

(19) **DANMARK**



Patent- og
Varemærkestyrelsen

(10) **DK/EP 3718565 T3**

(12) **Oversættelse af
europæisk patentskrift**

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- (51) Int.Cl.: **A 61 K 39/12 (2006.01)** **A 61 P 11/00 (2006.01)** **C 07 K 16/10 (2006.01)**
- (45) Oversættelsen bekendtgjort den: **2022-06-20**
- (80) Dato for Den Europæiske Patentmyndigheds bekendtgørelse om meddelelse af patentet: **2022-04-27**
- (86) Europæisk ansøgning nr.: **20164728.6**
- (86) Europæisk indleveringsdag: **2016-10-21**
- (87) Den europæiske ansøgnings publiceringsdag: **2020-10-07**
- (30) Prioritet: **2015-10-22 US 201562245031 P** **2015-10-22 US 201562244813 P**
2015-10-22 US 201562244946 P **2015-10-22 US 201562244802 P**
2015-10-22 US 201562244837 P **2015-10-28 US 201562247362 P**
2015-10-28 US 201562247483 P **2015-10-28 US 201562247394 P**
2015-10-28 US 201562247297 P
- (62) Stamansøgningsnr: **16858406.8**
- (84) Designerede stater: **AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR**
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- (54) Benævnelse: **VACCINER MOD RESPIRATORISK VIRUS**
- (56) Fremdragne publikationer:
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Description

BACKGROUND

5 **[0001]** 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.

10 **[0002]** 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.

15 **[0003]** 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.

20 **[0004]** 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 non-structural proteins (NS1 and NS2), which inhibit type I interferon activity as well as the M-2 protein.

25 **[0005]** 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.

30 **[0006]** 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).

35 **[0007]** 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

40 **[0008]** 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.

45 **[0009]** 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.

[0010] 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.

[0011] 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.

[0012] Shim et al., BMC Immunol, 11:65 (2010) discloses that intranasal immunization with plasmid DNA encoding spike protein of SARS-CoV/polyethylenimine nanoparticles elicits antigen-specific humoral and cellular immune responses in BALB/c mice.

[0013] Du et al., Virology, 353(1), 6-16 (2006) discloses that recombinant adeno-associated virus expressing the receptor-binding domain of SARS-CoV S protein is capable of eliciting neutralizing antibodies in BALB/c mice.

SUMMARY

[0014] Based on the disclosure that is contained herein, the present invention provides a betacoronavirus (BetaCoV) messenger RNA (mRNA) vaccine comprising at least one mRNA polynucleotide having an open reading frame encoding at least one BetaCoV antigenic polypeptide; wherein the at least one BetaCoV antigenic polypeptide is (a) a spike (S) protein or immunogenic fragment thereof, or (b) an S1 subunit or an S2 subunit of S protein or an immunogenic fragment thereof; wherein the BetaCoV vaccine is formulated in a lipid nanoparticle, wherein the lipid nanoparticle comprises 40-60% cationic lipid, 5-15% non-cationic lipid, 1-2% PEG lipid, and 30-50% cholesterol.

[0015] In another aspect, the present invention provides the BetaCoV mRNA vaccine of the invention for use in a method of preventing and/or treating a BetaCoV disease in a subject.

[0016] The present invention and some preferred embodiments thereof are set out in the appended claims.

DETAILED DESCRIPTION

[0017] The technical information set out below may in some respects go beyond the scope of the invention, which is defined exclusively by the appended claims. The additional technical information is provided to place the actual invention in a broader technical context and to illustrate possible related technical developments.

[0018] In addition, incidental references to methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body are not to be construed as claiming protection for such methods as such, but are instead to be construed as referring to products, in particular substances or compositions, for use in any of these methods.

[0019] Provided herein are ribonucleic acid (RNA) vaccines that build on the knowledge that 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 mRNA vaccines of the present disclosure may be used to induce a balanced immune response against BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1), 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.

[0020] The RNA (i.e., 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 (i.e., 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 (i.e., mRNA) vaccines, as mRNA polynucleotides, are better designed to produce the appropriate protein conformation upon translation as the RNA (i.e., mRNA) vaccines co-opt natural cellular machinery. Unlike traditional vaccines, which are manufactured *ex vivo* and may trigger unwanted cellular responses, RNA (i.e., mRNA) vaccines are presented to the cellular system in a more native fashion.

[0021] 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.

[0022] RNA (*i.e.*, mRNA) vaccines combined with the flagellin adjuvant (*i.e.*, 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 (*i.e.*, mRNA) vaccines, as mRNA polynucleotides, are better designed to produce the appropriate protein conformation upon translation, for both the antigen and the adjuvant, as the RNA (*i.e.*, mRNA) vaccines co-opt natural cellular machinery. Unlike traditional vaccines, which are manufactured *ex vivo* and may trigger unwanted cellular responses, RNA (*i.e.*, mRNA) vaccines are presented to the cellular system in a more native fashion.

[0023] Some embodiments of the present disclosure provide RNA (*i.e.*, mRNA) vaccines that include at least one RNA (*i.e.*, 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 (*i.e.*, mRNA polynucleotide) having an open reading frame encoding a flagellin adjuvant.

[0024] 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 (*i.e.*, mRNA) polynucleotide. In other embodiments, at least one flagellin polypeptide and at least one antigenic polypeptide are each encoded by a different RNA polynucleotide.

[0025] 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.

[0026] Provided herein, in some embodiments, is a ribonucleic acid (RNA) (*i.e.*, mRNA) vaccine, comprising at least one (*e.g.*, at least 2, 3, 4 or 5) RNA (*i.e.*, mRNA) polynucleotide having an open reading frame encoding at least one (*e.g.*, at least 2, 3, 4 or 5) BetaCoV (*e.g.*, MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide. Herein, use of the term "antigenic polypeptide" encompasses immunogenic fragments of the antigenic polypeptide (an immunogenic fragment that induces (or is capable of inducing) an immune response to BetaCoV, unless otherwise stated).

[0027] Also provided herein, in some embodiments, is a RNA (*i.e.*, 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) BetaCoV (*e.g.*, MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide or an immunogenic fragment thereof, linked to a signal peptide.

[0028] Further disclosed herein, in some instances, is a nucleic acid (*e.g.*, DNA) encoding at least one (*e.g.*, at least 2, 3, 4 or 5) BetaCoV (*e.g.*, MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) RNA (*e.g.*, mRNA) polynucleotide.

[0029] Further still, disclosed herein, in some instances, is a vaccine for use in 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 (*i.e.*, mRNA) polynucleotide having an open reading frame encoding at least one (*e.g.*, at least 2, 3, 4 or 5) BetaCoV (*e.g.*, MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide.

BetaCoV

[0030] In the invention, the RNA (*i.e.*, mRNA) vaccine comprises at least one RNA (*i.e.*, 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 the invention, the at least one antigenic polypeptide is a betacoronavirus structural protein. 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.

[0031] 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.

[0032] The invention provides 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 (*i.e.*, 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 (*i.e.*, 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,

5 **[0033]** In some embodiments, at least one antigenic polypeptide is a MERS-CoV structural protein. In some embodiments, the MERS-CoV structural protein is a spike protein (S) (*see, e.g.,* Coleman CM et al. *Vaccine* 2014;32:3169-74). 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).

10 **[0034]** 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).

15 **[0035]** 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).

[0036] 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).

20 **[0037]** In some embodiments, at least one antigenic polypeptide is obtained from MERS-CoV strain Riyadh_14_2013, 2cEMC/2012, or Hasa_1_2013.

[0038] In some embodiments, at least one antigenic polypeptide is a SARS-CoV structural protein. 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.

25 **[0039]** 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).

30 **[0040]** In some embodiments, at least one antigenic polypeptide is a HCoV-OC43 structural protein. 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.

35 **[0041]** 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).

[0042] In some embodiments, an antigenic polypeptide is a HCoV-HKU1 structural protein. 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.

40 **[0043]** 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).

[0044] In some embodiments, an open reading frame of a RNA (*i.e.,* mRNA) vaccine is codon-optimized.

[0045] In some embodiments, a RNA (*i.e.,* mRNA) vaccine further comprising an adjuvant.

45 **[0046]** 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.

50 **[0047]** 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 (*i.e.* 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), at least one 5'terminal cap and at least one chemical modification, formulated within a lipid nanoparticle,

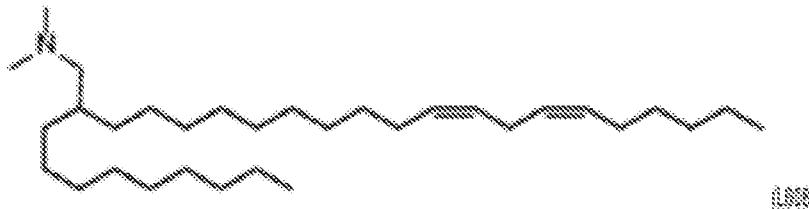
[0048] In some embodiments, a 5' terminal cap is 7mG(5')ppp(5')NImpNp.

55 **[0049]** 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-methyl-pseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-

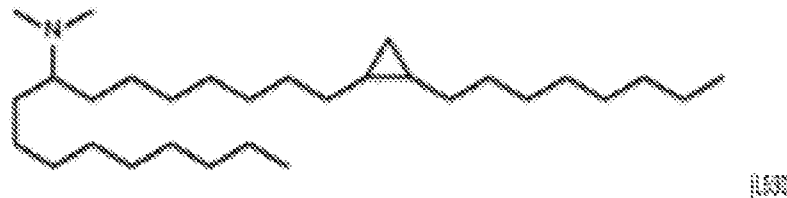
methyl uridine. In some embodiments, the chemical modification is in the 5-position of the uracil, In some embodiments, the chemical modification is a N1-methylpseudouridine. In some embodiments, the chemical modification is a N1-ethylpseudouridine.

[0050] In the invention, a lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a cholesterol 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. In some embodiments, a cationic lipid is selected from the group consisting of 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), (12Z,15Z)-N,N-dimethyl-2-nonylhenicosa-12,15-dien-1-amine (L608), and N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl]heptadecan-8-amine (L530).

[0051] In some embodiments, the lipid is



[0052] In some embodiments, the lipid is



[0053] In some embodiments, a lipid nanoparticle comprises compounds of Formula (I) and/or Formula (II), discussed below.

[0054] In some embodiments, the respiratory virus RNA (*i.e.*, mRNA) vaccine of the invention 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.

[0055] Some embodiments of the present disclosure provide a vaccine that includes at least one RNA (*i.e.*, mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide (*i.e.* 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), wherein at least 80% (*e.g.*, 85%, 90%, 95%, 98%, 99%) of the uracil in the open reading frame have a chemical modification, wherein the vaccine is formulated in a lipid nanoparticle (*i.e.*, a lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a cholesterol and a non-cationic lipid).

[0056] 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.

[0057] In some embodiments, an open reading frame of a RNA (*i.e.*, mRNA) polynucleotide encodes at least two antigenic polypeptides (*i.e.*, 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). 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.

[0058] In some embodiments, a vaccine comprises at least two RNA (*i.e.*, mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide (*i.e.* 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). In some embodiments, the vaccine comprises at least five or at least ten RNA (*i.e.*, 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 (*i.e.*, mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide. In some embodiments, the vaccine comprises 2-100 RNA (*i.e.*, mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide.

[0059] In some embodiments, at least one antigenic polypeptide (i.e. 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,) is fused to a signal peptide. In some embodiments, the signal peptide is selected from: a HulgGk signal peptide (MET-PAQLLFLLLLWLPDTTG; SEQ ID NO: 15); IgE heavy chain epsilon-1 signal peptide (MDWTWILFLVAAATRVHS; SEQ ID NO: 16); Japanese encephalitis PRM signal sequence (MLGSNSGQRVFTILLLVAPAYS; SEQ ID NO: 17), VSVg protein signal sequence (MKCLLYLAFLFIGVNCA; SEQ ID NO: 18) and Japanese encephalitis JEV signal sequence (MWLVSLAIVTACAGA; SEQ ID NO: 19).

[0060] 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.

[0061] In some embodiments, at least one antigenic polypeptide (i.e. 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,) comprises a mutated N-linked glycosylate site.

[0062] The invention provides a mRNA vaccine as set out in the claims formulated in a lipid nanoparticle, In some embodiments, the nanoparticle has a mean diameter of 50-200 nm. In some embodiments, the cationic lipid is an ionizable cationic lipid and the non-cationic lipid is a neutral lipid. 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-((t-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319).

[0063] In some embodiments, a lipid nanoparticle comprises compounds of Formula (I) and/or Formula (II), as discussed below.

[0064] In some embodiments, a lipid nanoparticle comprises Compounds 3,18,20,25,26,29,30,60,108-112, or 122, as discussed below.

[0065] 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),

[0066] In some embodiments, the nanoparticle has a net neutral charge at a neutral pH value.

[0067] In some embodiments, the respiratory virus vaccine is multivalent.

[0068] Some instances 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,

[0069] In some instances, an antigen-specific immune response comprises a T cell response or a B cell response,

[0070] In some instances, 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.

[0071] In some instances, 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.

[0072] In some instances, 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.

[0073] In some instances, a RNA (e.g., mRNA) vaccine is administered to a subject by intradermal or intramuscular injection.

[0074] Some instances 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 instances, 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 instances, the anti-antigenic polypeptide antibody titer produced in the subject is increased by at least 1 log relative to a control. In some instances, the anti-antigenic polypeptide antibody titer produced in the subject is increased by 1-3 log relative to a control.

[0075] In some instances, the anti-antigenic polypeptide antibody titer produced in a subject is increased at least 2 times relative to a control. In some instances, the anti-antigenic polypeptide antibody titer produced in the subject is increased at least 5 times relative to a control. In some instances, the anti-antigenic polypeptide antibody titer produced in the subject is increased at least 10 times relative to a control. In some instances, the anti-antigenic polypeptide antibody titer produced in the subject is increased 2-10 times relative to a control.

[0076] In some instances, 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 instances, the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered alive 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 tier produced in a subject who has been administered a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some instances, the control is an anti-antigenic polypeptide antibody tier 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 RG et al, J Virol 2014 Jun; 88(11): 6368-6379).

[0077] In some instances of the disclosure, 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 instances, 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 tier 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 instances, 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 tier 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.

[0078] In some instances, the control is an anti-antigenic polypeptide antibody tier 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.

[0079] In some embodiments, the mRNA vaccine of the invention is formulated in an effective amount to produce an antigen specific immune response in a subject.

[0080] 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.

[0081] In some embodiments, the efficacy (or effectiveness) of a mRNA vaccine is greater than 60%.

[0082] 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:

$$Efficacy = \left(\frac{ARU}{ARV} - 1 \right) \times 100;$$

and

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

[0083] 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:

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- 5 **[0084]** In some embodiments, the efficacy (or effectiveness) of a RNA (i.e., mRNA) vaccine is at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, or at least 90%.
- [0085]** In some embodiments, the vaccine immunizes the subject against BetaCoV (e.g., selected from MERS-Co V, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), for up to 2 years. In some
10 embodiments, the vaccine immunizes the subject against BetaCoV (e.g., selected from MERS-Co V, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), for more than 2 years, more than 3 years, more than 4 years, or for 5-10 years.
- [0086]** 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
15 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.
- [0087]** 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
20 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.
- [0088]** In some embodiments, the subject is pregnant (e.g., in the first, second or third trimester) when administered an RNA (ie, mRNA) vaccine. Thus, the present disclosure provides RNA (i.e., mRNA) vaccines for maternal immunization to improve mother-to-child transmission of protection against the virus.
- 25 **[0089]** 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).
- [0090]** 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).
- [0091]** In some embodiments, the subject is has a chronic pulmonary disease (e.g., chronic obstructive pulmonary
30 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 (i.e, mRNA) vaccine may have chronic bronchitis or emphysema.
- [0092]** In some embodiments, the subject has been exposed to BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1); the subject is infected with Beta-CoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1); or subject is at risk of infection by BetaCoV (e.g., selected from MERS-Co V, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).
- [0093]** In some embodiments, the subject is immuno compromised (has an impaired immune system, e.g., has an immune disorder or autoimmune disorder).
- 40 **[0094]** In some embodiments the nucleic acid vaccines described herein are chemically modified, In other embodiments the nucleic acid vaccines are unmodified.
- [0095]** The disclosure further relates to 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 $\mu\text{g}/\text{kg}$ and 400 pg/kg of the nucleic acid vaccine is admin-
45 istered to the subject, In some instances 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 instances, the nucleic acid vaccine is administered to the subject by intradermal or intramuscular injection, In some instances, the nucleic acid vaccine is administered to the subject on day zero, In some instances, a second dose of the nucleic acid vaccine is administered to the subject on
50 day twenty one.
- [0096]** In some instances, a dosage of 25 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject, In some instances, a dosage of 100 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some instances, a dosage of 50 micrograms of the RNA poly-
55 nucleotide is included in the nucleic acid vaccine administered to the subject. In some instances, a dosage of 75 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some instances, a dosage of 150 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the

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

[0097] The disclosure further relates to the 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 instances, the stabilization element is a histone stem-loop. In some instances, the stabilization element is a nucleic acid sequence having increased GC content relative to wild type sequence.

[0098] The disclosure further relates to 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 instances, the antibody titer produced by the mRNA vaccines of the disclosure is a neutralizing antibody tier. In some instances the neutralizing antibody titer is greater than a protein vaccine. In other instances the neutralizing antibody titer produced by the mRNA vaccines of the invention is greater than an adjuvanted protein vaccine. In yet other instances the neutralizing antibody titer produced by the mRNA vaccines of the disclosure 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, 2000-10,000, 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.

[0099] Also disclosed 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 instances, the RNA polynucleotide is formulated to produce a neutralizing antibodies within one week of a single administration, In some instances, the adjuvant is selected from a cationic peptide and an immunostimulatory nucleic acid. In some instances, the cationic peptide is protamine.

[0100] The disclosure further relates to 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.

[0101] The disclosure further relates to 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 tier. In some instances, the RNA polynucleotide is present in a dosage of 25-100 micrograms.

[0102] The disclosure further includes 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 atleast 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 instances, 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 instances, the administering step comprises contacting a muscle tissue of the subject with a device suitable for injection of the composition, In some instances, the administering step comprises contacting a muscle tissue of the subject with a device suitable for injection of the composition in combination with electroporation.

[0103] The disclosure further includes 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.

[0104] The disclosure further relates to 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 tier. In some instances, the RNA polynucleotide is present in a dosage of 25-100 micrograms.

[0105] The disclosure further relates to 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 instances, the RNA polynucleotide is present in a dosage of 25-100 micrograms.

[0106] 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.

[0107] The disclosure further includes 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 antigenic polypeptide in an effective amount to vaccinate the subject.

[0108] The disclosure includes 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.

[0109] The disclosure 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.

[0110] The disclosure includes 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 instances, the combined dosage is 25 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject, In some instances, the combined dosage is 100 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject, In some instances the combined dosage is 50 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject, In some instances, the combined dosage is 75 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject, In some instances, the combined dosage is 150 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject, In some instances, the combined dosage is 400 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject, In some instances, 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 instances the nucleic acid vaccine is chemically modified and in other embodiments the nucleic acid vaccine is not chemically modified.

[0111] In preferred aspects, vaccines of the invention (i.e., LNP-encapsulated mRNA vaccines) produce prophylactically- and/or therapeutically- efficacious levels, concentrations and/or tiers 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 tier is determined or measured by enzyme-linked immunosorbent assay (ELISA). In exemplary embodiments, antibody tier is determined or measured by neutralization assay, e.g., by microneutralization assay. In certain aspects, antibody tier measurement is expressed as a ratio, such as 1:40,1:100, etc.

[0112] 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 tier 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 tier 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.)

[0113] 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.

[0114] 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

[0115] 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.

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).

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 μ g or 10 μ g) on day 0 and were given a boost dose (2 μ g or 10 μ 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.

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.

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 μ g or a 2 μ g dose contained hMPV-neutralizing antibodies.

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 IL12 (Fig. 5C).

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), IL4 (Fig. 6C), IL-5 (Fig. 6D) and IL-6 (Fig. 6E).

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).

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).

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 \sim 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.

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.

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.

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.

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.

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.

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.

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 alevolitis and interstitial pneumonia was observed, indicating no antibody-dependent enhancement (ADE) of hMPV associated diseases.

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.

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.

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-Co V 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.

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-Co V mRNA vaccine encoding the full-length Spike protein, two 20 μ g doses (on day 0 and 21, Group 1b) of MERS-Co V 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-Co V 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.

Fig. 21 is a graph showing the MERS-Co V neutralizing antibody titers in New Zealand white rabbits immunized with MERS-CoV mRNA vaccine encoding the full-length Spike protein. Immunization of the in New Zealand white rabbits were carried out as described in Figs. 21A-21C. The results show that two doses of 20 μ g MERS-CoV mRNA vaccine induced a significant amount of neutralizing antibodies against MERS-CoV (EC_{50} 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.

FURTHER DETAILED DESCRIPTION

[0116] The present disclosure provides, in some embodiments, vaccines that comprise RNA (*i.e.*, mRNA) polynucleotides encoding 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.*, Esper F. et al. *Emerging Infectious Diseases*, 12(5), 2006; and Pyrc K. et al. *Journal of Virology*, 81(7):3051-57, 2007). In some embodiments, a RNA (*i.e.*, mRNA) vaccine comprises an adjuvant, such as a flagellin adjuvant, as provided herein,

[0117] The RNA (*i.e.*, mRNA) vaccines (*i.e.*, BetaCoV RNA vaccine), 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.

Human metapneumovirus (hMPV)

[0118] 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), 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 (HR1 and HR2), 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, KA et al. Mol. Cell 1999;3:309-319).

[0119] 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.

Human parainfluenza virus type 3 (PIV3)

[0120] 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).

[0121] 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 neuroaminidase, 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.

[0122] 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.

[0123] 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.

[0124] 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.

[0125] PIV3 V is a non-structural protein that blocks IFN signaling in the infected cell, therefore acting as a virulence factor.

[0126] 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.

Respiratory Syncytial Virus (RSV)

[0127] 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.

[0128] 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 (Krzyzaniak MA et al. PLoS Pathog 2013;9(4)).

Measles Virus (MeV)

[0129] 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, H1, and G3 have been detected in neighboring countries. Recently, MeV genotype B3 was detected in India (Kuttiatt VS et al. Emerg Infect Dis. 2014;20(10): 1764-66).

[0130] 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 MD 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).

Betacoronaviruses (BetaCoV)

[0131] *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. Dipeptidyl peptidase 4 (DDP4, 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.

[0132] 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 AL 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 VS et al. Nature 2013;495(7440):251-4).

[0133] In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (*i.e.*, mRNA) polynucleotide encoding S protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (*i.e.*, mRNA) polynucleotide encoding the S1 subunit of the S protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (*i.e.*, mRNA) polynucleotide encoding the S2 subunit of the S protein.

[0134] In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (*i.e.*, mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein, N protein and M protein.

[0135] In some embodiments, a MERS-Co V vaccine of the present disclosure comprises a RNA (*i.e.*, mRNA) poly-

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

[0136] In some embodiments, a MERS-Co V vaccine of the present disclosure comprises a RNA (i.e., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and M protein. In some embodiments, a MERS-Co V vaccine of the present disclosure comprises a RNA (i.e., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and N protein. In some embodiments, a MERS-Co V vaccine of the present disclosure comprises a RNA (i.e., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), M protein and N protein.

[0137] A MERS-Co V vaccine may comprise, for example, at least one RNA (i.e., mRNA) polynucleotide having an open reading frame encoding at least one MERS-Co V antigenic polypeptide identified by any one of SEQ ID NO: 24-38 or 33 (Table 11; see also amino acid sequences of Table 12).

[0138] A MERS-Co V vaccine may comprise, for example, at least one RNA (i.e., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 20-23 (Table 10).

[0139] The present disclosure is not limited by a particular strain of MERS-Co V. The strain of MERS-Co V used in a vaccine may be any strain of MERS-Co V. Non-limiting examples of strains of MERS-CoV for use as provide herein include Riyadh_14_2013, and 2cEMC/2012, Hasa_1_2013.

[0140] 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 (nucleocapsid). 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.

[0141] In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (i.e., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein, N protein and M protein.

[0142] In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (i.e., 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 (i.e., 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 (i.e., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and M protein.

[0143] In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (i.e., 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 (i.e., 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 (i.e., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), M protein and N protein.

[0144] A SARS-CoV vaccine may comprise, for example, at least one RNA (i.e., 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).

[0145] 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.

[0146] 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.

[0147] 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 (ORF8). The TRS is presumably located within the MUCUAAAC 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.

[0148] *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-NL63 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-NL63 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-NL63 is defined as AACUAAA. This sequence is situated upstream of every ORF except for the E ORF, which contains the suboptimal core sequence AACUAUA. Interestingly, a 13-nucleotide sequence with perfect homology to the leader sequence is situated upstream of the sub-optimal 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.

[0149] *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-NL63 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-NL63 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-NL63 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-NL63 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 Apr;108(4):270-9),

Combination Vaccines

[0150] Embodiments of the present disclosure also provide combination RNA (*i.e.*, mRNA) vaccines. A "combination RNA (*i.e.*, mRNA) vaccine" of the present disclosure refers to a vaccine comprising at least one (e.g., at least 2, 3, 4, or 5) RNA (*i.e.*, 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, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1). In the invention, at least one mRNA polynucleotide encodes at least one BetaCoV antigenic polypeptide.

[0151] In some embodiments, a combination RNA (*i.e.*, mRNA) vaccine comprises a RNA (*i.e.*, 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-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0152] In some embodiments, a combination RNA (*i.e.*, mRNA) vaccine comprises a RNA (*i.e.*, mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a BetaCoV antigenic polypeptide.

[0153] In some embodiments, a combination RNA (*i.e.*, mRNA) vaccine comprises a RNA (*i.e.*, 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-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0154] In some embodiments, a combination RNA (*i.e.*, mRNA) vaccine comprises a RNA (*i.e.*, 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-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0155] In some embodiments, a combination RNA (*i.e.*, mRNA) vaccine comprises a RNA (*i.e.*, 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-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0156] In some embodiments, a combination RNA (*i.e.*, mRNA) vaccine comprises a RNA (*i.e.*, 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-HKU1).

[0157] In some embodiments, a combination RNA (i.e., mRNA) vaccine comprises a RNA (i.e., 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-HKU1).

[0158] In some embodiments, a combination RNA (i.e., mRNA) vaccine comprises a RNA (i.e., 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-HKU1).

[0159] In some embodiments, a combination RNA (i.e., mRNA) vaccine comprises a RNA (i.e., 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-HKU1).

[0160] In some embodiments, a combination RNA (i.e., mRNA) vaccine comprises a RNA (i.e., 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-HKU1).

[0161] In some embodiments, a combination RNA (i.e., mRNA) vaccine comprises a RNA (i.e., 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-HKU1).

[0162] In some embodiments, a combination RNA (i.e., mRNA) vaccine comprises a RNA (i.e., 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-HKU1).

[0163] In some embodiments, a combination RNA (i.e., mRNA) vaccine comprises a RNA (i.e., mRNA) polynucleotide 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-HKU1).

[0164] In some embodiments, a combination RNA (i.e., mRNA) vaccine comprises a RNA (i.e., 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-HKU1).

[0165] Other combination respiratory virus RNA (i.e., mRNA) vaccines are encompassed by the present disclosure,

[0166] 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.

[0167] 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.

[0168] 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.

[0169] 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,

[0170] 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.

[0171] Two 20 µg doses of MERS-Co V mRNA LNP vaccine significantly reduced viral load and induced significant amount of neutralizing antibodies against MERS-CoV (EC₅₀ 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.

[0172] 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

[0173] Respiratory virus vaccines, as provided herein, comprise at least one (one or more) ribonucleic acid (RNA) (*i.e.*, mRNA) polynucleotide having an open reading frame encoding at least one BetaCoV (*e.g.*, selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1) antigenic polypeptide. 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.

[0174] 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 (ENA), cyclohexenyl nucleic acids (CeNA) or chimeras or combinations thereof.

[0175] Polynucleotides of the present invention function as messenger RNA (mRNA). "Messenger 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."

[0176] 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.

[0177] In some embodiments, a RNA polynucleotide of an RNA (*i.e.*, 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 (*i.e.*, 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 (*i.e.*, mRNA) polynucleotide of a respiratory virus vaccine encodes at least 100 or at least 200 antigenic polypeptides. In some embodiments, a RNA polynucleotide of an 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.

[0178] 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.* glycosylate 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 CA) and/or proprietary methods. In some embodiments, the open reading frame (ORF) sequence is optimized using optimization algorithms.

[0179] 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 naturally-occurring or wild-type mRNA sequence encoding a

polypeptide or protein of interest (e.g., an antigenic protein or antigenic polypeptide)).

[0180] 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)).

[0181] In some embodiments a codon-optimized RNA (i.e., 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

[0182] In some embodiments, an antigenic polypeptide (i.e., a 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, paralog, 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.

[0183] 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.

[0184] 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.

[0185] "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.

[0186] "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.

[0187] 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.

[0188] 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.

[0189] "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.

[0190] 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.

[0191] "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.

[0192] 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).

[0193] 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.

[0194] 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.

[0195] 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.

[0196] 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 (FOGSAA) 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.

[0197] 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.

[0198] 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.

[0199] 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*, Gribbskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991. 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, alternately, 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); . 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

[0200] The present disclosure encompasses respiratory virus vaccines comprising multiple RNA (*i.e.*, mRNA) polynucleotides, each encoding a single antigenic polypeptide, as well as respiratory virus vaccines comprising a single RNA (*i.e.*, mRNA) polynucleotide encoding more than one antigenic polypeptide (e.g., as a fusion polypeptide). Thus, a vaccine composition comprising a RNA (*i.e.*, mRNA) polynucleotide having an open reading frame encoding a first antigenic polypeptide and a RNA (*i.e.*, 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 (*i.e.*, 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, 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. In the invention, at least one mRNA polynucleotide encodes at least one BetaCoV antigenic polypeptide.

[0201] In some embodiments, a multicomponent vaccine comprises at least one RNA (*i.e.*, mRNA) polynucleotide encoding at least one antigenic polypeptide fused to a signal peptide (e.g., anyone 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

[0202] In some embodiments, antigenic polypeptides encoded by respiratory virus RNA (*i.e.*, 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.

[0203] Respiratory virus vaccines of the present disclosure may comprise, for example, RNA (*i.e.*, 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 (*i.e.*, 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.

[0204] 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 (*i.e.*, 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 (*i.e.*, mRNA) vaccine is an Ig heavy chain epsilon-1 signal peptide (IgE HC SP) having the sequence of: MDWTWILFLVAAATRVHS (SEQ ID NO: 16). In some embodiments, a signal peptide fused to the antigenic polypeptide encoded by the RNA (*i.e.*, mRNA) vaccine is

an IgGk chain V-III region HAH signal peptide (IgGk SP) having the sequence of METPAQLLFLLLLWLPDTTG (SEQ ID NO: 15). In some embodiments, the signal peptide is selected from: Japanese encephalitis PRM signal sequence (MLGSNSGQRVFTILLLLVAPAYS; SEQ ID NO: 17), VSVg protein signal sequence (MKCLLYLAFLFIGVNCA; SEQ ID NO: 18) and Japanese encephalitis JEV signal sequence (MWLVSLAIVTACAGA; SEQ ID NO: 19).

[0205] In some embodiments, the antigenic polypeptide encoded by a RNA (*i.e.*, 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.

[0206] 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.

[0207] 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 (*i.e.*, mRNA) vaccine of the present disclosure typically does not comprise a signal peptide.

Chemical Modifications

[0208] Respiratory virus vaccines of the present disclosure, in some embodiments, comprise at least RNA (*i.e.*, mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide that comprises at least one chemical modification.

[0209] 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.

[0210] Polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, 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 (*i.e.*, 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 (*i.e.*, 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).

[0211] Modifications of polynucleotides include, without limitation, those described herein. Polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, 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).

[0212] Polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, 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.

[0213] The present disclosure provides for modified nucleosides and nucleotides of a polynucleotide (*i.e.*, RNA polynucleotides, *i.e.*, 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.

[0214] 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.

[0215] Modifications of polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, 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 carbamoyladenosine; N6-glycinyllcarbamoyladenosine; 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-(propyl)adenine; 2'-Amino-2'-deoxy-ATP; 2'-Azido-2'-deoxy-ATP; 2'-Deoxy-2'-a-minoadenosine 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'-OMe-2-Amino-ATP; 2'O-methyl-N6-Bz-deoxyadenosine TP; 2'-a-Ethynyladenosine TP; 2-aminoadenine; 2-Aminoadenosine TP; 2-Amino-ATP; 2'-a-Trifluoromethyladenosine TP; 2-Azidoadenosine TP; 2'-b-Ethynyladenosine 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-mercaptopadenosine TP; 2'-Deoxy-2'-b-thiomethoxyadenosine TP; 2-Fluoroadenosine TP; 2-Iodoadenosine TP; 2-Mercaptopadenosine 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'-Ethynyladenosine 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-CTP; 2'-Azido-2'-deoxy-CTP; 2'-Deoxy-2'-a-aminocytidine TP; 2'-Deoxy-2'-a-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-aza-zebularine; 5-methylzebularine; pyrrolo-pseudoisocytidine; Zebularine; (E)-5-(2-Bromo-vinyl)cytidine TP; 2,2'-anhydro-cytidine TP hydrochloride; 2'Fluor-N4-Bz-cytidine TP; 2'Fluoro-N4-Acetyl-cytidine TP; 2'-O-Methyl-N4-Acetyl-cytidine TP; 2'O-methyl-N4-Bz-cytidine TP; 2'-a-Ethynylcytidine TP; 2'-a-Trifluoromethylcytidine TP; 2'-b-Ethynylcytidine TP; 2'-b-Trifluoromethylcytidine TP; 2'-Deoxy-2',2'-difluorocytidine TP; 2'-Deoxy-2'-a-mercaptopcytidine 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-mercaptopcytidine TP; 2'-Deoxy-2'-b-thiomethoxycytidine TP; 2'-O-Methyl-5-(1-propynyl)cytidine TP; 3'-Ethynylcytidine TP; 4'-Azidocytidine TP; 4'-Carbocyclic cytidine TP; 4'-Ethynylcytidine TP; 5-(1-Propynyl)ara-cytidine TP; 5-(2-Chloro-phenyl)-2-thiocytidine TP; 5-(4-Aminophenyl)-2-thiocytidine TP; 5-Aminoallyl-CTP; 5-Cyanocytidine TP; 5-Ethynylara-cytidine TP; 5-Ethynylcytidine TP; 5'-Homo-cytidine TP; 5-Methoxycytidine TP; 5-Trifluoromethyl-Cytidine TP; N4-Amino-cytidine TP; N4-Benzoyl-cytidine TP; Pseudoisocytidine; 7-methylguanosine; N2,2'-O-dimethylguanosine; N2-methylguanosine; Wyosine; 1,2-O-dimethylguanosine; 1-methylguanosine; 2'-O-methylguanosine; 2'-O-ribosylguanosine (phosphate); 2'-O-meth-

ylguanosine; 2'-O-riboseylguanosine (phosphate); 7-aminomethyl-7-deazaguanosine; 7-cyano-7-deazaguanosine; Archaeosine; Methylwyosine; N2,7-dimethylguanosine; N2,N2,2'-O-trimethylguanosine; N2,N2,7-trimethylguanosine; N2,N2-dimethylguanosine; N2,7,2'-O-trimethylguanosine; 6-thio-guanosine; 7-deaza-guanosine; 8-oxo-guanosine; N1-methyl-guanosine; α -thio-guanosine; 2(propyl)guanidine; 2-(alkyl)guanidine; 2'-Amino-2'-deoxy-GTP; 2'-Azido-2'-deoxy-GTP; 2'-Deoxy-2'-a-aminoguanosine TP; 2'-Deoxy-2'-a-azidoguanosine TP; 6(methyl)guanidine; 6-(alkyl)guanidine; 6-(methyl)guanidine; 6-methyl-guanosine; 7(alkyl)guanidine; 7 (deaza)guanidine; 7(methyl)guanidine; 7-(alkyl)guanidine; 7-(deaza)guanidine; 7-(methyl)guanidine; 8 (alkyl)guanidine; 8(alkynyl)guanidine; 8 (halo)guanidine; 8(thioalkyl)guanidine; 8-(alkenyl)guanidine; 8-(alkyl)guanidine; 8-(alkynyl)guanidine; 8-(amino)guanidine; 8-(halo)guanidine; 8-(hydroxyl)guanidine; 8-(thioalkyl)guanidine; 8-(thiol)guanidine; aza guanidine; deaza guanidine; N (methyl)guanidine; N-(methyl)guanidine; 1-methyl-6-thioguanosine; 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'Fluoro-N2-isobutyl-guanosine TP; 2'O-methyl-N2-isobutyl-guanosine TP; 2'-a-Ethynylguanosine TP; 2'-a-Tnfluoromethylguanosine TP; 2'-b-Ethynylguanosine 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'-Ethynylguanosine 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; galactosylqueuosine; Mannosylqueuosine; Queuosine; allyamino-thymidine; aza thymidine; deaza thymidine; deoxy-thymidine; 2'-O-methyluridine; 2-thiouridine; 3-methyluridine; 5-catoxymethyluridine; 5-hydroxyuridine; 5-methyluridine; 5-taufinomethyl-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; 5-carboxymethylaminomethyluridine; 5-Carbamoylmethyluridine TP; 5-methoxycarbonylmethyl-2'-O-methyluridine; 5-methoxycarbonylmethyl-2-thiouridine; 5-methoxycarbonylmethyluridine; 5-methoxyuridine; 5-methyl-2-thiouridine; 5-methylaminomethyl-2-selenouridine; 5-methylaminomethyl-2-thiouridine; 5-methylaminomethyluridine; 5-Methyldihydrouridine; 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-Amio-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; a-thio-uridine; 1 (aminoalkylaminocarbonylethyl)enyl)-2(thio)-pseudouracil; 1 (aminoalkylaminocarbonylethyl)enyl)-2,4-(dithio)pseudouracil; 1 (aminoalkylaminocarbonylethyl)enyl)-4 (thio)pseudouracil; 1 (aminoalkylaminocarbonylethyl)enyl)-pseudouracil; 1 (aminocarbonylethyl)enyl)-2(thio)-pseudouracil; 1 (aminocarbonylethyl)enyl)-2,4-(dithio)pseudouracil; 1 (aminocarbonylethyl)enyl)-4 (thio)pseudouracil; 1 (aminocarbonylethyl)enyl)-pseudouracil; 1 substituted 2(thio)-pseudouracil; 1 substituted 2,4-(dithio)pseudouracil; 1 substituted 4 (thio)pseudouracil; 1 substituted pseudouracil; 1-(aminoalkylamino-carbonylethyl)enyl)-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'fluro-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-amifoufidifidie 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-(methoxycarbonylmethyl)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; allyamino-uracil; aza uracil; deaza uracil; N3 (methyl)uracil; 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-dihydropseudouridine; 2-
 thio-dihydrouridine; 2-thio-pseudouridine; 4-methoxy-2-thio-pseudouridine; 4-methoxy-pseudouridine; 4-thio-1-methyl-
 5 pseudo-uridine; 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-urid-
 ine 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-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-
 10 UTP; 1-(2-Amino-2-carboxyethyl)pseudo-UTP; 1-(2-Aminoethyl)pseudo-UTP; 1-(2-Hydroxyethyl)pseudouridine TP;
 1-(2-Methoxyethyl)pseudouridine TP; 1-(3,4-Bis-trifluoromethoxybenzyl)pseudouridin TP; 1-(3,4-Dimethoxyben-
 zyl)pseudouridine TP; 1-(3-Amino-3-carboxypropyl)pseudo-UT P; 1-(3-Amino-propyl)pseudo-UTP; 1-(3-Cyclopropyl-
 prop-2-ynyl)pseu dourid ine TP; 1-(4-Amino-4-carboxybutyl)pseudo-U TP; 1-(4-Amino-benzyl)pseudo-UTP; 1-(4-Amino-
 butyl)pseudo-UTP; 1-(4-Amino-phenyl)pseudo-UTP; 1-(4-Azidoben zyl)pseudouridine TP; 1-(4-Bromobenzyl)pseudou-
 15 ridine 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)pseu-
 do-UTP; 1-(4-Methoxy-phenyl)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-Thiomethoxy-
 benzyl)pseudouridine TP; 1-(4-Trifluoromethoxybenzyl)pseudouridine TP; 1-(4-Trifluoromethylbenzyl)pseudouridine
 20 TP; 1-(5-Amino-pentyl)pseudo-UTP; 1-(6-Amino-hexyl)pseudo-UTP; 1,6-Dimethyl-pseudo-UTP; 1-[3-(2-[2-(2-Ami-
 noethoxy)-ethoxy]-ethoxy)-ethoxy]-propionyl]pseudouridine TP; 1-[3-[2-(2-
 Aminoethoxy)-ethoxy]-propionyl]pseudouridine TP; 1-Acetylpsudouridine 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-homoallyl-
 pseudo-UTP; 1-Alkyl-6-vinyl-pseudo-UTP; 1-Allylpseudouridine TP; 1-Aminomethyl-pseudo-UTP; 1-Benzoylpseudou-
 25 ridine TP; 1-Benzoyloxymethylpseudouridine TP; 1-Benzyl-pseudo-UTP; 1-Biotinyl-PEG2-pseudouridine TP; 1-Biotinylp-
 seudouridine TP; 1-Butyl-pseudo-UTP; 1-Cyanomethylpseudouridine TP; 1-Cyclobutylmethyl-pseudo-UTP; 1-Cy-
 clobutyl-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-
 30 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-Methanesulfonyl-
 methylpseudouridine 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-
 35 butyl-pseudo-UTP; 1-Methyl-6-chloro-pseudo-UTP; 1-Methyl-6-cyano-pseudo-UTP; 1-Methyl-6-dimethylamino-pseu-
 do-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-hy-
 droxy-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-Me-
 40 thyl-6-teft-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-pseu-
 do-UTP; 1-Thiomethoxy methylpseudouridine TP; 1-Thiomorpholinomethylpseudouridine TP; 1-Trifluoroacetylpsudou-
 45 ridine TP; 1-Trifluoromethyl-pseudo-UTP; 1-Vinylpseudouridine TP; 2,2'-anhydro-uridine TP; 2'-bromo-deoxyuridine TP;
 2'-F-5-Methyl-2'-deoxy-UTP; 2'-OMe-5-Me-UTP; 2'-OMe-pseudo-UTP; 2'-a-Ethynyluridine TP; 2'-a-Triluoromethylurid-
 ine TP; 2'-b-Ethynyluridine TP; 2'-b-Triluoromethyluridine TP; 2'-Deoxy-2',2'-difluorouridine TP; 2'-Deoxy-2'-a-mercap-
 touridine 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-fluorouridineTP; 2'-Deoxy-2'-b-iodouridine
 TP; 2'-Deoxy-2'-b-mercaptouridine TP; 2'-Deoxy-2'-b-thiomethoxyuridine TP; 2-methoxy-4-thio-uridine; 2-methoxyurid-
 50 ine; 2'-O-Methyl-5-(1-propynyl)uridine TP; 3-Alkyl-pseudo-UTP; 4'Azidouridine TP; 4'-Catocyclic uridine TP; 4'Ethyny-
 luridine 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-pseu do-UTP; 6-Azido-pseudo-
 55 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-UT P; 6-iso-Propyl-pseu-
 do-UTP; 6-Methoxy-pseudo-UTP; 6-Methylamino-pseudo-UTP; 6-Methyl-pseudo-UTP; 6-Phenyl-pseudo-UTP; 6-Phe-

nyl-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-ethoxy)-ethoxy)]propionic acid; Pseudouridine TP 1-methylphosphonic acid; Pseudouridine TP 1-methylphosphonic acid diethyl ester; Pseudo-UTP-N1-3-propionic acid; Pseudo-UTP-N1-4-butanolic acid; Pseudo-UTP-N1-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'-fluoro-modified bases; 2'-O-methyl-ribose; 2-oxo-7-aminopyridopyrimidin-3-yl; 2-oxo-pyridopyrimidine-3-yl; 2-pyridinone; 3 nitropyrrole; 3-(methyl)-7-(propynyl)isocarbostyrylyl; 3-(methyl)isocarbostyrylyl; 4-(fluoro)-6-(methyl)benzimidazole; 4-(methyl)benzimidazole; 4-(methyl)indolyl; 4,6-(dimethyl)indolyl; 5 nitroindole; 5 substituted pyrimidines; 5-(methyl)isocarbostyrylyl; 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-1-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)-phenoxazin-1-yl; 7-(guanidiniumalkylhydroxy)-1,3-(diazia)-2-(oxo)-phenoxazin-1-yl; 7-(propynyl)isocarbostyrylyl; 7-(propynyl)isocarbostyrylyl, 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; Isocarbostyrylyl; Isoguanisine; N2-substituted purines; N6-methyl-2-amino-purine; N6-substituted purines; N-alkylated derivative; Napthalenyl; Nitrobenzimidazolyl; Nitroimidazolyl; Nitroindazolyl; Nitropyrazolyl; 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; Pyrrolopyrizinyl; 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 ribonucleoside; 2-Amino-riboside-TP; Formycin A TP; Formycin B TP; Pyrrososine TP; 2'OH-ara-adenosine TP; 2'-OH-afacytidifilic TP; 2'OH-ara-uridine TP; 2'OH-ara-guanosine TP; 5-(2-carbomethoxyvinyl)uridine TP; and N6-(19-Amino-pentaaxanonadecyl)adenosine TP.

[0216] In some embodiments, polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) include a combination of at least two (*e.g.*, 2, 3, 4 or more) of the aforementioned modified nucleobases,

[0217] In some embodiments, modified nucleobases in polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, 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 (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) include a combination of at least two (*e.g.*, 2, 3, 4 or more) of the aforementioned modified nucleobases.

[0218] In some embodiments, modified nucleobases in polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, 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.

[0219] In some embodiments, polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) comprise pseudouridine (ψ) and 5-methyl-cytidine (m^5C). In some embodiments, polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) comprise 1-methyl-pseudouridine ($m^1\psi$). In some embodiments, polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) comprise 1-methyl-pseudouridine ($m^1\psi$) and 5-methyl-cytidine (m^5C). In some embodiments, polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) comprise 2-thiouridine (s^2U) In some

embodiments, polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) comprise 2-thiouridine and 5-methyl-cytidine (m⁵C). In some embodiments, polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) comprise methoxy-uridine (mo⁵U). In some embodiments, polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) comprise 5-methoxy-uridine (mo⁵U) and 5-methyl-cytidine (m⁵C). In some embodiments, polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) comprise 2'-O-methyl uridine. In some embodiments polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) comprise 2'-O-methyl uridine and 5-methyl-cytidine (m⁵C). In some embodiments, polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) comprise N6-methyl-adenosine (m⁶A). In some embodiments, polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, mRNA polynucleotides) comprise N6-methyl-adenosine (m⁶A) and 5-methyl-cytidine (m⁵C),

[0220] In some embodiments, polynucleotides (*i.e.*, RNA polynucleotides, *i.e.*, 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 (m⁵C), meaning that all cytosine residues in the mRNA sequence are replaced with 5-methyl-cytidine (m⁵C). 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.

[0221] Exemplary nucleobases and nucleosides having a modified cytosine include N4-acetyl-cytidine (ac4C), 5-methyl-cytidine (m⁵C), 5-halo-cytidine (*e.g.*, 5-iodo-cytidine), 5-hydroxymethyl-cytidine (hm5C), 1-methyl-pseudoisocytidine, 2-thio-cytidine (s2C), and 2-thio-5-methyl-cytidine.

[0222] 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.

[0223] 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 (m1A), 2-methyl-adenine (m2A), and N6-methyl-adenosine (m6A).

[0224] In some embodiments, a 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), 7-deaza-guanosine, 7-cyano-7-deaza-guanosine (preQ0), 7-aminomethyl-7-deaza-guanosine (preQ1), 7-methyl-guanosine (m7G), 1-methyl-guanosine (m1G), 8-oxo-guanosine, 7-methyl-8-oxo-guanosine.

[0225] 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 ora 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 anyone 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.

[0226] 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,

[0227] 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),

[0228] Thus, in some embodiments, the RNA (*i.e.*, 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.

[0229] 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-oxyacetic acid (cmo^5U), uridine 5-oxyacetic acid methyl ester ($mcmo^5U$), 5-carboxymethyl-uridine (cm^5U), 1-carboxymethyl-pseudouridine, 5-carboxyhydroxymethyl-uridine (chm^5U), 5-carboxyhydroxymethyl-uridinemethyl 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 (mnm^5U), 5-methylaminomethyl-2-thio-uridine (mnm^5s^2U), 5-methylaminomethyl-2-thio-uridine (mnm^5se^2U), 5-[carbamoylmethyl-uridine (ncm^5U), 5-carboxymethylaminomethyl-uridine ($cmnm^5U$), 5-carboxymethylaminomethyl-2-thio-uridine ($cmnm^5s^2U$), 5-propynyl-uridine, 1-propynyl-pseudouridine, 5-taurinomethyl-uridine (τm^5U), 1-taurinomethyl-pseudouridine, 5-taurinomethyl-2-thio-uridine (τm^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-oxo-3-oxopropyl)uridine (acp^3U), 1-methyl-3-(3-amino-3-carboxypropyl)pseudouridine ($acp^3\psi$), 5-(isopentenylaminomethyl)uridine (inm^5U), 5-(isopentenylaminomethyl)-2-thio-uridine (inm^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 (ncm^5Um), 5-carboxymethylaminomethyl-2'-O-methyl-uridine ($cmnm^5Um$), 3,2'-O-dimethyl-uridine (m^3Um), and 5-(isopentenylaminomethyl)-2'-O-methyl-uridine (inm^5Um), 1-thio-uridine, deoxythymidine, 2'-F-ara-uridine, 2'-F-uridine, 2'-OH-ara-uridine, 5-(2-carbomethoxyvinyl)uridine, and 5-[3-(1-E-propenylamino)]uridine,

[0230] 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^4_2Cm), 1-thio-cytidine, 2'-F-ara-cytidine, 2'-F-cytidine, and 2'-OH-ara-cytidine.

[0231] 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^6_2A), N6-hydroxynorvalylcarbamoyl-adenosine (hn^6A), 2-methylthio-N6-hydroxynorvalylcarbamoyl-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 (n^6_2Am), 1,2'-O-dimethyl-adenosine (m^1Am), 2'-O-ribosyladenosine (phosphate) (Ar(p)), 2-amino-N6-methyl-purine, 1-thio-adenosine, 8-azido-adenosine, 2'-F-aa-adenosine, 2'-F-adenosine, 2'-OH-ara-adenosine, and N6-(19-amino-pentaoxonadecyl)-adenosine.

[0232] In some embodiments, the modified nucleobase is a modified guanine. Exemplary nucleobases and nucleosides having a modified guanine include inosine (I), 1-methyl-inosine (m^1I), wyosine (imG), methylmyosine (mimG), 4-demethyl-wyosine (imG-14), isowyosine (imG2), wybutosine (yW), peroxywybutosine (o_2yW), hydroxywybutosine (OhyW), undermodified hydroxywybutosine (OhyW*), 7-deaza-guanosine, queuosine (Q), epoxyqueuosine (oQ), galactosyl-queuosine (galQ), mannosyl-queuosine (manQ), 7-cyano-7-deaza-guanosine (preQo), 7-aninomethyl-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 (m^7G), 6-thio-7-methyl-guanosine, 7-methyl-inosine, 6-methoxy-guanosine, 1-methyl-guanosine (m^1G), N2-methyl-guanosine (m^2G), N2,N2-dimethyl-guanosine (m^2_2G), N2,7-dimethyl-guanosine (m^2_7G), N2,N2,7-dimethyl-guanosine ($m^2_2_7G$), 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-riboseylguanosine (phosphate) (Gr(p)), 1-thio-guanosine, 06-methyl-guanosine, 2'-F-ara-guanosine, and 2'-F-guanosine.

N-Linked Glycosylation Site Mutants

[0233] 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 affect 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 (*i.e.*, mRNA) vaccines comprising nucleic acids (*i.e.*, mRNA) encoding antigenic polypeptides that comprise a deletion or modification at one or more N-linked glycosylation sites.

In vitro Transcription of RNA (i.e., mRNA)

[0234] Respiratory virus vaccines of the present disclosure comprise at least one RNA polynucleotide, such as a mRNA (*i.e.*, 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.

[0235] 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.

[0236] 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.

[0237] 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.

[0238] 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.

[0239] 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

[0240] 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 (TLR5) 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.

[0241] 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. clarridgeiae*, *P. Mirabilis*, *B. subtilis*, *L. monocytogenes*, *P. aeruginosa*, and *E. coli*, among others are known.

[0242] 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 *Sahonella typhi* (UniPro Entry number: Q56086), *Sahonella typhimurium* (A0A0C9DG09), *Salmonella enteritidis* (A0A0C9BAB7), and *Sahonella 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.

[0243] 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 TLR5 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 hypervariable 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.

[0244] 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 TLR5 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* FliC 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 TLR5 activation. Thus, immunogenic fragments of flagellin include flagellin like sequences that activate TLR5 and contain a 13 amino acid motif that is 53% or more identical to the *Samonella* sequence in 88-100 of FliC (LQRVRELAVQSAN; SEQ ID NO: 84).

[0245] In some embodiments, the RNA (*i.e.*, 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."

[0246] 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 (*i.e.*, 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.

[0247] In other embodiments the RNA (*i.e.*, mRNA) vaccine includes at least two separate RNA polynucleotides, one encoding one or more antigenic polypeptides and the other encoding the flagellin polypeptide, wherein the at least two RNA polynucleotides are co-formulated in a carrier such as a lipid nanoparticle.

Broad spectrum RNA (i.e., mRNA) vaccines

[0248] 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-Co V, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). RNA (*i.e.*, 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 (*i.e.*, 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 (*i.e.*, mRNA) can be co-formulated, for example, in a single lipid nanoparticle (LNP) or can be formulated in separate LNPs for co-administration.

Vaccines for use in Methods of Treatment

[0249] Respiratory virus RNA (*i.e.* 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. The present invention provides the mRNA vaccine defined in the claims for use in a method of preventing and/or treating a BetaCoV disease in a subject. In exemplary aspects, the RNA (*i.e.*, mRNA) vaccines of the present disclosure are used to provide prophylactic protection from BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E,

HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). Prophylactic protection from 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 (*i.e.*, mRNA) vaccine of the present disclosure. Respiratory virus RNA (*i.e.*, 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.

[0250] Disclosed 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-HKU1). 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. In some instances, 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).

[0251] 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 he/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).

[0252] In some instances 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).

[0253] In some instances 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).

[0254] Disclosed 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-HKU1). 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.

[0255] In some instances, 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.

In some instances 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.

[0256] In some instances the immune response is assessed by determining [protein] antibody titer in the subject.

[0257] In some instances 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-Co V, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). In some instances, 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 (*i.e.*, mRNA) vaccine.

[0258] In some instances, 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.

[0259] In some instances 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.

[0260] Also disclosed 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-HKU1) 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

[0261] The present invention provides the mRNA vaccine defined in the claims for use in a method of preventing and/or treating a BetaCoV disease in a subject.

[0262] In some embodiments, respiratory virus vaccine containing RNA (*i.e.*, mRNA) polynucleotides as described herein can be administered to a subject (e.g., a mammalian subject, such as a human subject), and the RNA (*i.e.*, mRNA) polynucleotides are translated *in vivo* to produce an antigenic polypeptide.

[0263] The respiratory virus RNA (*i.e.*, 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 (*i.e.*, mRNA) vaccine that contains a polynucleotide that has at least one a translatable region encoding an antigenic polypeptide.

[0264] An "effective amount" of a respiratory virus RNA (*i.e.* 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 (*i.e.*, 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.

[0265] In some embodiments, RNA (*i.e.* mRNA) vaccines (including polynucleotides their encoded polypeptides) in accordance with the present disclosure may be used for treatment of BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1).

[0266] Respiratory RNA (*i.e.* 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 (*i.e.*, mRNA) vaccine of the present disclosure provided to a cell, a tissue or a subject may be an amount effective for immune prophylaxis.

[0267] Respiratory virus RNA (*i.e.* 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.

[0268] In some embodiments, respiratory virus RNA (*i.e.* mRNA) vaccines may be administered intramuscularly or intradermally, similarly to the administration of inactivated vaccines known in the art,

[0269] 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. RNA (*i.e.*, mRNA) vaccines have superior properties in that they produce much larger antibody titers and produce responses early than commercially available anti-viral agents/compositions.

[0270] Disclosed 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.

[0271] Respiratory virus RNA (*i.e.* mRNA) vaccines may be formulated or administered alone or in conjunction with one or more other components.

[0272] In some embodiments, respiratory virus (*i.e.* mRNA) vaccines do not include an adjuvant (they are adjuvant free).

[0273] Respiratory virus RNA (*i.e.* 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.

[0274] In some instances, 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.

[0275] 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 (*i.e.*, 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.

[0276] 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.

[0277] Respiratory virus RNA (*i.e.* 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*.

Stabilizing Elements

[0278] 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.

[0279] In some embodiments the RNA (*i.e.* 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.

[0280] In some embodiments, the RNA (*i.e.* 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)).

[0281] 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.

[0282] In some embodiments, the RNA (*i.e.*, 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.

[0283] In some embodiments, the RNA (*i.e.*, 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 neighbored 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.

[0284] In other embodiments the RNA (*i.e.* 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 (*i.e.* mRNA) vaccines. Alternatively the AURES may remain in the RNA (*i.e.* mRNA) vaccine.

Nanoparticle Formulations

[0285] In the invention, respiratory virus RNA (*i.e.* mRNA) vaccines are formulated in a lipid nanoparticle. In some embodiments, respiratory virus RNA (*i.e.* 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).

[0286] 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% dipalmyoylphosphatidylcholine, 34.3% cholesterol, and 1.4% PEG-c-DMA. As another example, changing the composition of the cationic lipid can more effectively deliver siRNA to various antigen presenting cells (Basha et al. Mol Ther. 201119:2186-2200).

[0287] In some embodiments, the ratio of lipid to RNA (*i.e.* 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.

[0288] 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.

[0289] In the invention, the lipid comprises a cationic lipid such as, but not limited to, DLin-DMA, DLin-D-DMA, DLin-MC3-D MA, DLin-KC2-D MA, 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. 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. In the invention, the mRNA vaccine is formulated in a lipid nanoparticle as defined in the appended claims.

[0290] 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)butanoyloxy)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,

[0291] Examples of neutral lipids include, without limitation, DSPC, POPC, DPPC, DOPE and SM. An example of a sterol is cholesterol. 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)).

[0292] In some embodiments, lipid nanoparticle formulations include 60% of a cationic lipid 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)butanoyloxy)heptadecanedioate (L319), 7.5% of the neutral lipid, 31 % of the sterol, and 1.5% of the PEG or PEG-modified lipid on a molar basis.

[0293] In some embodiments, lipid nanoparticle formulations include 50% of a cationic lipid 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)butanoyloxy)heptadecanedioate (L319), 10% of the neutral lipid, 38.5% of the sterol, and 1.5% of the PEG or PEG-modified lipid on a molar basis.

[0294] In some embodiments, lipid nanoparticle formulations include 57.2% of a cationic lipid 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)butanoyloxy)heptadecanedioate (L319), 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.

[0295] In some embodiments, the molar lipid ratio is 50110138.511.5 (mol% cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG, PEG-DSG or PEG-DPG), or 57.217.1134.311.4 (mol% cationic lipid/neutral lipid, e.g., DPPC/Chol/PEG-modified lipid, e.g., PEG-cDMA).

[0296] 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., 51: 8529-8533; and Maier et al. (2013) Molecular Therapy 21,1570-1578.

[0297] In the invention, the lipid nanoparticle formulations described herein are 4 component lipid nanoparticles. The lipid nanoparticle comprises a cationic lipid, a non-cationic lipid, a PEG lipid and a structural lipid. In the invention, the lipid nanoparticle comprises 40-60% of cationic lipid, 5-15% of a non-cationic lipid, 1-2% of a PEG lipid and 30-50% of a structural lipid. As a non-limiting example, the lipid nanoparticle may comprise 50% cationic lipid, 10% non-cationic lipid, 1.5% PEG lipid and 38.5% 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 L319. In the invention, the structural lipid is cholesterol.

[0298] In the invention, the lipid nanoparticle formulations described herein comprise a cationic lipid, a non-cationic lipid, a PEG 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 PEG lipid PEG-DOMG 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 PEG lipid PEG-DOMG 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 PEG lipid PEG-DMG and 38.5% of the structural lipid cholesterol.

[0299] 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 .5 and 50%, between 1-30%, between 5-80%, at least 80% (w/w) active ingredient.

[0300] In some embodiments, the respiratory virus RNA (i.e. mRNA) vaccine composition may comprise the polynucleotide described herein, formulated in a lipid nanoparticle comprising MC3, Cholesterol, DSPC and PEG2000-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, 21.8 mg/mL of MC3, 10.1 mg/mL of cholesterol, 5.4 mg/mL of DSPC, 2.7 mg/mL of PEG2000-DMG, 5.16 mg/mL of trisodium citrate, 71 mg/mL of sucrose and 1.0 mL of water for injection.

[0301] In some embodiments, a nanoparticle (*i.e.*, 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 (*i.e.*, 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

[0302] In the invention, the lipid nanoparticle formulations described herein comprise a cationic lipid, a non-cationic lipid, a PEG lipid and cholesterol. 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-DOMG 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-DOMG 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.

[0303] 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-ene-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,21Z)-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, (21Z,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-dimethylheptacos-1-ene-10-amine, (20Z,23Z)-N-ethyl-N-methylnonacos-20,23-dien-10-amine, 1-[(11Z,14Z)-1-nonylicosa-11,14-dien-1-yl]pyrrolidine, (20Z)-N,N-dimethylheptacos-20-en-10-amine, (15Z)-N,N-dimethylheptacos-15-en-10-amine, (14Z)-N,N-dimethylnonacos-14-en-10-amine, (17Z)-N,N-dimethylnonacos-17-en-10-amine, (24Z)-N,N-dimethyltriaconta-24-en-10-amine, (20Z)-N,N-dimethylnonacos-20-en-10-amine, (22Z)-N,N-dimethylhentriaconta-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}azetidene, (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]-3-(hexyloxy)-N,N-dimethylpropan-2-amine, 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-H(1-metoyloctyloxy)-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, (2R)-1-[(3,7-dimethyloctyloxy)-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]octyloxy)propan-2-amine, N,N-dimethyl-1-[(8-(2-octylcyclopropyl)octyloxy)-3-(octyloxy)propan-2-amine and (1E,20Z,23Z)-N,N-dimethylnonacos-11,20,23-trien-10-amine or a pharmaceutically acceptable salt or stereoisomer thereof.

[0304] In some embodiments, the LNP formulations of the RNA (*e.g.*, mRNA) vaccines may contain PEG-c-DOMG

at 1.5% lipid molar ratio.

[0305] In some embodiments, the pharmaceutical compositions of the RNA (*i.e.*, mRNA) vaccines may include at least one of the PEGylated lipids described in International Publication No. WO2012099755.

[0306] In some embodiments, the LNP formulation may contain PEG-DMG 2000 (1,2-dimyristoyl-sn-glycero-3-phosphoetha no lamine-N-[methoxy(polyethylene glycol)-2000). 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, DLin-DMA, DSPC and cholesterol. As another non-limiting example the LNP formulation may contain PEG-DMG 2000, DLin-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).

[0307] The lipid nanoparticles described herein may be made in a sterile environment.

[0308] 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.

[0309] 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. 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. 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.

[0310] 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)). 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). 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,

[0311] In some embodiments, the RNA (*i.e.*, 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.

[0312] In some embodiments, a "self" peptide and/or CD47 protein may be conjugated to a virus-like particle or pseudovirion, as described herein for delivery of the RNA (*i.e.*, mRNA) vaccines of the present disclosure.

[0313] In some embodiments, RNA (*i.e.*, 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.

[0314] The nanoparticle formulations may be a carbohydrate nanoparticle comprising a carbohydrate carrier and a RNA (*i.e.*, 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).

[0315] 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 (*i.e.*, 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.

[0316] 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 (reLNP). Ionizable cationic lipids, such as, but not limited to, DLinDMA, DLin-KC2-DMA, and DLin-MC3-D MA, 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 reLNP 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.

[0317] In some embodiments, the internal ester linkage may be located on either side of the saturated carbon.

[0318] 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). 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.

[0319] 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). 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 International Patent Publication No. WO2013110028.

[0320] 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, polyethyleneimines, 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 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). 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 polyethylene glycol (PEG), polyalkylene oxides (PEO), polyalkylene terephthalates such as polyethylene terephthalate, polyvinyl alcohols (PVA), polyvinyl ethers, polyvinyl esters such as polyvinyl acetate, polyvinyl halides such as polyvinyl 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 polymethyl(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 Publication No. WO2013012476), and (polyethylene 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 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). 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).

[0321] 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).

[0322] 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, carbocisteine, eprazinone, mesna, ambroxol, soberol, dom-iodol, letosteine, stepronin, tiopronin, gelsolin, thymosin β 4 dornase alfa, neltenexine, erdosteine) 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).

[0323] 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.

[0324] 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.

[0325] 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 solution. Hypotonic solutions were found to increase the rate at which mucoinert 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).

[0326] 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 23:7M-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). 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). Formulations can also be selectively targeted through expression of different ligands on their surface as exemplified by, but not limited by, 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., Biomacro molecules. 2011 12:2708-2714; Zhao et al., Expert Opin Drug Deliv. 2008 5:309-319; Akinc et al., Mol Ther. 201018:1357-1364; 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 USA. 2007 104:4095-4100; Kim et al., Methods Mol Biol. 2011 721:339-353; Subramanya et al., Mol Ther. 201018:2028-2037; 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).

[0327] In some embodiments, the RNA (*i.e.*, 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 (*i.e.*, 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.

[0328] In some embodiments, the controlled release formulation may include, but is not limited to, tri-block co-polymers. As a non-limiting example, the formulation may include two different types of tri-block co-polymers (International Pub. No. WO2012131104 and WO2012131106).

[0329] In some embodiments, the RNA (*i.e.*, 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, GELSITE[®] (Nanotherapeutics, Inc. Alachua, FL), HYLENEX[®] (Halozyme Therapeutics, San Diego CA), surgical sealants such as fibrinogen polymers (Ethicon Inc. Cornelia, GA), TISSELL[®] (Baxter International, Inc Deerfield, IL), PEG-based sealants, and COSEAL[®] (Baxter International, Inc Deerfield, IL).

[0330] 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.

[0331] In some embodiments, the RNA (*i.e.*, 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[®]).

[0332] In some embodiments, the RNA (*i.e.*, 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.

[0333] In some embodiments, the RNA (*i.e.*, 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. Patent No. 8,404,222.

[0334] In some embodiments, the RNA (*i.e.*, mRNA) vaccine controlled release delivery formulation comprising at least one polynucleotide may be the controlled release polymer system described in US20130130348.

[0335] In some embodiments, the RNA (*i.e.*, 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. Patent No. 8,206,747, 8,293,276, 8,318,208 and 8,318,211. In some embodiments, therapeutic polymer nanoparticles may be identified by the methods described in US Pub No. US20120140790.

[0336] In some embodiments, the therapeutic nanoparticle RNA (*i.e.*, 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). 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).

[0337] In some embodiments, the therapeutic nanoparticle RNA (*i.e.*, 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). 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.

[0338] 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.

[0339] 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), polycyanoacrylates, polyvinyl alcohols, polyurethanes, polyphosphazenes, polyacrylates, polymethacrylates, polycyanoacrylates, polyureas, polystyrenes, polyamines, polylysine, polygene 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.

[0340] As a non-limiting example the therapeutic nanoparticle comprises a PLGA-PEG block copolymer (see U.S. Publication No. US20120004293 and U.S. Patent No. 8,236,330). 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. Patent No 8,246,968 and International Publication No. WO2012166923). 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.

[0341] In some embodiments, the therapeutic nanoparticle may comprise a multiblock copolymer (see *e.g.*, U.S. Pat. No. 8,263,665 and 8,287,910 and U.S. Patent Pub. No. US20130195987).

[0342] In 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-beta1 gene delivery vehicle in Lee et al. Thermosensitive Hydrogel as a Tgf-β1 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 RNA (*i.e.*, mRNA) vaccines of the present disclosure may be formulated in lipid nanoparticles comprising the PEG-PLGA-PEG block copolymer.

[0343] In some embodiments, the therapeutic nanoparticle may comprise a multiblock copolymer (see *e.g.*, U.S. Pat. No. 8,263,665 and 8,287,910 and U.S. Patent Pub. No. US20130195987).

[0344] 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).

[0345] 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.

[0346] 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. In some embodiments, the poly(vinyl ester) polymers may be conjugated to the polynucleotides described herein.

[0347] 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). As a non-limiting example, the therapeutic nanoparticle may be used to treat cancer (see International publication No. WO2013044219).

[0348] In some embodiments, the therapeutic nanoparticles may comprise at least one cationic polymer described herein and/or known in the art.

[0349] 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. Patent No. 8,287,849) and combinations thereof.

[0350] In some embodiments, the nanoparticles described herein may comprise an amine cationic lipid such as those described in International Patent Application No. WO2013059496. In some embodiments, the cationic lipids may have an amino-amine or an amino-amide moiety.

[0351] 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.

[0352] 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).

[0353] 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 International Publication Nos. WO2010138193 and WO2010138194 and US Pub Nos. US20110020388 and US20110027217).

[0354] 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.

[0355] In some embodiments, the RNA (i.e., 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. Patent No. 8,399,007.

[0356] 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.

[0357] In some embodiments, LNPs comprise the lipid KL52 (an amino-lipid disclosed in U.S. Application Publication No. 201210295832. 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 KL52 may be administered intravenously and/or in one or more doses. In some embodiments, administration of LNPs comprising KL52 results in equal or improved mRNA and/or protein expression as compared to LNPs comprising MC3.

[0358] In some embodiments, RNA (i.e., mRNA) vaccine may be delivered using smaller LNPs. Such particles may comprise a diameter from below 0.1 μm up to 100 nm 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 .

[0359] In some embodiments, RNA (i.e., 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.

[0360] 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) (Zhigaltsev, 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; Bellveau, 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). 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.

[0361] In some embodiments, the RNA (i.e., 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).

[0362] In some embodiments, the RNA (*i.e.*, 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). 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).

[0363] In some embodiments, the RNA (*i.e.*, 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, MA) 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.

[0364] In some embodiments, the RNA (*i.e.*, 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. Patent No. 8,440,614. The microspheres may comprise a compound of the formula (I), (II), (III), (IV), (V) or (VI) as described in International Patent Publication No. WO2013063468. In some embodiments, the amino acid, peptide, polypeptide, lipids (APPL) are useful in delivering the RNA (*i.e.*, mRNA) vaccines of the disclosure to cells (*see* International Patent Publication No. WO2013063468).

[0365] In some embodiments, the RNA (*i.e.*, 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 20 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 30 to about 100 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.

[0366] In some embodiments, the lipid nanoparticles may have a diameter from about 10 to 500 nm.

[0367] 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.

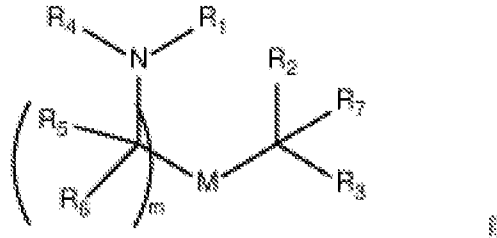
[0368] The nanoparticles of the present disclosure may further include nutrients such as, but not limited to, those which deficiencies can lead to health hazards from anemia to neural tube defects (*see, e.g.*, the nanoparticles described in International Patent Publication No WO2013072929). As a non-limiting example, the nutrient may be iron in the form of ferrous, ferric salts or elemental iron, iodine, folic acid, vitamins or micronutrients.

[0369] In some embodiments the RNA (*i.e.*, 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 Erns, HSV, VP22 (Herpes simplex), MAP, KALA or protein transduction domains (PTDs), PpT620, 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, pIsI, 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.* polyethyleneimine (PEI), cationic lipids, *e.g.* DOTMA: [1-(2,3-sioleyloxy)propyl]-N,N,N-trimethylammonium chloride, DMRIE, di-C14-amidine, DOTIM, SAINT, DC-Chol, BGTC, CTAP, DOPC, DODAP, DOPE: Dioleoyl phosphatidylethanol-amine, DOSPA, DODAB, DOIC, DMEPC, DOGS: Dioctadecylamidoglycylspermin, DIMRI: Dimyristooxypropyl dimethyl hydroxyethyl ammonium bromide, DOTAP: dioleoyloxy-3-(trimethylammonio)propane, DC-6-14: O,O-ditetradecanoyl-N-.alpha.-trimethylammonioacetyl)diethanolamine chloride, CLIP 1: rac-[(2,3-dioctadecyloxypropyl)(2-hydroxyethyl)]-dimethylammonium chloride, CLIP6: rac-[2(2,3-dihexadecyloxypropyloxymethyloxy)ethyl]-trimethylammonium, CLIP9: rac-[2(2,3-dihexadecyloxypropyloxysuccinyloxy)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 methacrylate)), etc., modified amidoamines such as pAMAM (poly(ami-

doamine)), 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-PDMS 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.

[0370] In other embodiments the RNA (i.e., mRNA) vaccine is not associated with a cationic or polycationic compounds.

[0371] In some embodiments, a nanoparticle comprises compounds of Formula (I):



or a salt or isomer thereof, wherein:

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

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;

R_4 is selected from the group consisting of a C_{3-6} carbocycle, $-(CH_2)_nQ$, $-(CH_2)_nCHQR$, $-CHQR$, $-CQ(R)_2$, and unsubstituted C_{1-6} alkyl, where Q is selected from a carbocycle, heterocycle, $-OR$, $-O(CH_2)_nN(R)_2$, $-C(O)OR$, -

$OC(O)R$, $-CX_3$, $-CX_2H$, $-CXH_2$, $-CN$, $-N(R)_2$,

$-C(O)N(R)_2$, $-N(R)C(O)R$, $-N(R)S(O)_2R$, $-N(R)C(O)N(R)_2$, $-N(R)C(S)N(R)_2$, $-N(R)R_8$,

$-O(CH_2)_nOR$, $-N(R)C(=NR_9)N(R)_2$, $-N(R)C(=CHR_9)N(R)_2$, $-OC(O)N(R)_2$, $-N(R)C(O)OR$,

$-N(OR)C(O)R$, $-N(OR)S(O)_2R$, $-N(OR)C(O)OR$, $-N(OR)C(O)N(R)_2$, $-N(OR)C(S)N(R)_2$,

$-N(OR)C(=NR_9)N(R)_2$, $-N(OR)C(=CHR_9)N(R)_2$, $-C(=NR_9)N(R)_2$, $-C(=NR_9)R$, $-C(O)N(R)OR$, and

$-C(R)N(R)_2C(O)OR$, and each n is independently selected from 1, 2, 3, 4, and 5;

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;

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;

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

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

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;

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

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

each R'' is independently selected from the group consisting of C_{3-14} alkyl and

C_{3-14} alkenyl;

each R' is independently selected from the group consisting of C_{1-12} alkyl and

C_{2-12} alkenyl;

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

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

m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13.

[0372] 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.

[0373] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0374] R₁ is selected from the group consisting of C₅₋₃₀ alkyl, C₅₋₂₀ alkenyl, -R*YR", -YR", and -R"M'R';

[0375] R₂ and R₃ are independently selected from the group consisting of H, C₁₋₁₄ alkyl, C₂₋₁₄ alkenyl, -R*YR", -YR", and -R'OR", or R₂ and R₃, together with the atom to which they are attached, form a heterocycle or carbocycle;

[0376] R₄ is selected from the group consisting of a C₃₋₆ carbocycle, -(CH₂)_nQ, -(CH₂)_nCHQR,

- 5
- CHQR, -CQ(R)₂, and unsubstituted C₁₋₆ alkyl, where Q is selected from a C₃₋₆ carbocycle, a 5- to 14-membered heteroaryl having one or more heteroatoms selected from N, O, and S, -OR,
 - O(CH₂)_nN(R)₂, -C(O)OR, -OC(O)R, -CX₃, -CX₂H, -CXH₂, -CN, -C(O)N(R)₂,
 - 10 - 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)R₈,
 - O(CH₂)_nOR, -N(R)C(=NR₉)N(R)₂, -N(R)C(=CHR₉)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,
 - 15 - N(OR)C(=NR₉)N(R)₂, -N(OR)C(=CHR₉)N(R)₂, -C(=NR₉)N(R)₂, -C(=NR₉)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 C₁₋₃ alkyl, and each n is independently selected from 1, 2, 3, 4, and 5;

each R₅ is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R₆ is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

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;

R₇ is selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

R₈ is selected from the group consisting of C₃₋₆ carbocycle and heterocycle;

R₉ is selected from the group consisting of H, CN, NO₂, C₁₋₆ alkyl, -OR, -S(O)₂R, -S(O)₂N(R)₂, C₂₋₆ alkenyl, C₃₋₆ carbocycle and heterocycle;

25 each R is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R' is independently selected from the group consisting of C₁₋₁₈ alkyl, C₂₋₁₈ alkenyl, -R*YR", -YR", and H;

each R" is independently selected from the group consisting of C₃₋₁₄ alkyl and C₃₋₁₄ alkenyl;

each R* is independently selected from the group consisting of C₁₋₁₂ alkyl and C₂₋₁₂ alkenyl;

each Y is independently a C₃₋₆ carbocycle;

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

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

or salts or isomers thereof.

[0377] In some embodiments, another subset of compounds of Formula (I) includes those in which

35 R₁ is selected from the group consisting of C₅₋₃₀ alkyl, C₅₋₂₀ alkenyl, -R*YR", -YR", and -R"M'R';

R₂ and R₃ are independently selected from the group consisting of H, C₁₋₁₄ alkyl, C₂₋₁₄ alkenyl, -R*YR", -YR", and -R'OR", or R₂ and R₃, together with the atom to which they are attached, form a heterocycle or carbocycle;

40 R₄ is selected from the group consisting of a C₃₋₆ carbocycle, -(CH₂)_nQ, -(CH₂)_nCHQR, -CHQR, -CQ(R)₂, and unsubstituted C₁₋₆ alkyl, where Q is selected from a C₃₋₆ carbocycle, a 5- to 14-membered heterocycle having one or more heteroatoms selected from N, O, and S, -OR,

-O(CH₂)_nN(R)₂, -C(O)OR, -OC(O)R, -CX₃, -CX₂H, -CXH₂, -CN, -C(O)N(R)₂,

45 -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)R₈,

-O(CH₂)_nOR, -N(R)C(=NR₉)N(R)₂, -N(R)C(=CHR₉)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,

50 -N(OR)C(=NR₉)N(R)₂, -N(OR)C(=CHR₉)N(R)₂, -C(=NR₉)R, -C(O)N(R)OR, and -C(=NR₉)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) R₄ is -(CH₂)_nQ in which n is 1 or 2, or (ii) R₄ is -(CH₂)_nCHQR in which n is 1, or (iii) R₄ is -CHQR, and -CQ(R)₂, then

Q is either a 5- to 14-membered heteroaryl or 8- to 14-membered heterocycloalkyl;

each R₅ is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R₆ is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

55 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;

R₇ is selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

R₈ is selected from the group consisting of C₃₋₆ carbocycle and heterocycle;

R₉ is selected from the group consisting of H, CN, NO₂, C₁₋₆ alkyl, -OR, -S(O)₂R, -S(O)₂N(R)₂, C₂₋₆ alkenyl, C₃₋₆

carbocycle and heterocycle;

each R is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R' is independently selected from the group consisting of C₁₋₁₈ alkyl, C₂₋₁₈ alkenyl, -R*YR", -YR", and H;

each R" is independently selected from the group consisting of C₃₋₁₄ alkyl and C₃₋₁₄ alkenyl;

5 each R* is independently selected from the group consisting of C₁₋₁₂ alkyl and C₂₋₁₂ alkenyl;

each Y is independently a C₃₋₆ carbocycle;

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

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

or salts or isomers thereof.

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[0378] In some embodiments, another subset of compounds of Formula (I) includes those in which

R₁ is selected from the group consisting of C₅₋₃₀ alkyl, C₅₋₂₀ alkenyl, -R*YR", -YR", and -R"M'R';

15 R₂ and R₃ are independently selected from the group consisting of H, C₁₋₁₄ alkyl, C₂₋₁₄ alkenyl, -R*YR", -YR", and -R'OR", or R₂ and R₃, together with the atom to which they are attached, form a heterocycle or carbocycle;

R₄ is selected from the group consisting of a C₃₋₆ carbocycle, -(CH₂)_nQ, -(CH₂)_nCHQR, -CHQR, -CQ(R)₂, and unsubstituted C₁₋₆ alkyl, where Q is selected from a C₃₋₆ carbocycle, a 5- to 14-membered heteroaryl having one or more heteroatoms selected from N, O, and S, -OR,

20 -O(CH₂)_nN(R)₂, -C(O)OR, -OC(O)R, -CX₃, -CX₂H, -CXH₂, -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)R₈,
-O(CH₂)_nOR, -N(R)C(=NR₉)N(R)₂, -N(R)C(=CHR₉)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(=NR₉)N(R)₂, -N(OR)C(=CHR₉)N(R)₂, -C(=NR₉)R, -C(O)N(R)OR, and -C(=NR₉)N(R)₂, and each n is
25 independently selected from 1, 2, 3, 4, and 5;

20

25

each R₅ is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R₆ is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

30 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;

30

R₇ is selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

R₈ is selected from the group consisting of C₃₋₆ carbocycle and heterocycle;

R₉ is selected from the group consisting of H, CN, NO₂, C₁₋₆ alkyl, -OR, -S(O)₂R, -S(O)₂N(R)₂, C₂₋₆ alkenyl, C₃₋₆ carbocycle and heterocycle;

35

each R is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R' is independently selected from the group consisting of C₁₋₁₈ alkyl, C₂₋₁₈ alkenyl, -R*YR", -YR", and H;

each R" is independently selected from the group consisting of C₃₋₁₄ alkyl and C₃₋₁₄ alkenyl;

each R* is independently selected from the group consisting of C₁₋₁₂ alkyl and C₂₋₁₂ alkenyl;

each Y is independently a C₃₋₆ carbocycle;

40

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

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

or salts or isomers thereof.

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

R₁ is selected from the group consisting of C₅₋₃₀ alkyl, C₅₋₂₀ alkenyl, -R*YR", -YR", and -R"M'R';

45 R₂ and R₃ are independently selected from the group consisting of H, C₂₋₁₄ alkyl, C₂₋₁₄ alkenyl, -R*YR", -YR", and -R'OR", or R₂ and R₃, together with the atom to which they are attached, form a heterocycle or carbocycle;

45

R₄ is -(CH₂)_nQ or -(CH₂)_nCHQR, where Q is -N(R)₂, and n is selected from 3, 4, and 5;

each R₅ is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R₆ is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

50 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;

50

R₇ is selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R' is independently selected from the group consisting of C₁₋₁₈ alkyl, C₂₋₁₈ alkenyl, -R*YR", -YR", and H;

55

each R" is independently selected from the group consisting of C₃₋₁₄ alkyl and C₃₋₁₄ alkenyl;

each R* is independently selected from the group consisting of C₁₋₁₂ alkyl and C₂₋₁₂ alkenyl;

each Y is independently a C₃₋₆ carbocycle;

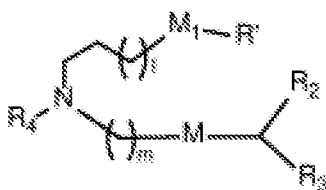
each X is independently selected from the group consisting of F, Cl, Br, and I; and

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

[0379] In some embodiments, another subset of compounds of Formula (I) includes those in which

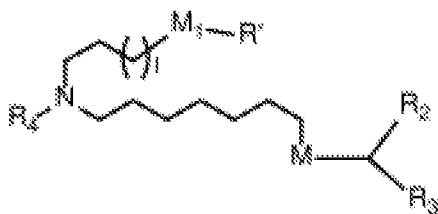
R_1 is selected from the group consisting of C_{5-30} alkyl, C_{5-20} alkenyl, $-R^*YR^*$, $-YR^*$, and $-R^*M'R^*$;
 R_2 and R_3 are independently selected from the group consisting of C_{1-14} alkyl, C_{2-14} alkenyl, $-R^*YR^*$, $-YR^*$, and $-R^*OR^*$, or R_2 and R_3 , together with the atom to which they are attached, form a heterocycle or carbocycle;
 R_4 is selected from the group consisting of $-(CH_2)_nQ$, $-(CH_2)_nCHQR$, $-CHQR$, and $-CQ(R)_2$, where Q is $-N(R)_2$, and n is selected from 1, 2, 3, 4, and 5;
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;
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;
 R_7 is selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;
each R is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;
each R' is independently selected from the group consisting of C_{1-18} alkyl, C_{2-18} alkenyl, $-R^*YR^*$, $-YR^*$, and H;
each R'' is independently selected from the group consisting of C_{3-14} alkyl and C_{3-14} alkenyl;
each R''' is independently selected from the group consisting of C_{1-12} alkyl and C_{1-12} alkenyl;
each Y is independently a C_{3-6} carbocycle;
each X is independently selected from the group consisting of F, Cl, Br, and I; and
m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,
or salts or isomers thereof.

[0380] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IA):



or a salt or isomer thereof, wherein l 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.

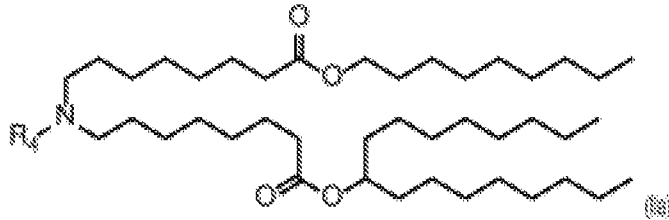
[0381] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (II):



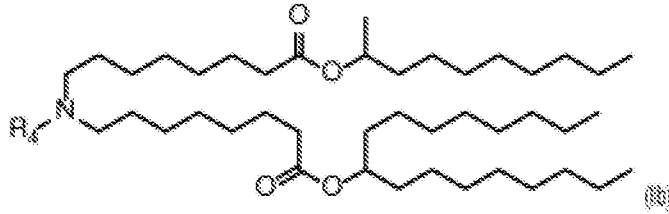
or a salt or isomer thereof, wherein l is selected from 1, 2, 3, 4, and 5; M_1 is a bond or M' ; R_4 is unsubstituted C_{1-3} alkyl, or $-(CH_2)_nQ$, in which n is 2, 3, or 4, and Q is OH, $-NHC(S)N(R)_2$, $-NHC(O)N(R)_2$, $-N(R)C(O)R$, $-N(R)S(O)_2R$, $-N(R)R_8$, $-NHC(=NR_9)N(R)_2$, $-NHC(=CHR_9)N(R)_2$, $-OC(O)N(R)_2$, $-N(R)C(O)OR$, 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 acyl 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.

[0382] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IIa), (IIb), (IIc), or (IIe):

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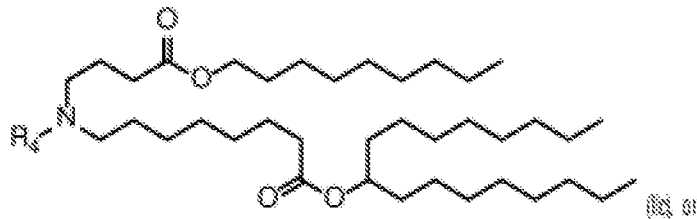


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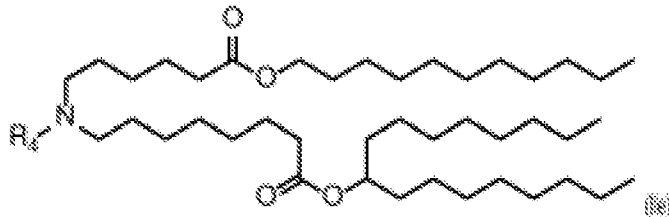
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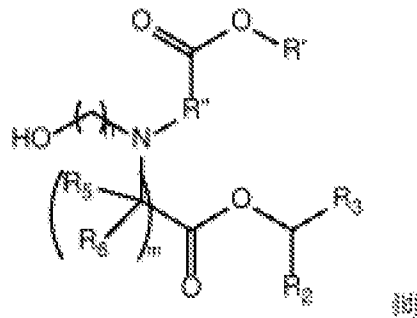


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or a salt or isomer thereof, wherein R_4 is as described herein.

[0383] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IIe):

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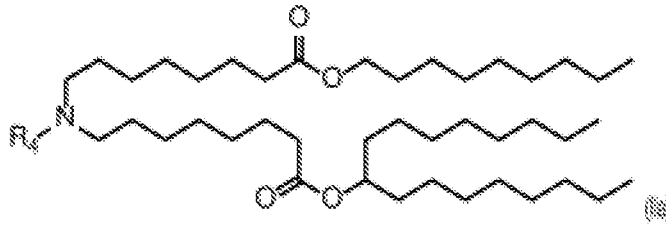
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or a salt or isomer thereof, wherein n is 2, 3, or 4; and m , R_1' , R_2 , and R_3 through R_6 are as described herein. For example, each of R_2 and R_3 may be independently selected from the group consisting of C_{5-14} alkyl and C_{5-14} alkenyl.

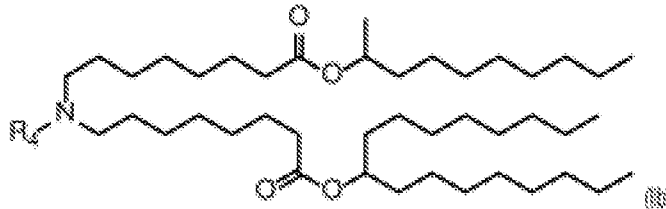
[0384] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IIa), (IIb), (IIc), or (IId):

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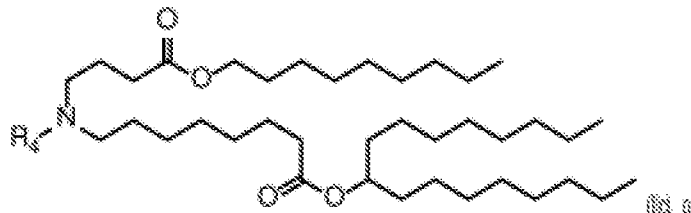


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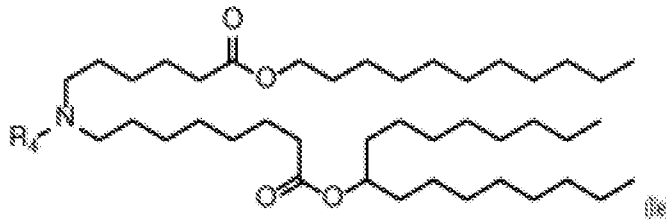
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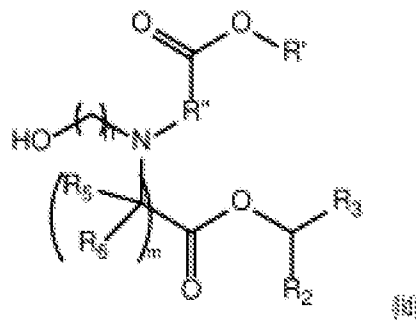


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or a salt or isomer thereof, wherein R_4 is as described herein.

[0385] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (II):

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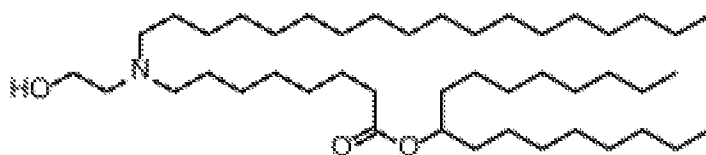
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or a salt or isomer thereof, wherein n is 2, 3, of 4; and m , R_1 , R_2 , and R_3 through R_6 are as described herein. For example, each of R_2 and R_3 may be independently selected from the group consisting of C_{5-14} alkyl and C_{5-14} alkenyl.

[0386] In some embodiments, the compound of Formula (I) is selected from the group consisting of:

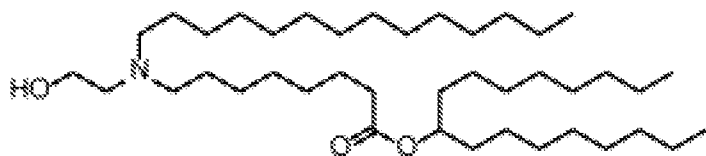
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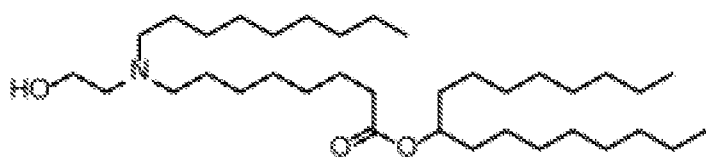
Compound 1)

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Compound 2)

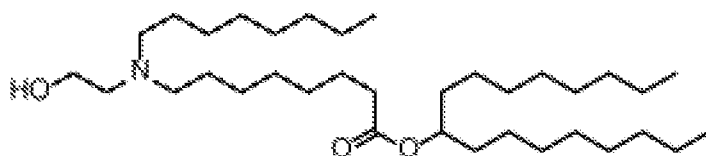
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Compound 3)

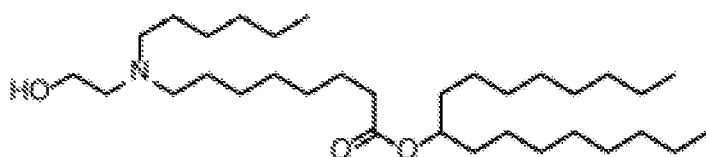
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Compound 4)

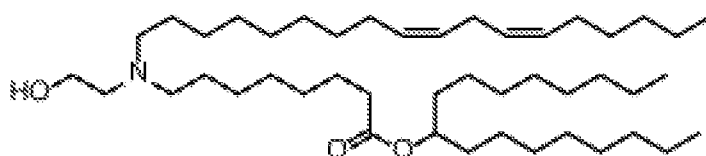
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Compound 5)

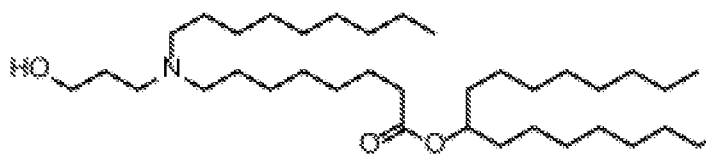
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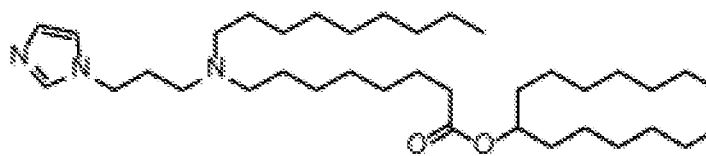
Compound 6)

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Compound 7)

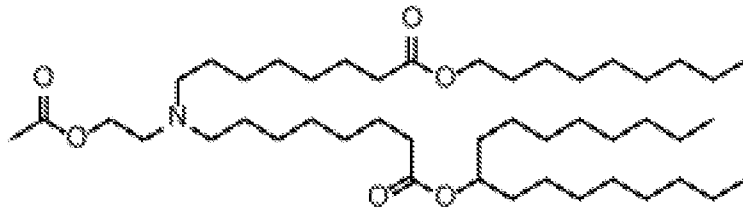
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Compound 8)

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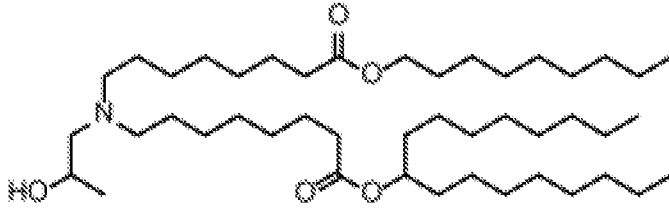
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Compound 9)

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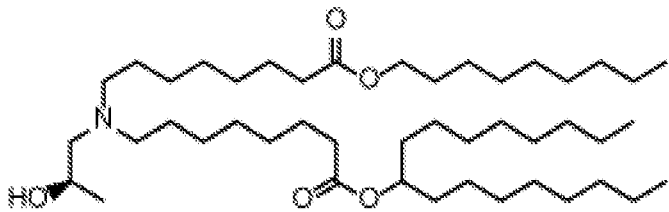
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Compound 10)

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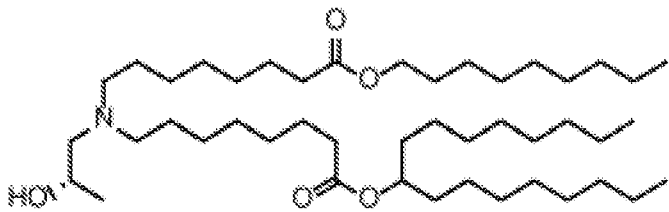
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Compound 11)

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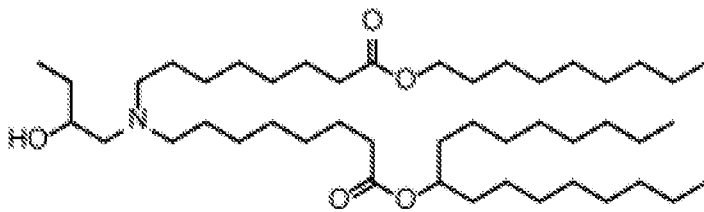
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Compound 12)

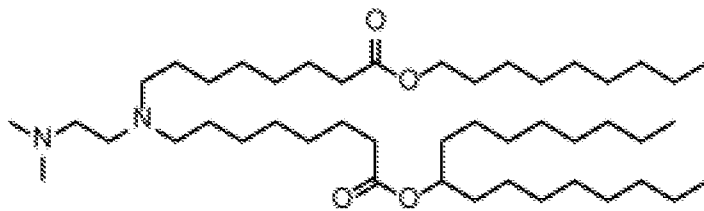
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Compound 13)

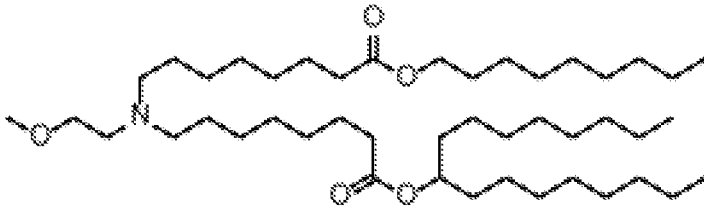
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Compound 14)

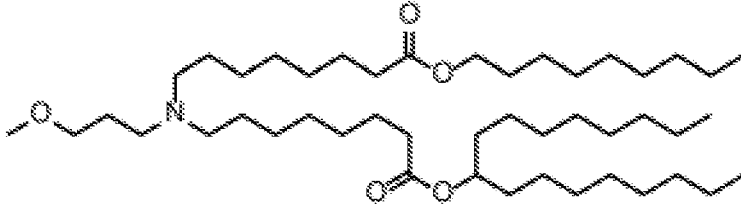
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(Compound 15)

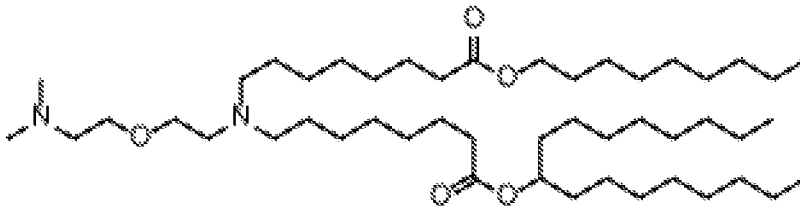
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(Compound 16)

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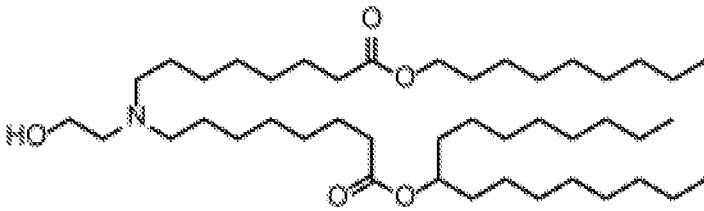
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(Compound 17)

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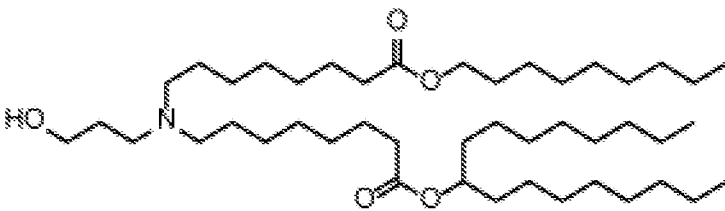
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(Compound 18)

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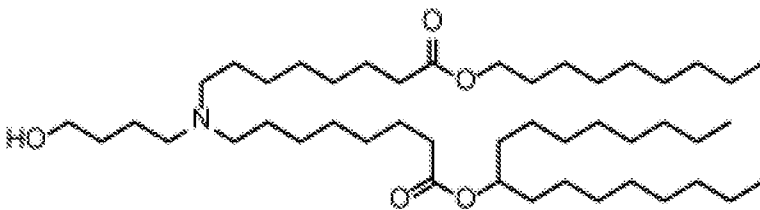
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(Compound 19)

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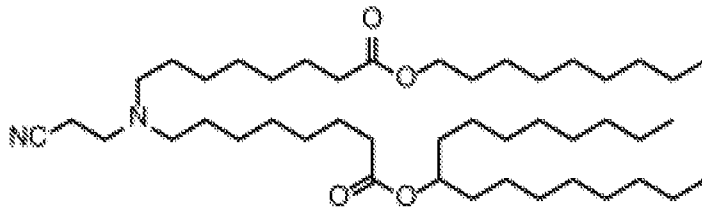
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(Compound 20)

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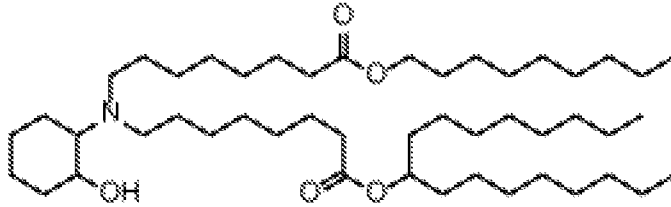
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(Compound 21)

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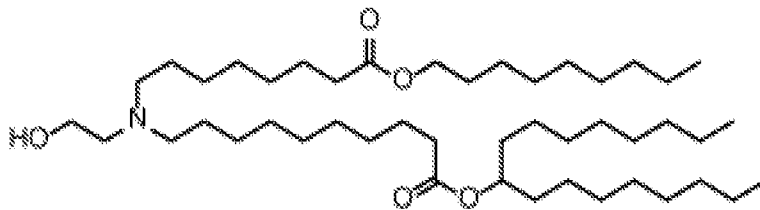
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(Compound 22)

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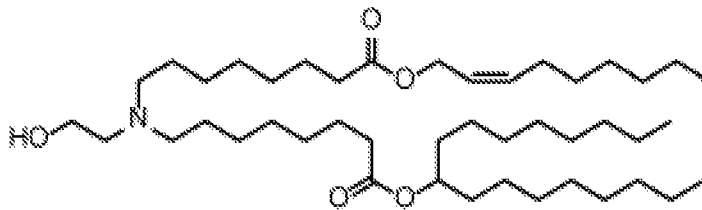
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(Compound 23)

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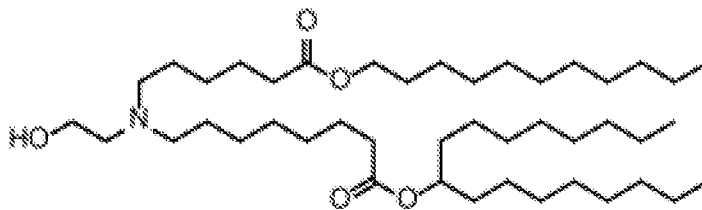
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(Compound 24)

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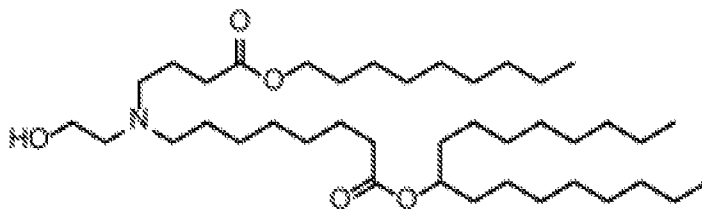
45



(Compound 25)

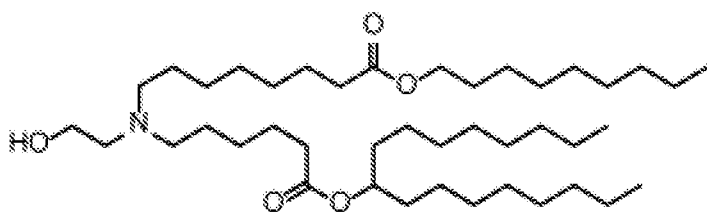
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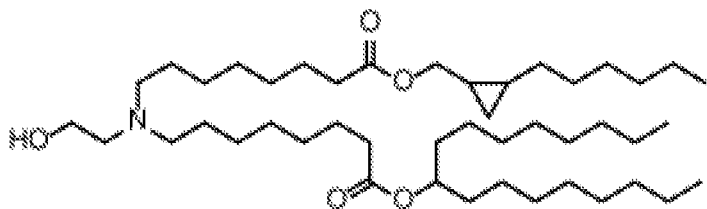
(Compound 26)

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(Compound 27)

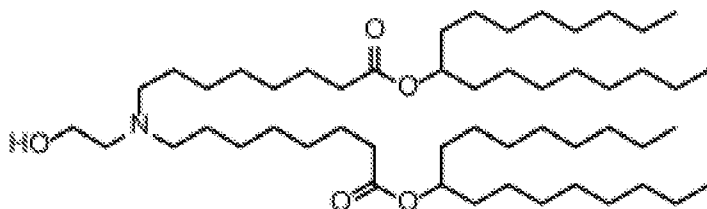
10



(Compound 28)

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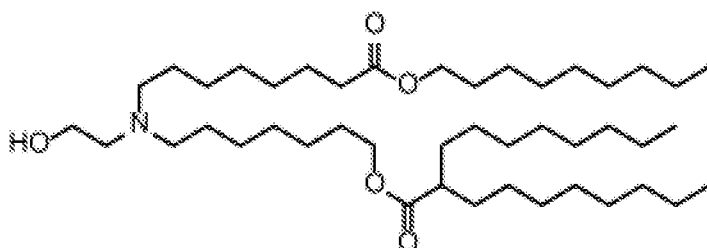
20



(Compound 29)

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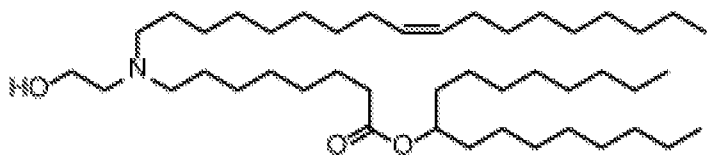
30



(Compound 30)

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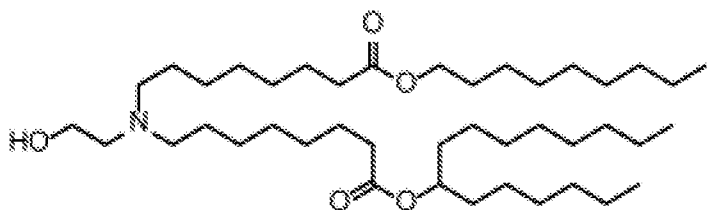
40



(Compound 31)

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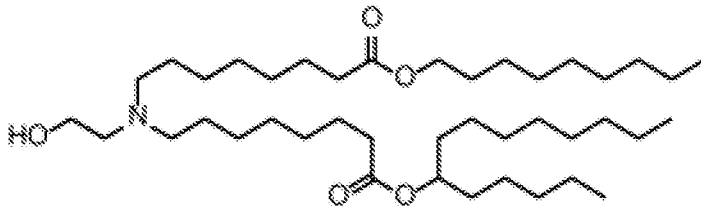
50



(Compound 32)

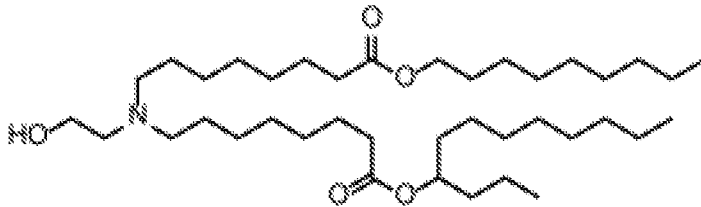
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Compound 33,

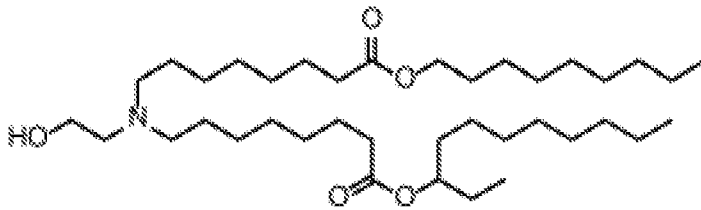
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Compound 34,

15

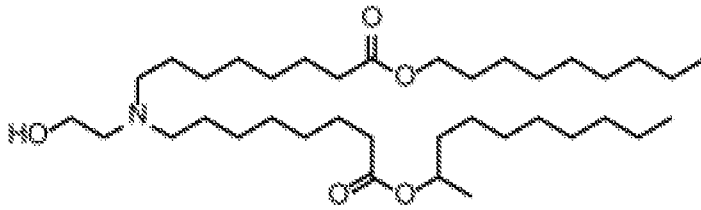
20



Compound 35,

25

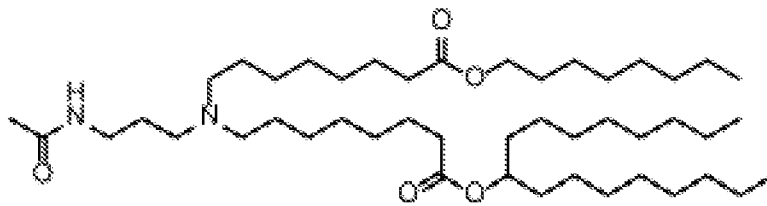
30



Compound 36,

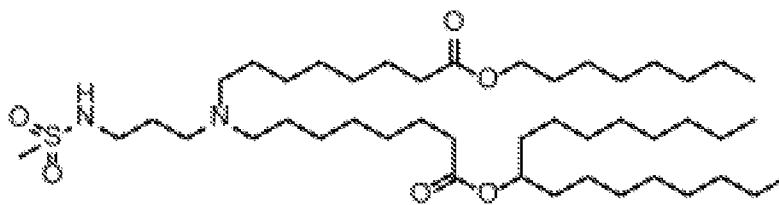
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Compound 37,

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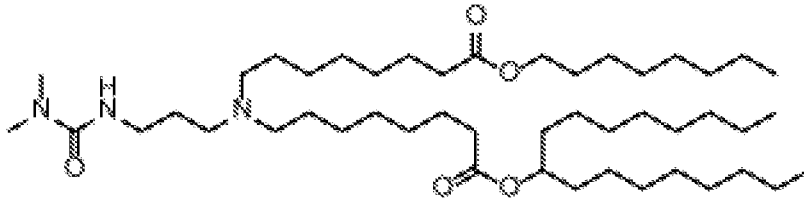


Compound 38,

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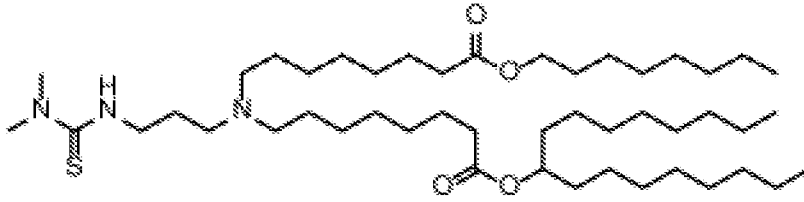
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Compound 38.

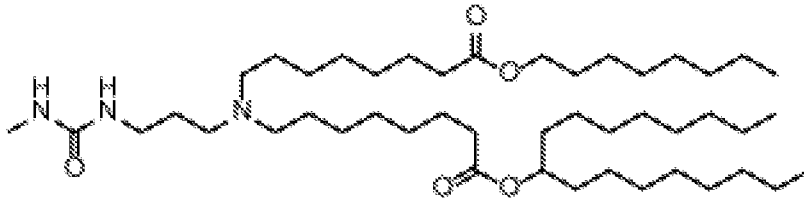
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Compound 39.

15

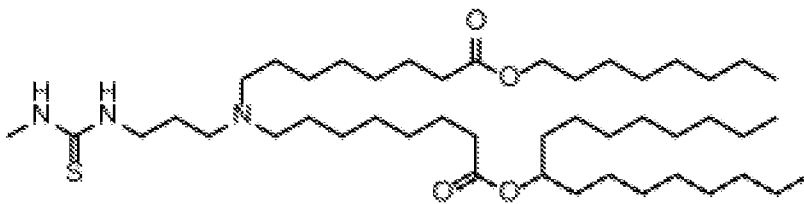
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Compound 40.

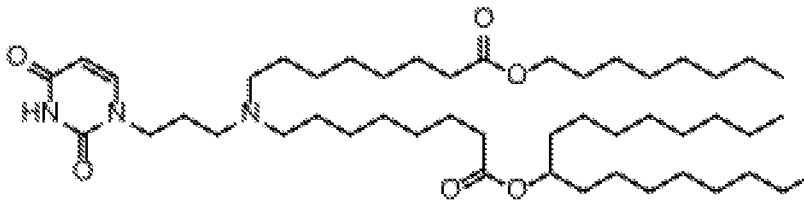
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Compound 41.

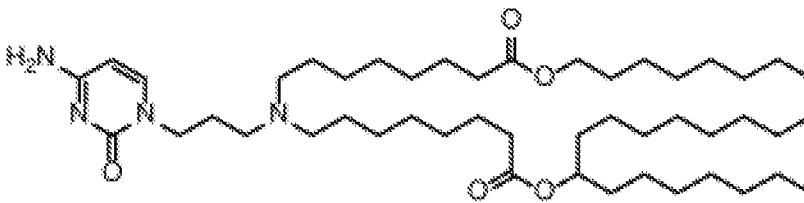
35



Compound 42.

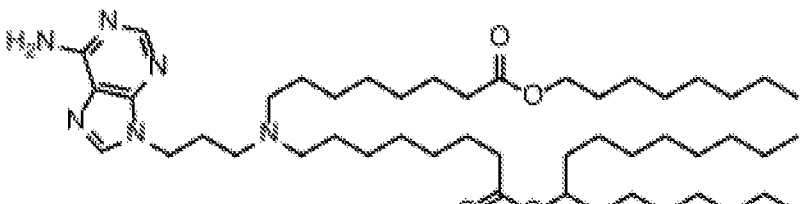
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Compound 43.

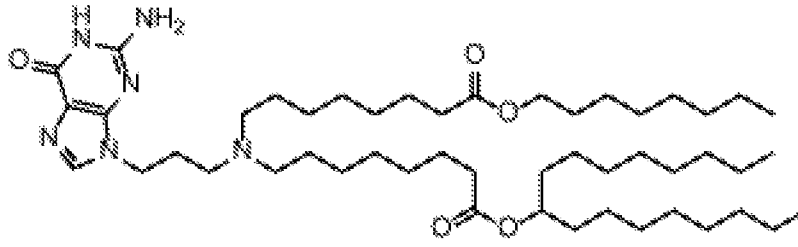
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Compound 44.

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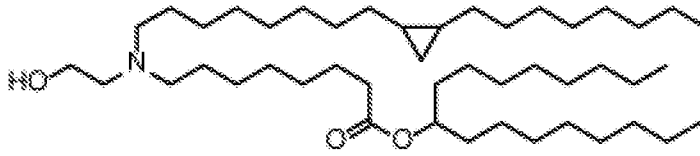
5



Compound 46,

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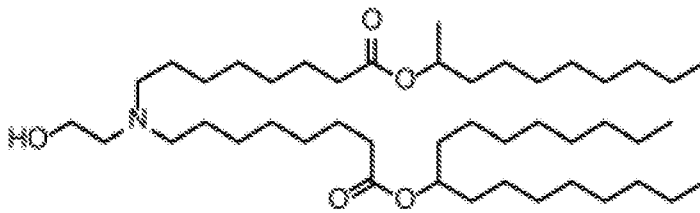
15



Compound 47,

20

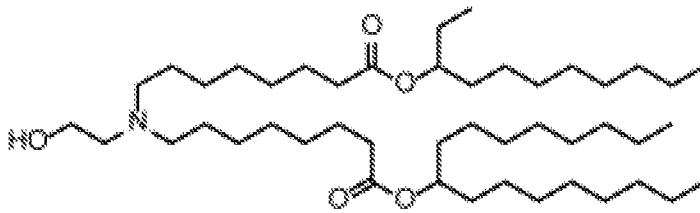
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Compound 48,

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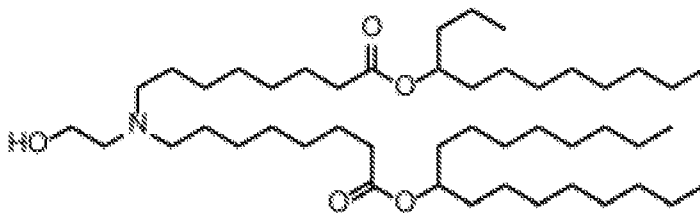
35



Compound 49,

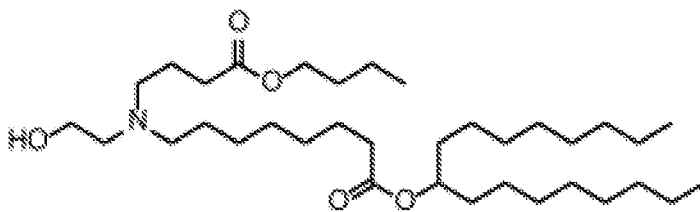
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Compound 50,

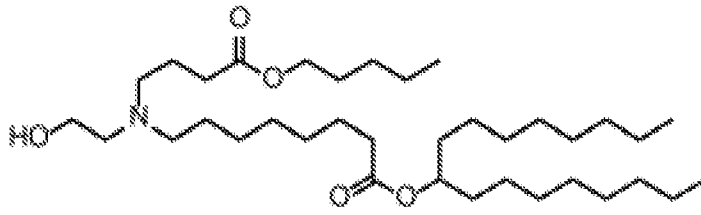
50



Compound 51,

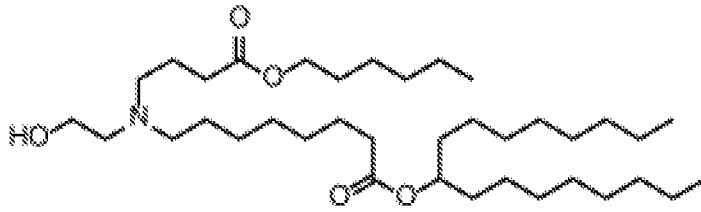
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Compound 53.

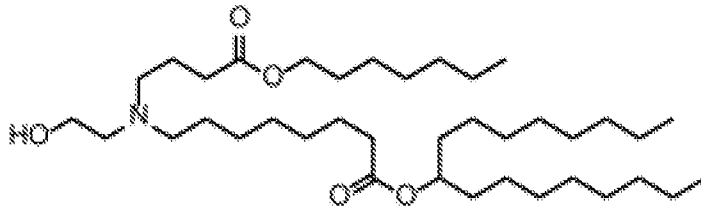
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Compound 54.

15

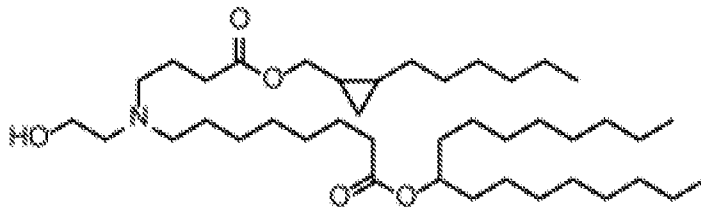
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Compound 55.

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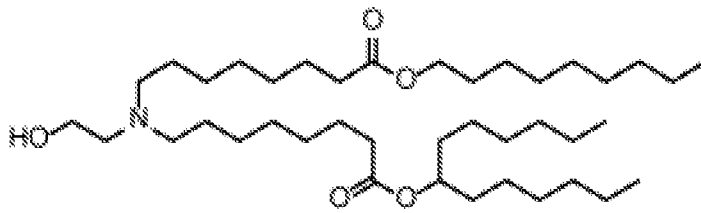
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Compound 56.

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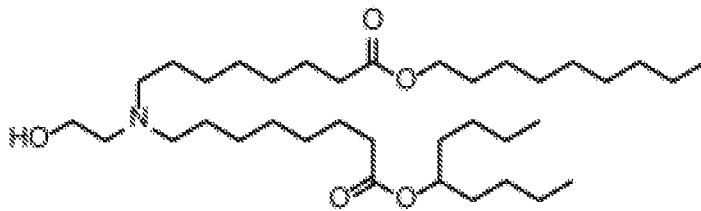
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Compound 57.

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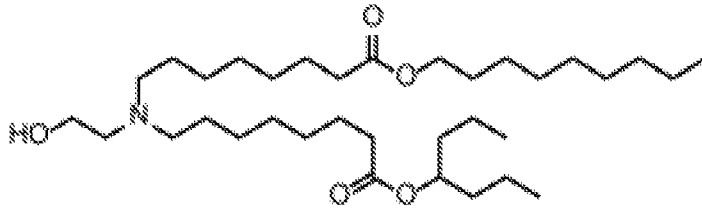
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Compound 58.

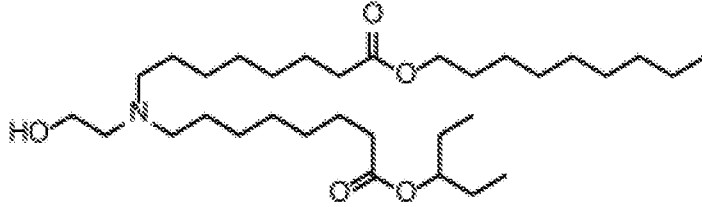
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(Compound 59),

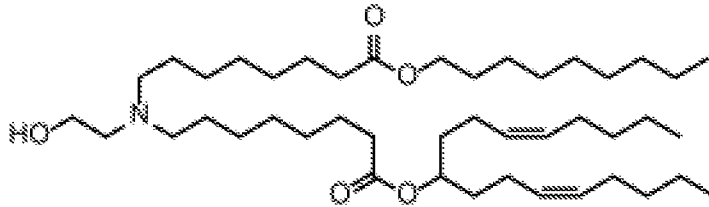
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(Compound 60),

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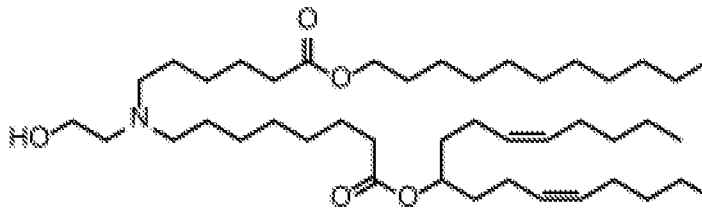
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(Compound 61), and

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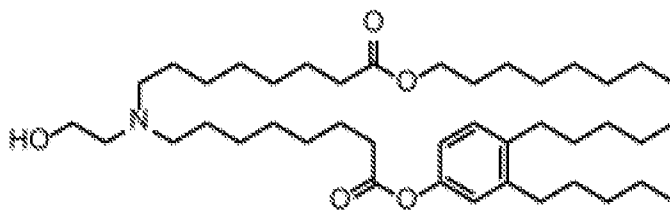


(Compound 62),

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[0387] In further embodiments, the compound of Formula (I) is selected from the group consisting of:

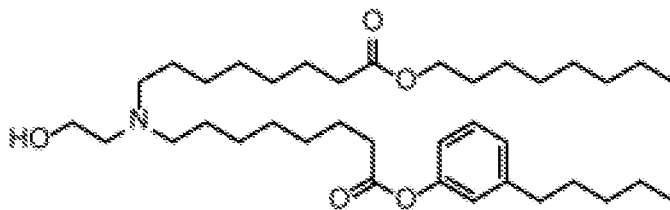
40



(Compound 63),

45

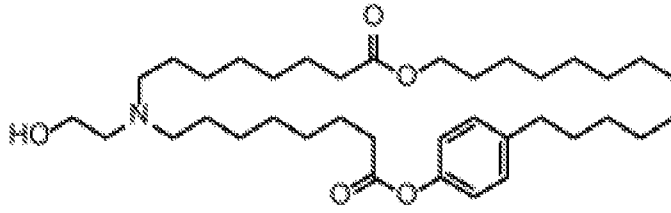
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(Compound 64), and

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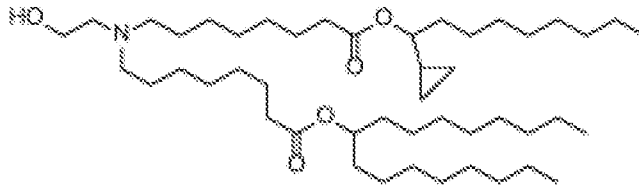


Compound 64.

10

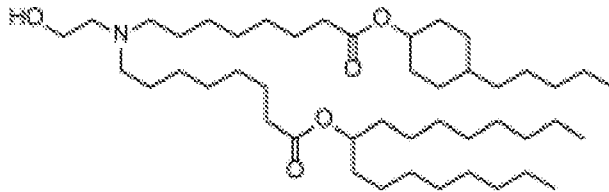
[0388] In some embodiments, the compound of Formula (I) is selected from the group consisting of:

15



Compound 65.

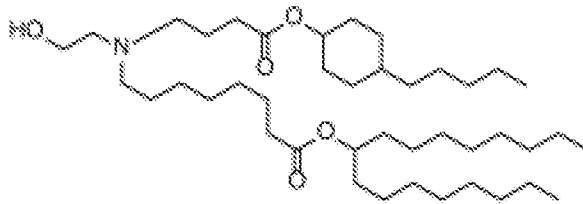
20



Compound 66.

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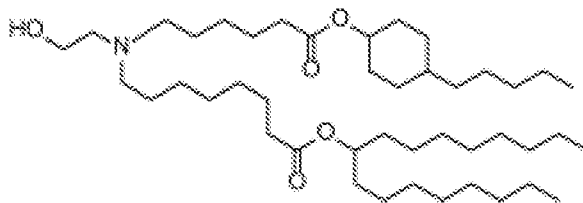
30



Compound 67.

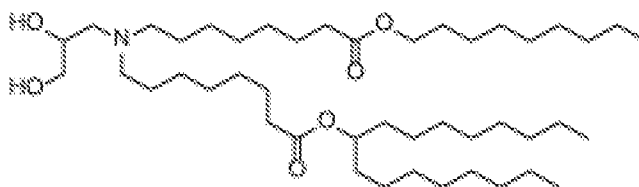
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Compound 68.

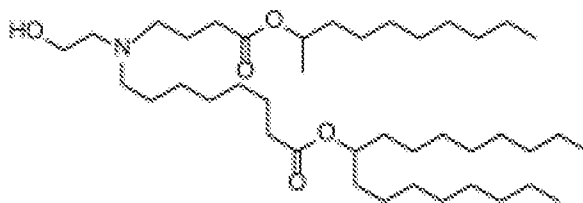
45



Compound 69.

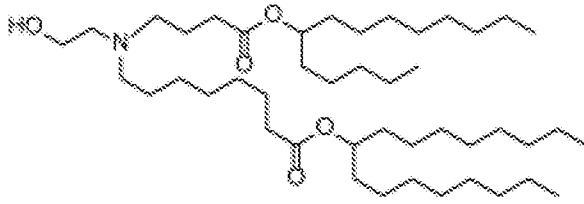
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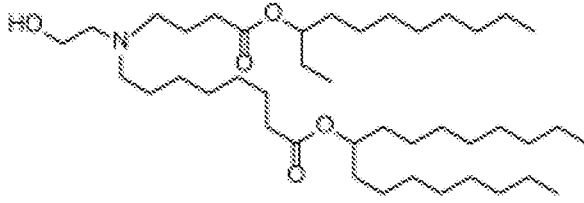
Compound 70.

5



Compound 71,

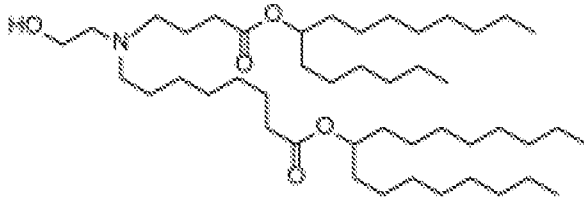
10



Compound 72,

15

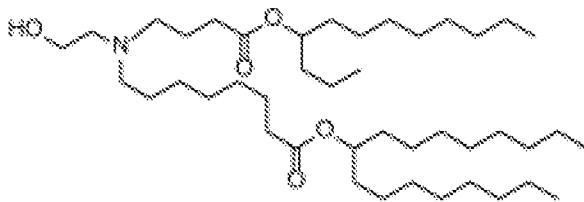
20



Compound 73,

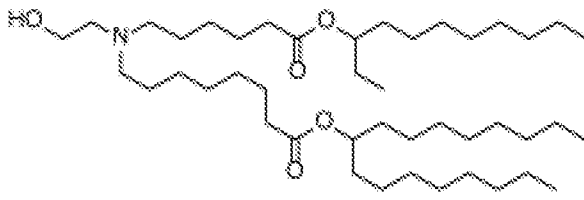
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Compound 74,

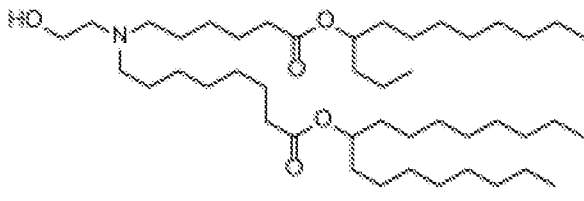
35



Compound 75,

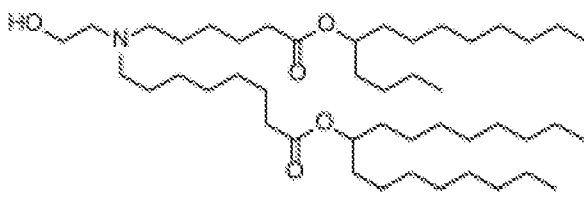
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Compound 76,

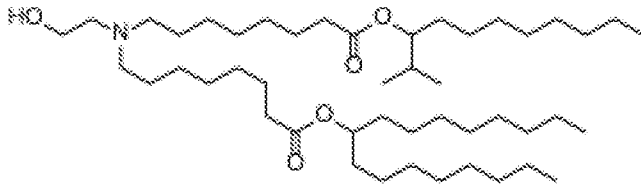
50



Compound 77,

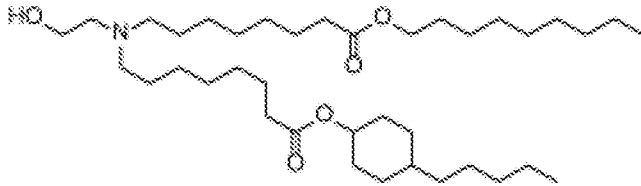
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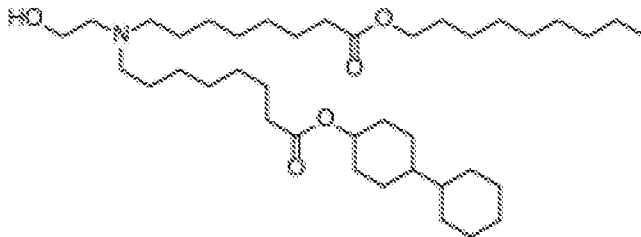
(Compound 78)

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(Compound 79)

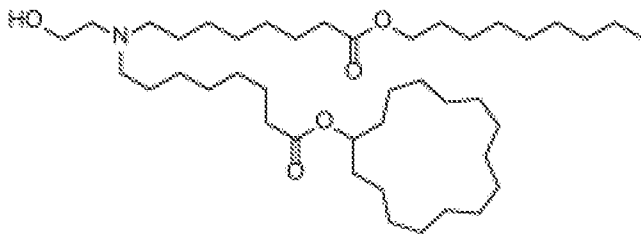
15



(Compound 80)

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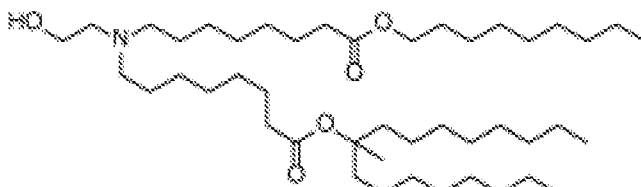
25



(Compound 81)

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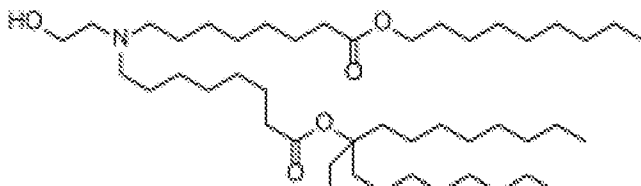
35



(Compound 82)

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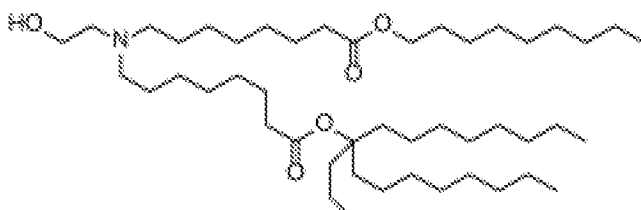
45



(Compound 83)

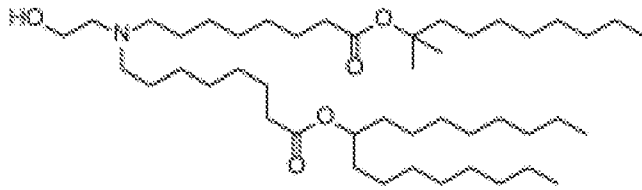
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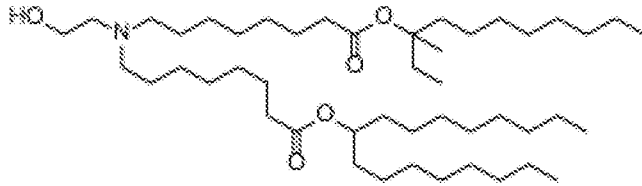
(Compound 84)

5



Compound 85,

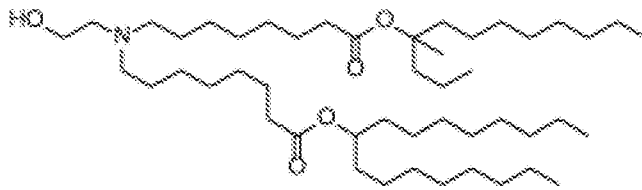
10



Compound 86,

15

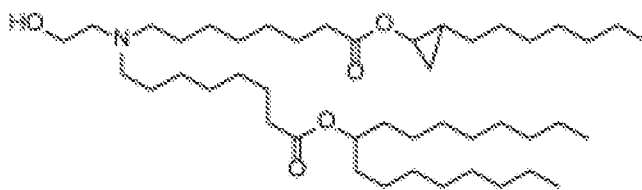
20



Compound 87,

25

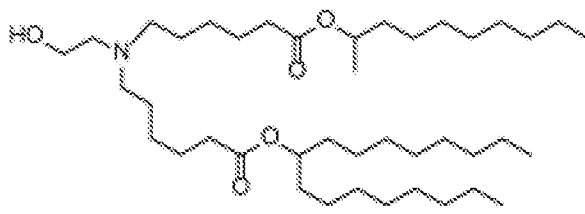
30



Compound 88,

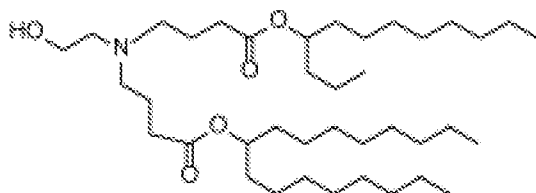
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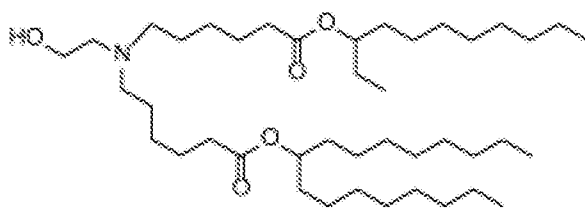
Compound 89,

45



Compound 90,

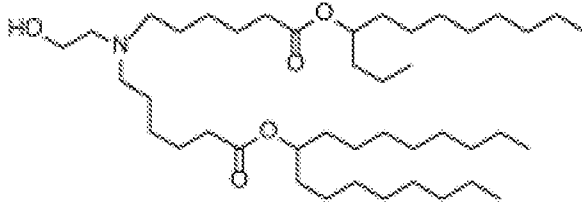
50



Compound 91,

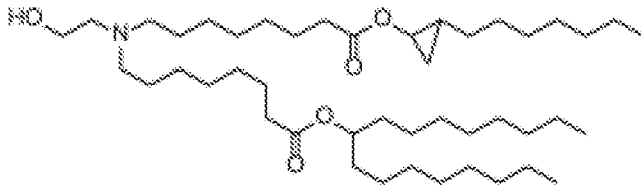
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Compound 92.

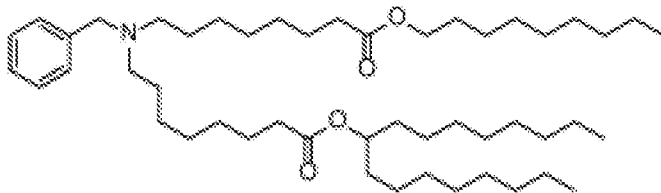
10



Compound 93.

15

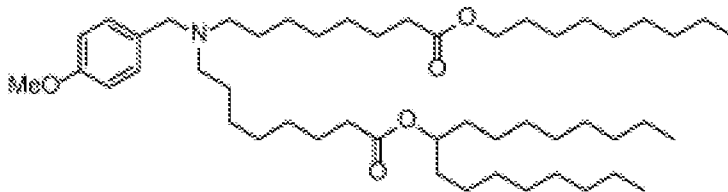
20



Compound 94.

25

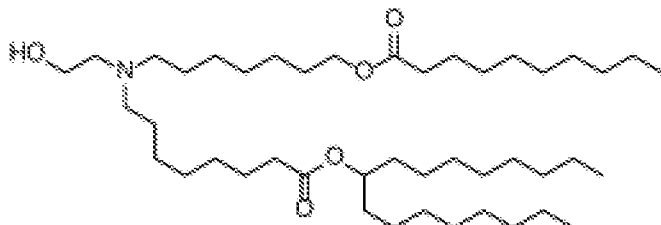
30



Compound 95.

35

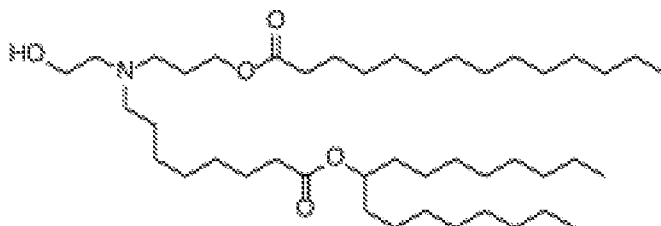
40



Compound 96.

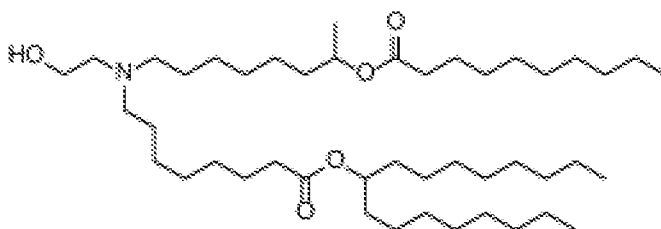
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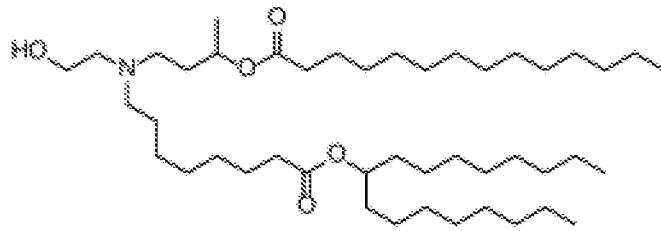
Compound 97.

55



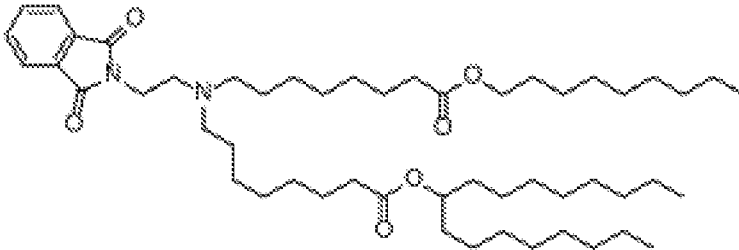
Compound 98.

5



Compound 99.

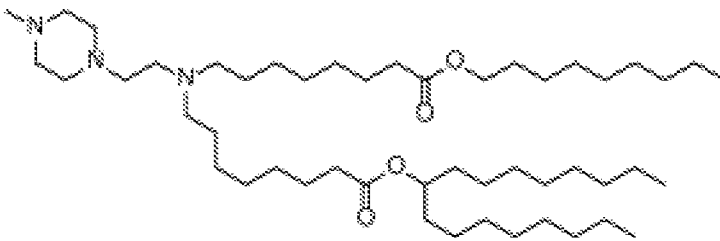
10



Compound 100.

15

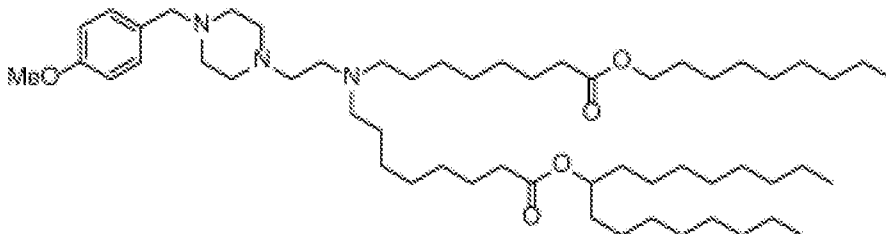
20



Compound 101.

25

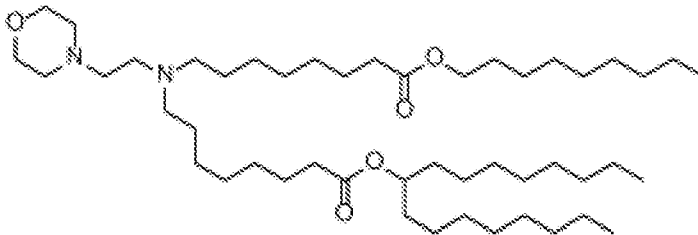
30



Compound 102.

35

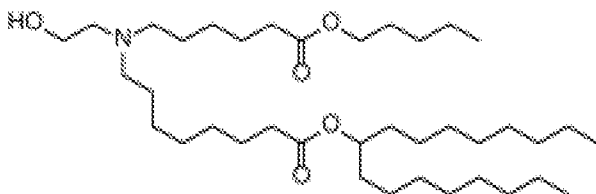
40



Compound 103.

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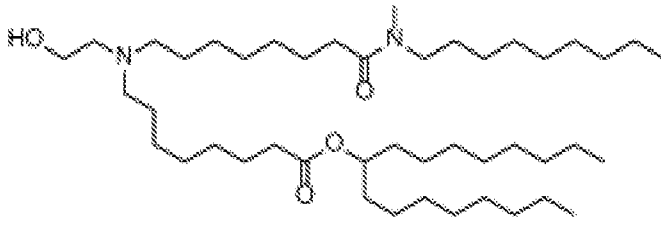
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Compound 104.

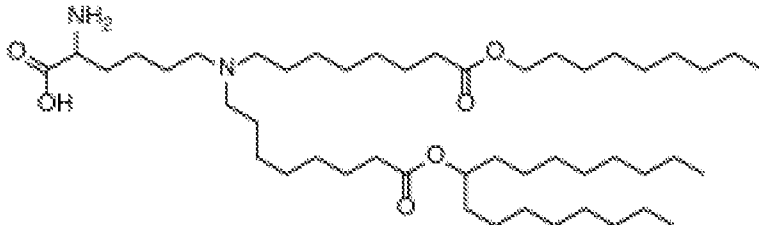
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(Compound 105)

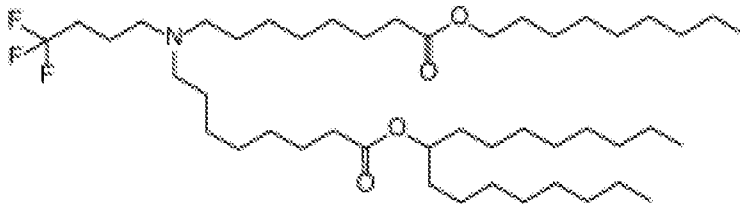
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(Compound 106)

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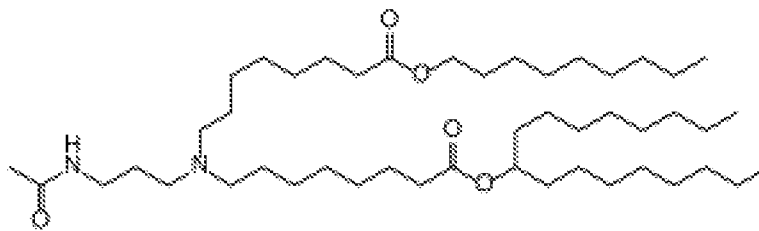
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(Compound 107)

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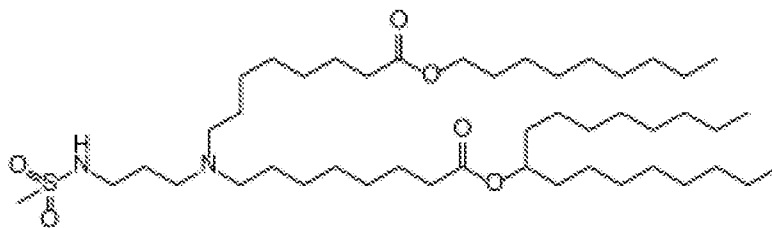
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(Compound 108)

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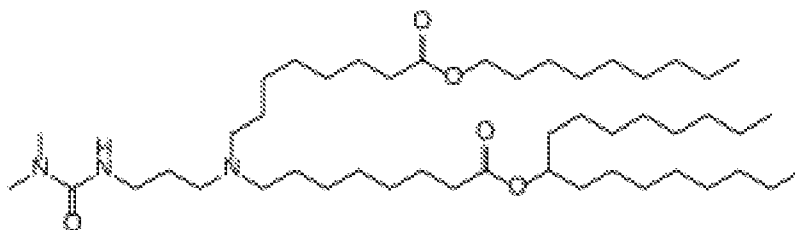
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(Compound 109)

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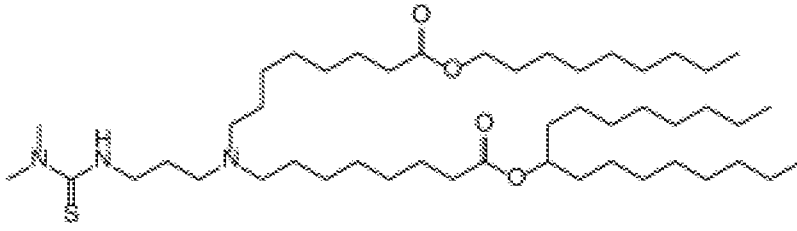
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(Compound 110)

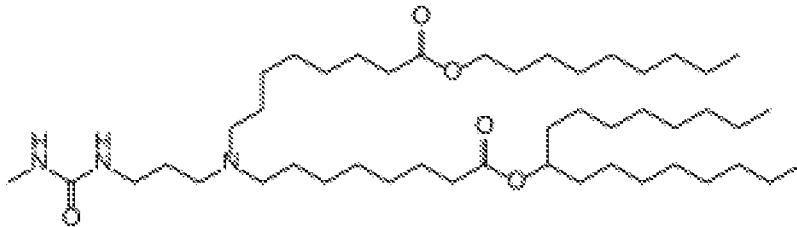
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Compound 111)

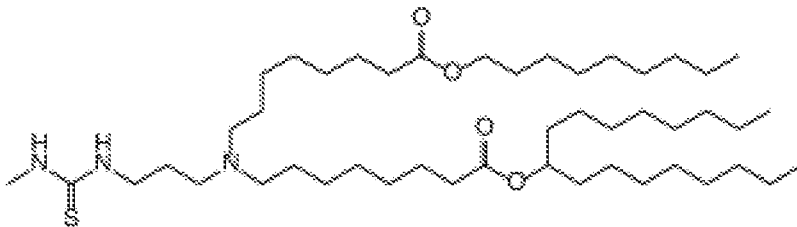
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Compound 112)

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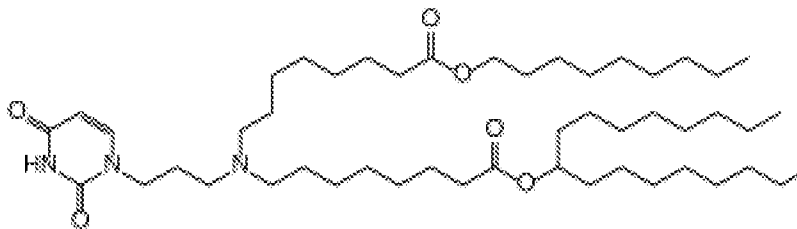
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Compound 113)

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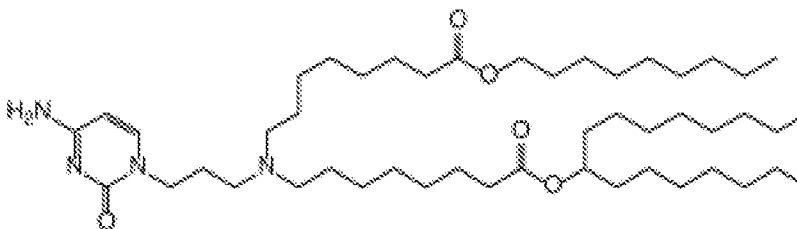
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Compound 114)

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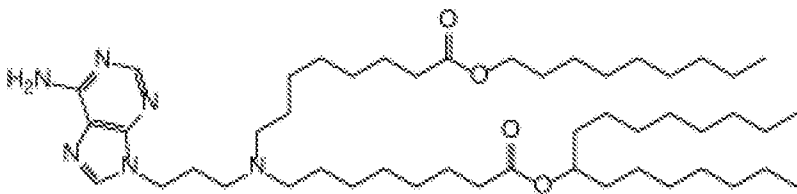
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Compound 115)

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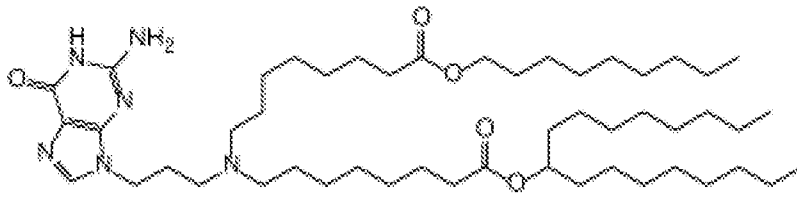
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Compound 116)

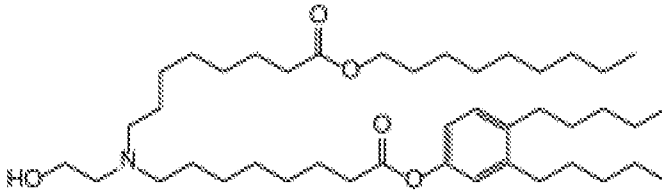
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(Compound 117)

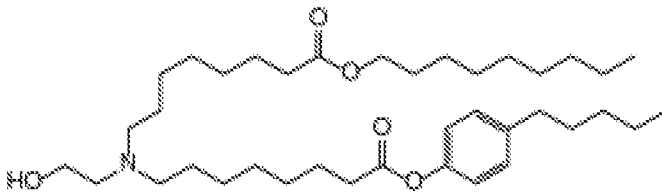
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(Compound 118)

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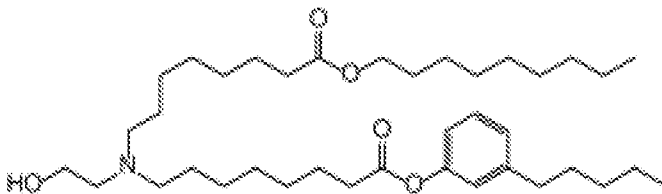
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(Compound 119)

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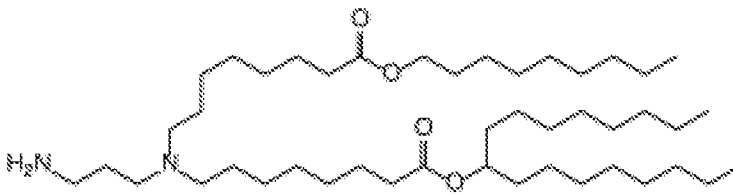
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(Compound 120)

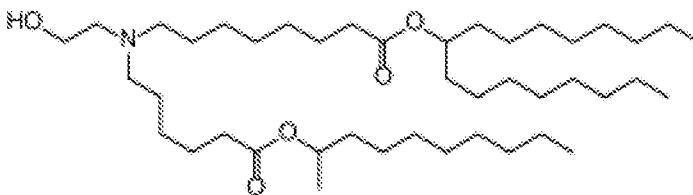
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(Compound 121)

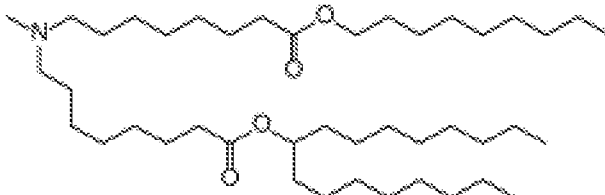
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(Compound 122)

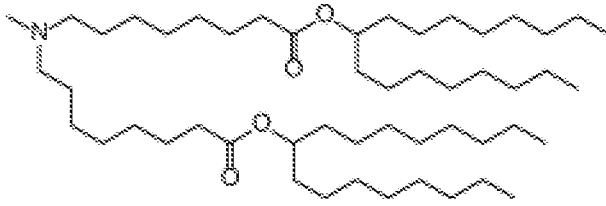
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(Compound 123)

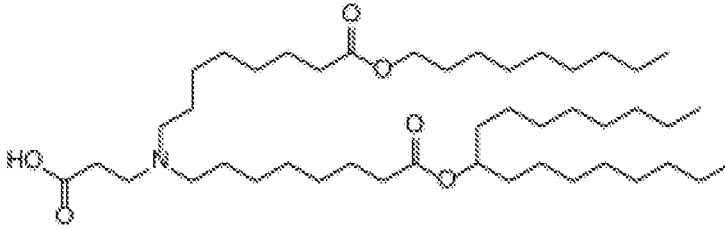
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(Compound 124)

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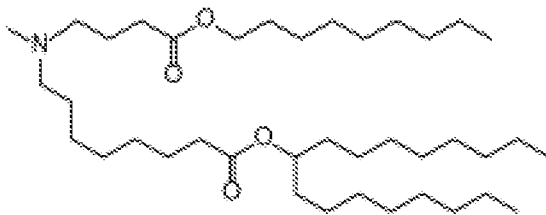
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(Compound 125)

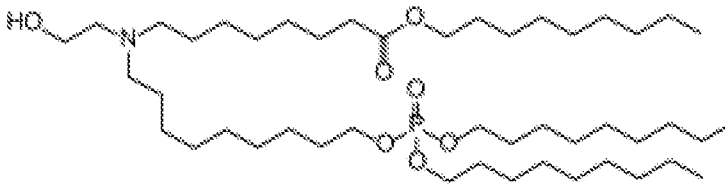
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(Compound 126)

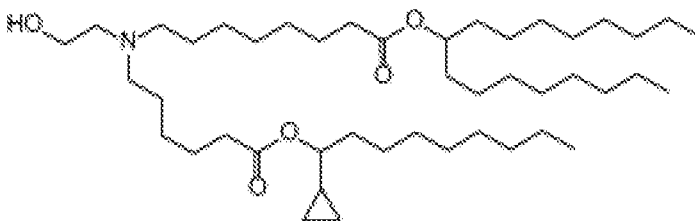
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(Compound 127)

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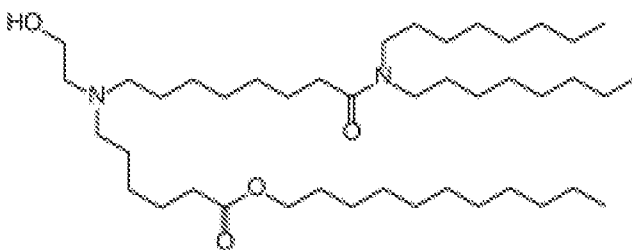
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(Compound 128)

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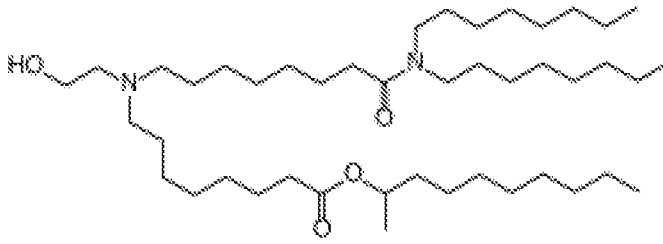
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(Compound 129)

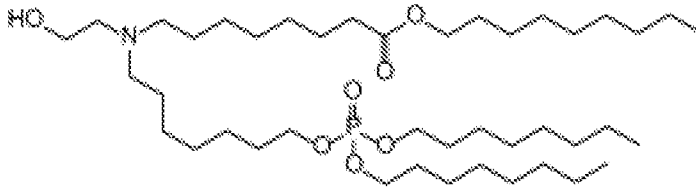
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(Compound 129)

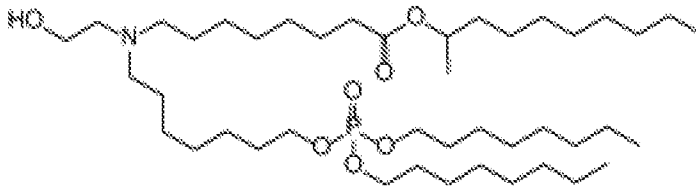
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(Compound 131)

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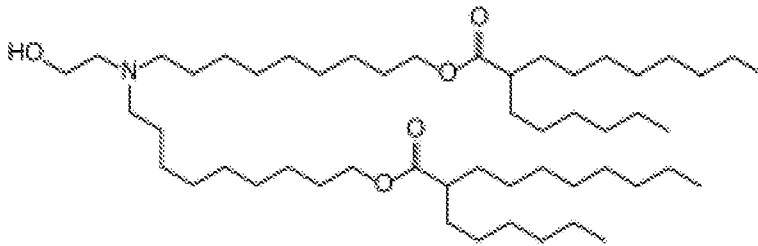
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(Compound 132)

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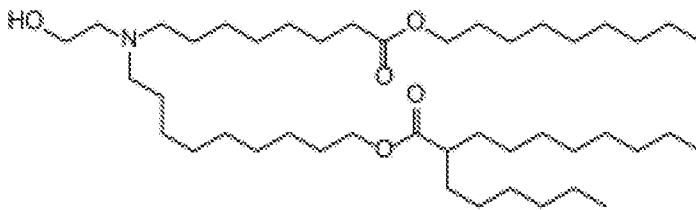
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(Compound 133)

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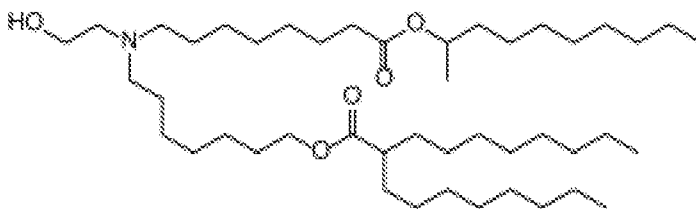
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(Compound 134)

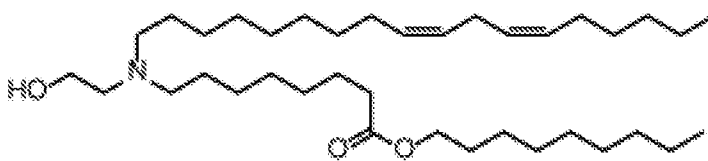
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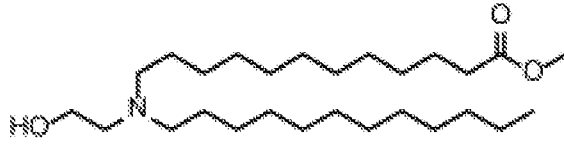
(Compound 135)

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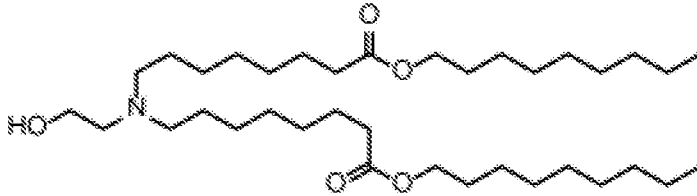
(Compound 136)

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(Compound 137)

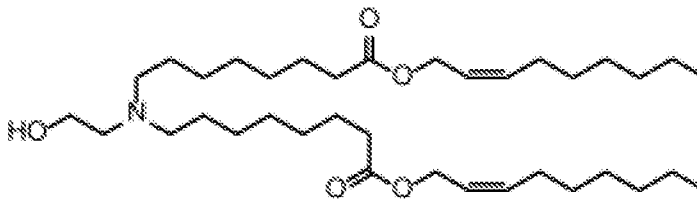
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(Compound 138)

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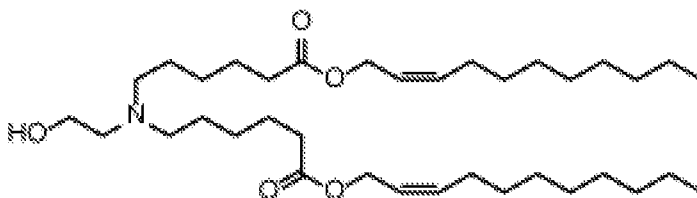
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(Compound 139)

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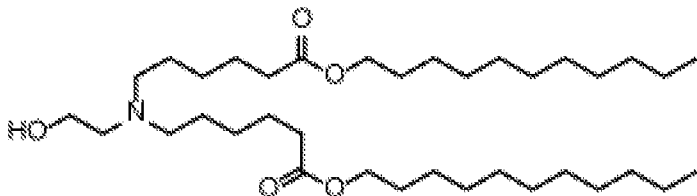
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(Compound 140)

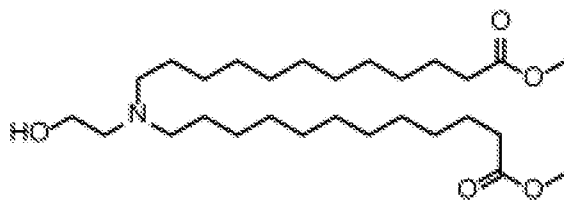
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(Compound 141)

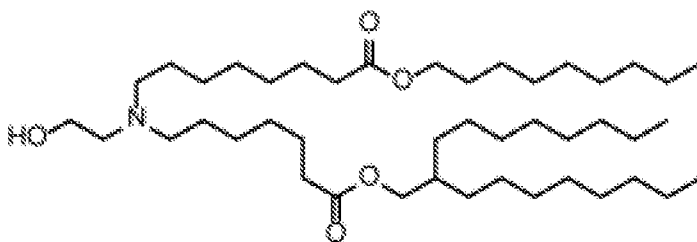
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(Compound 142)

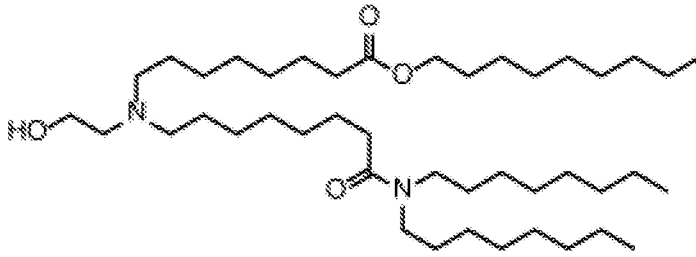
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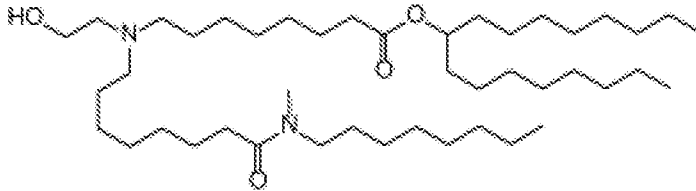
(Compound 143)

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(Compound 144)

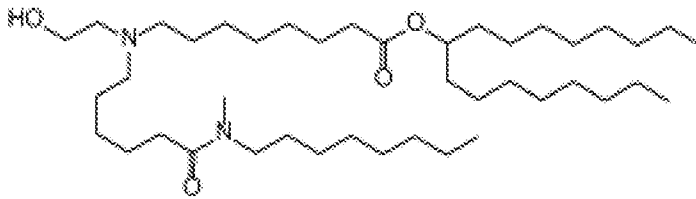
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(Compound 145)

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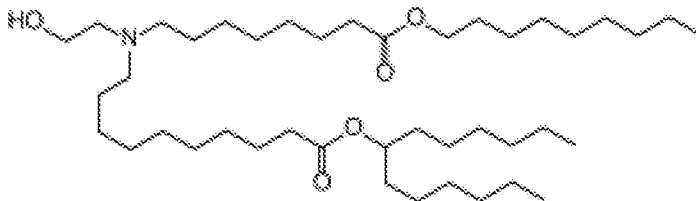
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(Compound 146)

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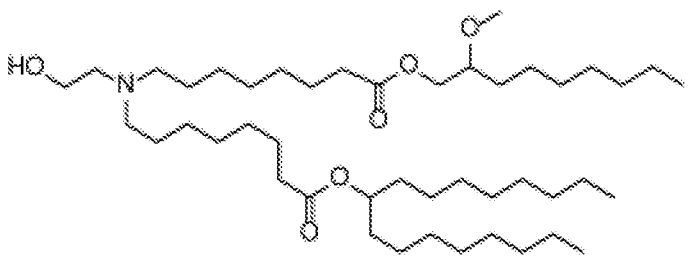
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(Compound 147)

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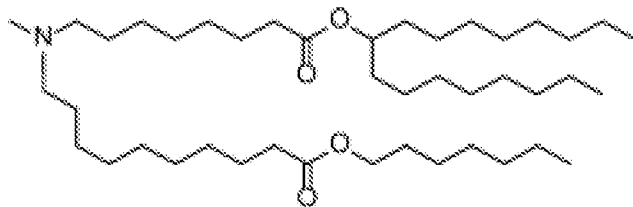
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(Compound 148)

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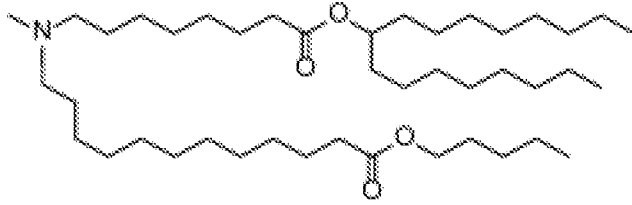
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(Compound 149)

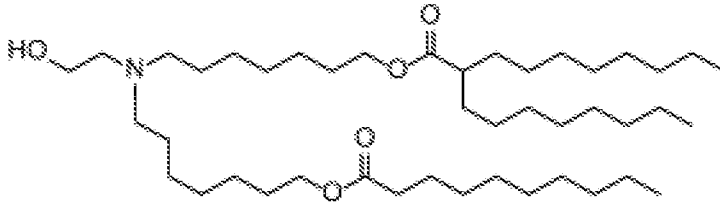
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(Compound 130)

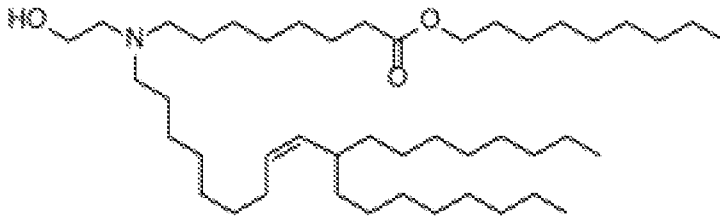
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(Compound 131)

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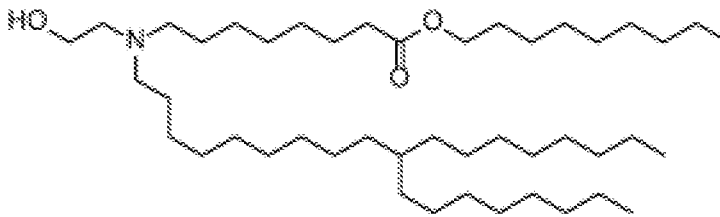
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(Compound 132)

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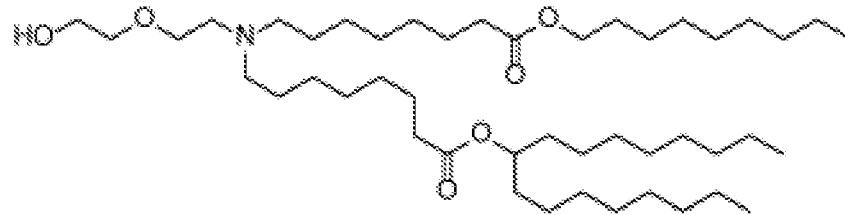
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(Compound 133)

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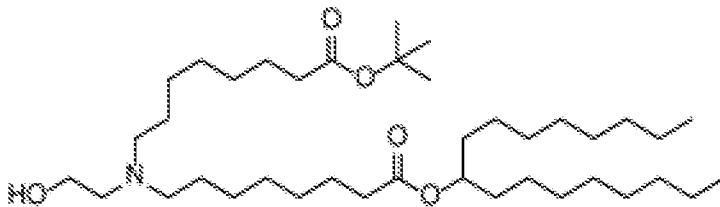
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(Compound 134)

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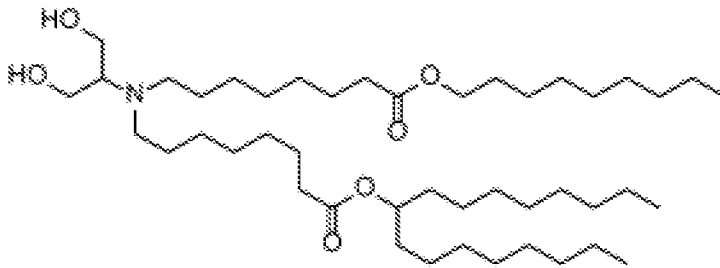
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(Compound 135)

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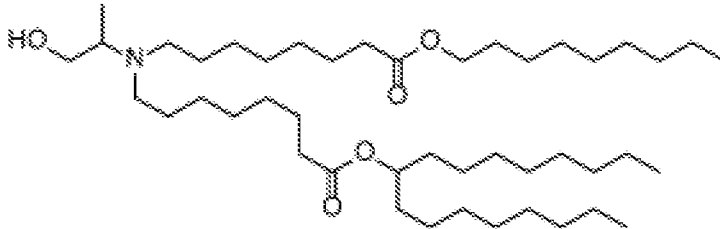
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(Compound 155)

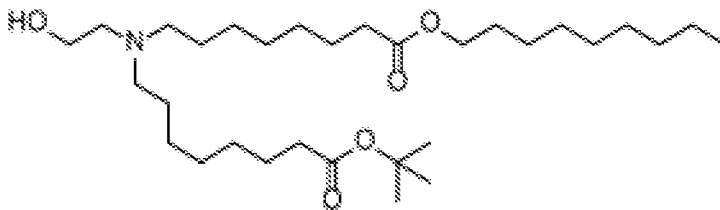
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(Compound 157)

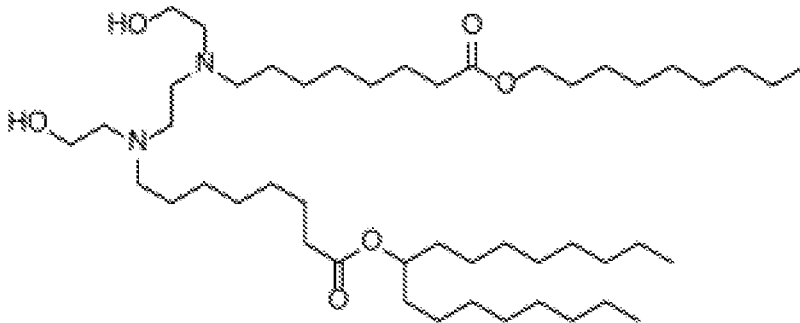
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(Compound 159)

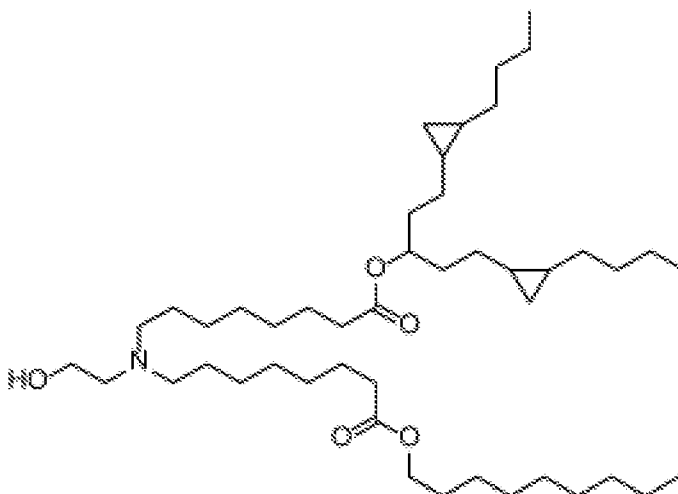
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(Compound 158)

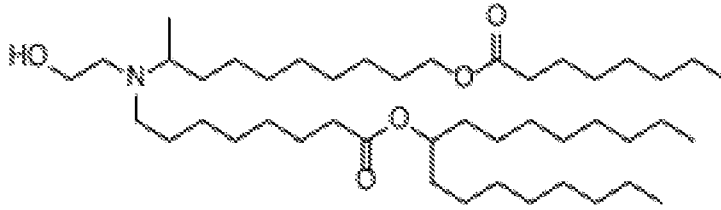
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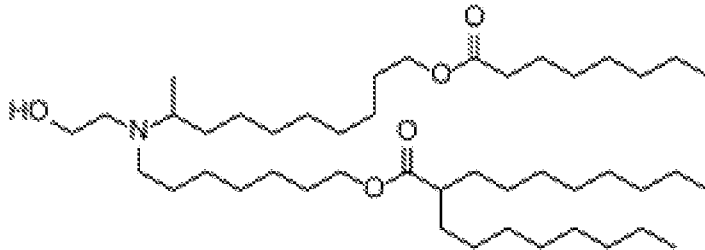
(Compound 156)

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(Compound 161)

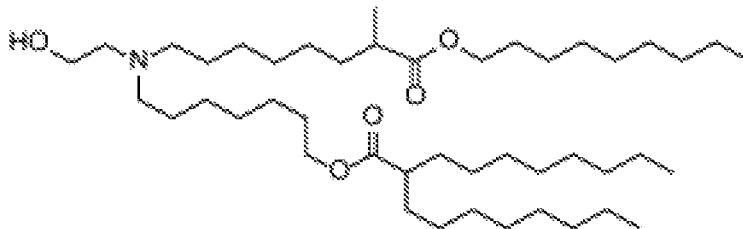
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(Compound 162)

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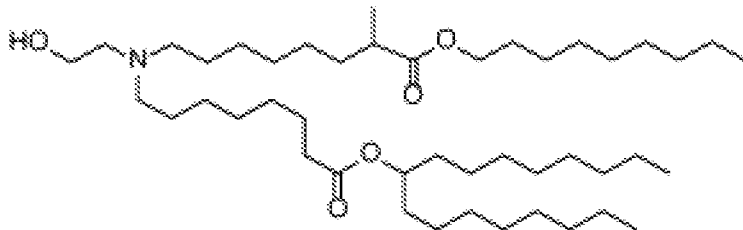
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(Compound 163)

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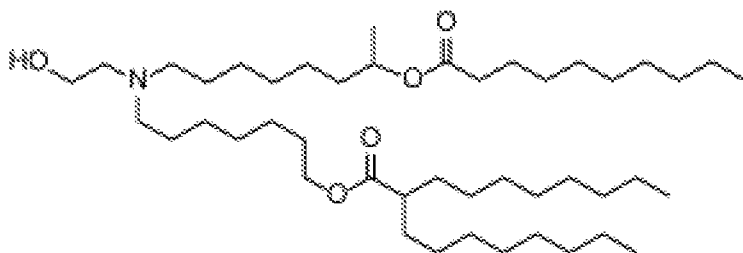
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(Compound 164)

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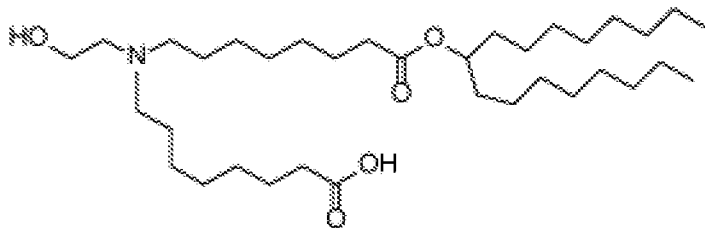
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(Compound 165)

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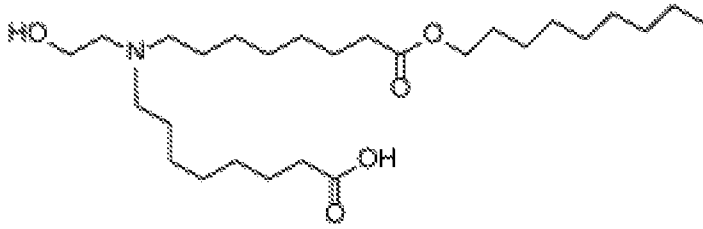
50



(Compound 166)

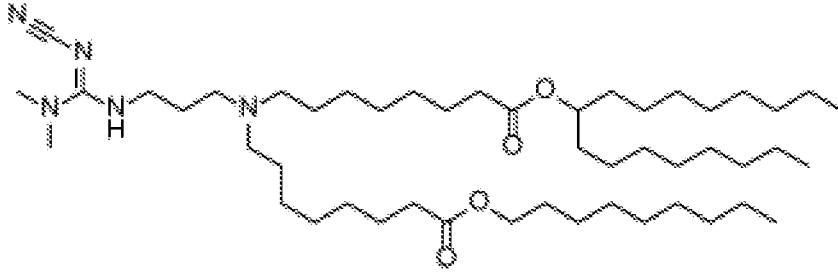
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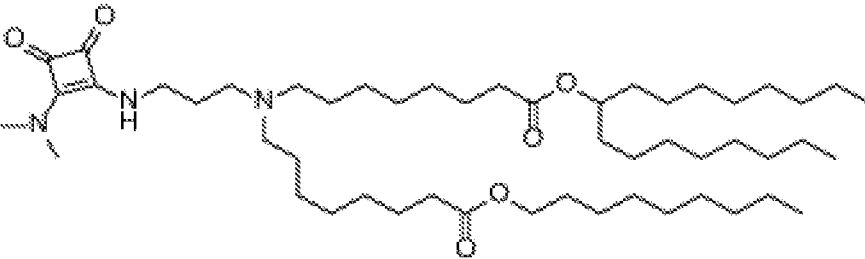
(Compound 167)

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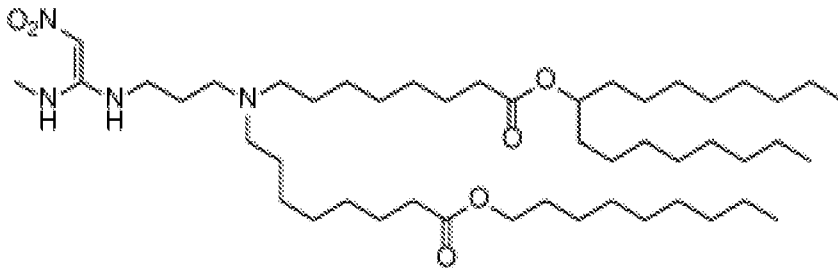
(Compound 168)

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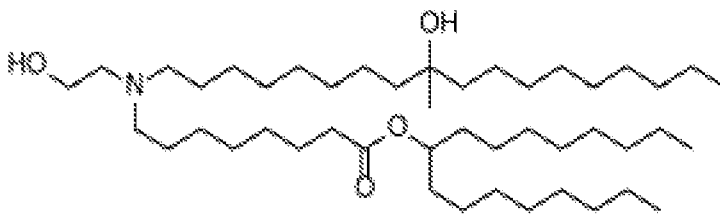
(Compound 169)

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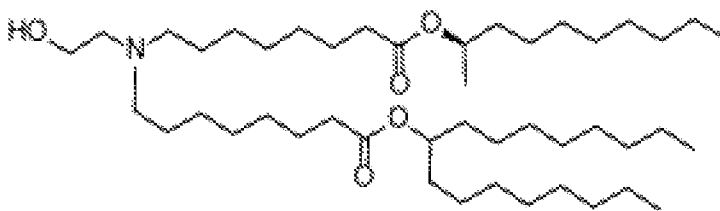
(Compound 170)

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(Compound 171)

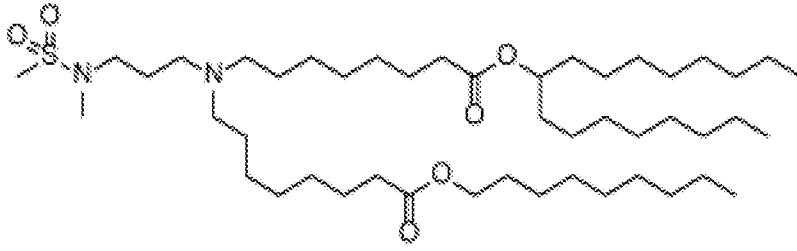
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(Compound 172)

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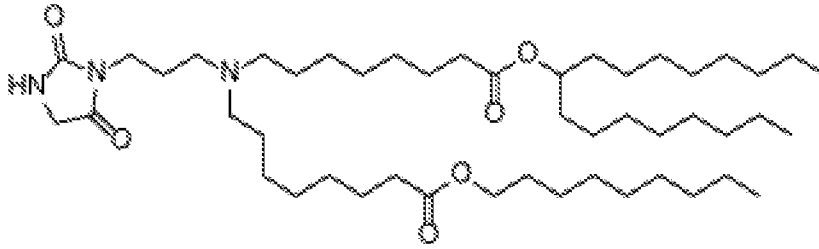
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(Compound 173)

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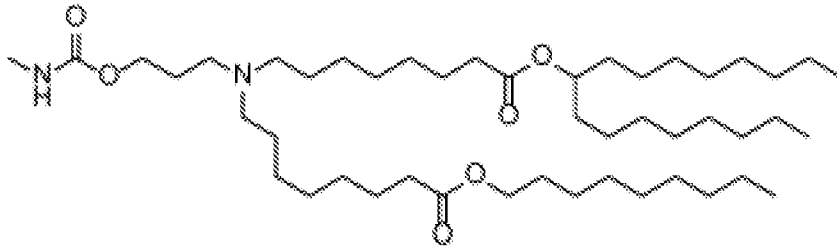
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(Compound 174)

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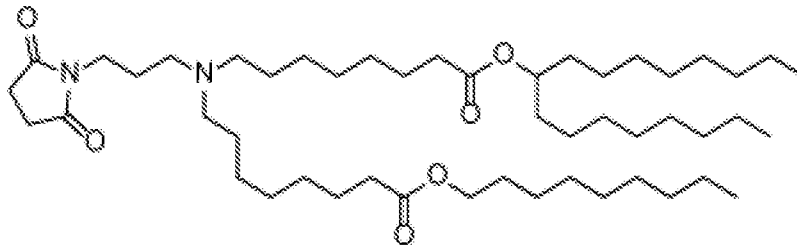
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(Compound 175)

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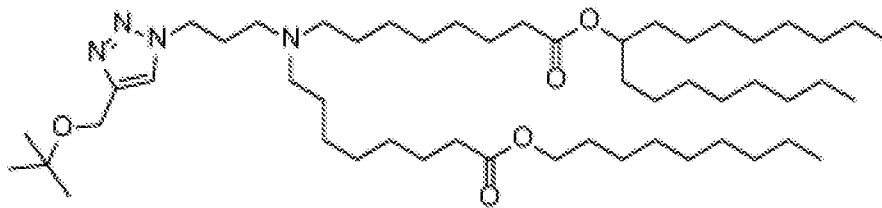
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(Compound 176)

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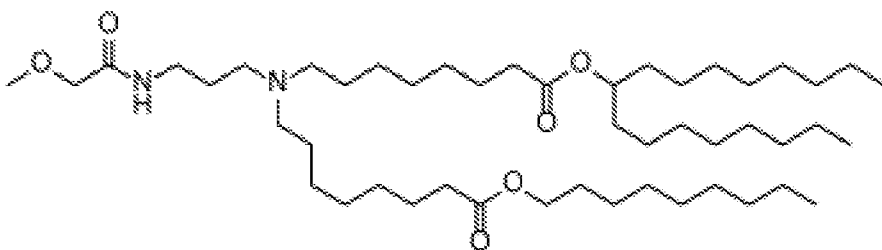
45



(Compound 177)

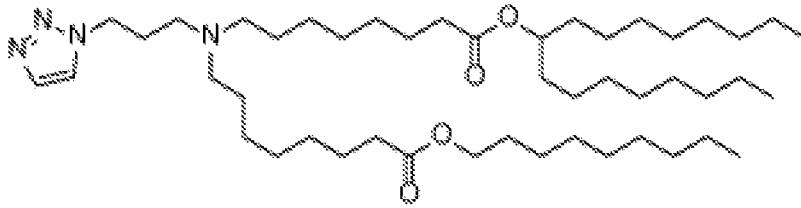
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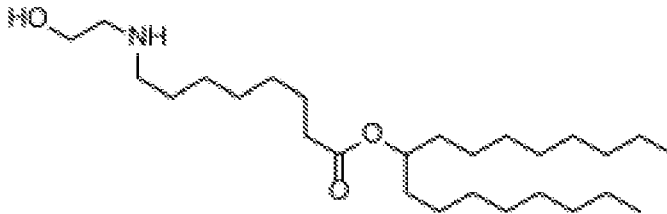
(Compound 178)

5



(Compound 179)

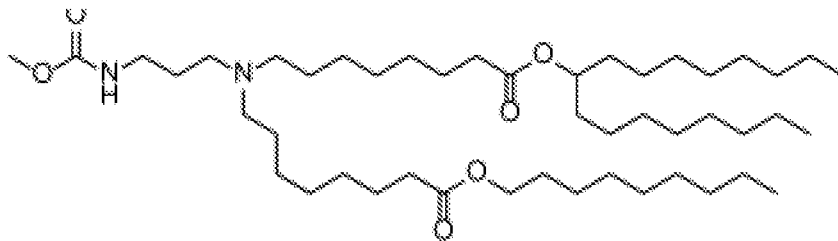
10



(Compound 180)

15

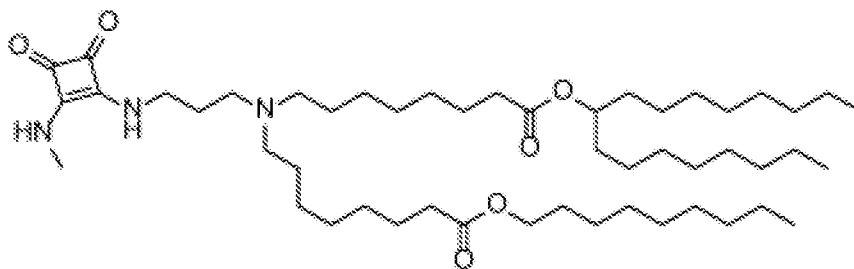
20



(Compound 181)

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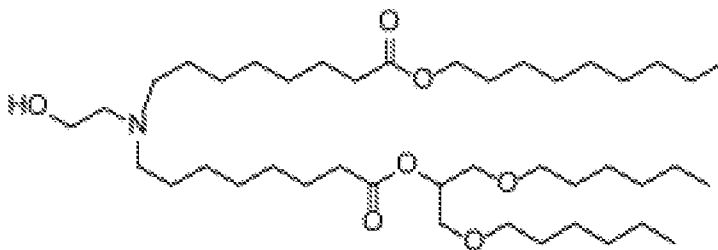
30



(Compound 182)

35

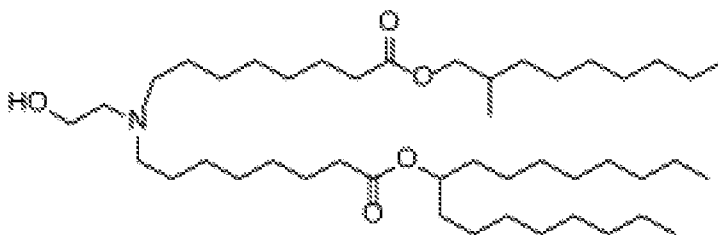
40



(Compound 183)

45

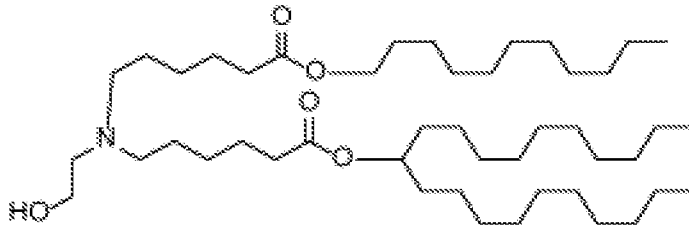
50



(Compound 184)

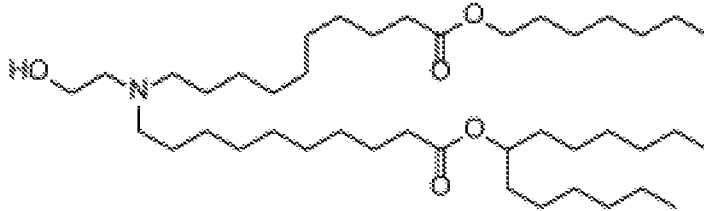
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5



(Compound 185)

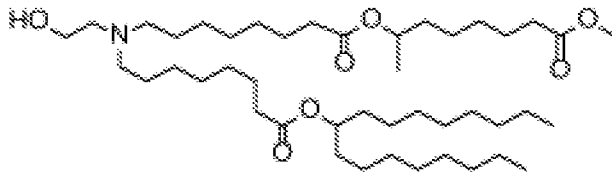
10



(Compound 186)

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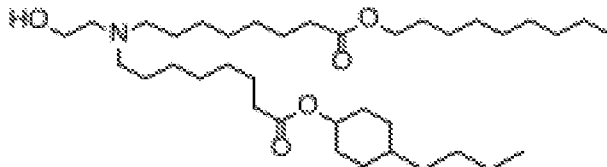
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(Compound 187)

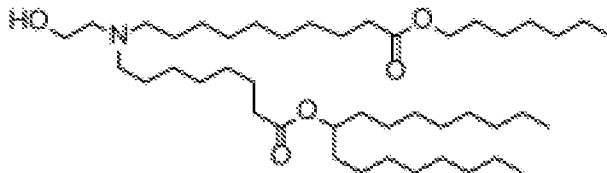
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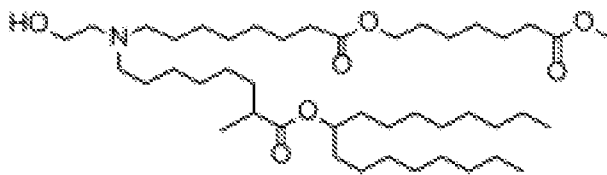
(Compound 188)

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(Compound 189)

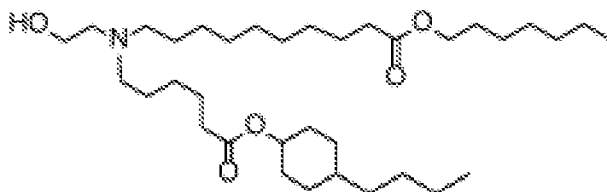
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(Compound 190)

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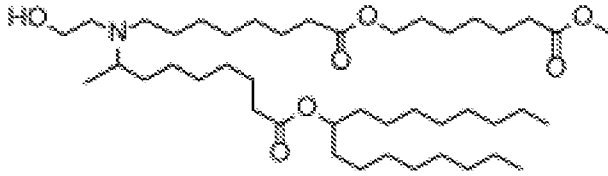
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(Compound 191)

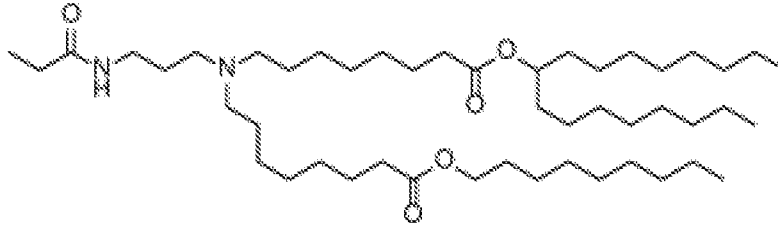
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(Compound 182)

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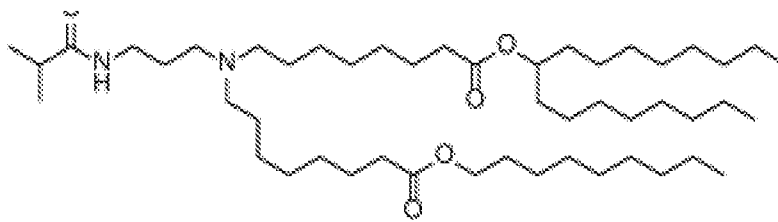


(Compound 183)

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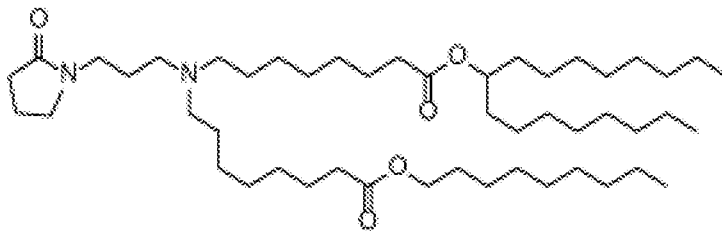
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(Compound 184)

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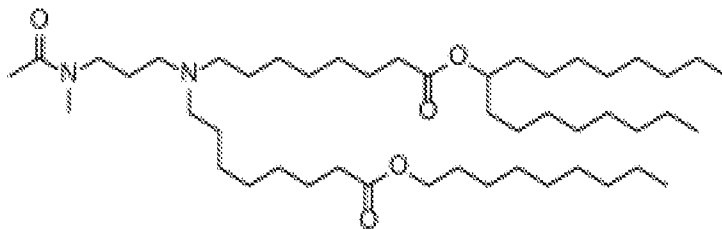
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(Compound 185)

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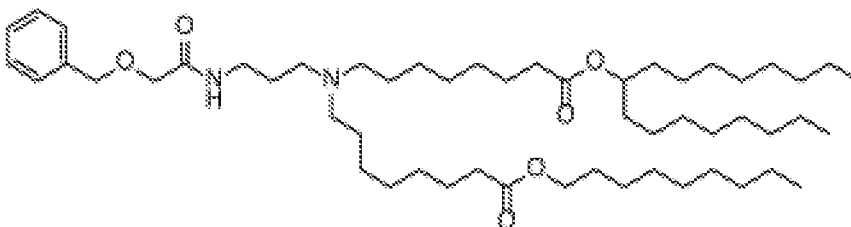
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(Compound 186)

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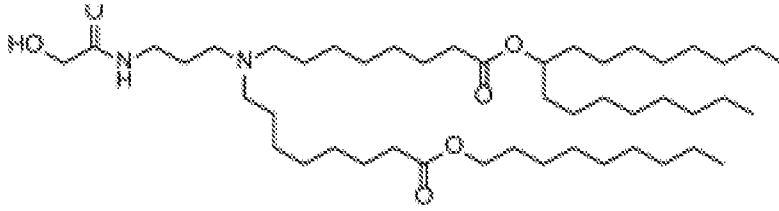
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(Compound 187)

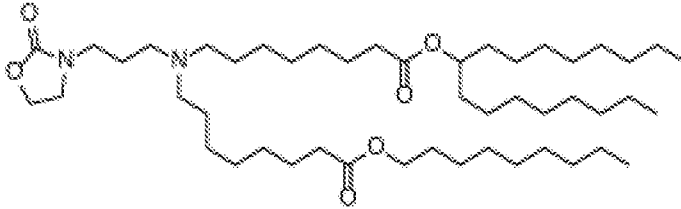
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(Compound 199)

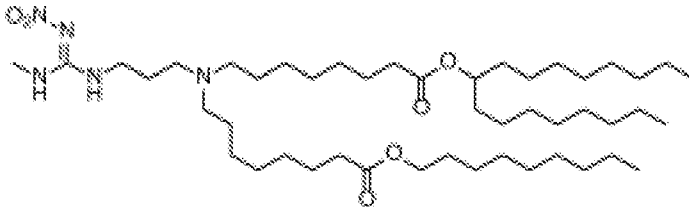
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(Compound 200)

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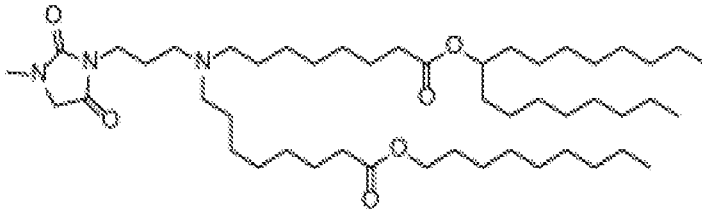
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(Compound 201)

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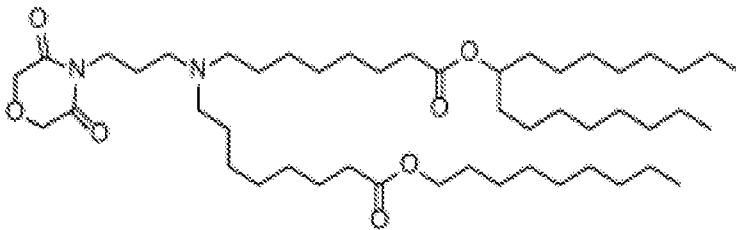
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(Compound 202)

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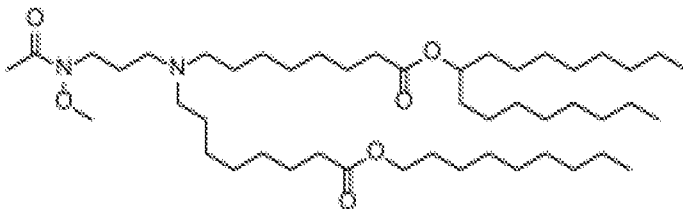
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(Compound 203)

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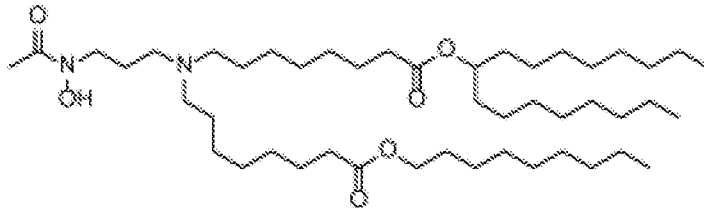
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(Compound 204)

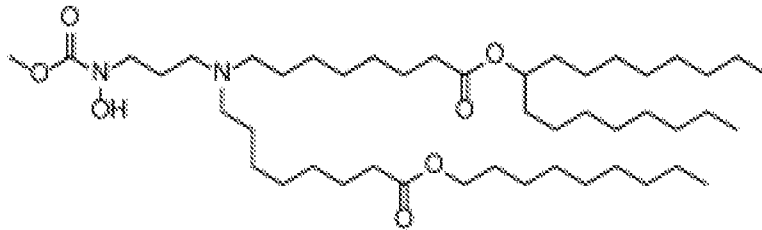
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(Compound 264)

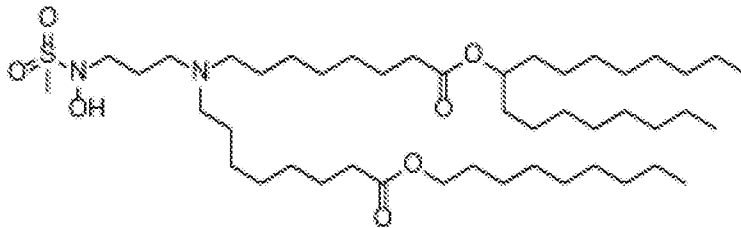
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(Compound 265)

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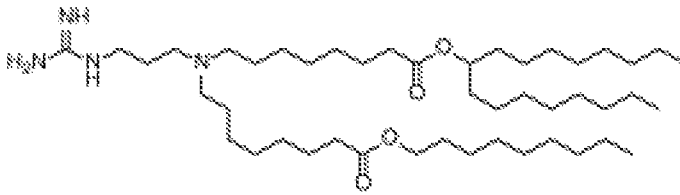
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(Compound 266)

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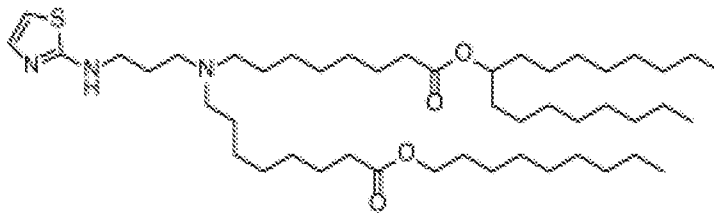
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(Compound 267)

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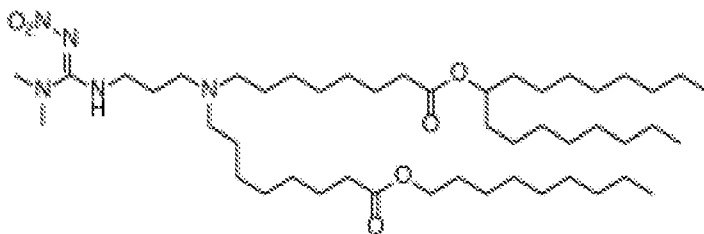
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(Compound 268)

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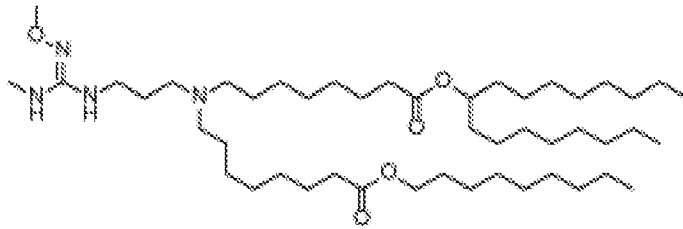
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(Compound 269)

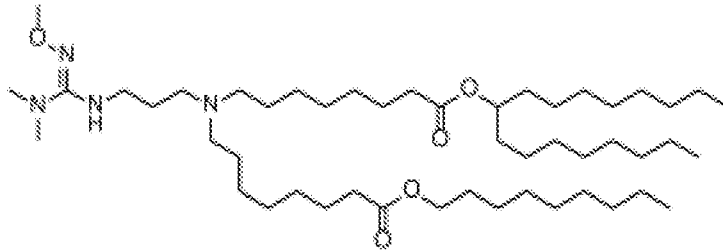
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(Compound 210)

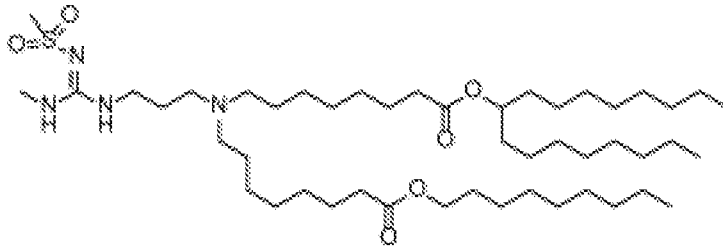
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(Compound 211)

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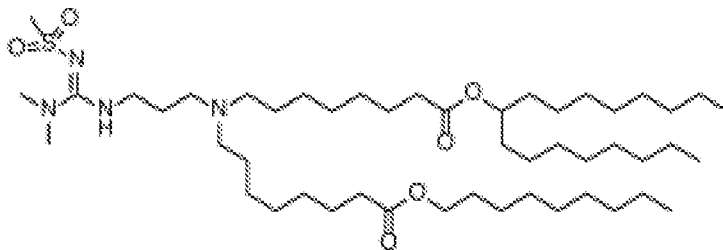
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(Compound 212)

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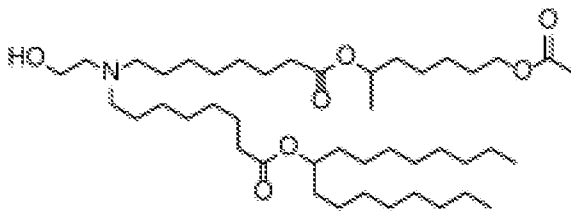
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(Compound 213)

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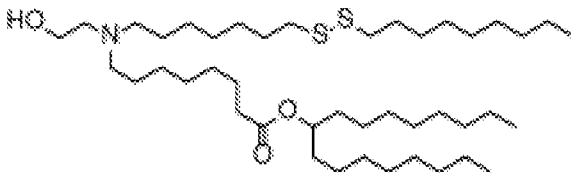
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(Compound 214)

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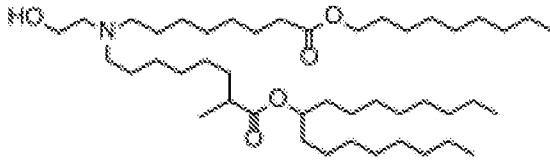
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(Compound 215)

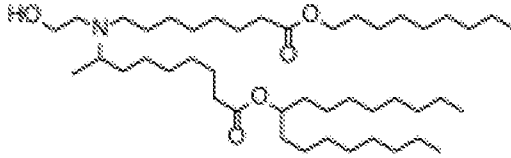
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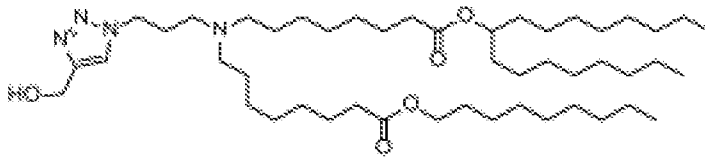
Compound 215.

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Compound 217.

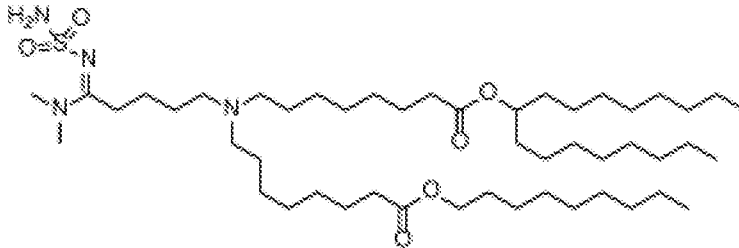
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Compound 218.

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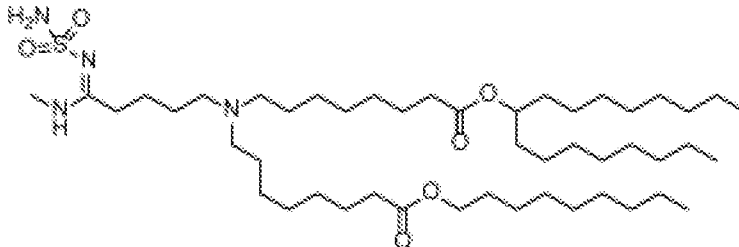
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Compound 219.

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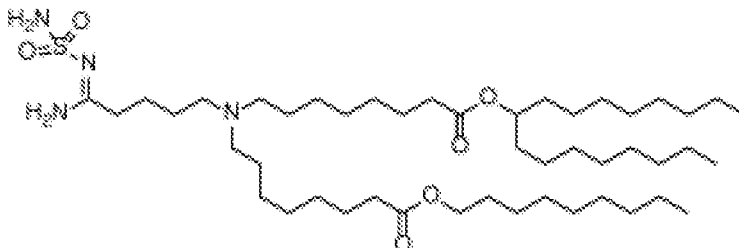
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Compound 220.

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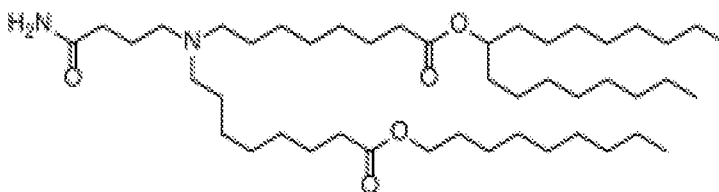
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Compound 221.

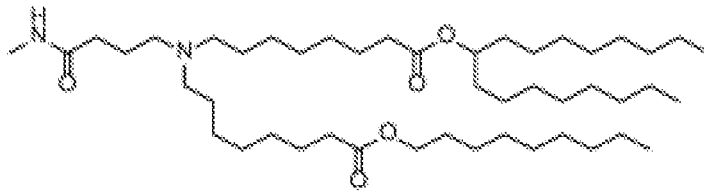
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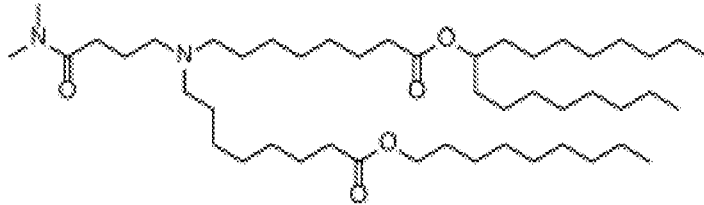
Compound 222.

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Compound 223)

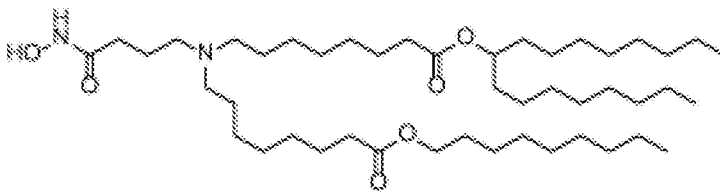
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Compound 224)

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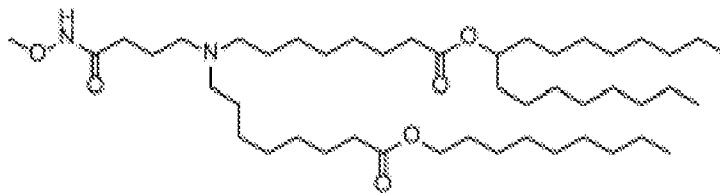
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Compound 225)

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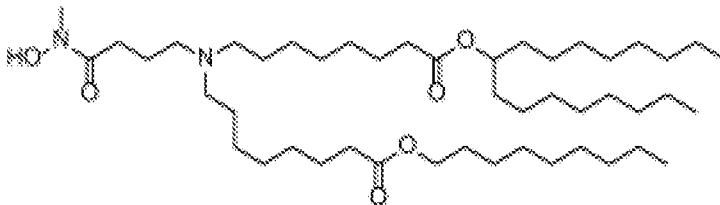
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Compound 226)

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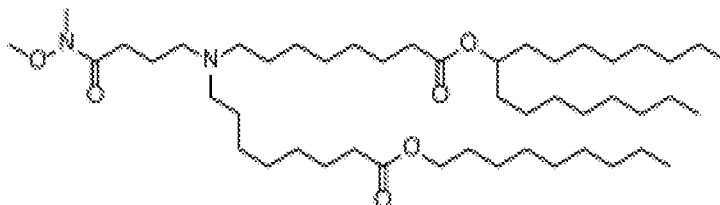
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Compound 227)

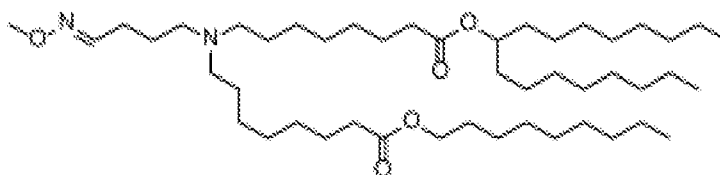
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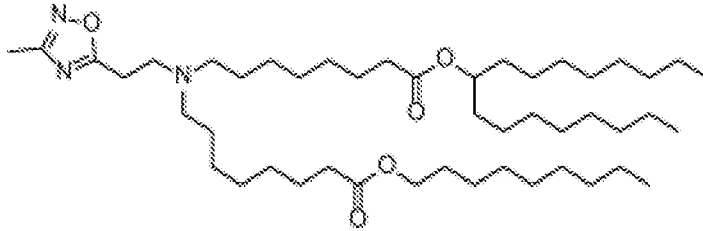
Compound 228)

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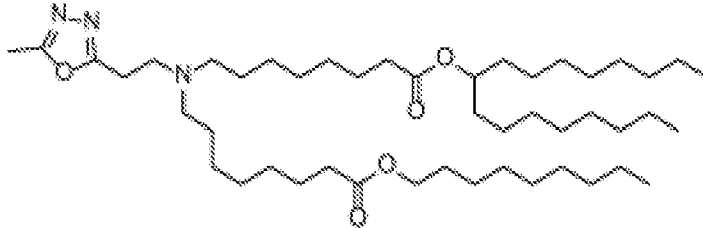
Compound 229)

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Compound 230

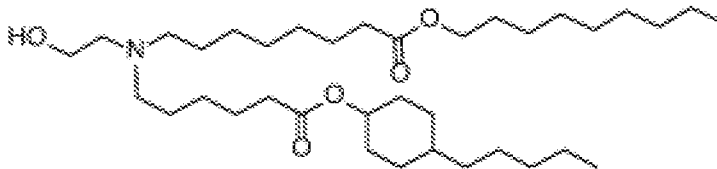
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Compound 231

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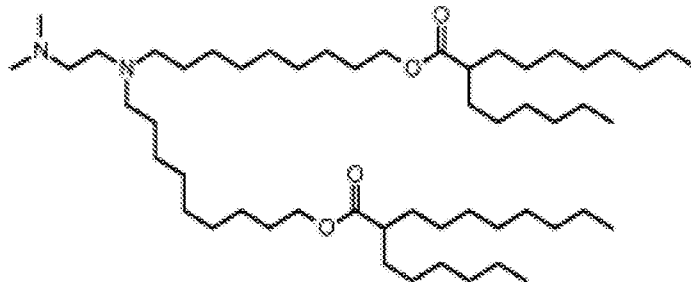
Compound 232

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and salts and isomers thereof.

[0389] In some embodiments, a nanoparticle comprises the following compound:

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Compound 233

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or salts and isomers thereof.

[0390] 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 (IIe)).

[0391] 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.

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[0392] The disclosure also includes methods of synthesizing a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe) and methods of making a nanoparticle composition including a lipid component comprising the compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe).

Modes of Vaccine Administration

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[0393] Respiratory virus RNA (i.e. mRNA) vaccines of the invention 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 invention provides vaccines for use in a method of preventing and/or treating a

BetaCoV disease, the method comprising administering the RNA (*i.e.*, 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 (*i.e.*, mRNA) vaccines compositions of the invention 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 (*i.e.*, mRNA) vaccine compositions of the invention may be decided by the attending physician within the scope of sound medical judgment. The specific therapeutically effects, 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.

[0394] In some embodiments, respiratory virus RNA (*i.e.* mRNA) vaccines compositions of the invention 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 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 (*i.e.*, mRNA) vaccines compositions of the invention 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.

[0395] In some embodiments, respiratory virus RNA (*i.e.*, mRNA) vaccine compositions of the invention 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.

[0396] In some embodiments, respiratory virus RNA (*i.e.*, mRNA) vaccine compositions of the invention 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 (*i.e.*, mRNA) vaccine composition of the invention may be administered three or four times.

[0397] In some embodiments, respiratory virus RNA (*i.e.* mRNA) vaccine compositions of the invention 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.

[0398] In some embodiments, the respiratory virus RNA (*i.e.*, mRNA) vaccine of the invention for use in a method of vaccinating a subject is administered to the subject as a single dosage of between 10 μ g/kg and 400 μ g/kg of the nucleic acid vaccine (in an effective amount to vaccinate the subject). In some embodiments the RNA (*i.e.*, mRNA) vaccine of the invention for use in a method of vaccinating a subject is administered to the subject as a single dosage of between 10 μ g and 400 μ g of the nucleic acid vaccine (in an effective amount to vaccinate the subject). In some embodiments, a respiratory virus RNA (*i.e.*, mRNA) vaccine of the invention for use in a method of vaccinating a subject is administered to the subject as a single dosage of 25-1000 μ g (*e.g.*, a single dosage of mRNA encoding hMPV, PIV3, RSV, MeV and/or BetaCoV antigen). In some embodiments, a respiratory virus RNA (*i.e.* mRNA) vaccine of the invention 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 μ g. For example, a respiratory virus RNA (*i.e.* mRNA) vaccine of the invention 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 μ g. In some instances, a respiratory virus RNA (*i.e.* mRNA) vaccine of the invention 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.

[0399] A respiratory virus RNA (*i.e.* 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

[0400] The present invention provides the mRNA vaccine defined in the claims for use in a method of preventing and/or treating a BetaCoV disease in a subject.

[0401] The technical information set out below may in some respects go beyond the scope of the invention, which is defined exclusively by the appended claims. The additional technical information is provided to place the actual invention in a broader technical context and to illustrate possible related technical developments.

[0402] In addition, incidental references to methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body are not to be construed as claiming protection for such methods as such, but are instead to be construed as referring to products, in particular substances or compositions, for use in any of these methods.

[0403] The present disclosure provides 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 disclosed herein are methods of inducing an antigen-specific immune response in a subject. In some instances, 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 disclosed 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.

[0404] In some instances, an antibody titer is used to assess whether a subject has had an infection or to determine whether immunizations are required. In some instances, an antibody titer is used to determine the strength of an auto-immune 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.

[0405] In some instances, 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 instances, 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 instances, 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 antibody 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.

[0406] In some instances, 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 instances, 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 instances, 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.

[0407] A control, in some instances, 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 instances, 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 instances, 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 instances, 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 instances, 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 RG et al., J Virol. 2014 Jun; 88(11): 6368-6379).

[0408] In some instances, an effective amount of a respiratory virus RNA (i.e., mRNA) vaccine is a dose that is reduced compared to the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. A "standard of care," as disclosed herein, refers to a medical or psychological treatment guideline and can be general or specific. "Standard of care" specifies appropriate treatment based on scientific evidence and collaboration between medical professionals involved in the treatment of a given condition. It is the diagnostic and treatment process that a physician/clinician should follow for a certain type of patient, illness or clinical circumstance. A "standard of care dose," as disclosed herein, refers to the 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, that a physician/clinician or other medical professional would administer to a subject to treat or prevent hMPV, PIV3, RSV, MeV and/or BetaCoV, or a hMPV-, PIV3-, RSV-, MeV- and/or BetaCoV-related condition, while following the standard of care guideline for treating or preventing hMPV, PIV3, RSV, MeV and/or BetaCoV, or a hMPV-, PIV3-, RSV-, MeV- and/or BetaCoV-related condition.

[0409] In some instances, 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 administered an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is equivalent to 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 control subject administered a 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.

[0410] In some instances, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to an at least 2-fold reduction in a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. For example, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine may be a dose equivalent to an at least 3-fold, at least 4-fold, at least 5-fold, at least 6-fold, at least 7-fold, at least 8-fold, at least 9-fold, or at least 10-fold reduction in a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some instances, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to an at least at least 100-fold, at least 500-fold, or at least 1000-fold reduction in a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some instances, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to a 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 20-, 50-, 100-, 250-, 500-, or 1000-fold reduction in a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some instances, the anti-antigenic polypeptide antibody titer produced in a subject administered an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant or protein 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 instances, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to a 2-fold to 1000-fold (e.g., 2-fold to 100-fold, 10-fold to 1000-fold) reduction in the standard of care dose of a recombinant or purified 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 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.

[0411] In some instances, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to a 2 to 1000-, 2 to 900-, 2 to 800-, 2 to 700-, 2 to 600-, 2 to 500-, 2 to 400-, 2 to 300-, 2 to 200-, 2 to 100-, 2 to 90-, 2 to 80-, 2 to 70-, 2 to 60-, 2 to 50-, 2 to 40-, 2 to 30-, 2 to 20-, 2 to 10-, 2 to 9-, 2 to 8-, 2 to 7-, 2 to 6-, 2 to 5-, 2 to 4-, 2 to 3-, 3 to 1000-, 3 to 900-, 3 to 800-, 3 to 700-, 3 to 600-, 3 to 500-, 3 to 400-, 3 to 3 to 00-, 3 to 200-, 3 to 100-, 3 to 90-, 3 to 80-, 3 to 70-, 3 to 60-, 3 to 50-, 3 to 40-, 3 to 30-, 3 to 20-, 3 to 10-, 3 to 9-, 3 to 8-, 3 to 7-, 3 to 6-, 3 to 5-, 3 to 4-, 4 to 1000-, 4 to 900-, 4 to 800-, 4 to 700-, 4 to 600-, 4 to 500-, 4 to 400-, 4 to 4 to 00-, 4 to 200-, 4 to 100-, 4 to 90-,

4 to 80-, 4 to 70-, 4 to 60-, 4 to 50-, 4 to 40-, 4 to 30-, 4 to 20-, 4 to 10-, 4 to 9-, 4 to 8-, 4 to 7-, 4 to 6-, 4 to 5-, 4 to 4-, 5 to 1000-, 5 to 900-, 5 to 800-, 5 to 700-, 5 to 600-, 5 to 500-, 5 to 400-, 5 to 300-, 5 to 200-, 5 to 100-, 5 to 90-, 5 to 80-, 5 to 70-, 5 to 60-, 5 to 50-, 5 to 40-, 5 to 30-, 5 to 20-, 5 to 10-, 5 to 9-, 5 to 8-, 5 to 7-, 5 to 6-, 6 to 1000-, 6 to 900-, 6 to 800-, 6 to 700-, 6 to 600-, 6 to 500-, 6 to 400-, 6 to 300-, 6 to 200-, 6 to 100-, 6 to 90-, 6 to 80-, 6 to 70-, 6 to 60-, 6 to 50-, 6 to 40-, 6 to 30-, 6 to 20-, 6 to 10-, 6 to 9-, 6 to 8-, 6 to 7-, 7 to 1000-, 7 to 900-, 7 to 800-, 7 to 700-, 7 to 600-, 7 to 500-, 7 to 400-, 7 to 300-, 7 to 200-, 7 to 100-, 7 to 90-, 7 to 80-, 7 to 70-, 7 to 60-, 7 to 50-, 7 to 40-, 7 to 30-, 7 to 20-, 7 to 10-, 7 to 9-, 7 to 8-, 8 to 1000-, 8 to 900-, 8 to 800-, 8 to 700-, 8 to 600-, 8 to 500-, 8 to 400-, 8 to 300-, 8 to 200-, 8 to 100-, 8 to 90-, 8 to 80-, 8 to 70-, 8 to 60-, 8 to 50-, 8 to 40-, 8 to 30-, 8 to 20-, 8 to 10-, 8 to 9-, 9 to 1000-, 9 to 900-, 9 to 800-, 9 to 700-, 9 to 600-, 9 to 500-, 9 to 400-, 9 to 300-, 9 to 200-, 9 to 100-, 9 to 90-, 9 to 80-, 9 to 70-, 9 to 60-, 9 to 50-, 9 to 40-, 9 to 30-, 9 to 20-, 9 to 10-, 10 to 1000-, 10 to 900-, 10 to 800-, 10 to 700-, 10 to 600-, 10 to 500-, 10 to 400-, 10 to 300-, 10 to 200-, 10 to 100-, 10 to 90-, 10 to 80-, 10 to 70-, 10 to 60-, 10 to 50-, 10 to 40-, 10 to 30-, 10 to 20-, 20 to 1000-, 20 to 900-, 20 to 800-, 20 to 700-, 20 to 600-, 20 to 500-, 20 to 400-, 20 to 300-, 20 to 200-, 20 to 100-, 20 to 90-, 20 to 80-, 20 to 70-, 20 to 60-, 20 to 50-, 20 to 40-, 20 to 30-, 30 to 1000-, 30 to 900-, 30 to 800-, 30 to 700-, 30 to 600-, 30 to 500-, 30 to 400-, 30 to 300-, 30 to 200-, 30 to 100-, 30 to 90-, 30 to 80-, 30 to 70-, 30 to 60-, 30 to 50-, 30 to 40-, 40 to 1000-, 40 to 900-, 40 to 800-, 40 to 700-, 40 to 600-, 40 to 500-, 40 to 400-, 40 to 300-, 40 to 200-, 40 to 100-, 40 to 90-, 40 to 80-, 40 to 70-, 40 to 60-, 40 to 50-, 50 to 1000-, 50 to 900-, 50 to 800-, 50 to 700-, 50 to 600-, 50 to 500-, 50 to 400-, 50 to 300-, 50 to 200-, 50 to 100-, 50 to 90-, 50 to 80-, 50 to 70-, 50 to 60-, 60 to 1000-, 60 to 900-, 60 to 800-, 60 to 700-, 60 to 600-, 60 to 500-, 60 to 400-, 60 to 300-, 60 to 200-, 60 to 100-, 60 to 90-, 60 to 80-, 60 to 70-, 70 to 1000-, 70 to 900-, 70 to 800-, 70 to 700-, 70 to 600-, 70 to 500-, 70 to 400-, 70 to 300-, 70 to 200-, 70 to 100-, 70 to 90-, 70 to 80-, 80 to 1000-, 80 to 900-, 80 to 800-, 80 to 700-, 80 to 600-, 80 to 500-, 80 to 400-, 80 to 300-, 80 to 200-, 80 to 100-, 80 to 90-, 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 instances, 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 instances, 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-, 1280-, 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 instances, 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.

[0412] In some instances, the effective amount of a respiratory virus RNA (*e.g.*, mRNA) vaccine is a total dose of 50-1000 μ g. In some instances, 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 μ g. In some instances, 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 μ g. In some instances, the effective amount is a dose of 25-500 μ g administered to the subject a total of two times. In some instances, 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 μ g administered to the subject a total of two times. In some instances, 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.

[0413] 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.

10 EXAMPL ES

Example 1: Manufacture of Polynucleotides

[0414] 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 "Manufacturing Methods for Production of RNA Transcripts".

[0415] Purification methods may include those taught in International Publication WO2014/152030 and International Publication WO2014/152031.

[0416] Detection and characterization methods of the polynucleotides may be performed as taught in International Publication WO2014/144039.

[0417] 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.

Example 2: Chimeric polynucleotide synthesis

[0418] 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.

[0419] 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.

[0420] Monophosphate protecting groups may be selected from any of those known in the art.

[0421] 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.

[0422] For ligation methods, ligation with DNA T4 ligase, followed by treatment with DNase should readily avoid concatenation.

[0423] 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.

[0424] Ligation is then performed using any known click chemistry, orthoclick chemistry, solulink, or other bioconjugate chemistries known to those in the art.

Synthetic route

[0425] The chimeric polynucleotide may be made using a series of starting segments. Such segments include:

- (a) a capped and protected 5' segment comprising a normal 3'OH (SEG. 1)
- (b) a 5'triphosphate segment, which may include the coding region of a polypeptide and a normal 3'OH (SEG. 2)
- (c) a 5' monophosphate segment for the 3'end of the chimeric polynucleotide (e.g., the tail) comprising cordycepin or no 3'OH (SEG. 3)

[0426] After synthesis (chemical or IVT), segment 3 (SEG. 3) may be treated with cordycepin and then with pyrophosphatase to create the 5' monophosphate.

[0427] Segment 2 (SEG. 2) may then be ligated to SEG. 3 using RNA ligase. The ligated polynucleotide is then purified and treated with pyrophosphatase to cleave the diphosphate. The treated SEG.2-SEG. 3 construct may then be purified

and SEG. 1 is ligated to the 5' terminus. A further purification step of the chimeric polynucleotide may be performed.

[0428] Where the chimeric polynucleotide encodes a polypeptide, the ligated or joined segments may be represented as: 5'UTR (SEG. 1), open reading frame or ORF (SEG. 2) and 3'UTR+PolyA (SEG. 3).

[0429] The yields of each step may be as much as 90-95%.

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Example 3: PCR for cDNA Production

[0430] PCR procedures for the preparation of cDNA may be performed using 2x KAPA HIFI™ HotStart ReadyMix by Kapa Biosystems (Woburn, MA). 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.

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[0431] The reaction may be cleaned up using Invitrogen's PURELINK™ PCR Micro Kit (Carlsbad, CA) 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,

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Example 4: *In vitro* Transcription (IVT)

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[0432] 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.

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[0433] 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 (25mM each) | | 02 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. | | | |

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[0434] 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 MEGACL EAR™ Kit (Austin, TX) 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,

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Example 5: Enzymatic Capping

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[0435] Capping of a RNA polynucleotide is performed as follows where the mixture includes: IVT RNA 60 μg-180μg 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.

[0436] 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 (400U); 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.

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[0437] The RNA polynucleotide may then be purified using Ambion's MEGACLEAR™ Kit (Austin, TX) following the manufacturer's instructions. Following the cleanup, the RNA may be quantified using the NANODROP™ (ThermoFisher, Waltham, MA) 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

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reverse-transcription-PCR to generate the cDNA for sequencing.

Example 6: PolyA Tailing Reaction

5 **[0438]** 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 μ l); RNase Inhibitor (20 U); 10x Tailing Buffer (0.5 M Tris-HCl (pH 8.0), 2.5 M NaCl, 100 mM MgCl₂) (12.0 μ l); 20 mM ATP (6.0 μ l); Poly-A Polymerase (20 U); dH₂O up to 123.5 μ l 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, TX) (up to 500 μ g). Poly-A Polymerase may be a recombinant enzyme expressed in yeast.

10 **[0439]** 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.

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Example 7; Natural 5' Caps and 5' Cap Analogues

[0440] 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, MA). 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, MA). 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.

20 **[0441]** 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.

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Example 8: Capping Assays

Protein Expression Assay

30 **[0442]** 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.

35 *Purify Analysis Synthesis*

[0443] 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.

40 *Cytokine Analysis*

[0444] 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.

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Capping Reaction Efficiency

50 **[0445]** RNA (e.g., mRNA) polynucleotides encoding a polypeptide, containing any of the caps taught herein can be

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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

[0446] Individual RNA polynucleotides (200-400 ng in a 20 μ l 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, CA) and run for 12-15 minutes, according to the manufacturer protocol.

Example 10: Nanodrop Modified RNA Quantification and UV Spectral Data

[0447] Chemically modified RNA polynucleotides in TE buffer (1 μ l) are used for Nanodrop UV absorbance readings to quantitate the yield of each polynucleotide from a chemical synthesis or *in vitro* transcription reaction.

Example 11: Formulation of Modified mRNA Using Lipidoids

[0448] 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 (Reference Example)

[0449] 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.

[0450] 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 (Reference Example)

[0451] 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.

[0452] 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.

[0453] 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 14: Immunogenicity of hMPV mRNA vaccine in BALB/c mice (Reference Example)

[0454] 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).

[0455] 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.

[0456] 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 (Reference Example)

[0457] 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.

[0458] 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.

[0459] 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 (Reference Example)

[0460] 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.

[0461] Cotton rats were immunized intramuscularly (IM) at week 0 and week 3 with the mRNA vaccines encoding hMPV fusion protein with either 2 µg or 10 µg 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 µg 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 µg dose of mRNA vaccine showed a 1 log reduction in lung viral titer in the cotton mice challenged.

[0462] 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 (Reference Example)

[0463] 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.

[0464] 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 (Reference Example)

[0465] 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.

[0466] 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.

[0467] 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 (Reference Example)

[0468] 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.

[0469] 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.

[0470] 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.

[0471] 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.

[0472] 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).

[0473] 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

[0474] 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).

[0475] 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).

[0476] 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 21: Betacoronavirus Challenge

[0477] 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 (10xLD₉₀; ~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).

[0478] 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 ~1 LD₉₀ 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

[0479] Nine serial 2-fold dilutions (1:50 -1:12,800) of rabbit serum are made in 50 µl 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 µl of 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

[0480] 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.

[0481] Mice were vaccinated with a 10 µg dose of MERS-Co V 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.

[0482] 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

[0483] 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 µg 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 µg 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.

[0484] 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-Co V mRNA vaccine resulted in a 2 log reduction of viral load, while two 20 µg doses of MERS-Co V mRNA vaccine resulted in an over 4 log reduction of viral load in the lungs of the New Zealand white rabbits (Fig. 19C).

[0485] 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).

[0486] Further, as shown in Fig. 21, two 20 µg doses of MERS-CoV mRNA vaccine induced significant amount of neutralizing antibodies against MERS-CoV (EC₅₀ 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 (Reference Example)

[0487] 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.

[0488] 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 (Reference Example)

[0489] 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 (Rail GF et al. PNAS USA 1997;94(9):4659-63). SLAM is a type 1 membrane glycoprotein belonging to the immunoglobulin superfamily. It is expressed on the surface of activated lymphocyte s, 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),

[0490] 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.

[0491] 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-DOMG (1.5 mol%) and the structural lipid is cholesterol (38.5 mol%), for example.

[0492] Each of the sequences described herein encompasses a chemically modified sequence or an unmodified sequence which includes no nucleotide modifications.

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(continued)

Description	Sequence	SEQ ID NO:
<p>gbIKJ723483.1:5586-7310 Human respiratory syncytial virus strain RSVA Homo sapiens/USA/841-215A-01/1984, complete genome</p>	<pre> ATGAGTTGCGAATGCTGAAAACAAATGCAATGACCAATGCGTCTGCAAGTCCAGTCAACAGTCTGTTG GGTTGAGTGAAGAGATGCTGAAAGATTTTATCATTGCAACATGCAATGCAATGCAATGCAATGCAAT GTTAGTGGTAAAGAGTGGTTGGTATACATAGTGTATAGTATAGTATAGTATAGTATAGTATAGTATAG AATAGCTGATATGAGACAGATGCTGAGGTAAATGATGATGATGATGATGATGATGATGATGATGATGAT GCTGAGCAGATTTGAGTGGTCAAGCAAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAG AGCAGCAAGGTTATGAAATATACAGCAATATGCTCAAGAAATGCTAATGCAATATGCAATATGCAATATG AGCAAGAGAGAGATTTGTTGTTTTGTTAGGTGTTGGATGCTGCAATGCGCAAGTGGTCTATGCTATGCTG TATGAGGTTGCTGCAAGTAAAG AGAGGTTAGTCAAGTATGCAAGTAAAG GTAAGAGATAG TGTGATAG GAGAGATAG TATGCTATAG TACTATAG TGTGATAG GGTCAAGT TGTGAGT TAAAGATAG ATTAG TATGAG TGTGAG AGCAG TGTGAG TTATGAG TACAG GTGAG GATTTGAG </pre>	<p>4</p>
<p>hMPV mRNA Sequences</p>		

Table 3. hMPV Amino Acid Sequences (Reference Example)

Description	Sequence	SEQ ID NO:
5 10 15 20 25 30 35 40 45 50 55	<p>gil122891979IgbIEF051124.1 Human metapneumovirus isolate TN/92-4 fusion protein gene, complete cds</p> <pre> MSKRVVPELLITPQHGLKESRL EESCSTITEGYL SMLRTGWTNWFLEVGQVDELTCSDGPSLXITE LQLTKSLRELKTVSADQLAREEGENPRQSRFLGALGVATAAAVNTAGYAIKTRLESEVTRNHA LKTNEAVSTLGNQVHRLATAVRELKDFVSKNLTRANKKCDIDDLKMAVSPSQFNRHFLNVRQFS DNAGTPIQLDLMTDAELARAVPNMPTSAQDHLML ENRAMVRRKGFGLIGVYQSSWYVQLRFGW NDTPCNIKAAPSCSEKNGNYACLLREDOGWYQKNIAGSTVYYPNEKDCETHGHWFCDTAAGNVAE GDFECNINISTNTPCKVSTGRHRSNVALSPLGALVACYKGVSCSTGSHVGHQLPKDCSYTNQD ADTYTIDNTVYQLSKVEGEQHWNGRPVSSDFPKFPEDQFNVALDQVFESENSEALVDQSNRLNS ASKQNTGFHILIAKLGSMMLVSEFNKTKRPTGAPPELNGVTNNGSFPHS </pre>	5
	<p>gblAY525843.11:3065-46 84 Human metapneumovirus isolate NL/1/99, complete cds</p> <pre> MSKRVVPELLITPQHGLKESYLEESCSTITEGYL SMLRTGWTNWFLEVGQVDELTCSDGPSLXITE LQLTKSLRELKTVSADQLAREEIDENPRQSRFLGALGVATAAAVNTAGIANKTRLESEVTRNHA LKTNEAVSTLGNQVHRLATAVRELKDFVSKNLTSANKKCDIADLKNMAYSPSQFNRHFLNVRQFS DNAGTPIQLDLMTDAELARAVPNMPTSAQDHLML ENRAMVRRKGFGLIGVYQSSWYVQLRFGW NDTPCNIKAAPSCSEKNGNYACLLREDOGWYQKNIAGSTVYYPNEKDCETHGHWFCDTAAGNVAE GDFECNINISTNTPCKVSTGRHRSNVALSPLGALVACYKGVSCSTGSHVGHQLPKDCSYTNQD ADTYTIDNTVYQLSKVEGEQHWNGRPVSSDFPKFPEDQFNVALDQVFESENSEALVDQSNRLNS ASKQNTGFHILIAKLGSMMLVSEFNKTKRPTGAPPELNGVTNNGSFPHS </pre>	6
	<p>gblKJ627414.11:3015-4634 Human metapneumovirus strain hMPV/Homo sapiens/PER/CFI0497/2010/ B, complete cds</p> <pre> MSKRVVPELLITPQHGLKESYLEESCSTITEGYL SMLRTGWTNWFLEVGQVDELTCSDGPSLXITE LQLTKSLRELKTVSADQLAREEIDENPRQSRFLGALGVATAAAVNTAGIANKTRLESEVTRNHA LKTNEAVSTLGNQVHRLATAVRELKDFVSKNLTSANKKCDIADLKNMAYSPSQFNRHFLNVRQFS DNAGTPIQLDLMTDAELARAVPNMPTSAQDHLML ENRAMVRRKGFGLIGVYQSSWYVQLRFGW NDTPCNIKAAPSCSEKNGNYACLLREDOGWYQKNIAGSTVYYPNEKDCETHGHWFCDTAAGNVAE GDFECNINISTNTPCKVSTGRHRSNVALSPLGALVACYKGVSCSTGSHVGHQLPKDCSYTNQD ADTYTIDNTVYQLSKVEGEQHWNGRPVSSDFPKFPEDQFNVALDQVFESENSEALVDQSNRLNS ASKQNTGFHILIAKLGSMMLVSEFNKTKRPTGAPPELNGVTNNGSFPHS </pre>	7
	<p>gblKJ723483,11:5586-7310 Human respiratory syncytial virus strain RSVA/Homo sapiens/USA/841-215A-01/1984, complete cds</p> <pre> MELPKTNVITLAAVTLQFASSQNTIEFYQITCSAVSKGKLSMLRTGWTNWFLEVGQVDELTCSDGPSLXITE LQLTKSLRELKTVSADQLAREEIDENPRQSRFLGALGVATAAAVNTAGIANKTRLESEVTRNHA LKTNEAVSTLGNQVHRLATAVRELKDFVSKNLTSANKKCDIADLKNMAYSPSQFNRHFLNVRQFS DNAGTPIQLDLMTDAELARAVPNMPTSAQDHLML ENRAMVRRKGFGLIGVYQSSWYVQLRFGW NDTPCNIKAAPSCSEKNGNYACLLREDOGWYQKNIAGSTVYYPNEKDCETHGHWFCDTAAGNVAE GDFECNINISTNTPCKVSTGRHRSNVALSPLGALVACYKGVSCSTGSHVGHQLPKDCSYTNQD ADTYTIDNTVYQLSKVEGEQHWNGRPVSSDFPKFPEDQFNVALDQVFESENSEALVDQSNRLNS ASKQNTGFHILIAKLGSMMLVSEFNKTKRPTGAPPELNGVTNNGSFPHS </pre>	8

Table 4. hMPV NCBI Accession Numbers (Amino Acid Sequences) (Reference Example)

Virus	GenBank Accession
F [Human metapneumovirus] [Human metapneumovirus]	AEK26895.1
fusion glycoprotein [Human metapneumovirus]	ACJ53565.1
fusion glycoprotein [Human metapneumovirus]	ACJ53566.1
fusion glycoprotein [Human metapneumovirus]	ACJ53569.1
fusion protein [Human metapneumovirus]	AEZ52347.1
fusion glycoprotein [Human metapneumovirus]	ACJ53574.1
fusion glycoprotein [Human metapneumovirus]	AHV79473.1

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	Virus	GenBank Accession
5	fusion glycoprotein [Human metapneumovirus]	ACJ53570.1
	fusion glycoprotein [Human metapneumovirus]	ACJ53567.1
	fusion protein [Human metapneumovirus]	AAS22125.1
	fusion glycoprotein [Human metapneumovirus]	AHV79795.1
10	fusion glycoprotein [Human metapneumovirus]	AHV79455.1
	fusion glycoprotein [Human metapneumovirus]	ACJ53568.1
	fusion protein [Human metapneumovirus]	AAS22109.1
15	fusion glycoprotein [Human metapneumovirus]	AGU68417.1
	fusion glycoprotein [Human metapneumovirus]	AGJ74228.1
	fusion glycoprotein [Human metapneumovirus]	ACJ53575.1
	fusion protein [Human metapneumovirus]	AAU25820.1
20	fusion glycoprotein [Human metapneumovirus]	AGU68377.1
	fusion glycoprotein [Human metapneumovirus]	AGU68371.1
	fusion glycoprotein [Human metapneumovirus]	AGJ74087.1
25	fusion glycoprotein [Human metapneumovirus]	ACJ53560.1
	fusion glycoprotein [Human metapneumovirus]	AHV79858.1
	fusion glycoprotein [Human metapneumovirus]	ACJ53577.1
	fusion protein [Human metapneumovirus]	AAS22085.1
30	fusion protein [Human metapneumovirus]	AEZ52348.1
	fusion glycoprotein [Human metapneumovirus]	AGJ74044.1
	fusion glycoprotein [Human metapneumovirus]	ACJ53563.1
35	fusion glycoprotein precursor [Human metapneumovirus]	YP_0126081
	fusion glycoprotein [Human metapneumovirus]	AGJ74053.1
	fusion protein [Human metapneumovirus]	BAM37562.1
	fusion glycoprotein [Human metapneumovirus]	ACJ53561.1
40	fusion glycoprotein [Human metapneumovirus]	AGU68387.1
	fusion [Human metapneumovirus]	AGL74060.1
	fusion glycoprotein precursor [Human metapneumovirus]	AAV88364.1
45	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
50	fusion protein [Human metapneumovirus]	AAQ90144.1
	fusion glycoprotein [Human metapneumovirus]	AHV79446.1
	fusion protein [Human metapneumovirus]	AEL87260.1
55	fusion glycoprotein [Human metapneumovirus]	AHV79867.1
	fusion protein [Human metapneumovirus]	ABQ66027.2
	fusion glycoprotein [Human metapneumovirus]	ACJ53621.1

(continued)

	Virus	GenBank Accession
5	fusion protein [Human metapneumovirus]	AAN52911.1
	fusion glycoprotein [Human metapneumovirus]	AHV79536.1
	fusion glycoprotein [Human metapneumovirus]	AGU68411.1
	fusion protein [Human metapneumovirus]	AEZ52346.1
10	fusion protein [Human metapneumovirus]	AAN52913.1
	fusion protein [Human metapneumovirus]	AAN52908.1
	fusion glycoprotein [Human metapneumovirus]	ACJ53553.1
15	fusion glycoprotein [Human metapneumovirus]	AIY25727.1
	fusion protein [Human metapneumovirus]	ABM67072.1
	fusion protein [Human metapneumovirus]	AEZ52361.1
	fusion protein [Human metapneumovirus]	AAS22093.1
20	fusion glycoprotein [Human metapneumovirus]	AGH27049.1
	fusion protein [Human metapneumovirus]	AAK62968.2
	fusion glycoprotein [Human metapneumovirus]	ACJ53556.1
25	fusion glycoprotein [Human metapneumovirus]	ACJ53620.1
	fusion protein [Human metapneumovirus]	ABQ58820.1
	F [Human metapneumovirus] [Human metapneumovirus]	AEK26886.1
	fusion glycoprotein [Human metapneumovirus]	ACJ53619.1
30	fusion glycoprotein [Human metapneumovirus]	ACJ53555.1
	fusion [Human metapneumovirus]	AGL74057.1
	fusion protein [Human metapneumovirus]	ABD27850.1
35	fusion protein [Human metapneumovirus]	AEZ52349.1
	fusion protein [Human metapneumovirus]	ABD27848.1
	fusion protein [Human metapneumovirus]	ABD27846.1
	fusion protein [Human metapneumovirus]	ABQ66021.1
40	fusion protein [Human metapneumovirus]	AFM57710.1
	fusion protein [Human metapneumovirus]	AFM57709.1
	fusion protein [Human metapneumovirus]	ABH05968.1
45	fusion protein [Human metapneumovirus]	AEZ52350.1
	fusion protein [Human metapneumovirus]	AFM57712.1
	fusion protein [Human metapneumovirus]	AEZ52364.1
	fusion protein [Human metapneumovirus]	AAN52912.1
50	fusion protein [Human metapneumovirus]	AEZ52363.1
	fusion [Human metapneumovirus]	AGL74059.1
	fusion glycoprotein [Human metapneumovirus]	ACJ53583.1
55	fusion protein [Human metapneumovirus]	AEZ52356.1
	fusion protein [Human metapneumovirus]	AEZ52353.1
	fusion glycoprotein [Human metapneumovirus]	ACJ53581.1

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	Virus	GenBank Accession
5	fusion glycoprotein [Human metapneumovirus]	ACJ53578.1
	fusion protein [Human metapneumovirus]	AAS22117.1
	fusion protein [Human metapneumovirus]	BAN75965.1
	fusion protein [Human metapneumovirus]	AGF92105.1
10	fusion protein [Human metapneumovirus]	AAS22077.1
	fusion protein [Human metapneumovirus]	AAN52909.1
	fusion glycoprotein [Human metapneumovirus]	ACJ53586.1
15	fusion protein [Human metapneumovirus]	AAQ90145.1
	fusion glycoprotein [Human metapneumovirus]	AGT75042.1
	fusion [Human metapneumovirus]	AGL74058.1
	fusion protein [Human metapneumovirus]	AEL87263.1
20	fusion glycoprotein [Human metapneumovirus]	AGH27057.1
	fusion glycoprotein [Human metapneumovirus]	AHV79491.1
	F [Human metapneumovirus] [Human metapneumovirus]	AEK26906.1
25	fusion glycoprotein [Human metapneumovirus]	ACJ53580.1
	fusion protein [Human metapneumovirus]	AEZ52354.1
	fusion protein [Human metapneumovirus]	AAN52914.1
	G [Human metapneumovirus] [Human metapneumovirus]	AEK26901.1
30	glycoprotein [Human metapneumovirus]	AFI56738.1
	glycoprotein [Human metapneumovirus]	AFI56739.1
	glycoprotein [Human metapneumovirus]	AFI56745.1
35	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
40	G protein [Human metapneumovirus]	AAQ62728.1
	glycoprotein [Human metapneumovirus]	AFI56753.1
	glycoprotein [Human metapneumovirus]	AFI56746.1
45	glycoprotein [Human metapneumovirus]	AFI56750.1
	glycoprotein [Human metapneumovirus]	AFI56747.1
	G protein [Human metapneumovirus]	AAQ62721.1
	glycoprotein [Human metapneumovirus]	AAT46573.1
50	glycoprotein [Human metapneumovirus]	AFI56748.1
	glycoprotein [Human metapneumovirus]	AFI56736.1
	glycoprotein [Human metapneumovirus]	AFI56749.1
55	attachment glycoprotein G [Human metapneumovirus]	AGH27131.1
	attachment glycoprotein G [Human metapneumovirus]	AHV79558.1
	glycoprotein [Human metapneumovirus]	AFI56740.1

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	Virus	GenBank Accession
5	glycoprotein [Human metapneumovirus]	AFI56741.1
	glycoprotein [Human metapneumovirus]	AFI56744.1
	attachment glycoprotein G [Human metapneumovirus]	AHV79790.1
	attachment glycoprotein G [Human metapneumovirus]	AGH27122.1
10	attachment glycoprotein G [Human metapneumovirus]	AHV79763.1
	attachment glycoprotein G [Human metapneumovirus]	AGZ48849.1
	glycoprotein [Human metapneumovirus]	AFI56743.1
15	attachment glycoprotein G [Human metapneumovirus]	AHV79450.1
	glycoprotein [Human metapneumovirus]	AFI56751.1
	attachment glycoprotein [Human metapneumovirus]	AAS48482.1
	attachment glycoprotein G [Human metapneumovirus]	AHV79889.1
20	attachment surface glycoprotein [Human metapneumovirus]	AGW43050.1
	glycoprotein [Human metapneumovirus]	AFI56754.1
	attachment glycoprotein G [Human metapneumovirus]	AHV79601.1
25	glycoprotein [Human metapneumovirus]	AFI56752.1
	attachment glycoprotein G [Human metapneumovirus]	AHV79871.1
	G protein [Human metapneumovirus]	AEZ68099.1
	attachment glycoprotein G [Human metapneumovirus]	AHV79817.1
30	attachment glycoprotein G [Human metapneumovirus]	AHV79943.1
	attachment glycoprotein G [Human metapneumovirus]	BAN75968.1
	attachment surface glycoprotein [Human metapneumovirus]	AGW43045.1
35	attachment glycoprotein G [Human metapneumovirus]	AHV79628.1
	attachment glycoprotein [Human metapneumovirus]	AFK49783.1
	G protein [Human metapneumovirus]	AAQ62723.1
	attachment glycoprotein [Human metapneumovirus]	ABD27839.1
40	attachment surface glycoprotein [Human metapneumovirus]	AGW43046.1
	G protein [Human metapneumovirus]	AAQ62717.1
	glycoprotein [Human metapneumovirus]	AFI56742.1
45	attachment protein [Human metapneumovirus]	ABQ44522.1
	glycoprotein [Human metapneumovirus]	AFI56735.1
	attachment surface glycoprotein [Human metapneumovirus]	AGW43065.1
	G protein [Human metapneumovirus]	AAQ62724.1
50	attachment surface glycoprotein [Human metapneumovirus]	AGW43075.1
	attachment surface glycoprotein [Human metapneumovirus]	AGW43062.1
	glycoprotein [Human metapneumovirus]	AAT46579.1
55	attachment surface glycoprotein [Human metapneumovirus]	AGW43064.1
	attachment surface glycoprotein [Human metapneumovirus]	AGW43054.1
	attachment surface glycoprotein [Human metapneumovirus]	AGW43042.1

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	Virus	GenBank Accession
5	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
10	glycoprotein [Human metapneumovirus]	AAT46571.1
	glycoprotein [Human metapneumovirus]	AAT46578.1
	attachment glycoprotein G [Human metapneumovirus]	AGJ74232.1
15	glycoprotein [Human metapneumovirus]	AAT46580.1
	glycoprotein [Human metapneumovirus]	AAT46574.1
	attachment surface glycoprotein [Human metapneumovirus]	AGW43061.1
	attachment glycoprotein [Human metapneumovirus]	AFK49791.1
20	attachment surface glycoprotein [Human metapneumovirus]	AGW43047.1
	glycoprotein [Human metapneumovirus]	ABC26386.1
	attachment glycoprotein [Human metapneumovirus]	AAS48466.1
25	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
30	attachment glycoprotein G [Human metapneumovirus]	AHV79442.1
	attachment glycoprotein G [Human metapneumovirus]	AGJ74091.1
	attachment glycoprotein G [Human metapneumovirus]	AHV79477.1
35	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
40	glycoprotein [Human metapneumovirus]	AAT46585.1
	attachment glycoprotein G [Human metapneumovirus]	AGU68409.1
	attachment glycoprotein G [Human metapneumovirus]	AGJ74223.1
45	attachment glycoprotein [Human metapneumovirus]	AAS22129.1
	attachment glycoprotein G [Human metapneumovirus]	AGJ74048.1
	G protein [Human metapneumovirus]	AAQ62725.1
	glycoprotein [Human metapneumovirus]	ABC26384.1
50	attachment protein [Human metapneumovirus]	ABQ44525.1
	attachment glycoprotein G [Human metapneumovirus]	YP_012612.1
	attachment surface glycoprotein [Human metapneumovirus]	AGW43071.1
55	attachment glycoprotein G [Human metapneumovirus]	AGJ74162.1
	attachment glycoprotein G [Human metapneumovirus]	AGH27095.1
	attachment glycoprotein G [Human metapneumovirus]	AHV79531.1

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	Virus	GenBank Accession
5	G protein [Human metapneumovirus]	AAQ62726.1
	attachment glycoprotein [Human metapneumovirus]	AAS48465.1
	attachment surface glycoprotein [Human metapneumovirus]	AGW43058.1
	P [Human metapneumovirus] [Human metapneumovirus]	AEK26894.1
10	phosphoprotein [Human metapneumovirus]	AHV79631.1
	phosphoprotein [Human metapneumovirus]	AHV79901.1
	phosphoprotein [Human metapneumovirus]	AHV79570.1
15	phosphoprotein [Human metapneumovirus]	AGJ74076.1
	phosphoprotein [Human metapneumovirus]	AAS22123.1
	phosphoprotein [Human metapneumovirus]	ABB16895.1
	phosphoprotein [Human metapneumovirus]	AHV79579.1
20	phosphoprotein [Human metapneumovirus]	AGJ74244.1
	phosphoprotein [Human metapneumovirus]	AHV79856.1
	phosphoprotein [Human metapneumovirus]	ACJ70113.1
25	phosphoprotein [Human metapneumovirus]	AGZ48843.1
	phosphoprotein [Human metapneumovirus]	AHV79498.1
	phosphoprotein [Human metapneumovirus]	AHV79480.1
	phosphoprotein [Human metapneumovirus]	ABQ43382.1
30	phosphoprotein [Human metapneumovirus]	AAS22107.1
	phosphoprotein [Human metapneumovirus]	ABB16898.1
	phosphoprotein [Human metapneumovirus]	AGH27134.1
35	phosphoprotein [Human metapneumovirus]	ABB16899.1
	phosphoprotein [Human metapneumovirus]	AGH27098.1
	phosphoprotein [Human metapneumovirus]	AAN52866.1
	phosphoprotein [Human metapneumovirus]	AAS22083.1
40	phosphoprotein [Human metapneumovirus]	YP_J12606.1
	phosphoprotein [Human metapneumovirus]	AHV79973.1
	phosphoprotein [Human metapneumovirus]	AHV79462.1
45	phosphoprotein [Human metapneumovirus]	AGJ74042.1
	phosphoprotein [Human metapneumovirus]	AAV88362.1
	P [Human metapneumovirus] [Human metapneumovirus]	AIL23591.1
	phosphoprotein [Human metapneumovirus]	AHV79453.1
50	phosphoprotein [Human metapneumovirus]	AGJ74261.1
	phosphoprotein [Human metapneumovirus]	AGH27116.1
	phosphoprotein [Human metapneumovirus]	ABB16444.1
55	phosphoprotein [Human metapneumovirus]	ABB16445.1
	phosphoprotein [Human metapneumovirus]	AHV79507.1
	phosphoprotein [Human metapneumovirus]	BAH59616.1

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	Virus	GenBank Accession
5	phosphoprotein [Human metapneumovirus]	ABB16443.1
	phosphoprotein [Human metapneumovirus]	ABQ43388.1
	phosphoprotein [Human metapneumovirus]	ABQ43389.1
	phosphoprotein [Human metapneumovirus]	ABQ43395.1
10	phosphoprotein [Human metapneumovirus]	ABQ43385.1
	phosphoprotein [Human metapneumovirus]	AAP84042.1
	phosphoprotein [Human metapneumovirus]	AAN52868.1
15	phosphoprotein [Human metapneumovirus]	AAP84041.1
	phosphoprotein [Human metapneumovirus]	AGH27080.1
	phosphoprotein [Human metapneumovirus]	ABQ43387.1
	phosphoprotein [Human metapneumovirus]	AAS22099.1
20	phosphoprotein [Human metapneumovirus]	ABB16896.1
	phosphoprotein [Human metapneumovirus]	AGJ74094.1
	phosphoprotein [Human metapneumovirus]	AEZ68089.1
25	phosphoprotein [Human metapneumovirus]	ABK97002.1
	phosphoprotein [Human metapneumovirus]	AAP13486.1
	phosphoprotein [Human metapneumovirus]	AHV79444.1
	phosphoprotein [Human metapneumovirus]	AHV79865.1
30	phosphoprotein [Human metapneumovirus]	AGJ74226.1
	phosphoprotein [Human metapneumovirus]	ABQ43383.1
	phosphoprotein [Human metapneumovirus]	AAN52863.1
35	phosphoprotein [Human metapneumovirus]	AHV79775.1
	phosphoprotein [Human metapneumovirus]	AEZ68094.1
	phosphoprotein [Human metapneumovirus]	AHV79883.1
	phosphoprotein [Human metapneumovirus]	AEZ68092.1
40	phosphoprotein [Human metapneumovirus]	ABQ43390.1
	phosphoprotein [Human metapneumovirus]	ABQ43386.1
	phosphoprotein [Human metapneumovirus]	ABQ43391.1
45	phosphoprotein [Human metapneumovirus]	ACS16062.1
	phosphoprotein [Human metapneumovirus]	AEZ68090.1
	phosphoprotein [Human metapneumovirus]	AAK62967.1
	phosphoprotein [Human metapneumovirus]	AEZ68093.1
50	phosphoprotein [Human metapneumovirus]	AEZ68088.1
	phosphoprotein [Human metapneumovirus]	ABQ43392.1
	phosphoprotein [Human metapneumovirus]	ABQ43393.1
55	phosphoprotein [Human metapneumovirus]	ABQ43384.1
	phosphoprotein [Human metapneumovirus]	ABQ43394.1
	phosphoprotein [Human metapneumovirus]	ABK96999.1

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	Virus	GenBank Accession
5	phosphoprotein [Human metapneumovirus]	AHV79489.1
	phosphoprotein [Human metapneumovirus]	AGJ74235.1
	phosphoprotein [Human metapneumovirus]	AAS22075.1
	phosphoprotein [Human metapneumovirus]	AAS22115.1
10	phosphoprotein [Human metapneumovirus]	All17601.1
	phosphoprotein [Human metapneumovirus]	ABK97000.1
	phosphoprotein [Human metapneumovirus]	AHV79561.1
15	phosphoprotein [Human metapneumovirus]	AGT75040.1
	phosphoprotein [Human metapneumovirus]	AAN52864.1
	phosphoprotein [Human metapneumovirus]	ABK97001.1
	phosphoprotein [Human metapneumovirus]	AGT74979.1
20	phosphoprotein [Human metapneumovirus]	AHV79955.1
	phosphoprotein [Human metapneumovirus]	AGH27055.1
	phosphoprotein [Human metapneumovirus]	AAV88361.1
25	phosphoprotein [Human metapneumovirus]	ABQ43397.1
	phosphoprotein [Human metapneumovirus]	AGJ74173.1
	P [Human metapneumovirus] [Human metapneumovirus]	AEK26904.1
	phosphoprotein [Human metapneumovirus]	ACJ70104.1
30	phosphoprotein [Human metapneumovirus]	ABK97003.1
	phosphoprotein [Human metapneumovirus]	AGT74955.1
	phosphoprotein [Human metapneumovirus]	AAN52856.1
35	phosphoprotein [Human metapneumovirus]	AAN52862.1
	phosphoprotein [Human metapneumovirus]	AGJ74138.1
	phosphoprotein [Human metapneumovirus]	AHV79613.1
	phosphoprotein [Human metapneumovirus]	AGJ74060.1
40	phosphoprotein [Human metapneumovirus]	AAQ67684.1
	phosphoprotein [Human metapneumovirus]	AEA02278.1
	N [Human metapneumovirus] [Human metapneumovirus]	AEK26899.1
45	nucleoprotein [Human metapneumovirus]	ACS16M1.1
	nucleoprotein [Human metapneumovirus]	AAS88425.1
	nucleoprotein [Human metapneumovirus]	YP_012605.1
	nucleoprotein [Human metapneumovirus]	AHV79882.1
50	nucleoprotein [Human metapneumovirus]	AHV79774.1
	nucleocapsid protein [Human metapneumovirus]	AAN52886.1
	nucleoprotein [Human metapneumovirus]	AAS22082.1
55	nucleoprotein [Human metapneumovirus]	AHV79864.1
	nucleoprotein [Human metapneumovirus]	AHV79828.1
	nucleoprotein [Human metapneumovirus]	AGJ74084.1

(continued)

	Virus	GenBank Accession
5	nucleocapsid protein [Human metapneumovirus]	AAN52888.1
	N [Human metapneumovirus] [Human metapneumovirus]	AIL23590.1
	nucleoprotein [Human metapneumovirus]	AAK62966.1
	nucleoprotein [Human metapneumovirus]	AHV79972.1
10	nucleoprotein [Human metapneumovirus]	AHV79470.1
	nucleoprotein [Human metapneumovirus]	AHV79452.1
	nucleoprotein [Human metapneumovirus]	AGJ74243.1
15	nucleoprotein [Human metapneumovirus]	AHV79533.1
	nucleoprotein [Human metapneumovirus]	AGJ74181.1
	nucleoprotein [Human metapneumovirus]	AHV79497.1
	nucleoprotein [Human metapneumovirus]	AHV79702.1
20	nucleoprotein [Human metapneumovirus]	AHV79648.1
	nucleoprotein [Human metapneumovirus]	AHV79435.1
	putative nucleoprotein [Human metapneumovirus]	AGJ74260.1
25	nucleocapsid protein [Human metapneumovirus]	AAN52887.1
	nucleoprotein [Human metapneumovirus]	AGU68386.1
	nucleocapsid protein [Human metapneumovirus]	AAN52899.1
	nucleoprotein [Human metapneumovirus]	AAR17673.1
30	nucleocapsid protein [Human metapneumovirus]	AAN52898.1
	nucleoprotein [Human metapneumovirus]	AEA02277.1
	nucleoprotein [Human metapneumovirus]	AHV79612.1
35	nucleoprotein [Human metapneumovirus]	AGU68416.1
	nucleoprotein [Human metapneumovirus]	AGU68408.1
	nucleoprotein [Human metapneumovirus]	AGU68370.1
	nucleoprotein [Human metapneumovirus]	AAQ67683.1
40	nucleoprotein [Human metapneumovirus]	AGJ74137.1
	nucleoprotein [Human metapneumovirus]	AGU68344.1
	nucleocapsid protein [Human metapneumovirus]	ABK96997.1
45	nucleoprotein [Human metapneumovirus]	AGU68413.1
	nucleocapsid protein [Human metapneumovirus]	AAN52891.1
	nucleoprotein [Human metapneumovirus]	AGU68360.1
	nucleoprotein [Human metapneumovirus]	AGU68353.1
50	nucleocapsid protein [Human metapneumovirus]	ABK96996.1
	nucleoprotein [Human metapneumovirus]	AAR17666.1
	N [Human metapneumovirus] [Human metapneumovirus]	AEK26903.1
55	nucleoprotein [Human metapneumovirus]	AGT75039.1
	nucleoprotein [Human metapneumovirus]	AGU68410.1
	nucleoprotein [Human metapneumovirus]	AAS22074.1

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	Virus	GenBank Accession
5	nucleoprotein [Human metapneumovirus]	AHV79560.1
	nucleoprotein [Human metapneumovirus]	AGT74978.1
	nucleoprotein [Human metapneumovirus]	AGJ74128.1
	nucleoprotein [Human metapneumovirus]	AAR17663.1
10	nucleoprotein [Human metapneumovirus]	AAR17662.1
	nucleoprotein [Human metapneumovirus]	AAR17664.1
	nucleoprotein [Human metapneumovirus]	AAR17657.1
15	nucleoprotein [Human metapneumovirus]	AAR17659.1
	nucleoprotein [Human metapneumovirus]	AAR17661.1
	nucleoprotein [Human metapneumovirus]	AGU68352.1
	nucleoprotein [Human metapneumovirus]	AGU68373.1
20	nucleoprotein [Human metapneumovirus]	AGU68376.1
	nucleoprotein [Human metapneumovirus]	AGU68342.1
	nucleoprotein [Human metapneumovirus]	AGU68365.1
25	nucleoprotein [Human metapneumovirus]	AGU68363.1
	nucleoprotein [Human metapneumovirus]	AGU68398.1
	nucleoprotein [Human metapneumovirus]	AGU68348.1
	nucleoprotein [Human metapneumovirus]	AGU68354.1
30	nucleoprotein [Human metapneumovirus]	AGU68391.1
	nucleoprotein [Human metapneumovirus]	AGU68389.1
	nucleoprotein [Human metapneumovirus]	AGU68399.1
35	nucleoprotein [Human metapneumovirus]	AGU68337.1
	nucleoprotein [Human metapneumovirus]	AAR17660.1
	nucleoprotein [Human metapneumovirus]	AAR17667.1
	nucleoprotein [Human metapneumovirus]	AGU68402.1
40	nucleoprotein [Avian metapneumovirus type C]	CDN30025.1
	nucleoprotein [Avian metapneumovirus]	AGZ87947.1
	Nucleoprotein [Avian metapneumovirus type C]	CAL25113.1
45	nucleocapsid protein [Avian metapneumovirus]	AB042286.1
	nucleocapsid protein [Avian metapneumovirus]	AAK38430.1
	nucleocapsid protein [Avian metapneumovirus]	AAK54155.1
	nucleocapsid protein [Avian metapneumovirus]	AAK38426.1
50	nucleocapsid protein [Avian metapneumovirus]	AAK38425.1
	nucleocapsid protein [Avian metapneumovirus]	AAK38424.1
	nucleocapsid protein [Avian metapneumovirus]	AAF05909.1
55	nucleocapsid protein [Avian metapneumovirus]	AAK38435.1
	nucleocapsid protein [Avian metapneumovirus]	AAK38428.1
	nucleoprotein [Human metapneumovirus]	AAR17669.1

(continued)

Virus	GenBank Accession
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]	AAL35389.3
nucleoprotein [Human metapneumovirus]	AEZ68064.1

Table 5. PIV3 Nucleic Acid Sequences (Reference Example)

Description	Sequence	SEQ ID NO:
>gbIKJ672601.11:4990-6609 Human parainfluenza virus 3 strain HPIV3/Homo sapiens/PER /FL A4815/2 008 [fusion glycoprotein F0]	<p>ATGCCAATTTC AATACTGTTAAATTATTACAAGCATGATCATGCGATGACACTGC CAATAGACAT CAGCAAC TACAGC AETABGTGTATTGTTCAACAGTCC CAAGGGATGAAAGATCAACAAC TTGGAAC AAGATATCTAATCCTGAGTC TCATACC AAAAATAGAAATCTAACTCTTGTGTTGA CCAGCAGATCAAGCAATCAAGAGGTTATTGATAGACTGATC ATTCCTTTATATGATGGACTAA GATTACAGAAAGSATGTGATAGTGAC TAATCAAGAAATCCAATGAAAACACTGATCCAGAACAG ACGATTCCTTGGAGGGGTAATTTGAACTATTGCTCTAGGAGTAGCAACCTEAGEACAAATAC GCAGCAGTTCTGCTGTTGAGGDC AAGCAGGC AAGATCAGACATTGAAAAC TC AAGGAAAC ATCAGGACAC AANTAAAGCAGTGCAGTCAAGTTCAGAGCTCTGTAGGAAATTTGATAGTAGC TTAATCAGTCCAGGATTATGTC AACAAGAAATCCTGTCATTCGATTCCGAGACTAGGTTGTGA AGCAGCAGGACTTCAGTTAGGGAATTGCATTAGCAGCATTACTCAGAAATTAACAATATATTG GTSATAACATAGGATCGTTAC AAGAAAGGGAATAAATTAACAAGGTATAGCATCATTATAGCGT ACAAATATCACAGAAATATTCAC AACATCAAGGTTGACAAATATGATATTATGATCTATATTT ACAGATCAATAAAGGTGAGAGTTATAGATGTTGATTTGATGATTACTCAATACCTCC AAGT CAGACTCCCTTTATGACCAGACTGCTGAGCAGTCAAAATCAAGAAATAGATTCATATCATAC ATATCCAAATAGAGATGTTATATCCCTTTCCAGCCATATCATGACGAAAAGGGGCATTTCT AGGTGAGCAGATGTC AAGSANTGCATAGAGCATTCAGCAGTTATATATGCCCCTTGTGATCA GGATTTGTACTAAACCATGAAATGAGAGCTGCTTATCAGGAAACATATCCCAATGTCCAGGAA CCAGCTCACATCAGACATAGTTGCTAGGTATGCAATTTGTC AATGGAGGAGTGGTTGCGAATTS TNTACAGCTACATGATACATGC AATGATATGGTAATAGATCAACCAAGCACCTGATCAGGA GTCAAATTTATACACATAAAGAAATGTANTAC AATAGGTATCAACGGAAATGCTATTCAACACAAA CAGGAAAGGAACTCTTGCATTTCAACACACAGAGACATAACATTAACAAATTCCTTTGCACCTG ATCCGATTTGACATATCATGAGGTCACAAAGGC AANNFCAGATCTTGGAGAAATCAAAAGATG GATAGAGGCTCAATCAAAAAGCTAGATTCTATTGGAAGTTGSCATCAATCTAGCCTAC AATCA TGGTTATTTGAT AATGATGATTTATATGTTTATATTAATATAACAAATTAATTC AATTTGCAATTA GTATTCAGAAATTC AAAAGAGAAATGAGTGGATCAAAATGAT AAGCCGTATGTTATTAACAAAC AG</p>	9

(continued)

Description	Sequence	SEQ ID NO:
<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p> <p>gil612507167IgbIAHX22430. 1I hemagglutinin- neuraminidase [Human parainfluenza virus 3]</p>	<p>ATGGGAAATACATGGAAGCACACC AACCCACGGAAAGGATGCTGGTAATGAGCTGGAGACATCCACA GGCACCTCATGGCACAGGCTCACCAACAGGATACATATATATTGTGGACGATAAACCTGGTGT THTTATCAATAGTCATTCATCATAGTGTAACTAATTCCATCAAAAAGTGAAGAGCCCGCGAATCA TTGCTCACAGACATAAATATAGTGGTTTATGGAGTTACAGAAAAGATCCAGGTGGCATCGSAT ATACTAATGATCTAATACAGTCAAGAGTGAATACAGGCTTCTTACAAATCAGAGTCAATGTCAG AHTTATATACCAATATCATTGACACACAAATATCGGATCTTAGGAAATTCATTAGTGAATAC ATTGAAATGATATACAGAGTSCACCCACAAAGAAATACACATGATGTGGGTATAAANCTTT AATCCAGATGATTTCAGAGATSCACGTCGGTCTTCATCTTTGATGAAAACCTCCAAAATAA GATTANTGCCGGGACAGGATTTATAGCTATGCCAACGACTGTTGATGGCTGATGTCAGAACCC CCGTCTTAGTGTAAATGATCTGATTTATGCTTACACCTCAAAATCTAATTAATCTCGAGGTTGCCAG GATATAGGGAAATCAATCAAGTATTACAGATAGGGCAATAACTGTAAAATCAGACTTGGTACCC TGACTTAATCTCTAGGATCTGATACCTTCAACATAAATGACAAATAGAAAGTCAATGTCCTGATG GACTCTAAATACAGATGTATATCAACTGTGTTCAACCCCAAAAAGTTGATGAAGATCAGATAT GCATCATCAGGCATAGAAATATGTACTTGTATATGTCGAATTAATGATGGCTCAATCTCGACAAC AAGATTTAAGAAATAAATATAAGTTTTGATCAACCATATGCGGCAATTAACCCATCTGTTGGAC CAGGATATACTACAAAGCCAAAATAAATTTCTCGGATATGGAGGCTTGAACATCCAAATAAAT GAGATGCATCTGCACACAACTGGGTGTCTGGGAAACACAGAGAGACTGTAAATGAAGCA TCTCATAGTCCATGGTTTTGATAGATAGAGGATGCTCACTCTATAATTTGTTGTCAGAGGGCT GAACTCAGTTCCAAAATGAAGGTATGGACGATATCTATGAGCAAAATTAATGGGGTCAAGAA GGAGATTACTTCTACTAGGTACAAAGATCTACATATACACAGATCTCAAGTTGGCACAGCA AGTACAAATAGGAATAATTGACATTACTGACTACAGTGAATAAAGGATAAATGGACATGGCAT ANTGTCTATCAAGACCAAGAAACAAATGATGTCCATGGGACATTCATGTCCGGATGGATGTA TANGGGAGTATATACCAGTGCATATCCACTCAATCCCACAGGAAGCATTGTATCTGTCAT ATTGGATCAAAAAATCGAGAGTCAACCCAGTCAATACTTACTCAACAGCAACCGAAGGGGTA AACGAGCTGCTATCCGAAACAAAACACTCTCAGCTGGGTACACAAACAACTGCTATTACAC ACTATAACAAAGGGTATTGTTTTTCATATAGTGAATAAATCATAAAAGCTTAAACACATTTCAAC CCTGTGTTCAAAACAGAGATTCCAAAAGCTGCAGT</p>	<p>10</p>

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Description	Sequence	SEQ ID NO:
<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p>	<p>ATGGAAATAC TGGAAAGCAC ACCAACCAC GGC AAGGAC GTC GGC AAGGAGCT GGAAC CAGC AC</p> <p>AGCCACAC AGGAC AAC AAGC TGACC AAC AAGATC ACCTAC ATCCTGT GGAAC ATC ACCTGGT</p> <p>GTTCCTGAGC ATC GTGTC ATC ATC GTGTC GACC AATAGC ATC AAGAGC GAG AAGGC CAGAGA</p> <p>GAGCTGCTGC AGGAC ATC AAC AAC GAGTTC ATGGAAATG GACC GAGAAAGATCC AGGTG GGC A</p> <p>GGACACAC AC AAG GACCTG ATCC AGAGG GGC GTG AAGC AGC GGTGCT GAC ATCC AGAGC</p> <p>CACCTGC AGA AC TAC ATCC CC ATC AGCCTG ACC CAGC AGATC AGC GACCTGC GG AAGTTC ATC</p> <p>AGCGAG ATC ACC ATCC GGAAGC ACAAC CAG AAGTGC CC CCC CAGAGA ATC AC CC AC GACGT</p> <p>GGGATC AAGC CC CTG AAGCC G GAC GATT TL TGCGGTGT AC AAGCGGCT TGGC CAGG CTGA</p> <p>TG AAGAC CC C AAGATC CGGC TGATGCTG GGCCTGGAC TGC TG GGC ATGC CTAGC ACAGT G</p> <p>GATGGCT GTGTGC GG AACC CC AGCC TC GTG ATC AAG GATGTG ATCTAC GDC TAC AC AGG AAG</p> <p>CTGATC AC CC GGGCT GGC AGGATATC GGC AAGAGCTAC C AGGTGCT GC AGATC GGC ATC AT</p> <p>CACCTG AAGC TC CGA COT GTGTG CC GACCTGA ACCCTG GG ATC AGCC AC AC CTLE AAC ATC AA</p> <p>CGACAC AGAAAGAGCTGC AAG CTGGCTCTGCTG AAC ACC GAGTGTG ACC AGCTGTGC AGC A</p> <p>CC CC AAGGTGGAC GAG AAGGCG ACTAGCC CAGC AGC GGC ATC GAGGATATC GTGCTGGAC</p> <p>ATGTTGACTAC GACGGC AGC ATC AGC AC C AC CC GGTTC AAGAAC AAC AAC ATCAGCTTGGAC</p> <p>CAGCCCTAGC GGC GGCCTGT ACC GTTC TGTTGG GGCCTGGC ATC TAC TAC AAGGGC AAGATC ATC</p> <p>TTCTGGG CTAC GGC GGC TGGAAC ACCC C ATC AAC GAG AAGG C C ATC TGC AAC AC C AGC GG</p> <p>CTG C C TGGC AAG AC CCAGAG AAG TGC AATC AAGCC AGCC AC AAGC C C TGTTC AAG G GACC</p> <p>GG AAGTGTG C AACTC ATC ATC GTGGTGGAC AAGGGCC TGAACAGC GTG C C AAGC TGA AAG</p> <p>TGTGGC AATC AAG ATGC GGC A GAACTACTGGGGC AGC GAGGGG A GACTTDTGC TGCTGGGA</p> <p>AACAGATC TAC ATC TAC ACC CGGTCC ACC AAG TGGC ACAGC AACCTGC AAG TGGG A ATC ATC</p> <p>GACATC ACC GACTAC AGC GAC ATC CCGATC AAGTGG ACC TGGC AC AAG GTGCTG AAGC AGAC</p> <p>CGGCAC AATG AATG C C TTG G GGC C ACAGC TGC CC C GATG GATGT ATC AC C GGC GTGTAC A</p> <p>CC GAC C C TACC CC CTG AATC CTACC GGC TC C ATC GTG TCC AGC GTG ATC CT G GAC AGCC A G A</p> <p>AAGCAG AGTGA ACC CC GTG ATC AC ATC AGC ACC GGC ACC GAGAG AATG AAG G AACTGGCC</p> <p>ATC A G A A C A A G A C C T G A G C G C C T A C A C C A A G C T G A T C A C A C A C T A A A C A A G</p> <p>GGCTACTGCTTC AC ATG GTG G A A A T C A A C C A A G T C C T G A A C A C C T T C A G C C C A T G C T G T</p> <p>TC AAGAC C GAG ATCC C A A G A G C T G C T G C</p>	<p>11</p>
<p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ATGCCCATC CAGC ATC CTGCTGATC ATC ACCAC AATGATC ATGGCCAGC CACTGC CAGATCGAC</p> <p>ATC AC CAAGCTT G C A G C A C G T G G G C G T G C T C G T G A A C A G C C C A A G G G C A T G A A G A T C A B C C A</p> <p>G A K T T C G A G A C A G C T A C C T G A T C C T G A C C C T G A T C C C C A A G A T C G A G G A C A G C A A C A G C T G</p> <p>C G G C A G C A G C A G A T E A N C A G T A C A A G C G G C T G C T G A C A G A E T G A T C A T C C C C T G T A C G</p> <p>A C G C C T G C G C C T G C A G A A A G A C G T G A T C G T G A C C A A C A G A A A A G C A A G A G A A C A C C G A C</p> <p>C C C C G A C C G A G A G A T T C T C G G C G C G T G A T C G G C A A A T C G C C T G G A A T G G C C A G A A G</p> <p>C G C C A B A T T A C A B C C C C T G T G C C C T G G T G G A A G C A A G C A G G C C A G A A G C G A C A T C G A G A</p> <p>A B C T G A A A G A G G G E A T C C G G A C A C A A C A A G G C E G T G C A G A G C T G C A G T C A G G C T G G E</p> <p>C A T T C G A T C G T G G C A T C A A G T C C G T G C A G G A C T A C G T G A A C A A A A A A T C G T G C C C T C A T</p> <p>C G C C G G C T G G C T G T G A A G C T G C G G A C T G C A G C T G G G E A T T G C C C T G A C A C A G C A C T A C A</p> <p>G C G A C T G A C C A A C A T C T T C G G C G A C A A C A T C G G C A B C T G C A G G A A A A G G G C A T T A A B C T G</p> <p>C A G G A A T C G C C A C C T G T A C C G A C C A A D A T C A C C G A G A T C T C A C C A C C A C C C G T G G A T</p> <p>A G T A C G A C A T C A C G A C C T G C T T C A C C G A G A B C A T C A A A G T G C G C G T G A T C G A C G T G G A C</p>	<p>12</p>

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Description	Sequence	SEQ ID NO:
<p>gil612507167IgbIAHX22430. 1I hemagglutinin-neuraminidase [Human parainfluenza virus 3]</p>	<p> AUGGAAUADUUGGAAAGC ACACCAACCACGGAAAGG AUGCUGGUAUU BAGDUIGGAGAC AUCC A CAGCCACUC AUGGG AACANGCUC ACCAACAASUAAC AUUUAUUUGUGNCGAU AACDCUS GUUAUUU AUCANUADUULCASC AUAGUGCUAACUA AUUUCCAUCAAAAAGU GAAAAGSDDCG CSANUCALUUCUAC AAGAC AUAAUAAUGABU UUUGGAAAUU ACAGAAAAGAUCC AAGUGG CALUGSUA AUUAG UANUGAKU AAUACAGUCAGSAGU GAUAC AAGGDUUC UUAUAAU UCAG AUUCABUUC CAGAAUU AUUAGC EAUUAE AUUGAC ACACAAAU AU CCGAUUCU UAGBAUU CAUAGUGAAUU ACAGUAGAANUGAU AUUC AAGAAUG GDC ACCAC AAAGA AU AACACUGA UGUUGUU UAAAAAC UUUAAAU CAGAU GAU UUUGGAGAU GAC GUCUUGUCUUUC AUUU UUGKUGAAAACUC CAAAAU AAGAUU AAUUGCCGSSAC CAGBAUU AUUAGC U UUGCCAAGSAC UGUUAGUUGGUCUUGUC AGAAC CDDGUCU UAGUENJAAUUGMUCU GAU UUUGGUU ACADC UC AAUUCU AAUU ACUCGAGGU UGC CAGGAU AUAGSAAAU C AUUUAAGU AUUACAG AUAGG GUNNUAC UGU AAACUC AGAEUUGG UGUC UGAC UUAAGUC UAGSACUUE UCAUCG UUCA ACUUAAGAC AUUAGAAAGUC AUGUUC UC UAGCACUCU AAUACAGAUU AUUACACUG UGUUCAC CC AAAAGUUGAU SAAGAUU CAGAUU UUGCUC AUUAGG CUAGGC AUAGSAAU AUUGU ACUAGNUAUGUC AAUUAU SAUGUC AUUCUGGAC AACAAAUUARGAAU AAUAAU AUA GUUAAGUC AAC AUUUGCGCAUU AUUCC AUGUUGUGAC CAGBAU UAGUAC AAGG CAAUUA AUUUUCUGG AUUGAGGUCUUGAAC AUCCAAUAAUAGAG AUUGCAAU UCSCA ACACACUCUGGUGUC CUUGSAAAC ACAGAGAGAUU GAUUCAGC AUGC AUAGUCCAU S GUULCAGAUAGAGG AUGGUCAC UC UUAUUUU GUUGUAGAC AAGGCUUGAUCU DACUU CC AAUUGAAGS U AUGGAC GAU AUUCUUGAGAC AAAAUUACUUGGGU CAGAAAGG AUU ACUCUACUAGGU AAC AAGAU UC AUUUAU ACACAG AUUCUAC AAGUU GGCACAGC AAGUAC AUUAGGAUAUU GACAUU ACUGACU ACAGUGAU UAAAGAU AAAAUUGGAC AUGGCU AAU GUGCUUUC AAGAC CAGSAAAC AUUGAUUGUC AUUGGGACAUUC AUUCUGG AUGSUAU UACGSGAGU AUUUC GAUUC AUUUCACUC AUUC CACAGSAAAGC AUGU UAUUC UC GUC AUUUGGACUC AC AAAAUUGAGAGUC AACCCAGUC AUUAC UUCUC AACAGC AACGSAAG GGUUACAGUCUGGU UUCGGAAAC AAAAC ACUCUCUCUUGGU ACACAC AACAGGUCGA UUUCACUC AUUAA CAAAGGUU AUUGUUCU AUUAGUAGAAU AAU CAUAAAAGCUUAAACA CAUUCACCC AUUGUUC AAAAAAGAU UC CAAAAAGCUGCAGU </p>	<p>62</p>

(continued)

	Description	GenBank Accession
5	hemagglutinin-neuraminidase [Human parainfluenza virus 3]	BA032044.1
	hemagglutinin-neuraminidase [Human parainfluenza virus 3]	BA032051.1
	C protein [Human parainfluenza virus 3]	NP.599251.1
	C protein [Human parainfluenza virus 3]	ABZ85670.1
10	C protein [Human parainfluenza virus 3]	AGT75164.1
	C protein [Human parainfluenza virus 3]	AAB48686.1
	C protein [Human parainfluenza virus 3]	AHX22115.1
15	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
20	C protein [Human parainfluenza virus 3]	AGW51218.1
	C protein [Human parainfluenza virus 3]	AGW51074.1
	C protein [Human parainfluenza virus 3]	AGT75323.1
25	C protein [Human parainfluenza virus 3]	AGT75307.1
	C protein [Human parainfluenza virus 3]	AHX22131.1
	C protein [Human parainfluenza virus 3]	AGW51243.1
	C protein [Human parainfluenza virus 3]	AGT75180.1
30	C protein [Human parainfluenza virus 3]	AGT75212.1
	C protein [Human parainfluenza virus 3]	AGW51186.1
	C protein [Human parainfluenza virus 3]	AHX22075.1
35	C protein [Human parainfluenza virus 3]	AHX22163.1
	C protein [Human parainfluenza virus 3]	AGT75196.1
	C protein [Human parainfluenza virus 3]	AHX22491.1
	C protein [Human parainfluenza virus 3]	AHX22139.1
40	C protein [Human parainfluenza virus 3]	AGW51138.1
	C protein [Human parainfluenza virus 3]	AGW51114.1
	C protein [Human parainfluenza virus 3]	AGT75220.1
45	C protein [Human parainfluenza virus 3]	AHX22251.1
	RecName: Full=Protein C; AltName: Full=VP18 protein	P06165.1
	C protein [Human parainfluenza virus 3]	AHX22187.1
	C protein [Human parainfluenza virus 3]	AGT75228.1
50	C protein [Human parainfluenza virus 3]	AHX22179.1
	C protein [Human parainfluenza virus 3]	AHX22427.1
	C protein [Human parainfluenza virus 3]	AGW51210.1
55	nonstructural protein C [Human parainfluenza virus 3]	BAA00922.1
	C protein [Human parainfluenza virus 3]	AHX22315.1
	C protein [Human parainfluenza virus 3]	AGW51259.1

(continued)

	Description	GenBank Accession
5	C protein [Human parainfluenza virus 3]	AHX22435.1
	C protein [Human parainfluenza virus 3]	AHX22123.1
	C protein [Human parainfluenza virus 3]	AHX22299.1
	C protein [Human parainfluenza virus 3]	AGW51267.1
10	unnamed protein product [Human parainfluenza virus 3]	CAA28430.1
	C protein [Human parainfluenza virus 3]	AGW51178.1
	C protein [Human parainfluenza virus 3]	AHX22411.1
15	RecName: Full=Protein C	P06164.1
	phosphoprotein [Human parainfluenza virus 3]	NP_067149.1
	phosphoprotein [Human parainfluenza virus 3]	AAB48685.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22498.1
20	phosphoprotein [Human parainfluenza virus 3]	AHX22490.1
	phosphoprotein [Human parainfluenza virus 3]	AGT75259.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51137.1
25	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
30	phosphoprotein [Human parainfluenza virus 3]	AGT75163.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22506.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51129.1
35	phosphoprotein [Human parainfluenza virus 3]	AHX22194.1
	phosphoprotein [Human parainfluenza virus 3]	AGT75211.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22258.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51121.1
40	phosphoprotein [Human parainfluenza virus 3]	AGT75282.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22146.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22138.1
45	phosphoprotein [Human parainfluenza virus 3]	AHX22322.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22370.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22098.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22130.1
50	phosphoprotein [Human parainfluenza virus 3]	AHX22418.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22114.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22410.1
55	phosphoprotein [Human parainfluenza virus 3]	AGT75306.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22170.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22266.1

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	Description	GenBank Accession
5	phosphoprotein [Human parainfluenza virus 3]	AHX22090.1
	phosphoprotein [Human parainfluenza virus 3]	AGT75195.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22226.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22178.1
10	phosphoprotein [Human parainfluenza virus 3]	AHX22122.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22186.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22066.1
15	phosphoprotein [Human parainfluenza virus 3]	AHX22522.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51225.1
	phosphoprotein [Human parainfluenza virus 3]	BAN29032.1
	phosphoprotein [Human parainfluenza virus 3]	ABZ85669.1
20	phosphoprotein [Human parainfluenza virus 3]	AHX22426.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22058.1
	phosphoprotein [Simian Agent 10]	ADR00400.1
25	phosphoprotein [Human parainfluenza virus 3]	AHX22250.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22434.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22298.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22442.1
30	phosphoprotein [Human parainfluenza virus 3]	AHX22074.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51153.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51241.1
35	phosphoprotein [Human parainfluenza virus 3]	AHX22210.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51105.1
	phosphoprotein [Human parainfluenza virus 3]	AGT75251.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22362.1
40	phosphoprotein [Human parainfluenza virus 3]	AHX22474.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51217.1
	phosphoprotein [Human parainfluenza virus 3]	AIG60038.1
45	phosphoprotein [Human parainfluenza virus 3]	AHX22378.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51057.1
	phosphoprotein [Human parainfluenza virus 3]	AGT75187.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51233.1
50	phosphoprotein [Human parainfluenza virus 3]	AHX22482.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51161.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22306.1
55	phosphoprotein [Human parainfluenza virus 3]	AHX22162.1
	phosphoprotein [Human parainfluenza virus 3]	ACJ70087.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22466.1

(continued)

	Description	GenBank Accession
5	phosphoprotein [Human parainfluenza virus 3]	AHX22346.1
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	phosphoprotein [Human parainfluenza virus 3]	AGW51073.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51185.1
10	phosphoprotein [Human parainfluenza virus 3]	AGW51065.1
	phosphoprotein [Human parainfluenza virus 3]	ABY47603.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51049.1
15	phosphoprotein [Human parainfluenza virus 3]	AHX22330.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51250.1
	phosphoprotein [Human parainfluenza virus 3]	AGT75227.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51282.1
20	phosphoprotein [Human parainfluenza virus 3]	AGW51209.1
	phosphoprotein [Human parainfluenza virus 3]	AGW51193.1
	phosphoprotein [Human parainfluenza virus 3]	AGT75322.1
25	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]	ACD99698.1
30	phosphoprotein [Human parainfluenza virus 3]	AGW51266.1
	phosphoprotein [Human parainfluenza virus 3]	AGT75179.1
	phosphoprotein [Human parainfluenza virus 3]	AHX22282.1
35	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
40	RecName: Full=Phosphoprotein; Short=Protein P	P06162.1
	P protein [Human parainfluenza virus 3]	AAA66818.1
	phosphoprotein [Human parainfluenza virus 3]	AAA46866.1
45	phosphoprotein [Human parainfluenza virus 3]	BAA00031.1
	polymerase-associated nucleocapsid phosphoprotein (version 2) - parainfluenza virus type 3 [Human parainfluenza virus 3]	RRNZP5
	phosphoprotein [Human parainfluenza virus 3]	AGT75171.1
50	phosphoprotein [Human parainfluenza virus 3]	BAA00921.1
	D protein [Human parainfluenza virus 3]	NP_599250.1
	D protein [Human parainfluenza virus 3]	AHX22377.1
55	D protein [Human parainfluenza virus 3]	AHX22121.1
	D protein [Human parainfluenza virus 3]	AGT75297.1
	D protein [Human parainfluenza virus 3]	AGW51136.1

(continued)

	Description	GenBank Accession
5	D protein [Human parainfluenza virus 3]	AGW51242.1
	D protein [Human parainfluenza virus 3]	AGW51112.1
	D protein [Human parainfluenza virus 3]	AHX22497.1
	D protein [Human parainfluenza virus 3]	AHX22145.1
10	D protein [Human parainfluenza virus 3]	AGT75202.1
	D protein [Human parainfluenza virus 3]	AHX22385.1
	D protein [Human parainfluenza virus 3]	AGW51216.1
15	D protein [Human parainfluenza virus 3]	AGT75281.1
	D protein [Human parainfluenza virus 3]	AGT75194.1
	D protein [Human parainfluenza virus 3]	AHX22521.1
	D protein [Human parainfluenza virus 3]	AGW51120.1
20	D protein [Human parainfluenza virus 3]	AGT75313.1
	D protein [Human parainfluenza virus 3]	AHX22249.1
	D protein [Human parainfluenza virus 3]	AHX22097.1
25	D protein [Human parainfluenza virus 3]	AGW51144.1
	D protein [Human parainfluenza virus 3]	AHX22089.1
	D protein [Human parainfluenza virus 3]	AHX22225.1
	D protein [Human parainfluenza virus 3]	AHX22137.1
30	D protein [Human parainfluenza virus 3]	AHX22065.1
	D protein [Human parainfluenza virus 3]	AGW51224.1
	D protein [Human parainfluenza virus 3]	AGT75210.1
35	D protein [Human parainfluenza virus 3]	AHX22393.1
	D protein [Human parainfluenza virus 3]	AGT75258.1
	D protein [Human parainfluenza virus 3]	AHX22345.1
	D protein [Human parainfluenza virus 3]	AGT75250.1
40	D protein [Human parainfluenza virus 3]	AHX22113.1
	D protein [Human parainfluenza virus 3]	AGW51232.1
	D protein [Human parainfluenza virus 3]	AHX22057.1
45	D protein [Human parainfluenza virus 3]	AHX22209.1
	D protein [Human parainfluenza virus 3]	AGW51056.1
	D protein [Human parainfluenza virus 3]	AHX22161.1
	D protein [Simian Agent 10]	ADR00402.1
50	D protein [Human parainfluenza virus 3]	AHX22361.1
	D protein [Human parainfluenza virus 3]	AGW51281.1
	D protein [Human parainfluenza virus 3]	AGW51184.1
55	D protein [Human parainfluenza virus 3]	AGW51160.1
	D protein [Human parainfluenza virus 3]	AHX22465.1
	D protein [Human parainfluenza virus 3]	AHX22329.1

(continued)

	Description	GenBank Accession
5	D protein [Human parainfluenza virus 3]	AGW51064.1
	D protein [Human parainfluenza virus 3]	AGW51040.1
	D protein [Human parainfluenza virus 3]	AGT75226.1
	D protein [Human parainfluenza virus 3]	AHX22425.1
10	D protein [Human parainfluenza virus 3]	AHX22305.1
	D protein [Human parainfluenza virus 3]	AGW51249.1
	D protein [Human parainfluenza virus 3]	AHX22481.1
15	D protein [Human parainfluenza virus 3]	AHX22281.1
	D protein [Human parainfluenza virus 3]	AGW51048.1
	D protein [Human parainfluenza virus 3]	AHX22297.1
	D protein [Human parainfluenza virus 3]	AGW51088.1
20	D protein [Human parainfluenza virus 3]	AGT75305.1
	D protein [Human parainfluenza virus 3]	AHX22185.1
	D protein [Human parainfluenza virus 3]	AGW51104.1
25	D protein [Human parainfluenza virus 3]	AHX22081.1
	D protein [Human parainfluenza virus 3]	AGW51192.1
	D protein [Human parainfluenza virus 3]	AHX22489.1
	D protein [Human parainfluenza virus 3]	AHX22441.1
30	D protein [Human parainfluenza virus 3]	AHX22409.1
	D protein [Human parainfluenza virus 3]	AHX22369.1
	D protein [Human parainfluenza virus 3]	AHX22321.1
35	D protein [Human parainfluenza virus 3]	AHX22073.1
	D protein [Human parainfluenza virus 3]	AGW51152.1
	D protein [Human parainfluenza virus 3]	AGW51072.1
	D protein [Human parainfluenza virus 3]	AGT75321.1
40	D protein [Human parainfluenza virus 3]	AHX22257.1
	D protein [Human parainfluenza virus 3]	AHX22129.1
	D protein [Human parainfluenza virus 3]	AHX22417.1
45	D protein [Human parainfluenza virus 3]	AGT75218.1
	D protein [Human parainfluenza virus 3]	AHX22265.1
	D protein [Human parainfluenza virus 3]	AGT75178.1
	D protein [Human parainfluenza virus 3]	AHX22433.1
50	D protein [Human parainfluenza virus 3]	AGW51273.1
	D protein [Human parainfluenza virus 3]	AGW51208.1
	D protein [Human parainfluenza virus 3]	AGT75170.1
55	D protein [Human parainfluenza virus 3]	AGT75162.1
	D protein [Human parainfluenza virus 3]	AGW51257.1
	D protein [Human parainfluenza virus 3]	AGW51200.1

(continued)

Description	GenBank Accession
D protein [Human parainfluenza virus 3]	AGW51176.1
D protein [Human parainfluenza virus 3]	AGT75186.1
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:
HulgGk signal peptide	METPAQLLFLLLLWLPDTTG	15
IgE heavy chain epsilon -1 signal peptide	MDWTWILFLVAAATRVHS	16
Japanese encephalitis PRM signal sequence	MLGSNSGQRVVFITLLLLVAPAYS	17
VSVg protein signal sequence	MKCLLYLAFLFIGVNCA	18
Japanese encephalitis JEV signal sequence	MWLVSLAIVTACAGA	19

Table 9. hMPV/PIV3 Cotton Rat Challenge Study Design (*Reference Example*)

Group	n	Test Article	[conc]/ μ g	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:
5 gblKJ156934.1l: 21405-25466 Middle East respiratory syndrome coronavirus isolate Riyadh_ 10 14_2013, spike protein (nucleotide) 15 20 25 30 35 40 45 50 55	ATGATACAGTCAGTGTTCCTACTGATGTCCTTGTAAACACTACAGAAAGTTACGTTGATGTAGGGC CAGNTCTGTTAAGTCCTCTTGTATTGAGGTTGATATACAAACAGACCTTCTTTGATAAAGTTGGCC TAGGCCAATTGATGTTTCTAAGGCTGACGGTATTATATACCCCTCAAGGCCGTACATATTCAAACATA ACTATCACTTATCAAGGCTCTTTTCCCTATCAGGGAGACCAATGAGTATATGATGTTTACCTGACG GACCTCTACAGGCACAACTCCACAAAATTTGTTGTAGCTAACATTCACAGGACGTCAAACAGT TTCTTANTGGGTTTGTGTCCTATAGGAGCAGCTGCAANTTCCACGAGACTGTTATATTAGCC CATCTKCCAGGCTACTATACGAAAAATTTACCTGCTTTTATGCTGGGTTCTTCAGTTGGTAATTT CTCAGATGGTAAAATGGCCGCTTCTTCAATCATACCTGATTCCTTTTGGCCGATGGATGTTGGCAC TTTACTTAGAGCTTTTTATTGTATTTAGAGCCCTCCCTCTGGAAATCATTGTCCTGCTGGCAATTCG TATACTGTTTGGCACTTATCACACTCCGCAACAGATTTGCTGATGGCAATTCACAACTGTAATG CCAGTCTGAACCTTTTTAAGGAGTATTTAATTTACCTAACTGCACTTTATAGTACACTTATAACTT ACCGAGATGAGATTTTAGAGTGGTTTGGCATTACAAACCTGCTCAAGGTTGTCACCTCTCTCTCAT CTCGGTATGTTGATTTGACGGGGCAATATGTTTCAATTTGOCACCCTTGGCTGTTTATGAGTAT TTAGTATTATCTATCATCTCCACAGTATCTGTTCTATCCAAAGTGATAGAAAAGCTTGGCCGTC TTCTACGTATATAAATCTCAACCGTTAACTTCTCTGTTGGATTTTCTGTTGATGGTTATATACGACG AGCTATAGACTGTGTTTAAATGATTTGTCACAACTCCACCTGCTCATATGAAATCTTCGATGTTGAA TCTGGASTTATTCAAGTTCTGCTTTCGAAACAAAACCTTCTGGCTCAGTTGTGGAAACAGGCTGAA GGTGTTGAATGTGATTTTTCAGCTCTTCTGCTGGCACCTCCCTAGGTTTATAAATTCAGGCTT TGGTTTTTACCAGTTGCAATATATGTTTACCAATTTGGTTTCACTTTTTTCTGTGAAAGATTTTACTT GTAGTCAAAATATCTCCAGCAGCAATTTGCTAGCAGCTGTTATCTTCTACTGATTTTGGATTTATTTTCA TACCAGCTTATGATGAAATCCGATCTCAGTGTAGTTCTGCTGGTCCAAATATCCAGTTTAAATATA AACACTCTTTTCAATCCACATGTTTATCTTAGCAGCTGTTCTCATAGCCTTACTACTTACT AAGCTCTTAAAGTACAGCTATATTAACAAGTGTCTCTGCTCTCTTTTCTGATGATGCTACTGAAAGTAC CTCAGTTAGTAAACGCTAATCAATACCTCACCCTGTTGATCTCATTTGCTCCCATCCACTGTTGGGAAAG ACGGTTGATTTATAGGAAACAACTATCTCCACTTGAAGGTTGGTGGCTGCTTGTGCTAGTGGCT CAACTGTTGCTATGACTGAGCAATTAAGATGGCTTTTGGTATTACAGTTCAATATGATACAGACAA CCATAGCTGTTTGGCCCAAGCTTGAATTTGCTAATGACACAAAATTTGCTCTCAATAGGCAATTTG GGTGGAAATATCCCTCTATGTTGTTTGGGCCGTGGTGTTTTCAGAAATTTGACAGCTGTAGGTTGT	20

(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p>	<p>TEGACGACAGCGCTTTGTTATGATGCGTACCAGAAATTTAGTTGGCTATTATTCTGATGAGGGCAAC TACNCTGTGTGCGTGGTTGTGTAGTGTTCCTGTTCCTGTCATCTATGATTAAGAAGAACAAAGACCC ACGGTACTCTATTTCGTAAGTGTGGATGTGAACACATTCTCTACCATGTCGCAATACCCGTTTC TACGGGATCAATGCTTAAACGGCGAGATCTACATATGGGCCCCCTTCAGACACCTGTTGTTGTGT CGTAGGACTTGTAAATTCCTTTGTGTGTAGAGGACTGCAGGTGGCTCTGCGCAATCTCTGT GGCTTTCCTGACACACTAGTACCTGTCACAGTCTGCGAGTGTGGCTCTGTGCGAGGTGAANTGGG GTGGCATCCATTGCTTTTAACTATCCATTCAGGTTGATCAACCTAATAGTAGTTATTTAANTAA GTGACCCACTAATTTTTGCTTTTGTGTGACCTGAGGATACATGAGACAGCCATTCAGAAAGTTAC TGTGATGTGAACAGTAGGTTCACATGGTTTCCAGAAAGTGTGAGCAATTACTGCGGAGTATGG CGAGTTTGTCCAAATTAACGAGGCTCTGCATGGTGGCAATTTACGCCAGGATGATTCTGTACG TAAATTTGTTTGGGAGGCTGAAAAGCTCTCAATCCTCTCTAGCATACAGGTTTGGAGGTGACTTT AATTGACACTCTAGAACCTGTCTCTATACCTACTGCGAGTCTGTAGTGGACGTAGTGTCTGTGAGG ATTGCTATTGACAAAGTCACTATAGCTGATCCTGGTTATATGCAAGGTTACGATGATGTAAGCA GCAGGTCGAGCATCAGCTGTGATCTTATTGTGCTCAATATGTGGCTGGTTATAAAGTATTACCT GCTCTTATGGATGTTAATATGGAAGCCGGTATACTCTATCTTTCCTGGCAGCATAGCAGGTTT GGCTGGACTGCTGGCTTACCTCTTGTGCTGATTCCTATTGCAAGAGTATTTTTATAGGTTAA ACGGTGTGGCATTACTCAACAGGTCTTTGAGGAAACAAAGCTTATTGCCAATAGSTTTAATCA GGCTGTGGAGCTATGCAACAGGCTTCACTACACAAATGAGGCTTTTGGGAGGTTCCAGGATGC TGTGACAAACAGTGCACAGGCTCTATCCAAATAGCTAGCGAGCTACTAATACTTTTGGTGTATT TCCGGCTCTATTGGAGACATCATCAAGCTCTTGTATGTTCTGCAACAGGACGGCCAAATAGACAG CTTATTAATGGCGTGTGACAACTAAATGCTTTTGTGTGACAGCAGCTTGTCTCTGAAATCAG GTGCTTTTGGCTCAATGGCTAAAGATAAAGTCAATGAGTGTGCAAGGCAACATCCAAAGGTT GTGATTTTGGGTCAGGCAACATATAGTGTCTTTGTTGTAAATGCGCCAAATGGCTTTACTT TATGAGTGTGTTATTACCTAGCAACCAACATTGAGGTTGTCTGTGTTATGGCTTTGGGATGCA GCTAACCTAGTAAATGTATAGCCTCTGTTAATGGCTACCTTATTAAAACATAACAGTAGGATTT TGAGAGTGGTCAATAGCTGGCTGCTCTCTATGCACTGAGCCCATCACCCTCTTAACTAAG TGTGTCAGCAGCAGGTTGACATCCAAACATTTCTACTAACCTCCCTGCTCTCTGCGCAATT CCACGGGATTAAGTCCAGGATGAGTGTGATGAGTTTTCAAAATGTTAGCACAGTATACCTAA TTTTGGTGTCTAACACAGATTAATACATATTACTCGATCACTAGGATGTTGCTCTCTAAC AAGTGTAAAAGCCCTAATGAGTGTACATAGACCTTAAAGAGCTTGGCANTTACTTATTACAA AATGGCGTGGTACATTTGCTTGGTTTCAATTTGTTGGCTTGTGCTTGGCTTATGGCTCTC TTCACTGTGTGCTGCTGTGTTGTGTCACAACTGTATGGGAAACCTAAGTGTAACTGTTGTGT GATAGATAGAGGAAATACGACCTCGAGCCGCATAAAGTTCAGTTCCTAA</p>	

(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGKACAC TC AGT GTT CTACT GAT GTT TTGTTAAC CTACAGAAAGTT AGTTGATGT AGGGC CAGATTC TGT TAAATCT GCTTTGATTT GAGGTTG AENTAC AACAAGACTT TGTGATAAA ACTTGGCC TGGGCCAATTA ATGTTTCTAAGGCT GAAGGTATT ATATADCCCTC AAGGCCGT AE ATATTCYAAE AT A ACTATCACTT ATCAAGGTCTTTTTCCTATCAGGGAGACCATG GTSATATGTATGTTTAC TC TCAG GNCATBCTAC AGGECACAE TCACAAAAGTTGTTTGTAGCTAACTATTCTCAGGACGTC AAAACGT TTGCTAATGGGTTTGTCTCCGTATAGGAGCAGCTGCCAATTCCAC TGGC ACTGTTATTATTAGCC CATCTACAGC GCTACTATACGAAAAATTTAC CCTGCTTTT ATGCTGGGTTCTTCAGTTGTAATTT CTCAGATGGTAAAATGGGC GCTTCCTCANTCATACTCTAGTTTC TTTTGGCCGATGGATGTGGCCAC TTTACTGAGAGCTTTTATTGTATTCTGGAGCC TCCTCTGGAAATCATTGCTCTCTGSCAATTC TATACTTC TTTGGCACTATC ACACCTCTGC AACAGMTTGTCTGATGGCAATTC AATCTGTAAATG CCAGTCTGAACCTCTTTTAAGGAGTATTTAATTTAC GTAACTGCACCTTATGTACACTT ATAACATY ACCGAGATGAGATTTTAGAGTGGTTTGGCATTACACAAAC TGCTCAAGGTGTTCCACCTCTCTCAT CTGGGTATGTTGATTTGTACGGC GGC AATATGTTTCAATTTGCCACTTGGCTGTTTATGATACTAT TATGATTAATTCATCATTCCTCACAGTATTCGTTCTATCCAAAGTATAGAAAGCTTGGGCTGCC TTCTACGTATATAACTTC AACC GTTAACTTGGCTGTTGGATTTTCTGTTGATGGTTATATACGCAG AGCTATAGACTGTGGT TTAATGATTTGTEACACCTC CACTGCTCATATGAAATCCTTCGATSTTGA TCTGGAGTTTATTCAGTTTCGTCTTTC SAAGCAAAACCTTCTGGCTCAGTTGTGGACAGGCTGAA GGTSTGAAATGTGATTTTCCACC TCTCTGTCTGGCACACTCC TCAAGTTTATAAATTC AAGCGTT TGGTTTTTACCAATTTGC AATTAATCTTACCAATTTGGTTTCACTTTTTTCTGTGAAATGATTTTACTY GTAGTCAAAATATCTCCAGCAGCAATTTGCTAGCAACTGTTATTC TTCACTGATTTGGATTACTTTCA TACCACTTASTATGAAATCCGATCTCAGTGTAGTTCTGCTGGTCCAAEATCCAGTTTAAATATA ANCACTCCTTTCTAATCCACATGTTTGTATTTAGCGACTGTTCC TELATAACCTTAC TACTATTACT ANGCTCTTAAAGTACAGCTATATTAACAGTGGCTCTGCTCTTCTTCTGATGATCTACTGAAAGTAC CTCAGTATGTAAGGCTAAATCAATAC TCACCSTGTGATCCATTTGCTCCATCCAC TGTGTGGGAAAG ACSTGATTTATTAAGBAACACTATCTCCACTTGAAGGTGGTGGCTGCTTGTTCCTAGTGGCT</p>	<p>21</p>

(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
5	<p> CACCTGTTGCGATGACCTGAGCAATTACAGATGCGCTTTGGTATTACAGTTCAAATATGCTACAGAC CGANTGTTGTTTGCCCAAGCCTTGAATTTGCTAATGACACAAAAATTGCCCTGCAATTAGGCANTTG CGTGGAAATAFTCCCTCTATGCTGTTTDCGGGCCSTGGTGTFTTCAGAAKTTGCACAGCTGTAGBTGT TEGNCAGCAGCAGCTTTGTTTATGATGCCTACCCAGAAATTTAGTTGGCTATTATTCTGATGATGGCAAC TACACTGTTTGGCTGCTTGTGTTAGTGTGCTGTTCTGTCATCTATGATAAAGAAACTAAAACCC AGCCTACTCTATTGCTAGTGTGCTATGTTGAACACATTCCTCTACCATGCTCTCAANTACCTGCTTC TACCGGATCAATGCTTAAACGGCGAGATTCTACATATGGCCCGCTTCAGACAGCTGTTGGTGTGT CCTAGGACTGTTAAATTCCTCTTTGTTCTGATAGSACTGCAAGTTGGCTCTGGGTCANTCTCTGT GCTCTTCCTGACACACCTAGTACCTCACAGCTGCTGCTGCTCAGGTGAATGCGC TTGGCAGCTATTGCTTTTAACTAATCTATTCAGGTTGATCAACTTAAATGATGTTATTAAATTAAGT ATCCACCAATTTCTTTGGTGTGACTCAGGAGTACATTCAGACAGCCATTCAGAAAGTACTG TTGATGTAAACAGTACGTTTGC AATGGTTCCAGAAAGTGTGAGCAATTAATGCTGGCGAGTATGGCC AGTGTGTTCCAAAATAAACGAGGCTCTCCATGGTGGCAATTAACGCCAGGATGATCTGTACGTAA TTTGTTGGCAGCGCTGAAAAGCTCTCANTCATCTCTATCAGGAGGTTTGGAGGTGACTTAAAT TTGACACTTCTGGAGCTGTTTCTATATCTACTGCGCAGTCTGATGTCAGTGTCTATTGAGGATT TECTATTGACAAAGCTACTATAGCTGATGCTGCTTATATGCAAGGTTACGATGATGCTGACAGCA AGGTCCAGCATCAGCTCCTGATCTTATTTGTGGTCAATATGTGGCTGGTTACAAAGTATTAACCTCT CTATGAGTGTAAATAGGAGCGCGCTATACCTCAGCTTGGCTTGGCAGCATAGCAGGTTGTTGGC TGGACTGCTGGCTTATCTCTCTTGTGCTGATTTCCATTTGCACAGAGTATCTTTTATAGGTTAAACG GTGTTGGCATTACTCACAGGCTCTTTCAGGAAACCAAAAGCTTATTGCCAATAAGTTTAACTAGGSC TCTGGGAGCTATSCAAACAGGCTCTACTACAGCAANTGAAAGCTTTTCAGAAAGTTTCAAGGATGCTGT GACACCAATGACAGGCTCTATCCAAATAGCTAGCGAGCTATCTAANTACTTTGGTGTCTATTTC GCTCTATGGAGACATCATACAGCTCTGATGCTCTGACAGGAGCGCCAAATAGACAGACTT ATTANTGGCTGTTTGAACACCAAAATGCTTTTGTGCTGACAGCAGCTTGTCTGTTCCGAATCAGCTG GTCTTCCGCTCAATGGCTAAAGATAAAGTCAAGGAGTGTGTCAAGGCAANTCCAAAGCTTCTG GATTTGGCGCTCAAGGCAACATATAGTGTCTTTGTTGTAAGGCGCCCTAATGGCTTACTCTAT GCTGTTGGTATTAGCTAGCAAGCACTGAGGTTTCTGCTTATGGCTCTTTGCTGATGCTCTGCTGCTG AACCTACTAATGATAGCCCTGTTAATGGCTACTTTATTAAACTAATAACACTAGGATTGTTGA TGGTGTCTATACTGCGCTCTCTCTCTATGCACTGAGCGCCTAGGCTCCCTTAACTAAGTAT GTTGACCCACAGGTCACATACAAAACATTTGTAAGCTCCCTGCTCTCTCTCTCTCTCTCTCTCTCTCT CCGGATGACTTCCAGATGAGTTGATGAGTTTTCAAAAATGTTAGCAGCAGTATACCTAATTT TGGTCCCTAAGACAGATTAATACTACATTACCTGATCTTACCAGAGATGTTGCTCTCTCTCTCTCTCT GTTGTAAAGCCCTAATGAGTCTTACATAGACCTTAAAGAGCTTGGCAATTAATCTTATTACAGCAA ATGGCGGTTGTTACATTGGCTTGGTTTCTATTGCTGAGGCTTGGTGGCTTGGCTTGGCTTGGCTTGGCT CATACTGTGCTG TACTAGAGGAACTAGGCTGAGCCTGAGCCTGATAGGTTCTATGCTCACTAA </p>	
10		
15		
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55		

(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
Novel_MERS_S2_subunit_trimeric vaccine (nucleotide)	<p>ATGATCCAGTCCGTGGTTCCCTCTCATGTTGGTGTGGAGCCCACTGAGTCAAGCTGCAAGGTCCTGG CTGGGACAGTCGTGTGTGGGCTGCTGAACACTCCTAGCAGTCTGGACCCACGCTCGTGGCTG GGTGCTTGGGGAAGTGCAGGCTGGCTCCATCAGCTTCAATCAGCCAAATCCAGTGGATCAGCTGA ATAGCTCGATTTCAAGCTGCTGACTCCAGGAACTGTCTGTTGGGCTCAAGCAGGACTAGCTCC AGCCACAAATTCAGAAAGTCAAGCTCGATTGCAAGCAATAGCTGTGCAAGCTGCTCAGAACTGC GAGCAGCTGCCTGAGAGAAATAGGGCTAGTTTTGAGCAAGATCAAGCAGGCTGCTGATGGAGCTAA CTGGGCTAGGACGACTCGTGCAGCAACTCTTTGGCTCTGTTGAATCAGCCAGTCTCTCCAA TCACTCCGAGATTCCGAGGGGACTTCAGCTGACCTTCTGAGGCCCTGCTGATGAGCACTGAGCACT TAGCAGATCGCTCCCTCAGCCATTGAAAGATCTTCTGTTCAAGAGCTCACATGCTCGATCCGG CCTCAGTGCAGGGATAGCAAGACTGTATGAGAGCAGGAGCAAGCTTCGCTGAGGGACTCATTG CGCGCAATAGCTGGCCGCTGCTCAAACTGCTGCTCTCTGATGGATGTGAACATGAGAGCTGCTT ATACTTGCTCCCTGCTGGCTCTATPCCGCTGTTGGGGTTGGAGCGCTGGCTTGTCTGCTGAG GCTATGCCCTTTGCTGCAATCTCATTTCTAGCGGCTCAAGGGCTGGGCAATTACTAGCAGCTCT GTGGAGAACTAGAAATGATGCAAGCAAGTTCAATCAGGGCTGTTGGGGCACTGAGAGCTGAT TCACTGAGACTAAGGAGCTTCCAGAAAGTCCAGGAGCTGTTGTAACAGCAAGCTCCAGGGCTCT TCAAGCTGGCTTCCAGACTAGCAAGCCTTCCAGGCTATCAAGCTGCTGAGGCTGACTAGCT TCAAGGCTGGAGCTGCTGGAGCAAGCAAGCTGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCT AGCTTGAATGCTTCCAGGCAAGCAAGCTGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCT GGGCAGGCAAGCAAGCTGAGGCAAGCAAGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCT GGAGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCT TTAGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCT GGTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCT GAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCTGAGGCT GGCCCGAGCAAGGATTGAGGAGATTCTGCTGAAAAATCTAGCAATGAAAAAGAGAGCTGGAGAA AGAGCTTATCGGCGAGGCC</p>	22

(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>MERS_S0_Full_length Spike protein (nucleotide, codon optimized)</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ATGGAAACC CCGTGC CAGCTGC TSTTTC CTGCTGC TGGTGTGTGCTGC CTGATAC CAGCGGCAGCTA TGTGACGTGGGCC CCGATAGCG GTBAAGTCCGCC TGTATC BAAGTGGAC ATCCAGC AGACCTTTT TGGACAGACC TGGCC CAGAGCC ATCGAC GTGTCC AAGGCG CAGC GGCATC ATCTATCC ACAAGGC CGGACCTAC AGE AATATC AC CATTAC CTACC AGGGG CTGTTCC C ATATC AAGGCG ACC AC GGC GA TATGTAC GTGTACTG TGC DGGCC AGGC ACCGGC ACCAC ACCAGAA ACTGTTTGTGGCCAACT ACAGCCAGGACG TBAAGC AGTTC BCCANCGGCTTCGTG CTGCG GGAATGGG GC CACTGCC AATAG GACCGGAC AGTGTATC ATC AGCCCC AGC ACC AGCGCC ACCATCC GGAAGATC TAC CCGGCC TTCA TCTGGGC AGCTCC CTGGGC ANTTTC AGC GACGGC AAGATGGGC CGGTTTTC CAGCCAC ACCG T GGTCTGCTGCC C GATGGCTGTGGC AC ACTGCTG GAGAGC CTTC ACTGCTATC CTGGAACCC AGAA GGGGACCC ACTGCC CTGCC GGC AATAGCTAC ACCAGC TTD GCCACCTAC CAGAC ACCCGCCAC CGATTGCTCC GACGGC AACTAC AACCGGAC GCCAGC CTGAAC AGCTTC AAGAGATC ATTC AAC C TCCGGACTGC ACCTTC ATGTAC ACCTAC AATATC ACCGAGGAC GAGATC CTGGAATGGCTTCGGC ATCACCCAG ACCGC CCAGGGGCTGGC ACCTGTTT AGCAGC AGATACGTGGAC CTGTAC GCGGCCA ACATGTTCC AGTTTGGC ACCCTGCC GTGTACGAC ACCATC AAGTACTAC AGCATC ATC CCGCAC A EATCCGGTC CATTCC AGAGGAC AGAAAAAGC CTGGCCCGCTTCCTAC GTGTAC AAGCTGCAGGCC CCTGACTTTCCTGCTGGACTTC AGC GTGGAC GGTAC ATC AGACGGGCCATC GACTGGGGCTTCA AGGACTGAGCC AGCTGC ACTGCTCTCTAC GAGAGCTTC GAC GTGGAAAGC GGGGTGTAC AGGGT GTCCAGCTTC GAGGC C AAGGC TABC GGC ACCGTGGTGGAC AGGCTGAGGGC GTGGANTGC BA CTTCAGCCCTGCTGTAAGCGGC ACCCTGCC CAGGTGTAC AACTTC AAGCGGCTGGTGTTC ACCA ACTGCAATTAACACCTGACCAAGCTGCTGAGCCGTGTTCTCC GTBAACGACTTCACCTGTAGCC AGA TCAGCCCTGCCGCC ATTGCC AGC AACTGCTACAGCAGC CTGATC CTGGACTACTC AGCTACCC C CTGAGCATGAAAGTCCGATCTGAGC GTGTGC TCCGCCGACCC ATCAGCCAGTTC AACTAC AAGCA GAGCTTCAAGCAGCCCTACCTGCCGTGATTC TGGCC ACCGTGCC CAC AATCTGACCC ACCATC ACCA AGCCCTGAAATACAGCTAC ATC AAC AAGTGCAGC AGACTGCTGTCC GACGACC GACCGA AGTG GCCAGTCTGTGAACGCCAAGCAGTACAGCCCTTGCCTGTC ATCTGTCC CAGCACC GTGTGGG AGGCGGCG GACTAGTACAGAAAGC AGCTGAGCC CCGTGGAGGCG GGC GGAATGGTGGTGGCTTC TGGAGC ACAGTGGCC ATGACC GAGCAGCTGC AGATGGGCTTTGGCATC ACCGGTCAGTACGGC ACCCAGACC AACAGC GTGTGCC CCAAGCTGG AATTGGCC ANTACACC AAGATC GCCAGCC AGCT GGGAAC TGC GTGG AATAC TCCTGTATGGC GTGTCC GGGAC GGGGC GTGTTCC AGAATTCAC A GCAGTGGGAGTGC GGCAGC AGAGATTC GTGTAC GATGCTTAC CAGNACCTC GTGGGCTACTAC A GCSAGAG GGC AATTACTACTGCC TGGGGCTGTGTGTGCC GTGCC CBTGTC GGTGATCTAG GAC AAGGAGAC AAGAGCC ACCGC CACACTGTTGGCTCC GTGGCCTGC GAGC ACATCAGCTCCAGC AT GAGCCAGTACTGCC GGTCC ACCG GGTCC ATGCTGAAGC GAGAGAGTAGC ACCTAGAGGCC CCGTG CAGACACTGTGGGATGTGTGCTGGGCC TCGTGAACAGCTCCTGTTTGTGGAAAGTTCAG AACT GCCCTGGGCC CAGAGCC TGTGTGCC CTGCCAGATACCC TABC ACCCTGAC CCCTAGAAAGCGTG GGCTCTGTGCC CAGC AAGTGC GGC TGCC TC TATGCCCTTCAATC ACCCCATCCAGGTGAGCC A GTTBANC TC CAGCTAC TTE AAGCTGAGC ATCCCCAC CAACTTC AGCTTC GGC GTGAGCC CAGGAT ACATCCAGAC CAC ATCCAGAA AGTGAN C GTGGAC TGC AAGCAGTAC GTGTGC AACGGCTTCAG AAGTGC GAACAGC TECTGC GTGASTACGGC CAGTTCTGCAGC AAGATC AACAGGC CCTGCAGC GGCCACCCCTGAGACAGGATGAC AGCTGCCGGAAACCTGTTCGCCAGCGTGAAGAGCAGCCAGTC CAGCCCATC ATC CCTGGCTTC GCGGGGAGCTTTAAC CTGACCC TGC TGGAACTGTGGTC ATCA GCACCGGC TC CAGAGGC GCGAGATCC GGC ATC GAGGACCTGC TGTTCGAC AAGTGAN C ATTC CGACCCGGCTAC ATGCAGGGCTAC GACGATTC ATGCAGC AGGGCCAGCCAGCGCCAGGAT CTGATCTGTGC CAGTATGTGGCC GGC TAC AAGGTGC TGGC CCGCTTANTGAGC GTBANCATGGA AGCCGGCTACACC TCCAGCCTGCTGGCTC TATTGCTGGC GTGGGATGGAC AGCCGGCTGTCT AGCTTTGCC GGC ATCCCTTTC CCGCAGAGC ATCTTCTAGC GGC TBAACGGC GTGGGCATC ACACA ACAGTGTCTGAGC GAGAACAGAACTGTATC GCGACAGTTT AACAGGC ACTGGCCCATG CAGACCCGCTTC ACCACAC CACAGGGCC TTCAGAAAGGTGCAGGAC GCGTGAAC AACAGC GGCAGGCTCTGAGC AAGCTGGCTCCGAGCTGAGC AATACCTTCGGGCCATCAGC GCGTCCAT CGGGAC ATC ATCCAGCGCTGGACGTGTAACAGGACGGCCAGATCGACC GCGTGAN C GGCAGACTGACAC CCGTGAAC GCCTTCGTGGCCACAGCAGCTC GTGCGGAGC GATCTGCCCTC</p>	<p>23</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>10</p> <p>15</p>	<pre> TGTCTGCTCAGCTGGCCAAAGGACAAAGTGAACGAGTGGGTGAAGGCCAGTCCAAAGCGAGGGG CTTFTGTGECAGGGCCACCCACATGCTGTCTTCTGTCGTGAATGECDCACAGGECCTGTACTTTAT GCACGTGGGCTATTACCCCAAGCAACACATCGAGGTGGTGTCCGGCTATGGCCTGTGACGGC GGCARTDCTACCAACTGTATGCGCCGGGTGAACGGCTACTTTCATCAAGACCAACAACACCGGGAT CGTGGACGAGTGGTCTACACAGGCAGCAGCTTCTACGGCCCGGAGGCCATCAGCTCCGACGCA CCAAATACGTGGCCCGCAAGTGACATACAGAGACATCTCCAGCAAGCTGGCCCTGCGACTGCTG GGAAHTCCACCGGCATCGACTTCCAGGACGAGCTGGACGAGTTCCTCAAGAACGTGTCCACTC CATGCGCAACTTCCGGCAGCTGACCCAGATCAACACACTCTGCTGGACCTGACCTAGSASATGC TGTCCGTGCACAGGTCGTGAAAGCCCGTGAACGAGAGCTACATCGACCTGAAAGAGCTGGGGAAC TACAGCTACGACAAAGTGGCCTTGGTACATTTGGCTGGGGTTTTATCGCGGGCTGGTGGCCCT GGCCGTGTGCTGTCTTCTATCGTGTGCTGACCGGGCTGGGGCCAGCAATTGCAATGGCCAAAGTGA ATGCAACCGGTGCTGCGACAGATACGAGGAATACGACCTGGAACCTCACAAAGTGCATGTGAC </pre>	
<p>20</p> <p>Betacoronavirus mRNA Sequences</p>		

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Strain	Nucleic Acid Sequence	SEQ ID NO:
5	<p> CUUGGACAGCAUAGCAGGUUUUGGCUUGGACUGCUUGGCUUAUCUUCUUUGGCUUGCUUAUCCAUU UGCAACAGAGUAUUYUUUUUAAGGUUUAANCUGUGUUGGCAUUNCUCACAGGUUUCUUCAGAGAA CCANAGCUUAUUUCANUAAGUUAUAUCAGGCUUCUGGGAGCUAUGCAANCAGGCUUCACUACA ACUNAGAAAGCUUUCUGAAGGUUCAGGAGGCUUGGAAACACAAUGCAAGGCUUCUUAUCCAAAU UAGCUAGCGAGCUAUCUUAUACUUUUUGGCUUAUUUCGCUUUAUUGGAGACAUCAUACAC GUUUGAUUUCUUCGAGCAGGACGCGCCAAUAAGACAGACUUAUUAAUGGCGUUUGACAGACU AAUGCUUUUGUUUCACAGCAGCUUUGUUUGUUCGAAUCAGCUGCUUUCUUCGCUUACUUGGC UAAAGAUAAAGUCAAUGAGUUGUUCAGGACAAUCCAGGCGUUUCUGGAGUUUGCGUCAAGG CACACUUAAGUUGCUUUUGUUUAAUGGCCUUAUUGGCCUUUACUUUAUGCAUUGUUGUUA UUAUCCUAGCAGCACAAUAGGCUUGUUUCUGCUUUAUGGCUUUGCGAUGCAGCUUAACCUAC UAAUUGUUAAGCCUUGUUAUUGGUAACUUUAUUAUUAAAACUAAUACACUAGGAGUUUGUUGAUGAG UGGUCAUUAUCUGGCUUCGUCUUCUUAUGCAUCCUGAGGCCAUCAUCCUUCUUUAUACUANGUUA GUUGCAUACAGGUAGCAUACCAAACAUUUCUACUACCUUCUUCUUCUUCUUCUUCGGAUU CCACCGGALUGACUUCCAGAGUGAGUUUGAGUAGUUUUUCAAAUUUUUAGCACCAGUAUAC CUAAUUUGGCUUCUACACAGAUUAUACUACAUUACUUGAUCUUAUCCUACGAGAUUUUGAC UCUUCACANGUUUUUAAGCCUUUAUGAGUUCUUACAUAGACUUUAAGAGCUUGGCAAUUUA ACUUAUACACAAUUGGCCUUGGUACAUUUUGUUUGGCUUUCUUCUUCUUCUUCUUCUUCUUA GCUUAUUCGUCUUCUUUUAUUGUUCUUCACUUGUUGGCAACAAUUGUUAUGGGAACUU AAGUUAUACGUUUUGUGAUAGAUACGAGGAAUACGACUUCGAGCCGUAUAGGCUUCUUGU CACUA </p>	

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Strain	Nucleic Acid Sequence	SEQ ID NO:
MERS S FL SPIKE 2cEMC/2012 (XbaI change(U to G)) (nucleotide)	<p> AUGGUAACACUAGUUGUUCUACUGGAGUCUCUUGUUAACACCCUACAGAAAGUACGUGGAGUAG GGGCCAGAUUCUGUUAAGGUCUGCUUGUAGUUGAGGCUUGAGUAUACACAGACUUCUUCUUGAAAA CUUGGCCCAGGGCCAAUUGGUGUUCUUAAGGCUUGACGGUAAUUAUAACCCUCAGGCGCUGACAU NGUCUACUAAACUACACUUAUUCAGGUCUUUUUUUCCUAACAGGAGACCAUUGUUAUGUUA UGUAUACUCUGACAGGACAUUCACAGGCACAACUCACAAAAGUUUGUUGUAAGGUAAACUUAUCU CAGGACUACAAACAGUUGUCUAAUUGGUUUGUCGUCUAGUUGAGAGCAGCGCCAAUUUCCACU GGCACUUGUUUUAUAGGCCAUCUACDAGGDCUACUUAACGAAAAGUUAGCCUGCUUUUUGGC UGGGUUCUUCAGUUGGUAUUUUCUCAGNUGGUAAGAGGGCCGUCUUCUAUCUAACUCUAG UUDUAUUGCCCGAUUGAUUGGGCAUUUACUUAAGAGC UUUAUAUGUUAUUCUGGAGCCUCCDU CUGGAAACAUUGGUCUUCUGCGCAAUUCUUAUACUUCUUUUGCCAGUUAUUCAGUCUGGCAAG AGUUGUUCUGAGUCGAAUUAACAAUCGUAAGGCCAGUCUGAACUUCUUUAAGGAGUUAUUUAAU UUNCGUAUCUCACUUAUUGUACUUAUAACAUUAACGAAGCAGUAGAUUUUAGAGUUGGUUUUG GCAUACACAAACUCUCAAAGGUGUUCACUUCUUUCUUCUCUGUUAAGUUUUUAGGGCG GCAUUNUGUUCAGUUGGCACUUUCUCUUGUUAUAGUUAUUAAGUUAUUAUUAUCAGUUC UCACAGUUAUCGUUCUUAUCCAAAGUGAUAGAAAAGCUUGGGCCUCUCUCUACGUUAUAACUU CACGCGUUAACUUUCUUGUUGAAUUUUUCUGUUAUGAUGGUAUAUACAGACUUAAGGCUUA GCUUAUAUGGAAUUUCACAAACUCCACUUCUCUUAUGGAAUCUUUCGAGUUGAAGUCUGGAGUU UUAACAGUUCUGUCUUCUUGACCAAAACUCUCUGGCUCAGUGUGUGGAAACAGGCHUAGAGUUGU GAAUGUGAAUUGUCACUUCUUCUGUCUUCUGGCACCCUCAGGCUUAUAUUAUCAGGCUUUG GUUUAUCCAAUUGCAUAUUAUCUJACEAAUUGCUIIUCUUAUUUCUUGUUAUUAUUUA CUUGUAGUCAAUUAUCUCCAGCAGCAUUGCUAGC AACUGUUUUUUUAUCUGAUUUGGUAUA CUUAUCUACCCACUUAUGUAUAAGAAUUCGAAUUCAGUUGUUAUUUCUGUGGUCCCAAUUCGC CAUUAUAUUAUAAACAGUCCUUUUUCUAAUCACAGUUAUGAUUUUUACGACUUUCUUCUUAAC CUUAUCUUAUUAACUAAGCCUUCUUAAGUACAGUUAUAUUAACAGGUCUCUCUGUUAUUAUG AGUCUGUAGUUAAGUACCUUCAGUUAGUGAAGGCUAUAUUAUUCUCUCUUGUUAUUAUCUUGU CCUUAUCUUGUUGUUGGAGACGGUGUUUAUUAAGGAAACAACHAUUCUCCAGUUAAGAGUGG UGGUUGGCUUUGUUGUAGUUGGUUCACUCUUUUUCCUUGACUAGACAAUUAACAGAGGUCUUUG GUUAUCAGUUCAGUUAUGUACAGACACCAAUAGUUGUUGGCCAAGCUUGAUAUUGCUUAUUA CACAAAUAUUCUCUUCAAUUUAGGCCAUUGGCCUGGAUAUUCUCUUAUUGGUAUUGGGCCG UGGUUGUUUUUCAGAAUUGCACAGGCUUGAGGUUGUUCGACAGGAGUUCUUGUUUUAUGUAGCUA CCAGAAUUAAGUUGCCUUAUUAUUCUUAUGAGGCAACUUAUAUCUUGUUGCCUUGUUUGUUAJAG UGUUCCUGUUUCUGUUAUUAUGAAAGAAACUAAAACTACCUUAUCUUAUUGGUAUUGUU GCAUGGAAACAAUUAUUCUUAACAGUUCUUAUAUCUCCGUUUCUACGCAUCARUGCUUAAC GGCAGAUUCUUAUUGGCCUUCUACAGACCTUUGUUGUUUGUUGUCCUAGGACUUGUUAUAU CCUUAUUGUUCUUAAGGACUUGCAAGUUUCUUAUGGUCANUCUUCUUGGUCUUCUUCUUAAC CACCUAGUACUCUCACACUUCAGUUGGCGUUCUUCUCAGGUGAAAUUCGCUUGGCACUA UUGCUUAUAUAACUUAUCUAGGUUGAUCAAGUUUAUAGUAGUUAUUAUAAGUUAAGUUAJACC CACUUAUAUUGCCUUUGGUUGACUCAGGAGUUAUUAUACAGACACCAAGUCAGAAAGUUAUCUUGU </p>	66

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Strain	Nucleic Acid Sequence	SEQ ID NO:
5	<p> GGUUGUAACAGUACGUUUGCAAUUGUUUCCAGAAAGUGUGAGCAGUUUCUUGCGCGAGUUAUGGC CAGUUUUUUUCCAAANUAAACAGGCUUCUCCAUUGUUUCCAGUUUACGCCAGGAGUUAUUUCUUA GGUAAUUUUUUUGCGAGCGUUGAAAAAGCUUCUCAAUCAGUCUUAUCAGUCCAGUUUUUGGAGGU GCUUUUAUUUGACAGUUCUUGGAAAGCUUUUUCUUAUUUCUACUUGGCAGUCGUAGUUCACGUAGU GCUUUUSAGGAGUUUCGUUUUGACAAAGUCCAUUAAGCUGAUGCGUUGUUUAUUCAGGCUUAC GAGUUUUCAGUCAGCAAGGUGCCAGCAGCAGCUCUGUUGUUAUUUUUUUGUCUUAUUUGUGGCU GGUUACAAAGUAUUUACCUCCUCUUUUGGAGUUUUAAUUAUGGAAAGCCGCGUAUACUUCAKCUUUUG CUUUGCAGCAAGGAGUUUUUUUUAAGGUUUAAACAGGCUUCUGGGAGCUUAUGCAACAGGCUUACAGCA ACUAAGGAAAGCUUUUUCAGAAAGUUUCAGGAGUUCUUAUAACAAACAGGCUUCUUAUCCAAUU UAGCUAGCGAGCUUAUAUACUUUUUGUUUCUUAUUUCUUCUUAUUUGGAGAGUUAUAACAGC GUUUUGAUUUUCUUCGAAAGGAGCGCCAAAUAGACAGACUUUAUUAAUGGCCUUUUGACAGAGCU AAUGCUUUUUGUUUCAGCAGCUUUUUUGUUUCGUAUCCGAAUCAGCUUGCUUUUUUCGUCUUAUUUGGC UAAAGUAAGAUCAGUAGUUGUUUCAGGCAACAUCCAGGCUUUUCUGGAGUUUUUCGGUAAAG CACAGUAUAAGUUCUUUUUUUUAAAUGCCCUAAUGGCCUUUACUUCAGUUAUUUUUUUUUA UUAACCUAGCAACCAAGUUAGGUUGUUUCUUGUUUAUUGUUUUUUUUUUUUUUUUUUUUUUUUUU UAAUUGUUAAGCCUUUUUAUUUGGUUACUUUUUUAAAACUAAUUAACAGUAGGAGUUUUUAUGAG UGGUUAUAUCUGGCUUCGUCUUCUUAUGCCACUAGGCUUUAUUCUUAUUUUUUUUUUUUUUUUUU GUUGCAGCAGGUGACAGUCCAAACUUUCUUAUACCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCU CCACCGGAGUUGACUUUCAGAGUAGUUUGGAGUAGUUUUUUUUUUUUUUUUUUUUUUUUUUUUUUUU GUUU UCUUCACAGUU ACUUUUUACAAAGGCGUGUUACUU GCUUU AGUUAUAUCGUUU CACUUA </p>	

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Strain	Nucleic Acid Sequence	SEQ ID NO:
Novel_MERS_S2_subunit_trimeric_vaccine_(nucleotide)	<p> AUGAUGC AOUCC GUGUUUCCUCCUC AUUUUCCUUBUUG ACC CCC ACUGAGUC AGAC UGC AAUCUC CCUCUGGAC AGUC CC UG UBU BC GOU GCU BAC AOUCC UAGC ADUCUG AC CCC AC GC UCC BU GC GUC GBU GC DU GBC GAA AUG C GOU GGC UUC AU C GC CUC UC AAUC ACC AAUC C AAGU GGA UC AGC UBA AU AGC UC BU AU UUC AAGC U BU CC AU CC CC AC GA ACU UC UC BU UC GGG BU C ACC A GCAGUC AUC C AG AC C AC AAH UC A GAAG GUC AC CG UC GA UUGC AAG C AU AC BU BU GC AAC GC CUUCC NGAUGUG GAGC AGC AGC UG GUG AGA BA AU C GGG C AUU UUGC AGC AAG AUC AAE D AGGC GCUGC AU G GAGC UAG UUC GDC AGG AC GA CU CC GU GGC AAC CU UGU UUG C CU UUG U G AAG UC AU CC AU UC CU CC CC AU UC AU CC G GGA UUG G AAG G GA UC AAG C U G ACC CU CC UG B AG CC CBUUUGAUC AGC AGC GBU AGC AGAU GGG C GC UC AGC CAUUGAG AUU UUGUUC G NCA A GBUCCAC AUC GGC AU CC GGG UAC A UGC A GGG AU AC GAC GA CUGU UUG C AGC AGG G ACC AGC CU CC GAG GAG ACC UC AU DUG C GC GC AAU AC GU GGC GGGU AC AAG BU SCU S DC UC CU U G AU GGA XUG AAC AUG G AGG C GC U U AU ACU UC C UCC U GC UC GGC UDUAG C GDC GGC GUG GGGU GAC GGC GGC CUGUC UC CU UC GC C GU AUH CC CU UUG C AC AU UC AU U UUC UAG C GGC A AC GGC BU GGG C AU UC UC AAC AG UC CU GUC GG AG ACC AGA AG UUG AUC GC AA C AAG UIC A AU C GGG CC UUG GGG C AU GC AG AC U G GAU UC AC U AC G ACU A C GA AG G UUC AC AAG BU CC AGAG GC UBU G AAC AAC AC GGC C AGGC BU UUC A AAG UUG GGC C G AUC AC C AAG ACC U UC GAG C AUC AGC GC AU UG AUC G GUG AC AU AUU C AGC G GOU G GAG GGC UG GAG C AGG AC GDC A G AUC G AC G C UC UC AU C AAG G AC G GUG AC C AC CU U G A U G C CU UD G GGC AC AAC AG CU G G C G G AG C GAU C AGC GGC ACU UC C GGC AAC UC GC C AAG C AAAG UIC AC GAU GC GUGAG GC CC AGUC C AAG NG G UCC GBU UUC G C G GUC AAG G AAE CC AU AUU GUGUCU UC GUC GUGAG CC G C C AAG G UDU G AC U U U AU GC AC GUC G GCU ACU AC CC G AGC AAUC AU AU GAA GUG G AUC C G C U AC G GC CU GUC G AU G C C U A ACC C ACU AAG UBU AUU G C C C U G U G AAG GGAU AU U AU U AAG C C AAC AAC ACC C GC AU U GUG AC GAU G GUC AU AC ACC G G U C G U CC UUC UNG G G C C G A G C C AUC AU UC ACUG AC ACC AAU AC BU G G C U C GC AAG U G A C U AC CAGAC AU CUC C AC CAU UH GC C GC CGCC GUG UC GAAAC AGC ACC GGA AUU G AUU CC AA GAU GA CUGG AC GA AUU C U C AAG AC U G U C ACU UCC AUU CC C AUC U G G A N G C O U G A C AC AGAUA C ACC ACC U U C U C ACC U G ACC U AC GAG U G C U G A G C C U U C A C AAG U G G U C AAG G CC U S A N C G A G A G U A C AU G AC CU GAAG G A G C U G G C A N C U A U A C U A C A A C A A G U G G E G G C A G A U G A G G A G A U C U S U C G A A A U C U A C C A C AU U G A A A C G A G AU C G C C A G A U C A A G A G C U U A U C G C C A A G C E </p>	67
MERS_S0_Full-length	<p> AUGGAACCC CU G C C C A G C U G C U G U U C C U C U G C U G C U G U G G C U G C U G A U A C C A C C G G C A G </p>	68

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Strain	Nucleic Acid Sequence	SEQ ID NO:
	<p>ACGAGCUGGACGAGUUCUUCAGAACGUUGCCACUCCAUCCCCAAUUCGGCAGCCUGACCC AGUACACACCACUUCUUGGACUUGACUUCGAGAGUGUGUCCGUCCACAGGUCUGUAGAG CCUUGACGAGAGCUACUUCGACUGGAGAGAGUUGGGGACUACACCUUCUACACACAGUUGCC UUGGUCAGUUGGCGGCGUUAUCGCCGCGUGGUGGCCUUGGCCUGUGCGUUGUUCUACA UCCUGUUCUCCACCGGCUUGCGGCACAGUUGCAGUGGCAAGUUGAAUUGACACCGUUGCGC GACGUAUCGAGAGAGUAGACCUGGACCCUACAAAGUGCAUGGUCAC</p>	

Table 11. Betacoronavirus Amino Acid Sequences

Strain	Amino Acid Sequence	SEQ ID NO:
<p>gbIKJ156934.11: 21405-25466 Middle East respiratory syndrome coronavirus isolate Riyadh_ 14_2013, spike protein (amino acid)</p>	<p>INHSYLLMFLLTPTESVYDVGPDVSKSACIEVDIQQTFQKTVPRPDVSKADGNYPGGRTYSNITTYQ QLPFYGGDHGDMYVYSAGHATSTTQKLFVANYSDVYKQFANGFVYRIGAAANSTGTMISPSTGATIR NYPAFLGSSVGNFSDGKMGFFNHTLWLLPSSGRTLHAFYDLERPSGNGCPAGNBYTSFATYHTP ATDCSDGNVYRNASLNSFKKYNLRNCTFMYTYNTEDELENFQITQTAQGVHVFSSRYVQLYGGNM FQKTLFYVDTKYYSIPHSRSDSDRKAWAAFYVYKLRPLTFLQFVVDGYRRADCGFNDLSQLHCS YESFDVESSGYSVSSFEAKPSSVVEQAESVEDDFSPLLSSTPPQVYVFNPLVFTNCNINLTKLLSLS VNCFCSDSPANAGNYSSLLDYFSYPLSMKSDLSVSSAGRSQFNYYKQSFNPTCLLATVPHLTI TRFLKYSYNNKSRLLSDRTEYFDLWNAQYSPCVSYVSTVWVEDGDYRKLSPLEGGHLYAGSS TWANTEQLWNGPQITVQYGTNTNSVCPKLEFANDTNASQLGNCVEYSLVGVSDRGVFNQSTAVGVR QDRFYDAYQHLVGYSDGNYICLRACVSYVPSVHYDKETKTHATLFGGVACEHISSTNSQYSRSTR SALKRRDSTYPLQTFVGCNLGLVNSL FVEDCKLPLGGSLCALPDTPTLTPRSVRSVYVPEMLASIA FRRPQVQLNSSYFLSIPTNFSGVYDQENQTTQKVTQCKQYVCHGFQKCEQLREYGGFCGMHJ ALHGAWLRQDDSVRNLFAVYKSSQSSPSPGFGDFNLTLLEPVISSTGSRAPSAIEDLLRQKYMADPG YMDSDDCMDDGFASARDUICADYVAGYKLPPLNDWNNEAAYTSLLGSDAGVGYTAQLSSFAVFP ACSFRLNGVGTQQVLSNCKLIANKFNQALGAMOTGFPTTNEAFKVGDAVWVNAQALSKLASELS NTFQASASGDHQRDLVLEQDADDRLINQRLLTNAFVAGQLVSESAAQSAQLAKDKVNECVKAGSK RSCFGCGTHVSPVYVAPNGLYFMHVGYYPSNHVVSAVGLCDAANPTNCLAPNGYRKTNNTRIV DENSYTSSSFYAPERTSLNTKYVAPQNTYQINSTNLPPRLGNSTGIDFQDELDEFFKNVSTSPNFGS LTQRITLLDLTYEMLSLQGVKALNESHDLKELGNYYVYKWPVYVLAGLVALACVFFILCCTG CSTNCMLKKNRCCDRYEEYDLEPHKVVH</p>	<p>24</p>

(continued)

Strain	Amino Acid Sequence	SEQ ID NO:
<p>5</p> <p>MERS S FL SPIKE 2cEMC/2012 (XbaI change(T to G)) (amino acid)</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p>	<p>MHSFLLMPLLTPTFESYVDVGPDSVKSACIEVDIQQTFFDKTWPRDQVSKADGNYPGQRTYSNITTYQ GLFPYGGDHGGMYVYSAGHATSTTFQKLFYANYSQDVKQFANGFVVRIGAAANSTGTVNSPSTSATIR KYPAPALGSSVGNFSDGKNGRFFNHTLWLPDSCGTLRAFYKOLEPRSGNHCPASGNYTBFATYHTP ATDCSDGNYNRNASLNSFKEVFLNRNCTFMYTYNTEDEL ENFGITDTAAGVHLFSSRYVDLYGONM FCFATLPVYDTIKYYSIPHSRSDSQRKAWAAFVYVYKLPRTFLLOFSDVGYYRWDGDFNLSQLHCS YESFDVESGYYVSSSEFAKPSGSEVVEQAEDVECDFSPLSGTTPQVYVFKL VFTNQNINLTNLLQLFS WDCFTCSQSPAAIASNCYSSLEDFYSYRGNKSDLVESAGPISQFNKQSPNPTCLLATVPNNLTTI TPLKYSYNNKCSRLLSQDRTEVPQLWNAQYSPCVSVPSTVWEDGQYRKLSPLEGGGRLVASSSS THANTEQLMGFGITVQYGTDTNSVCPKLEFANDTNASQLGNCVEYSLYGVSGRGVFNQCTAVGYR QCRPNDAYONLVGYSDDGNYYQLRACVSPVSVWYDKETKTHATLFGSVACEHISSTNSQYSRSTR SMLKRRDSTYGRLOTVYSCILGLVNSL FVEQCKLRLGQSLCALPDTPTLTPRSVRSVPGEMRLASIA FHPNDQLNSSYFLSPTNFSFGYTDENQTDIKVYKCKDYVYCHGPKCKEQLREYGGFCMIND ALHGANLRDDSVRNLFASVKSQSSPISGFGGDFNL TLEPVISITGSRBARSAIEDLLPKVYTIADPG YMGVYDCMQDGPASARDLICADYVAGYKLPRLMDWINEAAYTSLLGSIAGVGTAGLSSFAHFF ADSYRLNGVGTIQVLSNQKLIANKFNQALGAMQGTFTTNEAFQKVDVAVNNNAQALSKASELS NTFGASASISDHQRDLVLEQDADDRLINGRLTTLNAFVADQLVRSASAALSAQLAKDKVNECVKADSK RSCFGSDGTHVSPVWAPNGLYFNHVGYYPNH EVVSAYGLCAANPTNCLAPVNGYRKTNNTRIV DENSTGSSFYAPEPTSLSNTRYVAPNTYQNIHSTNLPRLGNSTGDFQDELDDEFFRNVSTSPNFQSS LTQNTLLDLTYEMLSLQGVVVALNESYDLKELGNVYTYNKNPWNVNLGFIAGLVALLCVFPLCCTG CSTNCKKLCNRCDDRYEEDLEPHKVMH</p>	<p>25</p>
<p>30</p> <p>Novel_MERS_S2_subunit_t rimeric vaccine (amino acid)</p> <p>35</p>	<p>MHSFLLMPLLTPTFESDCKPLGQSLCALPOTPSTLTPRSVRSVPGEMRLASIAFNHPDQVQLNSSFY KLSNINFSFQVYTDQYQTDIKQYVDCNDFQKCEQLREYGGFCMINDLHGANLRDDSVR NLFASVKSQSSPISGFGGDFNL TLEPVISITGSRBARSAIEDLLPKVYTIADPGYMGVYDCMQDGP ASARDLICADYVAGYKLPRLMDWINEAAYTSLLGSIAGVGTAGLSSFAHFFADSYRLNGVGTIQ VLSNQKLIANKFNQALGAMQGTFTTNEAFQKVDVAVNNNAQALSKASELSNTFGASASISDHQR DLVLEQDADDRLINGRLTTLNAFVADQLVRSASAALSAQLAKDKVNECVKADSKRSCFGSDGTHVSP VWAPNGLYFNHVGYYPNH EVVSAYGLCAANPTNCLAPVNGYRKTNNTRIVDENSTGSSFYAPE PTSLSNTRYVAPNTYQNIHSTNLPRLGNSTGDFQDELDDEFFRNVSTSPNFQSSLTQNTLLDLTYEML SLQGVVVALNESYDLKELGNVYTYNKNPWNVNLGFIAGLVALLCVFPLCCTG</p>	<p>26</p>
<p>40</p> <p>Isolate Al-Hasa_1_2013 (NCBI accession #AGN70962)</p> <p>45</p> <p>50</p> <p>55</p>	<p>MHSFLLMPLLTPTFESYVDVGPDSVKSACIEVDIQQTFFDKTWPRDQVSKADGNYPGQRTYSNITTYQ GLFPYGGDHGGMYVYSAGHATSTTFQKLFYANYSQDVKQFANGFVVRIGAAANSTGTVNSPSTSATIR KYPAPALGSSVGNFSDGKNGRFFNHTLWLPDSCGTLRAFYKOLEPRSGNHCPASGNYTBFATYHTP ATDCSDGNYNRNASLNSFKEVFLNRNCTFMYTYNTEDEL ENFGITDTAAGVHLFSSRYVDLYGONM FCFATLPVYDTIKYYSIPHSRSDSQRKAWAAFVYVYKLPRTFLLOFSDVGYYRWDGDFNLSQLHCS YESFDVESGYYVSSSEFAKPSGSEVVEQAEDVECDFSPLSGTTPQVYVFKL VFTNQNINLTNLLQLFS WDCFTCSQSPAAIASNCYSSLEDFYSYRGNKSDLVESAGPISQFNKQSPNPTCLLATVPNNLTTI TPLKYSYNNKCSRLLSQDRTEVPQLWNAQYSPCVSVPSTVWEDGQYRKLSPLEGGGRLVASSSS THANTEQLMGFGITVQYGTDTNSVCPKLEFANDTNASQLGNCVEYSLYGVSGRGVFNQCTAVGYR QCRPNDAYONLVGYSDDGNYYQLRACVSPVSVWYDKETKTHATLFGSVACEHISSTNSQYSRSTR SMLKRRDSTYGRLOTVYSCILGLVNSL FVEQCKLRLGQSLCALPDTPTLTPRSVRSVPGEMRLASIA FHPNDQLNSSYFLSPTNFSFGYTDENQTDIKVYKCKDYVYCHGPKCKEQLREYGGFCMIND ALHGANLRDDSVRNLFASVKSQSSPISGFGGDFNL TLEPVISITGSRBARSAIEDLLPKVYTIADPG YMGVYDCMQDGPASARDLICADYVAGYKLPRLMDWINEAAYTSLLGSIAGVGTAGLSSFAHFF ADSYRLNGVGTIQVLSNQKLIANKFNQALGAMQGTFTTNEAFQKVDVAVNNNAQALSKASELS NTFGASASISDHQRDLVLEQDADDRLINGRLTTLNAFVADQLVRSASAALSAQLAKDKVNECVKADSK RSCFGSDGTHVSPVWAPNGLYFNHVGYYPNH EVVSAYGLCAANPTNCLAPVNGYRKTNNTRIV DENSTGSSFYAPEPTSLSNTRYVAPNTYQNIHSTNLPRLGNSTGDFQDELDDEFFRNVSTSPNFQSS LTQNTLLDLTYEMLSLQGVVVALNESYDLKELGNVYTYNKNPWNVNLGFIAGLVALLCVFPLCCTG CSTNCKKLCNRCDDRYEEDLEPHKVMH</p>	<p>27</p>

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Strain	Amino Acid Sequence	SEQ ID NO:
<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p> <p>Middle East respiratory syndrome coronavirus S protein UniProtKB - R9UQ53</p>	<p>INHSFLLMPLLTPEESVYDVGPI SVKSAIEVDIQQTFFDKTWPHROVSKADGIIYPOGRTYSMTITVQ QLPFYGGDHGGIMVYVBSAGHATSTTFOKL FVANYSCDVRQF AVGFVVRIGAAAN STGTVISPSTSAITR KYPHFWL GSSVGNFSDGKVGRRFFNHTL WLPDSDGTL LRAFYQL EPRSDNHCPASNSYTSFATYHTP ATDCSDGNVNRNASLNSFKEYFLRINCTFMYTYNTEDELENFBIQTDAQGVHLFSSRYVDLYSGNW FQFATLPVYDTHKYYDHPHSRSGSSDRKAWAIFYVYKQLRPLTFLLDFSDVGIYRRADCGFNDLSQLHCS YESFDVESVHYVSSSFEAKPSSGVVEQAESVECDFORLLSSTPFDVYVNFKRLVFTNCSYMLTKLLSLFS VNCFTCSQHPAAIASNCYSELDYFSPYLNKSDLVSSSAGPI SQFNYYQDFQNPPTQLLATVPHLLTTI TPLKYSYNNKCSRLLSGDRTEYRDLWNAAGYSPCVSYVPSTVWEDGGYYR KQLSRL EGGGWL VASDS TWMTEDLQMGPGITVQYGTDTN SVPKLEFANDTNASQLGNCKEYSLNGVSGHGVNPGCTANGVR CGRPFDAYGNLVGYSDDGNYYQLRACVSYVPSWYD KETKTHATLFGSVADEHISSTNSQVSRSTR SMLKRRDSTYSPLOTFSVSCWGLVKSLSFVSDCKLRLGQSLCALPDTPTLTPSSVRSVPGEMRLASIA FHWFDNDGNSSYFLSIPTNFSDGYTSEYQTTIDKVTWCKADYYVCGFQKCEQLREYGGFCSNIND ALHGKLRDQD SVPRLFAGWKSQSSPPIPGFGGDFNLTL EPHYDGTGSR SARPASIEDLLPKYTTADPG YMGVYDQCMDQGPASARDLICADYYAGYKLPRLMDWINEAAYTSGLLSGIMGVGWTAGLSSFAWPF AOSPRLNGVGITQVLSNQKLIANKFNQALGAWGTGFTTNEAPR KVIDAVHNNAGALSKASELS NTFGASASISDHQRLDYLEQDADGR LINGRLTTLNAFVADQLVRSASAAL SAGLAKDKVNECVKADSK RSCFGSDGTHVDFVWAPNGLIFNHVGVYYPDHH EVVSAVGLCAANPTNCPINGYR KTHNTRIV DENSYTSSSFIAPERTSLNTRKYVAPHTYQNIETNLPPRLGNSTGDFQDELDEFKMYVSTSPNFGS LTQWNTLLDITVEMSLQGVVVKALNESHDLKELGNYYTRKKNPWYWRGFIAGLVALACVFPILCCTG CGTRNCMLKKNRCCDRYEEDLEPHKVVHW</p>	<p>28</p>
<p>Human SARS coronavirus (SARS-CoV) (Severe acute respiratory syndrome coronavirus) Spike glycoprotein UniProtKB - P59594</p>	<p>WFIPLFLTLTSGSDLRQCTTFOQVQAPHYTGHTSSNRGVYYPDEFFHSDTLKLTQDLRFPYVSVYGGPH TINHTFBNPFFRQGIYFAATEKENVWFQWVFGSTMNKKSQSYHNNSTNVMHACNFELCDNPFPAVS KPMGTQHTWFDNAFNCTFEYSDAFSLD VSEKSNFKMLREYVFNKIKDGLYNYKGYQDQVYRDLF SDFNTLXKFKLRLGNHTFRALTAFAQDHWGTSAAAAYVGYLKPTTFMLKYDENGTGTEAVDQSON PLAEKCSVKSFEQKGIYQTSNFFVYPSGQVYVFPNITNLCPGSEYFNATKFPDYYAWGRKKDNCVAG YSLVNSTFFSTFNDYEVSATKLN DLQFSNYYADSFVYKQEDVROAPGQGTQVADYNYLPODFMGE VLAHNTPKNDATSTENYNYKRYLRHGGKRPFERDISNYPFSPDQKPCTPPALNCSYRPLNGYGFYTTT GKYDFFRVVILSFEELNAPATYCGPKLSTDLKNDQVNFNFNGLTGTDLVLPSEKRFQPFQGFQRDVS DFTQSDQPKTSBLDHSFCFGGVSVITPGTNASSEYAWLYQDYNC TDVSTAHADQLTPANRYSTGN NNFQTLAGGLIGAEHVDTSYECGRGADICASYHTVSLLRSTQKQVAYTMDL GADSDIAYDNNTINPT NPSSTTEVN PVSMAKTSNDGNWYCGDSTECANELLQYGSFC TQLNHALSGAAECORNTREYFAQY KCMYKTPFLKYFGGFNFSQLPDPLKPTKREREDLLFNKYTLADAGFMKGYEELGONARDLICAGNF NGLTSLPRLTDDWAAAYTAALVSGTATAGWYTPGAGAAQLDIPFANQMAHYRFGGVTQNVLYENQKQIA NQFRKNSQIGESLTTTBALGKLDQYVHONAGLNTL VKQLSBNFSAISSNNDL SRLDHYEAEVQDR LITGRLQSLQTYTQQLRAABRASAKLAATKNSQCYL EDSKRQDFCGKGYHLMSFPCAAPHGVVFLH VTYNPDQERNFTTAPNCHESKATFPREGVYFNSTSWITQRNFFSPQITTDNTPVSONCDVYDQNN TWYDPLQPELDFKEELDKYFNIHSPDIDLCDISGNSASYVWQKEIDRLNEVAKNLNLSLQLGELGKY EQHKNPWHYVWLGFIASLAVNMTLLCCMTSCC SCLKGCSCGSECKPDEDDSEFVLKGVYKHYT</p>	<p>29</p>

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Strain	Amino Acid Sequence	SEQ ID NO:
<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>Human coronavirus OC43 (HCoV-OC43) Spike glycoprotein UniProtKB - P36334</p>	<p>MFLLLSLPTAFAWGDLKCTSDNNDKCTGPPPISTDTVDVTNGLQTYIWLQHYVLAITLFLNGYPTSG STYHNNALKQSVLLSRLWFKPFLSDFNGIFAKVNTKXNDRYWYSEFPAMGSDYVNTSYSVYQPR TINSTQDDNKLQGLLEVAVCDYNNMCEYPTQICHNLGNHAKELVHLDTGAVVSLYKPNFTYDWAQ YLYHFYQEGSPTFYAFTDTGVTKFLFNVYLGMLSHYYVMRLTONGKLEIYWYTRLSRQYLLAFN QDQIFNAEDCWSDFNSEKCKTCSAPPPTGVYELNGYTVQPIADVYRKPFLMNCNIEANLNDKSVSP LNWERKTFSNCFNFMNSLNSHDAQSFTDNDAAKHYMCFSSYDHFAPNQRKWLQQLQHLQYLS FVYRDTTATSCQLYYNLPANNVSVGRPNPSTNNKRFQFIEDSVFKPRPAQKTNHDVYVAQHCFAKAP KNFCPCXLSGCVGSGPCKNVGHSTCPAGTNYLTCQNLCTPQPTFTTGTTCPCQTKSLVQGEHCSQL AKSDYCGNSCTCRPQAFLENSADSCLODDKCNFANFLHDVNSQLTCSTDLCKANTDLGKCVNY DLYGLGDSIFVEVNAATYNSWQNLVDQNGMLYQFQDYNRTFMWRSQYDGRVGAFAFANSSSEPALF RHNKCNVFNISLITRQLQFNYYFSYLCVYVAHNSIAGVQTCDLTVGSGYCVDYSMNRHRSRQWTTG YRFTNFEPTWISVNDQLSPVSGLEYKDFSEFTIGNMVERICTGSPKVTDCAAFCGQDYAQCQSOLVE YGSPDNNWNLTEVNELELDTTQLQVANSLNNGYTLSTKLKGGVNFVDDNFSPVGLGSGECSNAGS RQWEDLFDKVKLSDVGFVEAYNCTGGAEFDLICYGQYKQKLPPLBENQISQYLAATSASLFPF NTAAGVFFYLKVDYRINQLGYTNDVLSQNRKLIANAFNHALYAIQEGFDATNSALVQDHYNANACA LHWLQDLNRPFGNISASLQELSPRLALEAQAQDRLINGRLTALNAVVSQQLSDSTLVKPSAQAMKX VNECWKQSSRNFCQNGHHSLVQNAFVSLYHFFSYVPTKYKTAHVSPQLCIAGQGIAPKSSYFIM WNTNMYTGGSYYPERTENNYVMSTCAVNYTKAPYYMLNLSFNLDFKKELDQWNFQDTSVAPD LQLDYNVTFDLQVEMHRLQEAIKVLDQSYMLKQDGTYYEYVWVWYVWMLLQLAGVAMLLPFDCC TDCGTSCKKCSGCCIDYTGYSQELVINTSDG</p>	<p>30</p>
<p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>Human coronavirus HKU1 (isolate N5) (HCoV-HKU1) Spike glycoprotein UniProtKB - QOZME7</p>	<p>MFLLPPTLAVGGDFNCTNSFINDYKTIPTISEDVVDVSLQLGTYIWLNRVYVNTLLELFTSIFPKSGAN FRLALKGSYVLSLWYKPPFLSDFRNGIFSKXKNTKLWNNLTYSEFSTIWSKAFVNTSYTVVQPHNGI LETAGDYTNACEYPTKCKSKSRNEGWHDSSEPLCLFKKNTFYNSVADWLKHFYQERGVFYAYVA DVQMPTEFLSLYLGTLSHYYVMRLTCNANSENTOINETLEYWYTRLSRQYLLNFDGHWTAADCCS SPLSECCXTQDFAPNFGVYDLSGFTVYVYATVYRIPNLPCDIDNWLNNVSNPSPNLNWERHFSNCH FRLSTLRLVHVDVSCSNLDRSKIFGSCRNSTVQKFAFNRRFDLQLGSSQFLQSSNYRDISSSCQ LYSLPLWVVTNHFNPSSVWNRVYGRGSRLLSVDVYVSDHCFSVNSDFPCADPQVYNCAKSKPFS NCFAGTKYRHCQLDTELYVNWCRCSCLPDRSTYSPNTPQQRKXVVDQGEHCPLGHNEEKGTQLN HSCPCSPDAFLGWSFDSCISNHCNMFQVFFNGNSGTTCSNDLLYNTBSTGVCVNYDLYSTGQG FRESAAVYNNWQNLVDQNGHIGFKDFLTKTYTLPCYSGRVSAAFYQWSSSFPALLVRLKCSVYLN NGRSOPPYFDQYLGCWLVANNLTSYVSSCDLRNGGSPQDYALPSRAKRRGSSPFRVYTFEPPNV SPVDSVETVSGLFEIQTNFTIAGHEEFIQTSBPKVTDCSAFCQSNVYACRGLSEYGTFCQNNQLN ENRDLDTQLQVANALMDGVTLSSNLNTLHSDVQNDQPKQLGCLGSDCGSSSRLLLELLFKVYKL SDVGPVEAYNCTGGSEMDLCCVGFNSIKNLPPILSETQSDYTTAATVAAMFPFWSAAADVFFSLNV QYRNLQVYTNQWLNKQKLIANAFNKALLSQNGFTAFNBLAQDQSYVAANAGALNSLQQLPKFCA SSELQELSPRLQNLDAQVQDFLNGRLTALNAVVSQQLSDITLKAGASRNEKYNECVKSQSPRNFCG NENLISLVQNAPEYLLFHFYKPTQFRTVLSVPLCLSGDQAPKQGYFKQNDQWNPFGSSYYP ERSXNVVFMNSQSVNFTKAPFVLSNDFEALSLWFKNNTSAPNLTFNQHINATFLDLYEM NWQESIKSLNSSFRLKGGTYENYKQVWYVWMLLWLPVLLWLPFCCTECGSAQFKCHNCDDEYV GHDFVKAHQD</p>	<p>31</p>
<p>50</p> <p>55</p> <p>Novel_SARS_S2</p>	<p>MFLLPLTLTSGSDLDRALEGIAAEQDRNTREXPAQVQKQWYKPTLKYFGGFNFSQQLPQPLKPTKHSP EDLLFNRTLADAGFMKQYGECLGDNARDLICAGKFNGLTWLPPLLTDDMIAAYTAALVSGTATAGWT FQAGALDFFAKQMAVHFNIGVYQVQVYENQKQANQFNKASQGEELTTTSTALQNLQVYVQNA QALNTLWQLSSNFGAIBSVLNDLSRLDKVEAEVQDRITGRLOSLQTYVQQLRAAERASANLAATK NEECALGQSNRVDFCGKGYHLWFFQAAPHGVVRLHYTYVPRQGRNFTTAPNCHEGSKATFPRFQV VPGSENRITQRNFPQNTDNTFVSNCDVWGHNTVYDFLQPELDFKQELKVFKNHTSPQVGL GQISGNASVWIKHEDRLEVAANLWESLIDLQELGXYEQHWVWYVWMLGFIAGLWVWVTLQDNT SCQCLNSACSCGCCNFDQDSEFNLKGVKHHIT</p>	<p>32</p>

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Strain	Amino Acid Sequence	SEQ ID NO:
Novel_MERS_S2	<p> MNSWFLIWFLLTPTEEDCKPLGQSLCALPQTPSTLTPHSHRDNVPGENHLAQAPWHRGVDQLNSSF NLSPTNFSFVYTDGEYDHTIQKYTDICNDYVCRSFQKCEQLLREYGGPESMNDKLGANLRGGDSVR NLPASWSSDSSPFGPFGDPLNLTLEPVNISTGSRBARSAEDLFDKYMADPGYMGDIDDCMGGSP ASARDLICQYVADYKYLPRNDVWNEAAYTSLLGGHAGYGVWTAGLSSFAAIFADSHFYRLNGVDTG QRLSENKLIANRFDALGANDTQFTTTNEAFQKVDVAVNNADALSKLASELNTTFGNASDSDHQR LDVLEQADQDRLINGRLTLNAFYVQDLVRSESAKSAQLAKDKYNECVKAGQSRGGFCGGDTHVVF VVWPNELYFNVGVYPPSNHENVSAVQLCDAAANPTNCLAPVNGWFKTNKTRHDENSYTGSSFYAPE PTLNTRYVAPQVTHQNIHNLPPRLGNSTGDFQDELEDFFNWVSTSPNFFGRLTQNTTLDLTYEK SLDGNYKALNEQMDLRELGNWYTYKWF </p>	33
Novel_Trimefic_SARS_S2	<p> WFFLLFLTLTSGSGLDRALSGIAEQSRNTRREYFAQVQKQMYKPTLKYFGGFNFSDLPDPLKPTKRSP EQLLFWKTLADAGFVWQYGEQLGDNARDLICQKFNGLTKPLPLITDDMIAAYTAAVSSATAGWT FQAGNALQPFANQMAVRFNIGVTONVYENQKQANCFNKNWSDQEBLTTTSTALGRLQDYNQNA QALMLIKQLSGNFGNISSVLDLRLDKVEAEVQIDRLTGRLOSLQTYVQQLHAAERASANLAKY NSECLGQGNRVDFCGKGYHLWFFQAAPHGVPVFLHNTYVPGERNFTTAPNCHESKAYFPEGVF VPGTENRTQRNFPSPQITDNTFYSGNCDVIRGIMNTYDPLQPELDSFKCEDKYFKNHTSPQKDL GQSDNASHVNIQKEIQRNEVARNLNEELDLQELDKYEQYRNFVYVYRLGFIAGLIMVWVTLCCNT SCCCKLNGACSCGSCCKFDQEDLSEPLKGVKLYHT </p>	34

Table 12. Full-length Spike Glycoprotein Amino Acid Sequences (*Homo sapiens* strains)

GenBank Accession	Country	Collection Date	Release Date	Virus Name
AFY13307	United Kingdom	2012/09/11	2012112105	Betacoronavirus England 1, complete genome
AFS88936		2012/06/13	2012/09/27	Human betacoronavirus 2c EMC/2012, complete genome
AGG22542	United Kingdom	2012/09/19	2013/02/27	Human betacoronavirus 2c England-Qatar/2012, complete genome
AHY21469	Jordan	2012	2014/05/04	Human betacoronavirus 2c Jordan-N3/2012 isolate MG167, complete genome
AGH58717	Jordan	2012/04	2013/03/25	Human betacoronavirus 2c Jordan-N3/2012, complete genome
AGV08444	Saudi Arabia	2013/05/07	2013/09/17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_12_2013, complete genome
AGV08546	Saudi Arabia	2013/05/11	2013/09/17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_15_2013, complete genome
AGV08535	Saudi Arabia	2013/05/12	2013/09/17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_16_2013, complete genome
AGV08558	Saudi Arabia	2013/05/15	2013/09/17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_17_2013, complete genome
AGV08573	Saudi Arabia	2013/05/23	2013/09/17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_18_2013, complete genome
AGV08480	Saudi Arabia	2013/05/23	2013/09/17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_19_2013, complete genome

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	GenBank Accession	Country	Collection Date	Release Date	Virus Name
5	AGN70962	Saudi Arabia	2013/05/09	2013/06/10	Middle East respiratory syndrome coronavirus isolate Al-Hasa_1_2013, complete genome
	AGV08492	Saudi Arabia	2013/05/30	2013/09/17	Middle East respiratory syndrome coronavirus isolate Al-Hasa_21_2013, complete genome
10	AHI48517	Saudi Arabia	2013/05/02	2014/02/06	Middle East respiratory syndrome coronavirus isolate Al-Hasa_25_2013, complete genome
	AGN70951	Saudi Arabia	2013/04/21	2013/06/10	Middle East respiratory syndrome coronavirus isolate Al-Hasa_2_2013, complete genome
15	AGN70973	Saudi Arabia	2013/04/22	2013/06/10	Middle East respiratory syndrome coronavirus isolate Al-Hasa_3_2013, complete genome
	AGN70929	Saudi Arabia	2013/05/01	2013/06/10	Middle East respiratory syndrome coronavirus isolate Al-Hasa_4_2013, complete genome
20	AGV08408	Saudi Arabia	2012/06/19	2013/09/17	Middle East respiratory syndrome coronavirus isolate Bisha_1_2012, complete genome
	AGV08467	Saudi Arabia	2013/05/13	2013/09/17	Middle East respiratory syndrome coronavirus isolate Buraidah_1_2013, complete genome
25	AID50418	United Kingdom	2013/02/10	2014/06/18	Middle East respiratory syndrome coronavirus isolate England/2/2013, complete genome
	AJD81451	United Kingdom	2013/02/10	2015/01/18	Middle East respiratory syndrome coronavirus isolate England/3/2013, complete genome
30	AJD81440	United Kingdom	2013/02/13	2015/01/18	Middle East respiratory syndrome coronavirus isolate England/4/2013, complete genome
	AHB33326	France	2013/05/07	2013/12/07	Middle East respiratory syndrome coronavirus isolate FRA/UAE, complete genome
35	AIZ48760	USA	2014/06	2014/12/14	Middle East respiratory syndrome coronavirus isolate Florida/USA-2_Saudi Arabia_2014, complete genome
	AGV08455	Saudi Arabia	2013/06/04	2013/09/17	Middle East respiratory syndrome coronavirus isolate Hafr_Al-Batin_1_2013, complete genome
40	AHI48561	Saudi Arabia	2013/08/05	2014/02/06	Middle East respiratory syndrome coronavirus isolate Hafr-Al-Batin_2_2013, complete genome
	AHI48539	Saudi Arabia	2013/08/28	2014/02/06	Middle East respiratory syndrome coronavirus isolate Hafr-Al-Batin_6_2013, complete genome
45	AIZ74417	France	2013/04/26	2015/03/10	Middle East respiratory syndrome coronavirus isolate Hu-France (UAE) - FRA1_1627-2013_BAL_Sanger, complete genome
	AIZ74433	France	2013/05/07	2015/03/10	Middle East respiratory syndrome coronavirus isolate Hu-France -FRA2_130569_2013_IS-HTS, complete genome
50	AIZ74439	France	2013/05/07	2015/03/10	Middle East respiratory syndrome coronavirus isolate Hu-France -FRA2_130569-2013_InSpu_Sanger, complete genome
55	AIZ74450	France	2013/05/07	2015/03/10	Middle East respiratory syndrome coronavirus isolate Hu-France -FRA2_130569_2013_Isolate_Sanger, complete genome

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	GenBank Accession	Country	Collection Date	Release Date	Virus Name
5	AKK52602	Saudi Arabia	2015/02/10	2015/06/08	Middle East respiratory syndrome coronavirus isolate Hu/Riyadh_KSA_2959_2015, complete genome
	AKK52612	Saudi Arabia	2015/03/01	2015/06/08	Middle East respiratory syndrome coronavirus isolate Hu/Riyadh_KSA_4050_2015, complete genome
10	AHN10812	Saudi Arabia	2013/11/06	2014/03/24	Middle East respiratory syndrome coronavirus isolate Jeddah_1_2013, complete genome
	AID55071	Saudi Arabia	2014/04/21	2014/11/12	Middle East respiratory syndrome coronavirus isolate Jeddah_C10306/KSA/2014-04-20, complete genome
15	AID55066	Saudi Arabia	2014	2014/11/12	Middle East respiratory syndrome coronavirus isolate Jeddah_C7149/KSA/2014-04-05, complete genome
	AID55067	Saudi Arabia	2014	2014/11/12	Middle East respiratory syndrome coronavirus isolate Jeddah_C756/KSA/2014-04-03, complete genome
20	AID55068	Saudi Arabia	2014/04/07	2014/11/12	Middle East respiratory syndrome coronavirus isolate Jeddah_C7770/KSA/2014-04-07, complete genome
	AID55069	Saudi Arabia	2014/04/1/12	2014/11/12	Middle East respiratory syndrome coronavirus isolate Jeddah_C8826/KSA/2014-04-12, complete genome
25	AID55070	Saudi Arabia	2014/04/14	2014/11/12	Middle East respiratory syndrome coronavirus isolate Jeddah_C9055/KSA/2014-04-14, complete genome
	AHE78108	Saudi Arabia	2013/11/05	2014/05/01	Middle East respiratory syndrome coronavirus isolate MERS-CoV-Jeddah-human-1, complete genome
30	AKL59401	South Korea	2015/05/20	2015/06/09	Middle East respiratory syndrome coronavirus isolate MERS-CoV/KOR/KNIH/002_05_2015, complete genome
	ALD51904	Thailand	2015/06/17	2015/07/07	Middle East respiratory syndrome coronavirus isolate MERS-CoV/THA/CU/17_06_2015, complete genome
35	AID55072	Saudi Arabia	2014/04/15	2014/11/12	Middle East respiratory syndrome coronavirus isolate Makkah_C9355/KSA/Makkah/2014-04-15, complete genome
	AHC74088	Qatar	2013/10/13	2013/12/23	Middle East respiratory syndrome coronavirus isolate Qatar3, complete genome
40	AHC74098	Qatar	2013/10/17	2013/12/23	Middle East respiratory syndrome coronavirus isolate Qatar4, complete genome
	AHI48572	Saudi Arabia	2013/08/15	2014/02/06	Middle East respiratory syndrome coronavirus isolate Riyadh_14_2013, complete genome
45	AGV08379	Saudi Arabia	2012/10/23	2013/09/17	Middle East respiratory syndrome coronavirus isolate Riyadh_1_2012, complete genome
	AID55073	Saudi Arabia	2014/04/22	2014/11/12	Middle East respiratory syndrome coronavirus isolate Riyadh_2014KSA_683/KSA/2014, complete genome
50	AGV08584	Saudi Arabia	2012/10/30	2013/09/17	Middle East respiratory syndrome coronavirus isolate Riyadh_2_2012, complete genome
	AGV08390	Saudi Arabia	2013/02/05	2013/09/17	Middle East respiratory syndrome coronavirus isolate Riyadh_3_2013, complete genome
55	AHI48605	Saudi Arabia	2013/03/01	2014/02/06	Middle East respiratory syndrome coronavirus isolate Riyadh_4_2013, complete genome

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	GenBank Accession	Country	Collection Date	Release Date	Virus Name
5	AHI48583	Saudi Arabia	2013/07/02	2014/02/06	Middle East respiratory syndrome coronavirus isolate Riyadh_5_2013, complete genome
	AHI48528	Saudi Arabia	2013/07/17	2014/02/06	Middle East respiratory syndrome coronavirus isolate Riyadh_9_2013, complete genome
10	AHI48594	Saudi Arabia	2013/06/12	2014/02/06	Middle East respiratory syndrome coronavirus isolate Taif_1_2013, complete genome
	AHI48550	Saudi Arabia	2013/06/12	2014/02/06	Middle East respiratory syndrome coronavirus isolate Wadi-Ad-Dawasir_1_2013, complete genome
15	AIY60558	United Arab Emirates	2014/03/07	2014/12/06	Middle East respiratory syndrome coronavirus strain Abu Dhabi/Gayathi_UAE_2_2014, complete genome
	AIY60538	United Arab Emirates	2014/04/10	2014/12/06	Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_16_2014, complete genome
20	AIY60528	United Arab Emirates	2014/04/10	2014/12/06	Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_18_2014, complete genome
	AIY60588	United Arab Emirates	2014/04/13	2014/12/06	Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_26_2014, complete genome
25	AIY60548	United Arab Emirates	2014/04/19	2014/12/06	Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_30_2014, complete genome
	AIY60568	United Arab Emirates	2014/04/17	2014/12/06	Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_33_2014, complete genome
30	AIY60518	United Arab Emirates	2014/04/07	2014/12/06	Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_8_2014, complete genome
	AIY60578	United Arab Emirates	2013/11/15	2014/12/06	Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_9_2013, complete genome
35	AKJ80137	China	2015/05/27	2015/06/05	Middle East respiratory syndrome coronavirus strain ChinaGD01, complete genome
	AHZ64057	USA	2014/05/10	2014/05/14	Middle East respiratory syndrome coronavirus strain Florida/USA-2_Saudi Arabia_2014, complete genome
40	AKM76229	Oman	2013/10/28	2015/06/23	Middle East respiratory syndrome coronavirus strain Hu/Oman_2285_2013, complete genome
	AKM76239	Oman	2013/12/28	2015/06/23	Middle East respiratory syndrome coronavirus strain Hu/Oman_2874_2013, complete genome
45	AKI29284	Saudi Arabia	2015/01/06	2015/05/27	Middle East respiratory syndrome coronavirus strain Hu/Riyadh-KSA-2049/2015, complete genome
	AKI29265	Saudi Arabia	2015/01/21	2015/05/27	Middle East respiratory syndrome coronavirus strain Hu/Riyadh-KSA-2343/2015, complete genome
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GenBank Accession	Country	Collection Date	Release Date	Virus Name
AKI29255	Saudi Arabia	2015/01/21	2015/05/27	Middle East respiratory syndrome coronavirus strain Hu/Riyadh-KSA-2345/2015, complete genome
AKI29275	Saudi Arabia	2015/01/26	2015/05/27	Middle East respiratory syndrome coronavirus strain Hu/Riyadh-KSA-2466/2015, complete genome
AKK52582	Saudi Arabia	2015/02/10	2015/06/08	Middle East respiratory syndrome coronavirus strain Hu/Riyadh_KSA_2959_2015, complete genome
AKK52592	Saudi Arabia	2015/03/01	2015/06/08	Middle East respiratory syndrome coronavirus strain Hu/Riyadh_KSA_4050_2015, complete genome
AHZ58501	USA	2014/04/30	2014/05/13	Middle East respiratory syndrome coronavirus strain Indiana/USA-1_Saudi Arabia_2014, complete genome
AGN52936	United Arab Emirates	2013	2013/06/10	Middle East respiratory syndrome coronavirus, complete genome

Table 13. MeV Nucleic Acid Sequences (Reference Example)

Description	Sequence	SEQ ID NO:
<p>GC_F_MEASLES_B3.1 Sequence, NT (5' UTR, ORF, 3' UTR) Sequence Length: 1864</p>	<p>TCAGGCTTTTGGACCTGCTGACAGAGGCTAATAAGGACTCACTATAGGGAAATAGAGAGAAAA GAGAGTAAAGAAATATAAGAGCCACCCATGCGGCTC AAGGTGAAACGTCTGTGCCATATTC ATGGCACTACTGTTAACTCTCCAAACACCCGCGGGTCAAAATTCATTGGGGCAATGCTCTAAG XTAGGGTGTAGTAAATAGGAAGTGC AAGGTACAAAGTTATGACCTGGTCCAGCCATCAATCA TTAGTCAATAAATTAATGCCCAATATAACTCTCTCAATAACAGCCAGGGGTAGAGATTGCA GATACAGGAGACTACTAAGAACAGTTTGGAACCAATTAGGGATGCAC TTAATGC AATGACC CAGAACATAAGGCCGGTTCAGAGCGTAGCTTC AAGTAGGAGACACAAAGAGATTGGGGAGT AGTCTGGCCAGGTGC GGCCCTAGGTTTGGCCACAGCTGCTAGATACAGCCGGCATTGCA CTTCACGGGTCCATGCTGAACCTCAGGCCATCGAC AATCAGAGAGCGAGCTTGGAAAGTAC TANTAGGC AATTGAGGC AATCAGAC AAGCAGGGCAGGAGATGATATTGGCTGTTGAGGGT TCAGAGCTACATCAATAATGAGCTGATAGCCTCTAGAACAGCTATCTTGTGATTAATG GTCCAGAGCTCGGGCTCAAAATGGCTAGATAGTATACAGAAATCCTGTCATATTGGCCCA GGCTAGGGGACCCATATCTGGGGAGATATCTATCCAGGC TTTGAGTTATGCACTTGGAGGA GATATCAATAAGGTGTAGAAAAGCTC GATACAGTGGAGGC GATTTACTAGGCATCTTAGAG AGCAGAGGAATAAAGGCTCGGATAACTCACCTCGACACAGAGTCTACTCTATAGTCTCAG TATAGCTATCCGACGCTGTCGAGATTAGGGGGGTGATTCACAGGGCTAGAGGGGTCT GGTACACATAGGCTCTCAAGAGTGGTATACC ACTGTGCCCAAGTATGTTGCACCCAGGG TACCCTATCTCGAATTTGATGAGTCAATAGTACTTTCATBCCAGAGGGACTGTTGTGAGC CAAAATGCTTTGATACCAGATGAGTCTCTGTC C AAGAAATGCTCCGGGGGTCCACCAGGTC GTGTGCTGTAGACTCGTATCCGGGTCTTTGGGAGCCGGTTCATTTATCACAGGGAGGCT AATAGCCAAATTTGCAATCAATTC TTTGTAAGTGTACACAAAGGTACGATTATTAATCAAGAC CTTCAAGATCTTACATACATTGCTGCCGATCCTGCCCGGTAGTCAAGGTGAACGGCT GACATCCAGGTCGGGACAGGAGGTATCCAGACGCTGTGTACTTGGACAGATTGACCTC GTCTTCCATATCATTTGAGAGGTGGAGGTAGGGACAAATCTGGGAAATGC AATTCGCAAA TTGGAGGATGCCAAGGAATGTTGGANTCAGCGACAGATATTGAGAATATGAAAAGGTTTA TGGAGACTAGCATAGTCTACATCTGATTTGAGTGTGCTTTGGAGGGTGTAGAGGGATCC CACTTAATATGTTGCTCAGGGGGCTTTGTAAACAAAAGGGAGAACAAATTTGGTATGTCAA GACCGGGCTAAAGCTGACCTTACAGGAACATCAAAATCCATGTAAGATGCTTTGATGAT AATAGGCTGGAGCTCGGTGGCCAAAGCTCTTGGCCCTTGGGGCTCCGCCAGGCCCTCT CCCTTCTGACACCGTACCCTGTTGGTCTTTGATAAAGTGTAGTGGCCGGC</p>	35

(continued)

Description	Sequence	SEQ ID NO:
<p>5 GC_F_MEASLES_B3.1 ORF Sequence, NT</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGGGTC TC AAGG TGAAC GTCT CTGCG GTATTC ATGGC AGTACT GTTAACTC TC C AAAC AC CC GCCGGTCAAATTC ATTGGGSC AATC TC TC TAAG ATAGGGGTAGTAGGAATAGGAASTGC AAG CTACAAAGTTATGACTCGTTCCAGCCATCAATCATTAGTC ATAAAATTAAATGCC AATATAACT CTCCCTANT AACTGCAAC GAGGGTAGAGATTGC ABAATAC AGGAGACTACTAAGAAAC AGT TTTG GAAACAHTTAGGGATGCAC TTAAATGC AATGACC CAGAAC ATAGGGCCGGTTCAGAGC GTAGC TTCAGTAGGAGACAC AAGAGATTTCGGGGAGTAGTC CTGGCAGSTGC GGC CCTAGSTGTT GCCACAGCTGCTCAGATAACAGCCGGCATTGCAC TTCACGGGTC CATGCTGAASTCTCAGGC CATGGACAACTCTGAGAGC GAGCC TGGAACTACTAATCAGGC AATTGAGGCAATCAGAC AAG CAGGGCAGGAGATGATA TTGGCTGTTCCAGGGTGTCCAAAGACTACATC AATAATGAGGTGATA GCGTCTGAGAC LAGCTATCTTGTGATCTAATC GGTCAAAAGCTC GGGCTCAAATTCCTAGA TACTATACAGAAATCTTCTATTATTGGCCACAGCCTACGGAGCCATATCTGGGAGATA TCTATCCAGCTTTGAGTTATGCAC TTGGAGGAGATATCAAT AAGSTGTTAGAAAAGCTC GBA TACAGTAGAGGC GATTTAC TAGGCATCTTAGAGAGC AGAGGAATAAAGGCTC GBAATACTCA GGTGACACAGAGTCTACTTCATAGTCTCAGTATAGCCTATCCGAC GCTGTGGGAGATTAA GGGGATGATTGTCCAGCCGCTAGAGGGGGTCTCTGTACAGC ATAGGCTCTC AAGAGTGGTAT ACCACTGTGGCC AAGTATGTTGCAACCC AAGGGTAGCTTACTGGAAATTTGATGAGTCATCA TGTACTTTCATGCCAGAGGGGACTGTGTGCAGCCAAAATGCCTTGTACCCGATGAGTCTCT GCTCCAGAAATGCTCCGGGGGTCCACC AAGTCTGTGGCTC GTACAGCTC GTATCCGGGTCTT TTGGGACCGTTTCAATTTATCACAGGGAAAGCTAANTAGCC AATTTGTCATCAATCTTTGTAA GTGTTCAC AAGAGGTAGCATTTAATCAAGAC CCTGAC AAGATGCTAKD ATACATTCGTC CGATGCTGCTCCGGTAGTGGAGGTAACGGCGGTGACC ATCCAGGTGGGAGCAGGAGGTAT GGNAGCCGTGTACTTTCACAGAAATGACCTCGGTCCCTCCATATCAATGGAGAGGTTGGA CCTAGGGAC AATCTGGGGAATGC AATTGC AAAATTGGAGGATGC AAGGAATTCTTGGAAAT CATCGGACCAGATATTAAGTATGAAAAGGTTTATC GAGC ACTAGCATAGTC TACATCCTGA TTGCAGTGTGCTTGGAGGGTTGATAGGGATCCCACTTTAATATGTTGCTGCAGGGGGCTGT TGTACAAAAGGGAGAAAGAGTTGATATGTC AAGACCAGGCTAAAGCC TGAACCTTACAGG AACATCAAAATCCTATGTAAGATCGCTTGA</p>	<p>36</p>

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Description	Sequence	SEQ ID NO:
<p>5 GC_F_MEASLES_B3.1 mRNA Sequence (assumes T100 tail) mRNA Sequence Length: 1925</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p>	<pre> GTGGCAATTAAGAGAGAAAAGAGAGTAAGCAAGAAATATAAGAGCCACCATGGGTCTCAAGG TGAAGTCTCTGCGGTATTCATGAGAGTACTGTTAACCTCCAAACACCCGCCGGTCAAAATC ATTGGGCAATGCTCTTAAGATAGGGGTAGTAGAATAGGAAGTGCAGGCTACAAAGTTATG ACTGTTCCAGCCATCAATCATTAGTCAATAAATTAAATGCCCAATATAACTCTCCATAAATCT GGACGAGGGTAGAGATTGCAGAAACAGGAGACTACTAAGAACAGTTTTGGAAACCAATTAGG GATCCACTTAATGCATGACCCAGAACATAAGGCAGGTTCCAGAGCCTTAGCTTCAGTAGGAG ACACAGGAGATTTGGGGAGTAGTCCAGGAGGTCAGGTCAGGCGGTAGGTTGGCACAGCTGCT CAGTAAACAGCCGGCATTCAGCTTCAGCGGTCATGCTGAACTCTCAGGCCATCGACAACTCT GAGAGCGAGCCTGGAAACTACTAATCAGGCATTTGAGGCATTCAGAACAGCCAGGAGGAG ATGATTAATGGTGTTCAGGGTGTCCAGAGCTACATCAATANTAGCTGATAGCCTCTATGAC CAGCTATCTTGTGATCTAATCGGTCAGAAAGCTCGGGCTCAAAATGCTTAGATACATACAGNA ATCTGTCTATTATTTGGCCAGCCAGCTACGGGACCCCATNATCTGCGGAGATATCTATCCAGGC TTGAGTTATGCACTTGGAGGAGATATCAATAGGTTTGGAAAGCTCAGATAGAGTGGAGG CGATTTACTAGGCTCTTAGAGAGCAGAGGAATAAAGGCTCGGATAACTCAGGTCAGACAG AGTCTCTATTCATAGTCTCTAGTATAGCCTATCCAGAGGCTGTCCAGATTAAAGGGGTGATTG TCCAGCCGCTAGAGGGGGTCTCTGACAACTAGAGCTCTCAGAGTGGTATACACTCTGTCCTC AGTATGTTGCAAGCCAGGGTACTTATCTGCAATTTTATGATGATCTATCATGTATTTTCATGC CAGGGGGACTGTGTGCAAGCAAAATGCCCTTGTACCCGATGAGTCTCTGTCTGCAAGATGTC CTCCGGGGTCCAGCAAGTCTGTGCTGACACTGATCCGGGCTTTTGGGAGCCGGTT CATTTATCACAGGGAGCTAATAGCCAAATGTGCTATCAATCTTTGTAAATGTTACAGAACN GGTACGATTTAATTAAGACCCGACAGGATCTAACATACATGCTGCCGATCGCTGCGCCG GTATGDBAGGTBAACGGCTGAGGATCCAGTCCGGAGCAGGAGGTATCCAGAGCCTGTST ACTTCCAGAGATTTGAGCTCGGTCCTCCATATCATGGGAGAGGTTGGACGTAGGGCAAAAT CTGGGGATGCATTTGCAAAATGGAGATGCGAGGAAATGTTGGATCATCGGACAGAT ATTGAGAGTATGAAAGGTTTATCAGGCATAGCATAGTCTACATCCGATTGCGAGTGTCT TGGGGGTTGATAGGGATCCCACTTAAATATGTTGCTGCAAGGGGGCTTGTAAACAAAAGG GAGAACAGTTGATGTCAGGACAGGCTAAAGGCTGACCTTACAGGAGATCAAAATCTCT ATGTAGATGCTTTGATGATAAATAGGCTGGAGCTCGGTCAGGCTTCTTGGCCCTTTGG GGCTGGGCGAGCCCTCTCCCTTCTGCAAGCCGACCCGCTGCTTTTGAATAAGTCT TGACTGGCGCAAA AATCTAG </pre>	<p>37</p>

(continued)

Description	Sequence	SEQ ID NO:
<p>5 GC_F_MEASLES_D8 Sequence, NT (5' UTR, ORF, 3' UTR) Sequence Length: 1864</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p>	<p>TCAGCCTTTTGGACCCTGCTACAGAGGTAAATACGACTCACATATAGGGAAATAGAGAGAAAA GAGAGTAAAGAAAGAAATATAGAGAGCCACCCATGCGGCTCAGAGGTGAAGGTCTCTCTGTAATATCA TGGCACTACTGTTAACTCTTCAAACACCCACCAGTCAAAATCCATGGGGCAATCTCTCTAAAGA TAGGGGTTGGTAGGGGTAGGAGTGCAGAGCTACAAAATATGAGCTCGTTCCAGCCATCAATCA TTAGTCAATAAGTTAATGCCCAATATAACTCTCTCAACAAATGCAAGAGGTAGGGATTGCA GANTCAGGAGAGCTACTGAGAACAGTCTGGAAACAAATAGAGATGCATTAATGCAATGACC CAGATATAAGACCAGTTCAGAGTGTAGCTTCAGGTAGGAGACACAGAGATTTTGCAGGAGT TGTCTGGCAGGTGCAGCCCTAGAGCTTGCACAGCTGCAAAATAGAGCCAGTATTGCA CTTCACAGTCCATGCTGAGCTCTCAAGCCATCGACAACTGGAGAGGAGCCTAGAAACTACT AATCAGGCAAATGAGGCAATCAGACAGCCAGGGCAGGAGATGATATTGGCTGTTCAGGCTGT CCAGACTACATCAATAAGAGCTGATACCTCTATGAACTACATCTTGTGATTTAATGAGC CAGAGCTAGGGCTAAATTTGCTCAGATACTATACAGAAATCTGTGTAATTTTGGCCACAGC TTAGGGAGCCCATATCTGCGAGATATCTATCCAGCCCTTGGAGCTATGCTTGGAGGAGA THTCAFAAGGTGTTGGAAAAGCTCAGATACAGTGGAGGTGATCTACTGGCCATCTTAGAGA GAGAGGAAATAAGGGCCGGATACCTCACGTCGACACAGAGTCTAATTCATTTGCTAGT ATAGCTATGCGAGGCTATCCGAGATTAGGGGGTGTATTGTCCACCGCTAGAGGGGGTCTC GTACACATAGGCTCTCAAGAGTGGTATACCACTGTGCACCAATATGTTCCAGCCAGGGGT ACCTTTCCTGAAATTTGATGAGTCACTATGCATTTCTATGGCAGAGGGGACTGTGTGAGCC AGATGCTTGTACCCGATGAGTCTCTGTCCCAAGAAATGCGTCCGGGGGTCACCTAAGTCC TGTGCTGTACACTCGATCCGGGCTTTTGGGAAACCGGTTCAATTTATCACAGGGGAGCTA ATAGCDAATTTGTCATCAATCTTTTGCAGGTGTTACACAAAGGAAACATCAATTAATCAAGAGC CTGCAAGATCTAATACATACATTCCTGCGGATCCAGCCCGGTGCTCGAGGTGAATGGGGT ACCATCCAGTCTGGGAGCAGGAGGTATCCGGAGGCTGTGTACTTGCACAGGATGACCTCG GTCTCCCATATCTTGGAGAGGTTGGACGTAGGGACAAATCTGGGGAAATGCAATTTGCTAAG TTGGAGGATGCCAAGGAAATGTTGGAGTCACTGGACCAGATATTGAGGAGTATGAAGGGTTT ATCGAGCACTAGTATAGTTTACATCTGATTCAGTGTGTCTTGGAGGATGATAGGGATCCC GGCTTTAATATGTTGCTGAGGGGGCTGTTGTAAACAGAGGGGAGAACAGTTGGTATGTCAA GACCGGCTAAAGCCGTGATCTTACAGGAAATCAAAATCTATGTAAGGTCACCTGATGAT AATAGGCTGAGGCCTCGGTGCGCAAGCTTCTTGCCTTGGGGCTCCCGAGCCCTCTCT CCCCTTCTGCACTGACCCGACCCGCTGGTCTTTGAAATAAGTCTGAGTGGGGGG</p>	<p>38</p>

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Description	Sequence	SEQ ID NO:
<p>5 GC_F_MEASLES_D8 ORF Sequence, NT</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGGGTCCTCAAGGTGAACGTCTCTGTGTCATATTCATGGCAAGTACTGTAACTCTTCAAAACACCC ACCGGTCAAATCCATTGCGGCANTCTCTTAAGATAGGGGTTGGTAGGGGTAGGAAAGTGCAGG CTACAAAGTTATGACTCGTTCCAGCCATCAATCATTAAGTCAATAAGTTAATGCCAANTATAACT CTCCCTAACAAATTGCAACGAGGGTAGGGATTGCAGAAACAGGAGACACTGAGAGACAGTTCT GGAACCATTAGAGATGCAGTTAATGCAAATGACCAGAAATAAGACCGCTTCAGAGTGTAGC TTCAGTAGGAGACACAAAGAAATTTGCGGGAGTTGCTCTGCGAGGTGCGGCCCTAGGGCTT GCGACAGCTGCCTAAATAACAGCCGGTATTGCACTTCCACAGTCCATGCTGAGCTCTCAAGC CATGACCACTGTGAGAGCGAGCCCTAGAAACTACTAATCAGGCAAATGAGGCCANTEAGACAGG CAGGGCAGGAGATGATATTGCGCTGTTCAAGGTGTCCAAAGCTACATCAATAATGAGCTGATA CCGTCTMTGAACTCACTATCTTGTGATTTAATCGGGCAGAAAGCTAGGGCTCAAAATGCTAGA TACTATACAGAAATCCCTGCTATTATTGGGCCAGCTTACGGGACCGEATKCTGCGGAGATA TCTATCCAGCTTTGAGCTATGCGCTTGGAGGAGATATCAATAAGGTGTTGGAAAAGCTCGG ATACAGTGGAGGTGATCTACTGGCACTTTAGAGAGCAGAGGAAATAAAGGCCCGGATACCTC AGCTGACACAGAGTCTTCTTCTATTGTACTAGTATAGCTATCCGACGCTATCCGAGATTA AGGGGTGATTGTCCAGCGCTAGAGGGGCTCTGCTACAGATAGGCTCTCAAGAGTGGTA TACACTGTGCGCAAGTATGTTGCAAGCCAGGGTACCTTATCTCGAATTTGATGAGTCACTC ATGCACTTTCATGCGCAGAGGGACTGTGTGAGCCAGAAATGCTTGTACCGGATGAGTCTC TCGTGGAAAGTGCCTCCGCGGGCTCCTAAGTCTCTGTCTGTACTGACTGCTATCCGCGCTC TTGGGAAAGCTGTTTATTTTACAGGGGAACTAATAGCCAAATGTGCACTCAATGCTTTGCG AAGTCTTACAGAGAGAAATCAATTAACTAAGAGCCGAGCAGATCTAAGATACATTGCT GCGGATCCTGCGCGGTGCTGAGGTGAATGGCTGACCTCCAAAGTGGAGCAGGAGGT ATCCGAGGCTGCTGTACTGACAGGAGTGAAGTGGCTGCTCCATATCTTTGGAGAGGTTG GAGGTAGGACAAATCTGGGGAATGCAATTGCTAAGTTGGAGGATGCAAGGAAATGTTGGA GTCACTGGACAGATATTGAGGAGTATGAAAGGTTTATCGAGCACTAGTATAGTTTACATCT GATTGCAAGTGTGCTTGGAGGATTGATAGGGATCCCGCTTCAATATGTTGCTGCGAGGGCC GTTGTACAAAGAGGGAGAACAGTTGCTATGTCAGAGCCAGGCCAAGGCCGTGATCTTACAG GGAACTCAAAATCTCTATGTAGGCTCACTCTGA</p>	<p>39</p>
<p>35 GC_F_MEASLES_D8 mRNA Sequence (assumes T100 tail) Sequence Length: 1925</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>GGGAAATAGAGAGAAAGAGAGTAAGAGAAATAAAGAGCCACCATGGGTCTCAAGG TGAGTCTCTCTCATATTCATGAGAGTACTGTTAACTCTTCAAAACACCCAGCGTCAAAATCC ATTGGGCAATCTCTCTAAGATAGGGTGTAGGGGTAGGAAAGTGCAGACTACAAAGTTATG ACTGTTCCAGCTATCAATCATTAAGTCAATAAGTTAATGCCAANTATAAGTCTCTCAAGAAAT GCAGAGGGTAGGGATTGCAGAAATACAGGAGACTACTGAGAGAGGTTCTGGAGCCAAATAGA GTGCACTTAAATGCAATGACCCAGAAATTAAGAGCCGCTAGAGTGTAGTCTCAAAATAGGAGA CACAGAGATTTGCGGGAGTTGCTCTGCGAGGTGCGGCCCTAGGCGTTGCGCACAGCTGCTC AANTACAGCCGCTATTGCACTTCACTAGCTCATGCTGAACTCTCAAGCCATCGACAACTGSA GAGCGAGCCTAGAAACTACTAATCAGCCAAATGAGGCANTCAGACAGGCGAGGAGAT GNTATTGGCTGTTCAAGGTTGCTCAAGACTACATCAATATGAGCTGATAGCGCTTATGAACTCA ACTATCTGTGATTTAATCGGCCAGAGCTAGGGCTCAAAATGCTCAAGTACTATACAGAAAT CCTGTATTTATTGCGCCAGCTTACGGGACCCTATATCTGGGAGATATCTATCCAGGCTTT GAGCTATGCGCTTGGAGGAGATHCAATAAGGTGTTGGAAAAGCTCGGATACAGTGGAGGTTG ATCACTGGCATCTTAGAGAGCAGAGGAAATAAGGCCCGGATAGCTAGGCTGACAGAGAG TCTACTTCAATTGTAAGTATAGCTTATCGGAGGCTATCCAGAGATTAAGGGGGTGAATTGTC CAGCGGCTAGAGGGGCTCTGTAACAGCTAGGCTCTEAGAGTGTATACACTGTGCTCAAA GTATGTTGCAAGCCAAAGGATCTTATCTCGAATTTTATGAGTCACTATGCACTTCTATGCCA GAGGGGACTGTGTGCAAGCAATGCTTGTATCCGATGAGTCTCTGCTCAAGAAATGCT CCGGGGCTCACTAAGTCTGTGCTGTAAGCTGATCCGGCTTTTCCGGAACCGGTTCA TTTTATCACAGGGGAAAGTAAATAGCCAAATTTGCTATCAATCTTTGCAAGGTTTAACTAACAG GACAACTAATAATCAAGAGCTGACAAAGATCTTAACTATCAATTTGCTGCGGATCACTGCGCG TGGTGAGGTTAATGCGGTGACATCTCAAGTGGAGCAGGAGTATCCGAGGCTGTGTA</p>	<p>40</p>

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Description	Sequence	SEQ ID NO:
<p>5</p> <p>10</p>	<p>CTTGCACAGGATTGACCTCGGTCCCTCCATATCTTTGGAGAGGTTGGACGTAGGGACAAATC TGGGGAATGCAAATTCCTAAGTTGGAGGATGCCAAGGAAATTTGTTGGAGTCAATGGGACAGATA TTGAGGAGTATGAAAGGTTTATCGGAGCACTAGTATAGTTTACATCCTGATTCAGGTGTGCTT GGAGGATTGATAGGGATCCCGCCCTTAAATATGTTGCTCCAGGGGGGCTTGTATACAAAGAGGG AGACAAAGTTGGTATGTCAGGACAGCCCTAAGGCGTGAATCTTACAGGAAACATCAAAATGCTA TGTANGGTCACCTGATGANTAGAGGCTGGAGCCCTCGGTGGCCAAAGTTCTTCCCTTGGG CCTCCGDDCAGCGCTCTCTCCCTCCCTTCCTGCAACCCGTCACCCGCTGGTCTTTGAAATAAGTCT GAGTGGCCGCTCAA AAATCTAG</p>	
<p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>TCAGCTTTTGGACCCCTGCTACAGAAAGCTAATACGACTCACTATAGGGAAATAGAGAGAAAA GAGGAGTANGAAGAAATATAAGAGCCACACATGTCACCCGCAACGAGAGCCGGATAAATGCTTC TCAAGGATAACCCCTTATCCAGGAGAGTAGGATAGTTATTACAGAGAACATCTTATGATTG ACAGACCTATATGTTGCTGGCTGGTGTGTTGTTGCTATGTTCTGAGCTTGAATGGATGCTGG CACTGCAAGGATTAGACTTCATGCGCCAGCCATCTACAGCGGGAGATCCATAAAAGCTC AGTACCAATCTGGATGTAAGTANGTCCATGCGAGCATCAGGTCAGGAGCTGGCTGACACCCACT CTTAATAATCAGCGGATGANGTGGGCTTGAGAACACCTCAGAGATTCAGTCACTAGTGTG AATTCATCTCGCAAGAAATTAATTCCTAATCCGGAATAGGGAGTACGACTTCAGAGATCTCA CTTGGTCAATCAACCGCCAGAGAGGATCAACCTAGATTAATGATCAACTCTGCAAGATG GCTGCTGAAGAGCTCATGAATGCATTGGTGAATCAACTCTACTGGAGACAGAGAACACAC TCAGTCCAGCTGCTCAAGGGGAACCTGCTAGGGCCACTACAAATAGAGGTAATTCCT AACATGTCCTGCTCTGTTGGACTTGTACTTAGGTCAGGCTTACAAATGCTGCTCATATAGT CACTATGACATCCAGGGAATGATGGGGGAACTACTAGTGAAGAGCTAATCTGACAA GCAGAGGCTCAGAGTGTCAACACTGAGCATGTACCAGATGTTTGAAGTAGGTTGTGATCA AACCGGCTTGGGGGCTCGGTGTTCCATATGACAAACTATTTTGAACACCCAGTCAAGTAAT GGTTCGCGCAAGTGTATGTTGGTTGGGGGAGGTCAAACTCCAGGCTTGTGTCACGGGG AGATTCATCATAAATCCCTATCAGGGATCAGGGAAAGGTTGTCAGCTTCCAGGCTGTCAGGC TGGGTGCTGGAAATCCCAAGCGACATGCAATGCTGGTCCCTTATCAAGCGATGATCCAA GTGGTAGACAGGGTTTACCTCTCATCTCACAGAGGTTGCTAGGCTGACAACTAAGCAAAATG GGCCTGTCAGCAACAGAGAGATGCAAGTTGCGAATGGAGACATGCTCCAGCAGCGG TGTAAAGGTAAAATCCAGCACTCTGGAGAACTCCGAGTGGTATCATTGAAGGATAAACAG GATTCCTCATAGGGGTCCTGCTGTTGATCTGAGTCTGACGGTTGAGCTTAAAATCAAAAT TGCCTDGGATTCGGGCCATTGATCAGACACAGGGTCCAGGGATGGACCTATCAAAATCCAACT GCACAAATGTTATTTGGCTGACTATCCGCAATGAGAAATCTAGCCTTAGGCTAATCAACA CATTGGAGTGGATACCAGATTCAGGTTAGTCCCAACCTTCACCTGCTCCAAATTAAGGAAAG CAGGCGAAGACTGACATGCCCAACATACCACCTGCGGAGGTTGACGGTATGTCAAACT CAGTTCAAGCTGGTGAATCTAGCTGGTCAAGATCTCAATATGTTTGGCAACCTACGATAC CTCAGGGTTGAGCATGCTGTGGTTTATTACGTTTACAGCCCAAGCCGCTATTTCTTACTTT TATGCTTTTAGGTTGCTATAAAGGGGCTCCAAATGAACTACAAGTGGAAATGCTTCAATGG GATCAAAATCTGGTGGCTGCTACTTCTGTTGCTTGGGAGTCAGAAATCGGTTGGACTTAT CACTCACTGTTGATGTTGGCTATGGAGTCAAGTCTGCAAGTACCCGGGAAAGTGGAAAC ATGCGCAGATAATGATAATAGGCTGGAGCTCGGTGGCCAAAGCTTCTTCCCTTGGGGCTC CCCCAGCCCTGCTCCCTCCCTGCTGAGCCGTACCCCTGTTGCTTGAATAAGTCTGAGT GGGCGGC</p>	<p>41</p>

(continued)

Description	Sequence	SEQ ID NO:
<p>5 GC_H_MEASLES_B3 ORF Sequence, NT</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p>	<p>ATGTCACC GCAAC GAGAC CCGAT AAATG CTTTC TAC AAAGAT AACCT TATC CC AAGGG AAGT AGGATAG TTTATT AAC AGAGAAC ATCTT ATGATT GACAG ACCCTAT GGTCT GCTGGCT GGTCTCT TCTGTGATG TTTCTGAGC TTGATC GGAATT GCTGGC AATGGC AGGC ATTAGACTTC ATC GGGC AG CCACTAC AC CCG GAGATCC AT AAAAGC CTCAGTAC CAATG TGATGTGACTAAGTCCATC G AGCATCAG GTC AAGGAC GTGC TGAC AC CAG TC TTTAAAA TC ATCGGGGATGAACTGSSCC TG AGACACC TCAGAGATTC ACTGACC TATGAAATTCATC TC GGC AAGATTAAATTCCTTATC CCGTAA GGGAGTAC GACTTC AGAGATC TC ACTTGGTGC ATCAACC CGCCAGAGAGATCAAA CTAGATT ATGATCAACTGTGC AGATG TGGCTGCTG AAGAGGTC ATGAAATGC ATTGGTGAAC TCACTCT ACTGGAGAC AGAACAAC CACTCASTTCCTASE TGTCTCAAAGGGAACCTGCTCA GGGCCACTACAATCAGAGGTC AATCTC AACATGTC GCTGCTCTCTGTTGGACTTGTAGTTA GGTGAGGTTAC AATGTGTC ATCTATAGTCACTATGACATC CCAGGGANTGTATGGGGGAC CTACTAGTTGAAAAGCTTATCTGAAACAGC AAGGGGTCAGAGTTGTCACACTGAGCATGTATA CCGAGTGTGAACTAGGTTGATCAGAAACCCGGGTTTGGGGGCTCGGCTGCTCATATGAA CAAGTATTTGAGC AACCAGTCAGTAATGCTCTCGGC AACTGATGATGGCTTTGGGGGAG CTCAACTG CAGCCCTTTGTCAGGGGAC GATTCTATC AATTCCTATCAGGGATCAGG GAAGGTGTCAGCTTCCAGCTC GTC AAGC TGGGTGCTG GAAATCC CCAACC GACATGCAAT CCTGGGTCCCTTATCAAC GGAATGATC CAGTGGTACAGGCTTTACCTCTC ATCTCAGAG GGTGTCATC GCTGAC AATC AAGCAAAATGGCTGTCC CAGCAACAC GACAGATGAC AAGTT GCGAATGGAGAC ATGCTTC CAGCAGGC GTGTAAGGTAAATCCAAAGC ACTCTCGGAGATC CCGAGTGGGTACC ATTTGAAGGATACAGGATTCCTTC ATACGGGGTCTG TGTGATCTG AGTCTGAC GGTGAGCTT AAAATC AAAATTGCTTCGGGATTCGGGCCATTGATCACACAGG CTCAGGGATGGACT ATACAAATCC AACTGCAAC AATGTGTATTGGCTGACT ATTCGCCAAT GAGAAATCTAGCTT TAGGCCTAATC AACACATTGGAGTGGATACCGAGATTC AAGGTTAGTCC CAGCTCTTCACTGTCC CANTTAAGGAGACAGG GAAAGCTGC ATGCCCAACATACCTAC CTGCGGAGGTGGAGGTTGATG TCAAACTCAGTTC CAAAGCTGGT GATTCTAGC TGGTAAAGAT CTCCATATGTTTTGGCAACCTAC GATACCTCCAGGGTTGAGCATGCTGTGGTTATACGTT TACAGCC AAGCCGC TCAATTTCTACTTTATCCTTTAGGTTGCTATAAAGGGGGTCCAA TDGACTAC AAGTGGANTGCTTAC ATGGATCAAAAAC TC TGCTGCCCTC ACTCTGTGTGC TTGGGACTCAGAAATCCGGTGGACTTATC ACTCACTCTGGGATGGTGGCATGGAGTCCAGC TGCACGCTACC GGGGAAGATGGAACTATC GCAGATAA</p>	<p>42</p>

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Description	Sequence	SEQ ID NO:
<p>5 GC_H_MEASLES_B3 mRNA Sequence (assumes T100 tail) Sequence Length: 2126</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p>	<p>GTGKRRAT KASGAGAAAAABRAGAG IARGAAGAAAI A IAAAGKUCACU B I B I C A U DUC AAC GAGACCGGAT AAATGCGCTTCACAAAGATA AGC CTTATCCG MAGGGAAGTAGGATAGSTATT A ACAGAGAACATGTTATGATGACAGACCCCTATGTTCTGCTGGCTGTTCTGTTGTCATGTTTCT GAGCTTGATC GGATTGCTGAGCAATTGCAGGCATTTAGACTTCATCGGGCAGCCATCTACACCG CGAGATGTCATAAAAGCCTCABTACC AATCTGGATGTGACTAAGTCCATCGAGCATCAGGTC AAGGACGTGCTGACACACCTTTAAAATCATCGGGGATGAAGTGGGCTGAGAACACCTCA GAGTTCACTEACCTAGTBAAATTCATCTCGAC AAGATTAAATTCCTTAAATCGGATAGGGA GTACAGCTTCAGAGATCTCACTTGGTGCATCAACCCGCCAGAGAGGATCAACAGTAGATTATGA TCANTACTGTGAGATGTGGCTGCTGAAAGACCTATGATGCAATTGGTGAAC TC AACTCTACT GGAGACTAGAACACACTACTAGTTCCAGCTGCTCA AAGGGAAAGTGC TCAGGGGCCACTA CAGTCAGAGGTC AATTCTCAAAACATGTCCTGCTCTGTTGTTGAC TTTAGTTAGGTC GAGGTT ACANTGTGTCATCTATAGTCACTATGACATCCAGGGAAATGATAGGGGAAAGCTACTAGTTG AAGGCTAATCTGAAAGCAAAAGGGTCAGAGTTGTCACAGTGAAGCATGACCGAGTGT GAGTTAGGTTGTGATCAGAAACCCGGGTTGGGGGCTCCGGTGTTCATATGACAAACTATT TGAGCAACAGTCAGTAATGGTCTCGCACCTGTATGTTGGCTTTGGGGAGCTCAAACTCG CAGGCTTTGTCAGGGGACGATTCATCTATAATTCCTATCAGGGATCAGGGAAAGGTTGTC AGCTTCAGCTGCTCAGCTGGGGTGTCTGGAAATCCCAACCGAGATGCAACTCTGGTCC GTTATCAAGGATGATCCAGTGGTAGACAGGCTTTACTCTCTCATCTCAGAGAGGTTGTCATGSC TGACATCAAGCAAAATGGCTGTCGGACACACAGACAGATGACAGGTTGCGAATGGAGGA CATGCTTCCAGCAAGGCTGTAAAGGTAAAATCCAAAGCCTCTGCGAGAAATCCGAGTGGGT CCATTGAAGGAT AACAGGATTCCTTCATAGGGGTCCTGTCTGTTGATGTGAGTGTGACGGTT GAGCTTAAATCAAAATTTCTGGGATTCGGGGCATTGATCACACAGGGCTCAGGGATGGA CCTATACAAATCCAACTGCAAC AATGTGTATTGGCTGACTATTGCGCCATGAGAAATCTAGC GTTAGGCGTAAATCAACACTTTGGAGTGGATACCGAGATTCAGGTTAGTCCCAAGCTCTTCAC TSTCCAAATTAAGGAAGCAGGCAGAGACTGCCCATGCCCCAACATAACTACTCTGCGGAGGTG GAGGTTGATGTC AAGCTAGTTCCAACTGGTATTCTACTGGTCAAGATCTCC AATATGTT TTGGCAGCTACGATACCTCAGGGTGAAGATGCTGTGGTTATTAGCTTTTACAGCCAAAGC GCTCATTTCTTAC TTTTATCTTTAGGTTGCTTAAAGGGGGTCCCAATCBAACTAC AAG TGGATCTTCACATGGATCAAAAACCTGGTGCCTCAGCTCTCTGTGCTTGGGGACTCA GATCCGGTGGACTTACTCTACCTCTGCGGATGGTGGCCATGGGAGTCAAGCTGACAGCTAC CCGGAGATGGAACTAATCCAGATATGATATAAGGCTGGAGCTGGGTGGCCAAAGCTTC TTGCTCTTGGGCTCCCCAGCCCCCTCTCCCTTCTGCAACCCGTACCCCTGTGGTCTT TGATTAAGCTTGAGTGGGCTGGCAAA AATCTAG</p>	<p>43</p>
<p>45 GC_H_MEASLES_D8 Sequence, NT (5' UTR, ORF, 3' UTR) Sequence Length: 2065</p> <p>50</p> <p>55</p>	<p>TCAGGCTTTTGGACCTCCTGACAGAGCTAATAGGACTCACTATAGGGAAATAGAGAGAAAA GAGAGTAAAGAAATATAAGAGCCACACTGTEACCAAGGAGACCGGATAAATGCCCTTC TACAGGACAGCCCTATCTAAGGGAAAGTAGGATAGTTATTAACAGAGAACATCTTATGANT GATGACCTTATGTTTGGTGGCTGTTCTATTGRTATGTTTGTAGCTTGATCGGGTTGCTA GCTATTCAGGCTATTAGACTTCATCGGGCAGCCATCTACAGGCGAGAGATCCATAAAAGCCT CAGCCAAATCTGGATSTAACTAACTAATCGAGCATCAGGTTAAGGACGTGCTGACACCCAC TCTTCAAGATCTCGGTGATGAAAGTGGGCTTGGAGACACTCAGAGATTCAGCTAGCTAGTG AAGTTCATCTGAC AAGATTAAATTCCTAATCCGGACAGGGAAATACGACTTCAGAGATCTC ACTGGTGTATCAAGCCGACAGAGAAATCAAAATGGATTATGATCAANTACTGTGAGATGTG</p>	<p>44</p>

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Description	Sequence	SEQ ID NO:
<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>GCTGCTGAAGAAATCATGAAATGCATTGCTGAACTAACCTCTACTGGAGACCAAGGCCAACCAA TTAGTTCCTAGGCTGTCTCAAGGAGGAAGCTGCTCAGGGCCCACTACAAATCAGAGGGCCAAATTC GAAGCATGTCGCTGTCCCTGTTGGACTTGTATTTAAGTCGAGGTACAAATGTGTCATCTATAGT CACTATGACATCCAGGGGAATGTACGGGGGAACTTAGCTAGTGGAAAAGGCTAATGTEAGCA GCAAAGGGTCAAGAGTTGTCAAACTGAGCAATGCAACCGAGTGTGTAAGTGTGTTATAGAA ATTCGGGTTTGGGGGCTCCGGTATTCCATATGACAAACTATGTTGAGCAACCAAGTCAAGTAT GATTTCAGCAACTGCAATGGTGGCTTGGGGGAGCTCAAGTTCCGAGCCCTCTGTCTCAGGGGA AGGTCTATCAGCAATTCCTATCAGGGATCAGGGGAAGGTGTGAGCTTCAGCTTGTCAAGCT AGGTGCTGGAAATCCCAACCGACATGCAATCCGAGGTCCCTTATCAACGGATGATCCAG TGAAGACAGGGCTTACGCTCAGTCAGAGGGCTTATGCTGACAACTAAGCAAAATGGGG CTGTCCCGCAACACGGACAGATGACAAATTCGGAATGGAGACATGCTTCAGCCAGGGCTGT AAGGTAATAATCCAAAGCACTTTGGGAAATCCGAGTGGACACCAATTGAAGGATACAGGAT TCCCTCAACGGGGTCTTGTCTGTTGATCTGAGTCTGACAGTTGAGCTTAAATCAAAATGTT TCAGGATTCGGGCAATGATCACACAGGTTCAAGGATGGAGCTATACAAATCCAGCCACAA CAGATGATTGAGCTGACTATCCCGCCAAAGGAAGAACCTGGCTTAGGTGTAAATCAACCAAT GGAGTGGATACCGAGATTCAAGGTTAGTCCCAAGCTTTCAGTGTTCCAATTAAAGGAAGCAG GCGAGGACGTCATGCCCCAAGATACCTAGCTGCGGAGGTGGATGCTGATGTCAAACTCAGT TCCATCTGGTGAATCTACTGCTCAAGGAGCTCCAAATATGTTCTGGCAAGCTACGATACTCC GAGTGGACATGCTGTAGTTTATTACGTTTACAGCCCAAGCCGCTCATTTCCTTACTTTATCC TTTTAGTTGCCGTAAAGGGGGGTCGCCATTGAATTACAAATGGAATGCTTCACATGGGAC AAAACTCTGCTGCCGTCACCTCTGTGCTGCTGGAGTCAAAATCTGGTGGACATATCAGTC ACTCTGGATGGTGGGATGGGAGTCAAGTGCACAGCCACTCAGGAGATGGGAAGGATGGGAAGC CAGTATGTATAATAGGCTGGAGCTCGGGTGGCCAAAGCTTCTTGGCCCTTGGGGCTCCGCC AGCCCTCCCTCCCTTCCGCAACCGTACCCCGTGGTCTTGGAAATAAGTCTGAGTGGGG GC</p>	
<p>35</p>		
<p>40</p>		
<p>45</p>		
<p>50</p>		
<p>55</p>		

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Description	Sequence	SEQ ID NO:
<p>5 GC_H_MEASLES_D8 ORF Sequence, NT</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p>	<p>ATGTCACCACAGCAGACGGGATAAATGCTTTGTCACAAAGACAAACCCCATCCCTAAGGGAGG TNGGATAGTTAATAACAGAGAACATCTEATGATGGATAGACCITATGTTTTGCTGCTGTGTTA TTGTCATGTTTCTGAGCTTGTATCGGTTGCTAGCCATTGCAAGGCAATTAGACTTCATCGGGCA GCCATGTACACCGCAGAGATCCATAAAAGCCTCAGGACCAAGCTGGATGTAACTAACTCAATC GAGCATCAGGTTAAGGACGTGCTGACACCACCTTCAGAGTCATCGGTGATGAGTGGGGTT GAGGACACCTCAGAGATTCAGTGAACCTAGTGAAGTTCATCTGTGACAGATTAAATTCCTTAA TCCGGACAGGGAAATACGACTTCAGAGATTCACCTTGGTGTATCAACCCGCCAGAGAGAACTA AATTGGATTATGATCAATACTGTGCAGATGTGGCTGCAGAGAACTCATGAATGCATTTGGTGA ACTCACTCTACTGGAGAGCCAGGGCAACCAATCAGTTCTAGCTGTCTCAAGGGGAACATGC TCAAGGGCCACTACANTEAGAGGCAAAATTCMAACATGTGCTGTCTCTGTTGGACTTGTAT TTAAGTCGAGGTTACAAATGTGTCTATATAGTCACTATGACATCCAGGGAAATGTAGGGGGAA ACTTACCTAGTGGAAAGCCATANTGTGAGCAGCAAAAGGGTCAGAGTTGTACAACTGAGCAT GCACCGAGTGTGTTGAGTAGGTGTTATCAGAAATCCGGGTTTGGGGGGCTCCGGTATTCCATA TGACAACTATCTTGGAGCAACAGTCAAGTATGATTTCAAGCACTGCAAGTGGGTTTGGGGG AGCTCAAGTTCGCAGGCCCTGTGTCACAGGGAGGATTCATCAAAATTCCTATCAGGGATCAG GGAAAGTGTGCACTTCCAGCTTGTCAAGCTAGGTGTCTGGAAATCCCAACCGACATGCAAA TCTGAGGTCCTCTATCAGGGATGATCCAGTATAGACAGGCTTTAGCTCCTCATCTCACAGAA GGCTTTATCGCTACAACTAAGCAAAATGGCTGTCCCGACAAACAGGAGATGACAGGTT GCGAATGGAGACATGCTTCCAGCAGGCGTGTAAAGGATAAATCCAGGCACTTTCGGAGAACTC CCGAGTGGACACCATTGAAGGATACAGGATTCCTTCATAGGGGTTGTTGTTGTTGATCTGA GTCTGACAGTTGAGCTTAAAATCAAAATGTTTCAGGATTCGGGCCATTGATCACACAGGTT CAGGGATGGACCTATACAAATCCAAACACAAATATGTATTGGCTGACTATCCCGCCATGSA AGACCTGGCTTATAGGTGTAAACACAGTTGGAATGGATACCAGATTCAGGTTAGTCCC AACCTCTCACCTGTCCAAATTAAGGAAGCAGGGGAGGACGCCCATCCGCCAACATACCTACCT GGGGAGTGGATGGTGTATGTCAAACTCAGTTCCAATCTGGTATTCATGCTGGTCAAGATCT CCANTGTGTTCTGGCAACCTACGATACCTCCAGAGTGGAAATGCTGTAGTTTATTACGTTTAC AGCCAAAGCCGCCTATTTCTTACTTTTATGCTTTTAGGTTGCTGTAAAGGGGGGTCCCAAT GATTTACAGTGGAAATGCTTACATGGGACAAAACCTCTGGTGGCTGCTACTCTGTGTGCTT GGGGCTCAGAACTCTGTGGACATATCACTCACCTCTGGGATGTTGGGATGGGAGTCAAGCT GCACAGCCACTCGGGAAGATGGACAGCCGCAAGATAG</p>	<p>45</p>
<p>GC_H_MEASLES_D8 mRNA Sequence (assumes</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>GGGGAAATAGAGAGAAAAGAGAGTAAGAAAGAAATATAAGGCCACCATGTCACCAAC GAGACGGGATAAATGCCCTTCTCAAAAGACAAACCCCATCCCTAAGGGGAAGTGGATAGTTA ACAGAGAACATGTTATGATTAAGACCTTATGTTTTGCTGGCTGTTCTATTCTATGTTCT</p>	<p>46</p>

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Description	Sequence	SEQ ID NO:
<p>5 T100 tail) Sequence Length: 2126 10 15 20 25 30 35</p>	<pre>GAGCTTGATCGGGTTGGTASGCCATTGGAGGCAATAGACTTCATCGGGCCAGCCATCTACACCG CAGNGATECATANAAGCCTCAGCACC AATCTGGSATGTANC TANCTCAATCGASEATCAGGTTA ASGAGGTGCTGACAC CACTCTTC AAGATC ATCGGTGATG AAGTGGGTTGAGGACACCTCAG AGATTCAC TBAICTAGTG AAGTTCATCTCTGAC AAGATTAAATTCCTTAATCGGGACAGGGA TAGGACTTCAGAGATCTCACCTTGGTTGTATCAACCCGGCCAGAGAGAAATCAAATTTGGATTATGAT CAGACTGTGTAAGATGTGGCTGGCTGAAGAATCCATGAATCCATTGGGTAACCTCAACTCTACTG GGAGCCAGGGCAACCAATCAGTTCTAGCTGTCTCAAAGGGAAGCTGCTCAGGGCCCACTAC ATCAGAGGC CAATTCACAACATGTCGCTGTCCTGTTTGGACTTGTATTAAAGTCGAGGTTA CAGTGTGTCATCTATAGTCACATATGACATCCAGGGAAATGTAAGGGGAACCTACCTAGTGA AAGGCDTAACTGAGCAGCAAGGGGTCCAGGTTGTCACAATCGAGCAGGCGCAGCTGTTG AAGTASGTTGATACAGAAATCCGGGTTTGGGGCTCCGGATTTCCATATGACAAACTATCTTG AGCAAGCAGTCAAGTAAGTATTCAGCAACTGCATGGTGGCTTTTGGGGAGCTCAAGTTCGCA GGCCCTGTTCACAGGGAAGATTCATACCAATTCCTATCACAGGATCAGGGAAAAAGTGTACAG CTTCCAGCTTGTCAAGCTAGGTGTGTGGAAATGCGCACAGCACATCCANTCCGGGTCGCC THTCACGGATGATCCAGTGAATGACAGGCTTACCTCTCATCTCACAGAGGCGTTATCGCTG ACANTCAACAAAATGGGGTGTCCGACAAACAGGACAGATGACAAGTTGCAANTCGAGAC TGCTTCAGCACAGCTGTGTAAAGGTTAAAATDCAAAGCACTTTCGAGANTCCAGAGTGCACAC ATTGAAGGATAACAGGATTCCTCATAAGGGGCTTGTGTGTGATCGTACGCTGACAGTTGA GCTTAAATCAAAATTTGTTACAGGATTCGGGCCATTGATCACACAGGTTCAAGSATGAGACCT ATACAAATCCAGCCAGCAATATATGTTGCTGACTATCCCGCCANTGAAGAACTGGGGT AGTTGTAAATCAACACATTTGAGTGGATACCAGGATTCAGGGTTAAGTCCCAACCTCTCACTGT TCCAAATTAAGGAAGCAGGGGAGAGACTGCCATGCCACCAGCACTCACTGCGAGAGGTTGAT GGTGATGTCAAACCTCAGTTCCAAATCTGGTGATTCTACC TGGTCAAGATETCAMATATGTCTG GGAGGTACGATACCTTCAGAGTTGAAACATGGTGADTTTATTACGTTACAGCAGCAGAGCCGC TCAATTGCTTACTTTTTACTTTTAAAGTTGGCTTGTAAAGGGGGTCCCAATTGAATTACAGCTGG AGTGGTTACAGATGGGACC AAAAAGCTGTGGTGCCGTC ACTTCTGTGTGCTTGGGAGTCAGAAAT CTGGTGGACATATCACTCACTCTGGGATGTTGGGACATGGGAGTCAAGCTGCACAGCCTCS GGAGATGGAGCACAGCCAGATAGTGAATAGGC TGGAGCCTCGGTGGCCAGGCCTTCTT GGCCCTTGGGCGCTCCCCAGGCCGCTCCCTCCCTCTGACAGCCGCTGGTCTTGG AATAAGTCTGAGTGGCCGCCAAA AATCTAG</pre>	

MeV mRNA Sequences

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Description	Sequence	SEQ ID NO:
<p>5 GC_F_MEASLES_B3.1 Sequence, NT (5' UTR, ORF, 3' UTR) Sequence Length: 1864</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p>	<p>UGAAGCUUJUGGAGCCUUCUACAGAAAGCUAAUACGACUCACUUAUAGGGAAAUUAGAGAGAA ANGASAGUAAAGAAAUUAAAGAGCCACCAUUGGGUCUCAAAGGUGAAGGUCUUCUGCCGU AUUCAUUGGCAGUAGUUGUUAACUCUCCAAACACCCGCCGUCAAAUUCAUUGGGGCAUCU CUUNAGUJAGGGGUAGUAGGAAUAGGAAUGCAAGCUCACAAAGUUAUGACUCUUGUCCAG CCACCAUCUUUAGUCUJAAAAGUUAUUCGCAAUUAUACUCUCUCUCAAUAACUCACAGGG GUAGAGUJUCAGAAUACAGGAGACUUAUAAAGAGUJUUUGAACCANUUAGGGAUUCA CUUAUUCANUAGCCACAGAACAUAAAGGCGGUCUACAGGCUJAGCUUCAAAGUAGGAGACAC ANGAGUJUCGGGAGUAGUCCUUGGCAGGUCGCGGCGUAGGUUUSCCACAGGUGGUC GAAACAGCCGGCAUUGCACUUCACCGUCCAUUGGUAACUUCAGGCUAUCGAGCAAUUCU GAGGCGGAGCUGGAAACUACUUAUUCAGGCANUUGAGGGAAGCAGACAGGAGGGAAGGA GUUCANUJUGGCUUUCAGGCUJCCAGACUACAUCAUUAUAGGAGGUGGAGUAGCUGUUAU GAKTASCUAUCUUUGUACUUAUUCGCGUCAGAGGUCGCGGUCUCAAUUUGUAGUUAUUA UACAGAAUUCUGUCAUJAUUUUGGCGCCAGCCUACGGGACCCAUAUUCUGCGGAGAUJUC UUCAGGCUUJAGUUAUJUCACUUGGAGGAGUUAUUAAGGUGUUAAGAAAGGUCGCG AUJAGUJGAGGCGAUUUAUUAAGGCUAUUCUUAAGAGAGAGAGGAAUAAAGGCUUCGAAUAC UCAAGUCACACAGAGUCUJACUUCUUAJUCUCUAGUUAJAGCUGAUCCGACGCGUGCCGA GAAUAAAGGGGUGUUAUUGCCACCGGCUAGAGGGGUGUCUUAACAAUAGGGUUCAGAA GUGGUUACACUGUUGGCAAGUUAUUGUACACCCAGGGUAGCUUAUUCUUAUUAUUGA UGAGUACUAGUUAUUCUAGGCGAGAGGGAGUUGUUGAGCCAAAAGGCGUUGUAGCC GAUAGUCCUCUGGUCUAGAGAGUUCUGGGGUGUCCAGAGUCCUGUUCUGUACAGU CUGUAGCGGUCUUAUUGGAAACCGUUCUUAUUAUACAAAGGAAACUUAUJAGCCANUUG UCCACANUCUUAUUAAGUUGUACACAAAGGUCAGGAGUUAUUAUUAUUAUUAUUAUUAUUA AUCCUACAUACAUUGCUUGCCGAAUCUUGCCCGGUAGUCGAGGUGAGAGCGGUGAGCCAU CAGUCCGAGCAGGAGGUUCCAGAGGCGUGUAGUUAUUAUUAUUAUUAUUAUUAUUAUUAU CCGACUACAGGAGAGGAGUJGACGUAGGACAAAUUCUGGGGAAUUCAGUCCAAAUUG GAGGAGCCAAAGGAAUUGUUGGAGUUAUUGGACAGAUUAUUAUUAUUAUUAUUAUUAUUAU UCGAGCUCUASCAGUUCUACAUUCUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAU CCCACUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAU UCAGACAGGCGUAAAGCCUAGACUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAU GAUGUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAU CCGUUCUUCUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAU GC</p>	<p>69</p>

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Description	Sequence	SEQ ID NO:
<p>5 GC_F_MEASLES_B3.1 ORF Sequence, NT</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<pre> AUGGGUUC AAGGUGAAC GUUUGGUC GU AUUC AUGGC AGUACUGUUAACUCUC CAACA CCDCCGCU CAANUUC AUUGGGGCAAUUUCUCUAAGAUAGGGGUAGUAGGAAUAGSAAU GCAGGUC AACAGUUUAGCAGUC GU UCCAGCC AUC AUUC AUUAGUC AUAAAUAUAGCC CA AUUUAUCUCUC UCANUAC UGC AC GAGGGU AGAGAUUCAGAAUUCAGGAGACUAGUAA AACAGUUAUGGAC CAUUAAGGAUUC AUUAAUGCAAGUACC CAGAAC AU AAGGCCGGU UCAGAGT GUAGCUU CAAGUAGGAG AC AC AAGAGAUUUCGGGAGUAGUCCUGGCGAGUUC GGCCUAGGUGUGUC AC AGUCUCUCAGAAACAGC GGGU AUUGCAUUC ACCGGUC CAU GUAGACUCUCAGGUC AUC GAC AUUC UGAGAGCGAGCCUGGAAACUACUUAUCAGGC AUU UGAGGCAALUCAGAC AAGCAGGUC AGGAGUUGAUUU GGU UGUUCAGGGUGUCCAAGAC UA CAUCANUUAAGAGUC UGUAJCT GU CUAUGAACAGCUUUCU UGU GAUCUUAUC GUUCAGAG CUUGGGUC AAAUUC UUGAGAUACU AUACAGAAUCCUGUC AU UAUUGGCC CAGCCUA CGGGCCC CAUAGUUC GGAGAUU CU AUCCAGGCCUU UGAGUUAUGC ACUUGGAGGAGAU AUCAUAAGGUGUUAGAAAAG UC GUAJAGUUGGAGGC GAUUAAGUAGGCAUC UUGAG AGCAGAGAGAAAGGCUUGGUAUCUC AGUC GAC AC AGAGUC CUADUUC AUAGUCUC A GUUAJGDCUUCUC GAC GUCUGUCAGAUU AAGGGGGUGAUUGUC ACCGGUCAGAGGG GUUCUGUC AACAUAGGCUUCAGAGUGUUAUC CACUGUC CAAAUUUC UUC AACCC CAGGGUACCUAUUC GAKUUU UCAUGAGUC AUC AUUUAUUC AUGCCAGAGGGACU GUUGUCAGC AAAUUC CUUUAUC CGAUGAGUCUC UGCUC AAGAAUUCUC C GGGGG UCCAGAGUC UGUUCUCGAC UC GU AUC CGGUC UUUUGGAAACC GGUC AUUUU A UCACAGGGAG UC AAUAGCC AAUUGUC AU CAUUCUUU GU AAGUUAUC AC AACAGU A CGAUUAUAUC AAGACCCUAG AAGAUUC AAC AUAC AUUCUUCGUC GUC GUCUC CCG UAGUCAGGUGAAAGGUC UGAC CAUC AAGUCGGAGCAGGAGUUAUC AGAGGUCUGG UAUUGGAGAGAAUUGACUCGGUC CUCCAUUC AUUGGAGAGGU UGGAC GUAGGAC A AUUUGGGAUUC AUUGCC AAUUGGAGAGG C AAGGAUUGUUGGAUUC AUGGAC CAGUUAUGGAGAGUUAUGAAAGGU UUAJGAGC AUAAGC AUAGUC UAC UC GAUUC A GUUGUCUUUGGAGGUGAU AGGALUC CU ACUUAUAU GUUGUCUCAGGGGUCUGG UACAAAAAGGAGAACAGU UGUUAUGUACAGAC CAGGUC UAAAGC UUGAC CUUACAGGA ACUCAAUUC UUAUGUAAGAUUCGULUGA </pre>	<p>70</p>
<p>35 GC_F_MEASLES_B3.1 mRNA Sequence (assumes T100 tail) mRNA Sequence Length: 1925</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<pre> GGGGAAU AAGACAGAA AAGAGAGUAGA AGAAU AUAGAGCC AC CAUGGGUUC AAG GUAGCUCUCUCGUUC GU AUUC AUGGC AGUACUGUUAACUCUC CAACAACC CGCC GGUC AA AUCAUUGGGCAUUCUCUCUAAGAUAGGGUAGUAGGAAUAGGAAUUC AAG UACAAA GUUUAUCUCUGUC AC CACA AUC AUUAGUC UAAAAUU AUUCUCCAUUAUC UCUC UCAUUACUC AC GAGGUUAGAGAUUC AGAAU AC AGGAGACU AU UAGAACAGUUAUG AACC AUUAGGAGUC AUUAUUC AUAGACC CAGAC AU AAGGCCGGUC AGAGC GUAG GUUCAGUAGGAG AC AAGAGAUUUC GGGAGUAGUUCUUCGCGGUC AGGUUCGGUC CUAGGU GUUGCCACAGUCUC AUUAAC ACCG GGC AUUGC AUUCACC GGGUC AUGGUAGAUUCU CAGGCUCAC AAUC UCAGAGCGAGCC UGGAAACU ACUUAUC AGCC AAUUGAGGC AUC AGCACGCAGGCGAGGAGUUAU UGGUUGUCAGGUGUC CAGAC UAC AUCAUAU GAGGUAUACUCUC UAU GAACAGC UAUUUGUUAU CUAAUCGUC AGAAGCU GGGGUC AAUUCUJAGAU ACUUAUC AGAAUUC UGUC AUUAUUGGGCC AC CUAAG GGGACCC A UUCUCGCGAG AUUCU AUC AGGCU UUGAGUUAUC ACUUGGAGGAG AUUAUAAUAGG UGUUAAGAAAG UC GUAJAGUUGGAGGC GAUUAAGUAGGC AUUUAAGAGAGCAGGAA UAGGCUUCGGAAUC UC ACUC GAC AC AGAGUC CUAUUC AUAGUCUC AU UAAGCCU A UCGAGUCUCAGAAUUAAGGGGUGAU UGUCAC CGGCU AAGGGGUC UC GUACA ACUAGUCUC AAGAGUGGUAUC ACUUGUC CAGUAGUGUC AACC AAGGGUAC UUUUCUCAAUU UUAUGAGUC AUC AUUAUC UUUU UUGCCAGAGGGACUUGUCAGC AAUUGCCUUGU ACC CUAUGAGUCUCUGUC CAAGAAUUC UC CCGGGUCC AC CAUJ GUUGUCUC GUACUUC GUUCCGGGUC UUGGGAAUC GU UC AUUUAUC AAGGGA ACUUAJAGCC AUUGUC AUC AUUCUUAUGUAAGUUAUC AACAGGUAUC GAUAUU AA UCAGACCUAGAC AAGAUUCUAUC AUAC AUUCUGCCG AU EGC UGCCGUUAAGUAGGAGU GACGUC GUGACC AUC CAGUCGGGAGCAGGAGUAUC CAGACCUUGUACUUCACAG </pre>	<p>71</p>

(continued)

Description	Sequence	SEQ ID NO:
5	<pre> MUUGACDUCGGUCCUCDCAUUUCNUUGGAGAGGUUGGACGUAGGGACAAUUCUUGGGAA UGCANUUGCCAAAUUGGAGGAGGCGAAAGGAAUUGUUGGAMJCAUCGGACCAGAUAGUAG MGGUUGAAAGGUGUUUAGUGAGGCACUAGCCAGUUCACAGCCUUGAUUGCAQUUGUUCUUGG AGGGUUGAUAGGGAUCCACUJUAUUAUAGUUGUCUUCAGGGGGGGHIGUANCAAAAGGG NGARCAAGUUGGUAGUCAGGACCAGGCUAAGAGGDUAGCCUUACAGGAAACAUCAAUUC UAGUAGAGGUCGCCUUUGAUGGAAAUAGGDUJGAGGCUCUGGUGGCCAAGCUUCUUGCCCU UGGGCCUCCCGCCAGCAGCCUCUCCCGUUCUCGCACCUGUACCUCUUGGUGUUUUGAAU AGUCUUAGUGGGCGGCAGAAAAAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAA AA </pre>	
<p>15 GC_F_MEASLES_D8 Sequence, NT (5' UTR, ORF, 3' UTR) Sequence Length: 1864</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<pre> UACGGCUUUGGACCUCGUCACAGAGCUAAUACGACUCACUUAAGGAAAUAGAGAGAAA MGASAGJAAGAAAGAAUUAAGAGGCAGCAUUGGUCUUCAGGUUGAACGUCUCUGUCUAU UUCAGGGCAGUACUUGUAGCUUUCAAACACCCAGCGUCAAUCCAUUGGGGGAAUCUC UCUAGUUAAGGGGUGUAGGGGUAGGAGUUCAGGUUCAAAGUUCAGGUCAGUCUGUCAGC CUCACAUCAUUGGCAGAAAGUUAAGUCCAGUAUAAGUCUCCUCACAAUUCGACGGGG UAGGUAUUCAGAAUACAGGAGACUADUGAGAAACAGUUCUGGAGACANUAGSAAUUCAC UUUAUGCCAGUGACCCAGAAUUAAGACGGUUCAGAGUUAAGCUUCAAAGUAGGAGACAA SAGUUUUCGGAGUGUUCUGUCGAGGUGCGGCCUAGGCUGUUCGACAGGUUCGCAA UACAGCGCGUAUUCACUUCACGAGUCAGUCUAGCUGAACUCUACAGCCAGUUCAGUA GAGCGACCUGAAACUUCUAUUCAGGCUAAUSAGGCCAUCAGACAGGAGGGSCAGGAGA UGAAUUGGGUGUUCAGGGUGUCCAGGACUACUCAAUAAUAGGUCUUAUAUCCUGUAUGA AUCACUUCUUAUUAUUAUCGGCCAGAAACUAGGGGCUCAAUUUGUCAGAAUACUUAUC AGAAUCCUGUCAUUAUUGGCGCCAGCUUACGGGACCCAUUCUUCGGGGAAUUAUCUUA CCAGGCUUGAGCUAUGCGCUUGGAGGAGAUUCAAUAGSUGUUGGAAGGCUUGGAAUA CAGUGGAGGUGUUCUUCUGGCUUAUAGAGACAGAGAAUAAAGGCCCGGUAUACUCUA GGUUGGACAGAGUCUGACUUAUUUUAUCAGUUAAGCCUUAUCGACCUUUCGAGUUC UAGGGGUGUUAUUCUCCAGCGAGAGGGGGUCUCGUACAGAGGUCUUCUUAAGGCU GGUUAUCCAGUGGCGAGGUAUGUUUGAACCCAGGGGUACCUUAUCUCGAUUUUGGAG AGUCACUAGUACUUCUAGGCAAGGGGACUUGUUGGAGGCGAAGCAGAAUGCCUUUGUACCC UAGNUGGCUUCUUGUCAAAGAAUUCGCCGGGGGUCCAUAAUGCUUUGUUCUGACUCUC UUAUCCGGUCUUUCGGAAACCGUUCUAUUUUAUCAGGGGAACCUAAUAGCCAAUUGUG CAUCACUUAUCUUCAGUUGUAACACAGAGAGGAAACUUAUAUUAAGAACCCUGACAGAU CCUAGCAUAGUCUAGCCGAGUCAGUCGGUUGGUCGAGGUGAAUUGGCGUGCACUCCAG AGUGGGAGGAGGAGGUAUCGGAGGCUUGUUAUCUUGCACAGGAAUUAUCUUCGGUCC CCAAUUCUUUGGAGGAGGUGGACGUAGGGACAAAUUUGGGAAUUGCAUUGGUAAGUUUG AGGAGUCGAGGGAUUGUUGGAGUCUUGGAGCAGAAUUGAGGAGUAUUAAGGGUUUUUJ GGACACUAGUUAAGUUUAUCUUCUGAUUGGAGUUGUUCUUGGAGGAAUUGAGGGAAUCC CCGUUUAAUUGUUGUUCAGGGGGCGUUAACAAAGAGGGAGAAACAGUUGGUAUUGU CAGATCCAGCCUAAGGCUUGAUUUACAGGAAACUCAAALUCUUAUGUUAAGGUCACUCUG AUGUAUAAGGCUUGGAGGCUUCGGGGCGAGGCUUCUUCCCGUUGGGCCUCCCGCCAGC CCUCCUGCCGUUCUUCACCCGUACCCCGUGGUUGUUGAAUAAAGUUCUAGUUGGGCC </pre>	72

(continued)

Description	Sequence	SEQ ID NO:
<p>5 GC_F_MEASLES_D8 ORF Sequence, NT</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>AUGGGUUC AAGGUUGAAC GUUUGUGUC AVALUC AU GGC AGUACUGUUAACU GU C AACA CCCACGGUUC AA AUCC AUUGGGCC ANUCUUCUUAAGAUAGGGGUGUAGG GGUJAGGAAAU GCANGUUC AAGUUU AUGACUUC GU UCCAGCC AUC AAUC AU UAGUC AUAAGUUA AU GCC R NUAIACUUCUC UC AACA AU UGC AC GAGGGU AGGG AU USCAGAAU ACAGGAGAUJACUGA GAKAGUUC UGGAKC AKAHAGAGAUUC AUU AAUCC AAU GACC CAGA AU UAGACC GGU UCASAGU GUAGCUUC AASUJAGGAGAC AC AAGAGAUUUGC GGGAGUGUC UCUGGCAGGU G CGGGCCUAGGC GU UGCC AC AGCUGUC AKAU AAC AGCC GGU AUUGC AC UUC ACC AGUC CA UGCUGACUUC AAGCC AUC GAC AAUUGAGAGGC GAGCCUJAGAAAUJACUAAUUCAGCCAAU UGAGGCAUUCAGAC AAGCAGGCC AGGAG AUGUA AUU GGC UGUUCAGGUGUCCAAAG AU A CAUCANUJAGAGUC UGUAJCC GU GUALCAAUC AADJAUUC GU GAUUA AUU GGC CAGAAG CUAAGGCUCAAU UGCUC AGUAU AUJACAG AAUCCUUC AUU AUUUGGCC CAGCUGUC GGGCCCAU AUUCU GC GAGAUJAU U AUCCAGCC UUU GAGCUAGGCCU UUGAGGAGAU A UCANUAGGUUUGU GAAAAGCUC GGAUACAGUGGAGGU GAUUAAGUGGC AUUCUJAGAGA GCAGAG BANJAAAGGCCCGAUJACUC AC GUC GAC ACAGAGUC CU AGUUC AU UGUJUCA GUUJAGCCU AUUC GAC GDUJUCGAGAUUAGGGGUG AUUGUCAC CGGCUJAGAGGG GUUCUGAC AAC AUAGGCUUC AAGAGUGGUAUC CACUGUGCC CAGAUU GU UGC AACC CAGGCUACCUJAUUC C GAKU UU UGAU GAGUC AUC AUUC ACUUC AUGCC AAGGGGACU GUUGCCAGCC CAGA AU GC GUUGUAC CC GAU GAGUCC UC UGCUCC AAGAAU GCUUC GGGG GUCCAGUAAGUCC UGU GC UC GUJAC AC UC GUJUC CGGGUC UUC GGGGACC GGUUC AGU UU AUCCAGGGGAAU CUAAUAGCC ANUUGUCCAU CAUUCU UU GC ANGU GUU AC ACACAGGA ACANUC AU AAUC AAGAC CC UGAC AAG AU CC UAC AU AC AUUCUGCC GAUC AC UGC CC GC UGGUCCAGG GU GAUUGGC GU GAC C AUCCAGUUC GGGAGCAGGAGU AUUC CGGAC GCUGUG UACUJGCACAGG AUU GAC CUC GGU UC CUCC AU AU CU UUGGAGAGGUUGGAC GUAGGGAC A AUUCUGG GGAUUGC ANUUGCU AAGU UGGAGG AUCC AAGGAAUUGU U GAGUUC AUC GGC CAGAUUUGAGGAG U AU GAAGGUU UAUCCAGCAC UAGU AUAGUU AC AUCC U GAUJCA GUUJUCU UUGAGG AUU GAUAGGALUC CC GGCU UJAU AU GUU GCUUCAGGGGCG GUJG UACAGAGG GGAAC AAGUU GGU AUJUC AAGAC CAGGCC UAAAGCC UG AU CUJACAGG AC AUCAA AUUC CUAUSUAAGGUCACUCU GA</p>	<p>73</p>

(continued)

Description	Sequence	SEQ ID NO:
<p>5 GC_H_MEASLES_B3 mRNA Sequence (assumes T100 Tail) Sequence Length: 2126</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p>	<pre> GTGGAAAUAAAGAGAGAAAGAAAGAGUAAGAAGAAAUAAAGAGCCACCGUGUCACCCGAA CGKACTGGAAAUAGCCUUCACAAAGAUAAACCCUUNLCCCAAGGGAAGUAGGAAUAGUU A UUACACAGAACAUUUUUGAUIIACAGACC CU AUGUUCUGUGUGGCUUUGUUGUGUUCGUC A UUUUUUGSAGDUAGAUCCGAAUUGCUUGGC AAU HECAGGCAGUAGACUUCXUCGCGGAGCC A UCUACACCCCGGAGAUCCAAUAAAAGCCUCAGUACC AUUCUGGAGUUGACUAAUCUCCAGCG A CCUUCAGGUCAGGACGIIICUUGACACCAGUEUUUAAAAGUAGUGGGAUAGAGUGGGCCU AGGAGAGGAG AUUCGGAGUAGGGAGUACGACUUCAGAGAUUCACUUGGUGGACACACCCGCCAGAGAGG NUCACUAGAUUAGUACAAUACUUGUGCAGAUUGUGGCUCCUGAABAGGUCAGUAGAUAGCA UUUGAGACUCAGUUCUUCUGGAGACAGAACACCCAGCAGUUECUGAGUUCUUCAGAG GGAGACUGUCAGGGCCACUACANUCAGAGGUCAAUUCUACAAAGUGUCUUGUUCUUG UUUGGCUUGUUCUAGGUCGAGGUAACANUGUGUACUEUAGAGUACUUGAGACUUCAGG GGAAUUAUGGGGGAACUACCUAGUUGAAAAGCCUAAUUGAGACAGCAAGGAGUUCAGAG UUUCACAGUGAGCAUUCAGCAGUUGUUGAAGUAGGUGUGAUCAGAAACCCGCGUUUG GGGGUCCGUGUUCAGUAGACAAACUUAUUGAGCAGCCAGUACAGUAGUAGGUCUCGCGC ACUUGUAGUGGCUUUUGGGAGGUCACACUCGACAGCGUUUGUACAGGGGAGGAGUUC UUCAGAAUUCUUAUCAGGAGUCAGGGAAAGGUGUAGCUUCCAGUUCUUCAGUUCUGG UUUCUGGAAUUCUCCAGCAGUUCAGUUCUGGUCUUCAGUUCAGUUCAGUUCAGUUCAGU GGUAGCAGGCUUUCUUCUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUC GGUUCUCCGACAGCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAG GUUAGAGUAAAUCAGCAGUUCUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAG CAGGAGUUCUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGU CAAAUUGUUCAGGAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAG AUCCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAG GUAUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUC CCUAAUAGGAG CGUAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAG UUUGGACCCUACAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUC AGCGGUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUC ACUACAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAG UCCGACUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAG GCUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAGUUCAG GGUUCGCAAGCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUCUUC CCUUCGCCCCUUGGUCUUUGAAUAAAGUUCUAGUUGGCGCCAAAAAAGAAAAAAGAAAAA AAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAA AAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAA </pre>	<p>77</p>

(continued)

Description	Sequence	SEQ ID NO:
<p>5 GC_H_MEASLES_D8 Sequence, NT (5' UTR, ORF, 3' UTR) Sequence Length: 2065</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p>	<pre> UCAGGCUUUUGGACCUCUCUACAGAGCUAAUACGACUCACUUAAGGGAJAHANGAGAGAA ANGMBAQJAGGAGAAAUHUANGAGCCACCAUUGUCACCAACAGAGACCAGGAAAUAGCC UUUUCAGAGAGACAAACCCCAUCCUAAAGGGAAGUAGGUAUAGUUUUUUAACAGAGAACAUUUA UOMJUGUJAGACCUUAGUJUGCCUUGGCUUUCUUAUUCUUCUAGUJUCUAGCUGUAGUAGC GGUAGCAGAGCCAUUGCAGGCALUJAGACUUCUUCAGGCAAGCUCUACACCCAGAGAHCC XUAMNGOCUEAGCACAAUEUGBAUJUAACUANCUCAAUEGAGCUCAGGUUAAAGGACBU GGUGACCCACUEUUCAGAUCAHUGGUGAUAAGUUGGCUUGAGGACACUCAGAGAUU CACUGACUJAGUGAAGUUCUUCUUCAGAGAUUAAUUCUUAUUCAGGACAGGGAUAC GACUJAGAGAGUUCACUUGGUGUUCACACCCGCCAGAGAGAAUCAAUUGGAAUUNJGAU CANKUJUGCCAGAUUGUGGUGGAGAGACUCAGUAGUUCAGUUGUAGACUACUUA CUGGAGACCAGGCAACCAUCAGUUCUJAGUUCUCAAAGGGAUACUUCUAGGACC ACUACAUACAGAGCCAAUUCUCAAACAUUCGCUUCUCCUGUUGGACUUGUUAUUUAGU CGAGUUUACAAUGUUCUUCUJUAUAGUCACUJAGACUUCAGGGAUUCAGGGGAAAU UACCUAGUGGAAAAGCUCUJAUUCUAGCAGCAGAGGUCAGAGUUGUCACACUUGAGCAG CAGGAGUUGUJAGAGHAGGUUUAUCAGAAAUUCGGGUUGGGGUCUCCGUUJUCA UUAJACAAACHAUUCUJAGACCACUAGUJAGUUAUJAGUUCAGCAAGUCUUGUUGGCUU GGGAGCUCUAGUUCGCAGCUCUUGUCACAGGGAAGAUUCUUAUCACAAUUCUUAUCA GGGACAGGGAAGGUGUUCAGCUUCAGCAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGG CGACUUCAGUUCUUGGUCUCCUUAUCAGGGAUAGUUCAGUGAUAGCAGGCUUUAUCU CUCAGUUCAGAGCCUUAJUCGCUAGCAALCAGCAGAAUGGGUUGUCCGACACAGCG GACAGUAGCAAGUUGCGAGUJGAGACAUUCUUCACAGGCGUUGAAGGUAAGAAUCCA AGCAGUUCGAGAAUUCGAGUGGACACCAGUJAGAGAUJAGAGAGUUCUUCUUCAGG GGUJUGUCUGUJAGUUCGAGUUCGAGAGUJAGCUUAAAACAAAUUUGUUUCAGGUAU CGGDCUUGAGACACAGGUCACAGGUAUGGACUUAACAAUUCAGCCACACAAUAGU UUAJGGUJAGUUCAGGUAAGAGAACUUGGCUUAGGUGUAUUCAGCAGUUGGAG UUGUUCGAGAGUCAGGUJAGUUCAGCAGCUCUUCACUJUCUCAAUUAAGGAAAGCAGC GAGGACUUCAGGUCUACAGUJAGUUCAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGG UCCAGUJAGUJAGUUCAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGG UCCAGUJAGUJAGUUCAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGG UUUUUUUUUUUAGGUUGGCUUAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGG ACUUGGACAAAACUUGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUA GGACAUUUCAGUUCAGUJAGUUCAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGG AGUJAGUUCAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGG CCUUGGACUUCAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGG GAAUJAGUUCAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGGUAAGG </pre>	<p>78</p>

(continued)

Description	Sequence	SEQ ID NO:
<p>5 GC_H_MEASLES_D8</p> <p>10 ORF Sequence, NT</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p>	<pre> ATGTCACCACACGAGACCGGAAAAAGCCCHUUCACAAACACAAACCCCAACCUAAGGGAA GUNGGAAGUUAAGUAAAGAGAAACAUUUAUSAVUGENJAGACUUNJGHHUUGCUGGCGU UUDLAUNDBJCAHGHUUCUGAGCUHUGAUCGGGUUGCUAGCCAUUCGAGGC AUUAGACUUC AUCGGGCAGCCACUCUACACCGCACAGAAUCCAUAAAGCCDUACAGCACANUCUUGENJAG UACUCANUCAGCACAUUCAGGUAUAGGACUGUCUAGCACACACUUCUUCAGGACUUCGGUAG UGANUUGGGCUUAGAGACACUCAGAAUUCACUAGACUAGUAGUAGUUGAUUCUUSACAA GUAUAUUCUUAUUCGGACAGGAAUACGACUUCAGAGAUUCACUUCUUCUUGUUAUUCUAC CCCCAGAGAGAAUUAUUGGGUUAUUGAUCAUUCUUGGCAUUGUUGGCUUCGUAAGAA CUCAGAUUCUUAUUGGUAUCUACUCUUCAGAGACACAGGACACCAUUCUUAUCUUA GCUGUCUUAAGGGAAUCUGGUCAGGCTCACUACAAUCAGAGCCAUUCUUAUCUUAUC UGGCUUUCUUGUAGACUUGUUAUUAAGGTCGAGGUUACAUUGUUCUUCUUAAGUACU AUGCACUCCAGGAAUUGUACGGGGAAUCUUCUUAUGGAAUAGCUUUAUUCUUCAGCAGC AAGGUCAGAGUUGUCACAUUCAGCCAUUCACUAGUUGUUAAGUAGGUGUUAUUCAGU AUCUGGGUUAUUGGGGCUUCUGUUAUCUUAUUCAGAAAGUUCUUGAGCACCAAGUAGU AUAUAUUCAGCACAUUCUUAUUCUUAUUCAGGAAUCAGGAAAGUUGUUCAGCUCUUGUAC AGGAAGAUUCUUAUCACAUUCUUAUCAGGAAUCAGGAAAGUUGUUCAGCUCUUGUAC GUCAGCUAAGUUGUUGGAAUUCACACCGCACUUGGAAUCUGGGUUCUUCUUAUCAGC GUAUAUCAGUUAUACACAGGCUUUCACUCUUCUUAUCACAGGAAUUCUUAUCUUCUUA CAGCAAAUUGGGUUGCCGACACACAGGACAGUAGCACAGUUGGUAUUGGAGCACUUC UUUCAGCAGCCGUGUUAAGGUAUUAUUCUUAAGCACUUCUUCAGGAAUCUUCAGGAAUCACCA UUGAAGGUAUUCAGGAAUCUUCACACUUCUUCUUAUCUUCUUCUUCUUCUUCUUCUUC GAGCUUAAAAUCAAAAUUGUUCUUAAGGAAUCGGGCAUUGAUCACACGCUUCAGGAAUC GACCUUUAUUAUUCUUAUCACAAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUAUUA UUGCCUUAAGGUUAUUCACAUUAAGGAACAGGGGAGGAGUUCUUAUGCCCAACUUAUCUUAUC CGGAAUUGGUGUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUA UUCUUAUUAUUAUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCU UUUCAGCCCAAGCAGUUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCU UCCUUAUUAUUAUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCU UUCUUAUUAUUAUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCU UUCUUAUUAUUAUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCU UUCUUAUUAUUAUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCU UUCUUAUUAUUAUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCUUAUCU </pre>	<p>79</p>

(continued)

Description	Sequence	SEQ ID NO:
<p>5 GC_H_MEASLES_D8 mRNA Sequence (assumes T100 tail) Sequence Length: 2126</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p>	<pre> GTGGAAGGAGAGAGAGAAAGAGAGAGUAGAGAGAAUAGAAAGAGCCACCCAGUCACCCAGC GAGACCGGAGUAAAGUCCUUCUACAAAGACAGCCCCAGUCCHAAAGGAAAGUAGGUAAGUUAU UACAGAGAGACAUUUUGAGUUAGUAGACCUUAGUGUUGUCUUGGUCUUAUUCUUCAGU UUUUUCUAGCCUAGAUUGAGUUGUCUAGGCCUUUGGAGGCCUUUAGACUACUAGCUGGAGCCAU GUACACCGCAGAGAUCCUAAAAGCCUUCAGCCACAAUCUGGAGUUAACUAAUUAUCAGUAG CUACAGUUUAAAGGAGUUGUCUGACAGCCUUCUUCAGAGUUCAGUCAGUAGUAGUUAGUUUG AGGACCCUAGAGAGUUCAGUCAGUAGUAGAUUCUUCUUCAGAGAGAGAGAGUUAGAAUUCUUAA NUCCGGACAGGAAUACAGUUCAGAGAUUCAGUUUGUUGUUUACCCGCCAGAGAGAA UCANUUGGAAUUAUAGUACAAUACUUCAGAGAUUGUCUUGUCUUGUAGAGAACUAGAAUAGCAG UUGUCAGUUCAGUCUAGUAGGAGACAGAGGACAGCAAGUAGUUUCUAGUUUCUAGUUUCUAGAGG GAAUCUUCAGGAGCCACUUCACAAUCAGAGGCCAAUUCUACAAUCAGUUCUUCUUCUUCUUCU UUGCUUUUUUUAUUAGUCAGAGUACAAUUCUUCUAGUUAUAGUACAUUAGAGAUUCAGUUCAGG GAKUUUACGGGAGGAAUUCUAGUUUAGUUAGGAAAGCUCUAGUAGCAGCAGAAAGGAGUAGAGU UUCACACAGUAGACUUCAGCCAGUUGUUUAGUAGUAGUUUUUAGUAGAAUUCUUGGAGUUUGG GGGUCUUGUUUUUUCUAAUAGAGAAACUUCUUGAGGAAACAGGAGUUCAGUUUUUAGUAGUUUUC CUUCAGUUUUUUCUUCUUGGAGAGUUCAGUUUUUCAGCCUUCUUCUACAGGAGAAUUCUUA UCACAAUUCUUCUUCAGGAGUUCAGGAAAGGAGUUUCAGUUCUUCAGUUUUCUAGUUUAGGUG UCUGGAAUUCUUCAGGAGUUCAGGAAAGGAGUUUCAGUUCUUCAGUUUUCUAGUUUAGGAGUA UAGGAGGAGUUUAGUUCUUCUUCAGGAGGAGUUUAGUUCUUCAGUUUUCUAGUUUAGGAGUA CUUCUUCAGGAGUUCAGGAGAGAGUUUCAGUUUCAGGAGAGUUCUUCUUCAGGAGGAGUUCU GUAGGAGUAAAAUCUAGCAGUUUCAGGAGUUUCUUCAGUUCAGUUCAGUUUUCUUCAGGAGUUA CA </pre>	<p>80</p>

Table 14. MeV Amino Acid Sequences (Reference Example)

Description	Sequence	SEQ ID NO:
<p>45 GC_F_MEASLES_B3.1 ORF Sequence, AA</p> <p>50</p> <p>55</p>	<pre> MGLKVVSYANFMALLTLQTPAGDHFHNGNLKSGVVGQGGASVYVMTBSSHQSLVHKWPNL TLLNQCIVSVEYPRILLRTVLEFRDANKAMQDNIHPVDSYASSRRHKRFAGVYLGAALG VMTAQTAGLHRSMINLQAIKLRABLETTNQRGHRDAGDEMLANVGGVDDYHNIELP MMLKSLDLDGKELKLLHYITELSLFQPSLHOPSAEISQALSYLGGDNIKLEKGYE GGDLGLESRGHARITWIDTESYFNLBAYPTLSEKSNVHLEGVSYNIGSGSWYTTVP KYNTQSYLISNFDSEECTFNPEGTNGBNALYPMKSLQEDLQGSTKSCARTLVSSSFG NHFLSQENLJANCAKELGNDYTTSTINGDPPMLTHAADRCPVYEWINGVTVNGSERRYPDA VLEHRIKLPPIKLERLDVSTNLDNAKAREDAKELIESSQKRSKIKLSTSVNLUAVLG GUSIPTLCCERSRDNRKNGEQQWNSRPLKPLTGTSTKSYKEL* </pre>	<p>47</p>

(continued)

Type	Virus Name	GenBank Accession	
5	hemagglutinin	hemagglutinin [Measles virus]	AAA74936.1
	hemagglutinin	hemagglutinin protein [Measles virus]	BAH56665.1
	hemagglutinin	hemagglutinin [Measles virus]	ACC86105.1
10	hemagglutinin	hemagglutinin [Measles virus strain Edmonston-Zagreb]	AAF85697.1
	hemagglutinin	hemagglutinin [Measles virus]	AAR89413.1
	hemagglutinin	hemagglutinin [Measles virus]	AAA56653.1
15	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
20	hemagglutinin	Hemagglutinin [Measles virus]	CAB94927.1
	hemagglutinin	Hemagglutinin [Measles virus]	CAB94925.1
	hemagglutinin	hemagglutinin protein [Measles virus]	BAB39835.1
25	hemagglutinin	Hemagglutinin [Measles virus]	CAB94931.1
	hemagglutinin	hemagglutinin [Measles virus genotype A]	AF084712.1
	hemagglutinin	hemagglutinin [Measles virus]	AAA56639.1
	hemagglutinin	Hemagglutinin [Measles virus]	CAB94926.1
30	hemagglutinin	hemagglutinin protein [Measles virus]	BAB39836.1
	hemagglutinin	Hemagglutinin [Measles virus]	CAB94929.1
	hemagglutinin	RecName: Full=Hemagglutinin glycoprotein	P06830.1
35	hemagglutinin	Hemagglutinin [Measles virus]	CAB94928.1
	hemagglutinin	hemagglutinin protein [Measles virus]	BAB39837.1
	hemagglutinin	hemagglutinin [Measles virus]	AAA74935.1
	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43780.1
40	hemagglutinin	hemagglutinin [Measles virus]	BAA09952.1
	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43815.1
	hemagglutinin	hemagglutinin [Measles virus]	AAF28390.1
45	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
50	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43781.1
	hemagglutinin	hemagglutinin [Measles virus]	BAH22353.1
	hemagglutinin	hemagglutinin [Measles virus]	AAC35878.2
55	hemagglutinin	hemagglutinin protein [Measles virus]	AAL86996.1
	hemagglutinin	hemagglutinin [Measles virus]	CAA76066.2
	hemagglutinin	hemagglutinin [Measles virus]	AAA46428.1

(continued)

Type	Virus Name	GenBank Accession	
5	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43803.1
	hemagglutinin	Hemagglutinin [Measles virus]	CAB94918.1
	hemagglutinin	hemagglutinin [Measles virus]	AAF72162.1
10	hemagglutinin	hemagglutinin [Measles virus]	AAM70154.1
	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43776.1
	hemagglutinin	hemagglutinin [Measles virus genotype D4]	ACT78395.1
	hemagglutinin	hemagglutinin [Measles virus genotype D7]	AAL02030.1
15	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43789.1
	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43774.1
	hemagglutinin	Hemagglutinin [Measles virus]	CAB94920.1
20	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
25	hemagglutinin	hemagglutinin [Measles virus]	AAX52048.1
	hemagglutinin	Hemagglutinin [Measles virus]	CAB94930.1
	hemagglutinin	hemagglutinin [Measles virus]	AAA74526.1
30	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43814.1
	hemagglutinin	hemagglutinin [Measles virus]	ABB59493.1
	hemagglutinin	hemagglutinin [Measles virus genotype D4]	AAL02019.1
	hemagglutinin	Hemagglutinin [Measles virus]	CAB94919.1
35	hemagglutinin	hemagglutinin protein [Measles virus]	AAL86997.1
	hemagglutinin	hemagglutinin [Measles virus genotype C2]	AAL02017.1
	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43769.1
40	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
45	hemagglutinin	hemagglutinin [Measles virus]	AAL67793.1
	hemagglutinin	hemagglutinin [Measles virus]	AAF89816.1
	hemagglutinin	hemagglutinin [Measles virus genotype D4]	AAL02020.1
50	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43786.1
	hemagglutinin	hemagglutinin protein [Measles virus strain MVi/New Jersey.USA/45.05]	AEP40452.1
	hemagglutinin	hemagglutinin [Measles virus]	AAA74531.1
	hemagglutinin	hemagglutinin [Measles virus]	AAB63800.1
55	hemagglutinin	hemagglutinin [Measles virus]	AA021711.1
	hemagglutinin	hemagglutinin [Measles virus genotype D8]	ALE27189.1

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Type	Virus Name	GenBank Accession	
5	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43810.1
	hemagglutinin	hemagglutinin [Measles virus]	AAF89817.1
	hemagglutinin	hemagglutinin [Measles virus genotype D6]	AAL02022.1
10	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43800.1
	hemagglutinin	hemagglutinin protein [Measles virus genotype B3]	AGA17219.1
	hemagglutinin	hemagglutinin protein [Measles virus]	CAB43770.1
15	hemagglutinin	hemagglutinin protein [Measles virus strain MVi/Texas. USA/4.07]	AEP40444.1
	hemagglutinin	hemagglutinin [Measles virus]	AAX52047.1
	hemagglutinin	hemagglutinin [Measles virus]	AAB63794.1
	hemagglutinin	hemagglutinin [Measles virus]	AAB63796.1
20	hemagglutinin	hemagglutinin [Measles virus]	AAA74528.1
	hemagglutinin	hemagglutinin [Measles virus]	AAB63774.1
	hemagglutinin	hemagglutinin [Measles virus]	AAB63795.1
25	hemagglutinin	hemagglutinin [Measles virus]	AAA74519.1
	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
30	fusion protein	fusion protein [Measles virus strain Rubeovax]	AAF85688.1
	fusion protein	fusion protein [Measles virus]	AAF85680.1
	fusion protein	fusion protein [Measles virus]	AEF30359.1
35	fusion protein	fusion protein [Measles virus]	BAA09957.1
	fusion protein	fusion protein [Measles virus]	AAV84957.1
	fusion protein	fusion protein [Measles virus MeV-eGFP_Edm-tag]	All16636.1
	fusion protein	fusion protein [Measles virus]	ABY58018.1
40	fusion protein	fusion protein [Measles virus]	BAA19838.1
	fusion protein	fusion protein [Measles virus]	AAA56641.1
	fusion protein	F protein [Measles virus]	ABK40529.1
45	fusion protein	fusion protein [Measles virus]	AAA56652.1
	fusion protein	fusion protein [Measles virus]	ABY58017.1
	fusion protein	fusion protein [Measles virus]	ABB71645.1
50	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]	BAB60865.1
	fusion protein	fusion protein [Measles virus]	BAA09950.1
55	fusion protein	fusion protein [Measles virus strain MVi/New York.USA/26.09/3]	AEP40403.1
	fusion protein	fusion protein [Measles virus]	AAA74934.1

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	Type	Virus Name	GenBank Accession
5	fusion protein	fusion protein [Measles virus]	CAB38075.1
	fusion protein	fusion protein [Measles virus strain MVI/Texas.USA/4.07]	AEP40443.1
	fusion protein	fusion protein [Measles virus]	AAF02695.1
10	fusion protein	fusion protein [Measles virus]	AAF02696.1
	fusion protein	fusion protein [Measles virus]	AAT99301.1
	fusion protein	fusion protein [Measles virus]	ABB71661.1
	fusion protein	fusion protein [Measles virus]	BAK08874.1
15	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]	AEP40467.1
20	fusion protein	fusion protein [Measles virus genotype D8]	AHN07989.1
	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
25	fusion protein	fusion protein [Measles virus genotype D8]	ALE27200.1
	fusion protein	fusion protein [Measles virus genotype D8]	AFY12695.1
	fusion protein	fusion protein [Measles virus genotype D8]	ALE27248.1
30	fusion protein	fusion protein [Measles virus genotype D8]	ALE27224.1
	fusion protein	fusion protein [Measles virus]	AAT99300.1
	fusion protein	fusion protein [Measles virus]	BAH96592.1
	fusion protein	fusion protein [Measles virus strain MVI/California.USA/8.04]	AEP40459.1
35	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]	ALE27194.1
40	fusion protein	fusion protein [Measles virus]	BAA33871.1
	fusion protein	fusion protein [Measles virus strain MVI/Washington,USA18.08/1]	AEP40427.1
	fusion protein	fusion protein [Measles virus]	ABY21182.1
	fusion protein	fusion protein [Measles virus genotype D8]	ALE27284.1
45	fusion protein	fusion protein [Measles virus]	ACA09725.1
	fusion protein	fusion protein [Measles virus genotype D8]	ALE27314.1
	fusion protein	fusion protein [Measles virus genotype G3]	AFY12712.1
50	fusion protein	fusion protein [Measles virus genotype D8]	ALE27368.1
	fusion protein	RecName: Full=Fusion glycoprotein F0; Contains: RecName: Full=Fusion glycoprotein F2; Contains: RecName: Full=Fusion glycoprotein F1; Flags: Precursor	P35973.1
55	fusion protein	fusion protein [Measles virus genotype H1]	AIG53713.1
		unnamed protein product [Measles virus]	CAA34588.1
	fusion protein	fusion protein [Measles virus]	CAA76888.1

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Type	Virus Name	GenBank Accession	
5	fusion protein	fusion protein [Measles virus genotype B3.1]	AIY55563.1
	fusion protein	fusion protein [Measles virus]	ADO17330.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53703.1
10	fusion protein	fusion protein [Measles virus genotype B3]	AGA17208.1
	fusion protein	fusion protein [Measles virus]	AAL29688.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53706.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53701.1
15	fusion protein	fusion protein [Measles virus genotype B3]	ALE27092.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53714.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53694.1
20	fusion protein	fusion protein [Measles virus genotype H1]	AIG53668.1
	fusion protein	fusion protein [Measles virus]	ACC86094.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53670.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53707.1
25	fusion protein	fusion protein [Measles virus genotype B3]	AGA17216.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53671.1
	fusion protein	fusion protein [Measles virus strain MVi/New Jersey.USA/45.05]	AEP40451.1
30	fusion protein	fusion protein [Measles virus genotype H1]	AIG53684.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53688.1
	fusion protein	fusion protein [Measles virus genotype B3]	AGA17214.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53683.1
35	fusion protein	fusion protein [Measles virus genotype H1]	AIG53667.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53686.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53685.1
40	fusion protein	fusion protein [Measles virus genotype H1]	AIG53681.1
		unnamed protein product [Measles virus]	CAA34589.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53678.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53710.1
45	fusion protein	fusion protein [Measles virus genotype H1]	AIG53669.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53664.1
	fusion protein	fusion protein [Measles virus]	AAA50547.1
50	fusion protein	fusion protein [Measles virus genotype H1]	AIG53679.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53709.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53672.1
55	fusion protein	fusion protein [Measles virus genotype H1]	AIG53697.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53689.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53676.1

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Type	Virus Name	GenBank Accession	
5	fusion protein	fusion protein [Measles virus genotype H1]	AIG53675.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53663.1
	fusion protein	fusion protein [Measles virus]	BAA19841.1
10	fusion protein	fusion protein [Measles virus]	AAF02701.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53680.1
	fusion protein	fusion protein [Measles virus genotype H1]	AIG53674.1
15	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
20	C protein	RecName: Full=Protein C	P35977.1
	C protein	C protein [Measles virus]	AAF85678.1
	C protein	C protein [Measles virus]	ABD33998.1
25	C protein	unnamed protein product [Measles virus]	CAA34586.1
	C protein	C proteer [Measles virus]	BAJ51786.1
	C protein	C protein [Measles virus]	BAA33869.1
	C protein	virulence factor [Measles virus]	ABO69700.1
30	C protein	C protein [Measles virus]	NP_056920.1
	C protein	C protein [Measles virus]	AD017333.1
	C protein	C protein [Measles virus]	ACC86082.1
35	C protein	C protein [Measles virus]	BAA33875.1
	C protein	C protein [Measles virus]	ABY21189.1
	C protein	C protein [Measles virus]	BAE98296.1
40	C protein	C protein [Measles virus]	ADU17782.1
	C protein	C protein [Measles virus strain MVi/Virginia.USA/15.09]	AEP40417.1
	C protein	C protein [Measles virus]	ADU17814.1
	C protein	C protein [Measles virus]	ADU17798.1
45	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.USA/16.03]	AEP40465.1
50	C protein	C protein [Measles virus]	ABB71643.1
	C protein	C protein [Measles virus]	AE191027.1
	C protein	C protein [Measles virus]	ADU17874.1
	C protein	C protein [Measles virus]	ADU17903.1
55	C protein	C protein [Measles virus]	CAA34579.1
	C protein	C protein [Measles virus]	ADU17790.1

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Type	Virus Name	GenBank Accession	
5	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
10	C protein	C protein [Measles virus strain MVi/Arizona.USA/11.08/2]	AEP40433.1
	C protein	C protein [Measles virus]	ADU17830.1
	C protein	C protein [Measles virus]	ADU17947.1
	C protein	C protein [Measles virus]	ADU17818.1
15	C protein	C protein [Measles virus strain MVi/New Jersey.USA/45.05]	AEP40449.1
	C protein	C protein [Measles virus strain MVi/Texas.USA/4.07]	AEP40441.1
	C protein	C protein [Measles virus]	ADU17864.1
20	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]	AEP40425.1
	C protein	C protein [Measles virus]	ADU17927.1
25	C protein	C protein [Measles virus]	ADU17953.1
	C protein	C protein [Measles virus]	ADU17889.1
	C protein	C protein [Measles virus]	ADU17963.1
30	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
35	C protein	C protein [Measles virus]	ADU17862.1
	C protein	C protein [Measles virus]	ADU17923.1
	C protein	C protein [Measles virus]	ADU17959.1
40	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
45	C protein	C protein [Measles virus]	ADU17901.1
	C protein	C protein [Measles virus]	ADU17887.1
	C protein	C protein [Measles virus]	ADU17832.1
50	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
55	C protein	C protein [Measles virus]	ADU17908.1
	C protein	C protein [Measles virus]	ADU17910.1

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	Type	Virus Name	GenBank Accession
5	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]	AEP40473.1
10	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]	ABA59559.1
15	C protein	RecName: Full=Protein C	Q00794.1
	C protein	nonstructural C protein [Measles virus]	ADO17934.1
	C protein	nonstructural C protein [Measles virus]	ACJ66773.1
20	C protein	C protein [Measles virus genotype G3]	AFY12708.1
	C protein	RecName: Full=Protein C	P26035.1
	C protein	C protein [Measles virus]	BAA84128.1
25	nucleoprotein	RecName: Full=Nucleoprotein; AltName: Full=Nucleocapsid protein; Short=NP; Short=Protein N	Q77M43.1
	nucleoprotein	nucleocapsid protein [Measles virus strain Rubeovax]	AAF85683.1
	nucleoprotein	RecName: Full=Nucleoprotein; AltName: Full=Nucleocapsid protein; Short=NP; Short=Protein N	Q89933.1
30	nucleoprotein	nucleocapsid protein [Measles virus strain AIK-C]	AAF85659.1
	nucleoprotein	nucleoprotein [Measles virus]	ABI54102.1
	nucleoprotein	nucleoprotein [Measles virus]	AAA56643.1
35	nucleoprotein	nucleoprotein [Measles virus]	AAC03050.1
	nucleoprotein	nucleoprotein [Measles virus]	AAA18990.1
	nucleoprotein	nucleoprotein [Measles virus]	AAA56640.1
40	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
45	nucleoprotein	RecName: Full=Nucleoprotein; AltName: Full=Nucleocapsid protein; Short=NP; Short=Protein N	B1AAA7.1
	nucleoprotein	nucleoprotein [Measles virus]	AAA18991.1
	nucleoprotein	nucleoprotein [Measles virus]	CAB46894.1
50	nucleoprotein	nucleoprotein [Measles virus]	CAB46871.1
	nucleoprotein	nucleoprotein [Measles virus]	CAB46872.1
	nucleoprotein	nucleoprotein [Measles virus]	ABU49606.1
55	nucleoprotein	nucleocapsid protein [Measles virus]	AAA75494.1
	nucleoprotein	nucleoprotein [Measles virus]	CAB46883.1

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Type	Virus Name	GenBank Accession
5	nucleoprotein [Measles virus]	CAB46892.1
	unnamed protein product [Measles virus]	CAA34584.1
	nucleoprotein [Measles virus]	AAA18997.1
10	nucleoprotein [Measles virus]	CAB46863.1
	nucleoprotein [Measles virus]	AEF30352.1
	nucleoprotein [Measles virus]	ABI54103.1
15	nucleocapsid protein [Measles virus]	AAA46433.1
	nucleoprotein [Measles virus]	CAB46902.1
	nucleoprotein [Measles virus]	CAB46873.1
	nucleoprotein [Measles virus]	CAB46906.1
20	nucleoprotein [Measles virus]	AAA74547.1
	nucleoprotein [Measles virus]	AAA74537.1
	nucleoprotein [Measles virus]	CAB46862.1
25	nucleocapsid protein [Measles virus]	BAA09961.1
	nucleoprotein [Measles virus]	AA015875.1
	nucleoprotein [Measles virus]	AA015871.1
	nucleoprotein [Measles virus]	CAB46882.1
30	nucleoprotein [Measles virus]	CAB60124.1
	nucleoprotein [Measles virus]	A8154104.1
	nucleoprotein [Measles virus]	CAB46869.1
	nucleoprotein [Measles virus]	CAB46880.1
35	nucleoprotein [Measles virus]	AAA74541.1
	nucleocapsid protein [Measles virus strain MVi/New Jersey.USA/45.05]	AEP40446.1
	nucleoprotein [Measles virus]	ABI54110.1
40	nucleoprotein [Measles virus]	CAB46903.1
	nucleoprotein [Measles virus]	CAB46899.1
	nucleoprotein [Measles virus]	CAB46901.1
45	nucleocapsid protein [Measles virus]	ABB71640.1
	nucleoprotein [Measles virus]	CAB60113.1
	nucleoprotein [Measles virus]	CAB60114.1
	nucleoprotein [Measles virus]	CAB60116.1
50	nucleoprotein [Measles virus]	CAB46895.1
	nucleoprotein [Measles virus]	CAB60121.1
	nucleoprotein [Measles virus]	ABI54111.1
55	nucleoprotein [Measles virus]	CAB46889.1
	nucleoprotein [Measles virus]	CAB46898.1
	nucleoprotein [Measles virus genotype B3]	ALE27083.1

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	Type	Virus Name	GenBank Accession
5	nucleoprotein	nucleoprotein [Measles virus]	CAB60118.1
	nucleoprotein	nucleocapsid protein [Measles virus]	CAA34570.1
	nucleoprotein	nucleoprotein [Measles virus]	AAC29443.1
10	nucleoprotein	nucleocapsid protein [Measles virus strain MVi/Washington.USA/18.08/1]	AEP40422.1
	nucleoprotein	nucleoprotein [Measles virus]	AA015872.1
	nucleoprotein	nucleoprotein [Measles virus]	CAB46874.1
	nucleoprotein	nucleoprotein [Measles virus]	AAA74550.1
15	nucleoprotein	nucleocapsid protein [Measles virus]	ABB71648.1
	nucleoprotein	nucleoprotein [Measles virus]	CAB46900.1
	nucleoprotein	nucleoprotein [Measles virus]	BAH22440.1
20	nucleoprotein	nucleocapsid protein [Measles virus]	AAA46432.1
	nucleoprotein	nucleocapsid protein [Measles virus]	BAA33867.1
	nucleoprotein	nucleoprotein [Measles virus]	AAA74539.1
	nucleoprotein	nucleoprotein [Measles virus]	CABM115.1
25	nucleoprotein	nucleoprotein [Measles virus]	CAB60123.1
	nucleoprotein	nucleocapsid protein [Measles virus]	ABB71664.1
	nucleoprotein	nucleoprotein [Measles virus]	CAB60125.1
30	nucleoprotein	nucleoprotein [Measles virus]	AAA74546.1
	nucleoprotein	nucleoprotein [Measles virus]	CAB46886.1
	nucleoprotein	nucleoprotein [Measles virus]	BAH22350.1
	nucleoprotein	nucleoprotein [Measles virus]	CAB46867.1
35	nucleoprotein	nucleocapsid protein [Measles virus]	BAA09954.1
	nucleoprotein	nucleoprotein [Measles virus]	AA015873.1
	nucleoprotein	nucleocapsid protein [Measles virus]	AEP95735.1
40	nucleoprotein	nucleoprotein [Measles virus]	AAL37726.1
	nucleoprotein	nucleoprotein [Measles virus]	AAA74549.1
	nucleoprotein	RecName: Full=Nucleoprotein; AltName: Full=Nucleocapsid protein; Short=NP; Short=Protein N	P26030.1
45	nucleoprotein	nucleoprotein [Measles virus ETH55/99]	AAK07777.1
	nucleoprotein	nucleoprotein [Measles virus genotype B3]	AGA17238.1
	nucleoprotein	nucleoprotein [Measles virus]	AEF30351.1
50	nucleoprotein	nucleoprotein [Measles virus genotype B3]	AGA17242.1
	nucleoprotein	nucleoprotein [Measles virus ETH54/98]	AAK07776.1
	nucleoprotein	nucleoprotein [Measles virus]	AAA74548.1
	nucleoprotein	nucleoprotein [Measles virus]	AAA19221.1
55	nucleoprotein	nucleoprotein [Measles virus]	AAC03039.1
	nucleoprotein	nucleoprotein [Measles virus]	AAA19223.1

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	Type	Virus Name	GenBank Accession
5	nucleoprotein	nucleoprotein [Measles virus genotype B3]	AGA17241.1
	nucleoprotein	nucleoprotein [Measles virus]	CAB60122.1
	nucleoprotein	nucleoprotein [Measles virus]	CAC34599.1
10	nucleoprotein	nucleoprotein [Measles virus]	AAC03042.1
	nucleoprotein	nucleoprotein [Measles virus]	CAC34604.1
	nucleoprotein	nucleoprotein [Measles virus]	AAA74544.1
15	nucleoprotein	nucleocapsid protein [Measles virus]	NP_056918.1
	V Protein	RecName: Full=Non-structural protein V	Q91C37.1
	V Protein	RecName: Full=Non-structural protein V	Q9EMA9.1
20	V Protein	V protein [Measles virus]	ACN54411.1
	V Protein	V protein [Measles virus]	ACN54403.1
	V Protein	V protein [Measles virus]	AEP95742.1
	V Protein	V protein [Measles virus strain MVi/Virginia.USA/15,09]	AEP40416.1
25	V Protein	V protein [Measles virus]	ADU17801.1
	V Protein	V protein [Measles virus]	ADU17849.1
	V Protein	V protein [Measles virus]	ABB71642.1
30	V Protein	V protein [Measles virus genotype D8]	AFY12693.1
	V Protein	V protein [Measles virus]	YP_M3873249.2
	V Protein	V protein [Measles virus strain MVi/Arizona.USA/11.08/2]	AEP4M32.1
35	V Protein	RecName: Full=Non-structural protein V	P26036.1
	V Protein	V protein [Measles virus strain MVi/California.USA/16.03]	AEP40464.1
	V Protein	V protein [Measles virus strain MVi/California.USA/8.04]	AEP40456.1
40	V Protein	V protein [Measles virus]	ABY21188.1
	V Protein	V protein [Measles virus strain MVi/Washington.USA/18.08/1]	AEP40424.1
	V Protein	V protein [Measles virus]	BAH96581.1
	V Protein	V protein [Measles virus]	ABB71666.1
45	V Protein	RecName: Full=Non-structural protein V	P60168.1
	V Protein	V protein [Measles virus]	BAH96589.1
	V Protein	V protein [Measles virus]	ADU17954.1
50	V Protein	V protein [Measles virus strain MVi/New York.USA/26.09/3]	AEP40400.1
	V Protein	V protein [Measles virus]	BY21196.1
	V Protein	virulence factor [Measles virus]	AB069701.1
	V Protein	V protein [Measles virus]	ABB71650.1
55	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]	AEP40448.1

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Type	Virus Name	GenBank Accession
V Protein	V protein [Measles virus]	BAE98295.1
V Protein	V protein [Measles virus]	ACC86083.1
V Protein	V protein [Measles virus]	ACU57139.1
V Protein	V protein [Measles virus]	AD017334.1
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]	AEP40472.1
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
	unnamed protein product [Measles virus]	CAA34585.1
V Protein	V protein [Measles virus]	ABD33997.1

Table 16. Flagellin Nucleic Acid Sequences

Name	Sequence	SEQ ID NO:
NT (5' UTR, ORF, 3' UTR)	<p>TCAGCTTTTGGACCTCGTAGAGAGGCTAATAGGACTACTATAGGGAAATANGAGAGAAAAGAGNATA NGAGAAATATAGAGCCAGCATGAGACAAAGTCAATTAAACAAACAGCCTGTGGCTGTAGACCCAGAAATAA CCTGACAAATCCAGTCCGCACCTGGGCACTGCTATCGAGGCTTTGTCTCCGGTGTGGCTATCAACAGGG GGGAGACGATGCGGGAGAGAGGCGATTGCTAAGCGTTTACCGGCAGACATCAAAAGTCTGTAGTCAAGGC TCCCGTACGCTAAACGAGGGTATCTCCATTGCGCAGACACTGAAGGGCGCGCTGAAGGAAATGAAACAA AACTGACGGTGTGTGGTGAAGTGGGGTTEAGTGTGGGAAATGGTACTAACTCCAGTGTGACCTCAAC CAGCCAGGCTGAAATGACCCAGCGCGCTGAACGAAATCGAGCGTGTATCCGGCAGACTGAGTCAACGGC GTGAAGTCTGTGGCGAGGACAAACAGCTGACCACTCCAGGTTGGTGGCAGAGAGGTTGAAACTATCGATA TGGATTAAGAGAAATGAGCTCTAAGACACTGGGACTTGATAAGCTTAATGTCCAAAGATGCCTACACCCGA AAGAACTGCTGTAAAGCGTTGTAAAGTACCTATAAAATGGTACAGATCTATTACAGCCGAGAGCAATA CTGATATCCAAAGTCCAAATGGCGGTGGTGCAGCAGGGGTTACTGGGGCTGATATCAAAATTAAGATGGT GATCTATTTAGATGTTAAAGGGCGTGCCTCTGCTGGTGTATATAAGCCACTTATGATGAAACTACAAAG AAGTTAATATGATAGGACTGATAAACTCCGTTGGCAACTGCGGAAGCTACAGCTATTCGGGGAGCGGC CACTTAACCCACAACCAAAATGCTGAAGTAAACAAAGAGGGTGTGATACGACCACAGTTCCGGGCTAAC TTGCTGCAGCAGGGGTTACTGGCGCCGATAAGGACAAATACAGCCCTTGTAAAGCTATCGTTTGAGGATAAA AAGGCTAAGGTTATGATGGTGGCTATGCAAGTGAAGTGGCGAGCAATTTCTATGCGCTACATATGATGA GAAACAGGTCGAATTACTGCTAAAACCCTACTTATACAGATGGTACGAGCGTTGCGTAAACTGGAGCTGT GAAATTTGGTGGCGCAANTGGTAAATCTGAAGTTGTTACTGCTACCGATGGTAAAGACTTACTAGCAAGCGA CTTGCAAAACATANDTTCAGAACAGGCGGTGAGCTTAAAGAGGTTAATACAGATAAGACTGAAAACCCACT GCAGAAATTTGATGCTGCCCTGGCAGAGGTTGATACACTCGTTGTGACCTGGGTGCGGTTCAAAACCGTT TCACTGCGCTATCCAGACCTGGGCAATACGTAATAACCTGTTCTGCGCCGTAGCCGTATGGAAGATT CGGACTAGCAACCGAAGTCTCCAAAGTGTCTGGCGCAGATTCGAGCAGGGCGGTAACCTCGGTTCT GGGCAGGCGAACCAGGTTCCGCAGAACGTCTCTCTTTACTGCGTTGATAAATAGGCTGGAGCCCTCGGTTG GCGATGCTTTGGCGCTTGGGCTCCCGCAGGCGCTCTGCGCTTCTGCAACCGGTAACCCGTTGGTC TTTGATAAAGTCTGAGTGGCGGCG</p>	51

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Name	Sequence	SEQ ID NO:
<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ORF Sequence, NT</p> <p>ATGSCACAAAGTCAATTAAATACAAACAGCCTGTCGCTGTTGACCCAGAAATAAGCTGAAACAATCCACATCCGC ACTSSGCACCTGCTATGCAGGCCTTTGCTCTGCCTGCTATGCAGAGCGCGAAAGAGCATGCGGSEAGSNA CAGSCGATTTGCTAAGCGTTTTACCGCGAACATCAAAAGGTCGACTCAGGCCTCCGCTAACGCTAACGACGG TATCTCATTTGCGCAGACACTGAAAGGGCGCTGAAAGAAAATAACAAEAACTGCAAGCGTGTGCCTGAA CTGSCGCTTCACTGCTGCAANTGGTACTAACTCCAGTCTGACCTCGACTCCATCCAGSCTGAAANTCAGCC GCGCTGAAAGCAAATCGACCTGTATCCGGCCAGACTCAGTTCAGCGCGGTGAAAGTCTCGCGCAGSAG AACACCTGACCATCGAGGTGCTGCAAGGACGGSTGAAACTATCGATATTGATTTAAAAGAAATCAGCTCT AAACACTGGGACTTGTAAAGCTTAATGTCDAAGATGCTACACCCGAAAGAAACTGCTGTAGCCTTGTAT AAACTACTATAAAAATGGTACAGATCTCTATTACAGCCAGAGCAANTACTGATATCCAACTGCAANTTGGC GGTGGTGCAGCGGGGCTTACTGGGGCTGATATCAAAATTTAAAGATGGTCAANTACTATTAGATGTTAAAGG CGGTGCTTGTGCTGGTGTTTATAAAGCCACTTATGATGAAACTACAAAGAAAGTTAATATTGATACGACTGA TAAACTCGTTGGCAACTGCGGAAAGTACAGCTATTCGGGAAAGCGCCACTATAAGCCACAACTAAATTTG CTGAGTAAACAAAGAGGGGTGTTGATACGACACAGTTCGGGCTCAGCTTGGCTGAGCGGGGTTACTGG CGCGATAGGACAACTACTAGCTTGTAAAACATGCTTTGAGGATAAAAACGGTAGGTTTGTGATGGTGG CTATGCGTGAATAATGGGCGAGCATTTCTATGCGCTACATATGATGAGAAACAGGTCGAANTACTGCTAA AGACTACTTATACAGATGGTACTGGCTTCTCAGACTGGAGETGTGAAATTTGGTGGCGCAATGGTA AATGTAAGTTGTTACTGCTACCGATGGTAAGACTTACTTACAGAGCGAGCTTGGCAAACTAATCTGAGAA CAGCGCGTGAAGTTAAAGAGGTTAATACAGATAAGACTGAAACCCACTGCAAGAAATTTGATGCTGCTTGG GCAAGGTTGATACATCGTCTGACCTGGGTGCGGTTGAGAACCGTTTCAGCTCCGCTATCCAACT GGGCATAGCTAAATACCTGCTCTGCGCCCTAGCCTATCGAAGATTCGAGACTGCAAGCCGAAGTCT CCAGCATGCTCTCGCGCAGAGTCTGAGAGGCGGCTACCTCGTTCTGGCGCAGCGCAAGCAAGGTTC CCAAACGTCCTCTCTTTACTGCT</p>	<p>52</p>
<p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>mRNA Sequence (assumes T100 tail)</p> <p>GTTGGAAAUANGAGAAANGANGASUANGANGAAUUNAAAGAGCCACCAUGGGACANGUCUUNAAUNACA ANGACCUUGUCGUUUGGUCAGAGAAUAAACUGAACAAAUCCAGUCGCGCACUUGGGCACUGUUNUGGAG CGUUGGUCUUGCGGUUUGACAGCGCGGAAAGAGCGUUGCGGGCAGGAGCGUUGGCUUAGCG UUUUACCGCGAACAUCAAAGGUUGAGUCAGAGCGUUCUGUAAAGCGUAAAGCACGGUUGUCUUCUUGCGG AGCCACUGAAGCGCGCGUGAACGAAAUCACAAACAGCUUCAGCGUGUGCGUGAAGUUGGGUUUCAG UUGCGAAUUGGUUAGUACUCCAGUUGAGACUUCAGUCCAUCCAGGCUUGAAAGACCCAGCGCTUGAAC GAAUCGACCGUUUUUUCGCGCAGACUCAGUUCACCGCGUGAAAGUUCUUGGCGCAGGACAAACAGCCU GACCAUCCAGGUUGGUUGCCAGCGAGCGUUUAAGCUUUCUUAUUUGUUUUAAAAGAAAAGCAGCUCUAAAAC ACUGGACUUGAUAAAGCUAAUUGUCGAAAGUUCGACACCCGAAAGAAACUGCGUUAAGCUGUUA ACUACCUUAAAANUGUACAGAGCGUUAUACAGCCGAGAGCAUACUUAUUGCCAAAGUUGCAALUGCG GGUGGUCAGCGGGGUUACUUGGGGUGAUUUCAAAUUUAAGAGUGGUCAAUACUUAUUJAGAUUUUAA NGCGGUGCUJUGGCUUGUUAUAAAGCAGUUAUGAUGAAGACUACAAAGAAAGUUAAUUAUUGUAC GACUGAAAAAACUCGUGGCAACUGCGGAAGCUACAGCUAUUCGGGAAAGGGCCAGUUAAGTCAAA CCAAUUGCUUAAGUACAAAAGAGGUGUUGUAUACGACACAGUUGCGGUCAGCUUGGUGCAAGCAG GGUUAUUGCGCGGAGUAAAGCACAUADUAGCCUUGUAAAACUUAUCGUGUAGGAAUAAAACGGUANGG UUUUGAUUGUGGCUUUGCAGUGAAMUUGGCGCACGAUUUCUUAUGCGGCUACUUAUGUUGAGAAACAA GGUCGAAUACUUGUAAAACGACUNCUUAUACAGAGUUGUACUGCGUUGCUAAACUGGAGCUGUGAAA UUUGUUGCGCGCAAUUGUAAGUGUGAAAGUUGUACUUGUACCGAUUGUAAAGCUUAACUUAAGCAAGCGA CUGGCAAAACUUAACUUCAGAACAGCGGUGGACCUUAAAGAGGUGUUAUACAGUAAAGACUGAAAACCC ACUGGCAAAAUUUGUGCGUGUUGGCTACAGGUUGUAACAGUUCGUUCUGAGCGUGGUGGUGGUGUUGA ACGUUUUCACUUCGCUUACAGACAGCCUGGCGAAUAGCGUAAAUAAACCUUGUUCUGCGCGUAGCCGUA UCCAGAUUCGACUACGCAACTGAGUUCACAGCUUGUUCGCGAGAGUUCUGCGAGCAGCGCGCG ACUUCGUGUGCGCGAGGCGAAGCAGGUCGCAAAACGUCCUGUUUAUCUGCGUUUGAUUAUAGCG UGGAGCGUCGUGGCGAGCGGAAAGCGGUGCGCAAAACGUCCUGUUUAUCUGCGUUUGAUUAUAGCG CGUAGCCCGUGGUGUUGUUAUUAAGUGUCUGAGUGGCGCGCAAAAAGAAAAAAAAAAAAAAAAAAAA AA \$</p>	<p>53</p>

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Name	Sequence	SEQ ID NO:
	<p>UAAAGAAAUAGAGUUCUAAAACACUGGGGACUUGAUAAAGCUUAUUGUCCANGAUAGCCUACACCCCGAAAG AACUGCCUUGUANCUGUUGAUAAAACUACUUNIAAANAUGGUACAGAUCCUUNUUACAGCCGAGAGCAGUAC UGAUACCAAAACUGCAAUUGGCUGUGUGUGCAGCAGGGGGUACUUGGGUGUGAUUACAAAUUUAAAAGUUG GUCAUUCUUAUUGAUAGUUAAAAGGCGGGUUCUUCUGUGUGUUUAUAAAAGCCACUUAUGAUAAACUUA CAAGCAAGUUAAUUAUAGAUAGGACUUNIAAAAACUCCGUUGGCAGCUGCCGGAAGCUCAGCCUUAUUCGGG GACGGCCACUAUAAACCACACACCAANUUGCUGAGGUAAACAAAGAGGGGUUGUUAUAGGACCACAGUU GGCCUCAACUUGCUAGCCAGGAGUUACUGGCCGCGAUAAAGGACAAUACUAGCCUUGUAAAACUUAUG UUUGAGGUAAAAAACGGUAAAGGUUAUUGAUUGUUUGGUUUGGUAGUUAGUUAAAAGGGCCGACUUAUUCU CGUACUAUUAUAGAAACAGGUAGCAUUAUAGUUGCUAAAACACUAUUAUACAGAUUGGUACUGGGGU UGCUCUACUUGGAGCUGUUAUUUGUGUGGCCAAAUUGUUAUUUCUGAAGUUGUUACUUGCUCACGAGU GUAGACUUACUUAAGCAAGCGACCUGGACAAACUAACUUCAGAACAGGGCGUGAGCUUAAAAGAGSUUA AUACAGUAAGACUGAAAACCCACUUGCAAAAUUUAUUGCUGCCUUGCCACAGGUUGUACACUUCGUU CUAGCCUGGGUGGGUUCAGAACCGUUCACUCCGCUAUCACCAACCUGGGCAAUACGUUAUUAAAC UGCUUUCUGCCGUAGCCGUAGUGAAGAUUCGGACUAGCCAGCCGAAAGUUCGCAACUUGUUCGCCCG CAGUAUCUGCAGCAGGCCGUAUCCUUGUUUGGGCCAGGCGAACAGGUCCGCAAAACGUCUUCU UUUACUGUU</p>	
mRNA Sequence (assumes T100 tail)	<p>GGGGAUUAAAGAGGAAAAGCAACAGUUAAGAAAGAAUUAAGAGCCACCAUGGCAAGUVCUUAUUAACAA AACGCCUGUUCGUGUUGGCCAGAAUAACAAUCCAGUCCCGACUUGGCUCUUGUGAGG GCUUUGGUGUUCGUUUGGUGUACAAAGGCGAAGAGACGAGUGCCAGGACAGGGUUAUUGCUAACC UUAUACCGCAACAUAAAGGUUGACUUGAGCCUCCGUAAACGUAAGGACGGUUAUCUUCUUGCGC AGACCUGAAGGGCGCGUGAACGAANUACAAACAGUUGGAGGGUUGUUGUUAAGUUUGGGUUGAG UUGCGUAGUUGAUUAACUUCUGAGUUGACUUCGACUCCAGCCAGGUGAANUACGCCAGCCUGAGAC GAUUGGCCGUGUUAUUGGGGCGAGUUCAGUUAACGGCGUGAAGGUUCUGGCGAGGACAGACGCU GCCUCCAGGGUUGGGCCAAAGCAGGUAAGUUUAGAUUUUAAGUUAAGAAAGUAGGUUCUAAAAC AGUGGACUUGUAAGGUUAUUUGGCAAGUUUCUAACCGCCGAAAGAAACUGUUGUUAACGUGUUA AAGUUCUUAUAAAAGUGUAACAGUUCUUAUACAGGECAGAGCAAAUACUGUAUUCGAAACUUGUUAUUGGG GGUGGUGCAACGGGGUUAUUGGGGUGUAUUAUCAAUUUUAAGAUUGGCAAAUACUUAUUAAGAUUA AGGUGUUGGUUUUGUGUUAUUAAGGCACUUAUUAUGAAAGUACAAAGAAAGUUUAUUAUGUUAAC GCUUAUAAAACUCCGUUGGCAACUGCGGAGGCUACAGCUUAUCGGGAAAGGGGACUUAUACCCACAA CCAAUUGCUUAAGUAACAAAGAGGGUUAUUAAGAAEACAGUUGCGGCUCAACUUGCUAGCAG GGUUACUGGCGCCGAUAAAGGACAAUACUAGCUGUUAUAAACUUAUCGUUUGAGGAUAAAACGGUAAAG UUUUAAGUUGGUUGGUUAUUGGCGGACGAUUUUAUUGCGCUACUAUUAUUAAGAAACUUAUUAAGGAAAC GUGCAAUUACUGCUAAAACACUACUUUAACAGAUUGUACUGCCUGUGGCUAAACUGGAGGUGUAAA UUUGGGGGCAAAUGUAUAUUGUAAAGUUUAUUGCUACGUUAUGGAAAGCUUAUUAAGCAAGCGA CCUGGACAAACUUAACUUCAGAACAGCGGUGGAGCUUAAGAGGUUAUUAACAGUAAGACUGAAAACCC ACUGGAGAAAUAUGUUGGUUGCUUGGCGACAGUUAUUAACAUUCUUCUGACCUUGGUUGGGUUCAG ACCGAUAUAUUCGUAUUCACACAGCUGGGCAGUACGUUAUUAAGGUGUUCUUAUUAAGGUGUUGG UUGAGUUAUCGADUAGCCAAACGAGUUCUUCACAGUUGUUCGGGGCAGAUUCUGCAGCAGGCUGU ACUUCUUGUUGGGUAGGCGAAGCAGGUUCGGCAAAACGUCUUCUUAUUAUUGUUUAUUAAGGCG UGGAGCCUUGGGUUGGCUAGGCUUUGGGUUGGCUUGCCCGAGGCCUUCUUCUUCUUCUUCUUGCGAGG CGUACCCCGUUGUUGUUAUUAAGUUCAGUUGGGGCGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAUCUA S</p>	83

Table 18. Human Metapneumovirus Mutant Amino Acid Sequences (Reference Example)

Strain	Sequence	SEQ ID NO:
HMPV_SC_DSCAV1_4MMV	<p> MSKRVFSGLLTPDAGLKEESVLEESVLEESVLSKNTGRTGNYTHVFLVGGDVEELTQSDGPRSLKTELEDAIKSAALRELKTYVSAQ QLKKEEEDKPSGSSFRKQALGVMAAAAVTASVYKATLRLLESETAVNNKAKTTRHAYSTLGGGQNVILKFAVRELKDFVSNMLT RLKRNKQDIDQLKRAYSSGDFPHHLYVPHGFSKRAASGTPKSLQIKTQKASLAKHAPHNPTASGQIKLQKAAHAKHAFKPSGL CGYKSSSRYVWLPKPSQNTTCWYKAAVSCSEKQDNYKLLREDDGQNTGQKAGSTYYVPRKQCETRGGHNFCDTAAAGNVA KQKQKESKRSSTTYTPKIVGSGRRHPSKPLGALVAGYKQVSCSGSHRYGQKLNKQCSNTRQDQNTYDQNTYDQNSVY EQDQYKGRPVSSDFPHFEDQVVALQDFEENKQALVDQSNRLSAGKQNTGPHWHLVGLSSMLVDFPHKATKPTT GPFELSGYTRNQGPPH </p>	85
HMPV_SC_DSTRIC_4MMV	<p> MSKRVFSGLLTPDAGLKEESVLEESVLEESVLSKNTGRTGNYTHVFLVGGDVEELTQSDGPRSLKTELEDAIKSAALRELKTYVSAQ QLKKEEEDKPSGSSFRKQALGVMAAAAVTASVYKATLRLLESETAVNNKAKTTRHAYSTLGGGQNVILKFAVRELKDFVSNMLT RLKRNKQDIDQLKRAYSSGDFPHHLYVPHGFSKRAASGTPKSLQIKTQKASLAKHAPHNPTASGQIKLQKAAHAKHAFKPSGL CGYKSSSRYVWLPKPSQNTTCWYKAAVSCSEKQDNYKLLREDDGQNTGQKAGSTYYVPRKQCETRGGHNFCDTAAAGNVA KQKQKESKRSSTTYTPKIVGSGRRHPSKPLGALVAGYKQVSCSGSHRYGQKLNKQCSNTRQDQNTYDQNTYDQNSVY EQDQYKGRPVSSDFPHFEDQVVALQDFEENKQALVDQSNRLSAGKQNTGPHWHLVGLSSMLVDFPHKATKPTT GPFELSGYTRNQGPPH </p>	86
HMPV_SC_DM_Krar up_T74LD185P	<p> MSKRVFSGLLTPDAGLKEESVLEESVLEESVLSKNTGRTGNYTHVFLVGGDVEELTQSDGPRSLKTELEDAIKSAALRELKTYVSAQ QLKKEEEDKPSGSSFRKQALGVMAAAAVTASVYKATLRLLESETAVNNKAKTTRHAYSTLGGGQNVILKFAVRELKDFVSNMLT RLKRNKQDIDQLKRAYSSGDFPHHLYVPHGFSKRAASGTPKSLQIKTQKASLAKHAPHNPTASGQIKLQKAAHAKHAFKPSGL CGYKSSSRYVWLPKPSQNTTCWYKAAVSCSEKQDNYKLLREDDGQNTGQKAGSTYYVPRKQCETRGGHNFCDTAAAGNVA KQKQKESKRSSTTYTPKIVGSGRRHPSKPLGALVAGYKQVSCSGSHRYGQKLNKQCSNTRQDQNTYDQNTYDQNSVY EQDQYKGRPVSSDFPHFEDQVVALQDFEENKQALVDQSNRLSAGKQNTGPHWHLVGLSSMLVDFPHKATKPTT GPFELSGYTRNQGPPH </p>	87
HMPV_SC_TM_Krar up_T74LD185PD454 N	<p> MSKRVFSGLLTPDAGLKEESVLEESVLEESVLSKNTGRTGNYTHVFLVGGDVEELTQSDGPRSLKTELEDAIKSAALRELKTYVSAQ QLKKEEEDKPSGSSFRKQALGVMAAAAVTASVYKATLRLLESETAVNNKAKTTRHAYSTLGGGQNVILKFAVRELKDFVSNMLT RLKRNKQDIDQLKRAYSSGDFPHHLYVPHGFSKRAASGTPKSLQIKTQKASLAKHAPHNPTASGQIKLQKAAHAKHAFKPSGL CGYKSSSRYVWLPKPSQNTTCWYKAAVSCSEKQDNYKLLREDDGQNTGQKAGSTYYVPRKQCETRGGHNFCDTAAAGNVA KQKQKESKRSSTTYTPKIVGSGRRHPSKPLGALVAGYKQVSCSGSHRYGQKLNKQCSNTRQDQNTYDQNTYDQNSVY EQDQYKGRPVSSDFPHFEDQVVALQDFEENKQALVDQSNRLSAGKQNTGPHWHLVGLSSMLVDFPHKATKPTT GPFELSGYTRNQGPPH </p>	88
HMPV_SC_4M_Krar up_	<p> MSKRVFSGLLTPDAGLKEESVLEESVLEESVLSKNTGRTGNYTHVFLVGGDVEELTQSDGPRSLKTELEDAIKSAALRELKTYVSAQ QLKKEEEDKPSGSSFRKQALGVMAAAAVTASVYKATLRLLESETAVNNKAKTTRHAYSTLGGGQNVILKFAVRELKDFVSNMLT RLKRNKQDIDQLKRAYSSGDFPHHLYVPHGFSKRAASGTPKSLQIKTQKASLAKHAPHNPTASGQIKLQKAAHAKHAFKPSGL CGYKSSSRYVWLPKPSQNTTCWYKAAVSCSEKQDNYKLLREDDGQNTGQKAGSTYYVPRKQCETRGGHNFCDTAAAGNVA KQKQKESKRSSTTYTPKIVGSGRRHPSKPLGALVAGYKQVSCSGSHRYGQKLNKQCSNTRQDQNTYDQNTYDQNSVY EQDQYKGRPVSSDFPHFEDQVVALQDFEENKQALVDQSNRLSAGKQNTGPHWHLVGLSSMLVDFPHKATKPTT GPFELSGYTRNQGPPH </p>	89

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Strain	Sequence	SEQ ID NO:
T74LS170LD185P	<p> HHHNNCCGEEELKAAAFEEEDFMRFLNYYRDFSDMAGTTPMSSLDLNTDLELRRAPVPMPTSGDQKLMENRANPPRNGFGLI GPPGSGRYWYVQDFRGGWDTPCWYKAPSCSEKKNZYACLLREDCGKQKAGSTYYYPHESDCETRQGHPCDTAAAGNVA EEDGECNNGSTTTPCKVSTGHHPSSWMLSPGLMVAQYKVSQSGSHRVRHQGNKDCSTNQQDADTYTQNHVYVQLSKVE GGDWKKSHPVSSDTPRFFDFQVNLQDFEFHNSQALVQDQWHLSSAEKQNTGTFHWHLLAGSSMLVSRHMKTKRPTG APTLGGYTHNGSPFHH </p>	90
HMPV_SC_5M_Krar up_T74LS170LD185 PD454N	<p> HHHNNCCGEEELKAAAFEEEDFMRFLNYYRDFSDMAGTTPMSSLDLNTDLELRRAPVPMPTSGDQKLMENRANPPRNGFGLI GPPGSGRYWYVQDFRGGWDTPCWYKAPSCSEKKNZYACLLREDCGKQKAGSTYYYPHESDCETRQGHPCDTAAAGNVA EEDGECNNGSTTTPCKVSTGHHPSSWMLSPGLMVAQYKVSQSGSHRVRHQGNKDCSTNQQDADTYTQNHVYVQLSKVE GGDWKKSHPVSSDTPRFFDFQVNLQDFEFHNSQALVQDQWHLSSAEKQNTGTFHWHLLAGSSMLVSRHMKTKRPTG APTLGGYTHNGSPFHH </p>	91
HMPV_SC_DM_Krar up_E51PT74L	<p> HHHNNCCGEEELKAAAFEEEDFMRFLNYYRDFSDMAGTTPMSSLDLNTDLELRRAPVPMPTSGDQKLMENRANPPRNGFGLI GPPGSGRYWYVQDFRGGWDTPCWYKAPSCSEKKNZYACLLREDCGKQKAGSTYYYPHESDCETRQGHPCDTAAAGNVA EEDGECNNGSTTTPCKVSTGHHPSSWMLSPGLMVAQYKVSQSGSHRVRHQGNKDCSTNQQDADTYTQNHVYVQLSKVE GGDWKKSHPVSSDTPRFFDFQVNLQDFEFHNSQALVQDQWHLSSAEKQNTGTFHWHLLAGSSMLVSRHMKTKRPTG APTLGGYTHNGSPFHH </p>	92
HMPV_SC_TM_Krar up_E51PT74LD454N	<p> HHHNNCCGEEELKAAAFEEEDFMRFLNYYRDFSDMAGTTPMSSLDLNTDLELRRAPVPMPTSGDQKLMENRANPPRNGFGLI GPPGSGRYWYVQDFRGGWDTPCWYKAPSCSEKKNZYACLLREDCGKQKAGSTYYYPHESDCETRQGHPCDTAAAGNVA EEDGECNNGSTTTPCKVSTGHHPSSWMLSPGLMVAQYKVSQSGSHRVRHQGNKDCSTNQQDADTYTQNHVYVQLSKVE GGDWKKSHPVSSDTPRFFDFQVNLQDFEFHNSQALVQDQWHLSSAEKQNTGTFHWHLLAGSSMLVSRHMKTKRPTG APTLGGYTHNGSPFHH </p>	

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Strain	Sequence	SEQ ID NO:
HMPV_SC_StabilizeAlpha_T74L	<p> MNNKVFSLITPQHLKESNLEESCSITTEGRLSRLRTGNTYTHFLKYGQVFAWCSQSPSLKTEBLTKSALRELKTVSAD CLAKTESEHPGSSSTVGLALGVAAAANKTADYAAKTRHLESETMNAKNTREASTLGMQVYRLATAVRELKDFVSRMLT HAKMMDQDELKKAASQSPNRRFLNYYRQFSDMASTPAGLQIMQALASAPYRHPPTSASQDLKSHRANRRKGFQSL GYQSSRYTVQDPTFGADPTGNTYKAPPSCSEKKNQYKALLREDGQKQKAGQTYYPWESDCEFRGSHVCDZTAAQDNYA EDSNCKMNSTTTPCKVSTGRHPSIMALSPISALVACVAGVCSGSHRVSQKKNKCSNINQDADTYTQNHVYVLSAVE GEDMNRHPVSSDTPFPEDQVHLQDFEHEEVSQALVQDQWPRLSAEKQNTQTFHMLLAKGSSMLVSPHINIKRPTQ APPLSGYTRNGSPFK </p>	93
HMPV_SC_StabilizeAlpha_V55L	<p> MNNKVFSLITPQHLKESNLEESCSITTEGRLSRLRTGNTYTHFLKYGQVFAWCSQSPSLKTEBLTKSALRELKTVSAD CLAKTESEHPGSSSTVGLALGVAAAANKTADYAAKTRHLESETMNAKNTREASTLGMQVYRLATAVRELKDFVSRMLT HAKMMDQDELKKAASQSPNRRFLNYYRQFSDMASTPAGLQIMQALASAPYRHPPTSASQDLKSHRANRRKGFQSL GYQSSRYTVQDPTFGADPTGNTYKAPPSCSEKKNQYKALLREDGQKQKAGQTYYPWESDCEFRGSHVCDZTAAQDNYA EDSNCKMNSTTTPCKVSTGRHPSIMALSPISALVACVAGVCSGSHRVSQKKNKCSNINQDADTYTQNHVYVLSAVE GEDMNRHPVSSDTPFPEDQVHLQDFEHEEVSQALVQDQWPRLSAEKQNTQTFHMLLAKGSSMLVSPHINIKRPTQ APPLSGYTRNGSPFK </p>	94
HMPV_SC_StabilizeAlpha_S170L	<p> MNNKVFSLITPQHLKESNLEESCSITTEGRLSRLRTGNTYTHFLKYGQVFAWCSQSPSLKTEBLTKSALRELKTVSAD CLAKTESEHPGSSSTVGLALGVAAAANKTADYAAKTRHLESETMNAKNTREASTLGMQVYRLATAVRELKDFVSRMLT HAKMMDQDELKKAASQSPNRRFLNYYRQFSDMASTPAGLQIMQALASAPYRHPPTSASQDLKSHRANRRKGFQSL GYQSSRYTVQDPTFGADPTGNTYKAPPSCSEKKNQYKALLREDGQKQKAGQTYYPWESDCEFRGSHVCDZTAAQDNYA EDSNCKMNSTTTPCKVSTGRHPSIMALSPISALVACVAGVCSGSHRVSQKKNKCSNINQDADTYTQNHVYVLSAVE GEDMNRHPVSSDTPFPEDQVHLQDFEHEEVSQALVQDQWPRLSAEKQNTQTFHMLLAKGSSMLVSPHINIKRPTQ APPLSGYTRNGSPFK </p>	95
HMPV_SC_StabilizeAlpha_T174W	<p> MNNKVFSLITPQHLKESNLEESCSITTEGRLSRLRTGNTYTHFLKYGQVFAWCSQSPSLKTEBLTKSALRELKTVSAD CLAKTESEHPGSSSTVGLALGVAAAANKTADYAAKTRHLESETMNAKNTREASTLGMQVYRLATAVRELKDFVSRML HAKMMDQDELKKAASQSPNRRFLNYYRQFSDMASTPAGLQIMQALASAPYRHPPTSASQDLKSHRANRRKGFQSL GYQSSRYTVQDPTFGADPTGNTYKAPPSCSEKKNQYKALLREDGQKQKAGQTYYPWESDCEFRGSHVCDZTAAQDNYA EDSNCKMNSTTTPCKVSTGRHPSIMALSPISALVACVAGVCSGSHRVSQKKNKCSNINQDADTYTQNHVYVLSAVE GEDMNRHPVSSDTPFPEDQVHLQDFEHEEVSQALVQDQWPRLSAEKQNTQTFHMLLAKGSSMLVSPHINIKRPTQ APPLSGYTRNGSPFK </p>	96

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Strain	Sequence	SEQ ID NO:
HMPV_SC_4M_Stablii zeAlpha_V55LT74L S170LT174W	<p> MNNKVFSLITPQALKEEYVEECSSTTESLGRHTGNTWYFTLGGDVEKTCSDGPTLITELTKSALRELKTYGAD CLAREDEEYFSSDPTLQALGVAAAANTAGYAAKTHLESETMNAKKTREASTLGRDVRWLAIAKELKDFVLLWLY RANRNDLDELKAAVSDPFRHFLWYRQSNAGTPASLIDLDTDELAPYPRMPTSAQDKLWENRANRRKGFGLI GYDSEVTVVQLPFGVDTPTWTKAAPSCSEKQNYKLLREDQWQCKADSTYYPHEDCETRQDHVFCQTAAGWVA EDSMCKMSTTVFKVSTGRHPSWMLSPGLVACVYKGSVSGSHRVSNGKAKCSYINQDADTYIIONTVYQLSKVE GEDMNRGHPVSSDPHPEDQVNLQDFEHEVSDALVQDQWRLSSAEKNTQTFWILLAKGSSMLYSPHMKTKPTG #PFLSSYTHNGSPFK </p>	97
HMPV_ProlineStab_E51P	<p> MNNKVFSLITPQALKEEYVEECSSTTESLGRHTGNTWYFTLGGDVEKTCSDGPTLITELTKSALRELKTYGAD CLAREDEEYFSSDPTLQALGVAAAANTAGYAAKTHLESETMNAKKTREASTLGRDVRWLAIAKELKDFVSSMLT RANRNDLDELKAAVSDPFRHFLWYRQSNAGTPASLIDLDTDELAPYPRMPTSAQDKLWENRANRRKGFGLI GYDSEVTVVQLPFGVDTPTWTKAAPSCSEKQNYKLLREDQWQCKADSTYYPHEDCETRQDHVFCQTAAGWVA EDSMCKMSTTVFKVSTGRHPSWMLSPGLVACVYKGSVSGSHRVSNGKAKCSYINQDADTYIIONTVYQLSKVE GEDMNRGHPVSSDPHPEDQVNLQDFEHEVSDALVQDQWRLSSAEKNTQTFWILLAKGSSMLYSPHMKTKPTG #PFLSSYTHNGSPFK </p>	98
HMPV_ProlineStab_D185P	<p> MNNKVFSLITPQALKEEYVEECSSTTESLGRHTGNTWYFTLGGDVEKTCSDGPTLITELTKSALRELKTYGAD CLAREDEEYFSSDPTLQALGVAAAANTAGYAAKTHLESETMNAKKTREASTLGRDVRWLAIAKELKDFVSSMLT RANRNDLDELKAAVSDPFRHFLWYRQSNAGTPASLIDLDTDELAPYPRMPTSAQDKLWENRANRRKGFGLI GYDSEVTVVQLPFGVDTPTWTKAAPSCSEKQNYKLLREDQWQCKADSTYYPHEDCETRQDHVFCQTAAGWVA EDSMCKMSTTVFKVSTGRHPSWMLSPGLVACVYKGSVSGSHRVSNGKAKCSYINQDADTYIIONTVYQLSKVE GEDMNRGHPVSSDPHPEDQVNLQDFEHEVSDALVQDQWRLSSAEKNTQTFWILLAKGSSMLYSPHMKTKPTG #PFLSSYTHNGSPFK </p>	99
HMPV_ProlineStab_D183P	<p> MNNKVFSLITPQALKEEYVEECSSTTESLGRHTGNTWYFTLGGDVEKTCSDGPTLITELTKSALRELKTYGAD CLAREDEEYFSSDPTLQALGVAAAANTAGYAAKTHLESETMNAKKTREASTLGRDVRWLAIAKELKDFVSSMLT RANRNDLDELKAAVSDPFRHFLWYRQSNAGTPASLIDLDTDELAPYPRMPTSAQDKLWENRANRRKGFGLI GYDSEVTVVQLPFGVDTPTWTKAAPSCSEKQNYKLLREDQWQCKADSTYYPHEDCETRQDHVFCQTAAGWVA EDSMCKMSTTVFKVSTGRHPSWMLSPGLVACVYKGSVSGSHRVSNGKAKCSYINQDADTYIIONTVYQLSKVE GEDMNRGHPVSSDPHPEDQVNLQDFEHEVSDALVQDQWRLSSAEKNTQTFWILLAKGSSMLYSPHMKTKPTG #PFLSSYTHNGSPFK </p>	100

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Strain	Sequence	SEQ ID NO:
HMPV_ProlineStab_E131P	<p> MNNWVPLUFPQHLKESNLEESCSITFEGVLSRHTGNTWTFLEYSQVEMTOSGQPSLNTBLSLTKSALREKTYVSAQ CLAFEESEHPGSSSTLGMALGVAAAANTAGYAAKTRHLESETMNMALKATREASTLGMGVRMLATAREELKDFVSNMLT HANNMCDLDEKKAAYSQSPNRRFLNRRDFSNMAGTTPASLDLMTQALEAPYPRMPTSAQDLMLKSHRANWRKNGFGLI GYQSSVRYVQLPFGVDTFCWTKMAPSCSEKRWYKLLREDGQWQKAGSTYYPIWESDCETRQDHVFCQTAADNVA EDSMCDMMSTTTPCKVSTGHHPISWMLSPGLAVQYQVCSGSHRVSNGCNKDCSTNQQDADTYTQNHVYVQLSAVE GSDMNRGHPVSSDFRPFQDFQVLDQFENENSDALVDQSRMLSSAEKGNTPMILLAKGSSMLVSPHMKTKPTG APFLSGYTRNGSPFK </p>	101
HMPV_ProlineStab_D447P	<p> MNNWVPLUFPQHLKESNLEESCSITFEGVLSRHTGNTWTFLEYSQVEMTOSGQPSLNTBLSLTKSALREKTYVSAQ CLAFEESEHPGSSSTLGMALGVAAAANTAGYAAKTRHLESETMNMALKATREASTLGMGVRMLATAREELKDFVSNMLT HANNMCDLDEKKAAYSQSPNRRFLNRRDFSNMAGTTPASLDLMTQALEAPYPRMPTSAQDLMLKSHRANWRKNGFGLI GYQSSVRYVQLPFGVDTFCWTKMAPSCSEKRWYKLLREDGQWQKAGSTYYPIWESDCETRQDHVFCQTAADNVA EDSMCDMMSTTTPCKVSTGHHPISWMLSPGLAVQYQVCSGSHRVSNGCNKDCSTNQQDADTYTQNHVYVQLSAVE GSDMNRGHPVSSDFRPFQDFQVLDQFENENSDALVDQSRMLSSAEKGNTPMILLAKGSSMLVSPHMKTKPTG APFLSGYTRNGSPFK </p>	102
HMPV_TrimerRepuls ionD454N	<p> MNNWVPLUFPQHLKESNLEESCSITFEGVLSRHTGNTWTFLEYSQVEMTOSGQPSLNTBLSLTKSALREKTYVSAQ CLAFEESEHPGSSSTLGMALGVAAAANTAGYAAKTRHLESETMNMALKATREASTLGMGVRMLATAREELKDFVSNMLT HANNMCDLDEKKAAYSQSPNRRFLNRRDFSNMAGTTPASLDLMTQALEAPYPRMPTSAQDLMLKSHRANWRKNGFGLI GYQSSVRYVQLPFGVDTFCWTKMAPSCSEKRWYKLLREDGQWQKAGSTYYPIWESDCETRQDHVFCQTAADNVA EDSMCDMMSTTTPCKVSTGHHPISWMLSPGLAVQYQVCSGSHRVSNGCNKDCSTNQQDADTYTQNHVYVQLSAVE GSDMNRGHPVSSDFRPFQDFQVLDQFENENSDALVDQSRMLSSAEKGNTPMILLAKGSSMLVSPHMKTKPTG APFLSGYTRNGSPFK </p>	103
HMPV_TrimerRepuls ionE453N	<p> MNNWVPLUFPQHLKESNLEESCSITFEGVLSRHTGNTWTFLEYSQVEMTOSGQPSLNTBLSLTKSALREKTYVSAQ CLAFEESEHPGSSSTLGMALGVAAAANTAGYAAKTRHLESETMNMALKATREASTLGMGVRMLATAREELKDFVSNMLT HANNMCDLDEKKAAYSQSPNRRFLNRRDFSNMAGTTPASLDLMTQALEAPYPRMPTSAQDLMLKSHRANWRKNGFGLI GYQSSVRYVQLPFGVDTFCWTKMAPSCSEKRWYKLLREDGQWQKAGSTYYPIWESDCETRQDHVFCQTAADNVA EDSMCDMMSTTTPCKVSTGHHPISWMLSPGLAVQYQVCSGSHRVSNGCNKDCSTNQQDADTYTQNHVYVQLSAVE GSDMNRGHPVSSDFRPFQDFQVLDQFENENSDALVDQSRMLSSAEKGNTPMILLAKGSSMLVSPHMKTKPTG APFLSGYTRNGSPFK </p>	104
HMPV_StabilizeAlph	<p> MNNWVPLUFPQHLKESNLEESCSITFEGVLSRHTGNTWTFLEYSQVEMTOSGQPSLNTBLSLTKSALREKTYVSAQ CLAFEESEHPGSSSTLGMALGVAAAANTAGYAAKTRHLESETMNMALKATREASTLGMGVRMLATAREELKDFVSNMLT HANNMCDLDEKKAAYSQSPNRRFLNRRDFSNMAGTTPASLDLMTQALEAPYPRMPTSAQDLMLKSHRANWRKNGFGLI GYQSSVRYVQLPFGVDTFCWTKMAPSCSEKRWYKLLREDGQWQKAGSTYYPIWESDCETRQDHVFCQTAADNVA EDSMCDMMSTTTPCKVSTGHHPISWMLSPGLAVQYQVCSGSHRVSNGCNKDCSTNQQDADTYTQNHVYVQLSAVE GSDMNRGHPVSSDFRPFQDFQVLDQFENENSDALVDQSRMLSSAEKGNTPMILLAKGSSMLVSPHMKTKPTG APFLSGYTRNGSPFK </p>	105

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Strain	Sequence	SEQ ID NO:
aF196W	<p> CLAFEEZ ENFISGDFVLCALGIAAAANTAGYAKTRLESEETAMWALWTKAEVETLGMKQVWVATKPEEKEFVGNKLT RHHKQDGLKAAVSRQWVAREKVVDFQSDHNSITFMQDQWYAEIAPAPVPSAGQKMLPRHAWPSRSPFLU QVSSWYVWLPFISVDTREWYAAPEVSEKIDRYADLRDQWVQWAGSTVYFREDVETFAQDVFQDVAQWVAA ESKEDMINISTHYSKVFQSPHPSVVALSPVQALVAGVYKVSQVSSVSRVSHVULKAGSNTWVQDAGTYDQWTVYDSEVYF GEDWQVPSSEDFPPEEDQVALDQVPEVNSQALVYQSKNELSEKEDVETDEVELLALDSSKLVSRHAKTQKPTG APPELSTVTKSRFPH </p>	

Table 19. Human Metapneumovirus Mutant Nucleic Acid Sequences (Reference Example)

Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGAGCTGGAAAGTGGTCAATCTTTCAGCCTGGTATCACCTCAGCACGGCTGAAAGAGAG CTACCTGGAAAGTCCCTGCAAGCACCATCACAGAGGGCTACCTGTCTGTCTGAGAACCGGCTGGT ACACCAACGTGTTCAACTGGAAGTGGGGGACGTGAGAACTGTGACATGCTCTGTATGGCCCTAGC CTGATCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAGAACTCAAGACCSTGTCTGCGGSA TLAGCTGGCCAGAGAGGAACAGATCAGAAATCTGGCAGCGGCAGCTTTGTGCTGGAGGCCATT GCTCTGGAGTGGCTGTCTGTGAGCTGTTACAGCAGGCSTGGCCATCTGCAAGACCATCAGACT GGAAGCAGAGTGAACGCCATCAACAGCCCTGAAAGAGACAAACGAGGCCTGAGCAGACTC GGCATGGCCTTAGAGTGGTGGCCTTTGGCCGTGGCAGAGTGAAGGACTTGTGTCCAGAACTT GACAGGGCCCTGAAACAGAAACAGTGGCAGACTGACGACCTGAAAGATGGCCGTGTCTTTAGCC AGTCAACCGGGGTTTGTGAACGTCTGTCGGCAGTTTAGCAGCAACGCGGAAATCACACAGCC ATCAGCCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGGCTAACATGCTCATCTGCG GGGCAGATCAAGCTGATGCTGAGAAATAGAGCCATGGTCCGACGGAAAGGCTGTGGCATCTGTT GTGGCCTGTACGGCAGCAGCCTGATCTATATGCTGAGCTGCTATGTTCCGGCCTGATCGACAC CCTGTGTTGATTTGTGAAGGGCGCTCCTAGCTGTAGCGAGAAAGAGGGCAATTACGCTGGCCGTCT GAGAGAGACCAAGGCTGATATTTGTCAGAACGCCGGCAGCAGCCTGTACTACCTAACAGAGAG GACTGGAGACAGAGAGCGGACCAAGTGTCTGTGATACCGCCGCTGGAAATCAATGTGGCCGAGC AGAGCAAGAGTGCACATCAACATCAGCACCACCAACTATCCCTGCAAGGTGTGCCAGCGGCAGG CACCCATTTCTATGTTGGCTCTGTCTCCCTGGAGGCCCTGGTGGCTGTGTTAAGGGCGTGTCC TGTAGCATCGCCAGCAGCAGAGTGGCCATCAGAGCAGCTGAACAGGGCTGCAAGTACATCAC CAGCAGGACGCCGATACCGTGCATCGACAGCAGCAGCTGTATCAGGTGAGCAAGGTGGAGAGCC GACAGCACGTGATCAAGGGCAGACCTGTGTCTCAGCAGCTTCGACCCATCAAGTTCCTGAGGA TCACTTCAAGGTGGCCCTGGACAGGTGTCTGAGAACATCAGAAATGCCAGGCTCTGTTGGACCC AGTCCAGCAGAACTCTGTACTGCGCCGAGAGGGGAAACACCAGCCTCACATGCTGATCTATCTG ATCGGCTGTCTGGCCAGCTCCATGATCCTGGTGTGCTATCTCATCATATCAAGAGACCAAGAA GCCACCGGGCTCTCCAGAACTGAGCGGAGTGCACCAAGATGGCTCTATCCCTCACAG</p>	<p>106</p>
<p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ATGAGCTGGAAAGTGGTCAATCTTTCAGCCTGGTATCACCTCAGCACGGCTGAAAGAGAG CTACCTGGAAAGTCCCTGCAAGCACCATCACAGAGGGCTACCTGTCTGTCTGAGAACCGGCTGGT ACACCAACGTGTTCAACTGGAAGTGGGGGACGTGAGAACTGTGACATGCTCTGTATGGCCCTAGC CTGATCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAGAACTCAAGACCSTGTCTGCGGSA TLAGCTGGCCAGAGAGGAACAGATCAGAAATCTGGCAGCGGCAGCTTTGTGCTGGAGGCCATT GCTCTGGAGTGGCTGTCTGTGAGCTGTTACAGCAGGCSTGGCCATCTGCAAGACCATCAGACT GGAAGCAGAGTGAACGCCATCAACAGCCCTGAAAGAGACAAACGAGGCCTGAGCAGACTC GGCATGGCCTTAGAGTGGTGGCCTTTGGCCGTGGCAGAGTGAAGGACTTGTGTCCAGAACTT TGAACGGCCATTAAACAGAAACAGTGGGACATCGACGACCTGAAAGATGGCCGTGTCTTTAGC CAGTTCAACCGGGGTTTGTGAACGTCTGTGGCAGTTTAAAGGACAGCCGGGAAATCACAGCAGC CATCAGCCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGGCTAACATGCTCATCTG CCGGCCAGATCAAGCTGATGCTGAGAAATAGAGCCATGGTCCGACGGAAAGGCTTGGCCATTCTG TGTGGCTGTACGGCAGCAGGCTGATCTATATGGTGCAGCTGCTATCTTGGCCGTGATCGACAC ACCCTGCTGATTTGTGAAGGCCTCTCCTAGCTGTAGGGAGAAAGAGGGCAATTACGCTGGCTG TGAAGAGGAGCACAGGCTGGTATTGTGACAGACGCCGGCAGCAGCAGCTGTACTACCCTAACGAGAA GACTGGAGACAGAGAGCGGACCAAGTGTCTGTGATACCGCCGCTGGAAATCAATGTGGCCGAGC AGAGCAAGAGTGCACATCAACATCAGCACCACCAACTATCCCTGCAAGGTGTGCCAGCGGCAGG CACCCATTTCTATGTTGGCTCTGTCTCCCTGGAGGCCCTGGTGGCTGTGTTAAGGGCGTGTCC TGTAGCATCGCCAGCAGCAGAGTGGCCATCAGAGCAGCTGAACAGGGCTGCAAGTACATCAC CAGCAGGACGCCGATACCGTGCATCGACAGCAGCAGCTGTATCAGGTGAGCAAGGTGGAGAGCC GACAGCACGTGATCAAGGGCAGACCTGTGTCTCAGCAGCTTCGACCCATCAAGTTCCTGAGGA CCACTGGCAGTGGCCCTGGACAGGTGTCTGAGAAACATCGAGAAATCCAGGCTCTGTGTGGAC CAGTCCACAGAAATCTGTCTTAGCAGCCGAGAAAGGAAACACCAGCCTCACATGCTGATCTATCC GATCGGCTGTCTGGCCAGCTCCATGATCTGGGTGTCACATTTCAATATCAAGAGACCAGAA GCCACCGGCGCTCTCCAGAACTGAGCGGAGTGCACCAAGATGGCTCTATCCCTCACAG</p>	<p>107</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5 HMPV_SC_DM_Krarup_T7 4LD185P</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGAGCTGGAAAGGTGGTCATCATTTCAGCCTGCTGATCACACCTCAGCACGGCCTGAAAGGAGAG CTACCTGGAAAGGTGCTGAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAGAAACGGGCTGGT ACACCAACGTGTTCACTGGAAGTGGGGCACGTGAGAACTGTGACATGCTCTGATGGCCCTAGC CTGATCAAGACCGAGCTGGATCTGCTCAAGAGCGGCCCTGAGAGAACTCAGACCGGTGCTGTGGAA TCAGCTGGCCAGAGAGGAAKAGATCGAGAATCTGGCCAGCGGCAGCTTTGTGCTGGAGGCCATT GCTCTGGAGTGGCTGCTGCTGAGCTGTTACAGCAGGCCTGGCCATCGCTAAGACCATCAGACT GGAAAGCGAAGTGAACGCCATCACAAAGCCCTGAAAGAAACAAACGAGGCCGTGAGCAGACTG GGCATTGGCGTTAAGAGTGGTGGCCACAGCCGTGGCCGAGCTGAAAGACTTCGTGTCCAAAGAAC TGACAGGGGCCATTAAACAAGAACAAAGTGGACATCCCTGACCTGAAGATGGCCGTGTGCTTTAGC CAGTTCAACCGGCCTTTCTGACGTCGTGCGCCAGTTTAAAGGACAAAGCCGGAAATCACAGCAGC CATCAGCCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGCTTAACTATGCTACATCTG CCGGCCAGATCAAGCTGATGCTCAGAAATAGAGCCATGGTCCGACGGAAAGGCTTGGCCATCTG ATTGGGTGTACGGCAGCAGCGTGTATATATGGTGGAGCTGCTATCTTGGCGTGTATGACAC ACCTGCTGGATTGTGAAGCCGCTCTCTAGCTGTAGGAGAAAGAGGGCAATTAAGCCTGCCCTGC TGAGAGAGGACCAAGGCTGGTATTGTCAAGAGCCGGCCAGCAGCAGCTGTACTAGCCTAAGGAGAG GACTGGGAGACAAAGAGCGGACCAGTGTCTGTGATACCGCCGCTGGAAATCAATGTGGCCGAGC AGAGCAAAAGAGTGCACATCAACATCAGCAGCCACCAACTATCCCTGCAAGGTGTCCAGCGCAGG CAGCCTATTTCTATGCTGGCTCTGTCTCCCTGAGAGCCCTGGTGGCTTGTATAAGGGCGTGTCC TGTAGCATCGGCAGCAAGAGTGGGCATCATCAAGCAGCTGAACAAGGGCTGCAAGCTACATCAC CAKCCAGGACGCCGATACCGTGAACATCGACAAACAGCTGTATCAGCTGAGCAAGGTGGAAAGCC GAKAGCACGTGATCAAGGGCAGACCTGTGTCCAGCAGCTTCGACCCATCAAGTTCCTTGAGGA TCAGTTCCAGGTGGCCCTGGAGCAGGTGTTCAGAAACATCAGAAATTCAGAGGCTGTGGTGGACC AGTCCAACAGAACTCTGTCTAGCGCCGAGAAAGGAAACAGCGGCTTCATCATCGTGTATCTCTG ATCGCGGTGCTGGCCAGCTCCATGATCCTGGTGTCCATCTTCATCATTAATCAAGAAAGCAAGAAAG CCCAAGGGCGCTCTCCAGAACTGAGCGGAGTGAACCAACAATGGCTTCATCCCTCACAG</p>	<p>108</p>
<p>HMPV_SC_TM_Kramp_T7 4LD185PD454N</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ATGAGCTGGAAAGGTGGTCATCATTTCAGCCTGCTGATCACACCTCAGCACGGCCTGAAAGGAGAG CTACCTGGAAAGGTGCTGAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAGAAACGGGCTGGT ACACCAACGTGTTCACTGGAAGTGGGGCACGTGAGAACTGTGACATGCTCTGATGGCCCTAGC CTGATCAAGACCGAGCTGGATCTGCTCAAGAGCGGCCCTGAGAGAACTCAGACCGGTGCTGTGGAA TCAGCTGGCCAGAGAGGAAKAGATCGAGAATCTGGCCAGCGGCAGCTTTGTGCTGGAGGCCATT GCTCTGGAGTGGCTGCTGCTGAGCTGTTACAGCAGGCCTGGCCATCGCTAAGACCATCAGACT GGAAAGCGAAGTGAACGCCATCACAAAGCCCTGAAAGAAACAAACGAGGCCGTGAGCAGACTG GGCATTGGCGTTAAGAGTGGTGGCCACAGCCGTGGCCGAGCTGAAAGACTTCGTGTCCAAAGAAC TGACAGGGGCCATTAAACAAGAACAAAGTGGACATCCCTGACCTGAAGATGGCCGTGTGCTTTAGC CAGTTCAACCGGCCTTTCTGACGTCGTGCGCCAGTTTAAAGGACAAAGCCGGAAATCACAGCAGC CATCAGCCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGCTTAACTATGCTACATCTG CCGGCCAGATCAAGCTGATGCTCAGAAATAGAGCCATGGTCCGACGGAAAGGCTTGGCCATCTG ATTGGGTGTACGGCAGCAGCGTGTATATATGGTGGAGCTGCTATCTTGGCGTGTATGACAC ACCTGCTGGATTGTGAAGCCGCTCTCTAGCTGTAGGAGAAAGAGGGCAATTAAGCCTGCCCTG TGAGAGAGGACCAAGGCTGGTATTGTCAAGAGCCGGCCAGCAGCAGCTGTACTAGCCTAAGGAGAG GACTGGGAGACAAAGAGCGGACCAGTGTCTGTGATACCGCCGCTGGAAATCAATGTGGCCGAGC AGAGCAAAAGAGTGCACATCAACATCAGCAGCCACCAACTATCCCTGCAAGGTGTCCAGCGCAGG CAGCCTATTTCTATGCTGGCTCTGTCTCCCTGAGAGCCCTGGTGGCTTGTATAAGGGCGTGTCC TGTAGCATCGGCAGCAAGAGTGGGCATCATCAAGCAGCTGAACAAGGGCTGCAAGCTACATCAC CAKCCAGGACGCCGATACCGTGAACATCGACAAACAGCTGTATCAGCTGAGCAAGGTGGAAAGCC GAKAGCACGTGATCAAGGGCAGACCTGTGTCCAGCAGCTTCGACCCATCAAGTTCCTTGAGGA CCAGTTCCAGGTGGCCCTGGAGCAGGTGTTCAGAAACATCAGAAATTCAGAGGCTGTGGTGGACC AGTCCAACAGAACTCTGTCTAGCGCCGAGAAAGGAAACAGCGGCTTCATCATCGTGTATCTCTG ATCGCGGTGCTGGCCAGCTCCATGATCCTGGTGTCCATCTTCATCATTAATCAAGAAAGCAAGAAAG CCCAAGGGCGCTCTCCAGAACTGAGCGGAGTGAACCAACAATGGCTTCATCCCTCACAG</p>	<p>109</p>

(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>HMPV_SC_4M_Krarup_T74LS170LD185P</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGAGCTGGAAAGTGGTCAATCATTTCAGCCTGCTGATCAACCTCAGCAGGGCTGAAAAGAGAG CTACCTGGAAAGTGGTGGAGCCATCAGAGAGGGCTACCTGTCTGTGAGAGACCGGGCTGGT ACACCAACGTGTTCAACTGGAAAGTGGGGCACGTGAGAAATCTGACATGCTCTGATGGCCCTAGC CTGATCAAGACCGAGCTGGATCTGCTCAAGAGCGGCCCTGAGAGAACTCAGACCGTGTCTGGCGA TCAGCTGGCCAGAGAGGAAACAGATCGAGAATCTGGGCAGCGGCAGCTTTGTGCTGGAGGCCATT GCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGCAGGCCTGGCCATCGCTAAGACCATCAGACT GGAAAGCGAAGTGAACGCCATCAACAAAGCCCTGAAGAGACAAACGAGGGCGGTAGCAGACTG GGCATTGGCGTTAGAGTGGTGGCCACAGCCGTGGCGGAGCTGAGGACTTCGTGCTTAAAGAAC TGACAGGGGCCATTAAACAAAGAACAGTGGGACATCCCTGAGCTGAGATGGCCGTGTGCTTTAGC CAGTTCAACCGGCCTTTCTGACGTCGTGGCGCAGTTTAGCGACAGCGCCGGAATCACAGCAGC CATCAAGCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGGCTAACATGCTACATGTG CCGGCCAGATCAAGCTGATGCTCGAGAAAGAGCCATGGTCCGACGGAAAGGCTTGGGCATCTG ATTGGGTGTACGGCAGCAGCGTATCTATATGGTGCAGCTGGCTATCTTGGCGTGTATGACAC ACCTGCTGGATTGTGAAGGCCTGCTCTAGCTGTAGCGAGAGAGAGGGCAATTACGGCTGCTGGC TGAGAGAGACCAAGGCCTGATTGTGACAGACGCCGGCAGCAGCCTGTACTAGCTAACGAGAAAG GACTGGAGACAGAGGGGACCACTGTTCTGTGATACCGCCGCTGGAAATCAATGTGGCCGAGC AGAGCAAGAGTGCACATCAACATCAGCAGCCACCAACTATCCCTGCAAGGTGTCCAGCGCAGG CAGCTGATTTCTATGGTGGCTCTGTCTCTCTGGAGCCCTGGTGGCTTGTATAAGGGCGTGTCC TGTAGCATCGGCAGCAAGAGTGGGCATCATCAAGCAGCTGAAACAGGGGCTGCAGCTACATCAC CAGCCAGGACGCCGATACCGTGAACATCGACAGCAGCCTGTATCAGCTGAGCAGGGTGGAGGGC GACAGCACGTGATCAAGGGCAGACCTGTGTCCAGCAGCTTCGACCTATCAAGTTCCTGAGGA TCAGTTCCAGGTGGCCCTGGAGCAGGTGTTGAGAACATCGAGAAATCCAGGGCTCTGGTGGACC AGTCCAGCAGAACTGCTAGCGCCGAGAGGGGAAACAGCGGCTTCATCATGCTGATCATCTG ATGGCGTCTGGCCAGCTCATGATCCTGGTGTCCATCTTATCATTAAGAGAGACCAAGAGG CCACCGGGCGCTCTCCAGAACTGAGCGGAGTGAACCAACAATGGCTTCATCCCTCACAG</p>	<p>110</p>
<p>35</p> <p>HMPV_SC_5M_Krarup_T74LS170LD185PD454N</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ATGAGCTGGAAAGTGGTCAATCATTTCAGCCTGCTGATCAACCTCAGCAGGGCTGAAAAGAGAG CTACCTGGAAAGTGGTGGAGCCATCAGAGAGGGCTACCTGTCTGTGAGAGACCGGGCTGGT ACACCAACGTGTTCAACTGGAAAGTGGGGCACGTGAGAAATCTGACATGCTCTGATGGCCCTAGC CTGATCAAGACCGAGCTGGATCTGCTCAAGAGCGGCCCTGAGAGAACTCAGACCGTGTCTGGCGA TCAGCTGGCCAGAGAGGAAACAGATCGAGAATCTGGGCAGCGGCAGCTTTGTGCTGGAGGCCATT GCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGCAGGCCTGGCCATCGCTAAGACCATCAGACT GGAAAGCGAAGTGAACGCCATCAACAAAGCCCTGAAGAGACAAACGAGGGCGGTAGCAGACTG GGCATTGGCGTTAGAGTGGTGGCCACAGCCGTGGCGGAGCTGAGGACTTCGTGCTTAAAGAAC TGACAGGGGCCATTAAACAAAGAACAGTGGGACATCCCTGAGCTGAGATGGCCGTGTGCTTTAGC CAGTTCAACCGGCCTTTCTGACGTCGTGGCGCAGTTTAGCGACAGCGCCGGAATCACAGCAGC CATCAAGCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGGCTAACATGCTACATGTG CCGGCCAGATCAAGCTGATGCTCGAGAAAGAGCCATGGTCCGACGGAAAGGCTTGGGCATCTG ATTGGGTGTACGGCAGCAGCGTATCTATATGGTGCAGCTGGCTATCTTGGCGTGTATGACAC ACCTGCTGGATTGTGAAGGCCTGCTCTAGCTGTAGCGAGAGAGAGGGCAATTACGGCTGCTGGC TGAGAGAGACCAAGGCCTGATTGTGACAGACGCCGGCAGCAGCCTGTACTAGCTAACGAGAAAG GACTGGAGACAGAGGGGACCACTGTTCTGTGATACCGCCGCTGGAAATCAATGTGGCCGAGC AGAGCAAGAGTGCACATCAACATCAGCAGCCACCAACTATCCCTGCAAGGTGTCCAGCGCAGG CAGCTGATTTCTATGGTGGCTCTGTCTCTCTGGAGCCCTGGTGGCTTGTATAAGGGCGTGTCC TGTAGCATCGGCAGCAAGAGTGGGCATCATCAAGCAGCTGAAACAGGGGCTGCAGCTACATCAC CAGCCAGGACGCCGATACCGTGAACATCGACAGCAGCCTGTATCAGCTGAGCAGGGTGGAGGGC GACAGCACGTGATCAAGGGCAGACCTGTGTCCAGCAGCTTCGACCTATCAAGTTCCTGAGGA CCAGTTCCAGGTGGCCCTGGAGCAGGTGTTGAGAACATCGAGAAATCCAGGGCTCTGGTGGACC AGTCCAGCAGAACTGCTAGCGCCGAGAGGGGAAACAGCGGCTTCATCATGCTGATCATCTG ATGGCGTCTGGCCAGCTCATGATCCTGGTGTCCATCTTATCATTAAGAGAGACCAAGAGG CCACCGGGCGCTCTCCAGAACTGAGCGGAGTGAACCAACAATGGCTTCATCCCTCACAG</p>	<p>111</p>

(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>HMPV_SC_DM_Krarup_E5 1 PT74L</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGAGCTGGAGGTTGGTCATCATCTTCAGCCTGCTGATCACACCTCAGCAGGGCTGAAAGAGAG CTACCTGGAAAGAGTCTGAGAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAGAACCGGCTGGT ACACCAAGGTGTTCACTGCTGTGGGGGACGCTCGAGAACTGACATGCTCTGATGGGCTAGC CTGATCAAGACCGAGCTGGATCTGCTCAAGAGCGGCCGAGAGAGACTCAAGACCGTGTCTGGCGA TCAGCTGGCCAGAGAGGAAACAGATCGAGAACTCTGGCCAGCGGCAGCTTTGTGCTGGAGGCCATT GGCTTGGAGTGGCTGCTGCTGCAAGCTGTTACAGCAGGCCTGGCCATGGCTAAGACCATCAGACT GGANAGCGAGGTGACCCTCAGCAACAGCGCTGAGAGAGACAAAGAGGGCGTCAAGCAGCTC GGCATTGGCTTTAGAGTGGCTGGCCACAGCCCTGGCGAGCTGAGAGCTGAGAGACTTGTGTCCAAAGAAC TGACAGGGGCTATTAAAGAGAAAGTGGAGACATCGACGACCTGAAGATGGCCGTGTCTTTAGC GAGTTCAAGCGGGGCTTTGTGAACGTCTGTGGCCAGTTTAAAGGACAAAGCCGGAAATCACAGGAGC CATCAGCCCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGGCTAACATGCTAGCTCTG CGGGCCAGATCAAGCTGATGCTCGAGAAATAGAGCCATGGCTCCGACGGAAAGGCTTGGGCTATCTG ATTGGCTGTACGGCAGCAGCCTGATCTATATGGTGGAGCTGCTATCTTGGCGTGTATGACAC ACCTGCTGGATTGTGAAGGCGCTCTCTAGCTGTAGCGAGAGAGAGGGCAATTAGCTGCTGCTGCG TGAGAGAGGACCAAGGCTGGTATTGTGCAAGACGCGGGCAGCACCCTGTACTAGCTAAGCAGAGAA GACTGGAGACAAAGAGGCGAGCCAGCTGTTCTGTGATACCGCGCTGGAAATCAATGTGGCGGAGC AGAGCAAGAGTGGCAACATCAACATCAGCACCACCAACTATCCCTGCAAGGTTGTCACCGGAGG CACCTTATTTCTATGGTGGCTCTGTCTCTCCCTGGAGGCGCTGGTGGCTGTTAAGGGGCGTGTCC TGTAGCATGGCCAGCAACAGAGTGGGCAATCATCAAGCAGCTGAACAAAGGGGTTGGAGCTACATCAC CAKCCAGGACGCCGATACCGTACCATCGACACACCCGTGTATCAGCTGAGCAAGGTTGGAGGGC GACAGCACGCTGATCAAGGGCGAGACCTGTGTCAGCAGCTTCGACCCATCAAGTTCCCTGAGGA TCAGTTCCAGGTGGCCCTGGACAGGTTGTGAGAACTCAGAAATTCAGGGCTCTGGTGGAGCC AGTCCAGCAGAACTCTGTCTAGCGCCGAGAAAGGAAACACCAGCTTCATCAAGTGTGATCTG ATCGGCTGTGGGGAGCTCCATGATCCTGGTGTCCATCTTCATCATATCAAGAAAGACCAAGAAAG CCCAAGGGGCTCTCCAGAACTGAGCGGAGTGAACCAACAAAGGCTTCAATCCCTCACAAAG</p>	<p>112</p>
<p>35</p> <p>HMPV_SC_TM_Krarup_E5 1FT74LD454N</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ATGAGCTGGAGGTTGGTCATCATCTTCAGCCTGCTGATCACACCTCAGCAGGGCTGAAAGAGAG CTACCTGGAAAGAGTCTGAGAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAGAACCGGCTGGT ACACCAAGGTGTTCACTGCTGTGGGGGACGCTCGAGAACTGACATGCTCTGATGGGCTAGC CTGATCAAGACCGAGCTGGATCTGCTCAAGAGCGGCCGAGAGAGACTCAAGACCGTGTCTGGCGA TCAGCTGGCCAGAGAGGAAACAGATCGAGAACTCTGGCCAGCGGCAGCTTTGTGCTGGAGGCCATT GGCTTGGAGTGGCTGCTGCTGCAAGCTGTTACAGCAGGCCTGGCCATGGCTAAGACCATCAGACT GGANAGCGAGGTGACCCTCAGCAACAGCGCTGAGAGAGACAAAGAGGGCGTCAAGCAGCTC GGCATTGGCTTTAGAGTGGCTGGCCACAGCCCTGGCGAGCTGAGAGCTGAGAGACTTGTGTCCAAAGAAC TGACAGGGGCTATTAAAGAGAAAGTGGAGACATCGACGACCTGAAGATGGCCGTGTCTTTAGC GAGTTCAAGCGGGGCTTTGTGAACGTCTGTGGCCAGTTTAAAGGACAAAGCCGGAAATCACAGGAGC CATCAGCCCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGGCTAACATGCTAGCTCTG CGGGCCAGATCAAGCTGATGCTCGAGAAATAGAGCCATGGCTCCGACGGAAAGGCTTGGGCTATCTG ATTGGCTGTACGGCAGCAGCCTGATCTATATGGTGGAGCTGCTATCTTGGCGTGTATGACAC ACCTGCTGGATTGTGAAGGCGCTCTCTAGCTGTAGCGAGAGAGAGGGCAATTAGCTGCTGCTGCG TGAGAGAGGACCAAGGCTGGTATTGTGCAAGACGCGGGCAGCACCCTGTACTAGCTAAGCAGAGAA GACTGGAGACAAAGAGGCGAGCCAGCTGTTCTGTGATACCGCGCTGGAAATCAATGTGGCGGAGC AGAGCAAGAGTGGCAACATCAACATCAGCACCACCAACTATCCCTGCAAGGTTGTCACCGGAGG CACCTTATTTCTATGGTGGCTCTGTCTCTCCCTGGAGGCGCTGGTGGCTGTTAAGGGGCGTGTCC TGTAGCATGGCCAGCAACAGAGTGGGCAATCATCAAGCAGCTGAACAAAGGGGTTGGAGCTACATCAC CAKCCAGGACGCCGATACCGTACCATCGACACACCCGTGTATCAGCTGAGCAAGGTTGGAGGGC GACAGCACGCTGATCAAGGGCGAGACCTGTGTCAGCAGCTTCGACCCATCAAGTTCCCTGAGGA CCAGTTCCAGGTGGCCCTGGACAGGTTGTGAGAACTCAGAAATTCAGGGCTCTGGTGGAGCC AGTCCAGCAGAACTCTGTCTAGCGCCGAGAAAGGAAACACCAGCTTCATCAAGTGTGATCTG ATCGGCTGTGGGGAGCTCCATGATCCTGGTGTCCATCTTCATCATATCAAGAAAGACCAAGAAAG CCCAAGGGGCTCTCCAGAACTGAGCGGAGTGAACCAACAAAGGCTTCAATCCCTCACAAAG</p>	<p>113</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>HMPV_SC_StabilizeAlpha_T74L</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGAGCTGGAAAGGTGGTCATCATTCTTACGCTGCTGATCAGCCTCAGCAGGGCTGAAAGAGAG CTACCTGGAAAGGTGCTGAGCCACCATCAGAGAGGGCTACCTGTCTGTGCTGAGAAACCGGGTGGT ACACCAACGTGTTCCACTGGAAGTGGGGGACCTGGAGAAATCTGACATGCTCTGATGGCCCTAGC CTGATCAAGACCGAGCTGGATCTGCTCAAGAGCGGCCCTGAGAGAACTCAAGACCGGTGCTGGCGA TCAGCTGGCCAGAGAGGAAACAGATCGAGAATCTGGCCAGCGGCAGCTTTGTGCTGGGAGCCATT GCTCTTGGAGTGGCTGCTGCTGCAAGCTGTTACAGCAGGCCTGGCCATCGCTAAGACCATCAGACT GGANAGCGAAGTGAACGCCATCAACAGCGCCCTGAAGAAACAAACGAGGCGGTGAGCACCTC GGCAATGGCTGTAGAGTGGCTGGCCACAGCCGTGGCCGAGCTGAAAGACTTGGTGCAGAAACC TGACAGGGGCCATTAAAGAAACAGTGGGACATCGACGACCTGAAGATGGCCGTGCTCTTTAGC CAGTTCAACCGGCCTTTCTGAACGTGCTGGCGCAGTTTGGGACAGCGCCGAAATCACAGCAGC CATCAGCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGCTAACATGCTACATCTG CCGGCCAGATCAGGCTGATGCTGAGNATAGAGCCATGGTCCGACGGAAAGGCTTCGGCATTCTG ATTGGGTGTACGGCAGCAGCTGATCTATATGGTGGAGCTGCTATCTTGGCGTGTAGCAGC ACCTGCTGGATTGTGAAGGCGCTCTAGCTGTAGCGAGAAAGAGGCAATTAACGCTGCTGGTGC TGAGAGAGGACCAAGGCTGGTATTGTGCAAGCGCCGGCAGCAGCCTGTACTACCTAAGGAGAAAG GACTGCGAGACAAAGAGGCGACCAAGTGTCTGTATACCGCCGCTGGAAATATGTGGCCGAGG AGAGCAAGAGTGCACATCAACATCAGCAGCCACCAACTATCCCTGCAAGGTGTCCAGCGGAGG GACCTTATTTCTATGGTGGCTCTGTCTCCCTGGAGGCCCTGGTGGCTTGTATTAAGGGCGGTGTCC TGAGCATCGCCAGCAACAGAGTGGGCATCAACAGCAGCTGAAACAGGGGCTGAGCTACATCAC CAACAGGACGCCGATACCGTGCATCGACACCAACAGCCGTGTATCAGCTGAGCAAGGTTGGAAGGC GACAGCACAGTGCATCAAGGGCAGACCTGTGTCCAGCAGCTTCGACCCATCAAGTTCCCTGAGGA TCAGTTCCAGGTGGCCCTGGACAGGTGTTCGAGAACATCGAGAAATCCAGGCTCTGGTGGAGCC AGTCCACAGATCCGTGCTAGCGCCGAGAAAGGAAACAGCCGGCTTCATCAGCTGATCAATCTG ATCGGCTGCTGGCCAGCTCCATGATCCTGGTGTCCATCTTCATCATTAATCAAGAAAGACCAAGAAAG CCCAAGGGCGCTCCCTCAGAACTGAGCGGAGTGCACCAACAAATGGCTTCATCCCTCACAG</p>	<p>114</p>
<p>35</p> <p>HMPV_SC_StabilizeAlpha_V55L</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ATGAGCTGGAAAGGTGGTCATCATTCTTACGCTGCTGATCAGCCTCAGCAGGGCTGAAAGAGAG CTACCTGGAAAGGTGCTGAGCCACCATCAGAGAGGGCTACCTGTCTGTGCTGAGAAACCGGGTGGT ACACCAACGTGTTCCACTGGAAGTGGGGGACCTGGAGAAATCTGACATGCTCTGATGGCCCTAGC CTGATCAAGACCGAGCTGGATCTGCTCAAGAGCGGCCCTGAGAGAACTCAAGACCGGTGCTGGCGA TCAGCTGGCCAGAGAGGAAACAGATCGAGAATCTGGCCAGCGGCAGCTTTGTGCTGGGAGCCATT GCTCTTGGAGTGGCTGCTGCTGCAAGCTGTTACAGCAGGCCTGGCCATCGCTAAGACCATCAGACT GGANAGCGAAGTGAACGCCATCAACAGCGCCCTGAAGAAACAAACGAGGCGGTGAGCACCTC GGCAATGGCTGTAGAGTGGCTGGCCACAGCCGTGGCCGAGCTGAAAGACTTGGTGCAGAAACC TGACAGGGGCCATTAAAGAAACAGTGGGACATCGACGACCTGAAGATGGCCGTGCTCTTTAGC CAGTTCAACCGGCCTTTCTGAACGTGCTGGCGCAGTTTGGGACAGCGCCGAAATCACAGCAGC CATCAGCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGCTAACATGCTACATCTG CCGGCCAGATCAGGCTGATGCTGAGNATAGAGCCATGGTCCGACGGAAAGGCTTCGGCATTCTG ATTGGGTGTACGGCAGCAGCTGATCTATATGGTGGAGCTGCTATCTTGGCGTGTAGCAGC ACCTGCTGGATTGTGAAGGCGCTCTAGCTGTAGCGAGAAAGAGGCAATTAACGCTGCTGGTGC TGAGAGAGGACCAAGGCTGGTATTGTGCAAGCGCCGGCAGCAGCCTGTACTACCTAAGGAGAAAG GACTGCGAGACAAAGAGGCGACCAAGTGTCTGTATACCGCCGCTGGAAATATGTGGCCGAGG AGAGCAAGAGTGCACATCAACATCAGCAGCCACCAACTATCCCTGCAAGGTGTCCAGCGGAGG GACCTTATTTCTATGGTGGCTCTGTCTCCCTGGAGGCCCTGGTGGCTTGTATTAAGGGCGGTGTCC TGAGCATCGCCAGCAACAGAGTGGGCATCAACAGCAGCTGAAACAGGGGCTGAGCTACATCAC CAACAGGACGCCGATACCGTGCATCGACACCAACAGCCGTGTATCAGCTGAGCAAGGTTGGAAGGC GACAGCACAGTGCATCAAGGGCAGACCTGTGTCCAGCAGCTTCGACCCATCAAGTTCCCTGAGGA TCAGTTCCAGGTGGCCCTGGACAGGTGTTCGAGAACATCGAGAAATCCAGGCTCTGGTGGAGCC AGTCCACAGATCCGTGCTAGCGCCGAGAAAGGAAACAGCCGGCTTCATCAGCTGATCAATCTG ATCGGCTGCTGGCCAGCTCCATGATCCTGGTGTCCATCTTCATCATTAATCAAGAAAGACCAAGAAAG CCCAAGGGCGCTCCCTCAGAACTGAGCGGAGTGCACCAACAAATGGCTTCATCCCTCACAG</p>	<p>115</p>

(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>HMPV_SC_StabilizeAlpha_S170L</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGAGCTGGAGGTGGTCATCATTTCAGCCTGCATCAGCCTCAGCAGGGCCTGAAGGAGAG CTACCTGGAAAGTCTCTGCAGCACCATCAGAGAGGGCTACCTGTCTGTCTGAGAAACCGGCTGGT ACACCAACGTGTTCCACTGAGAGTGGGCACGTGAGAAATCTGACATGCTCTGATGGCCCTAGC CTGATCAAGACCGAGCTGGATCTGACCAAGAGCAGCCTGAGAGAACTCAAGACCTGTCTGCGCA TCAGCTGGCCAGAGAGGAAACAGATCGAGAATCTGAGCAGCGCCAGCTTTGTGCTGGAGGCCATT GCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGCAGGCCTGGCCATCGCTAAGACCATCAGACT GGAAAGCGAAGTGAACGCCATCAACAGCGCCCTGAAGAAAGCAAAAGAGGCCTGAGCAGCCTC GGCATTGGCCTTAAAGTGGCTGGCCACAGCCGTGCAGCAGCTGAAAGACTTGGTCTTAAAGAAC TGACAGGGGCCATTAAAGAAACAAGTGGCAGCAGCAGCCTGAAGATGGCCGTGTCTTTAGC CAGTTCAACCGGCCTTTCTGAACTGTCGTGCGGCAGTTTAAAGCAGCAGCAGCAGCAGCAGCAGC CATCAGCCTGGAGCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGCTTAACTGCTACATCTG CTGGCCAGATCAGCTGATGCTGAGAAATAGAGCCATGGTCCAGCAGGAAAGAGCTTCCGCACTCTG ATTGGGTGTACGGCAGCAGCAGCTGATCTATATGGTGGAGCTGCTATCTTGGCTGATGACAGC ACCTGCTGGATTGTGAAGCCCGCTCTAGCTGTAGCGAGAAAGAGGGCAATTAAGCCTGCGCTGC TGAGAGAGGACCAAGGCCTGGTATTGTCAGAACGCCGCCAGCAGCAGCAGCAGCAGCAGCAGCAGC GACTGCGAGACAGAGAGCGAACCAGTGTCTGATGATGCTGCGCCTGGAACTAATGTGGCCGAGC AGAGCAAGAGAGTGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC CACCTTATTTCTATGGTGGCTGTCTCTCTCTGAGAGCCCTGGTGGCTGTTAATAGGGCTGTCTCC TGAGCAGTGGCCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC CAGC TGAGTCCAGCTGGCCCTGGAGCAGCTGTTCCAGCAATCTGAGAACTTCCAGGCTCTGGTGGACC AGTCCAGCAGAACTCTGTCTAGCGCCGAGAAAGGGAAGACCCGGCTTCATCAGCTGATCTCCTG ATCGCTGCTGGCCAGCTCCATGATCCTGCTGTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTG CCGACGGCCGCTCTCCAGAACTGAGCGGAGTGAACCAACAAATGGCTTCATCCCTCACAG</p>	<p>116</p>
<p>35</p> <p>HMPV_SC_StabilizeAlpha_T174W</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ATGAGCTGGAGGTGGTCATCATTTCAGCCTGCATCAGCCTCAGCAGGGCCTGAAGGAGAG CTACCTGGAAAGTCTCTGCAGCACCATCAGAGAGGGCTACCTGTCTGTCTGAGAAACCGGCTGGT ACACCAACGTGTTCCACTGAGAGTGGGCACGTGAGAAATCTGACATGCTCTGATGGCCCTAGC CTGATCAAGACCGAGCTGGATCTGACCAAGAGCAGCCTGAGAGAACTCAAGACCTGTCTGCGCA TCAGCTGGCCAGAGAGGAAACAGATCGAGAATCTGAGCAGCGCCAGCTTTGTGCTGGAGGCCATT GCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGCAGGCCTGGCCATCGCTAAGACCATCAGACT GGAAAGCGAAGTGAACGCCATCAACAGCGCCCTGAAGAAAGCAAAAGAGGCCTGAGCAGCCTC GGCATTGGCCTTAAAGTGGCTGGCCACAGCCGTGCAGCAGCTGAAAGACTTGGTCTTAAAGAAC TGAGAGGGGCCATTAAAGAAACAAGTGGCAGCAGCAGCCTGAAGATGGCCGTGTCTTTAGC CAGTTCAACCGGCCTTTCTGAACTGTCGTGCGGCAGTTTAAAGCAGCAGCAGCAGCAGCAGCAGC CATCAGCCTGGAGCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGCTTAACTGCTACATCTG CTGGCCAGATCAGCTGATGCTGAGAAATAGAGCCATGGTCCAGCAGGAAAGAGCTTCCGCACTCTG ATTGGGTGTACGGCAGCAGCAGCTGATCTATATGGTGGAGCTGCTATCTTGGCTGATGACAGC ACCTGCTGGATTGTGAAGCCCGCTCTAGCTGTAGCGAGAAAGAGGGCAATTAAGCCTGCGCTGC TGAGAGAGGACCAAGGCCTGGTATTGTCAGAACGCCGCCAGCAGCAGCAGCAGCAGCAGCAGCAGC GACTGCGAGACAGAGAGCGAACCAGTGTCTGATGATGCTGCGCCTGGAACTAATGTGGCCGAGC AGAGCAAGAGAGTGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC CACCTTATTTCTATGGTGGCTGTCT TGAGCAGTGGCCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC CAGC TGAGTCCAGCTGGCCCTGGAGCAGCTGTTCCAGCAATCTGAGAACTTCCAGGCTCTGGTGGACC AGTCCAGCAGAACTCTGTCTAGCGCCGAGAAAGGGAAGACCCGGCTTCATCAGCTGATCTCCTG ATCGCTGCTGGCCAGCTCCATGATCCTGCTGTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTG CCGACGGCCGCTCTCCAGAACTGAGCGGAGTGAACCAACAAATGGCTTCATCCCTCACAG</p>	<p>117</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5 HMPV_SC_4M_StabilizeAl pha_V55LT74LS170LT17 4 W</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGAGCTGGAAAGGTGGTCATCATTTCAGCCTGCTGATCAGCCTCAGCAGGGCCTGAAAGSAGAG CTACCTGGAAAGGTGCTGCAGCACCATCAGAGAGGGCTACCTGTCTGTGCTGAGAAACGGGCTGCT ACACCAACGTGTTCACTGGAAGTGGGGGACCTCGAGAATCTGACATGCTCTGATGGCCCTAGC CTGATCAAGAGCAGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGACTCAAGAGCCTGTCTGCTGGA TCAGCTGGCCAGAGAGGAACAGATCAGAAATCTGGCCAGCGGCAGCTTTGTGCTGGAGGCCATT GCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGCAGGCCTGGCCATGCTTAAGACCATCAGACT GGAAGCGAAGTGAACGCTATCAACAGCGCCCTGAAGAAAGCAAAAGAGGGCGTCAAGCAGCTC GGCATGGCTGTTAGAGTGGCTGGCCACAGCCGTGCAGAGCTGAAAGACTTGTGTGTTAAGAACCC TGTGGGGGGCCATTAAACAAGAACAGTGGCAGATCGAGCAGCCTGAAGATGGCCGTGTCTTTAGC CAGTTCAACCGCCGCTTCTGACGTCGTGCAGCAGTTTAGCGACAGCAGCGGAATCAGCAGCAGC CATCAAGCTGGAGCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGCTTAAATGCTACATCTG CCGCCAGATCAAGCTGATGCTGAGAAATAGAGCCATGGCTCGAGCGAAGAGCTTGGCATTCTG ATTGGGTGTGACGGCAGCAGCCTGATCTATATGGTGGAGCTGCTATCTTGGCGTGTAGCAGC ACCCTGCTGATTGTGAAGGCGCTCTCTAGCTGTAGCGAGAAAGAGGGCAATTAAGCCTGCCCTGC TENGAGAGGAGCAAGGCTGGTATTGTCAGAACGCCGCCAGCAGCAGCTGTACTACCCTAAGGAGAG GACTGGAGAGCAAGAGGCGAGCCAGCTGTTCTGTGATACCGCCCGCTGGAAATTAATGTGGCCGAGC AGAGCAAAAGAGTGCAGCATCAACATCAGCAGCAGCAGCAGCTATCCCTGCAAGGTGTCCAGCGCAGG CAGCCTATTTCTATGGTGGCTCTGTCTCTCTGCGAGCCCTGGTGGCTGTTATAGAGGGCTGTCTC TGTAGCATCGCCAGCAAGAGTGGGCTATCAGCAGCAGCTGAAAGAGGGCTGCAGCTACATCAC CAGCAGGAGCGCCGATACCGTGCATCTCGACAGCAGCAGCAGCTGATCAAGCTGAGCAGGCTGGAAGGG GAGCAGCAGCTGATCAAGGGCAGAGCTGTGCTCGAGCAGCTTCAGCAGCTATCAAGTTCCTGAGGA TCAGTTCAGCTGGCCCTGGAGCAGGTGTTGAGAAATCAGAAATTCAGGCTCTGGGTGGAGC AGTCCAGCAGAACTCTGTAGCGCCGAGAAAGGAAAGACCAGCAGCTTCATCAAGTGTGATCCTG ATCGGCTGTGGGAGCTCCATGATCCTGGTGTCTATCTTCATCAAGTATCAAGAAAGCAGAAAG CCCAGCGCCGCTCTCCAGAACTGAGCGGAGTGAACAGCAATGGCTTCATCCCTCACAG</p>	<p>118</p>
<p>HMPV_ProlineStab_E51P</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ATGAGCTGGAAAGGTGGTCATCATTTCAGCCTGCTGATCAGCCTCAGCAGGGCCTGAAAGSAGAG CTACCTGGAAAGGTGCTGCAGCACCATCAGAGAGGGCTACCTGTCTGTGCTGAGAAACGGGCTGCT ACACCAACGTGTTCACTGGAAGTGGGGGACCTCGAGAATCTGACATGCTCTGATGGCCCTAGC CTGATCAAGAGCAGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGACTCAAGAGCCTGTCTGCTGGA TCAGCTGGCCAGAGAGGAACAGATCAGAAATCTGGCCAGCGGCAGCTTTGTGCTGGAGGCCATT GCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGCAGGCCTGGCCATGCTTAAGACCATCAGACT GGAAGCGAAGTGAACGCTATCAACAGCGCCCTGAAGAAAGCAAAAGAGGGCGTCAAGCAGCTC GGCATGGCTGTTAGAGTGGCTGGCCACAGCCGTGCAGAGCTGAAAGACTTGTGTGTTAAGAACCC TGCAGCGGGCCATTAAACAAGAACAGTGGCAGATCGAGCAGCCTGAAGATGGCCGTGTCTTTAGC CAGTTCAACCGCCGCTTCTGACGTCGTGCAGCAGTTTAGCGACAGCAGCGGAATCAGCAGCAGC CATCAAGCTGGAGCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGCTTAAATGCTACATCTG CCGCCAGATCAAGCTGATGCTGAGAAATAGAGCCATGGCTCGAGCGAAGAGCTTGGCATTCTG ATTGGGTGTGACGGCAGCAGCCTGATCTATATGGTGGAGCTGCTATCTTGGCGTGTAGCAGCAGC ACCCTGCTGATTGTGAAGGCGCTCTCTAGCTGTAGCGAGAAAGAGGGCAATTAAGCCTGCCCTGC TENGAGAGGAGCAAGGCTGGTATTGTCAGAACGCCGCCAGCAGCAGCTGTACTACCCTAAGGAGAG GACTGGAGAGCAAGAGGCGAGCCAGCTGTTCTGTGATACCGCCCGCTGGAAATTAATGTGGCCGAGC AGAGCAAAAGAGTGCAGCATCAACATCAGCAGCAGCAGCAGCTATCCCTGCAAGGTGTCCAGCGCAGG CAGCCTATTTCTATGGTGGCTCTGTCTCTCTGCGAGCCCTGGTGGCTGTTATAGAGGGCTGTCTC TGTAGCATCGCCAGCAAGAGTGGGCTATCAGCAGCAGCTGAAAGAGGGCTGCAGCTACATCAC CAGCAGGAGCGCCGATACCGTGCATCTCGACAGCAGCAGCAGCTGATCAAGCTGAGCAGGCTGGAAGGG GAGCAGCAGCTGATCAAGGGCAGAGCTGTGCTCGAGCAGCTTCAGCAGCTATCAAGTTCCTGAGGA TCAGTTCAGCTGGCCCTGGAGCAGGTGTTGAGAAATCAGAAATTCAGGCTCTGGGTGGAGC AGTCCAGCAGAACTCTGTAGCGCCGAGAAAGGAAAGACCAGCAGCTTCATCAAGTGTGATCCTG ATCGGCTGTGGGAGCTCCATGATCCTGGTGTCTATCTTCATCAAGTATCAAGAAAGCAGAAAG CCCAGCGCCGCTCTCCAGAACTGAGCGGAGTGAACAGCAATGGCTTCATCCCTCACAG</p>	<p>119</p>

(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>HMPV_ProlineStab_D185P</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGAGCTGGAAAGGTGGTCATCACTTCAGCCTGCCTGATCACACCTCAGCAGGGCTGAAAGAGAG CTACCTGGAAAGAGTCCCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAGAAACGGGCTGGT ACACCAACGTGTTCACTGGAAGTGGGCACGTGAGAAATCTGACATGCTCTGATGGCCTTAGC CTGATCAAGACGAGCTGGATCTGACCAAGAGC GGCCTGAGAGAACTCAAGACC GTGTCTGGC GA TCAGCTGGCCAGAGAGGAAACAGATCGAATCTCTGGCAGCGGCAGCTTTGTGCTGGAGGCCATT GCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGCAGGCCTGGCCATCGCTAAGACCATCAGACT GGANAGCGAAGTGAACGCCATCACAAACGCCCTGAAGAAAGACAAACGAGGCCTGTCAGCACCTC GGCATTGGCCTTAAAGATGCTGGCCACAGCCGTGCAGCTGAGGACTTCGTGTCCAAAGACC TGACAGGGCCATTAAACAAAGCAAGTGGCACATCCCTGACCTGAGATGGCCGTGTCTTTAGC CAGTTCAACCGGCCTTTCTGAACTGTCTGGCCAGTTTAAAGCAACGCCGGAATCACAGCAGC CATCAACCTGGACCTGATGACAGATGCTGAGCTGGCTGAGGCCGTGCTTAACTATGCTACATCTG CCGCCAGATCAAGCTGATGCTCAGAAATAGAGCCATGGTCCGACGGAAAGGCTTCGGCCATCTG ATTGGCTGTACGGCAGCAGCTGATCTATATGGTGCAGCTGCCTATCTTCGGCTGATGACAC ACCTGCTGGATTGTGAAGGCCTCTCTAGCTGTAGCGAGAAAGAGGGCAATTCGCCCTGGC TGAGAGAGGACCAAGGCCTGATTGTGCAAGACGCCGGCAGCAGCAGCTGTACTACCCTAACGAGAAG GACTGGAGACAGAGAGCGACCACTGTTCTGTGATACCGCCCGCTGGAACTAATGTGGCCGAGC AGAGCAAGAGAGTCCAGCATCAACATCAGCAGCCACCAACTATCCCTGCAGGCTGTCCAGCGCAGG CACCTTATTTCTATGGTGGCTCTGTCTCCCTCGGAGCCCTGGTGGCTGTATTAAAGGGCTGTCC TGAGCATCGGCAGCAACAGAGTGGGCATCATCAAGCAGCTGAAACAAGGGCTGCAAGCTACATCAC CAGCCAGGACGCCGATACCGTGCATCTGACAGCAGCAGCTGTATCAGCTGAGCAAGGTTGAAGGG GACAGCACGTGATCAAGGGCAGACCTGTGTCCAGCAGCTTCGACCTTATCAAGTTCCCTGAGGA TCAGTTCAGGTGGCCCTGGACAGGTGTTGAGAACTCAGAAATTCAGGCTCTGGTGGACC AGTCCAGCAGATCTGTCTAGCGCCGAGAAAGGAAACAGCGCTTCATCACGCTGATCATCTG ATCGCCGTCTGGCCAGCTCCATGATCTGTGTCTCCATCTTCATCATTAATCAAGAAAGACAAAGAG CCCAAGGGCTCTCTCAGAACTGAGGGAGTGAACCAACAATGGCTTATCCCTCACAAAC</p>	<p>120</p>
<p>35</p> <p>HMPV_ProlineStab_D183P</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ATGAGCTGGAAAGGTGGTCATCACTTCAGCCTGCCTGATCACACCTCAGCAGGGCTGAAAGAGAG CTACCTGGAAAGAGTCCCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAGAAACGGGCTGGT ACACCAACGTGTTCACTGGAAGTGGGCACGTGAGAAATCTGACATGCTCTGATGGCCTTAGC CTGATCAAGACGAGCTGGATCTGACCAAGAGC GGCCTGAGAGAACTCAAGACC GTGTCTGGC GA TCAGCTGGCCAGAGAGGAAACAGATCGAATCTCTGGCAGCGGCAGCTTTGTGCTGGAGGCCATT GCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGCAGGCCTGGCCATCGCTAAGACCATCAGACT GGANAGCGAAGTGAACGCCATCACAAACGCCCTGAAGAAAGACAAACGAGGCCTGTCAGCACCTC GGCATTGGCCTTAAAGATGCTGGCCACAGCCGTGCAGCTGAGGACTTCGTGTCCAAAGACC TGACAGGGCCATTAAACAAAGCAAGTGGCACATCCCTGACCTGAGATGGCCGTGTCTTTAGC CAGTTCAACCGGCCTTTCTGAACTGTCTGGCCAGTTTAAAGCAACGCCGGAATCACAGCAGC CATCAACCTGGACCTGATGACAGATGCTGAGCTGGCTGAGGCCGTGCTTAACTATGCTACATCTG CCGCCAGATCAAGCTGATGCTCAGAAATAGAGCCATGGTCCGACGGAAAGGCTTCGGCCATCTG ATTGGCTGTACGGCAGCAGCTGATCTATATGGTGCAGCTGCCTATCTTCGGCTGATGACAC ACCTGCTGGATTGTGAAGGCCTCTCTAGCTGTAGCGAGAAAGAGGGCAATTCGCCCTGGC TGAGAGAGGACCAAGGCCTGATTGTGCAAGACGCCGGCAGCAGCAGCTGTACTACCCTAACGAGAAG GACTGGAGACAGAGAGCGACCACTGTTCTGTGATACCGCCCGCTGGAACTAATGTGGCCGAGC AGAGCAAGAGAGTCCAGCATCAACATCAGCAGCCACCAACTATCCCTGCAGGCTGTCCAGCGCAGG CACCTTATTTCTATGGTGGCTCTGTCTCCCTCGGAGCCCTGGTGGCTGTATTAAAGGGCTGTCC TGAGCATCGGCAGCAACAGAGTGGGCATCATCAAGCAGCTGAAACAAGGGCTGCAAGCTACATCAC CAGCCAGGACGCCGATACCGTGCATCTGACAGCAGCAGCTGTATCAGCTGAGCAAGGTTGAAGGG GACAGCACGTGATCAAGGGCAGACCTGTGTCCAGCAGCTTCGACCTTATCAAGTTCCCTGAGGA TCAGTTCAGGTGGCCCTGGACAGGTGTTGAGAACTCAGAAATTCAGGCTCTGGTGGACC AGTCCAGCAGATCTGTCTAGCGCCGAGAAAGGAAACAGCGCTTCATCACGCTGATCATCTG ATCGCCGTCTGGCCAGCTCCATGATCTGTGTCTCCATCTTCATCATTAATCAAGAAAGACAAAGAG CCCAAGGGCTCTCTCAGAACTGAGGGAGTGAACCAACAATGGCTTATCCCTCACAAAC</p>	<p>121</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>HMPV_ProlineStab_E131P</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGAGCTGGAAAGGTGGTCATCACTTCAGCCTGCCTGATCACACCTCAGCAGCGCCTGAAAGGAGAG CTACCTGGAAAGAGTCCCTGCAAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAGAAACCGGCTGGT ACACCAACGTGTTCACTGGAAGTGGGGCACGTGAGAGAACTGTGACATGCTCTGATGGGCTTAGC CTGATCAGAGACGAGCTGGATCTGACCAAGAGC GGCCTGAGAGAACTCAAGACTGTGTCTGCGCA TCAGCTGGCCAGAGAGGAACAGATCGAGAATCTGGGCAGCGGCAGCTTTGTGCTGGGAGCCATT GGCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGCAGGCCTGGCCATCGCTAAGACCATCAAGACT GGCTAGCGAAGTGAACGCCATCAACAAAGCGCTGAAGAAAGCAAAACGAGGCCGTGAGCACACTC GGCATGGCTTTAGAGTGGCTGGCCACAGCCGTGC GCGAGCTGAGAGACTTGGTGTCCAAAGAAC TGACAGGGGCATTAAKANGAACAGTGGACATCGACGACCTGAAGATGGCCGTGTCCCTTTAGC CAGTTCAACCGCGGCTTTCTGACGCTGCTGC GGCAGTTTAGGAGCAACGCCGGAACTCACACCAGC CATCAACCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGGCTAAKATGCTAGATCTG CGGCTCAGATCAAGCTGATGCTCAGAAATAGAGCCATGGCTCGACGGAAAGGCTTCGGCATCTG ATTGGCTGTACGGCAGCAGCTGATCTATATGGTGCAGCTGCCTATCTTCGGCTGTGATGACAC ACCTGCTGGATTGTGAAGGCCTGCTCCTAGCTGTAGCGAGAAAGGGCAATTAACGCTGGCTGC TGAGAGAGGACCAAGGCTGGATTGTCAGAACGCCGGCAGCAGCAGCTGACTACCTAAAGAGAAAG GACTGGAGACAGAGGCGACCAAGTGTCTGTGATACCGCCGCTGGAACTAATGTGGCCGAGC AGAGCAAGAGTGCACATCAACATCAGCAGCAGCAGCAGCTATCCCTGCAAGGTGTGCAAGCGCCAGG CAGCTTATTTCTATGGTGGCTGCTGTCTCCCTGGAGCCCTGGCTGGCTGGTTAAGAGGCGGTGTCC TGTAGCATCGCCAGCAACAGAGTGGGCATCATCAAGCAGCTGAAAGAGGGCTGCAAGCTACATCAC CAGCCAGGAGCCGATACCGTGCATCGACAGCAGCAGCTGTATCAGCTGAGCAAGGTGGAAGGGC GAKAGCACGTGATCAAGGGCAGACCTGTGTCCAGCAGCTTCGACCTATCAAGTTCCCTGAGGAA TCAGTTCAGGTGGCCTGGAGCAGGTGTTGAGAAACATCAGAAATTCAGAGGTCTGGTGGACC AGTCCAACAGAACTCTGTCTAGCGCCGAGAAAGGAAACAGCGGCTTCATCATCTGATCATCTG ATCGCGTGTGGCAGCTCCATGATCCTGGTGTCCATCTTCATCATTAAGAGAGCCAGAGAG CCACCGGGCTGCTCCAGAACTGAGCGGAGTGAACCAACAATGGCTTCATCCCTCACAC</p>	<p>122</p>
<p>35</p> <p>HMPV_ProlineStab_D447P</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ATGAGCTGGAAAGGTGGTCATCACTTCAGCCTGCCTGATCACACCTCAGCAGCGCCTGAAAGGAGAG CTACCTGGAAAGAGTCCCTGCAAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAGAAACCGGCTGGT ACACCAACGTGTTCACTGGAAGTGGGGCACGTGAGAGAACTGTGACATGCTCTGATGGGCTTAGC CTGATCAGAGACGAGCTGGATCTGACCAAGAGC GGCCTGAGAGAACTCAAGACTGTGTCTGCGCA TCAGCTGGCCAGAGAGGAACAGATCGAGAATCTGGGCAGCGGCAGCTTTGTGCTGGGAGCCATT GGCTCTGGAGTGGCTGCTGCTGCAGCTGTTACAGCAGGCCTGGCCATCGCTAAGACCATCAAGACT GGAAAGC GAAAGTGAACGCCATCAACAAAGCGCTGAAGAAAGCAAAACGAGGCCGTGAGCACACTC GGCATGGCTTTAGAGTGGCTGGCCACAGCCGTGC GCGAGCTGAGAGACTTGGTGTCCAAAGAAC TGACAGGGGCATTAAKANGAACAGTGGACATCGACGACCTGAAGATGGCCGTGTCCCTTTAGC CAGTTCAACCGCGGCTTTCTGACGCTGCTGC GGCAGTTTAGGAGCAACGCCGGAACTCACACCAGC CATCAACCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGGCTAAKATGCTAGATCTG CGGCTCAGATCAAGCTGATGCTCAGAAATAGAGCCATGGCTCGACGGAAAGGCTTCGGCATCTG ATTGGCTGTACGGCAGCAGCTGATCTATATGGTGCAGCTGCCTATCTTCGGCTGTGATGACAC ACCTGCTGGATTGTGAAGGCCTGCTCCTAGCTGTAGCGAGAAAGGGCAATTAACGCTGGCTGC TGAGAGAGGACCAAGGCTGGATTGTCAGAACGCCGGCAGCAGCAGCTGACTACCTAAAGAGAAAG GACTGGAGACAGAGGCGACCAAGTGTCTGTGATACCGCCGCTGGAACTAATGTGGCCGAGC AGAGCAAGAGTGCACATCAACATCAGCAGCAGCAGCAGCTATCCCTGCAAGGTGTGCAAGCGCCAGG CAGCTTATTTCTATGGTGGCTGCTGTCTCCCTGGAGCCCTGGCTGGCTGGTTAAGAGGCGGTGTCC TGTAGCATCGCCAGCAACAGAGTGGGCATCATCAAGCAGCTGAAAGAGGGCTGCAAGCTACATCAC CAGCCAGGAGCCGATACCGTGCATCGACAGCAGCAGCTGTATCAGCTGAGCAAGGTGGAAGGGC GAKAGCACGTGATCAAGGGCAGACCTGTGTCCAGCAGCTTCGACCTATCAAGTTCCCTGAGGAA TCAGTTCAGGTGGCCTGGAGCAGGTGTTGAGAAACATCAGAAATTCAGAGGTCTGGTGGACC AGTCCAACAGAACTCTGTCTAGCGCCGAGAAAGGAAACAGCGGCTTCATCATCTGATCATCTG ATCGCGTGTGGCAGCTCCATGATCCTGGTGTCCATCTTCATCATTAAGAGAGCCAGAGAG CCACCGGGCTGCTCCAGAACTGAGCGGAGTGAACCAACAATGGCTTCATCCCTCACAC</p>	<p>123</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>HMPV_TrimerRepulsionD4 54N</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>ATGAGCTGGAAAGGTGGTCATCACTTCAGCCTGCTGATCACACCTCAGCAGGGCTGAAAGAGAG CTACCTGGAAAGAGTCTGAGAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAGAAACGGGCTGT ACACCAACGTGTTCACTGGAAGTGGGGGACGTGAGAGAACTGTGACATGCTCTGATGGCCCTAGC CTGATCAAGACGAGCTGGATCTGACCAAGAGCAGCCTGAGAGAACTCAAGACCCTGTCTGAGCA TCAGCTGGCCAGAGAGGAAAGATCAGAAATCTGGCCAGCGGCAGCTTTGTGCTGGGAGCCATT GCTCTGGAGTGGCTGCTGCTGAGCTGTTACAGCAGGCCTGGCCATGCTCAAGACCATCAGACT GGAAGCAGAGTGAACGCCATCAACAGCGCTGGAAGAAACAAACGAGGCCTGAGCAGCACTC GGCATGGCTTAAAGTGGCTGGCCACAGCCGTGCAGCAGCTGAGAGACTTGTGTCCAAAGACC TGACAGGGCCATTAAACAGAAACAAGTGGCACATCGACGACCTGAAGATGGCCGTGTCTTTAGC CAGTTCAACCGCCGCTTTCTGAACGTCTGTGCGCAGTTTAAAGCAGCAGCCGGAAATCAAGCAGC CATCAACCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGCTAACATGCTACATCTG CCGCCAGATCAAGCTGATGCTCAGAAATAGAGCCATGGCTCCGACGGAAAGGCTTCGGCATCTG ATTGGGTGTACGGCAGCAGCTGATCTATATGGTGGAGCTGCTATCTTCGGCTGTGATGACAC ACCTGCTGATTTGTGAAGCCGCTCTAGCTGTAGGAGAAAGAGGCAATTAACGCTGCTGCTGC TGAAGAGGACCAAGGCTGGTATTGTCAAGAGCCGGCAGCAGCAGCTGTACTACCTAACGAGAAAG GACTGGGAGCAAGAGGCGACACCTGTTCTGTGATACCGCCGCTGGAAATCAATGTGGCCGAGC AGAGCAAGAGTGCACATCAACATCAGCAGCCAGCAACTATCCCTGCAGGCTGTCCAGCGAGG CAGCCATTTCTATGCTGCTCTGTCTCCCTGGAGCCCTGGCTGTGTTAAGAGGCTGTCTCC TGTAGCATCGCCAGCAGAGAGTGGGCATCAGCAGCAGCTGACAAAGGCTGCAAGCTACATCAC CAGCCAGGAGCCGATACCGTGCATCGACAGCAGCAGCTGTATCAGCTGAGCAGAGGTGGAGGGC GAGAGCACGCTGATCAAGGGCAGACCTGTGTCCAGCAGCTTCGACCTATCAAGTTCCCTGAGAA CCACTCCAGGTGGCCCTGGAGCAGGTGTGGAGAACATCAGAAATCCAGGCTCTGGTGGACC AGTCCAGCAGATCTGTCTAGCGCCGAGAAAGGAAACAGCCGGCTTCATCAGCTGTGATCCTG ATCGCGCTGTGGCAGCTCCATGATCCTGCTGTCCATCTTCATCATTAAGAGAGCCAGAAAG CCCACGGCGCTCTCCAGAACTGAGCGGAGTGCACACAAATGGCTTCATCCCTCACAG</p>	<p>124</p>
<p>35</p> <p>HMPV-TilmerRepulsionE45 3N</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>ATGAGCTGGAAAGGTGGTCATCACTTCAGCCTGCTGATCACACCTCAGCAGGGCTGAAAGAGAG CTACCTGGAAAGAGTCTGAGAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAGAAACGGGCTGT ACACCAACGTGTTCACTGGAAGTGGGGGACGTGAGAGAACTGTGACATGCTCTGATGGCCCTAGC CTGATCAAGACGAGCTGGATCTGACCAAGAGCAGCCTGAGAGAACTCAAGACCCTGTCTGAGCA TCAGCTGGCCAGAGAGGAAAGATCAGAAATCTGGCCAGCGGCAGCTTTGTGCTGGGAGCCATT GCTCTGGAGTGGCTGCTGCTGAGCTGTTACAGCAGGCCTGGCCATGCTCAAGACCATCAGACT GGAAGCAGAGTGAACGCCATCAACAGCGCTGGAAGAAACAAACGAGGCCTGAGCAGCACTC GGCATGGCTTAAAGTGGCTGGCCACAGCCGTGCAGCAGCTGAGAGACTTGTGTCCAAAGACC TGACAGGGCCATTAAACAGAAACAAGTGGCACATCGACGACCTGAAGATGGCCGTGTCTTTAGC CAGTTCAACCGCCGCTTTCTGAACGTCTGTGCGCAGTTTAAAGCAGCAGCCGGAAATCAAGCAGC CATCAACCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCGTGCTAACATGCTACATCTG CCGCCAGATCAAGCTGATGCTCAGAAATAGAGCCATGGCTCCGACGGAAAGGCTTCGGCATCTG ATTGGGTGTACGGCAGCAGCTGATCTATATGGTGGAGCTGCTATCTTCGGCTGTGATGACAC ACCTGCTGATTTGTGAAGCCGCTCTAGCTGTAGGAGAAAGAGGCAATTAACGCTGCTGCTGC TGAAGAGGACCAAGGCTGGTATTGTCAAGAGCCGGCAGCAGCAGCTGTACTACCTAACGAGAAAG GACTGGGAGCAAGAGGCGACACCTGTTCTGTGATACCGCCGCTGGAAATCAATGTGGCCGAGC AGAGCAAGAGTGCACATCAACATCAGCAGCCAGCAACTATCCCTGCAGGCTGTCCAGCGAGG CAGCCATTTCTATGCTGCTCTGTCTCCCTGGAGCCCTGGCTGTGTTAAGAGGCTGTCTCC TGTAGCATCGCCAGCAGAGAGTGGGCATCAGCAGCAGCTGACAAAGGCTGCAAGCTACATCAC CAGCCAGGAGCCGATACCGTGCATCGACAGCAGCAGCTGTATCAGCTGAGCAGAGGTGGAGGGC GAGAGCACGCTGATCAAGGGCAGACCTGTGTCCAGCAGCTTCGACCTATCAAGTTCCCTGAGAA TCACTCCAGGTGGCCCTGGAGCAGGTGTGGAGAACATCAGAAATCCAGGCTCTGGTGGACC AGTCCAGCAGATCTGTCTAGCGCCGAGAAAGGAAACAGCCGGCTTCATCAGCTGTGATCCTG ATCGCGCTGTGGCAGCTCCATGATCCTGCTGTCCATCTTCATCATTAAGAGAGCCAGAAAG CCCACGGCGCTCTCCAGAACTGAGCGGAGTGCACACAAATGGCTTCATCCCTCACAG</p>	<p>125</p>

(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>HMPV_StabilizeAlphaF196 W</p> <p>ATGAGCTGGAAAGGTGGTCATCACTTCAAGCTGCTGATCAGCCAGCAGCGCCCTGAAAGAGAG CTACCTGGAAAGAGTCCCTGCAAGCACCATCAAGAGAGGGTACCTGTCTGTGAGAACCGGGCTGCT ACACCAACGTGTTCACTGGAAGTGGGGCACGTGAGAGANTCTGACATGCTCTGATGGCCCTAGC CTGATCAAGAGCCGAGCTGGATCTGACCAAGAGCGCCCTGAGAGAACTCAAGAGCTGTGTCTGCTGA TCAGCTGGCCAGAGAGGAACAGATCGAGAATCTGGCCAGCGCCAGCTTTGTGCTGGGAGCCATT GCTCTTGGAGTGGCTGCTGCTGCAAGCTGTTACAGCAGGCCTGGCCATGCTCTAAGACCAATCAAGCT GGAAAGCGAAGTGAAGCGCCATCAACAAAGCCCTGAAAGAGAGCAAAAGAGAGCGCTGAGCACTC GGCAATGGCGTTAGAGTGGCTGGCCACAGCCGTGCGCCGAGCTGAAGGACTTCGTGTCCAAAGAAC TGACAGGGCCATTAAACAAAGAACAGTGGCACATCGACGAGCTGAAGGATGGCCGTGTCTTTAGC CACTGGAAACCGGCCTTTCTGAACGTCGTGCGCCAGTTTAGCGAACAGCCCGGAATCAACACAG CCATCAGCCCTGGACCTGATGACAGATGCTGAGCTGGCTAGAGCCCTGCTCAACATGCTTACATCT GGCGCCAGATCAAGCTGATGCTCGAGAAAGAGCCATGGTCGACGGAAAGGCTTCGGCATCT GATGCGGTGTACGGCAGCAGCGTGAATCTATATGGTGCAGCTGGCTATCTTCGGCGTATCGACA CACTTCTGGATTGGAAGGCCGCTCCTAGCTGTAGCGAGAAAGAGGGCAATTACGCTGCTTG CTGAGAGAGGAGCCAAAGCTGGTATTGTCAGAACGCCGGCAGCAGCCGTGTACTAGCCTAACGAGAA GGACTGCGAGACAAAGAGCGGACCAGCTGTCTGTGATACCGCCGCTGGAAATCAATGTGCCGAG CAGAGCAAGAGTGCAGCATCAACATCAAGCACCAGCAACTATCCCTGCAAGGTGTCAGCGCCAG GCACCTATTCTATGGCTGGCTGTGTCTCCCTGGGAGCCCTGGTGGCTGTATTAAAGGGCGTGT CCTGTAGCATCGCAGCAACAGAGTGGCAGTCAATCAAGCAGCTGAAACAAAGGCTGCAAGCTACATC ACCAGCCAGGAGCGCGATACCCTGACCATCAAGCAGCCCTGTGTATCAAGCTGAGCAAGGTGGAG GCGACAGCAGCTGATCAAGGGCAGACCTGTGTCAGCAGCTTCGACCCATCAAGGTGCTGTAG GATGCTTCAGAGTGGCCCTGGACCAGGTGTGAGAGCATCGAGAAATCCAGGGCTCTGGTGGAA CCAGTCCAGCAGAAATCCCTGAGCCGAGAGGGAAACACCGCCCTCAATCATGATGATCATCC TGATCGCCGTGCTGGCAGCTCCATGATCCCTGGTGTCCATCTCAATATCAAGAGAGCCAAAG AGCCACCGCCGCTCTCCAGAACTGAGCGGAGTCAACAAATGGCTTCATCCCTCAACAG</p>	<p>126</p>

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Human Metapneumovirus mRNA		
5 10 15 20 25 30	HMPV_SC_DSCAV1_4MM V AUGAGCUUGGGAAGGUGGGU C AUC AUC UUC AAGCCUGCU GAUC AC ACC UC AGC AC GGC CU GAAAGAG AGCUAGCUUGGGAAGAGUC CU GC AGC AC C AUC ACAGAGGGCU ACC UG UC U GU GCU GAGAACCGGC UGGUACACC AAC GUGUUC AC ACU GGAAGUGGGCCGAC GUC GAGAAUCU GAC AUGGC UC UG AU GGCC CUUGGCUUGAUC AAG ACC GAGC UG GAUC UG ACC AAG AGC GCC CUG GAGAGACUC AAGAC CGUG UCUGCCG AUCAGCU GGGCC AGAGAGG AAC AGAUC GAGA AUC CU GGC AGC GGC AGC UUU G U GCU G GGACCAUUGCUUUGGAGU GCU GCU GCU GC AGCU GUAAC AGC AGGC GUG GC CAUCU GC AA GACC AUC AGACU GGAAGGC GAAAG UG ACC GCC AU C AAC AAC GC CCUGAAGAGACAAAG GAGGCC GUCAGCACACUC GGC AAUGGGU AGAGU GCU GGC CUUU GGC GUC GCG GAGCU GAAAGGACUU CGU GAC AAGAC CU GAC AC GGC CC AU GAC AAGAAC AAGU GCGAC AUC GAC GAC CU GAAGAU GGCCGUGU CUU UAGCC AGU UCAACC GGC GGU UUCU GAAC GUC GUG GGC AGU UU AGC GACA AGCCGGAAUC ACC AGCC AU C AGCCUGGACC U GAUGACAGAU GC UGAGCU GGC UAGAGCGG UGCCU AAC AUG CC UAC AU GUG GC GGC C AGAUC AAGCU G AUG CU GA AAU UG A GGC AUGGGCC GACCGAAGGCU UUGGC AUUCUGUGUGGC GUGU AGGGCAGC AGC GUGAUCU AU AUGGUGCAG CUGCCU AUGUJC GGC GUSAU GAC AC ACC UGCUG GAUU GUGAAGGC CCG UCCU AGCU G UAGC GAGAAE AAGGGCAU U AC GC CU GC CU GUGAGAGAG GACC AAGGCUGG UUGUGC AGAAC GC C GGCAGCACCG UGUAC UAC CU A AC GAG AAGGACU GCGAGAC AAGAGGC GAC CAC GU G UUC U GU GAAUCGCC CGUGGAAUCAAUUGUGGC GGACAGAGCA AAGGAGU GCAAC AUC AAG AU C AGC ACC A CCANCUUCC U GC AAGGUGUJC ACC GGC AGC AC CCU AUUUCU AU GGU GCU CUG UC UC UC UC UGGAGCC CGUGUGGCU U GUU AUAGGGGC GUGUCC UGUAGC AUG GGC AGC AAC AGAGUGGGC AUCAU AAGCAGC UGAGAC AAGGGC UGC AGCUAC AUC ACC AAC CAGGAC GCGAUAC CGUGAC CA UGGACAC ACC GUGU AUC AGCUGAGC AAGGUUGAAGGC GAACAGC AGUGG AUC AAGGGCAGAC CUGUGUC CAGCAGCU UC GAC CCU AUC AAGGU CC CU GAGGALIC AUUU C AUC GUG GGG UGGACC AGGUGUC GAGAC AUC GAGAAUUC CCAGGCUUGGUGUGGACAGUC C AAGAGAU CC UGUUUA GGCCGAG AAGGG AAGS ACC GGC U UC AUC AUC GUG AUC AUCCUGAU GGC GUGCGGGG AGC U CGAUGACCUUGGGU CC AUUCUJC AUC AUU AUC AAGAAAGAC C AAGAGC CC AC CGGC CUC CC UC CGAUCUGAGCGGAGU GACC AAC AUUGGCUJC AUC CC UC AC A AC	127
35 40 45 50 55	HMPV_SC_DSURIC_4MM V AUGAGCUUGGGAAGGUGGGU C AUC AUC UUC AAGCCUGCU GAUC AC ACC UC AGC AC GGC CU GAAAGAG AGCUAGCUUGGGAAGAGUC CU GC AGC AC C AUC ACAGAGGGCU ACC UG UC U GU GCU GAGAACCGGC UGGUACACC AAC GUGUUC AC ACU GGAAGUGGGCCGAC GUC GAGAAUCU GAC AUGGC UC UG AU GGCC CUUGGCUUGAUC AAG ACC GAGC UG GAUC UG ACC AAG AGC GCC CUG GAGAGACUC AAGAC CGUG UCUGCCG AUCAGCU GGGCC AGAGAGG AAC AGAUC GAGA AUC CU GGC AGC GGC AGC UUU G U GCU G GGACCAUUGCUUUGGAGU GCU GCU GCU GC AGCU GUAAC AGC AGGC GUG GC CAUCU GC AA GACC AUC AGACU GGAAGGC GAAAG UG ACC GCC AU C AAC AAC GC CCUGAAGAGACAAAG GAGGCC GUCAGCACACUC GGC AAUGGGU AGAGU GCU GGC CA GGC C GUG GCG GAGCU GAAAGGAC UU CGU GAC AAGAC CU GAC AC GGC CC AUU AAG AAGAAC AAGU GCGAC AUC GAC GAC CU GAAGAU G GCCGUGUC CUU UAGCC AGU UCAACC GGC GGU UUCU GAAC GUC GUG GGC AGU UU AGC GAC AAC GGCGAAUC AC AC CAGCCALICAGCCUGGACCUUGAU GAC AGAUGCU GAGCUGCCUAGAGCC CUG CCUANC AUGCCU AC AUUCGCC GGC AGAUC AAGC U GAU GCU GAGAAU UGAGGCC AUGGUC GGA	128

(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
5	<p> CCGAAGGCUGGGCAUUCUGUGUGGCGUUGUACGGCAGCAGCGUUAUCUUAUUGUGUGCAGCU GCUAUGUACUGGGGUGAUCGACACACCCUGGUGGAAUUGUAAGGCGGUCUAGUUGUAGCGA GAKAAGGBCAAUUAACCCUGGCCUGGUGABAGAGAGAGCCAAAGGCGUGUUAUUGUAGAGACCCCG CAGCACCGUGUAGUACCCUAAAGSAGAAGGACUGGCGAGACAGAGGGCGACACAGSUGUUUGUGA UACCGCGCGUGGAAUUAUUGUGGCGGAGCAGAGCAAGAGAGUGCAACUACACAGCAGCAGCAGC ACUUAUCCUGGCAAGGUGUCCAGCGGCAAGGCAACCUUUAUUCUUGUGUGGUCUUGUCUCUUG GAGCCUUGUGUGUGUUAUUAAGGGCGUGUGGUGUAGCAUCGGCAGCAACAGAGUGGGCAU CAUCAGCAGCUUAACAGGGGCGUCAGCUACUACACCAACAGGACGCCGAUACCGUGAGCAGC GACACACCGUGUUAUAGCUGAGCAGGUGGAGAGGCGAAGCAGCACGUGAUCAGGGCAGACCU GUGACAGC GUGUAGCAGAACUAGSAGAUUCCAGGCUUGGUGGACAGUCCACAGSAGUCCUGUAGC GCGSAGAGGGAAACACCGGCGUCCAUCAUGUGUAGUACUUGUGGCGCGUGUGGCGAGCAGC AUGUUCUGUGUGGCAUCUUCUUAUUAUUAAGAAACCAAGAGGCCACCGGCGGUCUCCAGCA GACUGAGCGGAGUGACCAACAAGGGGUCUUCUCCUCACAAAC </p>	
20	<p> HMPV_SC_DM_Krarup_U7 4LD185P </p> <p> AUGAGCUGGAGGUGGUCUACUUCUUCAGCCUGCGUAGCACCCUCCAGCAGCGCGUUAAGAG AGCUACUGGAGAGAGUCUGGCGGCGACUACAGAGAGGCUACCGUGUUGUGUGUAGAGACCGGC UGGUAGCAGCAGCAGSUGUCCAGUAGAGUGGGCGAGCAGCAGSAGAUUCAGAGGCGUGUAGG CUGGCGUGUAGAGAGCGGAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC UCUGCGUAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GAGCAGUUGUGUUGGAGUGGUGGUGGUGGUGGUGGUGGUGGUGGUGGUGGUGGUGGUGGUGG GACUACAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GACUACAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GUCAGC CGUGGCGUAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GCGGAGC GCGGAGC CCGAAGGCUGGGCAUUCUGUGUGGCGUUGUACGGCAGCAGCGUUAUCUUAUUGUGUGCAGCU GCUAUGUACUGGGGUGAUCGACACACCCUGGUGGAAUUGUAAGGCGGUCUAGUUGUAGCGA GAKAAGGBCAAUUAACCCUGGCCUGGUGABAGAGAGAGCCAAAGGCGUGUUAUUGUAGAGACCCCG CAGCACCGUGUAGUACCCUAAAGSAGAAGGACUGGCGAGACAGAGGGCGACACAGSUGUUUGUGA UACCGCGCGUGGAAUUAUUGUGGCGGAGCAGAGCAAGAGAGUGCAACUACACAGCAGCAGCAGC ACUUAUCCUGGCAAGGUGUCCAGCGGCAAGGCAACCUUUAUUCUUGUGUGGUCUUGUCUCUUG GAGCCUUGUGUGUGUUAUUAAGGGCGUGUGGUGUAGCAUCGGCAGCAACAGAGUGGGCAU CAUCAGCAGCUUAACAGGGGCGUCAGCUACUACACCAACAGGACGCCGAUACCGUGAGCAGC GACACACCGUGUUAUAGCUGAGCAGGUGGAGAGGCGAAGCAGCACGUGAUCAGGGCAGACCU GUGACAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GUGUAGCAGAACUAGSAGAUUCCAGGCUUGGUGGACAGUCCACAGSAGUCCUGUAGC GCGSAGAGGGAAACACCGGCGUCCAUCAUGUGUAGUACUUGUGGCGCGUGUGGCGAGCAGC AUGUUCUGUGUGGCAUCUUCUUAUUAUUAAGAAACCAAGAGGCCACCGGCGGUCUCCAGCA GACUGAGCGGAGUGACCAACAAGGGGUCUUCUCCUCACAAAC </p>	129

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Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5 HMPV_SC_UM_Krarup_U7 4LD185PD454N</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>AUGAGCUUGGAAAGGUGGUC AUC AUC UUC AGCCUGCUGAUC AC ACCUC AGC AC GGCUC GAAAGAG AGCUNCCUGGAAAGAGUC CUGCAGC AC C AUC AC AGAGGCUACCCUGU UGUUCUGAGAACCCGCG UGCUACACCAAC GUGUUC AC ACU GAAAGUGGCGAC GUC GAGAAUCUGAC AUGCUC UG AUGGC CCUNGGCUGAUC AAGACCGAGCUGGUAUC UGCUAAGAGC CC CCGAGAGAACUC AAGACCGUG UCUCGCAUCAGCUGGCGAGAGAGGAC AGAUCGAGAAUC CUGGCAGCGGC AGC UUU GUUCUG GGACCAUUGCUC UUGGAGUG GCUUCUGUCUGG CAGCUGUAC AGC AGC GUGGC CAUC GCUAA GACCAUC AGACU GAAAGCG GAGUGACCGCC AUC AAC AAC GCGCCUGAAGAGAC AAG GAGGCC GUCAGC ACUC GGC AUGCUGUUGAGAGUGCUGG CAC AGCC GUGGC GC GAGUGGAGAGGAC UU CGUGGCAAGAAC CUGACACGGCC AUU AAC AAG AAC AAGU GGC AC AUCCU GAC CUGAAGAGU GCGAGUC UUAAGCC AGUUC AAC GGC GGUUUCUGAAGC UC GUGC GGC AGU UUA GAGAC AAC GCGCGAUC ACAC AGCC AUC AGCUGGACCGU AU GAC AGAUGCUG AGC UGGCUAGAGCC GUG CCUACAU GCU AC AUUCGC GGC A G AUC AAGC U GAUCUC GAGAAU AGAGCC AUGGUCGGA CGGAAAGC UUCGGC AU UCUGAUGGC GU GU AC GGC AGC AGC GUGAUCU AU AUGGUCAGC U GCUAUCUC GGC GUGAUC GAC AC ACC CUGUGG AUU GUGAAGGCGCC UC CUGAGCUGAGC GA GAGAAAGGC AAU UAC GCGUGCCUGCU GAGAGAGG ACC AAGGCUUGGU AUU GUC AGAAC GCG CG CAGCACCUGUGAUC CCU AAC G AAGAGGAC UGC GAGAC AAGAGGC GAC AC GUGUUCUGUGA UACCGCGC UGGAAUC AAUGUGGC CGAGC AGAGC AAGAGUGC AAC AUC AAC AUC AGC ACC ACC AUCUUC CUGC AAGGUGUC CAG GGC A G C AC C U AUUUCU AUGGU GGC UCUGUC UC CUCUG GGAGCCUGUGGCUUGU AU AAGGCG CUGUCU GUAAGC AUC GGC AGC AAC AGAGUGGCG AU CUCAGC AGCU GAAC AAGGCGU GC AGCUAC AUC ACC AAC AGGAC GCG AUU ACC GUGACC AUC GAC AAC AC CGUGU AUC AGCUGAGC AAGGUGGAGGC GAACAGC AC GU GAUC AAGGCG AGACCU GUGLCCAGC AGCUC GACCC U AUC AAGUCC CUG AGAAC CAGUCC AGGUGGCG CUG GAC C AG GUGLCCAGGAC AUC GAGAAUCC AGGCU CUGGUGAC C AGUCC AC AGAAUCC UGUACG GCGGAGAGGGAAC ACCGGCUUC AUC AUCUGAU C AUC CUGAUC GC CUGUCUGGCGAGC UCC AUGAUCCUGUGUC AUC UUC AUC AUU AUC AAGAGAC CAAG AAGCC ACC GCG CUCUC GAG GACUAGC GAGAGGAC AAC AAGGCUUC AUC CUC AAC</p>	<p>130</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>HMPV_SC_4M_Krarup_U74LS170LD185P</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>AUGAGUUGGAAAGGUGGUC AUC AUC UUC AGCCUUGUUGAUC ACCUC AGC AC GGC CUGAAAGAG AGCUNCUGGAAAGAGUC CUGC AGC AC C AUC AC AGAGGGDUACCGUUC UGUUCUGAGAACCGGC UGCUACACCAAC GUGUUC AC ACU GGAAGUGGGCGAC GUC GAGAAUCUGAC AUGC UC UGAVGGC CCUNGGCUG AUC AAGACCGAGCUGBAUC UGCUCAAGAGC GC CUGAGAGAACUC AAGACCGUG UGUCCCAUCAGCU GGGC AGAGAGGAAAC AGAUCGAGAAUC CUGGC AGCGGC AGC UUU GUUCUG GGACCCAUUGCU UUGGAGUUGUCUGUCUGUC AGCUUUAAC AGC AGGC GUGGC CAUC CUAA GACCAUC AGACH GGAAGC GAAGUGACCGCC AUC AAC AAC GC CUGAAGAGACAAAC GAGGCC GUCAGCAC ACUC GGC AUGC GCUUAGABUUGUCUGGC AC AGCC GUGGC GUGAGUGAAGGAC UU CGUCGUUAAGAAC CUGAC AC GGGCC AUUUAAC AAGAAC AAGU GGC AC AUCCUG AC CUGAAGAGU GCGUAGUC UUAAGCC AGUUC AACCGGC GGUUUCUGAAGGUC GUGCGGC AGUUAAGCGAC AAC GC CGAAUC AC AC CAGCC AUC AGCCUGGACCGU AUBAC AGAUGCUGAGCUGGCUAGAGCCGUG CCUANC AUCCU AC AUCUGCCGGCC AGAUC AAGC UG AUCUCUGAGAAUAGAGCC AUGGUC CGA CGGAAGGCUUGGCGC AU UGUAGUUGGC GU GU AC GGC AGC AGC GUGAUCU AU AUGGUGCAGC U GC UAUUCUGGC GUGAUC GAC AC ACC CUGC UGG AUU GUGAAGGCC GC UC CUGAGC UGU AGCGA GAGAAGGGC AU UAC GCUGCCUGUC GAGAGAGGAC AAGGCUUGGU AUU GUC AGAAC GCGCG CAGCACGUGUACU AC CCU AAC GAGAAAGC UGC GAGAC AAG AGGC GAC AC GUGUU CUGUGA UACCGCCUGGAAUC AUUGUGGCC GAGC AGAGC AAGAGUGGCAC AUC AAC AUC AGC ACC ACC ACUUAJCCUGC AAGGUGUC AC GGGC AGC ACC U AUUUCU AUGGU GGC UCUGUC UC CUCUG GGACCCUGGUGGCUUGU AU AAGGCC GUGU CCUGUAGC AUGGCC AGC AAC AGAGUGGGC AU CAUCAGC AGCU GAAC AAGGGCU GC AGCUAC AUG ACC AAC AGGAC GCG AU ACC GUGAGC AUC GACAC AC CUGU AU AGC UGAGC AAGGUGG AAGGC GAACAGC AC GU GAUC AAGGGC AGACCU GUGUCCAGC AGCUUC GACCU AUC AAGUUC CUGAGBAUC AGUUC AGGUGGCC CUGGAC AG GUGUCCAGAAC AUC GAGAAUUCGAGGCUUGGUGGAC CAGUCC AAC AGAAUCC UGUUAGC GCGGAAAGGGAAC ACCGGCUUC AUC AUGUUGAU C AUCUGAUC GC CUGUCUGGGCAGC UCC AUGUUCUGUGUC AUC UUC AUC AUU AUC AAGAAAC CAAGAGGCC ACCGGC GCUCC UC CA GANCUGAGC GAGUGAC CAACAUGGGUUC AUCCUC AC AAC</p>	<p>131</p>
<p>35</p> <p>HMPV_SC_5M_Krarup_U74LS170LD185PD454N</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>AUGAGUUGGAAAGGUGGUC AUC AUC UUC AGCCUUGUUGAUC ACCUC AGC AC GGC CUGAAAGAG AGCUNCUGGAAAGAGUC CUGC AGC AC C AUC AC AGAGGGDUACCGUUC UGUUCUGAGAACCGGC UGCUACACCAAC GUGUUC AC ACU GGAAGUGGGCGAC GUC GAGAAUCUGAC AUGC UC UGAVGGC CCUNGGCUG AUC AAGACCGAGCUGBAUC UGCUCAAGAGC GC CUGAGAGAACUC AAGACCGUG UGUCCCAUCAGCU GGGC AGAGAGGAAAC AGAUCGAGAAUC CUGGC AGCGGC AGC UUU GUUCUG GGACCCAUUGCU UUGGAGUUGUCUGUCUGUC AGCUUUAAC AGC AGGC GUGGC CAUC CUAA GACCAUC AGACH GGAAGC GAAGUGACCGCC AUC AAC AAC GC CUGAAGAGACAAAC GAGGCC GUCAGCAC ACUC GGC AUGC GCUUAGABUUGUCUGGC AC AGCC GUGGC GUGAGUGAAGGAC UU CGUCGUUAAGAAC CUGAC AC GGGCC AUUUAAC AAGAAC AAGU GGC AC AUCCUG AC CUGAAGAGU GCGUAGUC UUAAGCC AGUUC AACCGGC GGUUUCUGAAGGUC GUGCGGC AGUUAAGCGAC AAC GC CGAAUC AC AC CAGCC AUC AGCCUGGACCGU AUBAC AGAUGCUGAGCUGGCUAGAGCCGUG CCUANC AUCCU AC AUCUGCCGGCC AGAUC AAGC UG AUCUCUGAGAAUAGAGCC AUGGUC CGA CGGAAGGCUUGGCGC AU UGUAGUUGGC GU GU AC GGC AGC AGC GUGAUCU AU AUGGUGCAGC U GC UAUUCUGGC GUGAUC GAC AC ACC CUGC UGG AUU GUGAAGGCC GC UC CUGAGC UGU AGCGA GAGAAGGGC AU UAC GCUGCCUGUC GAGAGAGGAC AAGGCUUGGU AUU GUC AGAAC GCGCG CAGCACGUGUACU AC CCU AAC GAGAAAGC UGC GAGAC AAG AGGC GAC AC GUGUU CUGUGA UACCGCCUGGAAUC AUUGUGGCC GAGC AGAGC AAGAGUGGCAC AUC AAC AUC AGC ACC ACC ACUUAJCCUGC AAGGUGUC AC GGGC AGC ACC U AUUUCU AUGGU GGC UCUGUC UC CUCUG GGACCCUGGUGGCUUGU AU AAGGCC GUGU CCUGUAGC AUGGCC AGC AAC AGAGUGGGC AU CAUCAGC AGCU GAAC AAGGGCU GC AGCUAC AUG ACC AAC AGGAC GCG AU ACC GUGAGC AUC GACAC AC CUGU AU AGC UGAGC AAGGUGG AAGGC GAACAGC AC GU GAUC AAGGGC AGACCU GUGUCCAGC AGCUUC GACCU AUC AAGUUC CUGAGBAUC AGUUC AGGUGGCC CUGGAC AG GUGUCCAGAAC AUC GAGAAUUCGAGGCUUGGUGGAC CAGUCC AAC AGAAUCC UGUUAGC GCGGAAAGGGAAC ACCGGCUUC AUC AUGUUGAU C AUCUGAUC GC CUGUCUGGGCAGC UCC AUGUUCUGUGUC AUC UUC AUC AUU AUC AAGAAAC CAAGAGGCC ACCGGC GCUCC UC CA</p>	<p>132</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
5	AUGAUCUGGUGUCCAUUUCUAUC AUU AUC AAG AAG ACC AAG AAG GCC ACC CGG CGC UCC UCC A GACUGAGCGGAGUGACACACAAUGGGUUCAUCCUUCACAC	
HMPV_SC_DM_Krarup_E5 1PU74L 10 15 20 25 30 35 40 45 50 55	AUGAGCUUGGAAGGUGGUCAUC AUC UUC AGCCUGUUGAUCAC ACCUCAGC AC GCCCU GAAGAG AGCUNCCUGGAAGAGUCUGUCAGCACC AUCACAGAGGGCUACCUUGUCUUGUCUUGAGAACCGGC UGGUNCCACCAGGUGUUCACACUUCUCUGGGGGGACGUUGAGAAUCUGAC AUGCUCUGAUGGC CCUNGGUUGAUC AAGACC GACUUGBAUCUGUJCAAGAGC GCCUUGAGAGAACUC AAGACC GUG UCUCGCCAUCAGCUGGGCCAGAGAGGAAACAG AUCGAGAAUCUGGCAGCGGC AGCUUUUGUCUG GGACCAUUGUCUUGUGAGUGUCUCUGUCUGAGCUGUJACAGCAGGCUGGC AUUCGUA GACC AUCAGACUUGGAAGCGAAGUGACC GCCAUUC AAC AAC GCCUUGAAGAGAACAAAGGAGGCC GUCAGCACACUUCGGCAUGGGUGUAGAGUGUCUCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC CGUJLCAAGAACCUUGACAGGGCCAUUUAACAGAACAGGUCGGACAUCCAGCAGCAGCAGCAGCAGC GCGUGUCUUGAGCCAGUUC AACGGCCGUGUUCUGAAGCUCUGUCGGCAGUUGUAGCGACAGC GCGGAAUCACAGCAGCC AUCAGCCUGGACCUJG AUAGCAGAGUGUCUGAGCUGGCUAGAGCCUG CCUNCAUGCCUACAUUCUGCCGGCCAG AUCAGG UUGAUCUGAGAAUAGAGCC AUGGUCUGA GGGAAAGCCUUCGGCAUUCUGAUUGCCGUGUACGGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GCDUUCUUCGGCGUGAUCGACACACCUGGUGGAAUUGUAGGGCCGCCUUCUAGCUUGUAGCBA GAGAGAGGGCAUUAAGCCUUGCCUUGUAGAGAGGACC AAGGGUUGUUAUUGUAGAACGCCGG GAGCACCUGUJACUACCCUANCAGAGGGACUUCGAGACAGAGGCAGCACACGUGUUCUGUGA UACCGCCGUGGAAUC AUUGUGCCGAGCAGACAGACAAAGAGUJCAACAUUCACAGCAGCCAGC ACCUACCCUUGG AAGGUGUCCAGCGCCAGGCACCCUUAUUCUUGUGUUGGGUCUGUCUCUCUG GGAGCCUGUGUGGUGUUAU AAGGGCGUGUUCUGUAGCAUCGGCAGCAGCAGCAGCAGCAGCAGC CAUCAGCAGCUAAGCAGGGGCUUCAGCUACAUCC AACAGGACGCCAGUACCUGAGCCAUUC GACACACCGUGU AUCAGCUGAGC AAGGUGGAGGCGGACAGCACAGUAGUCAAAGGGCAGACCU GUGUCCAGCAGCUUCGACCCU AUC AAGUUCUGAGG AUCAGUCCAGGUGGCCUGGACCAAG GUGAUCGAGAACAUAGAAUUCAGGCUUGGUGGACAGUCCACAGAAUCCUUGUAGC GCGAAGGAGAACACC GGCUUC AUC AUUGUGAUC AUCCUGAUCGCCUGUCUUGGGCAGC UCC AUGAUCUGGUGUCCAUUUCUAUC AUU AUC AAG AAG ACC AAG AAG GCC ACC CGG CGC UCC UCC A GACUGAGCGGAGUGACACACAAUGGGUUCAUCCUUCACAC	133

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Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5 HMPV_SC_UM_Krarup_E5 1PU74LD454N</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>AUGAGUCUGGAAAGGUGGUC AUC AUC UUC AGCCUGCUGAUC ACACUUCAGC AC GGC CU GAAAGAG AGCUACCUUGGAAAGAGUC CUGCAGCAGC AUCACAGAGGGCUACCUUGUC UGUUCUGAGAAACGGC UGGUACACCAAC GUGUUCACACUUC CUGGGGGGACGUUCAGAAUCUGAC AUGCUCUGAGUGGC CCUAGCCUGAUC AAGACCGAGCUGGUAUC UGCUCAAGAGC CC CUUGAGAGAACUC AAGACCGUG UCUGCCCAUCAGCUGGGCC AGAGAGGAAAC AGAUCGAGAAUC CUGGCAGCGGC AGCUUUUUGUCUG GGACCAUUGUCUUGUGAGUUGGUCUGUCUC AGCUUUAACAGCAGGC GUGGC AUC GCUAA GACCAUCAGACUGGAAAGC GAAGUGACCGCC AUC AAC AAC GC CCUGAAGAGAAACA AAGCAGGCC GUCAGCAC ACUCGGC AAGUGGCUUAGAGUGGUGGC ACAGCCGUGGC GUGAGUGAAGGAC UU CGUGUCAGAAAC CUGACACGGCC AUUUAAC AAGAAC AAGUGGCAC AUCGAC GAC CUGAAGAGUG GGCGAGUC UUAAGCC AGUUCAGCCGGC GGUUUCUGAAGGUC GUGCGGC AGU UUAAGCAGCAAC GGCGAAUCACAC CAGCC AUCAGCCUGGACCUUGAU GACAGAGUCUGAGC UGGCUAGAGCCGUG CCUAGCAGCCUC AUCUGCCGGCC AGAUCAGC UGAGUUCUC GAGAAUAGAGCC AUGGUCGAG CGGAAAGCC UUGGCAUUCUGAUGGC GUUGACGGCAGCAGC GUGAUCUUAUGGUGCAGC U GCUAUUCUGGC GUGAUC GACAC ACC CUGCUGGAAUUGUGAAGGCC GCUCUGAGCUGAAGC GA GAGAAAGGC AAUUAAC CCUGCCUGUCUAGAGAGGAGCC AAGGDUGGU AUUUGUCAGAAC GC CG CAGCACCGUUGAUC AC CUUAGC GAGAAAGC ACUGC GAGACAGAGGC GAC CAGSUGUUGUGUA UACCGCCCGUGGAAUC AAUGUGGC C GAGCAGAGC AAAGAGUGCAAC AUC CAGC AUCAGCAGCCAGC AACUAUC CUGC AAGGUGUCAG GGGC ABECAACC U AUUUCU AUGGUGGC UCUGUC UC CUCUG GGAGCCUCUGUGGCUUGUUAU AAGGGC GUGUCUUGAUC AUCAGC AGC AACAGAGUGGC AU CAUCAGCAGCUGAAGC AAGGUGUC GACAGCUAC AUC ACCAACAGGAC GCGAU ACCGUGAACC AUC GACAC AC CUGU AUCAGCUGAGC AAGCUGGAAAGGS GANCAGCAGCUGAUC AAGGGC AGACCU GUGUCCAGCAGCUC GACCCU AUC AAGUUC CUGAGAAC CAGUUC AGGUGGCC CUGGAC CAG GUGAUCGAGAAC AUC GAGAAUUC CAGGCUUGGUGGAC CAGUCCAGCAGAAUUCUUGUAGC GGCAGAAAGGAAAC ACCGGCUC AUC AUGUGAUC AUC CUGAUC GC CUGUCUGGCGAGC UCC AUGNUCUGUGUC AUCUUC AUC AUU AUC AAGAAAGC CAGAAAGCC ACCGGC GCUCCUC A GACUGAGC GAGUGAC CAACAUGGUCUUC AUCCUC AC AAC</p>	<p>134</p>
<p>35 HMPV_SC_SUabilizeAlpha _U74L</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>AUGAGUCUGGAAAGGUGGUC AUC AUC UUC AGCCUGCUGAUC ACACUUCAGC AC GGC CU GAAAGAG AGCUACCUUGGAAAGAGUC CUGCAGCAGC AUCACAGAGGGCUACCUUGUC UGUUCUGAGAAACGGC UGGUACACCAAC GUGUUCACACUUC CUGGGGGGACGUUCAGAAUCUGAC AUGCUCUGAGUGGC CCUAGCCUGAUC AAGACCGAGCUGGUAUC UGCUCAAGAGC CC CUUGAGAGAACUC AAGACCGUG UCUGCCCAUCAGCUGGGCC AGAGAGGAAAC AGAUCGAGAAUC CUGGCAGCGGC AGCUUUUUGUCUG GGACCAUUGUCUUGUGAGUUGGUCUGUCUC AGCUUUAACAGCAGGC GUGGC AUC GCUAA GACCAUCAGACUGGAAAGC GAAGUGACCGCC AUC AAC AAC GC CCUGAAGAGAAACA AAGCAGGCC GUCAGCAC ACUCGGC AAGUGGCUUAGAGUGGUGGC ACAGCCGUGGC GUGAGUGAAGGAC UU CGUGUCAGAAAC CUGACACGGCC AUUUAAC AAGAAC AAGUGGCAC AUCGAC GAC CUGAAGAGUG GGCGAGUC UUAAGCC AGUUCAGCCGGC GGUUUCUGAAGGUC GUGCGGC AGU UUAAGCAGCAAC GGCGAAUCACAC CAGCC AUCAGCCUGGACCUUGAU GACAGAGUCUGAGC UGGCUAGAGCCGUG CCUAGCAGCCUC AUCUGCCGGCC AGAUCAGC UGAGUUCUC GAGAAUAGAGCC AUGGUCGAG CGGAAAGCC UUGGCAUUCUGAUGGC GUUGACGGCAGCAGC GUGAUCUUAUGGUGCAGC U GCUAUUCUGGC GUGAUC GACAC ACC CUGCUGGAAUUGUGAAGGCC GCUCUGAGCUGAAGC GA GAGAAAGGC AAUUAAC CCUGCCUGUCUAGAGAGGAGCC AAGGDUGGU AUUUGUCAGAAC GC CG CAGCACCGUUGAUC AC CUUAGC GAGAAAGC ACUGC GAGACAGAGGC GAC CAGSUGUUGUGUA UACCGCCCGUGGAAUC AAUGUGGC C GAGCAGAGC AAAGAGUGCAAC AUC CAGC AUCAGCAGCCAGC AACUAUC CUGC AAGGUGUCAG GGGC ABECAACC U AUUUCU AUGGUGGC UCUGUC UC CUCUG GGAGCCUCUGUGGCUUGUUAU AAGGGC GUGUCUUGAUC AUCAGC AGC AACAGAGUGGC AU CAUCAGCAGCUGAAGC AAGGUGUC GACAGCUAC AUC ACCAACAGGAC GCGAU ACCGUGAACC AUC GACAC AC CUGU AUCAGCUGAGC AAGCUGGAAAGGS GANCAGCAGCUGAUC AAGGGC AGACCU GUGUCCAGCAGCUC GACCCU AUC AAGUUC CUGAGAAC CAGUUC AGGUGGCC CUGGAC CAG GUGAUCGAGAAC AUC GAGAAUUC CAGGCUUGGUGGAC CAGUCCAGCAGAAUUCUUGUAGC GGCAGAAAGGAAAC ACCGGCUC AUC AUGUGAUC AUC CUGAUC GC CUGUCUGGCGAGC UCC AUGNUCUGUGUC AUCUUC AUC AUU AUC AAGAAAGC CAGAAAGCC ACCGGC GCUCCUC A GACUGAGC GAGUGAC CAACAUGGUCUUC AUCCUC AC AAC</p>	<p>135</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
5 10 15 20 25	<p>UCUGCCGAUCAGCUGGCGCAGAGAGGAAACAGNUGCAGAAUCCUCUGGCAGCGCCAGCUGUUSUGCUG GGAGCCAUUGUCUUCUUGGAGUUGUCUGCUGCUGCAGCUGUUAACAGCAGGCGUGGCGCAUCUCUAA GACCAUCAGACUUGGAAAGCGAAGUGACCGCCAUCAACAGCAGCCUUGAAGAGAGACAACAGAGCC GUCAGCACACUCGCGCAUGGCGUUAAGAGUGCUGGCACAGCCGUGCGCGAGGCUUGAAGGACUU CUGUCCCAAGAACUCAGACAGCGGCGCAUUAACAGAACAGUUGCGACAUCCAGACAGCUGAAGAGU GCCUGUCCUUAAGCCAGUUCAGCCGCGGUGUUCUGAAGCUCGUGCGCGCAGUUAAGCGACAGC GCCGGAAUCACACAGCCAUAGCCUUGAGCCUGAUAGACAGAGUCUGAGCCUUGCUAGAGCCUGG CCUAGCUGCCUACAUUCUGCCGCGCCAGALCAAGGUGAUGCUCGAGAAUAGAGCCAGUGUCGGA CGGAAAGCCUUCGCGCAUUCUGAUGGCGGUGUACGCGCAGCAGCGUGAUCUUAUGGUGCAGCCU GCCUUAUCUUCGCGCGUGAUCGACACAGCCUGCGUUGAAGUUGAAGGCGCCGCUUCUAGCUGUAGCGA GAGAAAGCGCAAUUACCGCUGCCUGCUGAGAGAGGAGCCAGGCGUGGUGUUAUGCAGAGCCCGG CAGCACCGUGUACUACCCUACAGAAAGGAGCUGCGAGACAGAGGCGGACACAGUUGUCUGUGA UACCGCCGCGUGGAUUAUUGUGGCGGAGCAGAGCAAGAGUUGCAACAUCAACAGCAGCAGCAGC ACUUAUCUGCGAAGGUGUCCAGCGCGAGCCAGCCUUAUUCUUAUGGUGGCGUCUGUCUCUGUG GGAGCCUGUGUGGUGUUAUAGGCGCGUGUCCUGAGCAUCGCGAGCAACAGAGUUGGCGAU CAUCAGCAGCUGAAGAGGCGUGAGCUCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GACACACCGUGUAGCUGAGCAGGUGGAGGCGGAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GUGUCCAGCAGCUGCAGCCUUAUCAGAGUUCUGAGGAGCAGUUCAGUUCAGGCGCGCGCGCCUGG GUGUUCAGAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GCCGAGAAAGGAGAACAGCGCGUUCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC AUGUUCUGUGUCCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GAGCUGAGCGAGAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC</p>	
30 35 40 45 50 55	<p>HMPV_SC_SUabilizeAlpha_V55L AUGAGCUGGAGGUGUGUCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC AGC UGGAGC CCUGGCGUGAUCAGGAGCGAGCUGGAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC UCUGCCGAUCAGCUGGCGCAGAGAGGAAACAGNUGCAGAAUCCUCUGGCAGCGCCAGCUGUUSUGCUG GGAGCCAUUGUCUUCUUGGAGUUGUCUGCUGCUGCAGCUGUUAACAGCAGGCGUGGCGCAUCUCUAA GACCAUCAGACUUGGAAAGCGAAGUGACCGCCAUCAACAGCAGCCUUGAAGAGAGACAACAGAGCC GUCAGCACACUCGCGCAUGGCGUUAAGAGUGCUGGCACAGCCGUGCGCGAGGCUUGAAGGACUU CUGUCCCAAGAACUCAGACAGCGGCGCAUUAACAGAACAGUUGCGACAUCCAGACAGCUGAAGAGU GCCUGUCCUUAAGCCAGUUCAGCCGCGGUGUUCUGAAGCUCGUGCGCGCAGUUAAGCGACAGC GCCGGAAUCACACAGCCAUAGCCUUGAGCCUGAUAGACAGAGUCUGAGCCUUGCUAGAGCCUGG CCUAGCUGCCUACAUUCUGCCGCGCCAGALCAAGGUGAUGCUCGAGAAUAGAGCCAGUGUCGGA CGGAAAGCCUUCGCGCAUUCUGAUGGCGGUGUACGCGCAGCAGCGUGAUCUUAUGGUGCAGCCU GCCUUAUCUUCGCGCGUGAUCGACACAGCCUGCGUUGAAGUUGAAGGCGCCGCUUCUAGCUGUAGCGA GAGAAAGCGCAAUUACCGCUGCCUGCUGAGAGAGGAGCCAGGCGUGGUGUUAUGCAGAGCCCGG CAGCACCGUGUACUACCCUACAGAAAGGAGCUGCGAGACAGAGGCGGACACAGUUGUCUGUGA UACCGCCGCGUGGAUUAUUGUGGCGGAGCAGAGCAAGAGUUGCAACAUCAACAGCAGCAGCAGC ACUUAUCUGCGAAGGUGUCCAGCGCGAGCCAGCCUUAUUCUUAUGGUGGCGUCUGUCUCUGUG GGAGCCUGUGUGGUGUUAUAGGCGCGUGUCCUGAGCAUCGCGAGCAACAGAGUUGGCGAU CAUCAGCAGCUGAAGAGGCGUGAGCUCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GACACACCGUGUAGCUGAGCAGGUGGAGGCGGAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GUGUCCAGCAGCUGCAGCCUUAUCAGAGUUCUGAGGAGCAGUUCAGUUCAGGCGCGCGCGCCUGG GUGUUCAGAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GCCGAGAAAGGAGAACAGCGCGUUCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC AUGUUCUGUGUCCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC GAGCUGAGCGAGAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC</p>	136

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Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>HMPV_SC_SUabilizeAlpha_S170L</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>AUGAGGUGGGAAGGGUGUC AUC AUC UUC AGCCUUGUGAUC ACACCUUC AGC AC GGC CU GAAGAG AGCUACDUAGGAGAGUUCUGCAGCAGC AUCACAGAGGGCUACCUUGUC UGUUCUGAGAACGGGC UGGUACACC AAC GUGUUC AC ACU GGAAGUGGGGC GAC GUC GAGANUCUGAC AUGGUCUGAGUGGC CUAGGCUUGAUCAGAACCCGAGCUGGAUCUGACC AAGAGCGCCUUGAGAGAACUC AAGACCGUG UCUGCCCAUCAGCU GGGC AGAGAGG AAC AGAUCGAGAAUC CUGGC AGCGGC AGC UUU GU GUG GGAGCCAUUGUC UUGGAGUGGCUUGGUCUC ACUCUGUAC AGC AGGC GUGGC CAUC GCUAA GACCAUCAGACU GGAAGAGC GAGUGACCGCC AU C AAC AAC GC CCUGAAGAGACA AAC GAGGCC GUCAGCAC ACUCGGC AUGGGGCUUAGAGUGGUGGC AC AGCC GUVGC GC GAGCUGAAGGAC UUU CGUCGUAAAG AAC CU GACACGGGCT AUU AAC AAG AAC AAGUGGCAC AUC GAC GAC CUGGAAAGUG GC CUGUC CUU AGCC AGUUC AAC GGG GGUUUCUGAACGUC GUGCGGC AGU UUAAGCGAC AAC GC CGG AUC AC AC CAGCC AUC AGGCUUGAGCCUGAU GAC AG AUGGUGAGGC UGGCUAGAGCC GUG GCUAACAUCC CU AC AU CUGCC GGGC AGAUC AAGG U GAUGCUC GAGAAUAGAGCC AUGGUCGAA GGGAAAGGC UUCGGC AU UCUGAUUGGC GU GU AC GGC AGC AGC GU GAUCU AU AUGGUGCAGCU GC CUGUCUGGCG GUGAUC GAC AC ACC CU GC UGGAUU GUGAAGGCC GC UC CU AGCU GUGAGC GA GAGAAAGGGC AUU UAC GC CUGCCU GCU GAGAGAGGACT AAGGCUUGGU AUU GUC AGAAC GCC GG CAGCACCUGU GUAUC ACCU AAC GAGAAAGGAC UGC GAGAC AAGAGGC GAC C AC GUGUU CUUGA UACCGCCGC UGGAAUC AUUGUGGC CGAGCAGAGC AAGAGUGGC AAC AUC AAC AUC AGC ACC ACC AUCUUC CUGC AAGGUGUC CAC GGGC AGGC ACC U AUUUC U AUGGU GGC UCUGUC UC CU CUG GGAGCCCU GUGGGCUUGU AU AAGGCGGUGU CUU GU AGC AUGGGC AGC AAC AGAGUGGGC AU CAUCAGC AGCU GAAC AAGGCU GC AGCUAC AUC ACC AAC AGGAC GCGAU ACC GUGACC AUC GACAC AC CGUGU AUC AGC UGAGC AAGGUGGAGGGC GANCAGC AC GU GAUC AAGGGC AGCCU GUGUCCAGC AGCUUC GACCCU AUC AAGUUCU CUGAGG AUC AGUUC AAGUGGCC CUGGACC AG GUGUUCGAGAAC AUC GAGAAUUCGAGGUCUGGUGGAC AGUCCAC AGAAUCC UGUUAGC GCCGAGAGGGAAAC ACCGGCUUC AU C AUCGUGAUC AUC CUGAUC GCG GUGGUGG CAGC UCC AUGAUUCUGGUGCC AUCUUC AUC AUU AUC AAGAAAC CAAGAA GCCC ACC GGC GCUCCUC CA GACUAGC GAGUGGAC C AAC AUUGGCUUC AUCC UUC AAC</p>	<p>137</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>HMPV_SC_SUabilizeAlpha_U174 W</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>AUGAGCUUGGAAAGGUGGUC AUC AUC UUC AGCCUGGUGAUC AC ACC UC AGC AC GGC CU GAAAGAG AGCUACCUUGGAAAGAGUC CUGC AGC AC C AUC AC AGAGGGCU ACC UGUC UGU GCU GAGAACCGGC UGLWACAC AAC GUGUUC AC ACU GGAAGUGGGCGAC GU C GAGANUCUGAC AUGC UC US AUGGC CCUNGGCUG AUC AAG ACC GAGC US SAUC UG ACC AAGAGC GDC CUG AGAGAAACUC AAG ACC GUG UCUGCCAU CAGCU GGGC AGAGAGGAAAC AGAUCGAGAAUC CUGGC AGCGGC AGC UUU G U GCU G GGACCAUUGCUC UUGGAGU G GCU GCU GCU GC AGCUGUJAC AGC AGG GUGGGC AUC GCUAA GACCAUC AGACH GGAAGCG GAA GUGACC GGC AUC AAC AAC GGC CU GAA GAGACA AAC GAGGGC GUCAGCAC ACUC GGC ANUGGCGUJAGABU GCU GGC AC AGC C GUGGC GC GAGCUGAAGGAC UU GUGUJCAAGAAC CU GUGGC GGGC AU U AAC AAGAAC AAGUGCGAC AUC GAC GAC UGAAGAU GGCCGUGU CCUJAGCC AGUUC ACC GGC GGUUUCUGAAC GUC GUGC GGC AGU UVA GCGACA ACGCCGAAUC AC ACC AGC C AUC AGCCUGGACC U G AUG ACAG AUGG UGAGCUGGC UAGAGCGG UGCCUAC AUGGC UAC AUCUGGC GGC CAGAUCAAGCUG AUGCUGAGAAUAGAGCC AUGGUC C GACCGAAGGCUUCGGC AUUCUGA UUGGC GUGUAC GGC AGC AGC GUGAUCU AU AUGGUGC AG CUGCCUACUUC GGC GUGAUC GAC AC ACC U GCU G A U U GUGAAGGC GCUCCUACGUGU AAG GAGAG AAGGGC AU U AC GC CUGC CU GUGGAGAGAGGACC AAGGC UG GU AUUGUC AGAAC GGC GGCAGCAC CUGUAC UAC CCUJAC GAG AAGGACU GCGAGAC AAGAGGC GACAC CU G UUCUGU GALNCGCC CUGUGA AUC A AUGUGGC GAGC AGAGC AAGAGUCC AAC AUC AAC AUC AGC ACC A CCANC AUCC U GC AAGGUGUC ACC GGC AGC AC CCU AUUUCU AU GGU GUC UC UGUC UC CUC UGGGAGC CC UGUGGCUUGU AU AAGGGC GUGUCC UGUJAGC AUG GGC AGC AAC AGAGUGGC AUCAUCAAGCAGC UG AAC AAGGGC UGC AGCUC AUC AC CAAGC AGGAC GCGAUAC CUGUAC CA UCGACAC ACC G UGU AUC AGCUGAGC AAGGUGGAAAGGC G AAC AGC AC GUGAUC AAGGGC AGAC CU GUGUCC AGC AGCU UC GAC CCU AUC AAGUUC CU GAGG AUC AGUUC AGGUGGC CC U GAGC AGGUGUC GAGAAC AUC GAGAAUUC CC AGGCUUCUGGUGGAC AGUC C AAC AGAAUC UGCUJA GGCCGAG AAGG GAAAC AC CGCCUUC AUC AUC GUG AUC AUCCUGAUC GGC GUGCUGGGG AGC U CC AUNGC UGUGUUC AUUCUAC AUC AUU AUC AAGAGAC AAGAGGCC AC GGGC GCUCC UC CAGACUGAGCC GAGU GACC AAC AUUGGCUACUC CC UC AC A AC</p>	<p>138</p>
<p>35</p> <p>HMPV_SC_4M_SUabilizeAl pha_V55LU74LS170LU174 W</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>AUGAGCUUGGAAAGGUGGUC AUC AUC UUC AGCCUGGUGAUC AC ACC UC AGC AC GGC CU GAAAGAG AGCUACCUUGGAAAGAGUC CUGC AGC AC C AUC AC AGAGGGCU ACC UGUC UGU GCU GAGAACCGGC UGLWACAC AAC GUGUUC AC ACU GGAAGUGGGCGAC CU C GAGANUCUGAC AUGC UC US AUGGC CCUNGGCUG AUC AAG ACC GAGC US SAUC UG ACC AAGAGC GDC CUG AGAGAAACUC AAG ACC GUG UCUGCCAU CAGCU GGGC AGAGAGGAAAC AGAUCGAGAAUC CUGGC AGCGGC AGC UUU G U GCU G GGACCAUUGCUC UUGGAGU G GCU GCU GCU GC AGCUGUJAC AGC AGG GUGGGC AUC GCUAA GACCAUC AGACH GGAAGCG GAA GUGACC GGC AUC AAC AAC GGC CU GAA GAGACA AAC GAGGGC GUCAGCAC ACUC GGC ANUGGCGUJAGABU GCU GGC AC AGC C GUGGC GC GAGCUGAAGGAC UU GUGUJCAAGAAC CU GUGGC GGGC AU U AAC AAGAAC AAGUGCGAC AUC GAC GAC UGAAGAU GGCCGUGU CCUJAGCC AGUUC ACC GGC GGUUUCUGAAC GUC GUGC GGC AGU UVA GCGACA ACGCCGAAUC AC ACC AGC C AUC AGCCUGGACC U G AUG ACAG AUGG UGAGCUGGC UAGAGCGG UGCCUAC AUGGC UAC AUCUGGC GGC CAGAUCAAGCUG AUGCUGAGAAUAGAGCC AUGGUC C GACCGAAGGCUUCGGC AUUCUGA UUGGC GUGUAC GGC AGC AGC GUGAUCU AU AUGGUGC AG CUGCCUACUUC GGC GUGAUC GAC AC ACC U GCU G A U U GUGAAGGC GCUCCUACGUGU AAG GAGAG AAGGGC AU U AC GC CUGC CU GUGGAGAGAGGACC AAGGC UG GU AUUGUC AGAAC GGC GGCAGCAC CUGUAC UAC CCUJAC GAG AAGGACU GCGAGAC AAGAGGC GACAC CU G UUCUGU</p>	<p>139</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
5	<p>GAAGCCCTCCUGGAAATCAATGUGGCTCAGCAGAGCAAAAAGUGCAACAUCAACAUCAAGCACC CCACUACUC UGC AAGGUUUKCACCCAGAGCACACUUAUUCUAUAGUUGGCUUGUUCUCUC UGGGAGCTCCUGGUGGCUUGUUUAUAGGGGCCGUGUCCUUBUAGCAUCGACAGCACAGAGUUGGGC AUCAUCAAGCAGCUGAACAAAGGGCUGCAGCUACAUACCCACACAGGACGCCGAAUCACCGUACCA UCACACACACCUGUUAUCAGCUGAGC AAGGUGGGAAGGGCAACAGCACGUBAUC AAGGGCAGAC CUUUGUCCAGCACGCUUCGACCCUAUCAGGUUCUGUAGGGAUCAGUUCAGGUGGCCUGUGACC AGCUGUUCGAGAACAUCCAGAAUUCGCCAGGUCUGGUGGAGCCAGUCAGAAUCCUGCUA GCGCCGAAAGGGAACACC GGUUGUUC AUCAUCUGAUC AUCCUGAUCGCCUGGUGGGCAGU CCAUGAUCUGGUGUCCAUUUC AUUUAUCAAGAAAGCACAGGAGGCCACCGGCGCUUCUCCUC CACACUUGACGGAGUACACAAUGGCUUUAUCUCCUCACAC</p>	
10		
15		
15	<p>HMPV_ProlineSUab_E51P</p>	140
20	<p>AUGAGUUGGGAAGGUUGGUCUUCUUCAGCCUGGUGAUACACCCUCAGCACGGCCUGAAGAG AGCUUCUUGAAGAGUUCUUCAGCACCAUCACAGAGGCUAGGCUUAGUUCUGAGACCCGGC UGGUACACCAGCUGUUCACACUCUGGUGGGGACGUGGAGAAUUGGAGAGGUGUUGAGUUGGC CCUGAGGUAUCAGGACGCCAGAGGUAUCUGACCAGAGAGCCGUGGAGAGUUCAGGAGCAGG UCUGCCCAUCAGCUUGGCCAGGAGGAAACAGUUGGAGAAUCCUGGCGAGCGAGCUGUUGG GAGCCAUUUGUCUUGAGUUGGCUUCUCUUCACACUCUUCUUCACAGGCGUGGCGAUCUCUAA GACCAUCAGACUGGAGAGGCAAGUGAACGCCAUCAGCAGCAGCCUGAAGAGAGACAAGAGGACC GUCAGCACUCGCAUGGCGUUAAGAGUGGUGGCCACAGCCUGUCCGAGGUGAGAGGACUU GGUUCCAGAGAACUUCACACAGCGCCAUUAACAGAGAACAGUUCGCAACUUCAGCUGAGAGU GCUUGUCCUUAAGCCAGUUCAGCCGGGAGUUCUUGAAGCAGCUCUGGCAGAGUUAAGGAGAAC GCGGUAUCACACAGCCAUAGCCUUGAGCCUUAUAGAGAGUUCUGAGCUGAGAGCUGG CCUAACUUGCCUUCAGUCCCGCCAGAUCAAGUGUUCUGAGAGAAUAGAGCCAGGUCUGA GGAAGAGCUGCGCAGUUCAGUUGGCGUUAUCAGGAGCAACUGUUCUUAUGGUGCAGCUG CCTUUCUUGCCGUGAUUCAGCACACCCUGGUGGAAUUGGAAAGGCCGCUUCUAGCUUGAAGC GAGAGAGGCAAUUAACGCUUGCCUGCUGABAGAGGACC AAGGCUUGUUAUUUCAGAACGCCGG CAGCCCGUUGACUACCCUAAAGGAGAGAGCCAGAGAAAGAGGACAGCAGCUGUUGGUGA UACCGCCCGUGGAAUC AAGUGGCGGAGCACAGCAAGAGAGUGCAACUACACAUAGCACCCAC AUCUACCCUGGCAAGGUGUACAGCGGCAGGCAAGCAAGAGAGUGCAACUACACAUAGCACCCAC AUCUACCCUGGCAAGGUGUUAUAGGGCCGUGUCCUGAAGAGGAGCCAGCAAGAGAGGAGGCU CAUCAGCACAGCUAGAACAGGGCCUGAGCUCUACACCAACAGGAGGCCGCAUCACCGUAGCC GACACACCGUUAUCAGCUGAGCAGAGUUGAGGCAAGGAGCACAGCACGUGAUCAGGAGAGGCU GUGUCCAGCACGUCAGCCUUAUCAGGUUCUGAGGAGUUCAGUUCAGGUUGGCCUGGAGCCAG GUGUUCGAGAACAUCCAGAAUUCAGGCCUCUGGUGGAGCACAGUCCACAGAAUCCUGUAGC GCGAAGAGGAAACACC GGCUCUUAUCAGUUGAUCAUCUUGAUCCGUGCUUGGCGAGCUC AUGAUCUGUGUCCAUUCUUCAUUAUCAGAAAGCACAGGAGGCCACCGGCGCUUCUCCAG GACUAGCGGAGUAGCACAAUGGGUUCUCUCUACAC</p>	
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(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>HMPV_ProlineSUab_D185 P</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>AUGAGCUUGGAAAGGUGGUC AUC AUC UUC AGCCUGGUGAUC AC ACCUC AGC AGG GGCUGAAAGAG</p> <p>AGC UAC UUG GAAG AGUC CUG C AGC AC C AUC AC AG AG GGC UAC C UG UC U GUC UG AG A NC C GGC</p> <p>UGG UAC ACC AAC GUG UUC AC ACU GAAAGUGGGCCGAC GUC GAG AUUCUGAC AUGC UC UG AUGGC</p> <p>CCUAGCCUG AUCAAG ACC GAGC UG GAUC UG ACC AAG AGC GGC CUG AG AG A NC UC AAG ACC GUG</p> <p>UCUGCCG AUC AGCU GGC AGAGAGG AAC AGAUC GAG A AUC CUGGC AGC GGC AGC UUU G U G CUG</p> <p>GGACCAUUGCUC UUG GAAGUG GCUUGCUGUC GC AGCU GUA AC AGC AGGC GUG GC AUC GCU AA</p> <p>GACC AUC AGACH GAAAGC GAAGUG ACC GGC AUC AAC AAC GC CCUGAAGAGAC AAC GAGGCC</p> <p>GUC AGC AC ACUC GGC AUUGG GCUU AGAGUG CUG GC AC AGCC GUG GC GAG CUG AAGG AC UU</p> <p>CGUGUC AAG AAC CU G AC AC GGC C AUU AAC AAG AAC AAGUG GC AC AUCCUG AC CUG AAG AU G</p> <p>GCUGAGUC UUAAGCC AGUUC AAC GGC GGUUUCUG AAGC UC GUGC GGC AGU UU A GC GAC AAC</p> <p>GC CGG AUC AC AC CAGCC AUC AGCCUG GAGCCUG AU GAC AG AUGCUG AGC U GGCU A GAGCC GUG</p> <p>CCUAC AU GC CU AC AU CUG C GGC C AGAUC AAGC U GAU GC UC GAG AAU AGAG CC AUGGUC GA</p> <p>CGG AAG GC UUG GC AU UCUG AUUGGC GU GU AC GGC AGC AGC GUG AUC UAU AUGGUC AGC U</p> <p>GC UAU CUC GGC GUG AUC GAC AC ACC CUG CUG AUUGUG AAGGCC CCUCU AGC UGUA GC GA</p> <p>GAG AAG GGC AAU U AC GC CUG CCU GCU GAGAG AGG ACC AAG GCU GGU AUU GUC AG AAC GC C GG</p> <p>CAGC ACC GUG A CU AC CCU AAC G AAGAG GAC UGC GAG AC AAG AG GC GAC AC G UG UU CUGUGA</p> <p>UACCGCC GUGG AAUC AAUGUGGC CGAGC AGAGC AAGAGUGC AAC AUC AAC AUC AGC ACC ACC</p> <p>AAC UUC CUGC AAGGUGUC AC GGC A GGC AC CC U AUU UC U AUGGU GGC UCUGUC UC CU CUG</p> <p>GGACCCUG GUGG CUGUU AU AAGG CCGGU CCUGU AGC AUGGC AGC AAC AAGUGGC AU</p> <p>CAU AAGC AGCU GAAC AAGG CUG GC AGCU AC AUC ACC AAC AGC AC GCG AU ACC GUG ACC AUC</p> <p>GAC AAC AC CGUGU AUC AGC UGAGC AAGGUGG AAGGC GAGC AGC AC GU GAUC AAGGGC AGCCU</p> <p>GUGGCCAGC AGCUUC GACCCU AUC AAGUUC CUG AAG AUC AGUUC CAGUUC CAGUUGGC CUGG ACC AG</p> <p>GUGUUC GAGANC AUC GAGANUCC CAGGCUCUGGUGGAC C AGUCC AAC AGAAUC U GUCUAGC</p> <p>GC GAG AAG GGAAC ACC GGCUC AUC AUUGUGAU C AUC CUGAUC GC C GUGCUUGG CAGC UCC</p> <p>AUGAUCCUGUGUC AUCUUC AUC AUU AUC AAG AAGAC CAAG AAGCC CACCGGC CCUCUC GA</p> <p>GACUAGC GAGUGAC C AAC AUGGCUC ACC CU C AC AAC</p>	<p>141</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>	<p>HMPV_Proline SUab_D183 P</p> <p>AUGAGUUGGAGGUGGUC AUC AUC UUC AGCCUCUGAUC ACCUCAGC AC GGC CU GAAGAG AGCUNCUUGGAGAGUC CUGCAGC AC C AUC ACAGAGGGCUACCUUGU UGUUCUGAGAACCGGC UGGUAACAC AAC GUGUUC AC ACU GGAAGUGGGCGAC GUC GAGAAUCUGAC AUGUCUUGAUGGC CCUNGGUCUGAUC AAGACCGAGCUGGUAUC UGACCAAGAGC GGC CUGAGAGAACUC AAGACCGUG UUCGUCACUCAGCUGGGCC AGAGAGGAAAC AGAUCGAGAAUC CUGGC AGCGGC AGC UUU GUUG GGACCAUUGUC UUGGAGUUGGUCUGUCUC GC AGCUUUAAC AGC AGGC GUGGC AUC GCUAA GACCAUC AGACU GGAAGC GAAGUGACCGCC AUC AAC AAC GC CCUGAAGAGAC AAC GAGGCC GUCAGC ACUC GGC AUUGGUCUUAAGAGUGGUGGC AC AGCC GUGGC GUGAGUGAAGGAC UU CGUCUCAGAGAC CU GAC AC GGGCC AUUAAC AAGAAC AAGU GGC UAUUGAC GAC CUGAAGAGU GGCGAGUC UUAUGCC AGUUC AAC GGC GGUUUCUGAAGUC UUGCGGC AGU UUAUC GAC AAC GGCGAUC ACAC CAGCC AUC AGCCUGGACCUU GAC AGAUGCUG AGC UGGCUGAGAGCC GUG CCUNAGUCUC AC AUCUGCCGGCC AGAUC AAG UGUAUCUC GAGAAUAGAGCC AUGGUCGGA CGGAAGGC UUGGC AUUCUGAUGGC GUUG AC GGC AGC AGC GUGAUCU AU AUGGUGCAGC U GCCUNUCUC GGC GUGAUC GAC AC ACC CUGCUGG AUUGUGAAGGCC CCUCUAGC UGUAAGC GA GAGAAAGGC AUU UAC GCUUGCCUGCUGAGAGAGGACT AAGGCUUGGU AUU GUC AGAC GGC GG CAGCACCGUUGAUC CCU AAC GAGAAAGGACUGC GAGAC AAGAGGC GAC CAC GUGUUCUGUGA UACCGCCGUGGAAUC AAUUGGCGGAGC AGAGC AAGAGUGCAAC AUC CAC AUC AUC ACC ACC AACUUC CUGC AAGGUGUC CAG GGC AAGC ACC U AUUCU AUGGU GGC UCUGUC UC CUUG GGAGCCUGGUGGUCUGUUAU AAGGCGGUGUCUUGAUC AUGGC AGC AAC AGAGUGGC AU CAUCAGC AGC U GAA C AAGGUC UC AGCUAC AUC ACC AAC AGGAC GCGCAU AUC GUG ACC AUC GACAC ACUGU AUU AGCUGAGC AAGGUGGAGGC GACAGC AGC GUAUC AAGGC AGACCU GUGUCCAGC AGCUC GACCU AUC AAGUUC CUGAGG AUC AGLUCC AGGUGGCCUGGAGC AG GUGUCCAGAAC AUC GAGAAUUC CAGGCUUGGUGGAC CAGUCCAC AGAAUUC UGUUAGC GCCGAGAGGGAAC ACCGGCUC AUC AUGUGAUC AUC CUGAUC GCGUGGUGGACAGC UCC AUGUUCUGGUGCC AUC UUC AUC AUU AUC AAGAGAC CAGAGGCC AC GGC GCUCUC CA GACUGAGC GAGUGAC C AAC AUUGGUC AUC CUC AC AAC</p>	<p>142</p>

(continued)

Strain	Nucleic Acid Sequence	SEQ ID NO:
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Strain	Nucleic Acid Sequence	SEQ ID NO:
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<p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>	<p>HMPV_Urimer RepulsionD4 54N</p> <p>AUGAGCUGG AAGGUGGU C AUC AUCUUC AGCC UGCU GAUC AC ACCUC AGC AC GGC CU GAAGAG AGCUAC CUGS AAGAGUC CUGC AGC AC C AUC AC AGAGGG CU ACCUGUC U GUGCUG A GANCC GGC UGBLNCACC AAC G UBUUC AC ACU GBAABUGGGCGAC GUC GAGANUCIGAC AUGGC UC UAUGGC CCUAGCCUGAUC AAGACC GAGC UGGAUC UGACC AAGAGC GCC CUGAGAGAAC UC AAGACC GUG UCUGCCBAUC AGCU GGGC AGAGAGG AAC AGAUC GAGAAUC CUGGC AGC GGC ACD UUU S U GCU G GGACC AUUGUC UUU G SAGU G GCU UGCU GCU GC AGC UGUUAC AGC AGGC GUGGC C AUC GCJAA GACC AUC AGACU GBAAGC GAAG UGACC GCC AUC AAC AAC GCC CU GBAAGAGACA AAG GAGGCC GUCAGCAC ACUC GGC AAUGGCGUWAGABU GCU GGC C AC AGC C GUC GC GAG CU GAAGG AC UU CGUGLCCAAG AAC CU GAC AC GGG CC AUVAAC AAGAAC AAGU GGC AC AUC GAC GAC CUGAGAGU G GCGUGUCC UUAAGCC AGUUC AAC GGC GBUUUCUGAAGS UC GUGCGGC AGU UUAAGC GAC AAC GCGGAAUC ACAC GAGCC AUC AGCCU GBAACCU GAU GAC AGAUGCU GAGC UGGCU A GAGCC C GUG CCUANC AUGC CU AC AUCUGC C GGC AGAUC AAGC U G AUGC UC GAG AAU AGAGCC AUGGUC CGA GGGAA GGC UJOGGC AU UCUG AUUGGC S U GU AC GGC AGC AGC GUGAUC UAU AUGGUC AGC U GCUUUCUUC GGC GUGAUC GAC AC ACC CU GC UGG AUU S UG AAGGCC GC UC CU AGC UGUAGC SA GAGAA GGGC AAU U AC GC CUGCC U GCU GAGAGAGG ACC AAGGCU GGU AUU GUC AGAAC GC C GG GAGC CCG UGUACU AC CCU AAC GAGAA GGC UGC GAGAC AAGAGGC GAC C AC G UBUU CUGUGA UACCGCC G UGAAUC AAUUGGC C GAGC AGAGC AAGAGU GC AAC AUC AAC AUC AGC ACC ACC AACUUC CUGG AAGGUGUC AC GGGC A GGC AC CC U AUULC U AUGGU GGC UCUGUC UC CU CUG GGACCCU GUGGGUUGU AU AAGGCG GUGU CCU GUA GC AUC GGC AGC AAC AGAUGGGC AU G AUCAGC AGCU GAAD AAGGGCU GC AGCU AC AUC ACC AAC AGG AC GCG AU ACC GUGACC AUC GACAC ACUGU AU AUC AGC UGAGC AAGGUGG AAGGC GACAGC AC GU GAUC AAGGGC AGACCU GUGLCCAGC AGCUUC G ACCU AUC AAGUUC CUGAGG AUCAGUUC C AGGU GGC CUUGS ACC AG GUGLUCGAGAAC AUC GAGAUUC C AGGUC UGGUGGAC C AGUC CAAC AGAAUCC UGUUAGC GCGGAAAG GGAAC ACC GGC UUC AUC AUCUGAU C AUC CUGAUC GC C GUGCU GGGC AGC UCC AUGAUCUGUGUC AUC UUC AUC AUU AUC AAGAA GAC C AAGAA GGC AC GGC GC UCC UC CA GACU S AGC GAGUG AC C AAC AAUGGCUUC AUCC CUC AC AAC</p>	<p>145</p>

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Strain	Nucleic Acid Sequence	SEQ ID NO:
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Strain	Nucleic Acid Sequence	SEQ ID NO:
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SEQUENCE LISTING

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<140> To be assigned

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 ttggtagatt gctaaaaagg gtttagctgc tggactggca gtaatcaggt tggaaatac 1200
 aacaaactac ctaaaagctg ctcatcata atcaaacagq acgcagacac tgtacaatt 1260
 gacaaactg tgtatcaact aagcaaatgt gagggtgaaq agratgtat aaaaaggaga 1320
 ccagtttcaa gaagttttga tcaaatcaag tttcctgagg atcagttcaa tgttgogctt 1380
 45 gatcaagtct ttgaaagcat tgaaaacagt caagcactag tggaccagtc aacaaaaatt 1440
 ctgaaacagt cagaaaaaag aacactggt ttcaattatg taataatctt gattgctgct 1500
 cttgggttaa caatgattc agtgaacata atcatcata tcaaaaaaaq aaggaagccc 1560
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<210> 4

<211> 1725

55 <212> DNA

<213> Human respiratory syncytial virus

<400> 4

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5	agcaaaagpct atcttagtgc tctaaagaact ggttgggtata ctagtgttat aactatagaa	180
	ttaagtaata tcaaggaaaa taagtgttat ggaacagatg ctacggtaaa attgataaaa	240
	caagaattag ataaatatca aastgctgta ccagaattgc agttgctcat gcaaaqcaca	300
10	ccagccagcca acactcagagc cagcaagagaa ctacccagggt ttatgtaata taccctcaat	360
	aataccacaaa ataccactgt accctcaagc agcaaaagga caagcaagatt ccttggctctt	420
15	ttgttaggtg ttggatctgc aatcgcacgt ggcatttctc tctctcaagggt cctgcaccca	480
	caagggggagc tgaacacaaat ccaaaagtgt ctactatcca caaaccaagga tcttagtccgc	540
	ttatcaaatg gagttagtgt cttaacccagc aaagtgttag aectcaaaaa ctatatagat	600
20	aaacagttgt taactattgt gaacaagcaa agctgcagca taccacaacat tgaacctgtg	660
	atagagttcc aacaaaaaga caacagacta ctagagatta ccagggcaatt tagtgttaat	720
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	atcaatgata tgcctataac aactgatcag aaaaagttca tgtccacaca tgttcaaaata	840
	gttagacagc aaagttaact taccatgtrc ataataaagc aggaagtctt agcaatctgta	900
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35	caatcgaatc ggttattttg tgacacaaatg accaghttca ccttcccaag tgaagtaaat	1140
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40	gatgtaagca gctccgttat cacactctca ggaagccattg tgtcattgta tggcaaaaact	1260
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	ttaattgcag ttggactgct cctatactgc aagggcagaa gcaaacccagt caaacctaagt	1680
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<210> 5
 <211> 539
 <212> PRT

<213> Human metapneumovirus isolate

<400> 5

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15 Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asp Val Phe
35 40 45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
50 55 60

20 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65 70 75 80

25

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Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95

5 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
 10 115 120 125

Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140

15 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160

20 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

25 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205

30 Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220

35 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

40 Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
 260 265 270

45 Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285

50 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

55 Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp

					325					330					335	
5	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
10			355					360					365			
	Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
		370					375					380				
15	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
20				405						410					415	
	Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
25				420					425					430		
	Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
			435					440					445			
30	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
35	465					470					475					480
	Leu	Ser	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile
40				485						490					495	
	Leu	Ile	Ala	Val	Leu	Gly	Ser	Ser	Met	Ile	Leu	Val	Ser	Ile	Phe	Ile
				500					505					510		
45	Ile	Ile	Lys	Lys	Thr	Lys	Lys	Pro	Thr	Gly	Ala	Pro	Pro	Glu	Leu	Ser
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<210> 6

<211> 539

<212> PRT

55 <213> Human metapneumovirus

<400> 6

Met Ser Trp Lys Val Met Ile Ile Ile Ser Leu Leu Ile Thr Pro Gln

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25

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45

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55

	1			5				10				15				
5	His	Gly	Leu	Lys	Glu	Ser	Tyr	Leu	Glu	Glu	Ser	Cys	Ser	Thr	Ile	Thr
				20				25						30		
10	Glu	Gly	Tyr	Leu	Ser	Val	Leu	Arg	Thr	Gly	Trp	Tyr	Thr	Asn	Val	Phe
			35					40						45		
15	Thr	Leu	Glu	Val	Gly	Asp	Val	Glu	Asn	Leu	Thr	Cys	Thr	Asp	Gly	Pro
			50				55						60			
20	Ser	Leu	Ile	Lys	Thr	Glu	Leu	Asp	Leu	Thr	Lys	Ser	Ala	Leu	Arg	Glu
	65					70					75					80
25	Leu	Lys	Thr	Val	Ser	Ala	Asp	Gln	Leu	Ala	Arg	Glu	Glu	Gln	Ile	Glu
				85						90					95	
30	Asn	Pro	Arg	Gln	Ser	Arg	Phe	Val	Leu	Gly	Ala	Ile	Ala	Leu	Gly	Val
				100					105					110		
35	Ala	Thr	Ala	Ala	Ala	Val	Thr	Ala	Gly	Ile	Ala	Ile	Ala	Lys	Thr	Ile
			115					120					125			
40	Arg	Leu	Glu	Ser	Glu	Val	Asn	Ala	Ile	Lys	Gly	Ala	Leu	Lys	Gln	Thr
		130					135					140				
45	Asn	Glu	Ala	Val	Ser	Thr	Leu	Gly	Asn	Gly	Val	Arg	Val	Leu	Ala	Thr
	145					150					155					160
50	Ala	Val	Arg	Glu	Leu	Lys	Glu	Phe	Val	Ser	Lys	Asn	Leu	Thr	Ser	Ala
				165						170					175	
55	Ile	Asn	Arg	Asn	Lys	Cys	Asp	Ile	Ala	Asp	Leu	Lys	Met	Ala	Val	Ser
			180						185					190		
60	Phe	Ser	Gln	Phe	Asn	Arg	Arg	Phe	Leu	Asn	Val	Val	Arg	Gln	Phe	Ser
			195					200					205			
65	Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Thr	Asp
		210					215					220				
70	Ala	Glu	Leu	Ala	Arg	Ala	Val	Ser	Tyr	Met	Pro	Thr	Ser	Ala	Gly	Gln
			225			230					235					240
75	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		
5	Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Ile	Lys	Ala
				275				280					285			
10	Ala	Pro	Ser	Cys	Ser	Glu	Lys	Asn	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
		290					295					300				
15	Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Lys	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
	305					310					315					320
20	Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp
					325					330					335	
25	Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Arg	Glu	Cys	Asn	Ile
				340					345					350		
30	Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
			355					360					365			
35	Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
		370					375					380				
40	Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Trp	Val	Gly	Ile	Ile
	385					390					395					400
45	Lys	Gln	Leu	Pro	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
				405						410					415	
50	Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
				420					425					430		
55	Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
				435				440						445		
60	Ile	Lys	Phe	Pro	Glu	Asp	Gln	Phe	Asn	Val	Ala	Leu	Asp	Gln	Val	Phe
	450						455					460				
65	Glu	Ser	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Lys	Ile
	465					470					475					480
70	Leu	Asn	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Val	Ile
				485						490					495	
75	Leu	Val	Ala	Val	Leu	Gly	Leu	Thr	Met	Ile	Ser	Val	Ser	Ile	Ile	Ile
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5 Gly Val Thr Asn Gly Gly Phe Ile Pro His Ser
 530 535

<210> 7

<211> 539

10 <212> PRT

<213> Human metapneumovirus

<400> 7

15 Met Ser Trp Lys Val Met Ile Ile Ile Ser Leu Leu Ile Thr Pro Gln
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20 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

25 Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Thr Asp Gly Pro
 50 55 60

30 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80

35 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

40 Ala Thr Ala Ala Ala Val Thr Ala Gly Ile Ala Ile Ala Lys Thr Ile
 115 120 125

45 Arg Leu Glu Ser Glu Val Asn Ala Ile Lys Gly Ala Leu Lys Thr Thr
 130 135 140

50 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

55 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			
5	Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Asn	Asp
			210				215					220				
10	Ala	Glu	Leu	Ala	Arg	Ala	Val	Ser	Tyr	Met	Pro	Thr	Ser	Ala	Gly	Gln
	225				230						235					240
15	Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe
				245						250					255	
20	Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln
				260				265						270		
25	Leu	Pro	Ile	Phe	Gly	Val	Ile	Asn	Thr	Pro	Cys	Trp	Ile	Ile	Lys	Ala
			275					280					285			
30	Ala	Pro	Ser	Cys	Ser	Glu	Lys	Asp	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
	290						295					300				
35	Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Lys	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
	305					310					315					320
40	Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp
				325						330					335	
45	Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Arg	Glu	Cys	Asn	Ile
			340					345						350		
50	Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
			355					360					365			
55	Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
			370				375					380				
60	Tyr	Lys	Gly	Val	Ser	Cys	Ser	Thr	Gly	Ser	Asn	Gln	Val	Gly	Ile	Ile
	385					390					395					400
65	Lys	Gln	Leu	Pro	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
				405						410					415	
70	Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
				420					425					430		
75	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

5
 Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Lys Ile
 465 470 475 480

10
 Leu Asn Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495

15
 Leu Ile 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

20
 Gly Val Thr Asn Gly Gly Phe Ile Pro His Ser
 530 535

<210> 8
 <211> 574
 25 <212> PRT
 <213> Human respiratory syncytial virus

<400> 8

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 Ala Val Thr Leu Cys Phe Ala Ser Ser Gln Asn Ile Thr Glu Glu Phe
 20 25 30

40
 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

45
 Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
 65 70 75 80

50
 Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
 85 90 95

55
 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
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 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
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 Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
 180 185 190
 15
 Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Val Asn
 195 200 205
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 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
 25
 Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
 245 250 255
 30
 Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
 260 265 270
 35
 Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
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 Met Ser Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
 290 295 300
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 Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
 305 310 315 320
 45
 Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
 325 330 335
 Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
 340 345 350
 50
 Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
 355 360 365
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 Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Ile

	370					375						380				
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	385					390					395					400
	Asp	Val	Ser	Ser	Ser	Val	Ile	Thr	Ser	Leu	Gly	Ala	Ile	Val	Ser	Cys
10					405					410					415	
	Tyr	Gly	Lys	Thr	Lys	Cys	Thr	Ala	Ser	Asn	Lys	Asn	Arg	Gly	Ile	Ile
				420				425						430		
15	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
20		450					455					460				
	Lys	Ser	Leu	Tyr	Val	Lys	Gly	Glu	Pro	Ile	Ile	Asn	Phe	Tyr	Asp	Pro
25						470					475					480
	Leu	Val	Phe	Pro	Ser	Asp	Glu	Phe	Asp	Ala	Ser	Ile	Ser	Gln	Val	Asn
					485					490					495	
30	Gln	Lys	Ile	Asn	Gln	Ser	Leu	Ala	Phe	Ile	Arg	Lys	Ser	Asp	Gln	Leu
				500					505					510		
	Leu	His	Asn	Val	Asn	Ala	Gly	Lys	Ser	Thr	Thr	Asn	Ile	Met	Ile	Thr
35			515					520					525			
	Thr	Ile	Ile	Ile	Val	Ile	Ile	Val	Ile	Leu	Leu	Ser	Leu	Ile	Ala	Val
40		530					535						540			
	Gly	Leu	Leu	Leu	Tyr	Cys	Lys	Ala	Arg	Ser	Thr	Pro	Val	Thr	Leu	Ser
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<210> 9
 <211> 1617
 <212> DNA
 <213> Human parainfluenza virus 3
 <400> 9

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 aactcttggtg gtgacaaaca gatcaagcaa tacaagaggt tattggatag actgatcatt 240
 10 ccttttatatg atggactaag attacagaaag gatgtgatag tgactaatca agaatacaat 300
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 15 agatcagaca ttgaaaaaact caaggaagca atcagggaca caaataaagc agtgcagtca 480
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 aagaaatcg tggcatoggt tggagagcta ggttgtgaaq cagcaggact tcagttaggg 600
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 25 gaaatattca caacctcaac agttgacaaa tatgatattc atgatctatt atttacagaa 780
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<213> Human parainfluenza virus 3

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S00

S05

S10

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	tggtaacttt	ggctgggctt	tatcgcggcc	ctgttggccc	tggccctgtg	cgtgtctctc	3960
55	atcctgtgct	gcaccggctg	cggcaccacat	tgcctgggca	agctgaaatg	caaccggctg	4020
	tgcgaacagc	accagggact	cgaacctggc	ctcaccagc	tgcctgtgca	c	4071

<210> 24
<211> 1353
<212> PRT
<213> Middle East respiratory syndrome coronavirus

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<400> 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
 5 Ser Tyr Val Asp Val Gly Pro Asp Ser Val Lys Ser Ala Cys Ile Glu
 20 25 30
 10 Val Asp Ile Gln Gln Thr Phe Phe Asp Lys Thr Trp Pro Arg Pro Ile
 35 40 45
 15 Asp Val Ser Lys Ala Asp Gly Ile Ile Tyr Pro Gln Gly Arg Thr Tyr
 50 55 60
 20 Ser Asn Ile Thr Ile Thr Tyr Gln Gly Leu Phe Pro Tyr Gln Gly Asp
 65 70 75 80
 25 His Gly Asp Met Tyr Val Tyr Ser Ala Gly His Ala Thr Gly Thr Thr
 85 90 95
 30 Pro Gln Lys Leu Phe Val Ala Asn Tyr Ser Gln Asp Val Lys Gln Phe
 100 105 110
 35 Ala Asn Gly Phe Val Val Arg Ile Gly Ala Ala Ala Asn Ser Thr Gly
 115 120 125
 40 Thr Val Ile Ile Ser Pro Ser Thr Ser Ala Thr Ile Arg Lys Ile Tyr
 130 135 140
 45 Pro Ala Phe Met Leu Gly Ser Ser Val Gly Asn Phe Ser Asp Gly Lys
 145 150 155 160
 50 Met Gly Arg Phe Phe Asn His Thr Leu Val Leu Leu Pro Asp Gly Cys
 165 170 175
 55 Gly Thr Leu Leu Arg Ala Phe Tyr Cys Ile Leu Glu Pro Arg Ser Gly
 180 185 190
 60 Asn His Cys Pro Ala Gly Asn Ser Tyr Thr Ser Phe Ala Thr Tyr His
 195 200 205
 65 Thr Pro Ala Thr Asp Cys Ser Asp Gly Asn Tyr Asn Arg Asn Ala Ser
 210 215 220
 70 Leu Asn Ser Phe Lys Glu Tyr Phe Asn Leu Arg Asn Cys Thr Phe Met
 225 230 235 240 245 250

	228				230					238					240	
5	Tyr	Thr	Tyr	Asn	Ile	Thr	Glu	Asp	Glu	Ile	Leu	Glu	Trp	Phe	Gly	Ile
				245						250					255	
10	Thr	Gln	Thr	Ala	Gln	Gly	Val	His	Leu	Phe	Ser	Ser	Arg	Tyr	Val	Asp
			260						265					270		
15	Leu	Tyr	Gly	Gly	Asn	Met	Phe	Gln	Phe	Ala	Thr	Leu	Pro	Val	Tyr	Asp
			275					280						285		
20	Thr	Ile	Lys	Tyr	Tyr	Ser	Ile	Ile	Pro	His	Ser	Ile	Arg	Ser	Ile	Gln
			290				295						300			
25	Ser	Asp	Arg	Lys	Ala	Trp	Ala	Ala	Phe	Tyr	Val	Tyr	Lys	Leu	Gln	Pro
	305					310					315					320
30	Leu	Thr	Phe	Leu	Leu	Asp	Phe	Ser	Val	Asp	Gly	Tyr	Ile	Arg	Arg	Ala
				325						330					335	
35	Ile	Asp	Cys	Gly	Phe	Asn	Asp	Leu	Ser	Gln	Leu	His	Cys	Ser	Tyr	Glu
			340						345					350		
40	Ser	Phe	Asp	Val	Glu	Ser	Gly	Val	Tyr	Ser	Val	Ser	Ser	Phe	Gln	Ala
			355					360						365		
45	Lys	Pro	Ser	Gly	Ser	Val	Val	Glu	Gln	Ala	Glu	Gly	Val	Glu	Cys	Asp
	370						375					380				
50	Phe	Ser	Pro	Leu	Leu	Ser	Gly	Thr	Pro	Pro	Gln	Val	Tyr	Asn	Phe	Lys
	385					390					395					400
55	Arg	Leu	Val	Phe	Thr	Asn	Cys	Asn	Tyr	Asn	Leu	Thr	Lys	Leu	Leu	Ser
				405						410						415
60	Leu	Phe	Ser	Val	Asn	Asp	Phe	Thr	Cys	Ser	Gln	Ile	Ser	Pro	Ala	Ala
				420					425					430		
65	Ile	Ala	Ser	Asn	Cys	Tyr	Ser	Ser	Leu	Ile	Leu	Asp	Tyr	Phe	Ser	Tyr
			435					440					445			
70	Pro	Leu	Ser	Met	Lys	Ser	Asp	Leu	Ser	Val	Ser	Ser	Ala	Gly	Pro	Ile
	450						455						460			
75	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

5 Tyr Ser Tyr Ile Asn Lys Cys Ser Arg Leu Leu Ser Asp Asp Arg Thr
 500 505 510

10 Glu Val Pro Gln Leu Val Asn Ala Asn Gln Tyr Ser Pro Cys Val Ser
 515 520 525

15 Ile Val Pro Ser Thr Val Trp Glu Asp Gly Asp Tyr Tyr Arg Lys Gln
 530 535 540

20 Leu Ser Pro Leu Glu Gly Gly Gly Trp Leu Val Ala Ser Gly Ser Thr
 545 550 555 560

25 Val Ala Met Thr Glu Gln Leu Gln Met Gly Phe Gly Ile Thr Val Gln
 565 570 575

30 Tyr Gly Thr Asp Thr Asn Ser Val Cys Pro Lys Leu Glu Phe Ala Asn
 580 585 590

35 Asp Thr Lys Ile Ala Ser Gln Leu Gly Asn Cys Val Glu Tyr Ser Leu
 595 600 605

40 Tyr Gly Val Ser Gly Arg Gly Val Phe Gln Asn Cys Thr Ala Val Gly
 610 615 620

45 Val Arg Gln Gln Arg Phe Val Tyr Asp Ala Tyr Gln Asn Leu Val Gly
 625 630 635 640

50 Tyr Tyr Ser Asp Asp Gly Asn Tyr Tyr Cys Leu Arg Ala Cys Val Ser
 645 650 655

55 Val Pro Val Ser Val Ile Tyr Asp Lys Glu Thr Lys Thr His Ala Thr
 660 665 670

60 Leu Phe Gly Ser Val Ala Cys Glu His Ile Ser Ser Thr Met Ser Gln
 675 680 685

65 Tyr Ser Arg Ser Thr Arg Ser Met Leu Lys Arg Arg Asp Ser Thr Tyr
 690 695 700

70 Gly Pro Leu Gln Thr Pro Val Gly Cys Val Leu Gly Leu Val Asn Ser
 705 710 715 720

75 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			
5	Val	Pro	Gly	Glu	Met	Arg	Leu	Ala	Ser	Ile	Ala	Phe	Asn	His	Pro	Ile	
			755					760					765				
10	Gln	Val	Asp	Gln	Leu	Asn	Ser	Ser	Tyr	Phe	Lys	Leu	Ser	Ile	Pro	Thr	
		770					775					780					
15	Asn	Phe	Ser	Phe	Gly	Val	Thr	Gln	Glu	Tyr	Ile	Gln	Thr	Thr	Ile	Gln	
	785					790					795					800	
20	Lys	Val	Thr	Val	Asp	Cys	Lys	Gln	Tyr	Val	Cys	Asn	Gly	Phe	Gln	Lys	
					805					810					815		
25	Cys	Gln	Gln	Leu	Leu	Arg	Glu	Tyr	Gly	Gln	Phe	Cys	Ser	Lys	Ile	Asn	
				820					825					830			
30	Gln	Ala	Leu	His	Gly	Ala	Asn	Leu	Arg	Gln	Asp	Asp	Ser	Val	Arg	Asn	
			835					840					845				
35	Leu	Phe	Ala	Ser	Val	Lys	Ser	Ser	Gln	Ser	Ser	Pro	Ile	Ile	Pro	Gly	
	850						855					860					
40	Phe	Gly	Gly	Asp	Phe	Asn	Leu	Thr	Leu	Leu	Glu	Pro	Val	Ser	Ile	Ser	
	865					870					875					880	
45	Thr	Gly	Ser	Arg	Ser	Ala	Arg	Ser	Ala	Ile	Glu	Asp	Leu	Leu	Phe	Asp	
					885					890					895		
50	Lys	Val	Thr	Ile	Ala	Asp	Pro	Gly	Tyr	Met	Gln	Gly	Tyr	Asp	Asp	Cys	
				900					905					910			
55	Met	Gln	Gln	Gly	Pro	Ala	Ser	Ala	Arg	Asp	Leu	Ile	Cys	Ala	Gln	Tyr	
			915					920					925				
60	Val	Ala	Gly	Tyr	Lys	Val	Leu	Pro	Pro	Leu	Met	Asp	Val	Asn	Met	Glu	
		930					935					940					
65	Ala	Ala	Tyr	Thr	Ser	Ser	Leu	Leu	Gly	Ser	Ile	Ala	Gly	Val	Gly	Trp	
	945					950					955					960	
70	Thr	Ala	Gly	Leu	Ser	Ser	Phe	Ala	Ala	Ile	Pro	Phe	Ala	Gln	Ser	Ile	
				965						970					975		
75	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			
5	Gln	Thr	Gly	Phe	Thr	Thr	Thr	Asn	Glu	Ala	Phe	Arg	Lys	Val	Gln	
	1010						1015					1020				
10	Asp	Ala	Val	Asn	Asn	Asn	Ala	Gln	Ala	Leu	Ser	Lys	Leu	Ala	Ser	
	1025						1030					1035				
15	Glu	Leu	Ser	Asn	Thr	Phe	Gly	Ala	Ile	Ser	Ala	Ser	Ile	Gly	Asp	
	1040						1045					1050				
20	Ile	Ile	Gln	Arg	Leu	Asp	Val	Leu	Glu	Gln	Asp	Ala	Gln	Ile	Asp	
	1055						1060					1065				
25	Arg	Leu	Ile	Asn	Gly	Arg	Leu	Thr	Thr	Leu	Asn	Ala	Phe	Val	Ala	
	1070						1075					1080				
30	Gln	Gln	Leu	Val	Arg	Ser	Glu	Ser	Ala	Ala	Leu	Ser	Ala	Gln	Leu	
	1085						1090					1095				
35	Ala	Lys	Asp	Lys	Val	Asn	Glu	Cys	Val	Lys	Ala	Gln	Ser	Lys	Arg	
	1100						1105					1110				
40	Ser	Gly	Phe	Cys	Gly	Gln	Gly	Thr	His	Ile	Val	Ser	Phe	Val	Val	
	1115						1120					1125				
45	Asn	Ala	Pro	Asn	Gly	Leu	Tyr	Phe	Met	His	Val	Gly	Tyr	Tyr	Pro	
	1130						1135					1140				
50	Ser	Asn	His	Ile	Glu	Val	Val	Ser	Ala	Tyr	Gly	Leu	Cys	Asp	Ala	
	1145						1150					1155				
55	Ala	Asn	Pro	Thr	Asn	Cys	Ile	Ala	Pro	Val	Asn	Gly	Tyr	Phe	Ile	
	1160						1165					1170				
60	Lys	Thr	Asn	Asn	Thr	Arg	Ile	Val	Asp	Glu	Trp	Ser	Tyr	Thr	Gly	
	1175						1180					1185				
65	Ser	Ser	Phe	Tyr	Ala	Pro	Glu	Pro	Ile	Thr	Ser	Leu	Asn	Thr	Lys	
	1190						1195					1200				
70	Tyr	Val	Ala	Pro	Gln	Val	Thr	Tyr	Gln	Asn	Ile	Ser	Thr	Asn	Leu	
	1205						1210					1215				
75	Pro	Pro	Pro	Leu	Leu	Gly	Asn	Ser	Thr	Gly	Ile	Asp	Phe	Gln	Asp	

	1220		1225		1230										
5	Glu	Leu	Asp	Glu	Phe	Phe	Lys	Asn	Val	Ser	Thr	Ser	Ile	Pro	Asn
	1235						1240					1245			
10	Phe	Gly	Ser	Leu	Thr	Gln	Ile	Asn	Thr	Thr	Leu	Leu	Asp	Leu	Thr
	1250						1255					1260			
15	Tyr	Glu	Met	Leu	Ser	Leu	Gln	Gln	Val	Val	Lys	Ala	Leu	Asn	Glu
	1265						1270					1275			
20	Ser	Tyr	Ile	Asp	Leu	Lys	Glu	Leu	Gly	Asn	Tyr	Thr	Tyr	Tyr	Asn
	1280						1285					1290			
25	Lys	Trp	Pro	Trp	Tyr	Ile	Trp	Leu	Gly	Phe	Ile	Ala	Gly	Leu	Val
	1295						1300					1305			
30	Ala	Leu	Ala	Leu	Cys	Val	Phe	Phe	Ile	Leu	Cys	Cys	Thr	Gly	Cys
	1310						1315					1320			
35	Gly	Thr	Asn	Cys	Met	Gly	Lys	Leu	Lys	Cys	Asn	Arg	Cys	Cys	Asp
	1325						1330					1335			
40	Arg	Tyr	Glu	Glu	Tyr	Asp	Leu	Glu	Pro	His	Lys	Val	His	Val	His
	1340						1345					1350			

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 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Polypeptide

<400> 25

	Met	Ile	His	Ser	Val	Phe	Leu	Leu	Met	Phe	Leu	Leu	Thr	Pro	Thr	Glu
	1				5					10					15	
5	Ser	Tyr	Val	Asp	Val	Gly	Pro	Asp	Ser	Val	Lys	Ser	Ala	Cys	Ile	Glu
				20					25					30		
10	Val	Asp	Ile	Gln	Gln	Thr	Phe	Phe	Asp	Lys	Thr	Trp	Pro	Arg	Pro	Ile
			35					40					45			
15	Asp	Val	Ser	Lys	Ala	Asp	Gly	Ile	Ile	Tyr	Pro	Gln	Gly	Arg	Thr	Tyr
	50						55					60				
20	Ser	Asn	Ile	Thr	Ile	Thr	Tyr	Gln	Gly	Leu	Phe	Pro	Tyr	Gln	Gly	Asp
	65					70					75					80
25																
30																
35																
40																
45																
50																
55																

His Gly Asp Met Tyr Val Tyr Ser Ala Gly His Ala Thr Gly Thr Thr
 85 90 95

5 Pro Gln Lys Leu Phe Val Ala Asn Tyr Ser Gln Asp Val Lys Gln Phe
 100 105 110

10 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

15 Pro Ala Phe Met Leu Gly Ser Ser Val Gly Asn Phe Ser Asp Gly Lys
 145 150 155 160

20 Met Gly Arg Phe Phe Asn His Thr Leu Val Leu Leu Pro Asp Gly Cys
 165 170 175

25 Gly Thr Leu Leu Arg Ala Phe Tyr Cys Ile Leu Glu Pro Arg Ser Gly
 180 185 190

30 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

35 Leu Asn Ser Phe Lys Glu Tyr Phe Asn Leu Arg Asn Cys Thr Phe Met
 225 230 235 240

40 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

45 Leu Tyr Gly Gly Asn Met Phe Gln Phe Ala Thr Leu Pro Val Tyr Asp
 275 280 285

50 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

55 Leu Thr Phe Leu Leu Asp Phe Ser Val Asp Gly Tyr Ile Arg Arg Ala

					328					330					338	
5	Ile	Asp	Cys	Gly	Phe	Asn	Asp	Leu	Ser	Gln	Leu	His	Cys	Ser	Tyr	Glu
				340					345					350		
10	Ser	Phe	Asp	Val	Glu	Ser	Gly	Val	Tyr	Ser	Val	Ser	Ser	Phe	Glu	Ala
			355					360					365			
15	Lys	Pro	Ser	Gly	Ser	Val	Val	Glu	Gln	Ala	Glu	Gly	Val	Glu	Cys	Asp
		370					375					380				
20	Phe	Ser	Pro	Leu	Leu	Ser	Gly	Thr	Pro	Pro	Gln	Val	Tyr	Asn	Phe	Lys
	385					390					395					400
25	Arg	Leu	Val	Phe	Thr	Asn	Cys	Asn	Tyr	Asn	Leu	Thr	Lys	Leu	Leu	Ser
					405					410						415
30	Leu	Phe	Ser	Val	Asn	Asp	Phe	Thr	Cys	Ser	Gln	Ile	Ser	Pro	Ala	Ala
			420						425					430		
35	Ile	Ala	Ser	Asn	Cys	Tyr	Ser	Ser	Leu	Ile	Leu	Asp	Tyr	Phe	Ser	Tyr
			435					440					445			
40	Pro	Leu	Ser	Met	Lys	Ser	Asp	Leu	Ser	Val	Ser	Ser	Ala	Gly	Pro	Ile
		450					455						460			
45	Ser	Gln	Phe	Asn	Tyr	Lys	Gln	Ser	Phe	Ser	Asn	Pro	Thr	Cys	Leu	Ile
	465				470						475					480
50	Leu	Ala	Thr	Val	Pro	His	Asn	Leu	Thr	Thr	Ile	Thr	Lys	Pro	Leu	Lys
					485					490						495
55	Tyr	Ser	Tyr	Ile	Asn	Lys	Cys	Ser	Arg	Leu	Leu	Ser	Asp	Asp	Arg	Thr
			500						505					510		
60	Glu	Val	Pro	Gln	Leu	Val	Asn	Ala	Asn	Gln	Tyr	Ser	Pro	Cys	Val	Ser
			515					520						525		
65	Ile	Val	Pro	Ser	Thr	Val	Trp	Glu	Asp	Gly	Asp	Tyr	Tyr	Arg	Lys	Gln
	530						535					540				
70	Leu	Ser	Pro	Leu	Glu	Gly	Gly	Gly	Trp	Leu	Val	Ala	Ser	Gly	Ser	Thr
	545					550					555					560
75	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

5 Asp Thr Lys Ile Ala Ser Gln Leu Gly Asn Cys Val Glu Tyr Ser Leu
 595 600 605

10 Tyr Gly Val Ser Gly Arg Gly Val Phe Gln Asn Cys Thr Ala Val Gly
 610 615 620

15 Val Arg Gln Gln Arg Phe Val Tyr Asp Ala Tyr Gln Asn Leu Val Gly
 625 630 635 640

20 Tyr Tyr Ser Asp Asp Gly Asn Tyr Tyr Cys Leu Arg Ala Cys Val Ser
 645 650 655

25 Val Pro Val Ser Val Ile Tyr Asp Lys Glu Thr Lys Thr His Ala Thr
 660 665 670

30 Leu Phe Gly Ser Val Ala Cys Glu His Ile Ser Ser Thr Met Ser Gln
 675 680 685

35 Tyr Ser Arg Ser Thr Arg Ser Met Leu Lys Arg Arg Asp Ser Thr Tyr
 690 695 700

40 Gly Pro Leu Gln Thr Pro Val Gly Cys Val Leu Gly Leu Val Asn Ser
 705 710 715 720

45 Ser Leu Phe Val Glu Asp Cys Lys Leu Pro Leu Gly Gln Ser Leu Cys
 725 730 735

50 Ala Leu Pro Asp Thr Pro Ser Thr Leu Thr Pro Arg Ser Val Arg Ser
 740 745 750

55 Val Pro Gly Glu Met Arg Leu Ala Ser Ile Ala Phe Asn His Pro Ile
 755 760 765

60 Gln Val Asp Gln Leu Asn Ser Ser Tyr Phe Lys Leu Ser Ile Pro Thr
 770 775 780

65 Asn Phe Ser Phe Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln
 785 790 795 800

70 Lys Val Thr Val Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys
 805 810 815

75 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
 5 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
 10 Thr Gly Ser Arg Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp
 885 890 895
 15 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
 20 Val Ala Gly Tyr Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu
 930 935 940
 25 Ala Ala Tyr Thr Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp
 945 950 955 960
 30 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
 35 Asn Gln Lys Leu Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met
 995 1000 1005
 40 Gln Thr Gly Phe Thr 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
 50 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			
5	Ala	Lys	Asp	Lys	Val	Asn	Glu	Cys	Val	Lys	Ala	Gln	Ser	Lys	Arg
	1100						1105					1110			
10	Ser	Gly	Phe	Cys	Gly	Gln	Gly	Thr	His	Ile	Val	Ser	Phe	Val	Val
	1115						1120					1125			
15	Asn	Ala	Pro	Asn	Gly	Leu	Tyr	Phe	Met	His	Val	Gly	Tyr	Tyr	Pro
	1130						1135					1140			
20	Ser	Asn	His	Ile	Glu	Val	Val	Ser	Ala	Tyr	Gly	Leu	Cys	Asp	Ala
	1145						1150					1155			
25	Ala	Asn	Pro	Thr	Asn	Cys	Ile	Ala	Pro	Val	Asn	Gly	Tyr	Phe	Ile
	1160						1165					1170			
30	Lys	Thr	Asn	Asn	Thr	Arg	Ile	Val	Asp	Glu	Trp	Ser	Tyr	Thr	Gly
	1175						1180					1185			
35	Ser	Ser	Phe	Tyr	Ala	Pro	Glu	Pro	Ile	Thr	Ser	Leu	Asn	Thr	Lys
	1190						1195					1200			
40	Tyr	Val	Ala	Pro	Gln	Val	Thr	Tyr	Gln	Asn	Ile	Ser	Thr	Asn	Leu
	1205						1210					1215			
45	Pro	Pro	Pro	Leu	Leu	Gly	Asn	Ser	Thr	Gly	Ile	Asp	Phe	Gln	Asp
	1220						1225					1230			
50	Glu	Leu	Asp	Glu	Phe	Phe	Lys	Asn	Val	Ser	Thr	Ser	Ile	Pro	Asn
	1235						1240					1245			
55	Phe	Gly	Ser	Leu	Thr	Gln	Ile	Asn	Thr	Thr	Leu	Leu	Asp	Leu	Thr
	1250						1255					1260			
60	Tyr	Glu	Met	Leu	Ser	Leu	Gln	Gln	Val	Val	Iys	Ala	Leu	Asn	Glu
	1265						1270					1275			
65	Ser	Tyr	Ile	Asp	Leu	Lys	Glu	Leu	Gly	Asn	Tyr	Thr	Tyr	Tyr	Asn
	1280						1285					1290			
70	Lys	Trp	Pro	Trp	Tyr	Ile	Trp	Leu	Gly	Phe	Ile	Ala	Gly	Leu	Val
	1295						1300					1305			
75	Ala	Leu	Ala	Leu	Cys	Val	Phe	Phe	Ile	Leu	Cys	Cys	Thr	Gly	Cys

	1310		1315		1320
5	Gly Thr Asn Cys Met Gly Lys Leu Lys Cys Asn Arg Cys Cys Asp				
	1325		1330		1335
10	Arg Tyr Glu Glu Tyr Asp Leu Glu Pro His Lys Val His Val His				
	1340		1345		1350

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 <211> 615
 <212> PRT
 <213> Artificial Sequence
 15
 <220>
 <223> Synthetic Polypeptide
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 <400> 26

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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 Asp Cys Lys Leu Pro Leu Gly Gln Ser Leu Cys Ala Leu Pro Asp
 5 20 25 30
 Thr Pro Ser Thr Leu Thr Pro Arg Ser Val Arg Ser Val Pro Gly Glu
 10 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
 20 85 90 95
 Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys Cys Glu Gln Leu
 25 100 105 110
 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
 5 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
 10 Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu Ala Ala Tyr Thr
 225 230 235 240
 15 Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp Thr Ala Gly Leu
 245 250 255
 20 Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile Phe Tyr Arg Leu
 260 265 270
 25 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
 30 Thr Thr Thr Asn Glu Ala Phe Gln Lys Val Gln Asp Ala Val Asn Asn
 305 310 315 320
 35 Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser Glu Leu Ser Asn Thr Phe
 325 330 335
 40 Gly Ala Ile Ser Ala Ser Ile Gly Asp Ile Ile Gln Arg Leu Asp Val
 340 345 350
 45 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
 50 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
 55 Ser Phe Val Val Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly

				420					425					430			
5	Tyr	Tyr	Pro	Ser	Asn	His	Ile	Glu	Val	Val	Ser	Ala	Tyr	Gly	Leu	Cys	
			435					440					445				
10	Asp	Ala	Ala	Asn	Pro	Thr	Asn	Cys	Ile	Ala	Pro	Val	Asn	Gly	Tyr	Phe	
		450					455					460					
15	Ile	Lys	Thr	Asn	Asn	Thr	Arg	Ile	Val	Asp	Glu	Trp	Ser	Tyr	Thr	Gly	
	465					470					475					480	
20	Ser	Ser	Phe	Tyr	Ala	Pro	Glu	Pro	Ile	Thr	Ser	Leu	Asn	Thr	Lys	Tyr	
					485					490					495		
25	Val	Ala	Pro	Gln	Val	Thr	Tyr	Gln	Asn	Ile	Ser	Thr	Asn	Leu	Pro	Pro	
				500					505					510			
30	Pro	Leu	Leu	Gly	Asn	Ser	Thr	Gly	Ile	Asp	Phe	Gln	Asp	Glu	Leu	Asp	
			515					520					525				
35	Gln	Phe	Phe	Lys	Asn	Val	Ser	Thr	Ser	Ile	Pro	Asn	Phe	Gly	Ser	Leu	
	530						535					540					
40	Thr	Gln	Ile	Asn	Thr	Thr	Leu	Leu	Asp	Leu	Thr	Tyr	Glu	Met	Leu	Ser	
	545					550					555					560	
45	Leu	Gln	Gln	Val	Val	Lys	Ala	Leu	Asn	Glu	Ser	Tyr	Ile	Asp	Leu	Lys	
				565						570					575		
50	Glu	Leu	Gly	Asn	Tyr	Thr	Tyr	Tyr	Asn	Lys	Trp	Pro	Asp	Lys	Ile	Glu	
			580						585					590			
55	Glu	Ile	Leu	Ser	Lys	Ile	Tyr	His	Ile	Glu	Asn	Glu	Ile	Ala	Arg	Ile	
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60	Lys	Lys	Leu	Ile	Gly	Glu	Ala										
	610						615										

<210> 27

<211> 1353

50 <212> PRT

<213> Middle East respiratory syndrome coronavirus

<400> 27

55

Met Ile His Ser Val Phe Leu Leu Met Phe Leu Leu Thr Pro Thr Glu
1 5 10 15

5

Ser Tyr Val Asp Val Gly Pro Asp Ser Val Lys Ser Ala Cys Ile Glu

10

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				20						25						30
5	Val	Asp	Ile	Gln	Gln	Thr	Phe	Phe	Asp	Lys	Thr	Trp	Pro	Arg	Pro	Ile
			35					40					45			
10	Asp	Val	Ser	Lys	Ala	Asp	Gly	Ile	Ile	Tyr	Pro	Gln	Gly	Arg	Thr	Tyr
		50					55					60				
15	Ser	Asn	Ile	Thr	Ile	Thr	Tyr	Gln	Gly	Leu	Phe	Pro	Tyr	Gln	Gly	Asp
	65					70					75					80
20	His	Gly	Asp	Met	Tyr	Val	Tyr	Ser	Ala	Gly	His	Ala	Thr	Gly	Thr	Thr
				85						90					95	
25	Pro	Gln	Lys	Leu	Phe	Val	Ala	Asn	Tyr	Ser	Gln	Asp	Val	Lys	Gln	Phe
			100						105					110		
30	Ala	Asn	Gly	Phe	Val	Val	Arg	Ile	Gly	Ala	Ala	Ala	Asn	Ser	Thr	Gly
			115					120					125			
35	Thr	Val	Ile	Ile	Ser	Pro	Ser	Thr	Ser	Ala	Thr	Ile	Arg	Lys	Ile	Tyr
	130						135					140				
40	Pro	Ala	Phe	Met	Leu	Gly	Ser	Ser	Val	Gly	Asn	Phe	Ser	Asp	Gly	Lys
	145					150					155					160
45	Met	Gly	Arg	Phe	Phe	Asn	His	Thr	Leu	Val	Leu	Leu	Pro	Asp	Gly	Cys
				165						170					175	
50	Gly	Thr	Leu	Leu	Arg	Ala	Phe	Tyr	Cys	Ile	Leu	Glu	Pro	Arg	Ser	Gly
			180						185					190		
55	Asn	His	Cys	Pro	Ala	Gly	Asn	Ser	Tyr	Thr	Ser	Phe	Ala	Thr	Tyr	His
			195					200					205			
60	Thr	Pro	Ala	Thr	Asp	Cys	Ser	Asp	Gly	Asn	Tyr	Asn	Arg	Asn	Ala	Ser
	210						215					220				
65	Leu	Asn	Ser	Phe	Lys	Glu	Tyr	Phe	Asn	Leu	Arg	Asn	Cys	Thr	Phe	Met
	225					230					235					240
70	Tyr	Thr	Tyr	Asn	Ile	Thr	Glu	Asp	Glu	Ile	Leu	Glu	Trp	Phe	Gly	Ile
				245					250						255	
75	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
 5 Thr Ile Lys Tyr Tyr Ser Ile Ile Pro His Ser Ile Arg Ser Ile Gln
 290 300
 Ser Asp Arg Lys Ala Trp Ala Ala Phe Tyr Val Tyr Lys Leu Gln Pro
 305 310 315 320
 10 Leu Thr Phe Leu Leu Asp Phe Ser Val Asp Gly Tyr Ile Arg Arg Ala
 325 330 335
 15 Ile Asp Cys Gly Phe Asn Asp Leu Ser Gln Leu His Cys Ser Tyr Glu
 340 345 350
 20 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
 25 Phe Ser Pro Leu Leu Ser Gly Thr Pro Pro Gln Val Tyr Asn Phe Lys
 385 390 395 400
 30 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
 35 Ile Ala Ser Asn Cys Tyr Ser Ser Leu Ile Leu Asp Tyr Phe Ser Tyr
 435 440 445
 40 Pro Leu Ser Met Lys Ser Asp Leu Ser Val Ser Ser Ala Gly Pro Ile
 450 455 460
 45 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
 50 Tyr Ser Tyr Ile Asn Lys Cys Ser Arg Leu Leu Ser Asp Asp Arg Thr
 500 505 510
 55 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				
5	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
10					565					570					575	
	Tyr	Gly	Thr	Asp	Thr	Asn	Ser	Val	Cys	Pro	Lys	Leu	Glu	Phe	Ala	Asn
15				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
20		610					615					620				
	Val	Arg	Gln	Gln	Arg	Phe	Val	Tyr	Asp	Ala	Tyr	Gln	Asn	Leu	Val	Gly
25						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
30				660					665					670		
	Leu	Phe	Gly	Ser	Val	Ala	Cys	Glu	His	Ile	Ser	Ser	Thr	Met	Ser	Gln
35			675					680					685			
	Tyr	Ser	Arg	Ser	Thr	Arg	Ser	Met	Leu	Lys	Arg	Arg	Asp	Ser	Thr	Tyr
40			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
45				725						730					735	
	Ala	Leu	Pro	Asp	Thr	Pro	Ser	Thr	Leu	Thr	Pro	Arg	Ser	Val	Arg	Ser
50				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
55							775					780				

Asn Phe Ser Phe Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln
 785 790 795 800
 5 Lys Val Thr Val Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys
 808 810 815
 10 Cys Glu Gln Leu Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn
 820 825 830
 15 Gln Ala Leu His Gly Ala Asn Leu Arg Gln Asp Asp Ser Val Arg Asn
 835 840 845
 20 Leu Phe Ala Ser Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly
 850 855 860
 25 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
 30 Lys Val Thr Ile Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys
 900 905 910
 35 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
 40 Ala Ala Tyr Thr Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp
 945 950 955 960
 45 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
 50 Asn Gln Lys Leu Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met
 995 1000 1005
 55 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				
5	Glu	Leu	Ser	Asn	Thr	Phe	Gly	Ala	Ile	Ser	Ala	Ser	Ile	Gly	Asp
		1040					1045					1050			
10	Ile	Ile	Gln	Arg	Leu	Asp	Val	Leu	Glu	Gln	Asp	Ala	Gln	Ile	Asp
		1055					1060					1065			
15	Arg	Leu	Ile	Asn	Gly	Arg	Leu	Thr	Thr	Leu	Asn	Ala	Phe	Val	Ala
		1070					1075					1080			
20	Gln	Gln	Leu	Val	Arg	Ser	Glu	Ser	Ala	Ala	Leu	Ser	Ala	Gln	Leu
		1085					1090					1095			
25	Ala	Lys	Asp	Lys	Val	Asn	Glu	Cys	Val	Lys	Ala	Gln	Ser	Lys	Arg
		1100					1105					1110			
30	Ser	Gly	Phe	Cys	Gly	Gln	Gly	Thr	His	Ile	Val	Ser	Phe	Val	Val
		1115					1120					1125			
35	Asn	Ala	Pro	Asn	Gly	Leu	Tyr	Phe	Met	His	Val	Gly	Tyr	Tyr	Pro
		1130					1135					1140			
40	Ser	Asn	His	Ile	Glu	Val	Val	Ser	Ala	Tyr	Gly	Leu	Cys	Asp	Ala
		1145					1150					1155			
45	Ala	Asn	Pro	Thr	Asn	Cys	Ile	Ala	Pro	Val	Asn	Gly	Tyr	Phe	Ile
		1160					1165					1170			
50	Lys	Thr	Asn	Asn	Thr	Arg	Ile	Val	Asp	Glu	Trp	Ser	Tyr	Thr	Gly
		1175					1180					1185			
55	Ser	Ser	Phe	Tyr	Ala	Pro	Glu	Pro	Ile	Thr	Ser	Leu	Asn	Thr	Lys
		1190					1195					1200			
60	Tyr	Val	Ala	Pro	His	Val	Thr	Tyr	Gln	Asn	Ile	Ser	Thr	Asn	Leu
		1205					1210					1215			
65	Pro	Pro	Pro	Leu	Leu	Gly	Asn	Ser	Thr	Gly	Ile	Asp	Phe	Gln	Asp
		1220					1225					1230			
70	Glu	Leu	Asp	Glu	Phe	Phe	Lys	Asn	Val	Ser	Thr	Ser	Ile	Pro	Asn
		1235					1240					1245			
75	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
 5 Ser Tyr Ile Asp Leu Lys Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn
 1280 1285 1290
 10 Lys Trp Pro Trp Tyr Ile Trp Leu Gly Phe Ile Ala Gly Leu Val
 1295 1300 1305
 15 Ala Leu Ala Leu Cys Val Phe Phe Ile Leu Cys Cys Thr Gly Cys
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 Arg Tyr Glu Glu Tyr Asp Leu Glu Pro His Lys Val His Val His
 1340 1345 1350
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 35 40 45
 45 Asp Val Ser Lys Ala Asp Gly Ile Ile Tyr Pro Gln Gly Arg Thr Tyr
 50 55 60
 50 Ser Asn Ile Thr Ile Thr Tyr Gln Gly Leu Phe Pro Tyr Gln Gly Asp
 65 70 75 80
 55 His Gly Asp Met Tyr Val Tyr Ser Ala Gly His Ala Thr Gly Thr Thr
 85 90 95
 60 Pro Gln Lys Leu Phe Val Ala Asn Tyr Ser Gln Asp Val Lys Gln Phe
 100 105 110
 65 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					
5	Pro	Ala	Phe	Met	Leu	Gly	Ser	Ser	Val	Gly	Asn	Phe	Ser	Asp	Gly	Lys	
	145					150					155					160	
10	Met	Gly	Arg	Phe	Phe	Asn	His	Thr	Leu	Val	Leu	Leu	Pro	Asp	Gly	Cys	
					165					170					175		
15	Gly	Thr	Leu	Leu	Arg	Ala	Phe	Tyr	Cys	Ile	Leu	Glu	Pro	Arg	Ser	Gly	
					180				185					190			
20	Asn	His	Cys	Pro	Ala	Gly	Asn	Ser	Tyr	Thr	Ser	Phe	Ala	Thr	Tyr	His	
			195					200					205				
25	Thr	Pro	Ala	Thr	Asp	Cys	Ser	Asp	Gly	Asn	Tyr	Asn	Arg	Asn	Ala	Ser	
		210					215					220					
30	Leu	Asn	Ser	Phe	Lys	Glu	Tyr	Phe	Asn	Leu	Arg	Asn	Cys	Thr	Phe	Met	
	225					230					235					240	
35	Tyr	Thr	Tyr	Asn	Ile	Thr	Glu	Asp	Glu	Ile	Leu	Glu	Trp	Phe	Gly	Ile	
					245					250					255		
40	Thr	Gln	Thr	Ala	Gln	Gly	Val	His	Leu	Phe	Ser	Ser	Arg	Tyr	Val	Asp	
				260					265					270			
45	Leu	Tyr	Gly	Gly	Asn	Met	Phe	Gln	Phe	Ala	Thr	Leu	Pro	Val	Tyr	Asp	
			275					280					285				
50	Thr	Ile	Lys	Tyr	Tyr	Ser	Ile	Ile	Pro	His	Ser	Ile	Arg	Ser	Ile	Gln	
	290						295					300					
55	Ser	Asp	Arg	Lys	Ala	Trp	Ala	Ala	Phe	Tyr	Val	Tyr	Lys	Leu	Gln	Pro	
	305					310					315					320	
60	Leu	Thr	Phe	Leu	Leu	Asp	Phe	Ser	Val	Asp	Gly	Tyr	Ile	Arg	Arg	Ala	
					325					330					335		
65	Ile	Asp	Cys	Gly	Phe	Asn	Asp	Leu	Ser	Gln	Leu	His	Cys	Ser	Tyr	Glu	
				340					345					350			
70	Ser	Phe	Asp	Val	Glu	Ser	Gly	Val	Tyr	Ser	Val	Ser	Ser	Phe	Glu	Ala	
			355				360						365				
75	Lys	Pro	Ser	Gly	Ser	Val	Val	Glu	Gln	Ala	Glu	Gly	Val	Glu	Cys	Asp	
							375					380					

	Phe	Ser	Pro	Leu	Leu	Ser	Gly	Thr	Pro	Pro	Gln	Val	Tyr	Asn	Phe	Lys
	385					390					395					400
5	Arg	Leu	Val	Phe	Thr	Asn	Cys	Asn	Tyr	Asn	Leu	Thr	Lys	Leu	Leu	Ser
					405					410						415
10	Leu	Phe	Ser	Val	Asn	Asp	Phe	Thr	Cys	Ser	Gln	Ile	Ser	Pro	Ala	Ala
				420					425					430		
15	Ile	Ala	Ser	Asn	Cys	Tyr	Ser	Ser	Leu	Ile	Leu	Asp	Tyr	Phe	Ser	Tyr
			435				440						445			
20	Pro	Leu	Ser	Met	Lys	Ser	Asp	Leu	Ser	Val	Ser	Ser	Ala	Gly	Pro	Ile
	450						455					460				
25	Ser	Gln	Phe	Asn	Tyr	Lys	Gln	Ser	Phe	Ser	Asn	Pro	Thr	Cys	Leu	Ile
	465					470					475					480
30	Leu	Ala	Thr	Val	Pro	His	Asn	Leu	Thr	Thr	Ile	Thr	Lys	Pro	Leu	Lys
				485						490					495	
35	Tyr	Ser	Tyr	Ile	Asn	Lys	Cys	Ser	Arg	Leu	Leu	Ser	Asp	Asp	Arg	Thr
				500					505					510		
40	Glu	Val	Pro	Gln	Leu	Val	Asn	Ala	Asn	Gln	Tyr	Ser	Pro	Cys	Val	Ser
			515					520					525			
45	Ile	Val	Pro	Ser	Thr	Val	Trp	Glu	Asp	Gly	Asp	Tyr	Tyr	Arg	Lys	Gln
	530						535					540				
50	Leu	Ser	Pro	Leu	Glu	Gly	Gly	Gly	Trp	Leu	Val	Ala	Ser	Gly	Ser	Thr
	545				550						555					560
55	Val	Ala	Met	Thr	Glu	Gln	Leu	Gln	Met	Gly	Phe	Gly	Ile	Thr	Val	Gln
				565						570					575	
60	Tyr	Gly	Thr	Asp	Thr	Asn	Ser	Val	Cys	Pro	Lys	Leu	Glu	Phe	Ala	Asn
				580					585					590		
65	Asp	Thr	Lys	Ile	Ala	Ser	Gln	Leu	Gly	Asn	Cys	Val	Glu	Tyr	Ser	Leu
			595					600					605			
70	Tyr	Gly	Val	Ser	Gly	Arg	Gly	Val	Phe	Gln	Asn	Cys	Thr	Ala	Val	Gly
	610					615						620				
75	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
 5 Val Pro Val Ser Val Ile Tyr Asp Lys Glu Thr Lys Thr His Ala Thr
 660 665 670
 10 Leu Phe Gly Ser Val Ala Cys Glu His Ile Ser Ser Thr Met Ser Gln
 675 680 685
 15 Tyr Ser Arg Ser Thr Arg Ser Met Leu Lys Arg Arg Asp Ser Thr Tyr
 690 695 700
 20 Gly Pro Leu Gln Thr Pro Val Gly Cys Val Leu Gly Leu Val Asn Ser
 705 710 715 720
 25 Ser Leu Phe Val Glu Asp Cys Lys Leu Pro Leu Gly Gln Ser Leu Cys
 725 730 735
 30 Ala Leu Pro Asp Thr Pro Ser Thr Leu Thr Pro Arg Ser Val Arg Ser
 740 745 750
 35 Val Pro Gly Glu Met Arg Leu Ala Ser Ile Ala Phe Asn His Pro Ile
 755 760 765
 40 Gln Val Asp Gln Leu Asn Ser Ser Tyr Phe Lys Leu Ser Ile Pro Thr
 770 775 780
 45 Asn Phe Ser Phe Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln
 785 790 795 800
 50 Lys Val Thr Val Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys
 805 810 815
 55 Cys Glu Gln Leu Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn
 820 825 830
 60 Gln Ala Leu His Gly Ala Asn Leu Arg Gln Asp Asp Ser Val Arg Asn
 835 840 845
 65 Leu Phe Ala Ser Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly
 850 855 860
 70 Phe Gly Gly Asp Phe Asn Leu Thr Leu Leu Glu Pro Val Ser Ile Ser
 865 870 875 880
 75 Thr Gly Ser Arg Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp

					888					890					898	
5	Lys	Val	Thr	Ile	Ala	Asp	Pro	Gly	Tyr	Met	Gln	Gly	Tyr	Asp	Asp	Cys
					900				908					910		
10	Met	Gln	Gln	Gly	Pro	Ala	Ser	Ala	Arg	Asp	Leu	Ile	Cys	Ala	Gln	Tyr
			915					920					925			
15	Val	Ala	Gly	Tyr	Lys	Val	Leu	Pro	Pro	Leu	Met	Asp	Val	Asn	Met	Glu
		930					935					940				
20	Ala	Ala	Tyr	Thr	Ser	Ser	Leu	Leu	Gly	Ser	Ile	Ala	Gly	Val	Gly	Trp
	945					950					955					960
25	Thr	Ala	Gly	Leu	Ser	Ser	Phe	Ala	Ala	Ile	Pro	Phe	Ala	Gln	Ser	Ile
					965					970					975	
30	Phe	Tyr	Arg	Leu	Asn	Gly	Val	Gly	Ile	Thr	Gln	Gln	Val	Leu	Ser	Glu
			980					985						990		
35	Asn	Gln	Lys	Leu	Ile	Ala	Asn	Lys	Phe	Asn	Gln	Ala	Leu	Gly	Ala	Met
			995					1000						1005		
40	Gln	Thr	Gly	Phe	Thr	Thr	Thr	Asn	Glu	Ala	Phe	Arg	Lys	Val	Gln	
	1010						1015					1020				
45	Asp	Ala	Val	Asn	Asn	Asn	Ala	Gln	Ala	Leu	Ser	Lys	Leu	Ala	Ser	
	1025						1030					1035				
50	Glu	Leu	Ser	Asn	Thr	Phe	Gly	Ala	Ile	Ser	Ala	Ser	Ile	Gly	Asp	
	1040						1045					1050				
55	Ile	Ile	Gln	Arg	Leu	Asp	Val	Leu	Glu	Gln	Asp	Ala	Gln	Ile	Asp	
	1055						1060					1065				
60	Arg	Leu	Ile	Asn	Gly	Arg	Leu	Thr	Thr	Leu	Asn	Ala	Phe	Val	Ala	
	1070						1075					1080				
65	Gln	Gln	Leu	Val	Arg	Ser	Glu	Ser	Ala	Ala	Leu	Ser	Ala	Gln	Leu	
	1085						1090					1095				
70	Ala	Lys	Asp	Lys	Val	Asn	Glu	Cys	Val	Lys	Ala	Gln	Ser	Lys	Arg	
	1100						1105					1110				
75	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			
5															
	Ser	Asn	His	Ile	Glu	Val	Val	Ser	Ala	Tyr	Gly	Leu	Cys	Asp	Ala
	1145						1150					1155			
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	1160						1165					1170			
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	1175						1180					1185			
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	Ser	Ser	Phe	Tyr	Ala	Pro	Glu	Pro	Ile	Thr	Ser	Leu	Asn	Thr	Lys
	1190						1195					1200			
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	Tyr	Val	Ala	Pro	His	Val	Thr	Tyr	Gln	Asn	Ile	Ser	Thr	Asn	Leu
	1205						1210					1215			
30															
	Pro	Pro	Pro	Leu	Leu	Gly	Asn	Ser	Thr	Gly	Ile	Asp	Phe	Gln	Asp
	1220						1225					1230			
35															
	Glu	Leu	Asp	Glu	Phe	Phe	Lys	Asn	Val	Ser	Thr	Ser	Ile	Pro	Asn
	1235						1240					1245			
40															
	Phe	Gly	Ser	Leu	Thr	Gln	Ile	Asn	Thr	Thr	Leu	Leu	Asp	Leu	Thr
	1250						1255					1260			
45															
	Tyr	Glu	Met	Leu	Ser	Leu	Gln	Gln	Val	Val	Lys	Ala	Leu	Asn	Glu
	1265						1270					1275			
50															
	Ser	Tyr	Ile	Asp	Leu	Lys	Glu	Leu	Gly	Asn	Tyr	Thr	Tyr	Tyr	Asn
	1280						1285					1290			
55															
	Lys	Trp	Pro	Trp	Tyr	Ile	Trp	Leu	Gly	Phe	Ile	Ala	Gly	Leu	Val
	1295						1300					1305			
60															
	Ala	Leu	Ala	Leu	Cys	Val	Phe	Phe	Ile	Leu	Cys	Cys	Thr	Gly	Cys
	1310						1315					1320			
65															
	Gly	Thr	Asn	Cys	Met	Gly	Lys	Leu	Lys	Cys	Asn	Arg	Cys	Cys	Asp
	1325						1330					1335			
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 5 Asp Arg Cys Thr Thr Phe Asp Asp Val Gln Ala Pro Asn Tyr Thr Gln
 20 25 30
 10 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
 15 Asn Val Thr Gly Phe His Thr Ile Asn His Thr Phe Gly Asn Pro Val
 65 70 75 80
 20 Ile Pro Phe Lys Asp Gly Ile Tyr Phe Ala Ala Thr Glu Lys Ser Asn
 85 90 95
 25 Val Val Arg Gly Trp Val Phe Gly Ser Thr Met Asn Asn Lys Ser Gln
 100 105 110
 30 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
 35 Gly Thr Gln Thr His Thr Met Ile Phe Asp Asn Ala Phe Asn Cys Thr
 145 150 155 160
 40 Phe Glu Tyr Ile Ser Asp Ala Phe Ser Leu Asp Val Ser Glu Lys Ser
 165 170 175
 45 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
 50 Leu Pro Ser Gly Phe Asn Thr Leu Lys Pro Ile Phe Lys Leu Pro Leu
 210 215 220
 55 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

5 Leu Lys Pro Thr Thr Phe Met Leu Lys Tyr Asp Glu Asn Gly Thr Ile
260 265 270

10 Thr Asp Ala Val Asp Cys Ser Gln Asn Pro Leu Ala Glu Leu Lys Cys
275 280 285

15 Ser Val Lys Ser Phe Glu Ile Asp Lys Gly Ile Tyr Gln Thr Ser Asn
290 295 300

20 Phe Arg Val Val Pro Ser Gly Asp Val Val Arg Phe Pro Asn Ile Thr
305 310 315 320

25 Asn Leu Cys Pro Phe Gly Glu Val Phe Asn Ala Thr Lys Phe Pro Ser
325 330 335

30 Val Tyr Ala Trp Glu Arg Lys Lys Ile Ser Asn Cys Val Ala Asp Tyr
340 345 350

35 Ser Val Leu Tyr Asn Ser Thr Phe Phe Ser Thr Phe Lys Cys Tyr Gly
355 360 365

40 Val Ser Ala Thr Lys Leu Asn Asp Leu Cys Phe Ser Asn Val Tyr Ala
370 375 380

45 Asp Ser Phe Val Val Lys Gly Asp Asp Val Arg Gln Ile Ala Pro Gly
385 390 395 400

50 Gln Thr Gly Val Ile Ala Asp Tyr Asn Tyr Lys Leu Pro Asp Asp Phe
405 410 415

55 Met Gly Cys Val Leu Ala Trp Asn Thr Arg Asn Ile Asp Ala Thr Ser
420 425 430

60 Thr Gly Asn Tyr Asn Tyr Lys Tyr Arg Tyr Leu Arg His Gly Lys Leu
435 440 445

65 Arg Pro Phe Glu Arg Asp Ile Ser Asn Val Pro Phe Ser Pro Asp Gly
450 455 460

70 Lys Pro Cys Thr Pro Pro Ala Leu Asn Cys Tyr Trp Pro Leu Asn Asp
465 470 475 480

75 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
 5
 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
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 Phe Gln Pro Phe Gln Gln Phe Gly Arg Asp Val Ser Asp Phe Thr Asp
 545 550 555 560
 15
 Ser Val Arg Asp Pro Lys Thr Ser Glu Ile Leu Asp Ile Ser Pro Cys
 565 570 575
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 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
 25
 Ala Ile His Ala Asp Gln Leu Thr Pro Ala Trp Arg Ile Tyr Ser Thr
 610 615 620
 30
 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
 35
 Cys Ala Ser Tyr His Thr Val Ser Leu Leu Arg Ser Thr Ser Gln Lys
 660 665 670
 40
 Ser Ile Val Ala Tyr Thr Met Ser Leu Gly Ala Asp Ser Ser Ile Ala
 675 680 685
 45
 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
 50
 Asn Met Tyr Ile Cys Gly Asp Ser Thr Glu Cys Ala Asn Leu Leu Leu
 725 730 735
 55
 Gln Tyr Gly Ser Phe Cys Thr Gln Leu Asn Arg Ala Leu Ser Gly Ile

				740					745					750			
5	Ala	Ala	Glu	Gln	Asp	Arg	Asn	Thr	Arg	Glu	Val	Phe	Ala	Gln	Val	Lys	
				755					760					765			
10	Gln	Met	Tyr	Lys	Thr	Pro	Thr	Leu	Lys	Tyr	Phe	Gly	Gly	Phe	Asn	Phe	
				770					775					780			
15	Ser	Gln	Ile	Leu	Pro	Asp	Pro	Leu	Lys	Pro	Thr	Lys	Arg	Ser	Phe	Ile	
				785					790					795		800	
20	Glu	Asp	Leu	Leu	Phe	Asn	Lys	Val	Thr	Leu	Ala	Asp	Ala	Gly	Phe	Met	
					805										810		
25	Lys	Gln	Tyr	Gly	Glu	Cys	Leu	Gly	Asp	Ile	Asn	Ala	Arg	Asp	Leu	Ile	
				820										825		830	
30	Cys	Ala	Gln	Lys	Phe	Asn	Gly	Leu	Thr	Val	Leu	Pro	Pro	Leu	Leu	Thr	
				835										840		845	
35	Asp	Asp	Met	Ile	Ala	Ala	Tyr	Thr	Ala	Ala	Leu	Val	Ser	Gly	Thr	Ala	
				850										855		860	
40	Thr	Ala	Gly	Trp	Thr	Phe	Gly	Ala	Gly	Ala	Ala	Leu	Gln	Ile	Pro	Phe	
				865										870		875	
45	Ala	Met	Gln	Met	Ala	Tyr	Arg	Phe	Asn	Gly	Ile	Gly	Val	Thr	Gln	Asn	
				885										890		895	
50	Val	Leu	Tyr	Glu	Asn	Gln	Lys	Gln	Ile	Ala	Asn	Gln	Phe	Asn	Lys	Ala	
				900										905		910	
55	Ile	Ser	Gln	Ile	Gln	Glu	Ser	Leu	Thr	Thr	Thr	Ser	Thr	Ala	Leu	Gly	
				915										920		925	
60	Lys	Leu	Gln	Asp	Val	Val	Asn	Gln	Asn	Ala	Gln	Ala	Leu	Asn	Thr	Leu	
				930										935		940	
65	Val	Lys	Gln	Leu	Ser	Ser	Asn	Phe	Gly	Ala	Ile	Ser	Ser	Val	Leu	Asn	
				945										950		955	
70	Asp	Ile	Leu	Ser	Arg	Leu	Asp	Lys	Val	Glu	Ala	Glu	Val	Gln	Ile	Asp	
				965										970		975	
75	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
 995 1000 1005

5 Thr Lys Met Ser Glu Cys Val Leu Gly Gln Ser Lys Arg Val Asp
 1010 1015 1020

10 Phe Cys Gly Lys Gly Tyr His Leu Met Ser Phe Pro Gln Ala Ala
 1025 1030 1035

15 Pro His Gly Val Val Phe Leu His Val Thr Tyr Val Pro Ser Gln
 1040 1045 1050

20 Glu Arg Asn Phe Thr Thr Ala Pro Ala Ile Cys His Glu Gly Lys
 1055 1060 1065

25 Ala Tyr Phe Pro Arg Glu Gly Val Phe Val Phe Asn Gly Thr Ser
 1070 1075 1080

30 Trp Phe Ile Thr Gln Arg Asn Phe Phe Ser Pro Gln Ile Ile Thr
 1085 1090 1095

35 Thr Asp Asn Thr Phe Val Ser Gly Asn Cys Asp Val Val Ile Gly
 1100 1105 1110

40 Ile Ile Asn Asn Thr Val Tyr Asp Pro Leu Gln Pro Glu Leu Asp
 1115 1120 1125

45 Ser Phe Lys Glu Glu Leu Asp Lys Tyr Phe Lys Asn His Thr Ser
 1130 1135 1140

50 Pro Asp Val Asp Leu Gly Asp Ile Ser Gly Ile Asn Ala Ser Val
 1145 1150 1155

55 Val Asn Ile Gln Lys Glu Ile Asp Arg Leu Asn Glu Val Ala Lys
 1160 1165 1170

60 Asn Leu Asn Glu Ser Leu Ile Asp Leu Gln Glu Leu Gly Lys Tyr
 1175 1180 1185

65 Glu Gln Tyr Ile Lys Trp Pro Trp Tyr Val Trp Leu Gly Phe Ile
 1190 1195 1200

70 Ala Gly Leu Ile Ala Ile Val Met Val Thr Ile Leu Leu Cys Cys
 1205 1210 1215

75 Met Thr Ser Cys Cys Ser Cys Leu Lys Gly Ala Cys Ser Cys Gly
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Ser Cys Cys Lys Phe Asp Glu Asp Asp Ser Glu Pro Val Leu Lys
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5 Gly Val Lys Leu His Tyr Thr
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25 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

30 Asn Gly Tyr Tyr Pro Thr Ser Gly Ser Thr Tyr Arg Asn Met Ala Leu
 65 70 75 80

35 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
 100 105 110

40 Ile Lys Asp Arg Val Met Tyr Ser Glu Phe Pro Ala Ile Thr Ile Gly
 115 120 125

45 Ser Thr Phe Val Asn Thr Ser Tyr Ser Val Val Val Gln Pro Arg Thr
 130 135 140

50 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

55 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			
5	Ala	Asp	Tyr	Leu	Tyr	Phe	His	Phe	Tyr	Gln	Glu	Gly	Gly	Thr	Phe	Tyr
		210				215						220				
10	Ala	Tyr	Phe	Thr	Asp	Thr	Gly	Val	Val	Thr	Lys	Phe	Leu	Phe	Asn	Val
	225				230						235					240
15	Tyr	Leu	Gly	Met	Ala	Leu	Ser	His	Tyr	Tyr	Val	Met	Pro	Leu	Thr	Cys
				245						250					255	
20	Asn	Ser	Lys	Leu	Thr	Leu	Glu	Tyr	Trp	Val	Thr	Pro	Leu	Thr	Ser	Arg
			260						265					270		
25	Gln	Tyr	Leu	Leu	Ala	Phe	Asn	Gln	Asp	Gly	Ile	Ile	Phe	Asn	Ala	Glu
			275					280					285			
30	Asp	Cys	Met	Ser	Asp	Phe	Met	Ser	Glu	Ile	Lys	Cys	Lys	Thr	Gln	Ser
	290						295					300				
35	Ile	Ala	Pro	Pro	Thr	Gly	Val	Tyr	Glu	Leu	Asn	Gly	Tyr	Thr	Val	Gln
	305				310						315					320
40	Pro	Ile	Ala	Asp	Val	Tyr	Arg	Arg	Lys	Pro	Asn	Leu	Pro	Asn	Cys	Asn
				325						330					335	
45	Ile	Gln	Ala	Trp	Leu	Asn	Asp	Lys	Ser	Val	Pro	Ser	Pro	Leu	Asn	Trp
			340					345						350		
50	Glu	Arg	Lys	Thr	Phe	Ser	Asn	Cys	Asn	Phe	Asn	Met	Ser	Ser	Leu	Met
			355					360					365			
55	Ser	Phe	Ile	Gln	Ala	Asp	Ser	Phe	Thr	Cys	Asn	Asn	Ile	Asp	Ala	Ala
	370					375						380				
60	Lys	Ile	Tyr	Gly	Met	Cys	Phe	Ser	Ser	Ile	Thr	Ile	Asp	Lys	Phe	Ala
	385				390						395					400
65	Ile	Pro	Asn	Gly	Arg	Lys	Val	Asp	Leu	Gln	Leu	Gly	Asn	Leu	Gly	Tyr
				405						410					415	
70	Leu	Gln	Ser	Phe	Asn	Tyr	Arg	Ile	Asp	Thr	Thr	Ala	Thr	Ser	Cys	Gln
			420						425					430		
75	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

5 Lys Pro Arg Pro Ala Gly Val Leu Thr Asn His Asp Val Val Tyr Ala
 465 470 475 480

10 Gln His Cys Phe Lys Ala Pro Lys Asn Phe Cys Pro Cys Lys Leu Asn
 485 490 495

15 Gly Ser Cys Val Gly Ser Gly Pro Gly Lys Asn Asn Gly Ile Gly Thr
 500 505 510

20 Cys Pro Ala Gly Thr Asn Tyr Leu Thr Cys Asp Asn Leu Cys Thr Pro
 515 520 525

25 Asp Pro Ile Thr Phe Thr Gly Thr Tyr Lys Cys Pro Gln Thr Lys Ser
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30 Leu Val Gly Ile Gly Glu His Cys Ser Gly Leu Ala Val Lys Ser Asp
 545 550 555 560

35 Tyr Cys Gly Gly Asn Ser Cys Thr Cys Arg Pro Gln Ala Phe Leu Gly
 565 570 575

40 Trp Ser Ala Asp Ser Cys Leu Gln Gly Asp Lys Cys Asn Ile Phe Ala
 580 585 590

45 Asn Phe Ile Leu His Asp Val Asn Ser Gly Leu Thr Cys Ser Thr Asp
 595 600 605

50 Leu Gln Lys Ala Asn Thr Asp Ile Ile Leu Gly Val Cys Val Asn Tyr
 610 615 620

55 Asp Leu Tyr Gly Ile Leu Gly Gln Gly Ile Phe Val Glu Val Asn Ala
 625 630 635 640

60 Thr Tyr Tyr Asn Ser Trp Gln Asn Leu Leu Tyr Asp Ser Asn Gly Asn
 645 650 655

65 Leu Tyr Gly Phe Arg Asp Tyr Ile Ile Asn Arg Thr Phe Met Ile Arg
 660 665 670

70 Ser Cys Tyr Ser Gly Arg Val Ser Ala Ala Phe His Ala Asn Ser Ser
 675 680 685

75 Glu Pro Ala Leu Leu Phe Arg Asn Ile Lys Cys Asn Tyr Val Phe Asn

	690		695		700												
5	Asn	Ser	Leu	Thr	Arg	Gln	Leu	Gln	Pro	Ile	Asn	Tyr	Phe	Asp	Ser	Tyr	
	705					710					715					720	
10	Leu	Gly	Cys	Val	Val	Asn	Ala	Tyr	Asn	Ser	Thr	Ala	Ile	Ser	Val	Gln	
					725					730					735		
15	Thr	Cys	Asp	Leu	Thr	Val	Gly	Ser	Gly	Tyr	Cys	Val	Asp	Tyr	Ser	Lys	
				740					745					750			
20	Asn	Arg	Arg	Ser	Arg	Gly	Ala	Ile	Thr	Thr	Gly	Tyr	Arg	Phe	Thr	Asn	
				755				760						765			
25	Phe	Glu	Pro	Phe	Thr	Val	Asn	Ser	Val	Asn	Asp	Ser	Leu	Glu	Pro	Val	
	770						775					780					
30	Gly	Gly	Leu	Tyr	Glu	Ile	Gln	Ile	Pro	Ser	Glu	Phe	Thr	Ile	Gly	Asn	
	785					790					795					800	
35	Met	Val	Glu	Phe	Ile	Gln	Thr	Ser	Ser	Pro	Lys	Val	Thr	Ile	Asp	Cys	
					805					810					815		
40	Ala	Ala	Phe	Val	Cys	Gly	Asp	Tyr	Ala	Ala	Cys	Lys	Ser	Gln	Leu	Val	
				820					825					830			
45	Glu	Tyr	Gly	Ser	Phe	Cys	Asp	Asn	Ile	Asn	Ala	Ile	Leu	Thr	Glu	Val	
			835					840					845				
50	Asn	Glu	Leu	Leu	Asp	Thr	Thr	Gln	Leu	Gln	Val	Ala	Asn	Ser	Leu	Met	
	850						855						860				
55	Asn	Gly	Val	Thr	Leu	Ser	Thr	Lys	Leu	Lys	Asp	Gly	Val	Asn	Phe	Asn	
	865					870					875					880	
60	Val	Asp	Asp	Ile	Asn	Phe	Ser	Pro	Val	Leu	Gly	Cys	Leu	Gly	Ser	Glu	
				885						890					895		
65	Cys	Ser	Lys	Ala	Ser	Ser	Arg	Ser	Ala	Ile	Glu	Asp	Leu	Leu	Phe	Asp	
				900					905					910			
70	Lys	Val	Lys	Leu	Ser	Asp	Val	Gly	Phe	Val	Glu	Ala	Tyr	Asn	Asn	Cys	
			915					920					925				
75	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

5 Tyr Thr Leu Ala Ala Thr Ser Ala Ser Leu Phe Pro Pro Trp Thr Ala
 965 970 975

10 Ala Ala Gly Val Pro Phe Tyr Leu Asn Val Gln Tyr Arg Ile Asn Gly
 980 985 990

15 Leu Gly Val Thr Met Asp Val Leu Ser Gln Asn Gln Lys Leu Ile Ala
 995 1000 1005

20 Asn Ala Phe Asn Asn Ala Leu Tyr Ala Ile Gln Glu Gly Phe Asp
 1010 1015 1020

25 Ala Thr Asn Ser Ala Leu Val Lys Ile Gln Ala Val Val Asn Ala
 1025 1030 1035

30 Asn Ala Glu Ala Leu Asn Asn Leu Leu Gln Gln Leu Ser Asn Arg
 1040 1045 1050

35 Phe Gly Ala Ile Ser Ala Ser Leu Gln Glu Ile Leu Ser Arg Leu
 1055 1060 1065

40 Asp Ala Leu Glu Ala Glu Ala Gln Ile Asp Arg Leu Ile Asn Gly
 1070 1075 1080

45 Arg Leu Thr Ala Leu Asn Ala Tyr Val Ser Gln Gln Leu Ser Asp
 1085 1090 1095

50 Ser Thr Leu Val Lys Phe Ser Ala Ala Gln Ala Met Glu Lys Val
 1100 1105 1110

55 Asn Glu Cys Val Lys Ser Gln Ser Ser Arg Ile Asn Phe Cys Gly
 1115 1120 1125

60 Asn Gly Asn His Ile Ile Ser Leu Val Gln Asn Ala Pro Tyr Gly
 1130 1135 1140

65 Leu Tyr Phe Ile His Phe Ser Tyr Val Pro Thr Lys Tyr Val Thr
 1145 1150 1155

70 Ala Arg Val Ser Pro Gly Leu Cys Ile Ala Gly Asp Arg Gly Ile
 1160 1165 1170

75 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
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 Asn Val Val Val Met Ser Thr Cys Ala Val Asn Tyr Thr Lys Ala
 1205 1210 1215
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 Pro Tyr Val Met Leu Asn Thr Ser Ile Pro Asn Leu Pro Asp Phe
 1220 1225 1230
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 Lys Glu Glu Leu Asp Gln Trp Phe Lys Asn Gln Thr Ser Val Ala
 1235 1240 1245
 20
 Pro Asp Leu Ser Leu Asp Tyr Ile Asn Val Thr Phe Leu Asp Leu
 1250 1255 1260
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 Gln Val Glu Met Asn Arg Leu Gln Glu Ala Ile Lys Val Leu Asn
 1265 1270 1275
 30
 Gln Ser Tyr Ile Asn Leu Lys Asp Ile Gly Thr Tyr Glu Tyr Tyr
 1280 1285 1290
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 Val Lys Trp Pro Trp Tyr Val Trp Leu Leu Ile Cys Leu Ala Gly
 1295 1300 1305
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 Val Ala Met Leu Val Leu Leu Phe Phe Ile Cys Cys Cys Thr Gly
 1310 1315 1320
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 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

5 Gly Tyr Phe Pro Lys Ser Gly Ala Asn Phe Arg Asp Leu Ala Leu Lys
 65 70 75 80

10 Gly Ser Ile Tyr Leu Ser Thr Leu Trp Tyr Lys Pro Pro Phe Leu Ser
 85 90 95

15 Asp Phe Asn Asn Gly Ile Phe Ser Lys Val Lys Asn Thr Lys Leu Tyr
 100 105 110

20 Val Asn Asn Thr Leu Tyr Ser Glu Phe Ser Thr Ile Val Ile Gly Ser
 115 120 125

25 Val Phe Val Asn Thr Ser Tyr Thr Ile Val Val Gln Pro His Asn Gly
 130 135 140

30 Ile Leu Glu Ile Thr Ala Cys Gln Tyr Thr Met Cys Glu Tyr Pro His
 145 150 155 160

35 Thr Val Cys Lys Ser Lys Gly Ser Ile Arg Asn Glu Ser Trp His Ile
 165 170 175

40 Asp Ser Ser Glu Pro Leu Cys Leu Phe Lys Lys Asn Phe Thr Tyr Asn
 180 185 190

45 Val Ser Ala Asp Trp Leu Tyr Phe His Phe Tyr Gln Glu Arg Gly Val
 195 200 205

50 Phe Tyr Ala Tyr Tyr Ala Asp Val Gly Met Pro Thr Thr Phe Leu Phe
 210 215 220

55 Ser Leu Tyr Leu Gly Thr Ile Leu Ser His Tyr Tyr Val Met Pro Leu
 225 230 235 240

60 Thr Cys Asn Ala Ile Ser Ser Asn Thr Asp Asn Glu Thr Leu Glu Tyr
 245 250 255

65 Trp Val Thr Pro Leu Ser Arg Arg Gln Tyr Leu Leu Asn Phe Asp Glu
 260 265 270

70 His Gly Val Ile Thr Asn Ala Val Asp Cys Ser Ser Ser Phe Leu Ser
 275 280 285

75 Glu Ile Gln Cys Lys Thr Gln Ser Phe Ala Pro Asn Thr Gly Val Tyr
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Asp Leu Ser Gly Phe Thr Val Lys Pro Val Ala Thr Val Tyr Arg Arg
 305 310 315 320
 5 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
 10 340 345 350
 Asn Phe Asn Leu Ser Thr Leu Leu Arg Leu Val His Val Asp Ser Phe
 15 355 360 365
 Ser Cys Asn Asn Leu Asp Lys Ser Lys Ile Phe Gly Ser Cys Phe Asn
 370 375 380
 20 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
 25 405 410 415
 Asp Ile Ser Ser Ser Ser Cys Gln Leu Tyr Tyr Ser Leu Pro Leu Val
 420 425 430
 30 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
 35 450 455 460
 His Cys Phe Ser Val Asn Ser Asp Phe Cys Pro Cys Ala Asp Pro Ser
 465 470 475 480
 40 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
 45 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
 55 His Cys Pro Gly Leu Gly Ile Asn Glu Glu Lys Cys Gly Thr Gln Leu

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10	Phe	Asp	Ser	Cys	Ile	Ser	Asn	Asn	Arg	Cys	Asn	Ile	Phe	Ser	Asn	Phe				
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15	Ile	Phe	Asn	Gly	Ile	Asn	Ser	Gly	Thr	Thr	Cys	Ser	Asn	Asp	Leu	Leu				
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30	Tyr	Asn	Asn	Trp	Gln	Asn	Leu	Leu	Tyr	Asp	Ser	Asn	Gly	Asn	Ile	Ile				
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35	Gly	Phe	Lys	Asp	Phe	Leu	Thr	Asn	Lys	Thr	Tyr	Thr	Ile	Leu	Pro	Cys				
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40	Tyr	Ser	Gly	Arg	Val	Ser	Ala	Ala	Phe	Tyr	Gln	Asn	Ser	Ser	Ser	Pro				
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50	Ser	Phe	Ile	Ser	Gln	Pro	Phe	Tyr	Phe	Asp	Ser	Tyr	Leu	Gly	Cys	Val				
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60	Arg	Met	Gly	Ser	Gly	Phe	Cys	Ile	Asp	Tyr	Ala	Leu	Pro	Ser	Ser	Arg				
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 5 Phe Val Cys Ser Asn Tyr Ala Ala Cys His Asp Leu Leu Ser Glu Tyr
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 10 Gly Thr Phe Cys Asp Asn Ile Asn Ser Ile Leu Asn Glu Val Asn Asp
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 15 Leu Leu Asp Ile Thr Gln Leu Gln Val Ala Asn Ala Leu Met Gln Gly
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 25 Asn Ile Asp Phe Lys Ser Leu Leu Gly Cys Leu Gly Ser Gln Cys Gly
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 30 Ser Ser Ser Arg Ser Leu Leu Glu Asp Leu Leu Phe Asn Lys Val Lys
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 35 Leu Ser Asp Val Gly Phe Val Glu Ala Tyr Asn Asn Cys Thr Gly Gly
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 40 Ser Glu Ile Arg Asp Leu Leu Cys Val Gln Ser Phe Asn Gly Ile Lys
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 60 Thr Met Asp Val Leu Asn Lys Asn Gln Lys Leu Ile Ala Asn Ala Phe
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 75 Ala Leu Asn Ser Leu Leu Gln Gln Leu Phe Asn Lys Phe Gly Ala
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5	Glu Ala Gln Val Gln Ile Asp Arg Leu Ile Asn Gly Arg Leu Thr	1070				1075				1080			
10	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			
15	Val Lys Ser Gln Ser Pro Arg Ile Asn Phe Cys Gly Asn Gly Asn	1115				1120				1125			
20	His Ile Leu Ser Leu Val Gln Asn Ala Pro Tyr Gly Leu Leu Phe	1130				1135				1140			
25	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			
30	Gln Gly Tyr Phe Ile Lys Gln Asn Asp Ser Trp Met Phe Thr Gly	1175				1180				1185			
35	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			
40	Tyr Leu Asn Asn Ser Ile Pro Asn Leu Ser Asp Phe Glu Ala Glu	1220				1225				1230			
45	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			
50	Glu Met Asn Val Ile Gln Glu Ser Ile Lys Ser Leu Asn Ser Ser	1265				1270				1275			
55	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
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 5 Phe Leu Met Ile Leu Phe Phe Ile Cys Cys Cys Thr Gly Cys Gly
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 35 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
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 40 Pro Thr Lys Arg Ser Phe Ile Glu Asp Leu Leu Phe Asn Lys Val Thr
 65 70 75 80
 45 Leu Ala Asp Ala Gly Phe Met Lys Gln Tyr Gly Glu Cys Leu Gly Asp
 85 90 95
 50 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
 55 Ala Leu Val Ser Gly Thr Ala Thr Ala Gly Trp Thr Phe Gly Ala Gly
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15	Thr	Thr	Ser	Thr	Ala	Leu	Gly	Lys	Leu	Gln	Asp	Val	Val	Asn	Gln	Asn
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20	Ala	Gln	Ala	Leu	Asn	Thr	Leu	Val	Lys	Gln	Leu	Ser	Ser	Asn	Phe	Gly
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25	Ala	Ile	Ser	Ser	Val	Leu	Asn	Asp	Ile	Leu	Ser	Arg	Leu	Asp	Lys	Val
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40	Ala	Ser	Ala	Asn	Leu	Ala	Ala	Thr	Lys	Met	Ser	Glu	Cys	Val	Leu	Gly
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45	Gln	Ser	Lys	Arg	Val	Asp	Phe	Cys	Gly	Lys	Gly	Tyr	His	Leu	Met	Ser
	290					295						300				
50	Phe	Pro	Gln	Ala	Ala	Pro	His	Gly	Val	Val	Phe	Leu	His	Val	Thr	Tyr
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55	Val	Pro	Ser	Gln	Glu	Arg	Asn	Phe	Thr	Thr	Ala	Pro	Ala	Ile	Cys	His
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60	Glu	Gly	Lys	Ala	Tyr	Phe	Pro	Arg	Glu	Gly	Val	Phe	Val	Phe	Asn	Gly
				340					345					350		
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			355					360					365			
70	Thr	Thr	Asp	Asn	Thr	Phe	Val	Ser	Gly	Asn	Cys	Asp	Val	Val	Ile	Gly
	370						375					380				
75	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
 5 Val Asp Leu Gly Asp Ile Ser Gly Ile Asn Ala Ser Val Val Asn Ile
 420 425 430
 10 Gln Lys Glu Ile Asp Arg Leu Asn Glu Val Ala Lys Asn Leu Asn Glu
 435 440 445
 15 Ser Leu Ile Asp Leu Gln Glu Leu Gly Lys Tyr Glu Gln Tyr Ile Lys
 450 455 460
 20 Trp Pro Trp Tyr Val Trp Leu Gly Phe Ile Ala Gly Leu Ile Ala Ile
 465 470 475 480
 25 Val Met Val Thr Ile Leu Leu Cys Cys Met Thr Ser Cys Cys Ser Cys
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 50 Thr Pro Ser Thr Leu Thr Pro Arg Ser Val Arg Ser Val Pro Gly Glu
 35 40 45
 55 Met Arg Leu Ala Ser Ile Ala Phe Asn His Pro Ile Gln Val Asp Gln
 50 55 60
 65 Leu Asn Ser Ser Tyr Phe Lys Leu Ser Ile Pro Thr Asn Phe Ser Phe
 70 75 80

Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln Lys Val Thr Val
 85 90 95

5 Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys Cys Glu Gln Leu
 100 105 110

10 Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn Gln Ala Leu His
 115 120 125

15 Gly Ala Asn Leu Arg Gln Asp Asp Ser Val Arg Asn Leu Phe Ala Ser
 130 135 140

20 Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly Phe Gly Gly Asp
 145 150 155 160

25 Phe Asn Leu Thr Leu Leu Glu Pro Val Ser Ile Ser Thr Gly Ser Arg
 165 170 175

30 Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp Lys Val Thr Ile
 180 185 190

35 Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys Met Gln Gln Gly
 195 200 205

40 Pro Ala Ser Ala Arg Asp Leu Ile Cys Ala Gln Tyr Val Ala Gly Tyr
 210 215 220

45 Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu Ala Ala Tyr Thr
 225 230 235 240

50 Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp Thr Ala Gly Leu
 245 250 255

55 Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile Phe Tyr Arg Leu
 260 265 270

60 Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu Asn Gln Lys Leu
 275 280 285

65 Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met Gln Thr Gly Phe
 290 295 300

70 Thr Thr Thr Asn Glu Ala Phe Gln Lys Val Gln Asp Ala Val Asn Asn
 305 310 315 320

75 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
 5 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
 10 Ala Leu Ser Ala Gln Leu Ala Lys Asp Lys Val Asn Glu Cys Val Lys
 385 390 395 400
 15 Ala Gln Ser Lys Arg Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val
 405 410 415
 20 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
 25 Asp Ala Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe
 450 455 460
 30 Ile Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly
 465 470 475 480
 Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys Tyr
 485 490 495
 35 Val Ala Pro Gln Val Thr Tyr Gln Asn Ile Ser Thr Asn Leu Pro Pro
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 40 Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp Glu Leu Asp
 515 520 525
 45 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
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 Glu Val Phe Ala Gln Val Lys Gln Met Tyr Lys Thr Pro Thr Leu Lys
 10 35 40 45
 Tyr Phe Gly Gly Phe Asn Phe Ser Gln Ile Leu Pro Asp Pro Leu Lys
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 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
 20 85 90 95
 Ile Asn Ala Arg Asp Leu Ile Cys Ala Gln Lys Phe Asn Gly Leu Thr
 25 100 105 110
 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

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Ala Gln Ala Leu Asn Thr Leu Val Lys Gln Leu Ser Ser Asn Phe Gly
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 Ala Ile Ser Ser Val Leu Asn Asp Ile Leu Ser Arg Leu Asp Lys Val
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 245 250 255
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 260 265 270
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 Ala Ser Ala Asn Leu Ala Ala Thr Lys Met Ser Glu Cys Val Leu Gly
 275 280 285
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 290 295 300
 Phe Pro Gln Ala Ala Pro His Gly Val Val Phe Leu His Val Thr Tyr
 305 310 315 320
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 Val Pro Ser Gln Glu Arg Asn Phe Thr Thr Ala Pro Ala Ile Cys His
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 Glu Gly Lys Ala Tyr Phe Pro Arg Glu Gly Val Phe Val Phe Asn Gly
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 Thr Thr Asp Asn Thr Phe Val Ser Gly Asn Cys Asp Val Val Ile Gly
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 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
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 Gln Lys Glu Ile Asp Arg Leu Asn Glu Val Ala Lys Asn Leu Asn Glu
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 Ser Leu Ile Asp Leu Gln Glu Leu Gly Lys Tyr Glu Gln Tyr Ile Lys

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5	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
10					485					490					495	
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<400> 44

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Ser Ser His Gln Ser Leu Val Ile Lys Leu Met Pro Asn Ile Thr Leu
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 40 Leu Ile Gly Leu Leu Ala Ile Ala Gly Ile Arg Leu His Arg Ala Ala
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 45 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
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 50 Lys Ile Ile Gly Asp Glu Val Gly Leu Arg Thr Pro Gln Arg Phe Thr
 100 105 110
 55 Asp Leu Val Lys Phe Ile Ser Asp Lys Ile Lys Phe Leu Asn Pro Asp
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	Leu	Val	Lys	Leu	Gly	Val	Trp	Lys	Ser	Pro	Thr	Asp	Met	Gln	Ser	Trp
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							375					380				

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 420 425 430

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 Pro Leu Ile Thr His Gly Ser Gly Met Asp Leu Tyr Lys Ser Asn Cys
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 Gly Val Ile Asn Thr Leu Glu Trp Ile Pro Arg Phe Lys Val Ser Pro
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 Asn Leu Phe Thr Val Pro Ile Lys Glu Ala Gly Glu Asp Cys His Ala
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 Pro Thr Tyr Leu Pro Ala Glu Val Asp Gly Asp Val Lys Leu Ser Ser
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 Tyr Asp Thr Ser Arg Val Glu His Ala Val Val Tyr Tyr Val Tyr Ser
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 Pro Ser Arg Ser Phe Ser Tyr Phe Tyr Pro Phe Arg Leu Pro Ile Lys
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15 Leu Ile Gly Leu Leu Ala Ile Ala Gly Ile Arg Leu His Arg Ala Ala
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Ile Tyr Thr Ala Glu Ile His Lys Ser Leu Ser Thr Asn Leu Asp Val
65 70 75 80

20 Thr Asn Ser Ile Glu His Gln Val Lys Asp Val Leu Thr Pro Leu Phe
85 90 95

25 Lys Ile Ile Gly Asp Glu Val Gly Leu Arg Thr Pro Gln Arg Phe Thr
100 105 110

30 Asp Leu Val Lys Phe Ile Ser Asp Lys Ile Lys Phe Leu Asn Pro Asp
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Arg Glu Tyr Asp Phe Arg Asp Leu Thr Trp Cys Ile Asn Pro Pro Glu
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35 Arg Ile Lys Leu Asp Tyr Asp Gln Tyr Cys Ala Asp Val Ala Ala Glu
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40 Glu Leu Met Asn Ala Leu Val Asn Ser Thr Leu Leu Glu Thr Arg Ala
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45 Thr Asn Gln Phe Leu Ala Val Ser Lys Gly Asn Cys Ser Gly Pro Thr
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Thr Ile Arg Gly Gln Phe Ser Asn Met Ser Leu Ser Leu Leu Asp Leu
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50 Tyr Leu Ser Arg Gly Tyr Asn Val Ser Ser Ile Val Thr Met Thr Ser
210 215 220

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Gln Gly Met Tyr Gly Gly Thr Tyr Leu Val Glu Lys Pro Asn Leu Ser
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5 Ser Lys Gly Ser Glu Leu Ser Gln Leu Ser Met His Arg Val Phe Glu
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10 Val Gly Val Ile Arg Asn Pro Gly Leu Gly Ala Pro Val Phe His Met
 260 265 270

15 Thr Asn Tyr Leu Glu Gln Pro Val Ser Asn Asp Phe Ser Asn Cys Met
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20 Val Ala Leu Gly Glu Leu Lys Phe Ala Ala Leu Cys His Arg Glu Asp
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25 Ser Ile Thr Ile Pro Tyr Gln Gly Ser Gly Lys Gly Val Ser Phe Gln
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30 Leu Val Lys Leu Gly Val Trp Lys Ser Pro Thr Asp Met Gln Ser Trp
 325 330 335

35 Val Pro Leu Ser Thr Asp Asp Pro Val Ile Asp Arg Leu Tyr Leu Ser
 340 345 350

40 Ser His Arg Gly Val Ile Ala Asp Asn Gln Ala Lys Trp Ala Val Pro
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45 Thr Thr Arg Thr Asp Asp Lys Leu Arg Met Glu Thr Cys Phe Gln Gln
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50 Ala Cys Lys Gly Lys Ile Gln Ala Leu Cys Glu Asn Pro Glu Trp Thr
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55 Pro Leu Lys Asp Asn Arg Ile Pro Ser Tyr Gly Val Leu Ser Val Asp
 405 410 415

60 Leu Ser Leu Thr Val Glu Leu Lys Ile Lys Ile Val Ser Gly Phe Gly
 420 425 430

65 Pro Leu Ile Thr His Gly Ser Gly Met Asp Leu Tyr Lys Ser Asn His
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70 Asn Asn Met Tyr Trp Leu Thr Ile Pro Pro Met Lys Asn Leu Ala Leu
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seqs 100 to 600

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    aacgaaatcg accgtgtatc cggccagact cagttcaacg gctgaaagt cctgggcagc      420
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    gcccgtagcc gtatogaaga ttcogactac gcaaccgaag totcaacat gctctogocg      1440
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5 Ser Ser Gly Leu Arg Ile Asn Ser Ala Lys Asp Asp Ala Ala Gly Gln
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Ala Ile Ala Asn Arg Phe Thr Ala Asn Ile Lys Gly Leu Thr Gln Ala
 50 55 60

10 Ser Arg Asn Ala Asn Asp Gly Ile Ser Ile Ala Gln Thr Thr Glu Gly
 65 70 75 80

15 Ala Leu Asn Glu Ile Asn Asn Asn Leu Gln Arg Val Arg Glu Leu Ala
 85 90 95

20 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

25 Gln Thr Gln Phe Asn Gly Val Lys Val Leu Ala Gln Asp Asn Thr Leu
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30 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

35 Asp Ala Tyr Thr Pro Lys Glu Thr Ala Val Thr Val Asp Lys Thr Thr
 180 185 190

40 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

50 Ala Gly Val Tyr Lys Ala Thr Tyr Asp Glu Thr Thr Lys Lys Val Asn
 245 250 255

55 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
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 Lys Glu Gly Val Asp Thr Thr Thr Val Ala Ala Gln Leu Ala Ala Ala
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 Gly Val Thr Gly Ala Asp Lys Asp Asn Thr Ser Leu Val Lys Leu Ser
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 Phe Glu Asp Lys Asn Gly Lys Val Ile Asp Gly Gly Tyr Ala Val Lys
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 Met Gly Asp Asp Phe Tyr Ala Ala Thr Tyr Asp Glu Lys Thr Gly Ala
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 Ile Thr Ala Lys Thr Thr Thr Tyr Thr Asp Gly Thr Gly Val Ala Gln
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 Thr Ala Thr Asp Gly Lys Thr Tyr Leu Ala Ser Asp Leu Asp Lys His
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 Asn Phe Arg Thr Gly Gly Glu Leu Lys Glu Val Asn Thr Asp Lys Thr
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 Glu Asn Pro Leu Gln Lys Ile Asp Ala Ala Leu Ala Gln Val Asp Thr
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 435 440 445
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 Thr Asn Leu Gly Asn Thr Val Asn Asn Leu Ser Ser Ala Arg Ser Arg
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Asn Leu Asn Lys Ser Gln Ser Ala Leu Gly Thr Ala Ile Glu Arg Leu
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Ser Ser Gly Leu Arg Ile Asn Ser Ala Lys Asp Asp Ala Ala Gly Gln
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Ala Ile Ala Asn Arg Phe Thr Ala Asn Ile Lys Gly Leu Thr Gln Ala
15 50 55 60

Ser Arg Asn Ala Asn Asp Gly Ile Ser Ile Ala Gln Thr Thr Glu Gly
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Ala Leu Asn Glu Ile Asn Asn Asn Leu Gln Arg Val Arg Glu Leu Ala
20 85 90 95

Val Gln Ser Ala Asn Ser Thr Asn Ser Gln Ser Asp Leu Asp Ser Ile
25 100 105 110

Gln Ala Glu Ile Thr Gln Arg Leu Asn Glu Ile Asp Arg Val Ser Gly
30 115 120 125

Gln Thr Gln Phe Asn Gly Val Lys Val Leu Ala Gln Asp Asn Thr Leu
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Thr Ile Gln Val Gly Ala Asn Asp Gly Glu Thr Ile Asp Ile Asp Leu
35 145 150 155 160

Lys Gln Ile Asn Ser Gln Thr Leu Gly Leu Asp Thr Leu Asn Val Gln
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Gln Lys Tyr Lys Val Ser Asp Thr Ala Ala Thr Val Thr Gly Tyr Ala
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Asp Thr Thr Ile Ala Leu Asp Asn Ser Thr Phe Lys Ala Ser Ala Thr
195 200 205

Gly Leu Gly Gly Thr Asp Gln Lys Ile Asp Gly Asp Leu Lys Phe Asp
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Asp Thr Thr Gly Lys Tyr Tyr Ala Lys Val Thr Val Thr Gly Gly Thr
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 245 250 255
 Val Thr Leu Ala Gly Gly Ala Thr Ser Pro Leu Thr Gly Gly Leu Pro
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	සලකායාලය	සලකායාලය	සලකායාලය	සලකායාලය	සලකායාලය	සලකායාලය	1320
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	සමස්තවලට	සමස්තවලට	සමස්තවලට	සමස්තවලට	සමස්තවලට	120
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	සමස්තවලට	සමස්තවලට	සමස්තවලට	සමස්තවලට	සමස්තවලට	240
	සමස්තවලට	සමස්තවලට	සමස්තවලට	සමස්තවලට	සමස්තවලට	300
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සහග්‍රහණයට සහග්‍රහණයට ප්‍රතිපත්තිමය මට්ටමකට පත්වීමට සහග්‍රහණය 60
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15 cuugacuuacaggg cuuucccguuac ccgcaaacccgac guuuuuuuuuuu uuugccagagac caccuuaacggcc 240

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15 Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
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 25 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Phe
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 30 Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
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 35 Leu Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
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 40 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
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 45 Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
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 50 Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240
 55 Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
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 60 Gly Ile Leu Cys Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
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 65 Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
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 Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
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 15 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
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 20 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
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 25 Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
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 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
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 40 Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
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 45 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
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Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
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 5 Gly Ile Leu Cys Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
 260 265 270
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 10 Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
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 15 Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
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 20 Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
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 Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
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 30 Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
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 405 410 415
 40 Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
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 45 Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
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Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
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15 Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu
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20 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
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25 Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
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30 Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
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35 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
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5 Ile Asn Lys Asn Lys Cys Asp Ile Pro Asp Leu Lys Met Ala Val Ser
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Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
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Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
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Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
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Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
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Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
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Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
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Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
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Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
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Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
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Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
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Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
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 1 5 10 15

5 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30

10 Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
 35 40 45

15 Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50 55 60

20 Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu
 65 70 75 80

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Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95
 5 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
 10 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140
 15 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160
 20 Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
 165 170 175
 25 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
 30 Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220
 35 Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240
 40 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
 45 Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285
 50 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
 55 Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp

				325					330					335		
5	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
10				355				360					365			
	Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
				370			375					380				
15	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
20				405						410					415	
	Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
25				420					425					430		
	Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
				435				440					445			
30	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
35				465		470					475					480
	Leu	Ser	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile
40				485						490					495	
	Leu	Ile	Ala	Val	Leu	Gly	Ser	Ser	Met	Ile	Leu	Val	Ser	Ile	Phe	Ile
				500					505					510		
45	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					
50				530			535									

<210> 89
 <211> 539
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Polypeptide

<400> 89

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Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15
 5 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30
 10 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
 15 Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu
 65 70 75 80
 20 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95
 25 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
 30 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140
 35 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160
 40 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
 45 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205
 50 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
 55 Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe

				248					280					288		
5	Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln
				260					268					270		
10	Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala
				278				280					288			
15	Ala	Pro	Ser	Cys	Ser	Glu	Lys	Lys	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
				290			295					300				
20	Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Gln	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
						310					315					320
25	Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp
					325					330					335	
30	Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Lys	Glu	Cys	Asn	Ile
				340					345					350		
35	Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
					355			360					365			
40	Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
					370		375					380				
45	Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile
						385					395					400
50	Lys	Gln	Leu	Asn	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
					405					410					415	
55	Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
				420					425					430		
60	Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
				435				440						445		
65	Ile	Lys	Phe	Pro	Glu	Asp	Gln	Phe	Gln	Val	Ala	Leu	Asp	Gln	Val	Phe
				450			455					460				
70	Glu	Asn	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Arg	Ile
						465					475					480
75	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

5 Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525

10 Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
 530 535

<210> 90

<211> 539

<212> PRT

15 <213> Artificial Sequence

<220>

<223> Synthetic Polypeptide

20 <400> 90

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Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15

5 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30

10 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

15 Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu
 65 70 75 80

20 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95

25 Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110

30 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

35 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160

40 Ala Val Arg Glu Leu Lys Asp Phe Val Leu Lys Asn Leu Thr Arg Ala

					168					170					178	
5	Ile	Asn	Lys	Asn	Lys	Cys	Asp	Ile	Pro	Asp	Leu	Lys	Met	Ala	Val	Ser
				180					185					190		
10	Phe	Ser	Gln	Phe	Asn	Arg	Arg	Phe	Leu	Asn	Val	Val	Arg	Gln	Phe	Ser
			195					200					205			
15	Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Thr	Asp
			210				215					220				
20	Ala	Glu	Leu	Ala	Arg	Ala	Val	Pro	Asn	Met	Pro	Thr	Ser	Ala	Gly	Gln
			225			230					235					240
25	Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe
				245						250					255	
30	Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln
				260					265					270		
35	Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala
			275					280					285			
40	Ala	Pro	Ser	Cys	Ser	Glu	Lys	Lys	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
			290				295					300				
45	Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Gln	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
			305			310					315					320
50	Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp
				325						330					335	
55	Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Lys	Glu	Cys	Asn	Ile
			340						345					350		
60	Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
			355				360						365			
65	Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
			370				375					380				
70	Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile
			385			390					395					400
75	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
 5
 Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445
 10
 Ile Lys Phe Pro Glu Asn Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460
 15
 Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480
 20
 Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495
 25
 Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510
 30
 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
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 <210> 91
 <211> 539
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 <400> 91

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15

5 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30

10 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

15 Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu
 65 70 75 80

20 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu

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				88					90				98			
5	Asn	Pro	Gly	Ser	Gly	Ser	Phe	Val	Leu	Gly	Ala	Ile	Ala	Leu	Gly	Val
				100					105					110		
10	Ala	Ala	Ala	Ala	Ala	Val	Thr	Ala	Gly	Val	Ala	Ile	Ala	Lys	Thr	Ile
				115					120					125		
15	Arg	Leu	Glu	Ser	Glu	Val	Thr	Ala	Ile	Asn	Asn	Ala	Leu	Lys	Lys	Thr
				130					135					140		
20	Ala	Val	Arg	Glu	Leu	Lys	Asp	Phe	Val	Ser	Lys	Asn	Leu	Thr	Arg	Ala
				165										170		175
25	Ile	Asn	Lys	Asn	Lys	Cys	Asp	Ile	Asp	Asp	Leu	Lys	Met	Ala	Val	Ser
				180										185		190
30	Phe	Ser	Gln	Phe	Asn	Arg	Arg	Phe	Leu	Asn	Val	Val	Arg	Gln	Phe	Ser
				195										200		205
35	Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Thr	Asp
				210										215		220
40	Ala	Glu	Leu	Ala	Arg	Ala	Val	Pro	Asn	Met	Pro	Thr	Ser	Ala	Gly	Gln
				225										230		235
45	Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe
				245										250		255
50	Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln
				260										265		270
55	Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala
				275										280		285
60	Ala	Pro	Ser	Cys	Ser	Glu	Lys	Lys	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
				290										295		300
65	Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Gln	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
				305										310		315
70	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
 5 Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365
 10 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
 15 Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415
 20 Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430
 25 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
 30 Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480
 35 Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495
 40 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
 45 Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
 530 535

<210> 92

50 <211> 539

<212> PRT

<213> Artificial Sequence

<220>

55 <223> Synthetic Polypeptide

<400> 92

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln

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5	His	Gly	Leu	Lys	Glu	Ser	Tyr	Leu	Glu	Glu	Ser	Cys	Ser	Thr	Ile	Thr
				20					25					30		
10	Glu	Gly	Tyr	Leu	Ser	Val	Leu	Arg	Thr	Gly	Trp	Tyr	Thr	Asn	Val	Phe
			35					40					45			
15	Thr	Leu	Pro	Val	Gly	Asp	Val	Glu	Asn	Leu	Thr	Cys	Ser	Asp	Gly	Pro
			50				55					60				
20	Ser	Leu	Ile	Lys	Thr	Glu	Leu	Asp	Leu	Leu	Lys	Ser	Ala	Leu	Arg	Glu
			65			70					75				80	
25	Leu	Lys	Thr	Val	Ser	Ala	Asp	Gln	Leu	Ala	Arg	Glu	Glu	Gln	Ile	Glu
			85							90					95	
30	Asn	Pro	Gly	Ser	Gly	Ser	Phe	Val	Leu	Gly	Ala	Ile	Ala	Leu	Gly	Val
			100						105					110		
35	Ala	Ala	Ala	Ala	Ala	Val	Thr	Ala	Gly	Val	Ala	Ile	Ala	Lys	Thr	Ile
			115					120					125			
40	Arg	Leu	Glu	Ser	Glu	Val	Thr	Ala	Ile	Asn	Asn	Ala	Leu	Lys	Lys	Thr
			130				135					140				
45	Asn	Glu	Ala	Val	Ser	Thr	Leu	Gly	Asn	Gly	Val	Arg	Val	Leu	Ala	Thr
			145			150					155				160	
50	Ala	Val	Arg	Glu	Leu	Lys	Asp	Phe	Val	Ser	Lys	Asn	Leu	Thr	Arg	Ala
			165							170					175	
55	Ile	Asn	Lys	Asn	Lys	Cys	Asp	Ile	Asp	Asp	Leu	Lys	Met	Ala	Val	Ser
			180						185					190		
60	Phe	Ser	Gln	Phe	Asn	Arg	Arg	Phe	Leu	Asn	Val	Val	Arg	Gln	Phe	Ser
			195					200					205			
65	Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Thr	Asp
			210				215					220				
70	Ala	Glu	Leu	Ala	Arg	Ala	Val	Pro	Asn	Met	Pro	Thr	Ser	Ala	Gly	Gln
			225			230					235				240	
75	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

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Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285

10

Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300

15

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320

20

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335

25

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350

30

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365

35

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380

40

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400

45

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415

50

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430

55

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445

60

Ile Lys Phe Pro Glu Asn Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460

65

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480

70

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495

75

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
315 320 325

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Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
530 535

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<210> 93

<211> 539

<212> PRT

<213> Artificial Sequence

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<220>

<223> Synthetic Polypeptide

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Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15
 5
 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30
 10
 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
 15
 Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu
 65 70 75 80
 20
 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95
 25
 Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110
 30
 Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125
 35
 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140
 40
 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160
 45
 Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
 165 170 175
 50
 55

180 Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
 185 190

5 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205

10 Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220

15 Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240

20 Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
 245 250 255

25 Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
 260 265 270

30 Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285

35 Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300

40 Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320

45 Pro Asn Gln Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335

50 Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350

55 Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365

60 Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380

65 Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400

70 Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415

75 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
 5
 Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460
 10
 Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480
 15
 Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495
 20
 Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510
 25
 Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525
 30
 Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
 530 535

<210> 94
 <211> 539
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Polypeptide

<400> 94

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15
 40
 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30
 45
 Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
 35 40 45
 50
 Thr Leu Glu Val Gly Asp Leu Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50 55 60
 55
 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80
 85
 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
 5 Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125
 10 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140
 15 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160
 20 Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
 165 170 175
 25 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
 30 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
 35 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
 40 Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285
 45 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
 50 Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335
 55 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			
5	Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
			370				375					380				
10	Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile
	385					390					395					400
15	Lys	Gln	Leu	Asn	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
				405						410					415	
20	Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
				420					425						430	
25	Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
			435					440					445			
30	Ile	Lys	Phe	Pro	Glu	Asp	Gln	Phe	Gln	Val	Ala	Leu	Asp	Gln	Val	Phe
	450						455					460				
35	Glu	Asn	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Arg	Ile
	465					470					475					480
40	Leu	Ser	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile
				485						490					495	
45	Leu	Ile	Ala	Val	Leu	Gly	Ser	Ser	Met	Ile	Leu	Val	Ser	Ile	Phe	Ile
			500						505					510		
50	Ile	Ile	Lys	Lys	Thr	Lys	Lys	Pro	Thr	Gly	Ala	Pro	Pro	Glu	Leu	Ser
			515					520					525			
55	Gly	Val	Thr	Asn	Asn	Gly	Phe	Ile	Pro	His	Asn					
	530						535									
55	<210>	95														
	<211>	539														
	<212>	PRT														
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50	<220>															
	<223>	Synthetic Polypeptide														
	<400>	95														
55	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

5 Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
 35 40 45

10 Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50 55 60

15 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80

20 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95

25 Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110

30 Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125

35 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140

40 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160

45 Ala Val Arg Glu Leu Lys Asp Phe Val Leu Lys Asn Leu Thr Arg Ala
 165 170 175

50 Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
 180 185 190

55 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205

60 Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220

65 Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240

70 Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
 245 250 255

75 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

5

Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300

10

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320

15

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335

20

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350

25

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365

30

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380

35

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400

40

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415

45

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430

50

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445

55

Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460

60

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480

65

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495

70

Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510

75

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> 96
- 5 <211> 539
- <212> PRT
- <213> Artificial Sequence

- <220>
- 10 <223> Synthetic Polypeptide

- <400> 96

15	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			20					25						30		
	Glu	Gly	Tyr	Leu	Ser	Val	Leu	Arg	Thr	Gly	Trp	Tyr	Thr	Asn	Val	Phe
			35					40						45		
25	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
30	65					70					75					80
	Leu	Lys	Thr	Val	Ser	Ala	Asp	Gln	Leu	Ala	Arg	Glu	Glu	Gln	Ile	Glu
35					85					90					95	
	Asn	Pro	Gly	Ser	Gly	Ser	Phe	Val	Leu	Gly	Ala	Ile	Ala	Leu	Gly	Val
				100					105					110		
40	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
45		130						135				140				
	Asn	Glu	Ala	Val	Ser	Thr	Leu	Gly	Asn	Gly	Val	Arg	Val	Leu	Ala	Thr
	145					150					155					160
50	Ala	Val	Arg	Glu	Leu	Lys	Asp	Phe	Val	Ser	Lys	Asn	Leu	Trp	Arg	Ala
				165						170					175	
55	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

5 Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220

10 Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240

15 Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
 245 250 255

20 Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
 260 265 270

25 Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285

30 Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300

35 Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320

40 Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335

45 Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350

50 Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365

55 Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380

60 Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400

65 Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415

70 Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430

75 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

5
Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
  465                               470                               475                               480

10
Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
  485                               490                               495

15
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

20
Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
  530                               535

<210> 97
<211> 539
25 <212> PRT
    <213> Artificial Sequence

<220>
<223> Synthetic Polypeptide
30
<400> 97

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
35  1      5      10      15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
40      20      25      30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
45      35      40      45

Thr Leu Glu Val Gly Asp Leu Glu Asn Leu Thr Cys Ser Asp Gly Pro
50      50      55      60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu
55      65      70      75      80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
85      90      95

60
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				
5	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	
10		145				150					155					160	
	Ala	Val	Arg	Glu	Leu	Lys	Asp	Phe	Val	Leu	Lys	Asn	Leu	Trp	Arg	Ala	
				165						170					175		
15	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	
20			195					200					205				
	Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Thr	Asp	
25		210					215					220					
	Ala	Glu	Leu	Ala	Arg	Ala	Val	Pro	Asn	Met	Pro	Thr	Ser	Ala	Gly	Gln	
		225			230						235					240	
30	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	
35			260					265						270			
	Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala	
			275					280					285				
40	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	
45		305				310					315					320	
	Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp	
50				325						330					335		
	Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Lys	Glu	Cys	Asn	Ile	
			340					345						350			
55	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

5 Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400

10 Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415

15 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

20 Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460

25 Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480

30 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

35 Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525

40 Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
 530 535

<210> 98

<211> 539

<212> PRT

45 <213> Artificial Sequence

<220>

<223> Synthetic Polypeptide

50 <400> 98

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15

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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
 5 Thr Leu Pro Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50 55 60
 10 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80
 15 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Gln Gln Ile Glu
 85 90 95
 20 Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110
 25 Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125
 30 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140
 35 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160
 40 Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
 165 170 175
 45 Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
 180 185 190
 50 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205
 55 Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220
 60 Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240
 65 Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
 245 250 255
 70 Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
 260 265 270
 75 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

5 Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320

10 Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335

15 Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350

20 Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365

25 Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380

30 Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400

35 Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415

40 Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430

45 Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445

50 Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460

55 Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480

60 Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495

65 Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510

70 Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525

75 Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn

530

538

5 <210> 99
<211> 539
<212> PRT
<213> Artificial Sequence

10 <220>
<223> Synthetic Polypeptide

<400> 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

5 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30

10 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

15 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80

20 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95

25 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

30 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140

35 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160

40 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

45 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205

50
 55

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220

5 Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240

10 Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
 245 250 255

15 Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
 260 265 270

20 Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285

25 Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300

30 Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320

35 Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335

40 Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
 340 345 350

45 Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365

50 Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
 370 375 380

55 Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
 385 390 395 400

60 Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415

65 Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430

70 Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445

75 Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe

	450		455		460											
5	Glu	Asn	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Arg	Ile
	465					470					475					480
10	Leu	Ser	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile
					485						490					495
15	Leu	Ile	Ala	Val	Leu	Gly	Ser	Ser	Met	Ile	Leu	Val	Ser	Ile	Phe	Ile
				500					505						510	
20	Ile	Ile	Lys	Lys	Thr	Lys	Lys	Phe	Thr	Gly	Ala	Phe	Phe	Glu	Leu	Ser
			515					520					525			
	Gly	Val	Thr	Asn	Asn	Gly	Phe	Ile	Phe	His	Asn					
	530						535									

<210> 100
 <211> 539
 <212> PRT
 25 <213> Artificial Sequence

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 30 <400> 100

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55

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15
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 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30
 10
 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
 15
 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80
 20
 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
 25
 Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125
 30
 35
 40
 45
 50
 55

Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140
 5
 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
 10
 Ile Asn Lys Asn Lys Cys Pro Ile Asp Asp Leu Lys Met Ala Val Ser
 180 185 190
 15
 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205
 20
 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
 25
 Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
 245 250 255
 30
 Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
 260 265 270
 35
 Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285
 40
 Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
 290 295 300
 45
 Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
 305 310 315 320
 50
 Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
 325 330 335
 55
 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
 60
 Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys

	370		375		380												
5	Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile	
	385					390					395					400	
10	Lys	Gln	Leu	Asn	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp	
				405						410					415		
15	Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly	
			420					425						430			
20	Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro	
			435					440						445			
25	Ile	Lys	Phe	Pro	Glu	Asp	Gln	Phe	Gln	Val	Ala	Leu	Asp	Gln	Val	Phe	
	450						455						460				
30	Glu	Asn	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Arg	Ile	
	465					470					475					480	
35	Leu	Ser	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile	
				485						490						495	
40	Leu	Ile	Ala	Val	Leu	Gly	Ser	Ser	Met	Ile	Leu	Val	Ser	Ile	Phe	Ile	
			500						505					510			
45	Ile	Ile	Lys	Lys	Thr	Lys	Lys	Pro	Thr	Gly	Ala	Pro	Pro	Glu	Leu	Ser	
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50	Gly	Val	Thr	Asn	Asn	Gly	Phe	Ile	Pro	His	Asn						
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<220>
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<400> 101

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5 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
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10 Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
 35 40 45

15

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Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
 50 55 60

5 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
 10 85 90 95

Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110

15 Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125

20 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
 145 150 155 160

25 Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
 165 170 175

30 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
 35 195 200 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 210 215 220

40 Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln
 225 230 235 240

45 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
 50 260 265 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
 275 280 285

55 Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg

	290		295		300												
5	Glu 305	Asp	Gln	Gly	Trp	Tyr 310	Cys	Gln	Asn	Ala	Gly 315	Ser	Thr	Val	Tyr	Tyr 320	
10	Pro	Asn	Glu	Lys	Asp 325	Cys	Glu	Thr	Arg	Gly 330	Asp	His	Val	Phe	Cys	Asp 335	
15	Thr	Ala	Ala	Gly 340	Ile	Asn	Val	Ala	Glu	Gln 345	Ser	Lys	Glu	Cys	Asn	Ile 350	
20	Asn	Ile	Ser	Thr	Thr	Asn	Tyr 355	Pro	Cys	Lys	Val 360	Ser	Thr	Gly	Arg	His 365	
25	Pro	Ile	Ser	Met	Val	Ala	Leu 370	Ser	Pro	Leu	Gly 375	Ala	Leu	Val	Ala	Cys 380	
30	Tyr	Lys	Gly	Val	Ser	Cys	Ser 385	Ile	Gly	Ser	Asn 390	Arg	Val	Gly	Ile	Ile 400	
35	Lys	Gln	Leu	Asn	Lys 405	Gly	Cys	Ser	Tyr	Ile 410	Thr	Asn	Gln	Asp	Ala	Asp 415	
40	Thr	Val	Thr	Ile 420	Asp	Asn	Thr	Val	Tyr	Gln 425	Leu	Ser	Lys	Val	Gln	Gly 430	
45	Glu	Gln	His	Val	Ile 435	Lys	Gly	Arg	Pro	Val 440	Ser	Ser	Ser	Phe	Asp	Pro 445	
50	Ile	Lys	Phe	Pro	Glu	Asp 450	Gln	Phe	Gln	Val 455	Ala	Leu	Asp	Gln	Val	Phe 460	
55	Glu	Asn	Ile	Glu	Asn	Ser 465	Gln	Ala	Leu	Val 470	Asp	Gln	Ser	Asn	Arg	Ile 475	
60	Leu	Ser	Ser	Ala	Glu 485	Lys	Gly	Asn	Thr	Gly 490	Phe	Ile	Ile	Val	Ile	Ile 495	
65	Leu	Ile	Ala	Val 500	Leu	Gly	Ser	Ser	Met	Ile 505	Leu	Val	Ser	Ile	Phe	Ile 510	
70	Ile	Ile	Lys	Lys	Thr	Lys	Lys	Pro	Thr	Gly 515	Ala	Pro	Pro	Glu	Leu	Ser 520	
75	Gly	Val	Thr	Asn	Asn	Gly	Phe 530	Ile	Pro	His	Asn						

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<220>
<223> Synthetic Polypeptide

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Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
 1 5 10 15
 5 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30
 10 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
 15 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80
 20 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95
 25 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
 30 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 130 135 140
 35 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
 145 150 155 160
 40 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
 45 Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
 195 200 205
 50 Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
 55

	210		215		220												
5	Ala 225	Glu	Leu	Ala	Arg	Ala	Val	Pro	Asn	Met	Pro	Thr	Ser	Ala	Gly	Gln	240
						230					235						
10	Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe	255
					245					250					255		
15	Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln	270
				260					265					270			
20	Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala	285
				275				280					285				
25	Ala	Pro	Ser	Cys	Ser	Glu	Lys	Lys	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg	300
	290						295					300					
30	Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Gln	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr	320
	305					310					315						
35	Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp	335
				325						330					335		
40	Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Gln	Gln	Ser	Lys	Glu	Cys	Asn	Ile	350
				340					345					350			
45	Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His	365
			355				360						365				
50	Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys	380
	370						375					380					
55	Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile	400
	385					390					395						
60	Lys	Gln	Leu	Asn	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp	415
				405						410					415		
65	Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly	430
				420					425					430			
70	Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Pro	Pro	445
			435					440					445				
75	Ile	Lys	Phe	Pro	Glu	Asp	Gln	Phe	Gln	Val	Ala	Leu	Asp	Gln	Val	Phe	460
	450						455					460					

	Glu	Asn	Ile	Glu	Asn	Ser	Gln	Ala	Leu	Val	Asp	Gln	Ser	Asn	Arg	Ile
	465					470					475					480
5																
	Leu	Ser	Ser	Ala	Glu	Lys	Gly	Asn	Thr	Gly	Phe	Ile	Ile	Val	Ile	Ile
					485					490						495
10																
	Leu	Ile	Ala	Val	Leu	Gly	Ser	Ser	Met	Ile	Leu	Val	Ser	Ile	Phe	Ile
				500					505					510		
15																
	Ile	Ile	Lys	Lys	Thr	Lys	Lys	Pro	Thr	Gly	Ala	Pro	Pro	Glu	Leu	Ser
			515					520					525			
20																
	Gly	Val	Thr	Asn	Asn	Gly	Phe	Ile	Pro	His	Asn					
	530						535									
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30	<400>	103														
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Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
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 5
 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30
 10
 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
 15
 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
 65 70 75 80
 20
 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
 85 90 95
 25
 Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
 100 105 110
 30
 Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
 115 120 125
 35
 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
 40
 45
 50
 55

	130					135						140					
5	Asn	Glu	Ala	Val	Ser	Thr	Leu	Gly	Asn	Gly	Val	Arg	Val	Leu	Ala	Thr	
	145					150					155					160	
10	Ala	Val	Arg	Glu	Leu	Lys	Asp	Phe	Val	Ser	Lys	Asn	Leu	Thr	Arg	Ala	
					165					170					175		
15	Ile	Asn	Lys	Asn	Lys	Cys	Asp	Ile	Asp	Asp	Leu	Lys	Met	Ala	Val	Ser	
				180					185					190			
20	Phe	Ser	Gln	Phe	Asn	Arg	Arg	Phe	Leu	Asn	Val	Val	Arg	Gln	Phe	Ser	
			195				200						205				
25	Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Thr	Asp	
	210					215						220					
30	Ala	Glu	Leu	Ala	Arg	Ala	Val	Pro	Asn	Met	Pro	Thr	Ser	Ala	Gly	Gln	
	225				230						235					240	
35	Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe	
				245						250					255		
40	Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln	
			260					265						270			
45	Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala	
			275					280					285				
50	Ala	Pro	Ser	Cys	Ser	Glu	Lys	Lys	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg	
	290						295					300					
55	Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Gln	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr	
	305					310					315					320	
60	Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp	
				325						330					335		
65	Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Lys	Glu	Cys	Asn	Ile	
			340						345					350			
70	Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His	
			355					360					365				
75	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
 5 Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 405 410 415
 10 Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430
 15 Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
 435 440 445
 20 Ile Lys Phe Pro Glu Asn Gln Phe Gln Val Ala Leu Asp Gln Val Phe
 450 455 460
 25 Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 465 470 475 480
 30 Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 485 490 495
 35 Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510
 40 Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525
 45 Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
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<211> 539

40 <212> PRT

<213> Artificial Sequence

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<223> Synthetic Polypeptide

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<400> 104

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Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
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 5 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
 20 25 30
 10 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
 15
 20
 25
 30
 35
 40
 45
 50
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	50		55		60														
5	Ser	Leu	Ile	Lys	Thr	Glu	Leu	Asp	Leu	Thr	Lys	Ser	Ala	Leu	Arg	Glu			
	65					70					75					80			
10	Leu	Lys	Thr	Val	Ser	Ala	Asp	Gln	Leu	Ala	Arg	Glu	Glu	Gln	Ile	Glu			
					85						90					95			
15	Asn	Pro	Gly	Ser	Gly	Ser	Phe	Val	Leu	Gly	Ala	Ile	Ala	Leu	Gly	Val			
				100					105					110					
20	Ala	Ala	Ala	Ala	Ala	Val	Thr	Ala	Gly	Val	Ala	Ile	Ala	Lys	Thr	Ile			
				115				120					125						
25	Arg	Leu	Glu	Ser	Glu	Val	Thr	Ala	Ile	Asn	Asn	Ala	Leu	Lys	Lys	Thr			
	130						135					140							
30	Asn	Glu	Ala	Val	Ser	Thr	Leu	Gly	Asn	Gly	Val	Arg	Val	Leu	Ala	Thr			
	145					150					155					160			
35	Ala	Val	Arg	Glu	Leu	Lys	Asp	Phe	Val	Ser	Lys	Asn	Leu	Thr	Arg	Ala			
				165						170					175				
40	Ile	Asn	Lys	Asn	Lys	Cys	Asp	Ile	Asp	Asp	Leu	Lys	Met	Ala	Val	Ser			
			180						185					190					
45	Phe	Ser	Gln	Phe	Asn	Arg	Arg	Phe	Leu	Asn	Val	Val	Arg	Gln	Phe	Ser			
	195						200						205						
50	Asp	Asn	Ala	Gly	Ile	Thr	Pro	Ala	Ile	Ser	Leu	Asp	Leu	Met	Thr	Asp			
	210						215					220							
55	Ala	Glu	Leu	Ala	Arg	Ala	Val	Pro	Asn	Met	Pro	Thr	Ser	Ala	Gly	Gln			
	225					230					235					240			
60	Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe			
				245						250					255				
65	Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln			
				260					265					270					
70	Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala			
	275							280					285						
75	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
 5
 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
 10 340 345 350
 Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
 355 360 365
 15
 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
 20 385 390 395 400
 Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
 25 405 410 415
 Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
 420 425 430
 30
 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
 35 450 455 460
 Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
 40 465 470 475 480
 Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
 45 485 490 495
 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
 55 530 535

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Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
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5 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
20 25 30

10 Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45

15 Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
50 55 60

20 Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65 70 75 80

25 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
85 90 95

30 Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100 105 110

35 Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
115 120 125

40 Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr
130 135 140

45 Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145 150 155 160

50 Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
165 170 175

55 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
5	Ile	Lys	Leu	Met	Leu	Glu	Asn	Arg	Ala	Met	Val	Arg	Arg	Lys	Gly	Phe
				245						250					255	
10	Gly	Ile	Leu	Ile	Gly	Val	Tyr	Gly	Ser	Ser	Val	Ile	Tyr	Met	Val	Gln
			260						265					270		
15	Leu	Pro	Ile	Phe	Gly	Val	Ile	Asp	Thr	Pro	Cys	Trp	Ile	Val	Lys	Ala
			275					280					285			
20	Ala	Pro	Ser	Cys	Ser	Glu	Lys	Lys	Gly	Asn	Tyr	Ala	Cys	Leu	Leu	Arg
	290						295					300				
25	Glu	Asp	Gln	Gly	Trp	Tyr	Cys	Gln	Asn	Ala	Gly	Ser	Thr	Val	Tyr	Tyr
	305					310					315					320
30	Pro	Asn	Glu	Lys	Asp	Cys	Glu	Thr	Arg	Gly	Asp	His	Val	Phe	Cys	Asp
				325						330					335	
35	Thr	Ala	Ala	Gly	Ile	Asn	Val	Ala	Glu	Gln	Ser	Lys	Glu	Cys	Asn	Ile
			340						345					350		
40	Asn	Ile	Ser	Thr	Thr	Asn	Tyr	Pro	Cys	Lys	Val	Ser	Thr	Gly	Arg	His
			355					360					365			
45	Pro	Ile	Ser	Met	Val	Ala	Leu	Ser	Pro	Leu	Gly	Ala	Leu	Val	Ala	Cys
	370						375					380				
50	Tyr	Lys	Gly	Val	Ser	Cys	Ser	Ile	Gly	Ser	Asn	Arg	Val	Gly	Ile	Ile
	385					390					395					400
55	Lys	Gln	Leu	Asn	Lys	Gly	Cys	Ser	Tyr	Ile	Thr	Asn	Gln	Asp	Ala	Asp
				405						410				415		
60	Thr	Val	Thr	Ile	Asp	Asn	Thr	Val	Tyr	Gln	Leu	Ser	Lys	Val	Glu	Gly
			420						425					430		
65	Glu	Gln	His	Val	Ile	Lys	Gly	Arg	Pro	Val	Ser	Ser	Ser	Phe	Asp	Pro
			435					440					445			
70	Ile	Lys	Phe	Pro	Glu	Asp	Gln	Phe	Gln	Val	Ala	Leu	Asp	Gln	Val	Phe
	450						455					460				
75	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

5 Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
 500 505 510

10 Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
 515 520 525

15 Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
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<400> 114

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<211> 1617

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<211> 1617

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35 <220>
 <223> Synthetic Polynucleotide

<400> 121

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<211> 1617

55 <212> DNA

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<220>

<223> Synthetic Polynucleotide

<400> 122

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<212> DNA

<213> Artificial Sequence

<220>

5 <223> Synthetic Polynucleotide

<400> 123

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35 <210> 124
 <211> 1617
 <212> DNA
 <213> Artificial Sequence

40 <220>
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<400> 124

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<210> 125
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 <212> DNA
 <213> Artificial Sequence

 <220>

<223> Synthetic Polynucleotide

<400> 125

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<211> 1617

<212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Polynucleotide

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<400> 126

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35 <210> 127
 <211> 1617
 <212> RNA
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40 <220>
 <223> Synthetic Polynucleotide

<400> 127

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<212> RNA
 <213> Artificial Sequence

<220>
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<400> 129

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<223> Synthetic Polynucleotide

<400> 131

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<210> 132

<211> 1617

<223> Synthetic Polynucleotide

<400> 134

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Patentkrav

1. Betacoronavirus-(BetaCoV)-messenger-RNA-(mRNA)-vaccine, der omfatter mindst ét mRNA-polynukleotid med en åben læseramme, der koder for mindst ét antigen BetaCoV-polypeptid;

hvor det mindst ene antigene BetaCoV-polypeptid er (a) et spike-(S)-protein eller et immunogent fragment deraf eller (b) en S1-underenhed eller en S2-underenhed af S-protein eller et immunogent fragment deraf;

hvor BetaCoV-vaccinen er formuleret i en lipidnanopartikel, hvor lipidnanopartiklen omfatter 40-60 % kationisk lipid, 5-15 % ikke-kationisk lipid, 1-2 % PEG-lipid og 30-50 % kolesterol.

2. Vaccine ifølge krav 1, hvor den åbne læseramme koder for et S-protein.

3. Vaccine ifølge krav 1, hvor den åbne læseramme koder for en S1-underenhed eller en S2-underenhed af S-protein.

4. Vaccine ifølge et hvilket som helst af kravene 1-3, hvor BetaCoV er MERS-CoV, SARS-CoV, HCoVOC43, HCoV-229E, HCoV-NL63 eller HCoV-HKU1.

5. Vaccine ifølge et hvilket som helst af kravene 1-4, hvor det mindst ene mRNA-polynukleotid omfatter en ikke-translateret 5'-region (UTR), en 3'-UTR, en 5'-cap og en poly(A)-hale.

6. Vaccine ifølge krav 5, hvor 5'-cap er en 5'-terminal-cap 7mG(5')ppp(5')NImpNp.

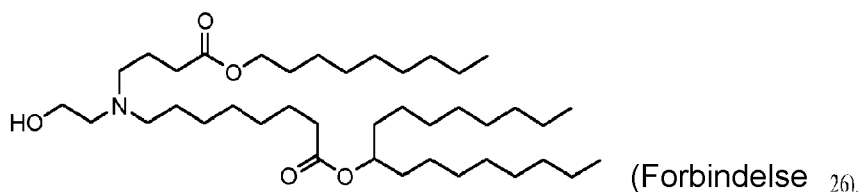
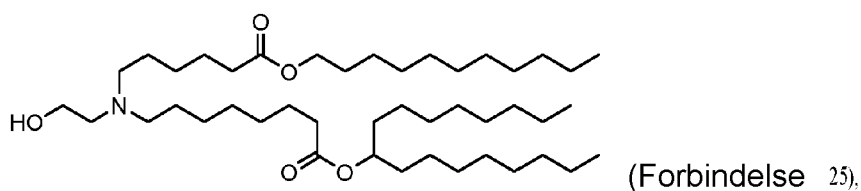
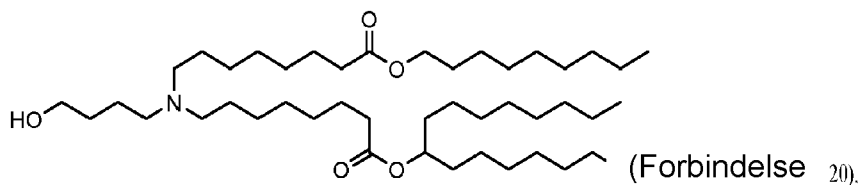
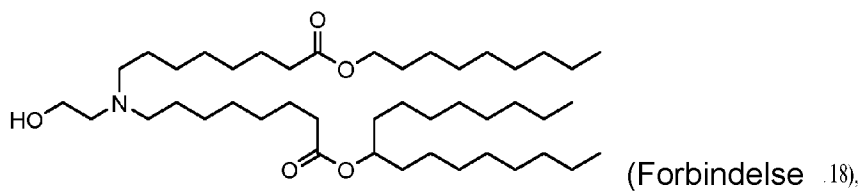
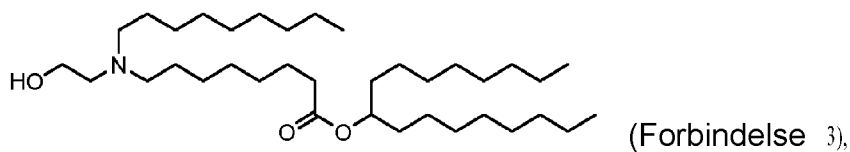
7. Vaccine ifølge et hvilket som helst af kravene 1-6, hvor det mindst ene mRNA-polynukleotid omfatter mindst én kemisk modifikation; eventuelt hvor den mindst ene kemiske modifikation er en N1-methylpseudouridinmodifikation eller en N1-ethylpseudouridinmodifikation.

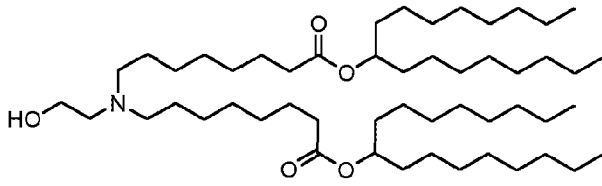
8. Vaccine ifølge krav 7, hvor mindst 80 % af uracil i den åbne læseramme har en kemisk modifikation.

9. Vaccine ifølge et hvilket som helst af kravene 1-8, hvor det kationiske lipid er et ioniserbart kationisk lipid, og det ikke-kationiske lipid er et neutralt lipid.

10. Vaccine ifølge krav 9, hvor det neutrale lipid er valgt blandt DSPC, DPPC, POPC, DOPE og SM.

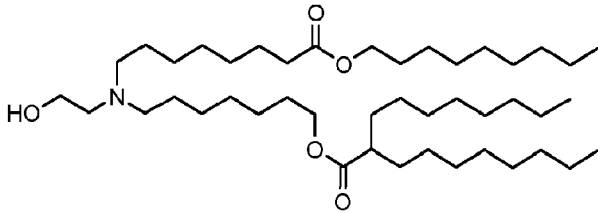
11. Vaccine ifølge et hvilket som helst af kravene 1-10, hvor lipidnanopartiklen omfatter en forbindelse af forbindelserne 3, 18, 20, 25, 26, 29, 30, 60, 108-112 eller 122:





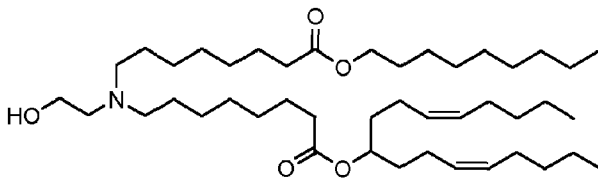
(Compound 29),

(Forbindelse)



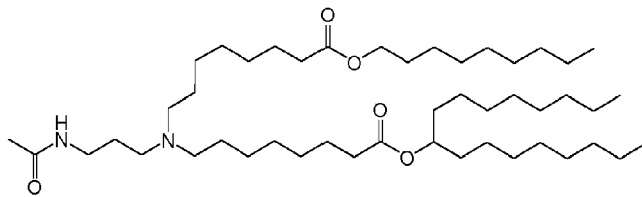
(Compound 30),

(Forbindelse)



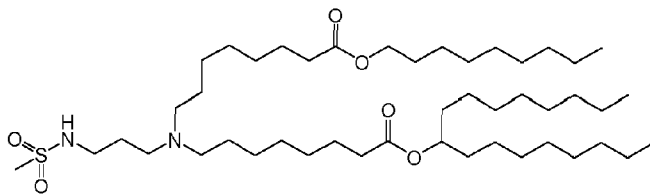
(Compound 60),

(Forbindelse)



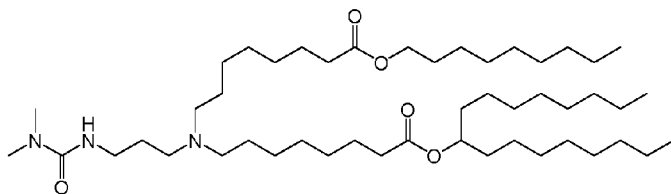
(Compound 108),

(Forbindelse)



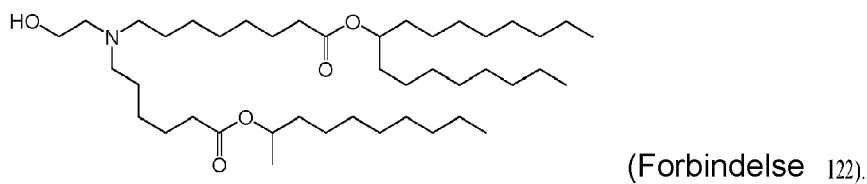
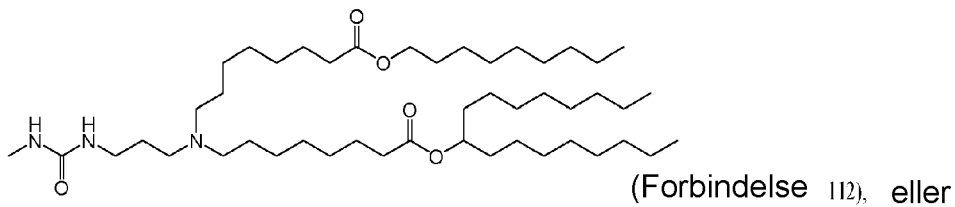
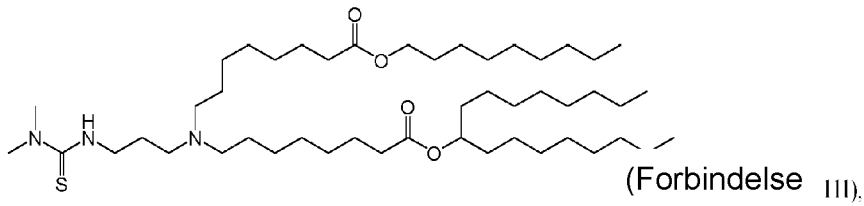
(Compound 109),

(Forbindelse)



(Compound 110),

(Forbindelse)



12. Vaccine ifølge et hvilket som helst af kravene 1-11 til anvendelse i en fremgangsmåde til forebyggelse og/eller behandling af en BetaCoV-sygdom hos et individ.

13. Vaccine til anvendelse ifølge krav 12, hvor vaccinen administreres til individet ved intradermal eller intramuskulær injektion.

DRAWINGS

Fig. 1

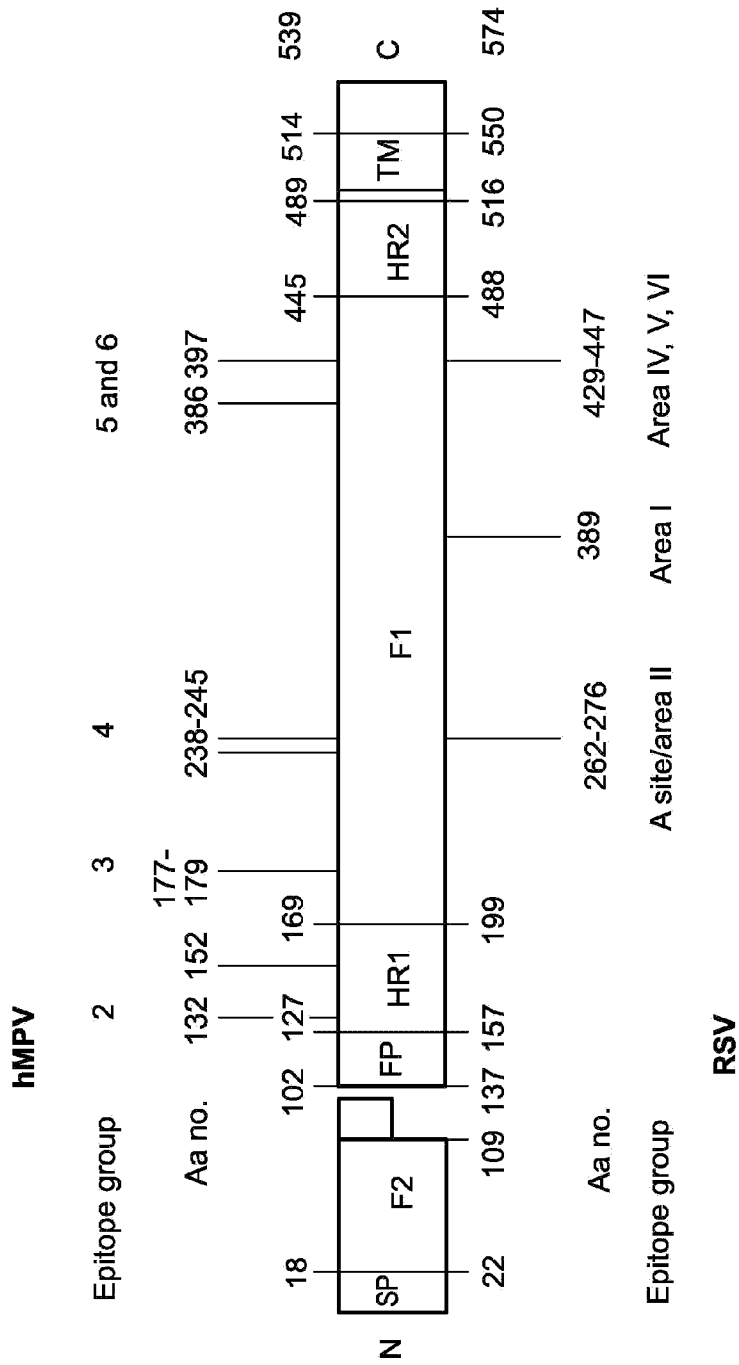


Fig. 2A

Day 0 serum titration

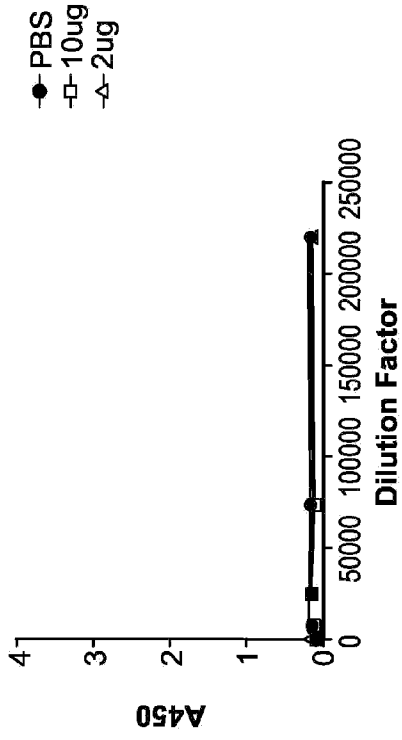


Fig. 2B

Day 14 serum titration

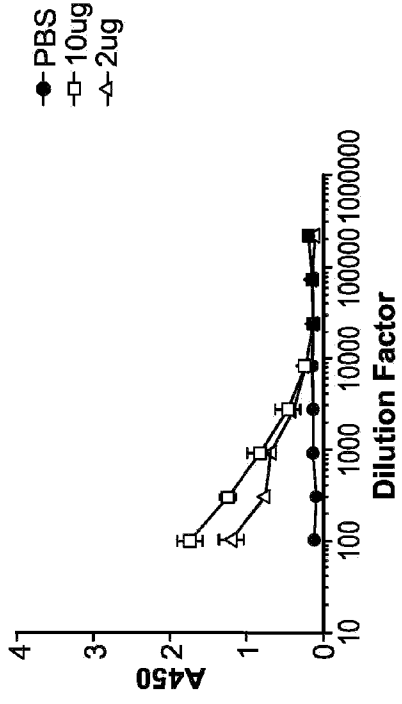


Fig. 2C Day 35 serum titration

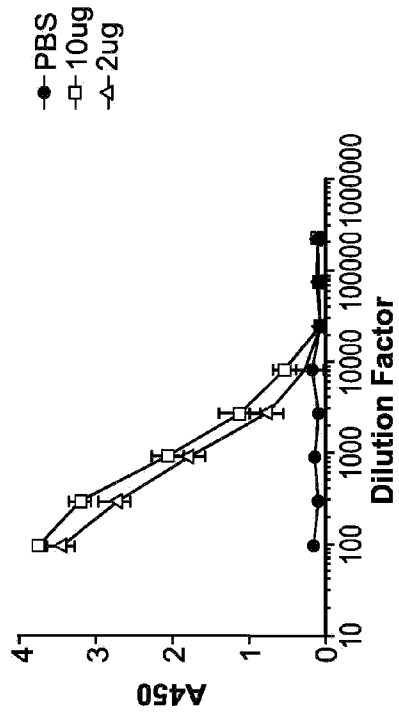


Fig. 3A

Mouse IgG2a - hMPV F specific



Fig. 3B

Mouse IgG1 - hMPV F specific

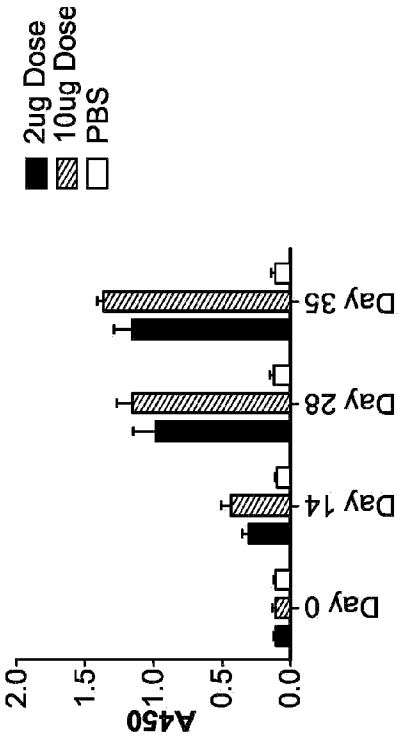


Fig. 3C

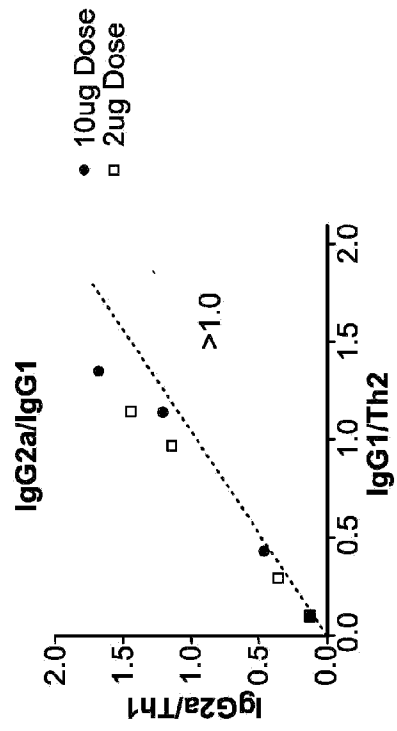


Fig. 4

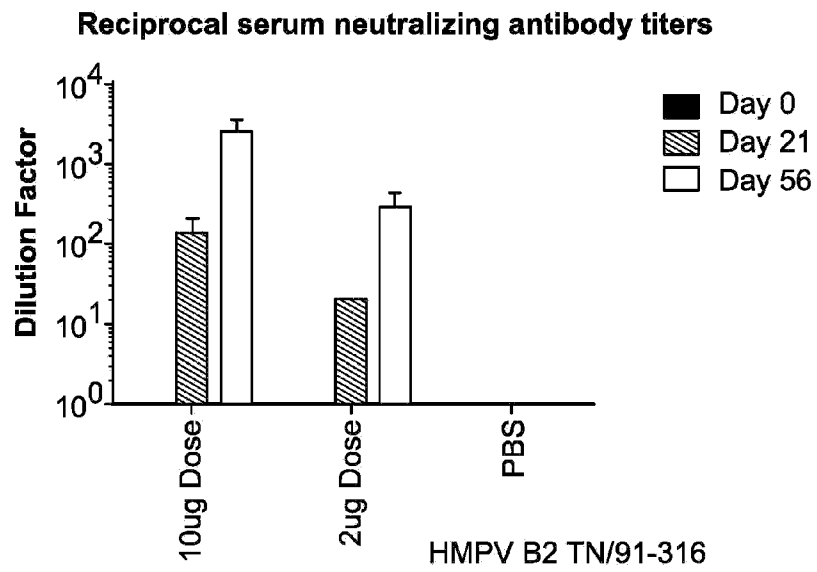
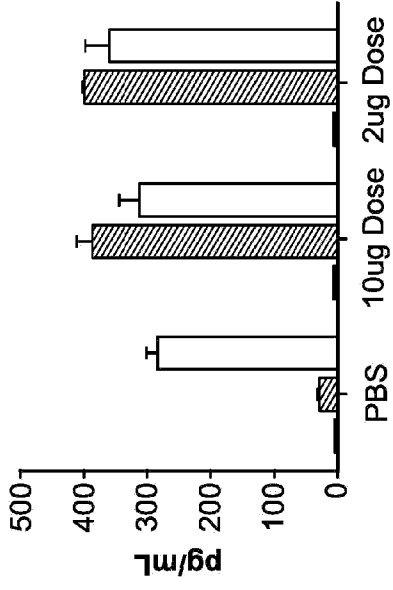


Fig. 5B

IL2



Media only
HMPV F peptide pool
Con-A

Fig. 5A

IFN- γ

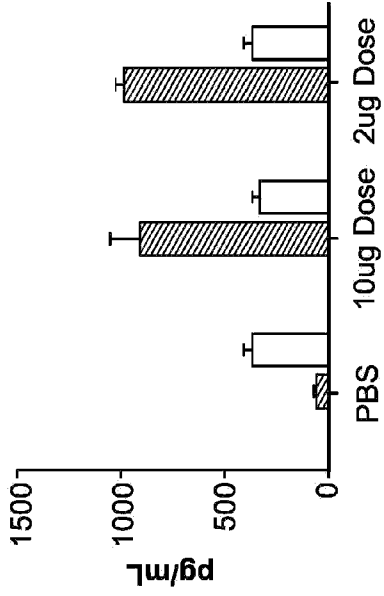
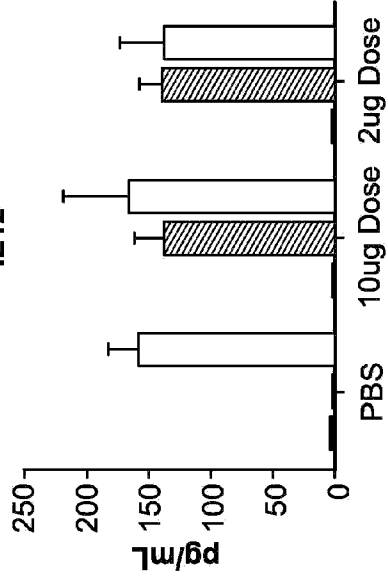
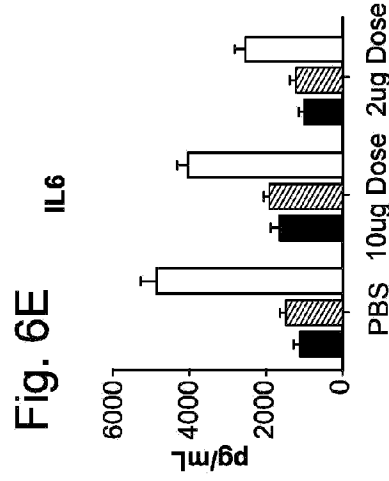
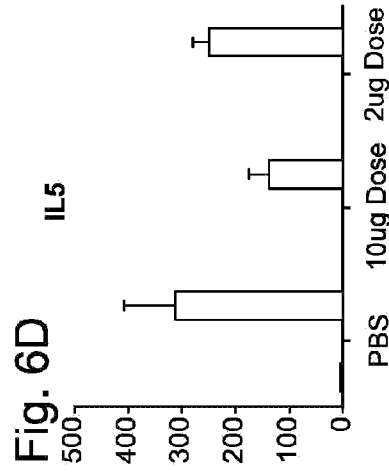
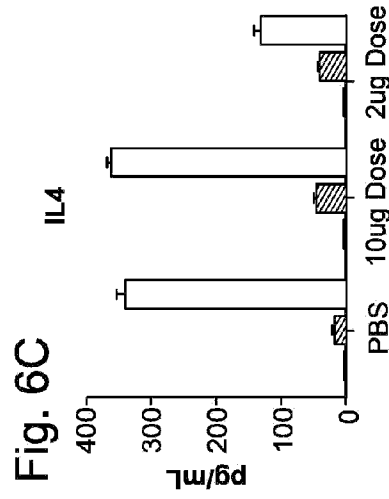
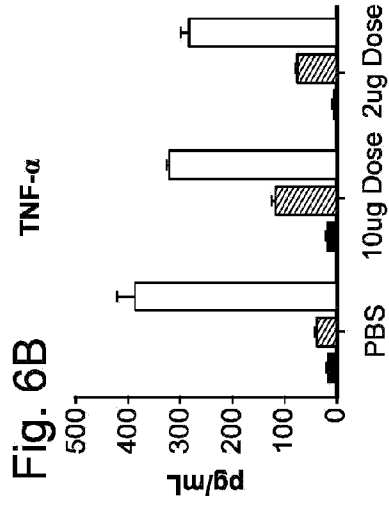
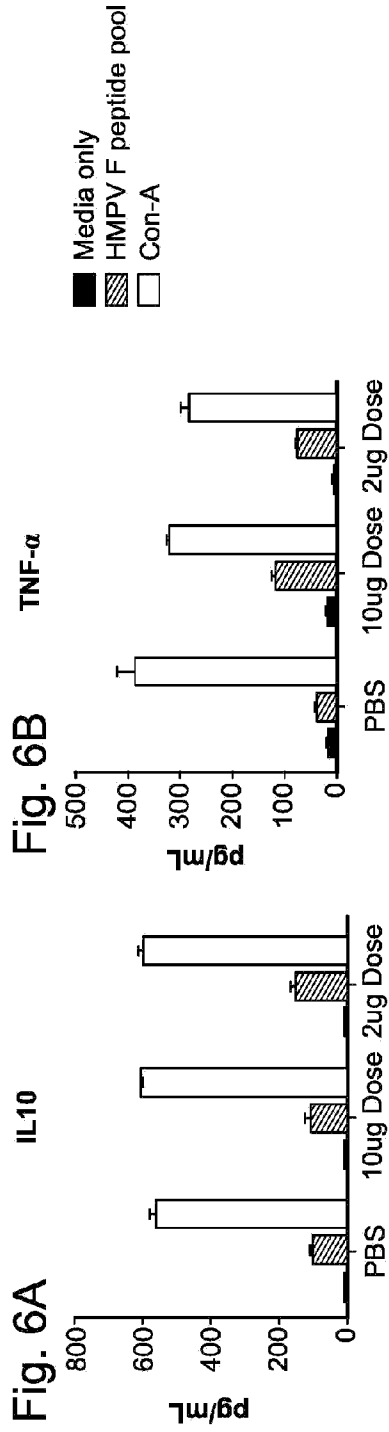
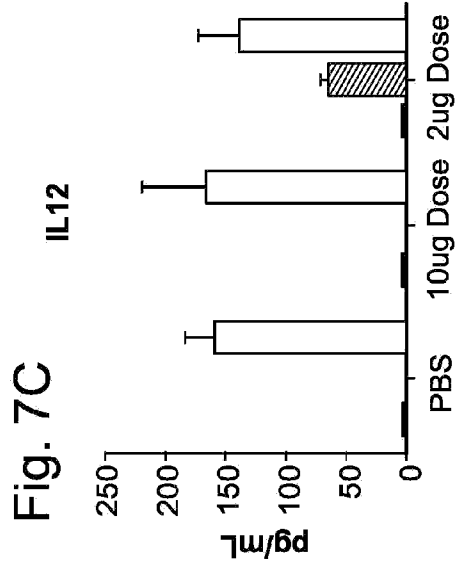
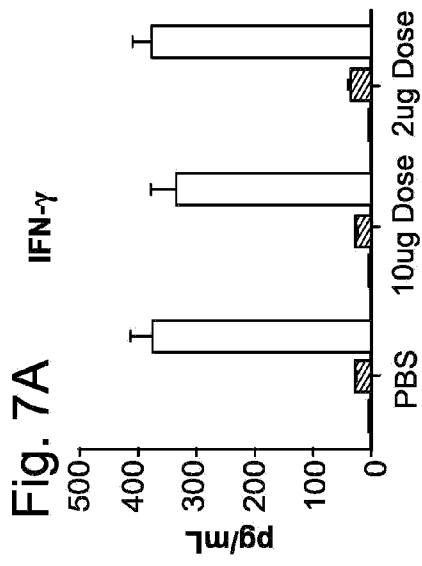
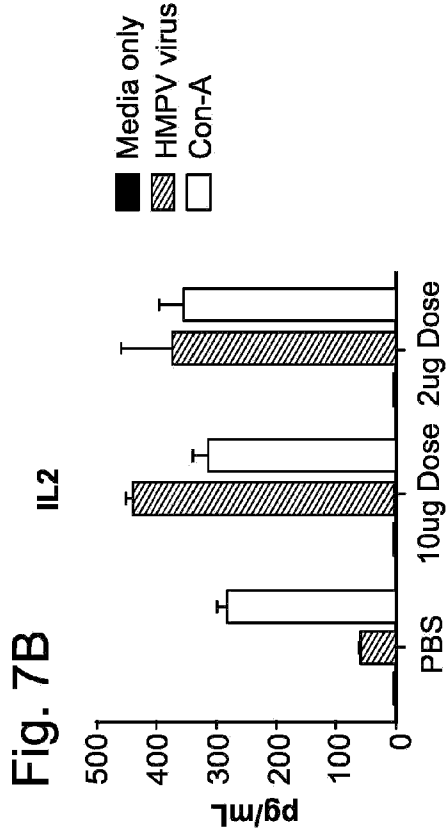


Fig. 5C

IL12







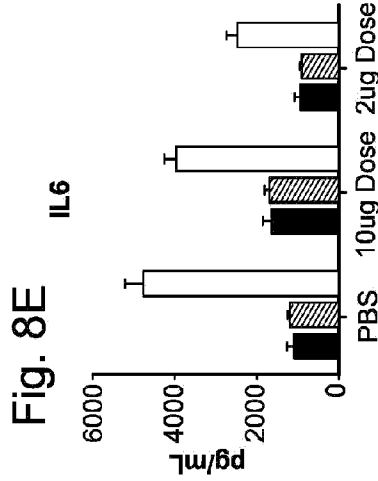
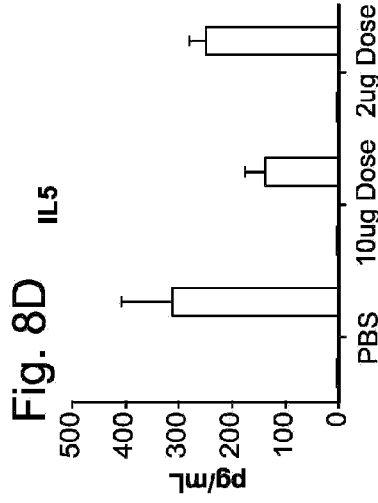
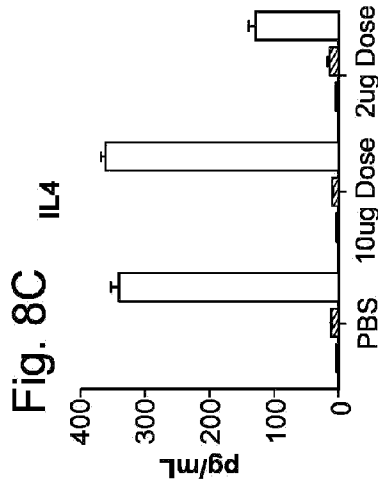
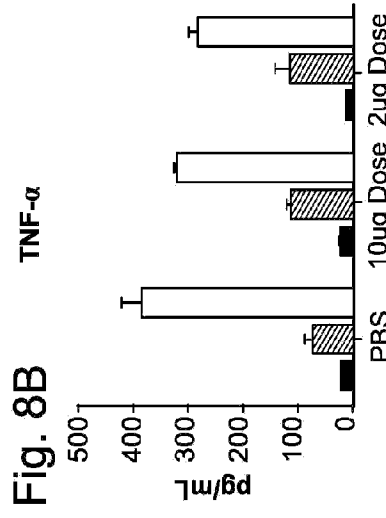
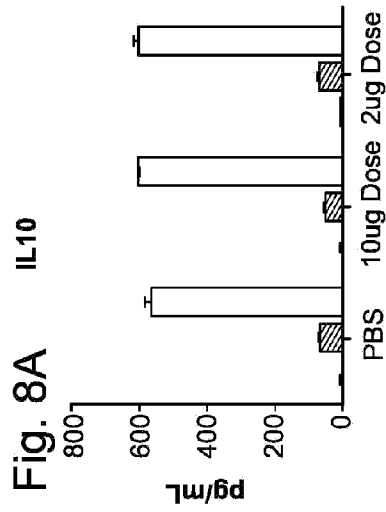


Fig. 9A

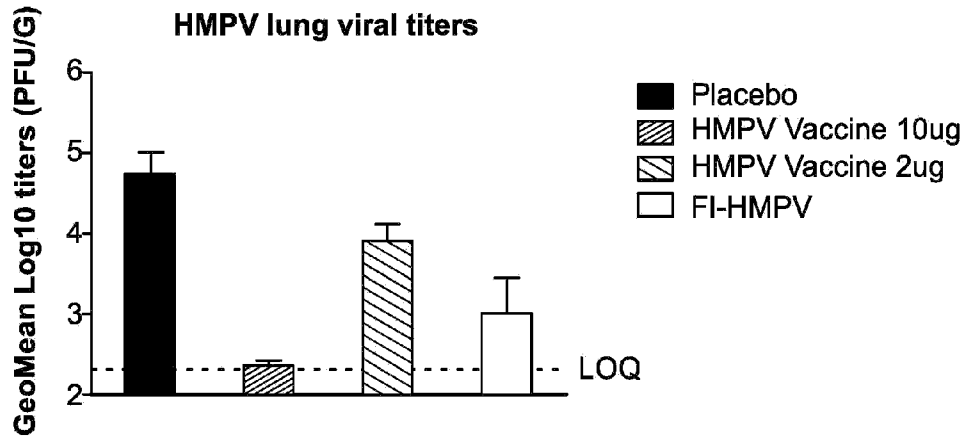


Fig. 9B

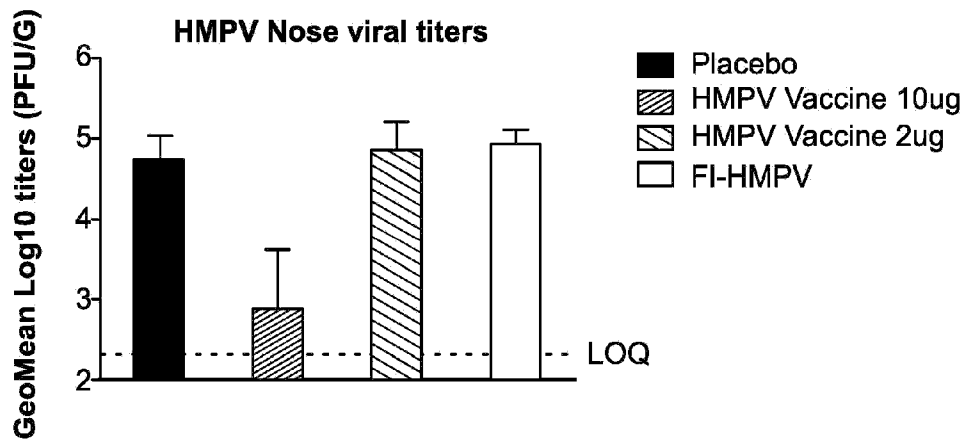


Fig. 10

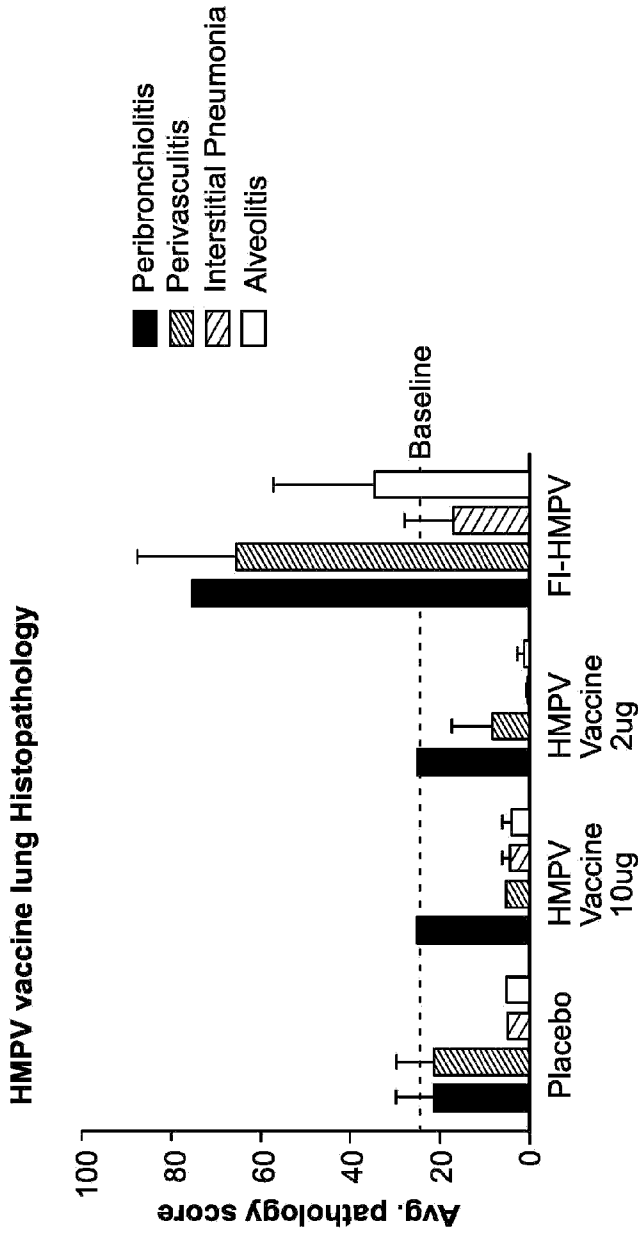
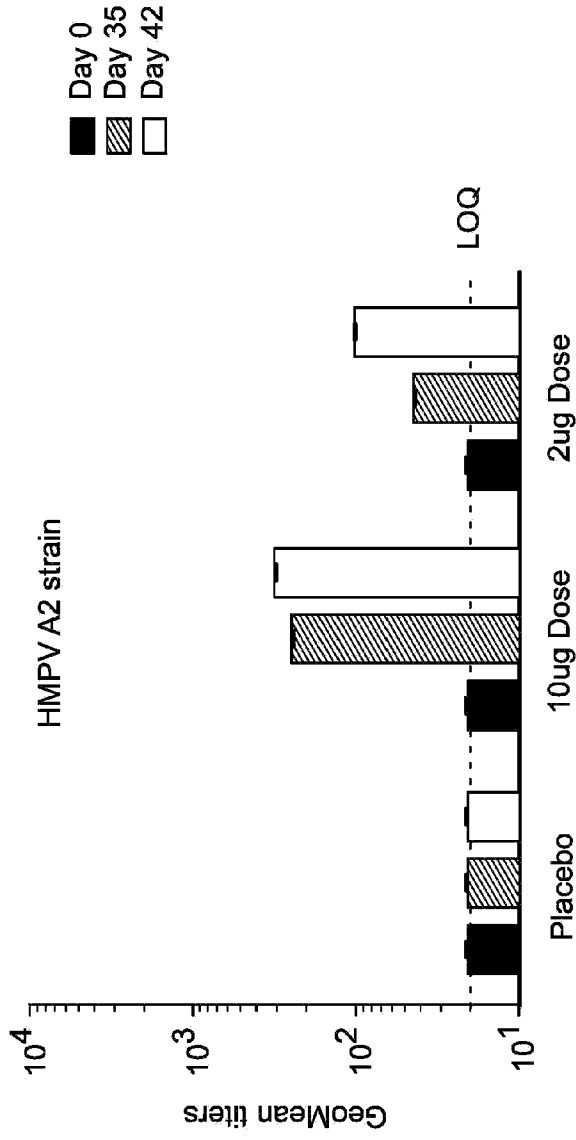


Fig. 11

HMPV neutralization antibody titers in cotton rats



Cotton rat viral load - HMPV challenge

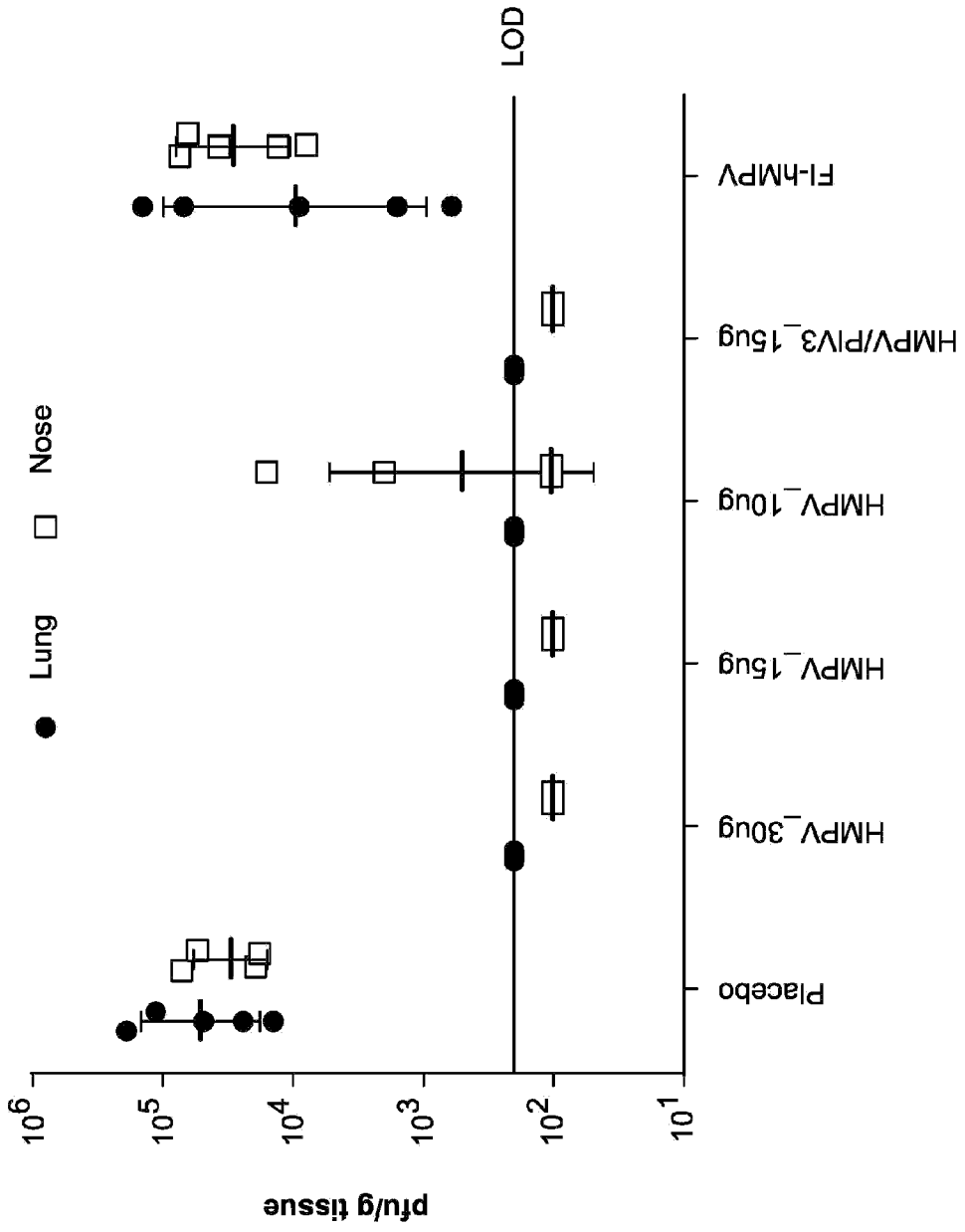


Fig. 12

Fig. 13

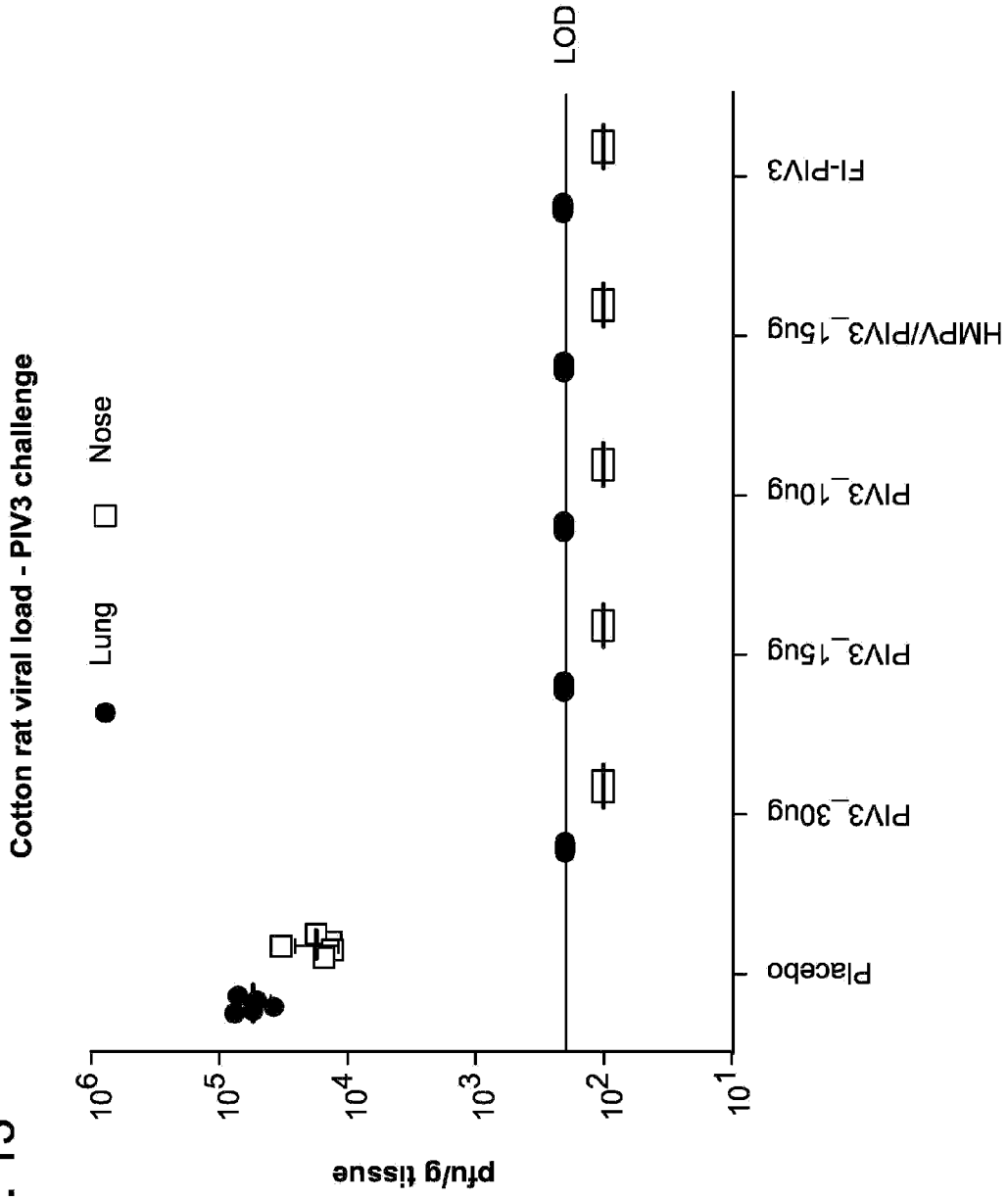


Fig. 14

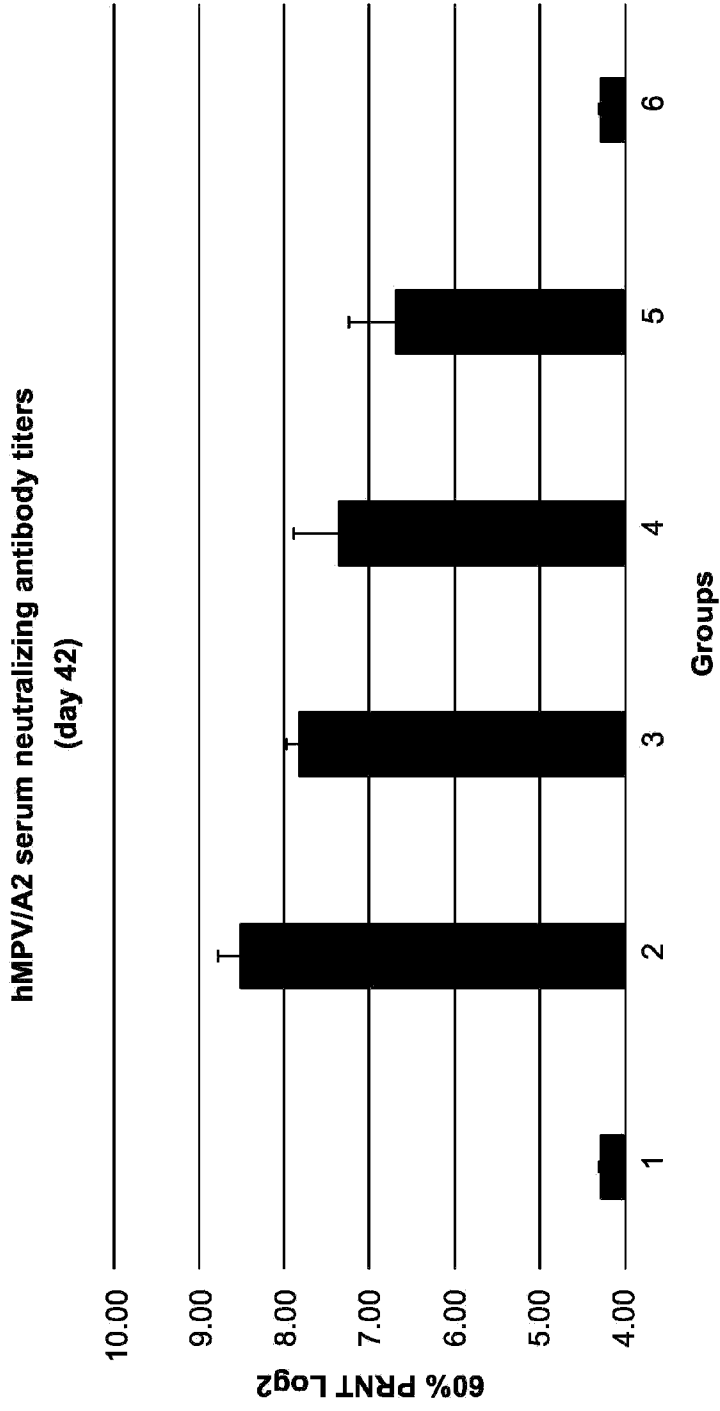


Fig. 15

PIV3 serum neutralizing antibody titers
(day 42)

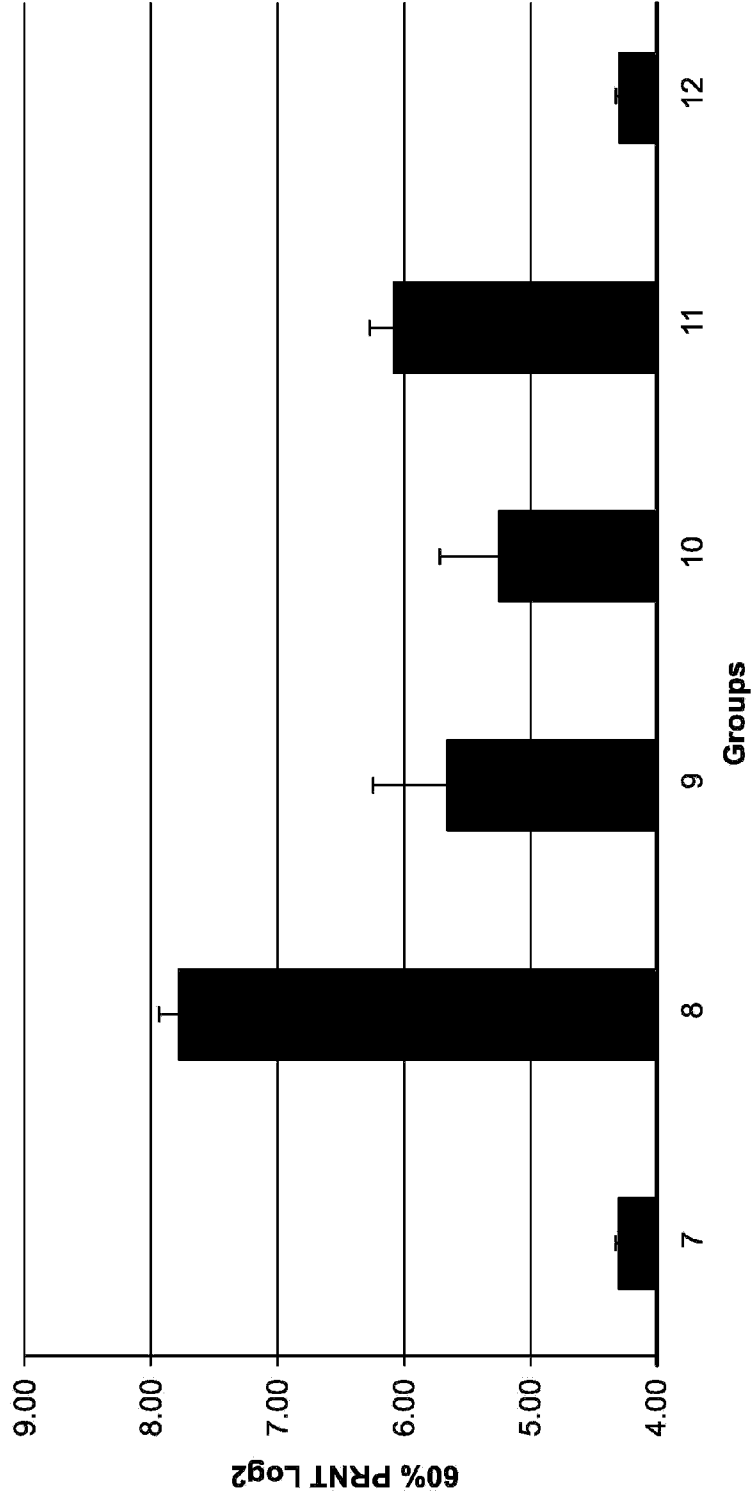


Fig. 16
Cotton rat lung histopathology

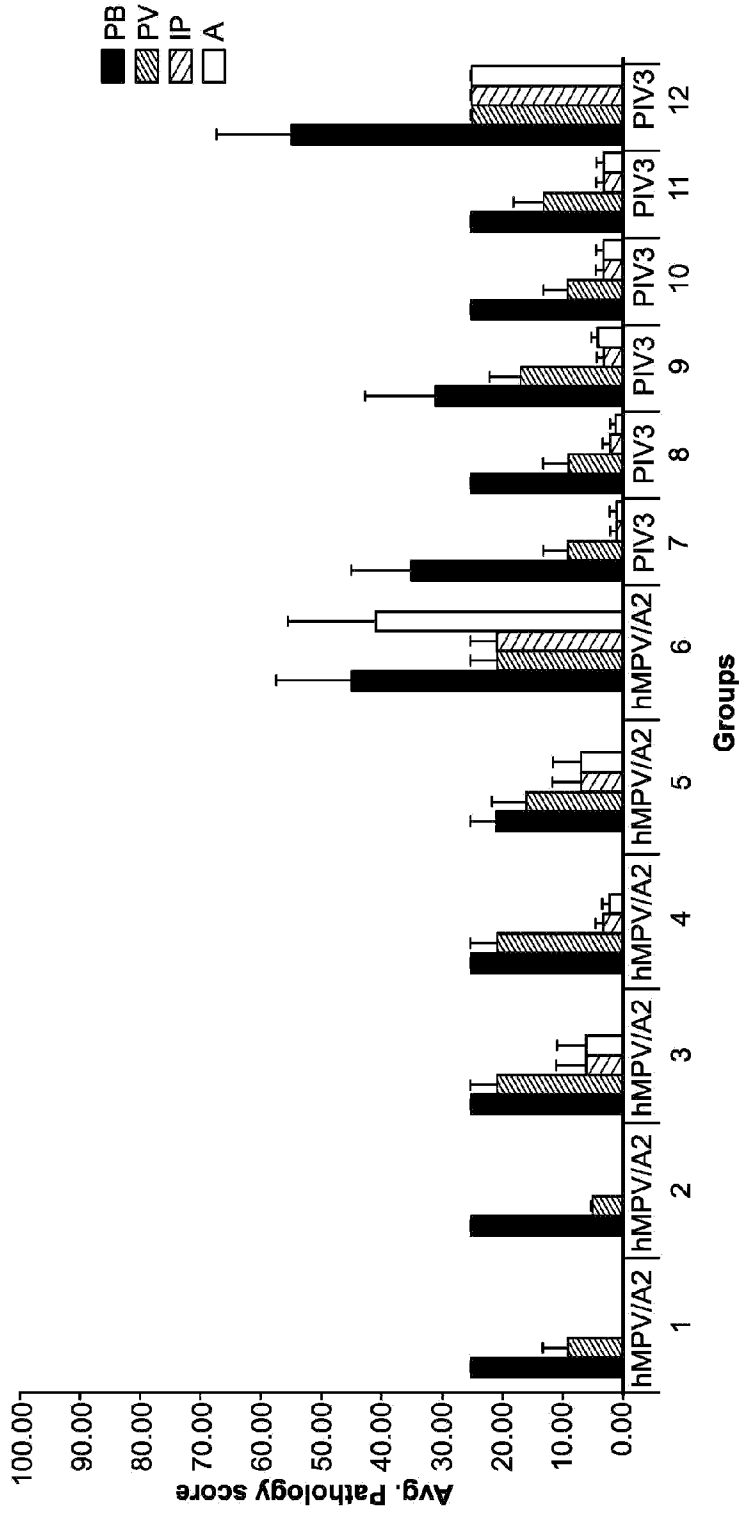


Fig. 17

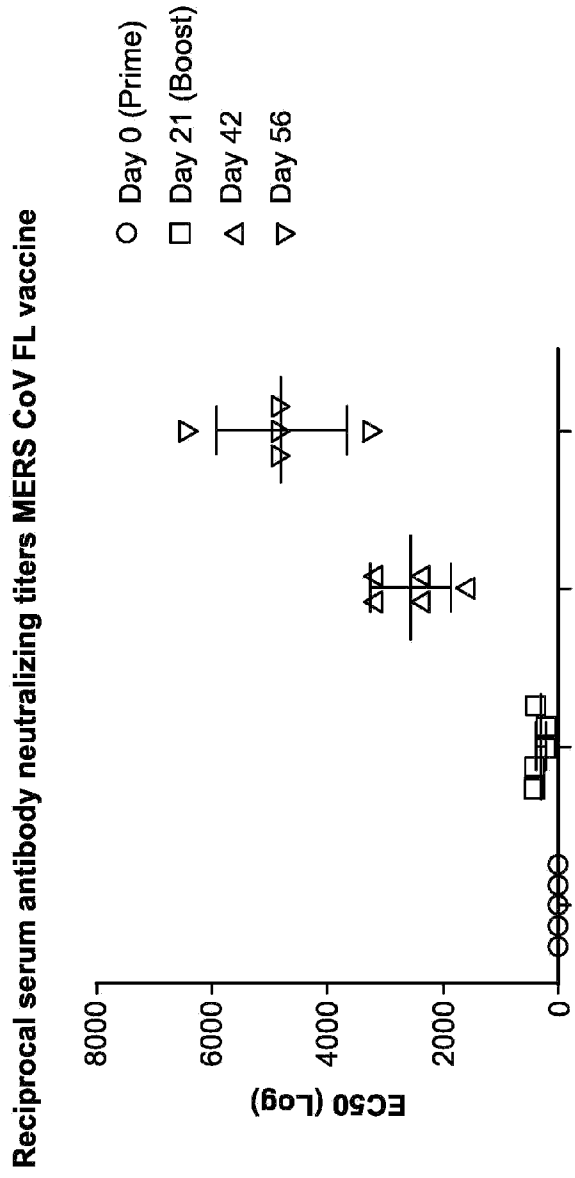


Fig.18

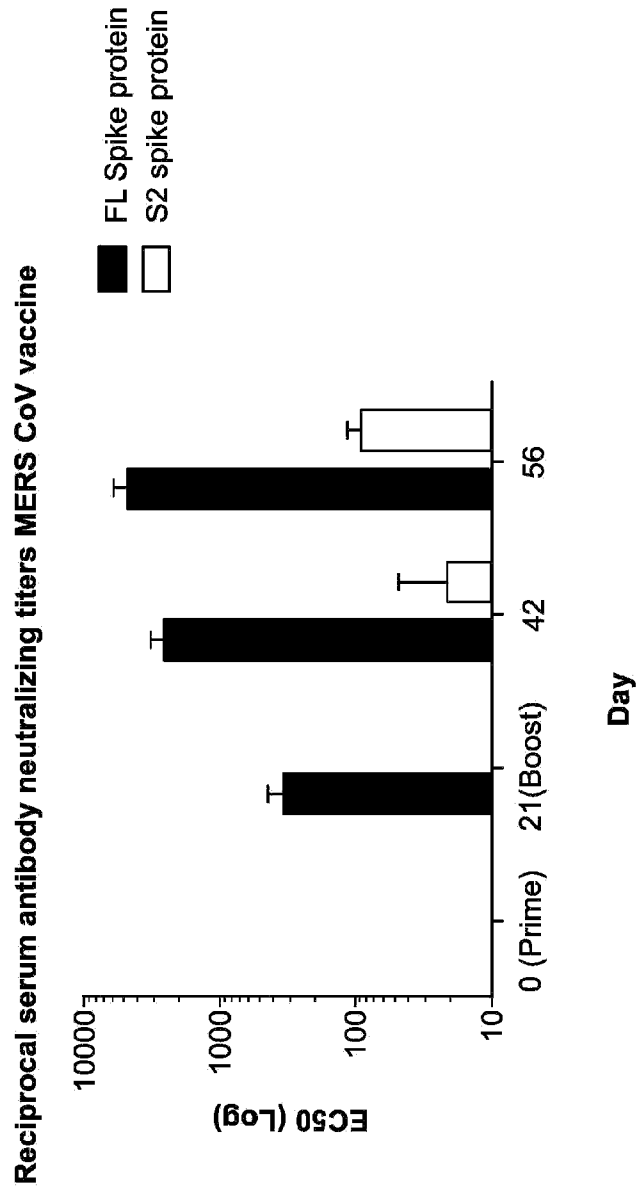


Fig. 19A

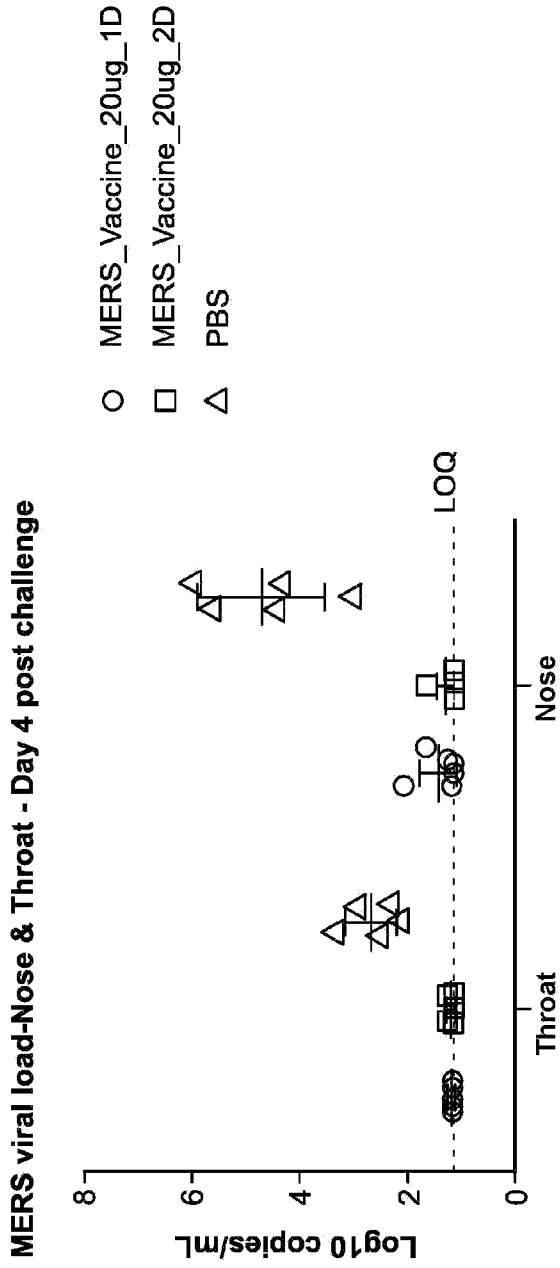


Fig. 19B

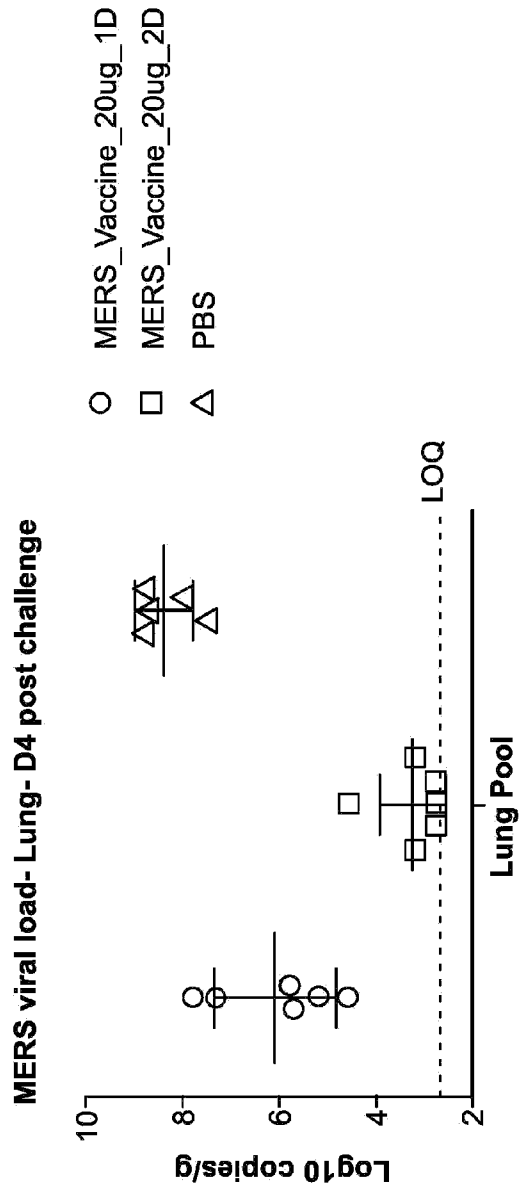


Fig. 19C

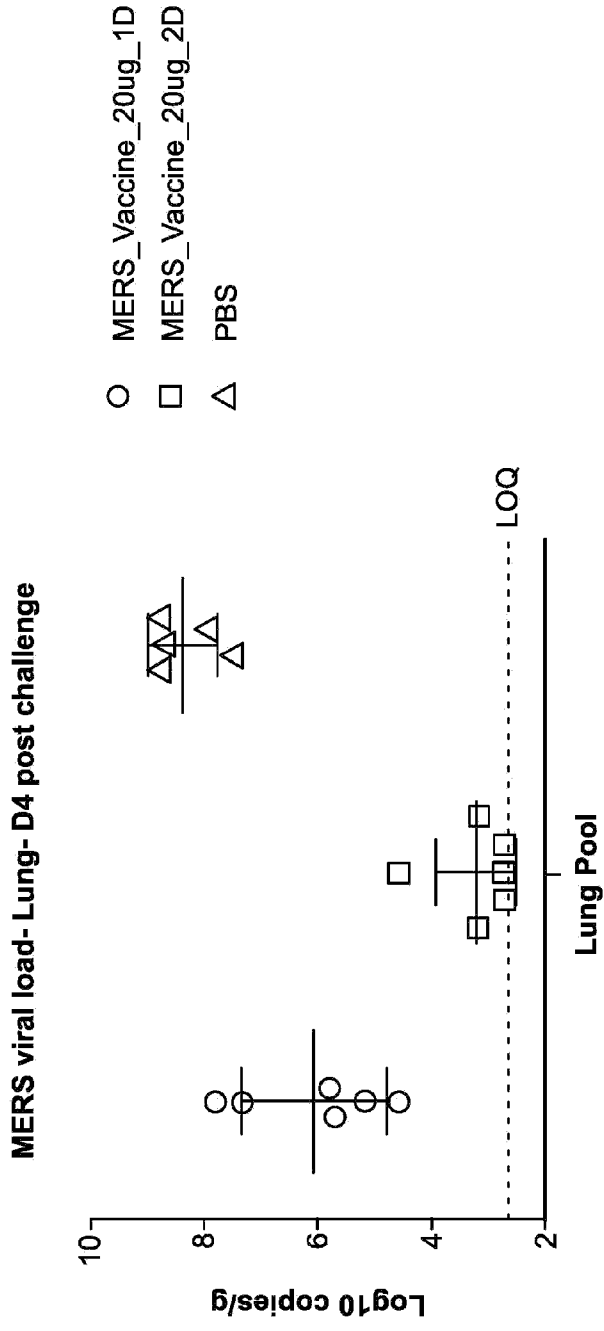
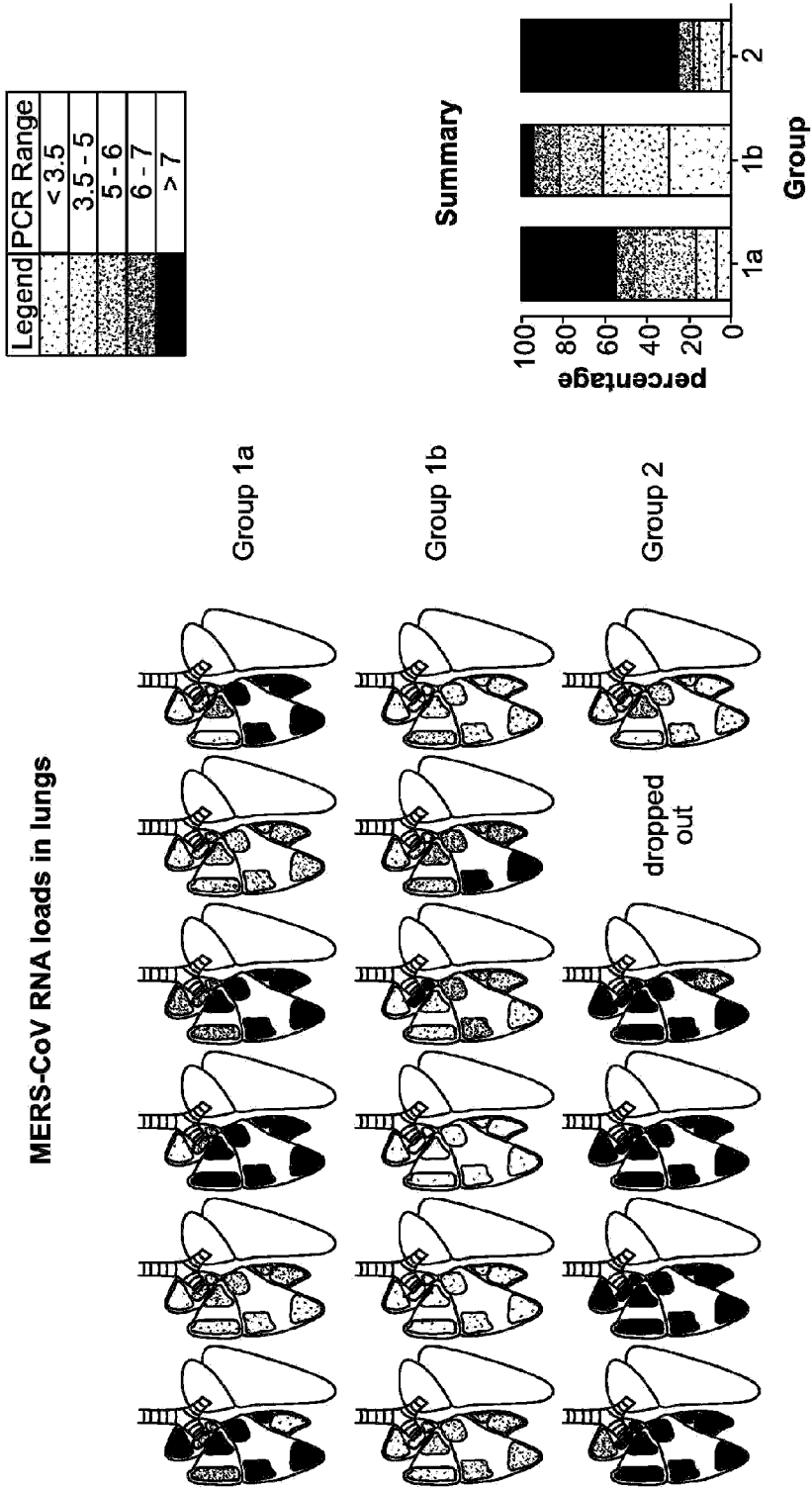


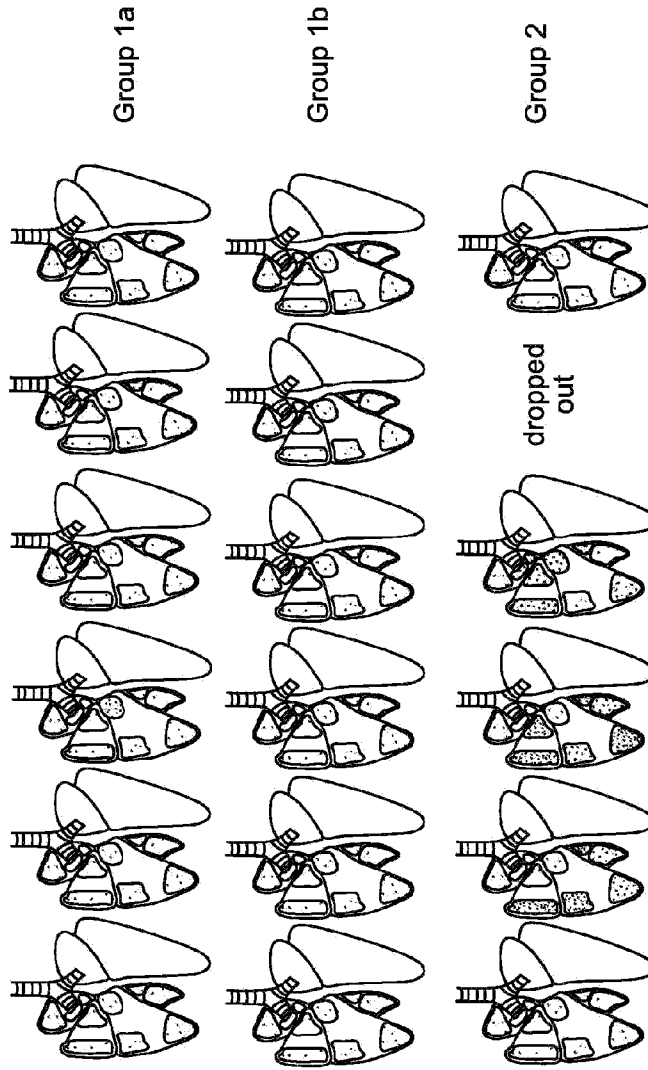
Fig. 20A



dropped out

Fig. 20B

MERS-CoV replication in lungs



Legend	TCID50 Range
[White box]	negative
[Light stippled box]	1 - 2
[Medium stippled box]	2 - 3
[Dark stippled box]	3 - 4
[Solid black box]	> 4

Summary

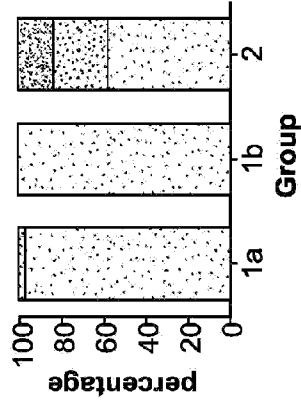


Fig. 21

