

Claims

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
5 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 on
position 203 into I.
2. The pre-fusion RSV F polypeptide according to claim 1, wherein the polypeptide further
10 comprises a mutation of amino acid residue S on position 215 to P.
3. The pre-fusion RSV F polypeptide according to claim 1, 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
15 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
20 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-fusion RSV F polypeptide according to claim 1, wherein the polypeptide is trimeric.
5. The pre-fusion RSV F polypeptide according to claim 1, comprising a truncated F1 domain, wherein the polypeptide comprises a heterologous trimerization domain linked to the truncated F1 domain.
6. The 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:
 - (a) a mutation of the amino acid residue S on position 46 into G;
 - (b) a mutation of the amino acid residue N/T on position 67 into I;
 - (c) a mutation of the amino acid residue L on position 83 into M;
 - (d) a mutation of the amino acid residue E on position 92 into D;
 - (e) a mutation of the amino acid residue G on position 184 into N;
 - (f) a mutation of the amino acid residue V on position 207 into I;
 - (g) a mutation of the amino acid residue D on position 486 into N; and
 - (h) a mutation of the amino acid residue E on position 487 into Q, N or I.

9. The pre-fusion RSV F polypeptide according to claim 1, wherein the F1 domain and/or the F2 domain are from an RSV A strain.

10. The pre-fusion RSV F polypeptide according to claim 1, wherein the F1 domain and/or the F2 domain are from an RSV B strain.

11. The pre-fusion RSV F polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 21, SEQ ID NO: 23 and SEQ ID NO: 24.

12. A composition comprising a pre-fusion RSV F polypeptide according to claim 1.

13. A pharmaceutical composition comprising the pre-fusion RSV F polypeptide according to claim 1, and a pharmaceutical carrier.