CLAIMS

What is claimed is:

1. An immunogenic composition comprising one or more respiratory syncytial virus F (RSV F) polypeptides in which amino acids 100-150 are replaced with the amino acid sequence of SEQ ID NO:9, SEQ ID NO:12, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7; SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:91 or SEQ ID NO:92.

2. The immunogenic composition of claim 1, wherein amino acids 100-150 of said RSV F are replaced with the amino acid sequence of SEQ ID NO:12.

3. The immunogenic composition of claim 1, wherein amino acids 100-150 of said RSV F are replaced with the amino acid sequence of SEQ ID NO:9, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7; SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13 or SEQ ID NO:92.

4. The immunogenic composition of claim 1, wherein amino acids 100-150 are replaced with the amino acid sequence of SEQ ID NO:9.

5. The immunogenic composition of claim 1 or claim 2, wherein the RSV F is in the form of a monomer, trimer, or combination of monomers and trimers.

6. The immunogenic composition of claim 3 or 4, wherein RSV F is in the form of a monomer, trimer, rosette or any combination thereof.

7. The immunogenic compositon of any one of claims 1-6, wherein said RSV F polypeptide is a soluble polypeptide comprising the RSV-F ectodomain.

8. The immunogenic composition of any one of claims 1-6, wherein said RSV F comprises amino acids 23-99 and 151-524 of SEQ ID NO:1 or SEQ ID NO:2.

9. An immunogenic composition comprising a polypeptide selected from the group consisting of SEQ ID NO:49, SEQ ID NO:68, SEQ ID NO:71, SEQ ID NO: 25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:93, any of the foregoing sequences in which the signal peptide and/or HIS tag is omitted, and combinations thereof.

10. The immunogenic composition of claim 9, wherein said polypeptide is SEQ ID NO:68 or SEQ ID NO:68 in which the signal peptide, and optionally the HIS tag, is omitted.

11. The immunogenic composition of claim 9, wherein said polypeptide is selected from the group consisting of SEQ ID NO:49, SEQ ID NO:71, and any of the foregoing sequences in which the signal peptide, and optionally the HIS tag, is omitted.

12. The immunogenic composition of any one of claims 1-11, further comprising an adjuvant.

13. The immunogenic composition of claim 12, wherein the adjuvant is selected from the group consisting of: an aluminum salt, a squalene-in-water emulsion, a benzonaphthyridine compound, a phospholipid compound, a small molecule immunopotentiator and combinations of any of the foregoing.

14. A recombinant respiratory syncytial virus F polypeptide (RSV F) in which amino acids 100-150 are replaced with the amino acid sequence of SEQ ID

NO:9, SEQ ID NO:12, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:91 or SEQ ID NO:92.

15. The recombinant RSV F of claim 14, wherein amino acids 100-150 of said RSV F are replaced with the amino acid sequence of SEQ ID NO:12.

16. The recombinant RSV F of claim 15, wherein amino acids 100-150 of said RSV F are replaced with the amino acid sequence of SEQ ID NO:9, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7; SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13 or SEQ ID NO:92.

17. The recombinant RSV F of claim 14, wherein amino acids 100-150 are replaced with the amino acid sequence of SEQ ID NO:9.

18. The recombinant RSV F of claim 14 or 15, wherein the RSV F is in the form of a monomer, trimer, or combination of monomers and trimers.

19. The recombinant RSV F of claim 16 or 17, wherein the RSV F is in the form of a monomer, trimer, rosette of trimers or combinations thereof.

20. A recombinant polypeptide selected from the group consisting of SEQ ID NO:49, SEQ ID NO:68, SEQ ID NO:71, SEQ ID NO: 25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:93, any of the foregoing

sequences in which the signal peptide and/or HIS tag is omitted, and combinations thereof.

21. The recombinant polypeptide of any one of claims 14-20, further comprising a heterologous oligomerization domain, an epitope, or a signal peptide.

22. The recombinant polypeptide of claim 21, wherein said heterologous oligomerization domain is selected from the group comprising a trimerization domain from influenza hemagglutinin, from SARS spike, or from HIV gp41, NadA, modified GCN4, or ATCase.

23. An isolated nucleic acid encoding the polypeptide of any of claims 14-21.

24. The isolated nucleic acid of claim 23, which is a self-replicating RNA molecule.

25. An immunogenic composition comprising the self-replicating RNA molecule of claim 24.

26. The immunogenic composition of claim 25, further comprising a delivery system.

27. The use of an immunogenic composition of any one of claims 1-14 in the manufacture of a medicament for inducing an immune response to RSV F in a subject.

28. The use of an immunogenic composition of claim 25 in the manufacture of a medicament for inducing an immune response to RSV F in a subject.

29. A method for producing a composition comprising cleaved RSV F protein ecto-domain polypeptides, the method comprising:

a) providing uncleaved RSV F protein ecto-domain polypeptides that contain a protease cleavage site that when cleaved produces F_1 and F_2 subunits, the amino acid sequence of said uncleaved soluble RSV F protein ecto-domain polypeptides comprising altered furin cleavage sites at positions 106-109 and 133-136, and said uncleaved soluble RSV F protein ecto-domain polypeptides are obtained from a cell that produces them uncleaved; and

b) cleaving the provided soluble RSV F protein ecto-domain polypeptides with a protease that cleaves said protease cleavage site, thereby producing a composition comprising cleaved soluble RSV F protein ecto-domain polypeptides.

30. The method of claim 29, wherein in step b) the provided uncleaved RSV F protein ecto-domain polypeptides are cleaved at one or more of positions from about position 101 to about position 161.

31. The method of claim 30, wherein the provided uncleaved RSV F protein ecto-domain polypeptides are cleaved at one or more of positions from about position 106 to about position 142.

32. The method of any one of claims 29-32, wherein the uncleaved RSV F protein ecto-domain polypeptides provided in a) are purified.

33. The method of any one of claims 29-32, wherein the uncleaved RSV F protein ecto-domain polypeptides provided in a) comprise an intact fusion peptide.

34. The method of claim 33, wherein the cleaving in step b) results in the formation of rosettes of trimers.

35. The method of claim 34, further comprising c) purifying said rosettes of trimers.

36. The method of claims 35, wherein purifying the rosettes of trimers comprises size exclusion chromatography.

37. The method of any one of claims 29-32, wherein the uncleaved RSV F protein ecto-domain polypeptides provided in a) comprise an altered fusion peptide.

38. The method of claim 37, wherein at least a portion of the fusion peptide is deleted in the uncleaved RSV F protein ecto-domain polypeptides.

39. The method of claim 37, wherein amino acids 137-153, amino acids 137-146, amino acids 137-145, or amino acids 137-142 are deleted from the fusion peptide.

40. The method of any one of claims 37-39, wherein the cleaving in step b) results in the formation of trimers.

41. The method of claim 40, further comprising c) purifying said trimers.

42. The method of claims 41, wherein purifying the trimers comprises size exclusion chromatography.

43. The method of any one of claims 29-42, wherein the uncleaved RSV F protein ecto-domain polypeptides provided in a) are expressed in insect cells, mammalian cells, avian cells, yeast cells, Tetrahymena cells or combinations thereof.

44. The method of claims 29-43, wherein the uncleaved RSV F protein ecto-domain polypeptides provided in a) are provided in cell culture conditioned media.

45. The method of claim 44, wherein said cell culture conditioned media is selected from the group consisting of insect cell culture conditioned media, mammalian cell culture conditioned media and combinations thereof.

46. The method of any one of claims 29-36 and 41, wherein the rosettes of trimers comprise F_1 and F_2 fragments of at least one polypeptide selected from the group consisting of Furdel and Delp23 furdel.

47. The method of any one of claims 29-46, wherein the cleaved RSV F protein ecto-domain polypeptides are substantially free of lipids and lipoproteins.

48. A composition comprising cleaved RSV F protein ecto-domain polypeptides produced using the method of any one of claims 29-47.

49. The composition of claim 48, wherein the composition is an immunogenic composition.

50. A method for producing a composition comprising uncleaved RSV F protein ecto-domain polypeptide monomers, trimers or a combination of monomers and trimers, the method comprising:

a) providing a biological material that contains uncleaved RSV F protein ecto-domain polypeptides, the amino acid sequence of said uncleaved soluble RSV F protein ecto-domain polypeptides comprising altered furin cleavage sites at positions 106-109 and 133-136, and said uncleaved soluble RSV F protein ecto-domain polypeptides are secreted from a cell that produces them uncleaved; and

b) purifying uncleaved RSV F protein ecto-domain polypeptide monomers or trimers from the biological material, thereby producing the composition.

51. The method of claim 50, wherein the biological material is selected from the group consisting of insect cell culture conditioned medium or cell lysate, mammalian cell culture conditioned medium or cell lysate, avian cell culture conditioned medium or cell lysate, yeast cell conditioned medium or cell lysate, Tetrahymena cell culture conditioned medium or cell lysate, and combinations thereof.

52. The method of claim 50 or 51, wherein in b) uncleaved RSV F protein ecto-domain polypeptide trimers are purified.

53. The method of claim 50 or 51, wherein in b) uncleaved RSV F protein ecto-domain polypeptide monomers are purified.

54. The method of claim 50, wherein purifying in b) comprises size exclusion chromatography.

55. The method of any one of claims 50-54, wherein the uncleaved RSV F protein ecto-domain polypeptides further comprise an altered fusion peptide.

56. The method of claim 50, wherein said soluble uncleaved RSV F protein ecto-domain polypeptides comprise at least one polypeptide selected from the group consisting of furmt, furdel, Delp21 furx, Delp23 furx, Delp21 furdel, Delp23 furdel, and the factor Xa construct.

57. The method of any one of claims 50-56, wherein the composition comprising uncleaved RSV F protein ecto-domain polypeptides is substantially free of lipids and lipoproteins.

58. A composition comprising soluble uncleaved RSV F protein ecto-domain polypeptide monomers or trimers produced using the method of any one of claims 50-57.

59. The composition of claim 58, wherein the composition is an immunogenic composition.

60. A method for producing a composition comprising uncleaved RSV F protein ecto-domain polypeptide monomers, trimers or a combination of monomers and trimers, the method comprising:
a) providing a biological material that contains uncleaved RSV F protein ecto-domain polypeptides, wherein the amino acid sequence of the uncleaved RSV F protein ecto-domain polypeptide contains altered furin cleavage sites, lysine and arginine residues present between about position 101 and about position 161 are deleted or replaced with an amino acid that is not lysine or arginine, the RSV F protein ecto-domain polypeptides are obtained from a host cell that produces them uncleaved between about

position 101 and about position 161, and the RSV F protein ecto-domain polypeptides are not cleaved between about position 101 and about position 161; and
b) purifying uncleaved RSV F protein ecto-domain polypeptide monomers, trimers or a combination of monomers and trimers from the biological material.

61. The method of claim 60, wherein the biological material is selected from the group consisting of insect cell culture conditioned medium or cell lysate, mammalian cell culture conditioned medium or cell lysate, avian cell culture conditioned medium or cell lysate, yeast cell conditioned medium or cell lysate, Tetrahymena cell culture conditioned medium or cell lysate, and combinations thereof.

62. The method of claim 60 or 61, wherein in b) uncleaved RSV F protein ecto-domain polypeptide trimers are purified.

63. The method of claim 60 or 61, wherein in b) uncleaved RSV F protein ecto-domain polypeptide monomers are purified.

64. The method of claim 60 or 61, wherein in b) uncleaved RSV F protein ecto-domain polypeptide monomers and uncleaved RSV F protein ecto-domain polypeptide trimers are purified.

65. The method of any one of claims 60-64, wherein purifying in b) comprises size exclusion chromatography.

66. The method of any one of claims 60-64, wherein the uncleaved RSV F protein ecto-domain polypeptides further comprise an altered fusion peptide.

67. The method of claim 60, wherein said uncleaved RSV F protein ecto-domain polypeptides comprise at least one polypeptide selected from the group consisting of Furx, Furx R113Q K123N K124N, Delp21 furx and Delp23 furx.

68. The method of any one of claims 60-67, wherein the composition comprising uncleaved RSV F protein ecto-domain polypeptides is substantially free of lipids and lipoproteins.

69. A composition comprising soluble uncleaved RSV F protein ecto-domain polypeptides produced using the method of any one of claims 60-68.

70. The composition of claim 69, wherein the composition is an immunogenic composition.

71. A method for producing a composition comprising cleaved RSV F protein ecto-domain polypeptide monomers, trimers or a combination of monomers and trimers, the method comprising:
a) providing biological material that contains cleaved RSV F protein ecto-domain polypeptides that contain an altered fusion peptide; and
b) purifying cleaved RSV F protein ecto-domain polypeptides from the biological material.

72. The method of claim 71, wherein the RSV F protein ecto-domain polypeptide comprises an amino acid sequence in which about amino acids 137-152 are deleted, about amino acids 137-153 are deleted, about amino acids 137-145 are deleted, about amino acids 137-146 are deleted or about amino acids 137-142 are deleted.

73. The method of claim 71 or 72, wherein the biological material is selected from the group consisting of insect cell culture conditioned medium or cell lysate, mammalian cell culture conditioned medium or cell lysate, avian cell culture conditioned medium or cell lysate, yeast cell conditioned medium or cell lysate, Tetrahymena cell culture conditioned medium or cell lysate, and combinations thereof.

74. The method of any one of claims 71-73, wherein in b) cleaved RSV F protein ecto-domain polypeptide trimers are purified.

75. The method of any one of claims 71-73, wherein in b) cleaved RSV F protein ecto-domain polypeptide monomers are purified.

76. The method of any one of claims 71-73, wherein in b) cleaved RSV F protein ecto-domain polypeptide monomers and cleaved RSV F protein ecto-domain polypeptide trimers are purified.

77. The method of any one of claims 71-73, wherein purifying in b) comprises size exclusion chromatography.

78. The method of claim 71, wherein said uncleaved RSV F protein ecto-domain polypeptides comprise at least the Fusion Peptide deletion polypeptide.

79. The method of any one of claims 71-78, wherein the composition comprising uncleaved RSV F protein ecto-domain polypeptides is substantially free of lipids and lipoproteins.

80. A composition comprising soluble uncleaved RSV F protein ecto-domain polypeptides produced using the method of any one of claims 71-79.

81. The composition of claim 80, wherein the composition is an immunogenic composition.

82. A method for producing a composition comprising RSV F protein ecto-domain polypeptides, the method comprising:

a) providing RSV F protein ecto-domain polypeptides that comprises an altered furin cleavage site at positions 133-136, and said soluble RSV F protein ecto-domain polypeptides are secreted from a cell that produces them in the form of an F_2 fragment that is associated with a subunit that comprises F_1 but is uncleaved at position 136/137; and

b) cleaving the provided RSV F protein ecto-domain polypeptides with a protease that cleaves RSV F protein ecto-domain at a site between positions 101 and 161, thereby producing said composition.

83. The method of claim 82, wherein the RSV F protein ecto-domain polypeptides provided in a) are purified.

84. The method claim 82 or 83, wherein the RSV F protein ecto-domain polypeptides provided in a) are expressed in insect cells, mammalian cells, avian cells, yeast cells, Tetrahymena cells or combinations thereof.

85. The method of any one of claims 82-84, wherein the RSV F protein ecto-domain polypeptides provided in a) are provided in cell culture conditioned media, cell extract or a combination thereof.

86. The method of claim 85, wherein the RSV F protein ecto-domain polypeptides are provided in cell culture conditioned media is selected from the group consisting of insect cell culture conditioned media, mammalian cell culture conditioned media, avian cell culture conditioned media, yeast cell culture conditioned media, Tetrahymena cell culture conditioned media and combinations thereof.

87. The method of any one of claims 82-86, wherein the RSV F protein ecto-domain polypeptides include at least the C-term Furin polypeptide.

88. The method of any one of claims 82-87, wherein the cleaved RSV F protein ecto-domain polypeptides produced in b) are substantially free of lipids and lipoproteins.

89. A composition comprising cleaved RSV F protein ecto-domain polypeptides produced using the method of any one of claims 82-88.

90. The composition of claim 89, wherein the composition is an immunogenic composition.

91. A method for producing a composition comprising RSV F protein ecto-domain polypeptides, the method comprising:

a) providing biological material that contains RSV F protein ecto-domain polypeptides that comprise an altered furin cleavage site at positions 133-136, and said soluble RSV F protein ecto-domain polypeptides are secreted from a cell that produces them in the form of an F_2 fragment that is associated with a subunit that comprises F_1 but is uncleaved at position 136/137, with the proviso that the altered furin cleavage site is not deletion of amino acids 131-134; and

b) purifying the RSV F protein ecto-domain polypeptides from the biological material, thereby producing the composition.

92. The method of claim 91, wherein the biological material is selected from the group consisting of insect cell culture conditioned medium or cell lysate, mammalian cell culture conditioned medium or cell lysate, avian cell culture conditioned medium or cell lysate, yeast cell conditioned medium or cell lysate, Tetrahymena cell culture conditioned medium or cell lysate, and combinations thereof.

93. The method of claim 91 or 92, wherein in b) RSV F protein ecto-domain polypeptide monomers, trimers or a combination of monomers and trimers are purified.

94. The method of claim 93, wherein purifying in b) comprises size exclusion chromatography.

95. The method of any one of claims 91-94, wherein the RSV F protein ecto-domain polypeptides include at least the C-term Furin polypeptide.

96. The method of any one of claims 91-95, wherein the composition comprising RSV F protein ecto-domain polypeptides is substantially free of lipids and lipoproteins.

97. A composition comprising RSV F protein ecto-domain polypeptide produced using the method of any one of claims 92-96.

98. The composition of claim 97, wherein the composition is an immunogenic composition.

CLAIMS

1. An immunogenic composition comprising one or more respiratory syncytial virus F (RSV F) soluble ectodomain polypeptides in which, relative to SEQ ID NO:1 or SEQ ID NO:2, amino acids 100-150 are replaced with the amino acid sequence of SEQ ID NO: 9, SEQ ID NO: 12, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7; SEQ ID NO:8, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO:91 or SEQ ID NO:92, wherein the RSV F polypeptides are i) substantially free of contaminating lipids and lipoproteins and ii) exhibit a crutch, golf tee, or rosette conformation by electron microscopy.

2. The immunogenic composition of claim 1, wherein amino acids 100-150 of said RSV F are replaced with the amino acid sequence of SEQ ID NO: 12.

3. The immunogenic composition of claim 1, wherein amino acids 100-150 of said RSV F are replaced with the amino acid sequence of SEQ ID NO:9, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7; SEQ ID NO:8, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 13 or SEQ ID NO:92.

4. The immunogenic composition of claim 1, wherein amino acids 100-150 are replaced with the amino acid sequence of SEQ ID NO:9.

5. The immunogenic composition of claim 1 or claim 2, wherein the RSV F is in the form of a monomer, trimer, or combination of monomers and trimers.

6. The immunogenic composition of claim 3 or 4, wherein RSV F is in the form of a monomer, trimer, rosette or any combination thereof.

7. The immunogenic composition of any one of claims 1-6, wherein said RSV F comprises amino acids 23-99 and 151-524 of SEQ ID NO: 1 or SEQ ID NO:2.

8. An immunogenic composition comprising a soluble polypeptide selected from the group consisting of SEQ ID NO:49, SEQ ID NO:68, SEQ ID NO:71, SEQ ID NO: 25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ

ID NO:46, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:93, any of the foregoing sequences in which the signal peptide and/or HIS tag is omitted, and combinations thereof, wherein the polypeptide is i) substantially free of contaminating lipids and lipoproteins and ii) exhibit a crutch, golf tee, or rosette conformation by electron microscopy.

9. The immunogenic composition of claim 8, wherein said polypeptide is SEQ ID NO:68 or SEQ ID NO:68 in which the signal peptide, and optionally the HIS tag, is omitted.

10. The immunogenic composition of claim 8, wherein said polypeptide is selected from the group consisting of SEQ ID NO:49, SEQ ID NO:71, and any of the foregoing sequences in which the signal peptide, and optionally the HIS tag, is omitted.

11. The immunogenic composition of any one of claims 1-10, further comprising an adjuvant.

12. The immunogenic composition of claim 11, wherein the adjuvant is selected from the group consisting of: an aluminum salt, a squalene-in-water emulsion, a benzonaphthyridine compound, a phospholipid compound, a small molecule immunopotentiator and combinations of any of the foregoing.

13. A recombinant soluble ectodomain respiratory syncytial virus F polypeptide (RSV F) in which amino acids 100-150 are replaced with the amino acid sequence of SEQ ID NO:9, SEQ ID NO: 12, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO:91 or SEQ ID NO:92, wherein the RSV F polypeptide is i) substantially free of contaminating lipids and lipoproteins and ii) exhibit a crutch, golf tee, or rosette conformation by electron microscopy.

14. The recombinant RSV F of claim 13, wherein amino acids 100-150 of said RSV F are replaced with the amino acid sequence of SEQ ID NO: 12.

15. The recombinant RSV F of claim 13, wherein amino acids 100-150 of said RSV F are replaced with the amino acid sequence of SEQ ID NO: 9, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7; SEQ ID NO:8, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 13 or SEQ ID NO:92.

16. The recombinant RSV F of claim 13, wherein amino acids 100-150 are replaced with the amino acid sequence of SEQ ID NO:9.

17. The recombinant RSV F of claim 13 or 14, wherein the RSV F is in the form of a monomer, trimer, or combination of monomers and trimers.

18. The recombinant RSV F of claim 15 or 16, wherein the RSV F is in the form of a monomer, trimer, rosette of trimers or combinations thereof.

19. A recombinant soluble polypeptide selected from the group consisting of SEQ ID NO:49, SEQ ID NO:68, SEQ ID NO:71, SEQ ID NO: 25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:93, any of the foregoing sequences in which the signal peptide and/or HIS tag is omitted, and combinations thereof, wherein the polypeptide is i) substantially free of contaminating lipids and lipoproteins and ii) exhibit a crutch, golf tee, or rosette conformation by electron microscopy.

20. The recombinant polypeptide of any one of claims 13-19, further comprising a heterologous oligomerization domain, an epitope, or a signal peptide.

21. The recombinant polypeptide of claim 20, wherein said heterologous oligomerization domain is selected from the group comprising a trimerization domain from influenza hemagglutinin, from SARS spike, or from HIV gp41, NadA, modified GCN4, or ATCase.

22. An isolated nucleic acid encoding the polypeptide of any of claims 13-20.

23. The isolated nucleic acid of claim 22, which is a self-replicating RNA molecule.

24. An immunogenic composition comprising the self-replicating RNA molecule of claim 23.

25. The immunogenic composition of claim 24, further comprising a delivery system.

26. The composition of Claim 25, wherein the delivery system comprises (i) liposomes (ii) non-toxic and biodegradable polymer microparticles, or (iii) cationic submicron oil-in-water emulsions.

27. The use of an immunogenic composition of any one of claims 1-13 in the manufacture of a medicament for inducing an immune response to RSV F in a subject.

28. The use of an immunogenic composition of any one of claims 25-27 in the manufacture of a medicament for inducing an immune response to RSV F in a subject.