A need still remains for efficient vaccines against RSV, in particular vaccines based on or comprising RSV F proteins in the pre-fusion conformation. The present invention aims at providing such stable pre-fusion RSV F proteins for use in vaccinating against RSV.

SUMMARY

Provided herein are vaccine components that can be used to induce an immune response against RSV.

The present disclosure provides respiratory syncytial virus (RSV) F proteins, comprising a head region and a stem region, wherein the protein comprises at least one amino acid substitution in the stem region relative to the amino acid sequence of a wild-type RSV F protein, wherein the at least one substitution in the stem region comprises a substitution of the amino acid residue at position 509 into F, I or L, and wherein amino acid positions are numbered according to the numbering of the amino acid residues in SEQ ID NO:1.

In one aspect, the present disclosure provides a respiratory syncytial virus (RSV) F protein, comprising a head region and a stem region, wherein the protein comprises at least two amino acid mutations in the stem region relative to the amino acid sequence of a wild-type RSV F protein and amino acid mutations in the head region, wherein the at least two amino acid mutations in the stem region comprises a mutation of the amino acid residue at position 509 into F, I or L and a mutation of the amino acid residue at position 505 into W, wherein the amino acid mutations in the head region comprises a mutation of the amino at residue 215 into P, a mutation of the amino acid residue at position 486 into N, a mutation of the amino acid residue at position 101 into Q, S, T, A, or G, a mutation of the amino acid residue at position 354 into L, a mutation of the amino acid at position 487 into L, and a mutation of the amino acid residue at position 489 into Y, wherein amino acid positions are numbered according to

the numbering of the amino acid residues in SEQ ID NO:1, and wherein the protein does not comprise a heterologous trimerization domain.

The disclosure further provides nucleic acids encoding the proteins according to the disclosure, as well as vectors comprising such nucleic acids.

In another aspect, the present disclosure provides a nucleic acid encoding a protein as defined herein.

In another aspect, the present disclosure provides a vector comprising a nucleic acid as defined herein.

Compositions comprising the protein(s), nucleic acid(s) and/or vector(s) according to the disclosure, as well as the use thereof are also provided.

In another aspect, the present disclosure provides a composition comprising a protein as defined herein, a nucleic acid as defined herein or a vector as defined herein.

The disclosure also provides isolated host cells comprising a nucleic acid according to the disclosure.

In another aspect, the present disclosure provides an isolated host cell comprising a nucleic acid as defined herein

In another aspect, the present disclosure provides a composition as defined herein for use as a vaccine.

In another aspect, the present disclosure provides use of the composition as defined herein in the manufacture of a medicament for preventing infection and/or replication of RSV.

In another aspect, the present disclosure provides a composition as defined herein for use in preventing infection and/or replication of RSV.

BRIEF DESCRIPTION OF THE FIGURES

The foregoing summary, as well as the following detailed description of the invention, will be better understood when read in conjunction with the appended figures. It should be understood that the invention is not limited to the precise embodiments shown in the examples.

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CLAIMS

1. A respiratory syncytial virus (RSV) F protein, comprising a head region and a stem region, wherein the protein comprises at least two amino acid mutations in the stem region relative to the amino acid sequence of a wild-type RSV F protein and amino acid mutations in the head region, wherein the at least two amino acid mutations in the stem region comprises a mutation of the amino acid residue at position 509 into F, I or L and a mutation of the amino acid residue at position 505 into W, wherein the amino acid mutations in the head region comprises a mutation of the amino at residue 215 into P, a mutation of the amino acid residue at position 486 into N, a mutation of the amino acid residue at position 101 into Q, S, T, A, or G, a mutation of the amino acid residue at position 354 into L, a mutation of the amino acid at position 487 into L, and a mutation of the amino acid residue at position 489 into Y, wherein amino acid positions are numbered according to the numbering of the amino acid residues in SEQ ID NO:1, and wherein the protein does not comprise a heterologous trimerization domain.

2. The protein according to claim 1, wherein the RSV F protein is an F protein of an RSV A subtype.

3. The protein according to claim 1, wherein the RSV F protein is an F protein of an RSV B subtype.

4. The protein according to any one of claims 1-3, wherein the protein further comprises at least one additional mutation in the head region selected from the group consisting of a mutation of the amino acid residue at position 152 into M, and a mutation of the amino acid

residue at position 203 into I, and wherein amino acid positions are numbered according to the numbering of the amino acid residues in SEQ ID NO:1.

5. The protein according to claims 1 or 4, wherein the protein further comprises at least one additional mutation in the stem region selected from the group consisting of a mutation of the amino acid residue at position 519 into V and a mutation of the amino acid residue 523 into I, and wherein amino acid positions are numbered according to the numbering of the amino acid residues in SEQ ID NO:1.

6. The protein according to any one of claims 1-5, wherein the mutation of the amino acid residue in the stem region at position 509 is a mutation into F.

7. The protein according to any one of claims claim 1-6, wherein the protein has been truncated after the amino acid residue 524.

8. The protein according to any one of claims 1-4 or 6, wherein the protein has been truncated at the C-terminus after amino acid residue 513.

9. The protein according to any one of the preceding claims wherein the protein is trimeric.

10. The protein according to claim 9, comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 18, 43 and 44, or a fragment thereof.

11. A nucleic acid encoding a protein according to any one of claims 1-10.

12. The nucleic acid according to claim 11, wherein the nucleic acid is DNA or RNA.

13. The nucleic acid according to claim 12, wherein the RNA is mRNA, modified mRNA, self-replicating RNA, or circular mRNA.

14. A vector comprising a nucleic acid according to any one of claims 11-13.

15. A composition comprising a protein according to any one of claims 1-10, a nucleic acid according to any one of claims 11-13 or a vector according to claim 14.

16. A composition according to claim 15 for use as a vaccine.

17. Use of the composition according to claim 15 in the manufacture of a medicament for preventing infection and/or replication of RSV.

18. An isolated host cell comprising a nucleic acid according to any one of claims 11-13.

19. A composition according to claim 15 for use in preventing infection and/or replication of RSV.