We claim:

1. A recombinant respiratory syncytial virus (RSV) antigen comprising a soluble F protein polypeptide comprising an F_2 domain and an F_1 domain of an RSV F protein polypeptide, wherein the F protein polypeptide comprises at least one modification that alters glycosylation.

2. The recombinant RSV antigen of claim 1, wherein the F protein polypeptide comprises at least one modification selected from:

(i) an addition of an amino acid sequence comprising a heterologous trimerization domain;

(ii) a deletion of at least one furin cleavage site;

(iii) a deletion of at least one non-furin cleavage site;

(iv) a deletion of one or more amino acids of the pep27 domain; and

(v) at least one substitution or addition of a hydrophilic amino acid in a hydrophobic domain of the F protein extracellular domain.

3. The recombinant RSV antigen of claim 1, wherein the modification that alters glycosylation comprises a substitution of one or amino acids comprising and/or adjacent to the amino acid corresponding position 500 of SEQ ID NO:2.

4. The recombinant RSV antigen of caim 1 or 3, wherein amino acids corresponding to positions 500-502 of SEQ ID NO:2 are selected from: NGS; NKS; NGT; NKT.

5. The recombinant RSV antigen of any one of claims 1-4, wherein the modification that alters glycosylation comprises a substitution of glutamine at the amino acid corresponding to position 500 of SEQ ID NO:2.

6. The recombinant RSV antigen of any one of claims 1-5, wherein the soluble F protein polypeptide comprises an intact fusion peptide between the F2 domain and the F1 domain.

7. The recombinant RSV antigen of any one of claims 1-6, wherein the at least one modification comprises the addition of an amino acid sequence comprising a heterologous trimerization domain.

8. The recombinant RSV antigen of claim 7, wherein the heterologous trimerization domain is positioned C-terminal to the F_1 domain.

9. The recombinant RSV antigen of any one of claims 1-8, comprising an F2 domain and an F1 domain with no intervening furin cleavage site.

10. The recombinant RSV antigen of any one of claims 1-9, wherein the RSV antigen assembles into a multimer

11. The recombinant RSV antigen of any one of claims 1-10, wherein the RSV antigen assembles into a trimer.

12. The recombinant RSV antigen of any one of claims 1-11, wherein the F_2 domain comprises at least a portion of an RSV F protein polypeptide corresponding to amino acids 26-105 of the reference F protein precursor polypeptide (F_0) of SEQ ID NO:2.

13. The recombinant RSV antigen of any one of claims 1-12 and wherein the F_1 domain comprises at least a portion of an RSV F protein polypeptide corresponding to amino acids 137-516 of the reference F protein precursor polypeptide (F_0) of SEQ ID NO:2.

14. The recombinant RSV antigen of any one of claims 1-13, wherein the F_2 domain comprises an RSV F protein polypeptide corresponding to amino acids 26-105 and/or wherein the F_1 domain comprises an RSV F protein polypeptide corresponding to amino acids 137-516 of the reference F protein precursor polypeptide (F_0) of SEQ ID NO:2.

15. The recombinant RSV antigen of any one of claims 1-14, wherein the RSV antigen is selected from the group of:

a) a polypeptide comprising SEQ ID NO:22;

b) a polypeptide encoded by SEQ ID NO:21 or by a polynucleotide sequence that hybridizes under stringent conditions over substantially its entire length to SEQ ID NO:21;

c) a polypeptide with at least 95% sequence identity to SEQ ID NO:22.

16. The recombinant RSV antigen of any one of claims 1-15, wherein the F2 domain comprises amino acids 1-105 of the RSV F protein polypeptide.

17. The recombinant RSV antigen of any one of claims 1-16, wherein the F_2 domain and the F_1 domain are positioned with an intact fusion peptide and without an intervening pep27 domain.

18. The recombinant RSV antigen of any one of claims 1-17, wherein the heterologous trimerization domain comprises a coiled-coil domain.

19. The recombinant RSV antigen of claim 18, wherein the multimerization domain comprises an isoleucine zipper.

20. .The recombinant RSV antigen of claim 19, wherein the isoleucine zipper domain comprises the amino acid sequence of SEQ ID NO:11.

21. The recombinant RSV antigen of any one of claims 1-20, wherein the RSV antigen comprises at least one substitution or addition of a hydrophilic amino acid in a hydrophobic domain of the F protein extracellular domain.

22. The recombinant RSV antigen of claim 21, wherein the hydrophobic domain is the HRB coiled-coil domain of the F protein extracellular domain.

23. The recombinant RSV antigen of claim 22, wherein the HRB coiled-coil domain comprises the substitution of a charged residue in place of a neutral residue at the position corresponding to amino acid 512 of the reference F protein precursor (F_0) of SEQ ID NO:2.

24. The RSV antigen of claim 23, wherein the HRB coiled-coil domain comprises a substitution of lysine or glutamine for leucine at the position corresponding to amino acid 512 of the reference F protein precursor (F_0) of SEQ ID NO:2.

25. The recombinant RSV antigen of claim 21, wherein the hydrophobic domain is the HRA domain of the F protein extracellular domain.

26. The recombinant RSV antigen of claim 25, wherein the HRA domain comprises the addition of a charged residue following the position corresponding to amino acid 105 of the reference F protein precursor (F_0) of SEQ ID NO:2.

27. The recombinant RSV antigen of claim 26, wherein the HRA domain comprises the addition of a lysine following the position corresponding to amino acid 105 of the reference F protein precursor (F_0) of SEQ ID NO:2.

28. The recombinant RSV antigen of any one of claims 21-27, wherein the RSV antigen comprises at least a first substitution or addition of a hydrophilic amino acid in the HRA domain and at least a second substitution or addition of a hydrophilic amino acid in the HRB domain of the F protein extracellular domain.

29. The recombinant RSV antigen of any one of claims 1-28, wherein the RSV antigen comprises at least one amino acid addition, deletion or substitution that eliminates a furin cleavage site present in a naturally occuring F protein precursor (F_0).

30. The recombinant RSV antigen of 29, wherein the RSV antigen comprises an amino acid addition, deletion or substitutionat that eliminates a furin cleavage site at a position corresponding to amino acids 105-109, a position corresponding to amino acids 133-136, or at both positions corresponding to amino acids 105-109 and 133-136 of the reference F protein precursor (F_0) of SEQ ID NO:2.

31. The recombinant RSV antigen of any one of claims 1-30, wherein the F_1 and F_2 polypeptide domains correspond in sequence to the RSV A Long strain.

32. The recombinant RSV antigen of any one of claims 1-31, wherein the RSV antigen comprises a multimer of polypeptides.

33. The recombinant RSV antigen of any one of claims 1-31, wherein the RSV antigen comprises a trimer of polypeptides.

34. An immunogenic composition comprising the recombinant RSV antigen of any one of claims 1-33, and a pharmaceutically acceptable carrier or excipient.

35. The immunogenic composition of claim 34, further comprising an adjuvant.

36. The immunogenic composition of claim 35, wherein the adjuvant comprises at least one of: 3D-MPL, QS21, an oil-in-water emulsion, and Alum.

37. The immunogenic composition of claim 36, wherein the adjuvant comprises an oil-in-water emulsion.

38. The immunogenic composition of claim 36 or 37, wherein the oil-in-water emulsion comprises a tocol.

39. The immunogenic composition of any one of claims 36-38, wherein the oil-in-water emulsion comprises less than 5 mg squalene per human dose.

40. The immunogenic composition of any one of claims 35-39, wherein the adjuvant is suitable for administration to a neonate.

41. The immunogenic composition of any one of claims 34-40, wherein when the immunogenic composition comprises the recombinant RSV antigen of any one of claims 1-33 the immunogenic composition further comprises a G protein polypeptide comprising an amino acid sequence corresponding to amino acid positions 149 to 229 of an RSV G protein polypeptide.

42. The immunogenic composition of any one of claims 34-41, further comprising at least one additional antigen of a pathogenic organism other than RSV.

43. A recombinant nucleic acid comprising a polynucleotide sequence that encodes the recombinant RSV antigen of any one of claims 1-33.

44. The recombinant nucleic acid of claim 43, wherein the polynucleotide sequence that encodes the RSV antigen is codon optimized for expression in a selected host cell.

45. The recombinant nucleic acid of claim 43 or 44, wherein the nuclec acid comprises a polynucleotide sequence selected from:

a) a polynucleotide sequence comprising SEQ ID NO:21;
b) a polynucleotide sequence that encodes SEQ ID NO:22;
c) a polynucleotide sequence that hybridizes under stringent conditions over substantially its entire length to SEQ ID NO:21;
d) a polynucleotide sequence with at least 95% sequence identity to SEQ ID NO:21, which polynucleotide sequence does not correspond to a naturally occurring RSV strain.

46. A vector comprising the recombinant nucleic acid of any one of claims 43-45.

47. A host cell comprising the nucleic acid of claim 43 or 44 or the vector of claim 46.

48. The use of the RSV antigen of any one of claims 1-33 in the preparation of a medicament for treating an RSV infection.

49. The use of the RSV antigen or nucleic acid of claim 48, wherein the medicament is administered for the purpose of prophylactically treating an RSV infection.

50. A method for eliciting an immune response against Respiratory Syncytial Virus (RSV), the method comprising:

administering to a subject a composition comprising the recombinant RSV antigen of any one of claims 1-33 or the immunogenic composition of any one of claims 34-42.

51. The method of claim 50, wherein administering the composition comprising the RSV antigen elicits an immune response specific for RSV without enhancing viral disease following contact with RSV.

52. The method of claims 50 or 51, wherein the immune response comprises a protective immune response that reduces or prevents infection with a RSV and/or reduces or prevents a pathological response following infection with a RSV.

53. The method of any one of claims 50-52, wherein the subject is a human subject.

54. The recombinant RSV antigen of any one of claims 1-33 or the immunogenic composition of any one of claims 34-42 for use in medicine.

55. The recombinant RSV antigen of any one of claims 1-33 or the immunogenic composition of any one of claims 34-42 for the prevention or treatment of RSV-associated diseases.

56. A method for producing a recombinant RSV antigen with an altered glycosylation pattern, the method comprising:

(i) expressing a nucleic acid of any one of claims 43-45 in a host cell; and

(ii) isolating the recombinant RSV antigen expressed thereby.

57. A method for increasing expression of an RSV fusion protein polypeptide, the method comprising:

expressing in a host cell an a nucleic acid encoding an RSV fusion protein polypeptide comprising at least one mutation that produces an amino acid addition, deletion or substitution, which amino acid addition, deletion or substitution alters a glycosylation site of the encoded RSV fusion protein polypeptide as compared to a a naturally occurring RSV fusion protein, whereby altering the glycosylation site increases expression of the RSV fusion protein polypeptide as compared to an RSV fusion protein without the amino acid addition, deletion or substitution.

58. The method of claim 57, wherein the nucleic acid encoding the RSV fusion protein polypeptide further comprises an additional mutation that produces an amino acid addition, deletion or substitution that eliminates a peptidase cleavage site within the encoded RSV fusion protein polypeptide.

59. The method of claim 57 or 58, wherein the RSV fusion protein polypeptide is a recombinant fusion protein polypeptide stabilized in the prefusion conformation.

We claim:

1. A recombinant respiratory syncytial virus (RSV) antigen comprising an RSV F protein polypeptide without a transmembrane domain, comprising an F_2 domain and an F_1 domain of an RSV F protein polypeptide, wherein the F protein polypeptide comprises at least one modification that increases glycosylation, which at least one modification that increases glycosylation comprises a substitution of one or more amino acids comprising and/or adjacent to the amino acid corresponding position 500 of SEQ ID NO:2.

2. The recombinant RSV antigen of claim 1, wherein the F protein polypeptide comprises at least one modification selected from:

(i) an addition of an amino acid sequence comprising a heterologous trimerization domain;

(ii) a deletion of at least one furin protease cleavage site;

(iii) a deletion of at least one non-furin protease cleavage site;

(iv) a deletion of one or more amino acids of the pep27 domain; and

(v) at least one substitution or addition of a hydrophilic amino acid in a hydrophobic domain of the F protein extracellular domain.

3. The recombinant RSV antigen of any one of claims 1 or 2, wherein amino acids corresponding to positions 500-502 of SEQ ID NO:2 are selected from: NGS; NKS; NGT; NKT.

4. The recombinant RSV antigen of any one of claims 1-3, wherein the modification that increases glycosylation comprises a substitution of glutamine at the amino acid corresponding to position 500 of SEQ ID NO:2.

5. The recombinant RSV antigen of any one of claims 1-4, wherein the soluble F protein polypeptide comprises an intact fusion peptide between the F2 domain and the F1 domain.

6. The recombinant RSV antigen of any one of claims 1-5, wherein the at least one modification comprises the addition of an amino acid sequence comprising a heterologous trimerization domain.

7. The recombinant RSV antigen of claim 6, wherein the heterologous trimerization domain is positioned C-terminal to the F_1 domain.

8. The recombinant RSV antigen of any one of claims 1-7, comprising an F2 domain and an F1 domain with no intervening furin cleavage site.

9. The recombinant RSV antigen of any one of claims 1-8, wherein the F_2 domain comprises at least a portion of an RSV F protein polypeptide corresponding to amino acids 26-105 of the reference F protein precursor polypeptide (F_0) of SEQ ID NO:2.

10. The recombinant RSV antigen of any one of claims 1-9, wherein the F_1 domain comprises at least a portion of an RSV F protein polypeptide corresponding to amino acids 137-516 of the reference F protein precursor polypeptide (F_0) of SEQ ID NO:2.

11. The recombinant RSV antigen of any one of claims 1-10, wherein the RSV antigen is selected from the group of:

a) a polypeptide comprising SEQ ID NO:22;

b) a polypeptide encoded by SEQ ID NO:21 or by a polynucleotide sequence that hybridizes under stringent conditions over substantially its entire length to SEQ ID NO:21;

c) a polypeptide with at least 95% sequence identity to SEQ ID NO:22.

12. The recombinant RSV antigen of any one of claims 1-11, wherein the RSV antigen comprises at least one amino acid addition, deletion or substitution that eliminates a furin cleavage site present in a naturally occurring F protein precursor (F_0).

13. The recombinant RSV antigen of claim 12, wherein the RSV antigen comprises an amino acid addition, deletion or substitution that eliminates a furin cleavage site at a position corresponding to amino acids 105-109, a position corresponding to amino acids 133-136, or at both positions corresponding to amino acids 105-109 and 133-136 of the reference F protein precursor (F_0) of SEQ ID NO:2.

14. The recombinant RSV antigen of any one of claims 1-13, wherein the RSV antigen comprises a multimer of polypeptides.

15. The recombinant RSV antigen of any one of claims 1-14, wherein the RSV antigen comprises a trimer of polypeptides.

16. An immunogenic composition comprising the recombinant RSV antigen of any one of claims 0-15, and a pharmaceutically acceptable carrier or excipient.

17. The immunogenic composition of claim 16, further comprising an adjuvant.

18. A recombinant nucleic acid comprising a polynucleotide sequence that encodes the recombinant RSV antigen of any one of claims 1-17.

19. The recombinant nucleic acid of claim 18, wherein the nucleic acid comprises a polynucleotide sequence selected from:

a) a polynucleotide sequence comprising SEQ ID NO:21;

b) a polynucleotide sequence that encodes SEQ ID NO:22;

c) a polynucleotide sequence that hybridizes under stringent conditions over substantially its entire length to SEQ ID NO:21;

d) a polynucleotide sequence with at least 95% sequence identity to SEQ ID NO:21, which polynucleotide sequence does not correspond to a naturally occurring RSV strain.

20. The use of the RSV antigen of any one of claims 1-15 or the nucleic acid of claim 19 in the preparation of a medicament for treating an RSV infection.

21. The use of claim 20, wherein the medicament is administered for the purpose of prophylactically treating an RSV infection.

22. The recombinant RSV antigen of any one of claims 1-15 or the immunogenic composition of any one of claims 16 or 17 for use in medicine.

23. The recombinant RSV antigen of any one of claims 1-15 or the immunogenic composition of any one of claims 16 or 17 for the prevention or treatment of RSV-associated diseases.

24. A method for producing a recombinant RSV antigen with an altered glycosylation pattern, the method comprising:

(i) expressing a nucleic acid of claim in a host cell; and

(ii) isolating the recombinant RSV antigen expressed thereby.

25. A method for increasing expression of an RSV fusion protein polypeptide, the method comprising:

expressing in a host cell a nucleic acid encoding an RSV fusion protein polypeptide comprising at least one mutation that produces an amino acid addition, deletion or substitution, which amino acid addition, deletion or substitution alters a glycosylation site of the encoded RSV fusion protein polypeptide as compared to a a naturally occurring RSV fusion protein, whereby altering the glycosylation site increases expression of the RSV fusion protein polypeptide as compared to an RSV fusion protein without the amino acid addition, deletion or substitution.

26. The method of claim 25, wherein the nucleic acid encoding the RSV fusion protein polypeptide further comprises an additional mutation that produces an amino acid addition, deletion or substitution that eliminates a peptidase cleavage site within the encoded RSV fusion protein polypeptide.