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile	385	390	395
Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp	405	410	415

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Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445

Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495

Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510

Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525

Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
 530 535

<210> SEQ ID NO 96
 <211> LENGTH: 539
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 96

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
 35 40 45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50 55 60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95

Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110

Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125

Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140

Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160

Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Trp Arg Ala
 165 170 175

Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
 180 185 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220

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Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
 245 250 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
 260 265 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285

Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445

Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495

Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510

Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525

Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
 530 535

<210> SEQ ID NO 97

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 97

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30

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Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445
 Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460
 Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480
 Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495
 Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510
 Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525
 Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
 530 535

<210> SEQ ID NO 98
 <211> LENGTH: 539
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 98

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15
 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30
 Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
 35 40 45
 Thr Leu Pro Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50 55 60
 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80
 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95
 Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110
 Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125
 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140
 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160
 Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
 165 170 175
 Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
 180 185 190
 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205
 Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220
 Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240

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Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
      245                               250                255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
      260                               265                270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
      275                               280                285

Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
      290                               295                300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
      305                               310                315                320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
      325                               330                335

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
      340                               345                350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
      355                               360                365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
      370                               375                380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
      385                               390                395                400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
      405                               410                415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
      420                               425                430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
      435                               440                445

Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe
      450                               455                460

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
      465                               470                475                480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
      485                               490                495

Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
      500                               505                510

Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
      515                               520                525

Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
      530                               535

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<210> SEQ ID NO 99

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 99

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Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1      5      10      15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
      20      25      30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
      35      40      45

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Thr	Leu	Glu	Val	Gly	Asp	Val	Glu	Asn	Leu	Thr	Cys	Ser	Asp	Gly	Pro
50						55					60				
Ser	Leu	Ile	Lys	Thr	Glu	Leu	Asp	Leu	Thr	Lys	Ser	Ala	Leu	Arg	Glu
65					70					75					80
Leu	Lys	Thr	Val	Ser	Ala	Asp	Gln	Leu	Ala	Arg	Glu	Glu	Gln	Ile	Glu
				85					90					95	
Asn	Pro	Gly	Ser	Gly	Ser	Phe	Val	Leu	Gly	Ala	Ile	Ala	Leu	Gly	Val
			100					105					110		
Ala	Ala	Ala	Ala	Ala	Val	Thr	Ala	Gly	Val	Ala	Ile	Ala	Lys	Thr	Ile
			115				120					125			
Arg	Leu	Glu	Ser	Glu	Val	Thr	Ala	Ile	Asn	Asn	Ala	Leu	Lys	Lys	Thr
	130					135					140				
Asn	Glu	Ala	Val	Ser	Thr	Leu	Gly	Asn	Gly	Val	Arg	Val	Leu	Ala	Thr
145					150					155					160
Ala	Val	Arg	Glu	Leu	Lys	Asp	Phe	Val	Ser	Lys	Asn	Leu	Thr	Arg	Ala
				165					170					175	
Ile	Asn	Lys	Asn	Lys	Cys	Asp	Ile	Pro	Asp	Leu	Lys	Met	Ala	Val	Ser
			180					185					190		
Phe	Ser	Gln	Phe	Asn	Arg	Arg	Phe	Leu	Asn	Val	Val	Arg	Gln	Phe	Ser
		195					200					205			
Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Thr	Asp
		210				215					220				
Ala	Glu	Leu	Ala	Arg	Ala	Val	Pro	Asn	Met	Pro	Thr	Ser	Ala	Gly	Gln
225					230					235					240
Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe
				245					250					255	
Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln
			260					265					270		
Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala
		275					280					285			
Ala	Pro	Ser	Cys	Ser	Glu	Lys	Lys	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
		290				295					300				
Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Gln	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
305					310					315					320
Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp
				325					330					335	
Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Lys	Glu	Cys	Asn	Ile
			340					345					350		
Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
			355				360					365			
Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
			370			375					380				
Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile
385					390					395					400
Lys	Gln	Leu	Asn	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
				405					410					415	
Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
			420					425					430		
Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
			435				440					445			
Ile	Lys	Phe	Pro	Glu	Asp	Gln	Phe	Gln	Val	Ala	Leu	Asp	Gln	Val	Phe

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450	455	460
Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile		
465	470	475 480
Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile		
	485	490 495
Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile		
	500	505 510
Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser		
	515	520 525
Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn		
	530	535

<210> SEQ ID NO 100

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 100

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln		
1	5	10 15
His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr		
	20	25 30
Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe		
	35	40 45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro		
	50	55 60
Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu		
	65	70 75 80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu		
	85	90 95
Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val		
	100	105 110
Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile		
	115	120 125
Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr		
	130	135 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr		
	145	150 155 160
Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala		
	165	170 175
Ile Asn Lys Asn Lys Cys Pro Ile Asp Asp Leu Lys Met Ala Val Ser		
	180	185 190
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser		
	195	200 205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp		
	210	215 220
Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln		
	225	230 235 240
Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe		
	245	250 255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln		

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260					265					270					
Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala
	275						280					285			
Ala	Pro	Ser	Cys	Ser	Glu	Lys	Lys	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
	290					295						300			
Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Gln	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
305					310					315					320
Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp
				325					330					335	
Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Lys	Glu	Cys	Asn	Ile
			340					345					350		
Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
		355					360					365			
Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
	370					375						380			
Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile
385					390					395					400
Lys	Gln	Leu	Asn	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
				405					410					415	
Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
			420					425					430		
Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
		435					440						445		
Ile	Lys	Phe	Pro	Glu	Asp	Gln	Phe	Gln	Val	Ala	Leu	Asp	Gln	Val	Phe
	450					455						460			
Glu	Asn	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Arg	Ile
465				470						475					480
Leu	Ser	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile
				485					490					495	
Leu	Ile	Ala	Val	Leu	Gly	Ser	Ser	Met	Ile	Leu	Val	Ser	Ile	Phe	Ile
		500						505					510		
Ile	Ile	Lys	Lys	Thr	Lys	Lys	Pro	Thr	Gly	Ala	Pro	Pro	Glu	Leu	Ser
		515					520					525			
Gly	Val	Thr	Asn	Asn	Gly	Phe	Ile	Pro	His	Asn					
	530					535									

<210> SEQ ID NO 101

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 101

Met	Ser	Trp	Lys	Val	Val	Ile	Ile	Phe	Ser	Leu	Leu	Ile	Thr	Pro	Gln
1				5					10					15	
His	Gly	Leu	Lys	Glu	Ser	Tyr	Leu	Glu	Glu	Ser	Cys	Ser	Thr	Ile	Thr
			20				25						30		
Glu	Gly	Tyr	Leu	Ser	Val	Leu	Arg	Thr	Gly	Trp	Tyr	Thr	Asn	Val	Phe
		35					40					45			
Thr	Leu	Glu	Val	Gly	Asp	Val	Glu	Asn	Leu	Thr	Cys	Ser	Asp	Gly	Pro
	50					55						60			
Ser	Leu	Ile	Lys	Thr	Glu	Leu	Asp	Leu	Thr	Lys	Ser	Ala	Leu	Arg	Glu

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65	70				75				80			
Leu Lys Thr	Val Ser	Ala Asp	Gln Leu	Ala Arg	Glu Glu	Gln Ile	Glu	95				
	85			90								
Asn Pro Gly	Ser Gly	Ser Phe	Val Leu	Gly Ala	Ile Ala	Leu Gly	Val	110				
	100			105								
Ala Ala Ala	Ala Ala	Val Thr	Ala Gly	Val Ala	Ile Ala	Lys Thr	Ile					
	115		120			125						
Arg Leu Pro	Ser Glu	Val Thr	Ala Ile	Asn Asn	Ala Leu	Lys Lys	Thr					
	130		135			140						
Asn Glu Ala	Val Ser	Thr Leu	Gly Asn	Gly Val	Arg Val	Leu Ala	Thr					
	145		150			155						
Ala Val Arg	Glu Leu	Lys Asp	Phe Val	Ser Lys	Asn Leu	Thr Arg	Ala					
	165			170			175					
Ile Asn Lys	Asn Lys	Cys Asp	Ile Asp	Asp Leu	Lys Met	Ala Val	Ser					
	180		185			190						
Phe Ser Gln	Phe Asn	Arg Arg	Phe Leu	Asn Val	Val Arg	Gln Phe	Ser					
	195		200			205						
Asp Asn Ala	Gly Ile	Thr Pro	Ala Ile	Ser Leu	Asp Leu	Met Thr	Asp					
	210		215			220						
Ala Glu Leu	Ala Arg	Ala Val	Pro Asn	Met Pro	Thr Ser	Ala Gly	Gln					
	225		230			235						
Ile Lys Leu	Met Leu	Glu Asn	Arg Ala	Met Val	Arg Arg	Lys Gly	Phe					
	245			250			255					
Gly Ile Leu	Ile Gly	Val Tyr	Gly Ser	Ser Val	Ile Tyr	Met Val	Gln					
	260		265			270						
Leu Pro Ile	Phe Gly	Val Ile	Asp Thr	Pro Cys	Trp Ile	Val Lys	Ala					
	275		280			285						
Ala Pro Ser	Cys Ser	Glu Lys	Lys Gly	Asn Tyr	Ala Cys	Leu Leu	Arg					
	290		295			300						
Glu Asp Gln	Gly Trp	Tyr Cys	Gln Asn	Ala Gly	Ser Thr	Val Tyr	Tyr					
	305		310			315						
Pro Asn Glu	Lys Asp	Cys Glu	Thr Arg	Gly Asp	His Val	Phe Cys	Asp					
	325			330			335					
Thr Ala Ala	Gly Ile	Asn Val	Ala Glu	Gln Ser	Lys Glu	Cys Asn	Ile					
	340		345			350						
Asn Ile Ser	Thr Thr	Asn Tyr	Pro Cys	Lys Val	Ser Thr	Gly Arg	His					
	355		360			365						
Pro Ile Ser	Met Val	Ala Leu	Ser Pro	Leu Gly	Ala Leu	Val Ala	Cys					
	370		375			380						
Tyr Lys Gly	Val Ser	Cys Ser	Ile Gly	Ser Asn	Arg Val	Gly Ile	Ile					
	385		390			395						
Lys Gln Leu	Asn Lys	Gly Cys	Ser Tyr	Ile Thr	Asn Gln	Asp Ala	Asp					
	405			410			415					
Thr Val Thr	Ile Asp	Asn Thr	Val Tyr	Gln Leu	Ser Lys	Val Glu	Gly					
	420			425			430					
Glu Gln His	Val Ile	Lys Gly	Arg Pro	Val Ser	Ser Ser	Phe Asp	Pro					
	435		440			445						
Ile Lys Phe	Pro Glu	Asp Gln	Phe Gln	Val Ala	Leu Asp	Gln Val	Phe					
	450		455			460						
Glu Asn Ile	Glu Asn	Ser Gln	Ala Leu	Val Asp	Gln Ser	Asn Arg	Ile					
	465		470			475						480

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Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
      485                               490                               495

Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
      500                               505                               510

Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
      515                               520                               525

Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
      530                               535

<210> SEQ ID NO 102
<211> LENGTH: 539
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 102

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1      5      10      15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
      20      25      30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
      35      40      45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
      50      55      60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
      65      70      75      80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
      85      90      95

Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
      100     105     110

Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
      115     120     125

Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
      130     135     140

Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
      145     150     155     160

Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
      165     170     175

Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
      180     185     190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
      195     200     205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
      210     215     220

Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
      225     230     235     240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
      245     250     255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
      260     265     270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
      275     280     285

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Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Pro Pro
 435 440 445

Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495

Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510

Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525

Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
 530 535

<210> SEQ ID NO 103

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 103

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
 35 40 45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50 55 60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95

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Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110

Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125

Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140

Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160

Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
 165 170 175

Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
 180 185 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220

Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
 245 250 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
 260 265 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285

Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445

Ile Lys Phe Pro Glu Asn Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495

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Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510

Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525

Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
 530 535

<210> SEQ ID NO 104
 <211> LENGTH: 539
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 104

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
 35 40 45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50 55 60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95

Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110

Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125

Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140

Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160

Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
 165 170 175

Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
 180 185 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220

Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
 245 250 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
 260 265 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285

Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300

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Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320
 Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335
 Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350
 Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365
 Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380
 Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400
 Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415
 Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430
 Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445
 Ile Lys Phe Pro Gln Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460
 Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480
 Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495
 Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510
 Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525
 Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
 530 535

<210> SEQ ID NO 105

<211> LENGTH: 539

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 105

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15
 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30
 Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
 35 40 45
 Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50 55 60
 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80
 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95
 Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110

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Ala	Ala	Ala	Ala	Ala	Val	Thr	Ala	Gly	Val	Ala	Ile	Ala	Lys	Thr	Ile
		115					120					125			
Arg	Leu	Glu	Ser	Glu	Val	Thr	Ala	Ile	Asn	Asn	Ala	Leu	Lys	Lys	Thr
	130					135					140				
Asn	Glu	Ala	Val	Ser	Thr	Leu	Gly	Asn	Gly	Val	Arg	Val	Leu	Ala	Thr
145					150					155					160
Ala	Val	Arg	Glu	Leu	Lys	Asp	Phe	Val	Ser	Lys	Asn	Leu	Thr	Arg	Ala
			165						170					175	
Ile	Asn	Lys	Asn	Lys	Cys	Asp	Ile	Asp	Asp	Leu	Lys	Met	Ala	Val	Ser
		180					185						190		
Phe	Ser	Gln	Trp	Asn	Arg	Arg	Phe	Leu	Asn	Val	Val	Arg	Gln	Phe	Ser
		195					200					205			
Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Thr	Asp
	210					215					220				
Ala	Glu	Leu	Ala	Arg	Ala	Val	Pro	Asn	Met	Pro	Thr	Ser	Ala	Gly	Gln
225					230					235					240
Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe
			245						250					255	
Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln
		260						265					270		
Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala
		275					280					285			
Ala	Pro	Ser	Cys	Ser	Glu	Lys	Lys	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
	290					295					300				
Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Gln	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
305					310					315					320
Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp
			325						330					335	
Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Lys	Glu	Cys	Asn	Ile
			340					345					350		
Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
		355					360					365			
Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
	370					375					380				
Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile
385					390					395					400
Lys	Gln	Leu	Asn	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
			405						410					415	
Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
			420					425					430		
Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
		435					440					445			
Ile	Lys	Phe	Pro	Glu	Asp	Gln	Phe	Gln	Val	Ala	Leu	Asp	Gln	Val	Phe
	450					455					460				
Glu	Asn	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Arg	Ile
465					470					475					480
Leu	Ser	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile
			485						490					495	
Leu	Ile	Ala	Val	Leu	Gly	Ser	Ser	Met	Ile	Leu	Val	Ser	Ile	Phe	Ile
		500						505					510		
Ile	Ile	Lys	Lys	Thr	Lys	Lys	Pro	Thr	Gly	Ala	Pro	Pro	Glu	Leu	Ser

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515	520	525	
Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn			
530	535		
<210> SEQ ID NO 106 <211> LENGTH: 1617 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide			
<400> SEQUENCE: 106			
atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa			60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga			120
accggctggt acaccaactg gttcacactg gaagtgggag acgtcgagaa tctgacatgc			180
tctgatggcc ctagectgat caagaccgag ctggtatctga ccaagagggc cctgagagaa			240
ctcaagaccg tgtctgcoga tcagctggcc agagaggaac agatcgagaa tcttggcagc			300
ggcagctttg tctggggagc ctttctcttt ggagtggctg ctgctgcagc tgttacagca			360
ggcgtggcca tctgcaagac catcagactg gaaagcgaag tgaccgccat caaccaagcc			420
ctgaagaaga caaacgaggc cgtcagcaca ctggcaatg gcgttagagt gctggccttt			480
gccgtgcggg agctgaagga ctctgtgtcc aagaacctga caccggccct gaacaagaa			540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt			600
ctgaacgtgc tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac			660
ctgatgacag atgctgagct ggttagagcc gtgcctaaca tgcctacatc tgcgggccag			720
atcaagctga tgcctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgtgt			780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac			840
acaccctgct ggattgtgaa ggcctctctt agctgtagcy agaagaaggg caattacgcc			900
tgcctgctga gagaggacca aggctggat tgtcagaacg ccggcagcac cgtgtactac			960
cctaacyaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgcctctgga			1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc			1080
tgaaggtgt ccaccggcag gcacctatt tctatggtgg ctctgtctcc tctgggagcc			1140
ctggtggcct gttataaggg cgtgtcctgt agcatcgcca gcaacagagt gggcctcctc			1200
aagcagctga acaaggctg cagctacatc accaaccagg acgcccatac cgtgaccatc			1260
gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga			1320
cctgtgtcca gcagcttcga cctatcaag ttccctgagg atcagttcaa cgtggccctg			1380
gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc			1440
ctgtctagcy ccgagaaggg aaacaccggc ttcctcctcg tgateatcct gatcgccgtg			1500
ctgggcagct ccatgatcct ggtgtccatc ttcctcatta tcaagaagac caagaagccc			1560
accggcgtc ctcagaact gagcggagtg accaacaatg gcttcctccc tcacaac			1617

<210> SEQ ID NO 107
 <211> LENGTH: 1617
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Polynucleotide

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<400> SEQUENCE: 107

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atgagctgga aggtggteat catcttcagc ctgctgatca cacctcagca cggcctgaaa    60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga    120
accggctggt acaccaacgt gttccacty gaagtgggcy acgtcgagaa tctgacatgc    180
tctgatggcc ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa    240
ctcaagaccg tgtctgcoga tcagctggcc agagaggaac agatcgagaa tcttggcagc    300
ggcagctttg tctggggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca    360
ggcgtggcca tctgcaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc    420
ctgaagaaga caaacgaggc cgtcagcaca ctccgcaatg gcgttagagt gctggccaca    480
gcccgtgcgc agctgaagga ctctgtgtcc aagaacctga caccggccat taacaagaac    540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt    600
ctgaacgtgc tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac    660
ctgatgacag atgctgagct ggcctagagcc gtgcctaaca tgctacatc tgcggccag    720
atcaagctga tctctgagaa tagagccatg gtccgacgga aagccttcgg cattctgtgt    780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac    840
acacctgct ggattgtgaa ggcctctcct agctgtagcg agaagaaggy caattacgcc    900
tgctctgctg gagaggacca agcctggtat tctcagaacg ccggcagcac cgtgtactac    960
cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgcctctgga    1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc    1080
tgcaaggtgt ccaccggcag gcacctatt tctatggtgg ctctgtctcc tctgggagcc    1140
ctgggtggctt gttataaggg cgtgtcctgt agcatcgcca gcaacagagt gggcaccatc    1200
aagcagctga acaaggctg cagctacatc accaaccagc acgcccatac cgtgaccatc    1260
gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga    1320
cctgtgtcca gcagcttcga cctatcaag tccctgagc accagtggca tgtggcctg    1380
gaccaggtgt tcgagaacat cyagaattcc caggtctctg tggaccagtc caacagaatc    1440
ctgtctagcg ccgagaaggy aaacaccggc ttcacatcog tgatcactct gatcgccgtg    1500
ctgggcagct ccatgactct ggtgtccatc ttcacatta tcaagaagac caagaagccc    1560
accggcgcct ctcagaact gagcggagtg accaacaatg gcttcatccc tcacaac    1617
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<210> SEQ ID NO 108

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 108

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atgagctgga aggtggteat catcttcagc ctgctgatca cacctcagca cggcctgaaa    60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga    120
accggctggt acaccaacgt gttccacty gaagtgggcy acgtcgagaa tctgacatgc    180
tctgatggcc ctgacctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa    240
ctcaagaccg tgtctgcoga tcagctggcc agagaggaac agatcgagaa tcttggcagc    300
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ggcagctttg tgcgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360
ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420
ctgaagaaga caaacgaggc cgtcagcaca ctccgcaatg gcgttagagt gctggccaca 480
gccgtgctcg agctgaagga ctctgtgtcc aagaacctga cacgggccat taacaagaac 540
aagtgcgaca tcctgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600
ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660
ctgatgacag atgctgagct ggttagagcc gtgcctaaca tgccctacate tgcggccag 720
atcaagctga tgcctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840
acacctgct ggattgtgaa ggcgctctct agctgtagcg agaagaaggg caattacgcc 900
tgctgtctga gagaggacca aggtcgttat tgtcagaacg ccggcagcac cgtgtaactc 960
cctaacgaga aggactcgca gacaagaggc gaccacgtgt tctgtgatac cgcgcctgga 1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080
tgcaaggtgt ccaccggcag gcacctatt tctatggtgg ctctgtctcc tctgggagcc 1140
ctggtggcct gttataaggg cgtgtctctgt agcatcggca gcaacagagt gggcatcatc 1200
aagcagctga acaagggctg cagctacate accaaccagg acgcccatac cgtgaccate 1260
gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320
cctgtgtcca gcagcttcga cctatcaag ttcctgagg atcagttcca ggtggccctg 1380
gaccaggtgt tcgagaacat cgagaattcc caggtctctg tggaccagtc caacagaate 1440
ctgtctagcg ccgagaaggg aaacaccggc ttcacatcg tgatcactct gatcgcctg 1500
ctgggcagct ccatgatcct ggtgtccatc ttcacatta tcaagaagac caagaagccc 1560
accggcgtcc ctccagaact gagcggagtg accaacaatg gcttcacccc tcacaac 1617

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<210> SEQ ID NO 109

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 109

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atgagctgga aggtggctcat catcttcagc ctgctgatac cacctcagca cggcctgaaa 60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120
accggctggt acaccaactg gttcacactg gaagtgggcy acgtcgagaa tctgacatgc 180
tctgatggcc ctgacctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240
ctcaagaccg tgtctgccga tcagctggcc agayaggaac agatcgagaa tcttggcagc 300
ggcagctttg tgcgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360
ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420
ctgaagaaga caaacgaggc cgtcagcaca ctccgcaatg gcgttagagt gctggccaca 480
gccgtgctcg agctgaagga ctctgtgtcc aagaacctga cacgggccat taacaagaac 540
aagtgcgaca tcctgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600
ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660

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ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgcggccag 720
atcaagctga tgcctgagaa tagagccatg gtccgacgga aaggettcgg cattctgatt 780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840
acacctgct ggattgtgaa ggcgctcct agctgtagcg agaagaaggg caattacgcc 900
tgcttctga gagaggacca aggetggat tgtcagaacg ccggcagcac cgtgtactac 960
cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgcctctgga 1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagccaccac caactatccc 1080
tgcaaggtgt ccaccggcag gcacctatt tctatggtgg ctctgtctcc tctgggagcc 1140
ctggtggcct gttataaggg cgtgtcctgt agcatcgga gcaacagagt gggcatcatc 1200
aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260
gacaacaccg tgtatcagct gagcaaggtg gaaggogaac agcactgat caagggcaga 1320
cctgtgtcca gcagcttoga cctatcaag ttccctgaga accagttcca ggtggccctg 1380
gaccaggtgt tcgagaacat cgagaattcc caggetctgg tggaccagtc caacagaatc 1440
ctgtctagcg ccgagaaggg aacaccggc ttcactatcg tgatcactct gatcgcctg 1500
ctgggcagct ccctgatcct ggtgtccatc ttcactatta tcaagaagac caagaagccc 1560
accggcctc ctcagaact gagcggagtg accaacaatg gcttcctcc tcacaac 1617

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<210> SEQ ID NO 110

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 110

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atgagctgga aggtggtcat catcttcage ctgctgatac cacctcagca cggcctgaaa 60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120
accggctggt acaccaacgt gttcacacty gaagtgggcy acgtcgagaa tctgacatgc 180
tctgatggcc ctgacctgat caagaccyag ctggatctgc tcaagagcyc cctgagagaa 240
ctcaagaccg tgtctgcoga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300
ggcagctttg tctggggagc cattgtctct ggagtggctg ctgctgcagc tgttacagca 360
ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420
ctgaagaaga caaacgagcc cgtcagcaca ctoggcaatg gcgttagagt gctggccaca 480
gccytgcgcy agctgaagga cttcctgctt aagaacctga cacgggccat taacaagaac 540
aagtgcgaca tcctgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600
ctgaacgtcg tgcggcagtt tagcgadaac gccggaatca caccagccat cagcctggac 660
ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgcggccag 720
atcaagctga tgcctgagaa tagagccatg gtccgacgga aaggettcgg cattctgatt 780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840
acacctgct ggattgtgaa ggcgctcct agctgtagcg agaagaaggg caattacgcc 900
tgcttctga gagaggacca aggetggat tgtcagaacg ccggcagcac cgtgtactac 960
cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgcctctgga 1020

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atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080
tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140
ctggtggcctt gttataaggg cgtgtcctgt agcatcgcca gcaacagagt gggcatcacc 1200
aagcagctga acaagggctg cagctacacc accaaccagg acgcccatac cgtgaccacc 1260
gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320
cctgtgtcca gcagcttcga cctatcaag tccctgagg atcagttcca ggtggccctg 1380
gaccaggtgt togagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440
ctgtctagcg cggagaaggg aaacaccggc ttcacatcg tgatcaccct gatcgccgtg 1500
ctgggcagct ccctgatcct ggtgtccacc ttcacatta tcaagaagac caagaagccc 1560
accggcgctc ctccagaact gagcggagtg accaacaatg gcttcacccc tcacaac 1617

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<210> SEQ ID NO 111

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 111

```

atgagctgga aggtggtcat catctcage ctgctgata cacctcagca cggcctgaaa 60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120
accggctggt acaccaactg gttcacactg gaagtggggc acgtcgagaa tctgacatgc 180
tctgatggcc ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240
ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300
ggcagctttg tctggggagc cattgtctct ggagtggctg ctgctgcagc tgttacagca 360
ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420
ctgaagaaga caaacgaggc cgtcagcaca ctccgcaatg gcgttagagt gctggccaca 480
gcccgtgcgc agctgaagga ctctgtgctt aagaacctga cacggggccat taacaagaa 540
aagtgcgaca tccctgacct gaagatggcc gtgtccttta gccagttcaa cggcggttt 600
ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660
ctgatgacag atgtgtgact ggttagagcc gtgcctaaca tgcctacacc tgcggccag 720
atcaagctga tctctgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780
ggcgtgtacg gcagcagcgt gatctatag gtgcagctgc ctatcttcgg cgtgatcgac 840
acaccctgct ggattgtgaa ggcgcctcct agctgtagcg agaagaaggg caattacgcc 900
tgctctgctg gagaggacca aggctgggat tgtcagaacg ccggcagcac cgtgtactac 960
cctaaccgaga aggactgcga gacaagaggc gaccaogtgt tctgtgatac cgcctctgga 1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080
tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140
ctggtggcctt gttataaggg cgtgtcctgt agcatcgcca gcaacagagt gggcatcacc 1200
aagcagctga acaagggctg cagctacacc accaaccagg acgcccatac cgtgaccacc 1260
gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320
cctgtgtcca gcagcttcga cctatcaag tccctgaga accagttcca ggtggccctg 1380

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gaccagggtg  tggagaacat  cgagaattcc  caggctctgg  tggaccagtc  caacagaatc  1440
ctgtctagcg  cggagaaggg  aaacaccggc  ttcateatcg  tgateatcct  gatcgccgtg  1500
ctgggcagct  ccattgaccc  ggtgtccacc  ttcateatta  tcaagaagac  caagaagccc  1560
accggcgctc  ctccagaact  gagcggagtg  accaacaatg  gcttcatccc  tcacaac    1617

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<210> SEQ ID NO 112
<211> LENGTH: 1617
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

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<400> SEQUENCE: 112

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atgagctgga  aggtggctat  catcttcage  ctgctgatac  cacctcagca  cggcctgaaa  60
gagagctacc  tggagaagtc  ctgcagcacc  atcacagagg  gctacctgtc  tgtgctgaga  120
accggctggt  acaccaacgt  gttcacactg  cctgtgggag  acgtogagaa  tctgacatgc  180
tetgatggcc  ctgacctgat  caagaccgag  ctggatctgc  tcaagagcgc  cctgagagaa  240
ctcaagaccg  tgtctgcccg  tcagctggcc  agagaggaac  agatcgagaa  tcttggcagc  300
ggcagctttg  tctggggagc  cattgtctct  ggagtggctg  ctgctgcagc  tgttacagca  360
ggcgtggcca  tgcctaagac  catcagactg  gaaagcgaag  tgaccgccat  caacaacgcc  420
ctgaagaaga  caaacgaggg  cgtcagcaca  ctccgcaatg  gcgttagagt  gctggccaca  480
gcccgtgcgc  agctgaagga  ctctgtgtcc  aagaacctga  caccggccat  taacaagaac  540
aagtgcgaca  tcgacgacct  gaagatggcc  gtgtccttta  gccagttcaa  ccggcggttt  600
ctgaacgtcg  tgcggcagtt  tagcgacaac  gccggaatca  caccagccat  cagcctggac  660
ctgatgacag  atgctgagct  ggtctagagc  gtgcctaaca  tgccctacac  tgccggccag  720
atcaagctga  tgcctgagaa  tagagccatg  gtcgcagcga  aaggcttcgg  cattctgatt  780
ggcgtgtacg  gcagcagcgt  gatctatatg  gtgcagctgc  ctatcttcgg  cgtgatcgac  840
acaccctgct  ggattgtgaa  ggcctctcct  agctgtagcg  agaagaaggg  caattacgcc  900
tgctctgctg  gagaggacca  aggctgggat  tgtcagaacg  ccggcagcac  cgtgtactac  960
cctaacgaga  aggactgcga  gacaagaggg  gaccacgtgt  tctgtgatac  cgcctctgga  1020
atcaatgtgg  ccgagcagag  caaagagtgc  aacatcaaca  tcagcaccac  caactatccc  1080
tgcaagggtg  ccaccggcag  gcaacctatt  tctatgggtg  ctctgtctcc  tctgggagcc  1140
ctggtggctt  gttataaggg  cgtgtcctgt  agcatcggca  gcaacagagt  gggcatcacc  1200
aagcagctga  acaaggctcg  cagctacacc  accaaccagg  acgcccagac  cgtgaccacc  1260
gacaacaccg  tgtatcagct  gagcaaggtg  gaaggcgaac  agcacgtgat  caagggcaga  1320
cctgtgtcca  gcagcttcga  cctatcaag  ttcctgagg  atcagttcca  ggtggccttg  1380
gaccagggtg  tggagaacat  cgagaattcc  caggctctgg  tggaccagtc  caacagaatc  1440
ctgtctagcg  cggagaaggg  aaacaccggc  ttcateatcg  tgateatcct  gatcgccgtg  1500
ctgggcagct  ccattgaccc  ggtgtccacc  ttcateatta  tcaagaagac  caagaagccc  1560
accggcgctc  ctccagaact  gagcggagtg  accaacaatg  gcttcatccc  tcacaac    1617

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<210> SEQ ID NO 113
<211> LENGTH: 1617

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 113
atgagctgga aggtggtcat catcttcage ctgctgatea cacctcagca cggcctgaaa    60
gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga    120
accggctggt acaccaactg gttcacactg cctgtggggc acgtogagaa tctgacatgc    180
tctgatggcc ctgacctgat caagacogag ctggatctgc tcaagagcgc cctgagagaa    240
ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatogagaa tcttggcagc    300
ggcagctttg tgctgggagc cattgtctct ggagtggctg ctgctgcagc tgttacagca    360
ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc    420
ctgaagaaga caaacgaggc cgtcagcaca ctccgcaatg gcgttagagt gctggccaca    480
gocgtgcgcg agctgaagga ctctgtgtcc aagaacctga cacgggccat taacaagaac    540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt    600
ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac    660
ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc tgccggccag    720
atcaagctga tgctogagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt    780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac    840
acaccctgct ggattgtgaa ggcgcctcct agctgtagcg agaagaaggg caattacgcc    900
tgctctgctg gagaggacca aggctgggtat tgtcagaacg ccggcagcac cgtgtactac    960
cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgcgctgga    1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc    1080
tgcaagggtg ccaccgycag gcaccctatt tctatgggtg ctctgtctcc tctgggagcc    1140
ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcacc    1200
aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc    1260
gacaacaccg tgtatcagct gagcaagytg gaaggcgaac agcacgtgat caagggcaga    1320
cctgtgtcca gcagcttoga cctatcaag ttccctgaga accagttcca ggtggcctg    1380
gaccagytgt tcgagaacat cgagaattcc caggtctctg tggaccagtc caacagaatc    1440
ctgtctagcg ccgagaaggg aaacaccggc ttcacatcog tgatcctcct gatcgccgtg    1500
ctgggcagct ccatgatcct ggtgtccatc ttcacatta tcaagaagac caagaagccc    1560
accggcgctc ctccagaact gagcggagtg accaacaatg gcttccatccc tcacaac    1617

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<210> SEQ ID NO 114
<211> LENGTH: 1617
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

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<400> SEQUENCE: 114
atgagctgga aggtggtcat catcttcage ctgctgatea cacctcagca cggcctgaaa    60
gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga    120
accggctggt acaccaactg gttcacactg gaagtggggc acgtogagaa tctgacatgc    180

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tctgatggcc ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa	240
ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc	300
ggcagctttg tgctggggagc cattgtctctt ggagtggctg ctgctgcagc tgttacagca	360
ggcgtggcca tgcctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc	420
ctgaagaaga caaacgaggc cgtcagcaca ctccgcaatg gcgttagagt gctggccaca	480
gcgctgcgcy agctgaagga ctctgtgtcc aagaacctga cacgggccat taacaagaac	540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa cggcggttt	600
ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac	660
ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgccctacatc tgccggccag	720
atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt	780
ggcgtgtacy gcagcagcgt gatctataty gtgcagctgc ctatcttcgg cgtgatcgac	840
acacctgct ggatttgtaa ggcgcctcct agctgtagcg agaagaaggg caattacgcc	900
tgctgtctga gagaggacca aggctgggat tgtcagaacg ccggcagcac cgtgtactac	960
cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgcgctgga	1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc	1080
tgcaaggtgt ccacggcag gcaccctatt tctatgggtg ctctgtctcc tctgggagcc	1140
ctggtggctt gttataaggg cgtgtcctgt agcatcgga gcaacagagt gggcatcatc	1200
aagcagctga acaagggctg cagctacatc accaaccagg acgcccatac cgtgaccatc	1260
gacaacaccc tgatcagct gagcaaggtg gaaggogaac agcactgat caagggcaga	1320
cctgtgtoca gcagcttoga cctatcaag ttcctgagg atcagttcca ggtggcctg	1380
gaccaggtgt tcgagaacat cgagaattcc caggetctgg tggaccagtc caacagaatc	1440
ctgtctagcg ccgagaaggg aaacaccgyc ttcctatctg tgatcctctt gatcgcctg	1500
ctgggcagct ccatgatcct ggtgtccatc ttcctcatta tcaagaagac caagaagccc	1560
accggcgcct ctcagaact gagcggagtg accaacaatg gcttcatccc tcacaac	1617

<210> SEQ ID NO 115

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 115

atgagctgga aggtggctcat catcttcagc ctgctgatca cacctcagca cggcctgaaa	60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga	120
accggctggt acaccaacgt gttcacactg gaagtgggcy acctcgagaa tctgacatgc	180
tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa	240
ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc	300
ggcagctttg tgctggggagc cattgtctctt ggagtggctg ctgctgcagc tgttacagca	360
ggcgtggcca tgcctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc	420
ctgaagaaga caaacgaggc cgtcagcaca ctccgcaatg gcgttagagt gctggccaca	480
gcgctgcgcy agctgaagga ctctgtgtcc aagaacctga cacgggccat taacaagaac	540

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aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa cggcggttt 600
ctgaaactcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660
ctgatgacag atgctgagct ggttagagcc gtgcctaaca tgccctacac tgcggccag 720
atcaagctga tgcctgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840
acaccctgct ggatttgtgaa ggcgcctcct agctgtagcg agaagaaggg caattaogcc 900
tgctgtctga gagaggacca aggctgggat tgtcagaacg ccggcagcac cgtgtactac 960
cctaacgaga aggactgcga gacaagagge gaccacgtgt tctgtgatac gcgcgctgga 1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080
tgcaagggtg ccaccggcag gcaccctatt tctatgggtg ctctgtctcc tctgggagcc 1140
ctggtggctt gttataaggg cgtgtcctgt agcatogcca gcaacagagt gggcatcacc 1200
aagcagctga acaaggctcg cagctacacc accaaccagg acgcogatac cgtgaccacc 1260
gacaacaccc tgtatcagct gagcaagggt gaaggcgaaac agcagctgat caagggcaga 1320
cctgtgtcca gcagcttcga cctatcaag ttcctgagg atcagttcca ggtggcctg 1380
gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440
ctgtctagcg ccgagaaggg aaacaccggc ttcctcctcg tgatcctct gatcgccctg 1500
ctgggcagct ccatgatcct ggtgtccacc ttcctcatta tcaagaagac caagaagccc 1560
accggcgctc ctccagaact gagcggagtg accaacaatg gcttcctccc tcacaac 1617

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<210> SEQ ID NO 116

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 116

```

atgagctgga aggtggctcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60
gagagctacc tggaaagagtc ctgcagcacc atcacagagg gctacctgct tgtgctgaga 120
accggctggt acaccacagc gttcaccactg gaagtgggag acgtcgagaa tctgacatgc 180
tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240
ctcaagaccg tgtctgcoga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300
ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360
ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420
ctgaagaaga caaacgaggc cgtcagcaca ctggccaatg gcgcttagagt gctggccaca 480
ggcgtgagcg agctgaagga ctctgtgctt aagaaactga caaggccat taacaagaa 540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa cggcggttt 600
ctgaaactcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660
ctgatgacag atgctgagct ggttagagcc gtgcctaaca tgccctacac tgcggccag 720
atcaagctga tgcctgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840
acaccctgct ggatttgtgaa ggcgcctcct agctgtagcg agaagaaggg caattaogcc 900

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tgccctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac	960
cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cggcgtgga	1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc	1080
tgcaaggtgt ccacggcag gcaacctatt tctatggtgg ctctgtctcc tctgggagcc	1140
ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcaccatc	1200
aagcagctga acaagggctg cagctacatc accaaccagg acgcogatac cgtgaccatc	1260
gacaacaccc tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga	1320
cctgtgtcca gcagcttoga cctatcaag ttcctgagg atcagttcca ggtggcctg	1380
gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc	1440
ctgtctagcg ccgagaaggg aaacaccggc ttcctcctcg tgatcctcct gatcggcgtg	1500
ctgggcagct ccatgatcct ggtgtccatc ttcctcatta tcaagaagac caagaagccc	1560
accggcgcctc ctccagaact gagcggagtg accaacaatg gcttcctccc tcacaac	1617

<210> SEQ ID NO 117

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 117

atgagctgga aggtggctcat catcttcagc ctgctgatca cacctcagca ccggcctgaaa	60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga	120
accggctggt acaccaacgt gttcacactg gaagtggcg acgtogagaa tctgacatgc	180
tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa	240
ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc	300
ggcagctttg tctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca	360
ggcgtggcca tcgctaagac catcagacty gaaagcgaag tgaccgcat caacaacgcc	420
ctgaagaaga caaacgaggc cgtcagcaca ctccgcaaty gcgttagagt gctggccaca	480
gocgtgocgc agctgaagga ctctgtgtcc aagaacctgt ggggggccat taacaagaac	540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt	600
ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac	660
ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgccctacatc tgccggccag	720
atcaagctga tgcctgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt	780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac	840
acacctgct ggattgtgaa ggcogctcct agctgtagcg agaagaaggg caattaacgcc	900
tgccctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac	960
cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cggcgtgga	1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc	1080
tgcaaggtgt ccacggcag gcaacctatt tctatggtgg ctctgtctcc tctgggagcc	1140
ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcaccatc	1200
aagcagctga acaagggctg cagctacatc accaaccagg acgcogatac cgtgaccatc	1260

-continued

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gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320
cctgtgtcca gcagcttcca cccatcaag tccctgagg atcagttcca ggtggcctg 1380
gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440
ctgtctagcg ccgagaaggg aaacaccggc ttcateatcg tgatcatcct gatcgccgtg 1500
ctgggcagct ccatgatcct ggtgtccate ttcateatta tcaagaagac caagaagccc 1560
accggcgctc ctcagaact gagcggagtg accaacaatg gcttcacccc tcacaac 1617

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<210> SEQ ID NO 118

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 118

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atgagctgga aggtggctcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120
accggctggt acaccaacgt gttcacactg gaagtgggag acctcgagaa tctgacatgc 180
tctgatggcc ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240
ctcaagaccg tgtctgcccga tcagctggcc agagaggaac agatcgagaa tctggcagc 300
ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360
ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420
ctgaagaaga caaacgaggc cgtcagcaca ctggcaatg gcgttagagt gctggccaca 480
gcctgcccgc agctgaagga ctctgtgctt aagaacctgt ggcgggccat taacaagaac 540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600
ctgaacgtcg tgcggcagtt tagcgcacaac gccggaatca caccagccat cagcctggac 660
ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgccctacatc tgcggccag 720
atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780
ggcgtgtacy gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840
acacctgct ggattgtgaa ggcctctcct agctgtagcg agaagaaggg caattacgcc 900
tgccctgctg gagaggacca aggctgggat tgtcagaacg ccggcagcac cgtgtactac 960
cctaaccgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cggcctgga 1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080
tgcaagggtg ccaccgycag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140
ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcacc 1200
aagcagctga acaagggctg cagctacatc accaaccagg acgcccatac cgtgaccate 1260
gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320
cctgtgtcca gcagcttcca cccatcaag tccctgagg atcagttcca ggtggcctg 1380
gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440
ctgtctagcg ccgagaaggg aaacaccggc ttcateatcg tgatcatcct gatcgccgtg 1500
ctgggcagct ccatgatcct ggtgtccate ttcateatta tcaagaagac caagaagccc 1560
accggcgctc ctcagaact gagcggagtg accaacaatg gcttcacccc tcacaac 1617

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<210> SEQ ID NO 119
<211> LENGTH: 1617
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 119

atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa	60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga	120
accgctggtt acaccaacgt gttcacactg cctgtgggag acgtogagaa tctgacatgc	180
tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa	240
ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc	300
ggcagctttg tcttgggagc catttctctt ggagtggctg ctgctgcagc tgttacagca	360
ggcgtggcca togetaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc	420
ctgaagaaga caaacgagge cgtcagcaca ctccgcaatg gcgttagagt gctggccaca	480
gcccgtgcgc agctgaagga ctctgtgtcc aagaacctga cacgggccat taacaagaac	540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa cggcggttt	600
ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac	660
ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc tgcgggccag	720
atcaagctga tctctgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt	780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac	840
acacctgctt ggattgtgaa ggcgctcctt agctgtagcg agaagaagg caattacgcc	900
tgctctgctg gagaggacca aggctgggat tgtcagaacg ccggcagcac cgtgtactac	960
cctaacgaga aggactgcga gacaagagge gaccacgtgt tctgtgatac cggcctgga	1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc	1080
tgcaaggtgt ccacccgag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc	1140
ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcacc	1200
aagcagctga acaagggctg cagctacatc accaaccagg acgcccatac cgtgaccatc	1260
gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga	1320
cctgtgtcca gcagcttoga cctatcaag ttcctgagg atcagttcca ggtggcctg	1380
gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc	1440
ctgtctagcy ccgagaaggg aaacaccgyc ttcacatcgy tgatcaccct gatcgcctg	1500
ctgggcagct ccatgatcct ggtgtccatc ttcacatta tcaagaagac caagaagccc	1560
accggcgcct ctcagaact gagcggagty accaacaatg gcttcacccc tcacaac	1617

<210> SEQ ID NO 120
<211> LENGTH: 1617
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 120

atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa	60
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gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120
accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180
tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240
ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tctgggcagc 300
ggcagctttg tgcctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360
ggcgtggcca togetaagac catcagactg gaaagogaag tgaccgccat caacaacgcc 420
ctgaagaaga caaacgaggc cgtcagcaca ctggcaatg gcgttagagt gctggccaca 480
gccgtgcccg agctgaagga ctctgtgtcc aagaacctga cacgggccat taacaagaac 540
aagtgcgaca tccctgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600
ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660
ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc tgccggccag 720
atcaagctga tgcctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780
ggcgtgtaag gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840
acacctgctt ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900
tgccctgctg gagaggacca aggctgggat tgtcagaacg ccggcagcac cgtgtactac 960
cctaacgaga aggactgcga gacaagagge gaccacgtgt tctgtgatac cgcgcctgga 1020
atcaatgttg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080
tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140
ctggtggctt gttataaggg cgtgtcctgt agcatoggca gcaacagagt gggcatcacc 1200
aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260
gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320
cctgtgtcca gcagcttcga cctatcaag ttcctgaggy atcagttcca ggtggccctg 1380
gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440
ctgtctagcg ccgagaaggg aaacaccggc ttcacatcag tgatcatcct gatcgccgtg 1500
ctgggcagct ccatgatcct ggtgtccatc ttcacatta tcaagaagac caagaagccc 1560
accggcgcct cccagaact gagcggagtg accaacaatg gcttcacccc tcacaac 1617

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<210> SEQ ID NO 121

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 121

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atgagctgga aggtggctcat catcttcagc ctgctgatac caactcagca cggcctgaaa 60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120
accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180
tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240
ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tctgggcagc 300
ggcagctttg tgcctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360
ggcgtggcca togetaagac catcagactg gaaagogaag tgaccgccat caacaacgcc 420

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ctgaagaaga caaacgaggc cgtcagcaca ctggcaatg gcgttagagt gctggccaca 480
gccgtgcgcg agctgaagga ctctgtgtcc aagaacctga cacgggcat taacaagaac 540
aagtgcaccta tcgacgacct gaagatggcc gtgtccttta gccagttcaa cggcggttt
ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660
ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc tgcggccag 720
atcaagctga tgetcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780
ggcgtgtaag gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840
acacctgct ggattgtgaa gcccgctcct agctgtagcg agaagaagg caattacgcc 900
tgcctgctga gagaggacca aggctggat tgtcagaacg ccggcagcac cgtgtactac 960
cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cggcctgga 1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080
tgcaagggtg ccaccgagc gacccctatt tctatgggtg ctctgtctcc tctgggagcc 1140
ctgggtggett gttataaggg cgtgtcctgt agcatcgcca gcaacagagt gggcaccac 1200
aagcagctga acaagggctg cagctacatc accaaccagg acgcccatac cgtgaccatc 1260
gacaacaccg tgtatcagct gagcaaggts gaaggcgaac agcacgtgat caagggcaga 1320
cctgtgtcca gcagcttcga cctatcaag tccctgagg atcagttcca ggtggcctg 1380
gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440
ctgtctagcg ccgagaaggg aaacaccggc ttcateatcg tgatcactc gatcgccgtg 1500
ctgggcagct ccctgactc ggtgtccate ttcateatta tcaagaagac caagaagccc 1560
accggcgcct ctcagaact gagcggagt accaacaatg gcttcatccc tcacaac 1617

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<210> SEQ ID NO 122

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 122

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gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgct tgtgtgaga 120
accggctggt acaccaacgt gttcacactg gaagtggggc acgtcgagaa tctgacatgc 180
tctgatggcc ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240
ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300
ggcagctttg tctggggagc catttctctt ggagtggctg ctgctgcagc tgttacagca 360
ggcgtggcca tcgctaagac catcagactg cctagogaag tgaccgccat caacaaagcc 420
ctgaagaaga caaacgaggc cgtcagcaca ctggcaatg gcgttagagt gctggccaca 480
gccgtgcgcg agctgaagga ctctgtgtcc aagaacctga cacgggcat taacaagaac 540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa cggcggttt
ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660
ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc tgcggccag 720
atcaagctga tgetcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780

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ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840
acaccctgct ggatttgtgaa ggcgcctcct agctgttagcg agaagaaggg caattacgcc 900
tgccctgctga gagaggacca aggctggat  tgtcagaacg ccggcagcac cgtgtactac 960
cctaacygaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgcgcctgga 1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080
tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140
ctggtggcct gttataaggg cgtgtcctgt agcatcgga gcaacagagt gggcatcacc 1200
aagcagctga acaagggctg cagctacacc accaaccagg acgcagatac cgtgaccacc 1260
gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320
cctgtgtcca gcagcttcga cccatacaag ttcctgagg atcagttcca ggtggccctg 1380
gaccaggtgt tcgagaacat cyagaattcc caggtctctg tggaccagtc caacagaacc 1440
ctgtctagcg ccgagaaggg aaacaccggc ttcctcctcg tgatcaccct gatcgccgtg 1500
ctgggcagct ccctgacct ggtgtccacc ttcctcatta tcaagaagac caagaagccc 1560
accggcgcct ctcagaact gagcggagt accaacaatg gcttccatccc tcacaac 1617

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<210> SEQ ID NO 123

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 123

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atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60
gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgtgagaa 120
accggctggt acaccaacgt gttccactg gaagtgggcy acgtcgagaa tctgacatgc 180
tctgatggcc ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240
ctcaagaccg tgtctgcgga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300
ggcagctttg tgctgggagc cattgctctt ggagtggcty ctgctgcagc tgttacagca 360
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ctgaagaaga caaacgaggc cgtcagcaca ctccgcaatg gcgttagagt gctggccaca 480
gcogtgcgag agctgaagga ctctgtgtcc aagaacctga caccggccat taacaagaac 540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600
ctgaacgtcy tgcggcagtt tagcgcacaac gccggaatca caccagccat cagcctggac 660
ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacacc tgcggccag 720
atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840
acaccctgct ggatttgtgaa ggcgcctcct agctgttagcg agaagaaggg caattacgcc 900
tgccctgctga gagaggacca aggctggat  tgtcagaacg ccggcagcac cgtgtactac 960
cctaacygaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgcgcctgga 1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080
tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140

```

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ctggtggctt gttataaggg cgtgtcctgt agcatcgcca gcaacagagt gggcatcacc 1200
aagcagctga acaagggctg cagctacacc accaaccagg acgcccagac cgtgaccacc 1260
gacaacaccg tgtatcagct gagcaaggty gaaggcgaac agcacgtgat caagggcaga 1320
cctgtgtcca gcagcttccc acctatcaag ttccttgagg atcagttcca ggtggccctg 1380
gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaacc 1440
ctgtctagcg ccgagaaggg aaacaccggc ttcctcctcg tgatcctcct gatccgctg 1500
ctgggcagct ccatgatcct ggtgtccacc ttcctcatta tcaagaagac caagaagccc 1560
accggcctcc ctccagaact gagcggagt accaacaatg gcttccacc tcacaac 1617

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<210> SEQ ID NO 124

<211> LENGTH: 1617

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 124

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atgagctgga aggtggctcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120
accggctggt acaccaacgt gttccacty gaagtggggc acgtcgagaa totgacatgc 180
tctgatggcc ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240
ctcaagaccg tgtctgcoga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300
ggcagctttg tcttgggagc catttctctt ggagtggctg ctgctgcagc tgttacagca 360
ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420
ctgaagaaga caaacggggc cgtcagcaca ctccgcaatg gcgttagagt gctggccaca 480
gcccgtgcgc agctgaagga ctctgtgtcc aagaacctga cccgggccat taacaagaac 540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600
ctgaacgtcg tgcggcagtt tagcgcacaac gccggaatca caccagccat cagcctggac 660
ctgatgacag atgctgagct ggttagagcc gtgcctaaca tgctacacc tgcggccag 720
atcaagctga tctctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780
ggcgtgtacc gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840
acaccctgct ggattgtgaa ggcgcctcct agctgtagcg agaagaaggg caattacgcc 900
tgcttctga gagaggacca aggtgggtat tgtcagaacg ccggcagcac cgtgtactac 960
cctaaccgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cggcctgga 1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080
tgcaaggtgt ccaccggcag gcaacctatt tctatggtgg ctctgtctcc tctgggagcc 1140
ctggtggctt gttataaggg cgtgtcctgt agcatcgcca gcaacagagt gggcatcacc 1200
aagcagctga acaagggctg cagctacacc accaaccagg acgcccagac cgtgaccacc 1260
gacaacaccg tgtatcagct gagcaaggty gaaggcgaac agcacgtgat caagggcaga 1320
cctgtgtcca gcagcttccc acctatcaag ttccttgagg accagttcca ggtggccctg 1380
gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaacc 1440
ctgtctagcg ccgagaaggg aaacaccggc ttcctcctcg tgatcctcct gatccgctg 1500

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```
ctgggcagct ccatgatcct ggtgtccate ttcatacatta tcaagaagac caagaagccc 1560
accggcgctc ctccagaact gaggcgagt acccaacaatg gcttcacccc tcacaac 1617
```

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<210> SEQ ID NO 125
<211> LENGTH: 1617
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide
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<400> SEQUENCE: 125
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gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120
accggctggt acaccaacgt gttcacactg gaagtgggag acgtcgagaa tetgacatgc 180
tctgatggcc ctagectgat caagaccgag ctggtatctga ccaagagggc cctgagagaa 240
ctcaagaccg tgtctgcoga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300
ggcagccttg tctggggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360
ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420
ctgaagaaga caaacgaggc cgtcagcaca ctggcaatg gcgttagagt gctggccaca 480
gcccgtcgcg agctgaagga ctctgtgtcc aagaacctga caccggccat taacaagaa 540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600
ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660
ctgatgacag atgctgagct ggttagagcc gtgcctaaca tgcctacatc tgcggccag 720
atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840
acaccctgct ggattgtgaa ggcgctcctt agctgtagcy agaagaaggg caattacgcc 900
tgcttctga gagaggacca aggctggat tgtcagaacg ccggcagcac cgtgtactac 960
cctaacyaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgcgctgga 1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080
tgcaaggtgt ccaccggcag gcacctatt tctatggtgg ctctgtctcc tctgggagcc 1140
ctggtggcct gttataaggg cgtgtcctgt agcatcgcca gcaacagagt gggcaccatc 1200
aagcagctga acaaggctg cagctacatc accaaccagg acgcccatac cgtgaccatc 1260
gacaacaccg tgtatcagct gagcaagggt gaaggcgaac agcacgtgat caagggcaga 1320
cctgtgtcca gcagcttcga cctatcaag ttcctcagc atcagttcca ggtggccctg 1380
gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440
ctgtctagcy ccgagaaggg aaacaccggc ttcatactcg tgateatcct gatcgccgtg 1500
ctgggcagct ccatgatcct ggtgtccate ttcatacatta tcaagaagac caagaagccc 1560
accggcgctc ctccagaact gaggcgagt acccaacaatg gcttcacccc tcacaac 1617
```

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<210> SEQ ID NO 126
<211> LENGTH: 1617
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide
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<400> SEQUENCE: 126

```

atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa    60
gagagctacc tggaaagatc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga    120
accggctggt acaccaacgt gttcacactg gaagtgggag acgtcagaaa tctgacatgc    180
tctgatggcc ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa    240
ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcagaaa tctctggcagc    300
ggcagctttg tgcctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca    360
ggcgtggcca togctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc    420
ctgaagaaga caaacgaggc cgtcagcaca ctccgcaatg gcgttagagt gctggccaca    480
gcccgtgcgc agctgaagga ctctgtgtcc aagaacctga caccggccat taacaagaac    540
aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagtggaa ccggcggttt    600
ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac    660
ctgatgacag atgctgagct ggcctagagc gtgcctaaca tgcctacatc tgcggccag    720
atcaagctga tgcctcagaa tagagccatg gtccgacgga aagccttcgg cattctgatt    780
ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac    840
acacctgctt ggattgtgaa ggcctgctct agctgtagcg agaagaaggg caattacgcc    900
tgctctgctg gagaggacca agcctggtat tgtcagaacg ccggcagcac cgtgtactac    960
cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgcctctgga   1020
atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc   1080
tgcaaggtgt ccaccggcag gcacctatt tctatggtgg ctctgtctcc tctgggagcc   1140
ctggtggcct gttataaggg cgtgtcctgt agcatcgcca gcaacagagt gggcaccatc   1200
aagcagctga acaagggtcg cagctacatc accaaccagg acgcccatac cgtgaccatc   1260
gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga   1320
cctgtgtcca gcagcttcga cctatcaag ttcctgagg atcagttcca ggtggcctcg   1380
gaccaggtgt tcgagaacat cyagaattcc caggtctctg tggaccagtc caacagaatc   1440
ctgtctagcg ccgagaaggg aaacaccggc ttcacatcag tgatcactct gatcgcctg   1500
ctgggcagct ccatgactct ggtgtccatc ttcacatta tcaagaagac caagaagccc   1560
accggcgcct ctcagaact gagcggagtg accaacaatg gcttcacccc tcacaac    1617

```

<210> SEQ ID NO 127

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 127

```

augagcugga agguggucan caucucagc cugcugauca caccucagca cggccugaaa    60
gagagcuacc uggaagaguc cugcagcacc aacacagagg gcuaaccuguc ugugcugaga    120
accggcuggu acaccaacgu guucacacug gaagugggag acguccagaa ucugacaugc    180
ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa    240
cucaagaccg uguucgccga ucagcuggcc agagaggaac agaucagaaa ucucggcagc    300

```

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ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca 360
ggcguggcca ucugcaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420
cugaagaaga caaacgaggc cguacagaca cucggcaaug gcguuagagu gcuggccuuu 480
gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggcccu gaacaagaa 540
aagugcgaca ucgacgaccu gaagauggcc guguccuuu gccaguucua ccggcgguuu 600
cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660
cugaugacag augcugagcu ggcugagacc guggcuauca ugccuacauc ugcggccag 720
aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugugu 780
ggcgugucg gcagcagcgu gaucuauaug gucgagcugc cuauucucgg cugaugcgac 840
acaccucgcu ggauugugaa ggcgcucucu agcugugagcg agaagaaggg caauuacgcc 900
ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguaucua 960
cuuaacgaga aggacugcga gacaagagcc gaccacgugu ucugugauac cgcgcugga 1020
aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080
ugcaaggugu ccaccggcag gcaccuuuu ucuauggugg cucugucucc ucugggagcc 1140
cugguggcuu guuuaaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200
aagcagcuga acaaggcgug cagcuacauc accaaccagg acgcccgauc cgugaccauc 1260
gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcagcugau caagggcaga 1320
ccugugucca gcagcuucga cccuaucaag ucccugagg aucaguucua cguggccucg 1380
gaccaggugu ucgagaacau cgagaaucc caggcucugg uggaccaguc caacagaauc 1440
cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucuuccu gaucgcccug 1500
cugggcagcu ccaugauccu gguguccauc uucaucaua ucaagaagac caagaagccc 1560
accggcgcuc cuccagaacu gagcggagug accaacaauy gcuucauucc ucacaac 1617

```

<210> SEQ ID NO 128

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 128

```

augagcugga aggugguau caucuucagc cugcugauca caccucagca cggccugaaa 60
gagagcuacc uggaaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120
accggcuggu acaccaacgu guucacacug gaagugggcy acgucgagaa ucugacaugc 180
ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240
cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300
ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca 360
ggcguggcca ucugcaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420
cugaagaaga caaacgaggc cguacagaca cucggcaaug gcguuagagu gcuggccaca 480
gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaa 540
aagugcgaca ucgacgaccu gaagauggcc guguccuuu gccaguucua ccggcgguuu 600
cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660

```

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cugaugacag augcugagcu ggcuaagagcc gugccuaaca ugccuacauc ugccggccag 720
aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugugu 780
ggcguguaac gcagcagcgu gaucuaauug gugcagcugc cuaucuuogg cgugaucgac 840
acaccucgcu ggauugugaa ggcgcgucuu agcuguagcg agaagaaggg caauuacgcc 900
ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguaucac 960
ccuaacgaga aggcucgca gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020
aucaaugugg ccgagcagag caaagagugc aacaucaca ucagcaccac caacuauccc 1080
ugcaaggugu ccaccggcag gcacccuaau ucuauggugg cucugucucc ucugggagcc 1140
cugguggcuu guuaaaaggg cguguccgu agcaucggca gcaacagagu gggcaucauc 1200
aagcagcuga acaaggcgug cagcuacauc accaaccagg acgcccgauc cgugaccac 1260
gacaacaccg uguaucagcu gagcaaggug gaaggogaac agcagcugau caagggcaga 1320
ccugugucca gcagcuucga cccuaucaag ucccugagc accaguggca uguggcccug 1380
gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440
cugucuaagc ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgcccug 1500
cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc 1560
accggcguc cuccagaacu gagcggagug accaacaauug gcuucaucc ucacaac 1617

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<210> SEQ ID NO 129

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 129

```

augagcugga agguggucau caucucagc cugcugauca caccucagca cggccugaaa 60
gagagcuacc uggaagaguc cugcagcacc aacacagagg gcuaccuguc ugugcugaga 120
accggcuggu acaccaacgu guucacacug gaaguggggcg acgucgagaa ucugacaugc 180
ucugauggcc cuagccugau caagaccyag cuggaucugc ucaagagcgc ccugagagaa 240
cucaagaccg uguucgcca ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300
ggcagcuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca 360
ggcguggcca ucgcuagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420
cugaagaaga caaacgagcc cgucagcaca cucggcaaug gcuuagagu gcuggccaca 480
gccyugcgcy agcugaagga cuucyugucc aagaaccuga cacgggccau uaacaagaac 540
aagugcgaca ucccugaccu gaagauggcc guguccuuu gccaguuca cggcgguuu 600
cugaacgucg ugccggcaguu uagcgadaac gccggauca caccagccau cagccuggac 660
cugaugacag augcugagcu ggcuaagagcc gugccuaaca ugccuacauc ugccggccag 720
aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780
ggcguguaac gcagcagcgu gaucuaauug gugcagcugc cuaucuuogg cgugaucgac 840
acaccucgcu ggauugugaa ggcgcgucuu agcuguagcg agaagaaggg caauuacgcc 900
ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguaucac 960
ccuaacgaga aggcucgca gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020

```

-continued

aucaaugugg ccgagcagag caaagagugc aacaaucaaca ucagcaccac caacuauccc	1080
ugcaaggugu ccaccggcag gcaccuuuu ucuauggugg cucugucucc ucugggagcc	1140
cugguggcuu guuaaaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc	1200
aagcagcuga acaagggcug cagcuacauc accaaccagg acgcccgauc cgugaccauc	1260
gacaacaccg uguauacagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga	1320
ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug	1380
gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc	1440
cugucucg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgcccug	1500
cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc	1560
accggcgcuc cuccagaacu gagcggagug accaacaauug gcuucauccc ucacaac	1617

<210> SEQ ID NO 130

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 130

augagcugga agguggucou caucuuacagc cugcugauca caccucagca cggccugaaa	60
gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga	120
accggcuggu acaccaacgu guucacacug gaaguggggc acgucgagaa ucugacaugc	180
ucugauggcc cuagccugau caagaccgag cuggaucucg ucaagagcgc ccugagagaa	240
cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc	300
ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca	360
ggcugggcca ucyuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc	420
cugaagaaga caaacgaggc cugcagcaca cucggcaaug gcuuagagu gcuggccaca	480
gcccugcgcg agcugaagga cuucgugucc aagaaccuga caccggccau uaacaagaa	540
aagugcycaca ucccugaccu gaagauggcc guguccuuu gccaguucaa cggcgguuu	600
cugaacgucg ugcggcaguu uagcgcacaac gccggaauca caccagccau cagccuggac	660
cugaugacag augcugagcu ggcugagacc gugccuaaca ugccuacauc ugcccgccag	720
aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu	780
ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac	840
acaccucgcu ggauugugaa ggccgcuccu agcuguaagc agaagaaggg caauuacgcc	900
ugccucguga gagaggacca aggcugguau ugucagaacg cggcagcagc cguguaucac	960
ccuaacgaga aggacugcga gacaagaggc gaccaogugu ucugugauac cgcgcgugga	1020
aucaaugugg ccgagcagag caaagagugc aacaaucaaca ucagcaccac caacuauccc	1080
ugcaaggugu ccaccggcag gcaccuuuu ucuauggugg cucugucucc ucugggagcc	1140
cugguggcuu guuaaaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc	1200
aagcagcuga acaagggcug cagcuacauc accaaccagg acgcccgauc cgugaccauc	1260
gacaacaccg uguauacagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga	1320
ccugugucca gcagcuucga cccuaucaag uucccugaga accaguucca gguggcccug	1380

-continued

```

gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440
cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgcccug 1500
cugggcagcu ccaugauccu gguguccauc uucaucauaa ucaagaagac caagaagccc 1560
accggcgcuc cuccagaacu gagcggagug accaacaauug gcuucauccc ucacaac 1617

```

```

<210> SEQ ID NO 131
<211> LENGTH: 1617
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

```

```

<400> SEQUENCE: 131

```

```

augagcugga agguggucou caucucagc cugcugauc caccucagca cggccugaaa 60
gagagcuacc uggaagaguc cugcagcacc auctacagag gcuaccuguc ugugcugaga 120
accggcuggu acaccaacgu guucacacug gaaguggggcg acgucgagaa ucugacaucg 180
ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240
cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300
ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca 360
ggcguggcca ucguaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420
cugaagaaga caaacgaggg cugcagcaca cucggcaaug gcuuagagu gcuggccaca 480
gccgugcgcg agcugaagga cuucgugcuu aagaaccuga cacgggccau uaacaagaac 540
aagugcgaca uccugaccu gaagauggcc gugucuuua gccaguuaa ccggcgguuu 600
cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660
cugaugacag augcugagcu ggcuaagacc gugccuaaca ugccuacauc ugccggccag 720
aucaagcuga ugcucgagaa uagagccaug guccagcggg aaggcuucgg cauucugauu 780
ggcguguacg gcagcagcgu gaucuauaug gucgagcugc cuaucuucgg cgugaucgac 840
acaccucgcu ggauugugaa ggcgcgucuu agcuguagcg agaagaaggg caauuacgcc 900
ugccucguga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguaucac 960
ccuaacgaga aggacugcga gacaaagggc gaccacgugu ucugugauac cgcgcgugga 1020
aucaaugugg ccgagcagag caaagagugc aacaaucaaa ucagcaccac caacuauccc 1080
ugcaaggugu ccaccggcag gcaaccuuuu ucuauuggug cucugucucc ucugggagcc 1140
cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200
aagcagcuga acaaggcgug cagcuacauc accaaccagg acgcccgauc cgugaccauc 1260
gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320
ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguuca gguggcccug 1380
gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440
cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgcccug 1500
cugggcagcu ccaugauccu gguguccauc uucaucauaa ucaagaagac caagaagccc 1560
accggcgcuc cuccagaacu gagcggagug accaacaauug gcuucauccc ucacaac 1617

```

```

<210> SEQ ID NO 132
<211> LENGTH: 1617

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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 132
augagcugga agguggucau caucuucage cugcugauca caccucagca cggccugaaa    60
gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga    120
accggcuggu acaccaacgu guucacacug gaaguggggcg acgucgagaa ucugacaugc    180
ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa    240
cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc    300
ggcagcuuug ugcugggagc cauugcucu ggagugggucg cugcugcagc uguuacagca    360
ggcuguggcca ucguaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc    420
cugaagaaga caaacgaggg cguacgcaca cuccggcaaug gcguuagagu gcuggccaca    480
gccugcgcgc agcugaagga cuucugucuu aagaaccuga cacgggccau uaacaagaac    540
aagugcgaca ucccgaccu gaagauggcc guguccuuua gccaguucua ccggcgguuu    600
cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac    660
cugaugacag augcugagcu ggcuaagacc guggcuaaca ugccuacauc ugccggccag    720
aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu    780
ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cugauucgac    840
acaccucgcu ggauuugaa ggcgcucucc agcuguagcg agaagaaggg caauuacgcc    900
ugccucguga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuaa    960
ccuaacgaga aggacucgga gacaagaggg gaccacgugu ucugugauac cgccgcugga   1020
aucaaugugg ccagcagagc caaagagugc aacaucuaa ucagcaccac caacuauccc   1080
ugcaaggugu ccaccggcag gcaccuuuu ucuauuggug cucugucucc ucugggagcc   1140
cugguggcuu guuuuaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc   1200
aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc   1260
gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga   1320
ccugugucca gcagcuucga ccuaucaag ucccugaga accaguucca gguggccucg   1380
gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc   1440
cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug   1500
cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc   1560
accggcgcuc cuccagaacu gagcggagug accaacaauy gcuucauccc ucacaac   1617

```

```

<210> SEQ ID NO 133
<211> LENGTH: 1617
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

```

```

<400> SEQUENCE: 133
augagcugga agguggucau caucuucage cugcugauca caccucagca cggccugaaa    60
gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga    120
accggcuggu acaccaacgu guucacacug ccuguggggcg acgucgagaa ucugacaugc    180

```

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ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa	240
cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc	300
ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca	360
ggcguggcca ucgcuagac caucagacug gaaagcgaag ugaccgccau caacaacgcc	420
cugaagaaga caaacgaggc cguccagcaca cucggcaaug gcguuagagu gcuggccaca	480
gccugcgcg agcugaagga cuucuguguc aagaaccuga cacgggccau uaacaagaac	540
aagugcgaca ucgacgaccu gaagauggcc guguccuuu gccaguuca cggcgguuu	600
cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac	660
cugaugacag augcugagcu ggcuagagcc guggcuaca ugccuacauc ugccggccag	720
aucaagcuga ugcugagaa uagagccaug guccgacgga aaggcuucgg cauucugauu	780
ggcguguaag gcagcagcgu gaucuauaug gucgagcugc cuaucuucgg cgugaucgac	840
acaccucgcu ggauuguaa ggcgcucucu agcuguagcg agaagaagg caauuacgcc	900
ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguaucac	960
ccuaacgaga aggacucgca gacaagaggc gaccacgugu ucugugauac cggcgugga	1020
aucaaugugg ccgagcagag caaagagugc aacaucaca ucagcaccac caacuauccc	1080
ugcaaggugu ccaccggcag gcaaccuauu ucuauuggug cucugucucc ucugggagcc	1140
cugguggcuu guuuuaaggc cguguccugu agcaucggca gcaacagagu gggcaucauc	1200
aagcagcuga acaaggcgug cagcuacauc accaaccagg accgccauac cgugaccauc	1260
gacaacaccg uguaucagcu gagcaaggug gaaggogaac agcacugau caagggcaga	1320
ccugugucca gcagcuuca cccuaucaag ucccugagg aucaguucca gguggccoug	1380
gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc	1440
cugucuagcg ccgagaaggg aaacaccgyc uucaucaucy ugaucauccu gaucgcccug	1500
cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc	1560
accggcgcuc cuccagaacu gagcggagug accaacaauug gcuucaucc ucacaac	1617

<210> SEQ ID NO 134

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 134

augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa	60
gagagcuacc uggaaagaguc cugcagcacc aucacagagg gcuaaccuguc ugugcugaga	120
accggcuggu accaccaacgu guuacacacug ccugugggag acguccagaa ucugacaugc	180
ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa	240
cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc	300
ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca	360
ggcguggcca ucgcuagac caucagacug gaaagcgaag ugaccgccau caacaacgcc	420
cugaagaaga caaacgaggc cguccagcaca cucggcaaug gcguuagagu gcuggccaca	480
gccugcgcg agcugaagga cuucuguguc aagaaccuga cacgggccau uaacaagaac	540

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aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucua cggcgguuu 600
cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660
cugaugacag augcugagcu ggcuaagacc gugccuaaca ugccuacauc ugccggccag 720
aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780
ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840
acaccucgcu ggaauuguaa ggcgcgucuu agcuguagcg agaagaaggg caauuacgcc 900
ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960
ccuaacgaga aggacucgca gacaagagge gaccacgugu ucugugauac cgccgcugga 1020
aucaaugugg ccgagcagag caaagagugc aacaucaca ucagcaccac caacuauccc 1080
ugcaaggugu ccaccggcag gcaaccuuuu ucuauuggug cucugucucc ucggggagcc 1140
cugguggcuu guuuuaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200
aagcagcuga acaagggcug cagcuacauc accaaccagg acgcogauac cgugaccauc 1260
gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320
ccugugucca gcagcuucga ccuaucaag ucccugaga accaguuca gguggccucg 1380
gaccaggugu ucgagaacau cgagaaucc caggcucugg uggaccaguc caacagaauc 1440
cugucuaagc ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucggcgug 1500
cugggcagcu ccaugauccu gguguccauc uucaucauuu ucaagaagac caagaagccc 1560
accggcguc cuccagaacu gagcggagug accaacaauug gcuucauccc ucacaac 1617

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<210> SEQ ID NO 135

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 135

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augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60
gagagcuacc uggaaagaguc cugcagcacc aucacagagg gcuaaccuguc ugugcugaga 120
accggcuggu acaccacagc guucacacug gaagugggagc acgucgagaa ucugacaugc 180
ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240
cucaagaccg ugucugcga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300
ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca 360
ggcugggcca ugcuaagac caucagacug gaaagcgaag ugaccgcca caacaacgcc 420
cugaagaaga caaacgaggc cgucagcaca cugggcaaug gcguaagagu gcuggccaca 480
gccgugcgcg agcugaagga cuucugucuc aagaaccuga cacgggcca uaaacaagaa 540
aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucua cggcgguuu 600
cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660
cugaugacag augcugagcu ggcuaagacc gugccuaaca ugccuacauc ugccggccag 720
aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780
ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840
acaccucgcu ggaauuguaa ggcgcgucuu agcuguagcg agaagaaggg caauuacgcc 900

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ugccugcuga gagaggacca aggcugguau ugucagaacg cggcagcac cguguacua	960
ccuaacgaga aggcugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga	1020
aucaaugugg ccgagcagag caaagagugc aacaaucaaca ucagcaccac caacuauccc	1080
ugcaaggugu ccaccggcag gcaeccuauu ucuauggugg cucugucucc ucugggagcc	1140
cugguggcuu guuauaaggg cguguccgu agcaucggca gcaacagagu gggcaucauc	1200
aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc	1260
gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga	1320
ccugugucca gcagcuuca cccuaucaag ucccugagg aucaguucca gguggccug	1380
gaccaggugu ucgagaacau cgagaaucc caggcucugg uggaccaguc caacagaau	1440
cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug	1500
cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc	1560
accggcgcuc cuccagaacu gagcggagug accaacaau gcuucaucc ucacaac	1617

<210> SEQ ID NO 136

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 136

augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa	60
gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaaccuguc ugugcugaga	120
accggcuggu acaccaacgu guucacacug gaagugggcg accucgagaa ucugacaugc	180
ucugauggcc cuagccgau caagaccgag cuggaucuga ccaagagcgc ccugagagaa	240
cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc	300
ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca	360
ggcguggcca ugcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc	420
cugaagaaga caaacgaggg cugcagcaca cucggcaaug gcguaagagu gcuggccaca	480
gcccugccgc agcugaagga cuucgugucc aagaaccuga caccggccau uaacaagaac	540
aagugcgaca ucgacgaccu gaagauggcc guguccuuu gccaguucaa ccggcgguuu	600
cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac	660
cugaugacag augcugagcu ggcuaagacc guggcuuaca ugccuacauc ugccggccag	720
aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu	780
ggcguguaag gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac	840
acaccucgu ggauugugaa ggcgcuccu agcuguagcg agaagaaggg cauuuacgcc	900
ugccugcuga gagaggacca aggcugguau ugucagaacg cggcagcac cguguacua	960
ccuaacgaga aggcugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga	1020
aucaaugugg ccgagcagag caaagagugc aacaaucaaca ucagcaccac caacuauccc	1080
ugcaaggugu ccaccggcag gcaeccuauu ucuauggugg cucugucucc ucugggagcc	1140
cugguggcuu guuauaaggg cguguccgu agcaucggca gcaacagagu gggcaucauc	1200
aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc	1260

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gacaacaccg	uguauacgcu	gagcaaggug	gaaggcgaac	agcacgugau	caagggcaga	1320
ccugugucca	gcagcuucga	cccuaucaag	uucccugagg	aucaguucca	gguggccug	1380
gaccaggugu	ucgagaacau	cgagaauucc	caggcucugg	uggaccaguc	caacagaauc	1440
cugucuagcg	ccgagaaggg	aaacaccggc	uucaucaucg	ugaucuuccu	gaucgccgug	1500
cugggcagcu	ccaugauccu	gguguccauc	uucaucuuu	ucaagaagac	caagaagccc	1560
accggcgcuc	cuccagaacu	gagcggagug	accaacaau	gcuuauccc	ucacaac	1617

<210> SEQ ID NO 137

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 137

augagcugga	aggugguac	caucuucagc	cugcugauca	caccucagca	cggccugaaa	60
gagagcuacc	uggaagaguc	cugcagcacc	aucacagagg	gcuaccuguc	ugugcugaga	120
accggcuggu	acaccaacgu	guucacacug	gaagugggcg	acgucgagaa	ucugacaugc	180
ucugauggcc	cuagccugau	caagaccgag	cuggaucuga	ccaagagcgc	ccugagagaa	240
cucaagaccg	ugucugccga	ucagcuggcc	agagaggaac	agaucgagaa	uccuggcagc	300
ggcagcuuug	ugcugggagc	cauugcucu	ggaguggcug	cugcugcagc	uguuacagca	360
ggcugggcca	ucgcuaagac	caucagacug	gaaagcgaag	ugaccgccau	caacaacgcc	420
cugaagaaga	caaacgaggc	cugcagcaca	cucggcaaug	gcguuagagu	gcuggccaca	480
gccgugcgcg	agcugaagga	cuucgugcu	aagaaccuga	caccggccau	uaacaagaac	540
aagugcgaca	ucgacgaccu	gaagauggcc	guguccuuu	gccaguucaa	ccggcgguuu	600
cugaacgucg	ugcggcaguu	uagcgacaac	gccggaauca	caccagccau	cagccuggac	660
cugaugacag	augcugagcu	ggcuagagcc	gugccuaaca	ugccuacauc	ugccggccag	720
aucaagcuga	ugcucgagaa	uagagccaug	guccgacgga	aaggcuucgg	cauucugauu	780
ggcguguaacg	gcagcagcgu	gaucuauaug	gugcagcugc	cuaucuucgg	cgugaucgac	840
acaccucgcu	ggauugugaa	ggccgcuccu	agcuguaagc	agaagaaggg	cauuuacgcc	900
ugccugcuga	gagaggacca	aggcugguau	ugucagaacg	ccggcagcac	cguguaucuc	960
ccuaacgaga	aggacugcga	gacaagaggc	gaccacgugu	ucugugauac	cgccgcugga	1020
aucaaugugg	ccgagcagag	caaagagugc	aacaucaaca	ucagcaccac	caacuauccc	1080
ugcaaggugu	ccaccggcag	gcaccuuuu	ucuauuggug	cucugucucc	ucugggagcc	1140
cuggguggcu	guuauaaggg	cguguccugu	agcaucggca	gcaacagagu	gggcaucauc	1200
aagcagcuga	acaagggcug	cagcuadauc	accaaaccag	acgcccgauc	cgugaccauc	1260
gacaacaccg	uguauacgcu	gagcaaggug	gaaggcgaac	agcacgugau	caagggcaga	1320
ccugugucca	gcagcuucga	cccuaucaag	uucccugagg	aucaguucca	gguggccug	1380
gaccaggugu	ucgagaacau	cgagaauucc	caggcucugg	uggaccaguc	caacagaauc	1440
cugucuagcg	ccgagaaggg	aaacaccggc	uucaucaucg	ugaucuuccu	gaucgccgug	1500
cugggcagcu	ccaugauccu	gguguccauc	uucaucuuu	ucaagaagac	caagaagccc	1560
accggcgcuc	cuccagaacu	gagcggagug	accaacaau	gcuuauccc	ucacaac	1617

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<210> SEQ ID NO 138
<211> LENGTH: 1617
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 138
augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa   60
gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga   120
accggcuggu acaccaacgu guucacacug gaagugggcg acguocgagaa ucugacaugc   180
ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa   240
cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc   300
ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca   360
ggcguggcca uocuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc   420
cugaagaaga caaacgaggc cugcagcaca cucggcaaug gcguuagagu gcuggccaca   480
gccgugcgcg agcugaagga cuucgugucc aagaaccugu ggcgggccau uaacaagaac   540
aagugcgaca ucgacgaccu gaagauggcc guguccuuu gccaguucca cggcgguuu   600
cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac   660
cugaugacag augcugagcu ggcugagcc guggcuuaca ugccuacauc ugccggccag   720
aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu   780
ggcguguaac gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cugaugcagc   840
acaccucgcu ggauugugaa ggcgcuccu agcuguagcg agaagaaggg cauuuacgcc   900
ugccucguga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuaC   960
ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cggcgugga   1020
aucaaugugg ccgagcagag caaagagugc aacaucaca ucagcaccac caacuauccc   1080
ugcaaggugu ccacccgagc gcaccuauu ucuauuggug cucugucucc ucugggagcc   1140
cugguggcuu guuauaaggc cugucuccgu agcaucggca gcaacagagu gggcaucauc   1200
aagcagcuga acaagggcug cagcuacauc accaacagc agcccgauac cugagccauc   1260
gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga   1320
ccugugucca gcagcuucga ccuaucaag ucccugagg aucaguucca gguggccug   1380
gaccaggugu ucgagaacau cgagaaucc caggcucugg uggaccaguc caacagaauC   1440
cugucuaagc ccgagaaggc aaacaccgyc uucaucaucy ugaucauccu gaucgcccug   1500
cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc   1560
accggcguc cuccagaacu gagcggagug accaacaauC gcuucaucc ucacaac   1617

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<210> SEQ ID NO 139
<211> LENGTH: 1617
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 139
augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa   60

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gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120
accggcuggu acaccaacgu guucacacug gaagugggcg accucgagaa ucugacaugc 180
ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240
cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300
ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca 360
ggcguggcca ugcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420
cugaagaaga caaacgaggc cgcagcaca cucggcaaug gcguuagagu gcuggccaca 480
gccgugcgcg agcugaagga cuucugucu aagaaccugu ggcgggccau uaacaagaac 540
aagugcgaca ucgacgaccu gaagauggcc guguccuuu gccaguuaa ccggcgguuu 600
cugaacgucg ugcggcaguu uagcgacaac gccggaaua caccagccau cagccuggac 660
cugaugacag augcugagcu ggcuaagacc gugcuaaca ugccuacauc ugccggccag 720
aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780
ggcguguaag gcagcagcgu gaucuaauug gugcagcugc cuaucuucgg cugugaucgac 840
acaccucgcu ggauugugaa ggcgcuccu agcuguaagc agaagaaggg cauuuacgcc 900
ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960
ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgcgcuggga 1020
aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080
ugcaaggugu ccaccggcag gcaccuuuu ucuauggugg cucugucucc ucugggagcc 1140
cugguggcuu guuauaaggg cguguccugu agcauoggca gcaacagagu gggcaucauc 1200
aagcagcuga acaagggcug cagcuacauc accaaccagg acgcggauac cgugaccauc 1260
gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320
ccugugucca gcagcuucga ccuaucaag ucccugagg aucaguucca gggggcccug 1380
gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440
cugucuaagc ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgcgug 1500
cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc 1560
accggcgcuc cuccagaacu gagcggagug accaacaau gcuucauccc ucacaac 1617

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<210> SEQ ID NO 140

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 140

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augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60
gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120
accggcuggu acaccaacgu guucacacug ccugugggcg accucgagaa ucugacaugc 180
ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240
cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300
ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca 360
ggcguggcca ugcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420

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cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguaagagu gcuggccaca 480
gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540
aagugcgaca ucgacgaccu gaagauggcc guguccuuu gccaguucua cggcgguuu 600
cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660
cugaugacag augcugagcu ggcuaagacc gugccuaaca ugccuacauc ugccggccag 720
aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780
ggcguguaag gcagcagcgu gaucuaauaug gugcagcugc cuaucuucgg cgugaucgac 840
acaccucgcu ggauugugaa ggcgcuccu agcuguagcg agaagaaggg cauuuacgcc 900
ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuaac 960
ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cggcgugga 1020
aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080
ugcaaggugu ccaccgagc gacccuauu ucuauuggug cucugucucc ucugggagcc 1140
cugggugcuu guuauaaggg cgugucucgu agcaucggca gcaacagagu gggcauac 1200
aagcagcuga acaaggcgug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260
gacaacaccg uguaucgcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320
ccugugucca gcagcuucga cccuaucaag ucccugagg aucaguucca gggggcccug 1380
gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440
cugucagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgcccug 1500
cugggagcgu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc 1560
accggcguc cuccagaacu gagcgagug accaacaau gcuucaucc ucacaac 1617

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<210> SEQ ID NO 141

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 141

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augagcugga aggugguacau caucuucagc cugcugauca caccucagca cggccugaaa 60
gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120
accggcuggu acaccaacgu guucacacug gaaguggggcg acgucgagaa ucugacaugc 180
ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240
cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300
ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca 360
ggcguggcca ugcuaagac caucagacug gaaagcgaag ugaccgccau caaccaagcc 420
cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguaagagu gcuggccaca 480
gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540
aagugcgaca ucccugaccu gaagauggcc guguccuuu gccaguucua cggcgguuu 600
cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660
cugaugacag augcugagcu ggcuaagacc gugccuaaca ugccuacauc ugccggccag 720
aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780

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ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cugaucgac      840
acaccucgcu ggauugugaa ggccgcuccu agcugugagc agaagaaggg cauuuacgcc      900
ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac      960
ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgcgcugga      1020
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ugcaaggugu ccaccggcag gcaccuauu ucuauuggug cucugucucc ucugggagcc      1140
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cugucugagc cggagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgcccug      1500
cugggcagcu ccaugauccu gguguccauc uucaucaua ucaagaagac caagaagccc      1560
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<210> SEQ ID NO 142

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 142

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cugaacgucy ugccggcaguu uagcgcacaac gccggaauca caccagccau cagccuggac      660
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cugggcagcu ccaugauccu gguguccauc uucaucaua ucaagaagac caagaagccc 1560
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<210> SEQ ID NO 143

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 143

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gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540
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cugaacgucg ugccggcaguu uagcgcacaac gccggaauca caccagccau cagccuggac 660
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<211> LENGTH: 1617
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide
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<400> SEQUENCE: 144
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide
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<400> SEQUENCE: 145

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<210> SEQ ID NO 146

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 146

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<210> SEQ ID NO 147

<211> LENGTH: 1617

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 147

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accggcgcuc cuccagaacu gagcggagug accaacaau gcuucaucc ucacaac	1617

1.-12. (canceled)

33. A human parainfluenza virus type 3 (hPIV3) vaccine, comprising:

an isolated ribonucleic acid (RNA) polynucleotide comprising an open reading frame encoding an antigenic hPIV3 Fusion (F) protein formulated in a lipid nanoparticle that comprises a molar ratio of 20-60% ionizable cationic lipid, 5-25% non-cationic lipid, 25-55% sterol, and 0.5-15% PEG-modified lipid, wherein the isolated mRNA polynucleotide is not self-replicating RNA.

34.-95. (canceled)

96. A method of inducing an antigen-specific immune response in a subject, the method comprising administering to the subject the vaccine of claim 33 in an amount effective to produce an antigen-specific immune response in the subject.

97.-135. (canceled)

136. The hPIV3 vaccine of claim 33, wherein the isolated mRNA polynucleotide further encodes a 5' terminal cap, 7mG(5')ppp(5')NlmpNp.

137. The hPIV3 vaccine of claim 33, wherein at least 80% of the uracil in the open reading frame comprises a chemical modification selected from N1-methyl-pseudouridine and N1-ethyl-pseudouridine.

138. The hPIV3 vaccine of claim 33, wherein the chemical modification is in the 5-position of the uracil.

139. The hPIV3 vaccine of claim 33, wherein the open reading frame encoding an antigenic hPIV3 F protein comprises a RNA sequence that has at least 90% identity to the RNA sequence set forth in SEQ ID NO: 64.

140. The hPIV3 vaccine of claim 139, wherein the open reading frame encoding an antigenic hPIV3 F protein comprises a RNA sequence set forth as SEQ ID NO: 64.

141. The hPIV3 vaccine of claim 33, wherein the antigenic hPIV3 F protein comprises an amino acid sequence that has at least 90% identity to the amino acid sequence set forth as SEQ ID NO: 13.

142. The hPIV3 vaccine of claim 141, wherein the antigenic hPIV3 F protein comprises an amino acid sequence set forth as SEQ ID NO: 13.

143. The hPIV3 vaccine of claim 33, formulated in an effective amount, wherein the effective amount is a total dose of 25 µg-200 µg.

144. The hPIV3 vaccine of claim 33, wherein the isolated RNA polynucleotide further comprises 5' terminal cap, a 5' UTR, a 3' UTR, and a polyA tail.

145. The hPIV3 vaccine of claim 144, wherein the open reading frame encoding an antigenic hPIV3 F protein comprises a RNA sequence that has at least 90% identity to the RNA sequence set forth in SEQ ID NO: 64.

146. The hPIV3 vaccine of claim 145, wherein the open reading frame encoding an antigenic hPIV3 F protein comprises a RNA sequence set forth as SEQ ID NO: 64.

147. The hPIV3 vaccine of claim 33, wherein the efficacy of the vaccine in vaccinated subjects is at least 60%, relative to unvaccinated subjects, following a single dose of the vaccine.

148. The hPIV3 vaccine of claim 33, wherein a single dose of the vaccine administered to a subject is sufficient to produce detectable levels of hPIV3 F protein as measured in serum of a subject vaccinated with at least one dose of the vaccine at 1-72 hours post administration.

149. The hPIV3 vaccine of claim 33, wherein a single dose of the vaccine administered to a subject is sufficient to produce a 1,000-10,000 neutralization titer produced by neutralizing antibody against the antigenic hPIV3 F protein as measured in serum of a subject vaccinated with at least one dose of the vaccine at 1-72 hours post administration.

150. The hPIV3 vaccine of claim 149, wherein the 1,000-10,000 neutralization titer is produced in the absence of antibody-dependent enhancement (ADE) of a hPIV3-associated disease.

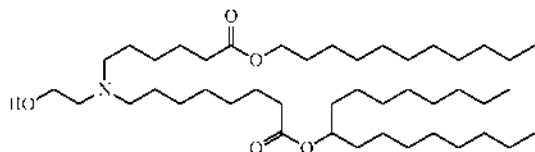
151. The hPIV3 vaccine of claim 150, wherein the hPIV3-associated disease is alevolitis interstitial pneumonia.

152. The hPIV3 vaccine of claim 33, wherein an anti-hPIV3 F protein antibody titer produced in a subject vaccinated with at least one dose of the vaccine is increased by at least 1 log relative to a control, wherein the control is an anti-hPIV3 F protein antibody titer produced in a subject who has not been administered a vaccine against hPIV3.

153. The hPIV3 vaccine of claim 33, wherein an anti-hPIV3 F protein antibody titer produced in a subject vaccinated with at least one dose of the vaccine is increased at least 2 times relative to a control, wherein the control is an anti-hPIV3 F protein antibody titer produced in a subject who has not been administered a vaccine against hPIV3.

154. The hPIV3 vaccine of claim 33, wherein the ionizable cationic lipid comprises the following compound:

(Compound 25)



155. The hPIV3 vaccine of claim 33, wherein the noncationic lipid is DSPC (1,2-Distearoyl-sn-glycero-3-phosphocholine).

156. The hPIV3 vaccine of claim 33, wherein the PEG-modified lipid is DMG-PEG (1,2-dimyristoyl-racglycero-3-methoxypolyethylene glycol-2000).

157. The method of claim 33, wherein the lipid nanoparticle comprises 40-50% ionizable cationic lipid, 5-15% DSPC, 25-40% cholesterol, and 1-3.5% DMG-PEG.

158. The method of claim 157, wherein the lipid nanoparticle comprises 50% ionizable cationic lipid, 10% DSPC, 38.5% cholesterol, and 1.5% DMG-PEG.

* * * * *