CLAIMS

1. A nucleic acid vaccine, comprising:

one or more RNA polynucleotides having an open reading frame encoding an antigenic polypeptide, formulated in a cationic lipid nanoparticle having a molar ratio of about 20-60% cationic lipid: about 5-25% non-cationic lipid: about 25-55% sterol; and about 0.5-15% PEG-modified lipid.

2. The vaccine of claim 1, wherein the cationic lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid.

3. The vaccine of claim 2, wherein the 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), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319).

4. The vaccine of claim 2 or 3, wherein the cationic lipid nanoparticle has a molar ratio of about 20-60% cationic lipid: about 5-25% non-cationic lipid: about 25-55% sterol; and about 0.5-15% PEG-modified lipid.

5. The vaccine of claim 2 or 3, wherein the cationic lipid nanoparticle comprises a molar ratio of about 50% cationic lipid, about 1.5% PEG-modified lipid, about 38.5% cholesterol and about 10% non-cationic lipid.

6. The vaccine of claim 2 or 3, wherein the cationic lipid nanoparticle comprises a molar ratio of about 55% cationic lipid, about 2.5% PEG lipid, about 32.5% cholesterol and about 10% non-cationic lipid.

7. The vaccine of claim 2, wherein the cationic lipid is an ionizable cationic lipid and the non-cationic lipid is a neutral lipid, and the sterol is a cholesterol.

8. The vaccine of any one of claims 1-7, wherein the open reading frame is codon-optimized.

9. The vaccine of any one of claims 1-8, wherein the antigenic polypeptide is derived from an infectious agent.

10. The vaccine of claim 9, wherein the infectious agent is selected from a member of the group consisting of strains of viruses and strains of bacteria.

11. The vaccine of any one of claims 1-8, wherein the one or more RNA polynucleotides encode a further antigenic polypeptide.

12. The vaccine of claim 1-8, wherein the one or more RNA polynucleotides comprise at least one chemical modification.

13. The vaccine of any one of claims 1-8, wherein the antigenic polypeptide is selected from those proteins listed in Tables 6-14, Tables 29-30, or antigenic fragments thereof.

14. The vaccine of any one of claims 1-8, wherein the open reading frame of the one or more RNA polynucleotides encodes an antigenic polypeptide selected from Tables 6-11, Tables 22-23, or antigenic fragments thereof.

15. The vaccine of any one of claims 1-8, wherein each of the open reading frame of the one or more RNA polynucleotides is selected from any of the RNA sequences from Table 28, or antigenic fragments thereof.

16. The vaccine of any one of claims 9-10, wherein the infectious agent is a strain of Influenza A or Influenza B or combinations thereof.

17. The vaccine of claim 16, wherein the strain of Influenza A or Influenza B is associated with birds, pigs, horses, dogs, humans or non-human primates.

18. The vaccine of any one of claims 1-16, wherein the antigenic polypeptide encodes a hemagglutinin protein or fragment thereof.

19. The vaccine of claim 18, wherein the hemagglutinin protein is H1, H2, H3, H4, H5, H6, H7, H8, H9, H10, H11, H12, H13, H14, H15, H16, H17, H18, or a fragment thereof.

20. The vaccine of claim 18 or 19, wherein the hemagglutinin protein does not comprise a head domain (HA1).

21. The vaccine of claim 18 or 19, wherein the hemagglutinin protein comprises a portion of the head domain (HA1).

22. The vaccine of any one of claim 18-21, wherein the hemagglutinin protein does not comprise a cytoplasmic domain.

23. The vaccine of any one of claim 18-21, wherein the hemagglutinin protein comprises a portion of the cytoplasmic domain.

24. The vaccine of any one of claims 18-23, wherein the truncated hemagglutinin protein.

25. The vaccine of any one of claims 18-23, wherein the truncated hemagglutinin protein comprises a portion of the transmembrane domain.

26. The vaccine of any one of claims 18- 25, wherein the amino acid sequence of the hemagglutinin protein or fragment thereof comprises at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97% 98%, or 99% identify with any of the amino acid sequences provided in Table 14-16.

27. The vaccine of claim 18, wherein the virus is selected from the group consisting of H1N1, H3N2, H7N9, and H10N8.

28. The vaccine of claim 18, wherein the antigenic polypeptide is selected from those proteins listed in Tables 6-12, or fragments thereof.

29. The vaccine of any one of claims 1-28, wherein the nucleic acid vaccine is multivalent.

30. The vaccine of claim 29, wherein the open reading frame of the one or more RNA polynucleotides encode at least 2, 3, 4, 5, 6, 7, 8, 9 or 10 antigenic polypeptides.

31. The vaccine of claim 29, wherein the open reading frame of the one or more RNA polynucleotides encode at least 10, 15, 20 or 50 antigenic polypeptides.

32. The vaccine of claim 29, wherein the open reading frame of the one or more RNA polynucleotides encode 2-10, 10-15, 15-20, 20-50, 50-100 or 100-200 antigenic polypeptides.

33. The vaccine of any one of claims 1-32, wherein the RNA polynucleotide includes a chemical modification and the chemical modification is selected from any of those listed in Tables 22 and 23.

34. The vaccine of claim 33, wherein the chemical modification is selected from the group consisting of pseudouridine, N1-methylpseudouridine, 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.

35. The vaccine of claim 34, further comprising a second chemical modification wherein said second chemical modification is selected from any of those listed in Tables 22 and 23.

36. The vaccine of claim 35, wherein the combination of first and second chemical modification is selected from those listed in Table 25.

37. A nucleic acid vaccine, comprising:

one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide, formulated within a nanoparticle, wherein the nanoparticle has a mean diameter of 50-200nm.

38. The vaccine of claim 37, wherein the nanoparticle has a polydiversity value of less than 0.4.

39. The vaccine of claim 37, wherein the nanoparticle has a net neutral charge at a neutral pH.

40. The vaccine of claim 37, wherein the nanoparticle has a mean diameter of 80-100nm.

41. The vaccine of claim 37, wherein the nanoparticle is a cationic lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid.

42. The vaccine of claim 41,wherein the 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), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319).

43. A nucleic acid vaccine, comprising:

one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide, wherein at least 80% of the uracil in the open reading frame have a chemical modification.

44. The vaccine of claim 43, wherein 100% of the uracil in the open reading frame have a chemical modification.

45. The vaccine of claim 43 or 44, wherein the chemical modification is in the 5-position of the uracil.

46. The vaccine of any of claims 43 - 44, wherein the chemical modification is a N1-methyl pseudouridine.

47. The vaccine of any one of claims 43-46, which is formulated within a cationic lipid complex or cationic lipid nanoparticle.

48. A nucleic acid vaccine, comprising:

one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide, at least one 5′ terminal cap and at least one chemical modification, formulated within a cationic lipid nanoparticle.

49. The vaccine of claim 48, wherein the 5' terminal cap is 7mG(5')ppp(5')NlmpNp.

50. The vaccine of any one of claims 48-49, wherein the chemical modification is selected from any of those listed in Tables 22 and 23.

51. The vaccine of claim 50, wherein the chemical modification is selected from the group consisting of pseudouridine, N1-methylpseudouridine, 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.

52. The vaccine of claim 50, further comprising a second chemical modification wherein said second chemical modification is selected from any of those listed in Tables 22 and 23.

53. The vaccine of claim 52, wherein the combination of first and second chemical modification is selected from those listed in Table 25.

54. The vaccine of claim 48, wherein the cationic lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid.

55. The vaccine of claim 54, wherein the 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), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319).

56. The vaccine of claim 54 or 55, wherein the cationic lipid nanoparticle has a molar ratio of about 20-60% cationic lipid: about 5-25% non-cationic lipid: about 25-55% sterol; and about 0.5-15% PEG-modified lipid.

57. A nucleic acid vaccine, comprising:

one or more RNA polynucleotides having an open reading frame encoding a hemagglutinin protein and a pharmaceutically acceptable carrier or excipient, formulated within a cationic lipid nanoparticle.

58. The vaccine of claim 57, wherein the hemagglutinin protein is selected from HA1, HA7 and HA 10.

59. The vaccine of claim 57 or 58, wherein the RNA polynucleotide does not encode F protein.

60. The vaccine of any one of claims 57-59, wherein the RNA polynucleotide further encodes neuraminidase protein.

61. The vaccine of any one of claims 57-60, wherein the hemagglutinin protein is derived from a strain of Influenza A virus or Influenza B virus or combinations thereof.

62. The vaccine of claim 61, wherein the Influenza virus is selected from H1N1, H3N2, H7N9, and H10N8.

63. The vaccine of any one of claims 57-62, wherein the RNA polynucleotide includes a chemical modification and the chemical modification is selected from any of those listed in Tables 22 and 23.

64. The vaccine of claim 63 wherein the chemical modification is selected from the group consisting of pseudouridine, N1-methylpseudouridine, 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.

65. The vaccine of claim 63, further comprising a second chemical modification wherein said second chemical modification is selected from any of those listed in Tables 22 and 23.

66. The vaccine of claim 65, wherein the combination of first and second chemical modification is selected from those listed in Table 25.

67. The vaccine of claim 57, wherein the cationic lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid.

68. The vaccine of claim 67, wherein the 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), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319).

69. The vaccine of claim 67 or 68, wherein the cationic lipid nanoparticle has a molar ratio of about 20-60% cationic lipid: about 5-25% non-cationic lipid: about 25-55% sterol; and about 0.5-15% PEG-modified lipid.

70. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises SEQ ID NOs 2459-2621.

71. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide having at least 80% sequence identity to SEQ ID NOs 2459-2621.

72. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide encoding an amino acid sequence having at least 90% sequence identity to SEQ ID NO 2254.

73. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide encoding the amino acid sequence of SEQ ID NO 2254.

74. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide encoding an amino acid sequence having at least 90% sequence identity to SEQ ID NO 2259.

75. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide encoding the amino acid sequence of SEQ ID NO 2259.

76. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide encoding an amino acid sequence having at least 90% sequence identity to SEQ ID NO 2192.

77. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide encoding the amino acid sequence of SEQ ID NO 2192.

78. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide encoding an amino acid sequence having at least 90% sequence identity to SEQ ID NO 2200.

79. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide encoding the amino acid sequence of SEQ ID NO 2200.

80. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises SEQ ID NO 2046.

81. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide having 80-98% sequence identity to SEQ ID NO 2046.

82. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises SEQ ID NO 2119.

83. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide having 80-98% sequence identity to SEQ ID NO 2119.

84. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises SEQ ID NO 2054.

85. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide having 80-98% sequence identity to SEQ ID NO 2054.

86. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises SEQ ID NO 2127.

87. The vaccine of any one of claims 57-69, wherein the RNA polynucleotide comprises a polynucleotide having 80-98% sequence identity to SEQ ID NO 2127.

88. A nucleic acid comprising 80-95% sequence identity to SEQ ID NO 2127 or SEQ ID NO 2054.

89. A nucleic acid comprising SEQ ID NO: 2624.

90. A vaccine of any one of claims 1-89 for use in inducing an antigen specific immune response in a subject.

91. Use of a vaccine of any one of claims 1-89 in the manufacture of a medicament for use in inducing an antigen specific immune response in a subject.

92. A vaccine of any of claims 57-89 for use in preventing or treating influenza viral infection.

93. Use of a vaccine of any of claims 57-89 in the manufacture of a medicament for use in preventing or treating influenza viral infection.

94. A nucleic acid vaccine for use in a method of vaccinating a subject

wherein the nucleic acid vaccine comprises a first RNA polynucleotide 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 coformulated or co-administered with the vaccine.

95. Use of a nucleic acid vaccine in the manufacture of a medicament for use in a method of vaccinating a subject

wherein the nucleic acid vaccine comprises a first RNA polynucleotide 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 coformulated or co-administered with the vaccine.

96. An antigenic memory booster nucleic acid vaccine for use in creating, maintaining or restoring antigenic memory to an influenza strain in an individual or population of individuals

wherein the antigenic memory booster nucleic acid vaccine comprises

(a) at least one RNA polynucleotide, said polynucleotide comprising at least one chemical 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

and wherein the method comprises administering to said individual or population the antigenic memory booster nucleic acid vaccine.

97. Use of an antigenic memory booster nucleic acid vaccine in the manufacture of a medicament for use in creating, maintaining or restoring antigenic memory to an influenza strain in an individual or population of individuals

wherein the antigenic memory booster nucleic acid vaccine comprises

(a) at least one RNA polynucleotide, said polynucleotide comprising at least one chemical 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

and wherein the method comprises administering to said individual or population the antigenic memory booster nucleic acid vaccine.

98. A nucleic acid vaccine for use in vaccinating a subject

wherein the nucleic acid vaccine comprises a first RNA polynucleotide having an open reading frame encoding a first antigenic polypeptide

and wherein the method comprises administering to the subject a single dosage of between 25 ug/kg and 400 ug/kg of the nucleic acid vaccine in an effective amount to vaccinate the subject.

99. Use of a nucleic acid vaccine in the manufacture of a medicament for use in vaccinating a subject

wherein the nucleic acid vaccine comprises a first RNA polynucleotide having an open reading frame encoding a first antigenic polypeptide

and wherein the method comprises administering to the subject a single dosage of between 25 ug/kg and 400 ug/kg of the nucleic acid vaccine in an effective amount to vaccinate the subject.

100. A nucleic acid vaccine, comprising:

one or more RNA polynucleotides having an open reading frame encoding a hemagglutinin protein fragment, wherein the hemagglutinin protein includes only a portion of at least one of: a head domain (HA1), a cytoplasmic domain, or a transmembrane domain.

101. The vaccine of claim 100, wherein the hemagglutinin protein is H1, H2, H3, H4, H5, H6, H7, H8, H9, H10, H11, H12, H13, H14, H15, H16, H17, H18.

102. The vaccine of claim 100, wherein the hemagglutinin protein does not comprise the head domain (HA1).

103. The vaccine of claim 100, wherein the hemagglutinin protein does not comprise the cytoplasmic domain.

104. The vaccine of any one of claims 100-103, wherein the truncated hemagglutinin protein does not comprise the transmembrane domain.

105. The vaccine of any one of claims 100-104, wherein the amino acid sequence of the hemagglutinin protein comprises at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97% 98%, or 99% identify with any of the amino acid sequences provided in 14-16.

106. The vaccine of any one of claims 100-105, wherein the vaccine is formulated within a cationic lipid complex or cationic lipid nanoparticle.

107. The vaccine of any one of claims 100-106, wherein the polynucleotide comprises at least one 5′ terminal cap and at least one chemical modification.