

Claims

1. ~~1.~~ A recombinant pre-fusion respiratory ~~syncytial~~ virus (RSV) Fusion (F) polypeptide, wherein the polypeptide comprises at least two stabilizing mutations in the F1 and/or F2 domain as compared to the RSV F1 and/or F2 domain in a wild-type RSV F protein, wherein at least one of the stabilizing mutations is a mutation of amino acid residue L ~~at~~ on position 203 ~~to~~ into I.
2. ~~The pre~~
2. ~~Pre-fusion RSV F polypeptide according to claim 1, wherein the polypeptide further comprises a mutation of amino acid residue S ~~at~~ on position 215 ~~to~~, preferably a mutation of the amino acid residue S ~~on~~ position 215 into P.~~
3. ~~The pre~~
3. ~~Pre-fusion RSV F polypeptide according to claim 1 ~~or~~ 2, wherein the polypeptide comprises at least one epitope that is specific to the pre-fusion conformation F protein, wherein the at least one epitope is recognized by a pre-fusion specific monoclonal antibody, comprising a heavy chain CDR1 region of SEQ ID NO: 1, a heavy chain CDR2 region of SEQ ID NO: 2, a heavy chain CDR3 region of SEQ ID NO: 3 and a light chain CDR1 region of SEQ ID NO: 4, a light chain CDR2 region of SEQ ID NO: 5, and a light chain CDR3 region of SEQ ID NO: 6~~

and/or a pre-fusion specific monoclonal antibody, comprising a heavy chain CDR1 region of SEQ ID NO: 7, a heavy chain CDR2 region of SEQ ID NO: 8, a heavy chain CDR3 region of SEQ ID NO: 9 and a light chain CDR1 region of SEQ ID NO: 10, a light chain CDR2 region of SEQ ID NO: 67, and a light chain CDR3 region of SEQ ID NO: 11._

4. The pre

~~4. Pre-fusion RSV F polypeptide according to claim 1, 2 or 3, wherein the polypeptide is trimeric.~~

5. The pre

~~5. Pre-fusion RSV F polypeptide according to claim any one of claims 1-4, comprising a truncated F1 domain, wherein the polypeptide comprises a heterologous trimerization domain linked to thesaid truncated F1 domain.~~

6. The pre

~~6. Pre-fusion RSV F polypeptide according to claim 5, wherein the heterologous trimerization domain comprises the amino acid sequence~~

~~GYIPEAPRDGQAYVRKDGEWVLLSTFL (SEQ ID NO: 14).~~

7. The pre-fusion RSV F polypeptide according to claim 5, wherein the trimerization domain is linked to the truncated F1 domain at amino acid residue 513 of the RSV F protein.

8. The pre-fusion RSV F polypeptide according to claim 1, wherein the at least one further mutation is selected from the group consisting of:

~~7. Pre-fusion RSV F polypeptide according to claim 5 or 6, wherein the trimerization domain is linked to amino acid residue 513 of the RSV F protein.~~

~~8. Pre fusion RSV F polypeptide according to any one of the claims 1-7, wherein the polypeptide comprises at least one further mutation, wherein said mutation is selected from the group consisting of:~~

~~(a) a mutation of the amino acid residue on position 46;~~

~~(b) a mutation of the amino acid residue on position 67;~~

~~(c) a mutation of the amino acid residue on position 83;~~

~~(d) a mutation of the amino acid residue on position 92;~~

~~(e) a mutation of the amino acid residue on position 184;~~

~~(f) a mutation of the amino acid residue on position 207;~~

~~(g) a mutation of the amino acid residue on position 486; and~~

~~(h) a mutation of the amino acid residue on position 487.~~

~~9. Pre-fusion RSV F polypeptide according to claim 8, wherein the at least one further mutation is selected from the group consisting of:~~

(a) a mutation of the amino acid residue S ~~at~~ position 46

~~to~~ G;

(b) a mutation of the amino acid residue N/T ~~at~~ position

67 ~~to~~ I;

(c) a mutation of the amino acid residue L ~~at~~ position 83

~~to~~ M;

(d) a mutation of the amino acid residue E ~~at~~ position 92

~~to~~ D;

(e) a mutation of the amino acid residue G ~~at~~ position 184

~~to~~ N;

(f) a mutation of the amino acid residue V ~~at~~ position 207

~~to~~ I;

(g) a mutation of the amino acid residue D ~~at~~ position 486

~~to~~ N; and

(h) a mutation of the amino acid residue E ~~at~~ position 487 ~~to~~ Q, N or I.

9. The pre

~~10. Pre-fusion RSV F polypeptide according to claim 1 any of the preceding claims, wherein the F1 domain and/or the F2 domain are from an RSV A strain.~~

10. The pre

~~11. Pre-fusion RSV F polypeptide according to claim 1 any of the preceding claims, wherein the F1 domain and/or the F2 domain are from an RSV B strain.~~

11. The pre

~~12. Pre-fusion RSV F polypeptide according to claim 1 any one of the preceding claims, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 20, ~~SEQ ID NO: 21~~, SEQ ID NO: 23 and SEQ ID NO: 24.~~

12. A composition comprising a

- ~~13. Nucleic acid molecule encoding a pre-fusion RSV F polypeptide according to any one of the preceding claims 1-12.~~
- ~~14. Nucleic acid molecule according to claim 13, wherein the nucleic acid molecule has been codon-optimized for expression in mammalian cells.~~
- ~~15. Vector comprising a nucleic acid molecule according to claim 13 or claim 14.~~
- ~~16. Composition comprising a pre-fusion RSV F polypeptide according to any of the claims 1-12, a nucleic acid molecule according to claim 13 or claim 14 and/or a vector according to claim 15.~~
- ~~17. Pre-fusion RSV F polypeptide according to any of the claims 1,~~

~~-12, a nucleic acid molecule according to claim 13. A pharmaceutical composition comprising the pre-~~
~~or claim 14, and/or a vector according to claim 15 for use in inducing an immune~~
~~response against RSV F protein.~~
- ~~18. Pre-fusion RSV F polypeptide according to claim any of the claims 1, and a pharmaceutical carrier~~
~~-12, a nucleic acid molecule according to claim 13 or claim 14, and/or a vector~~
~~according to claim 15 for use as a vaccine.~~
- ~~19. Pre-fusion RSV F polypeptide according to any of the claims 1-12, a nucleic acid molecule according to claim 13 or claim 14, and/or a vector according to claim 15 for use in the prophylaxis and/or treatment of RSV infection.~~