

Claims

1. Recombinant pre-fusion SARS-CoV-2 S protein, or a fragment thereof, comprising an S1 and an S2 domain, and comprising at least one mutation selected from the group consisting of a mutation of at least one amino acid in the loop region corresponding to amino acid residues 941 – 945 into P, a mutation of the amino acid at position 892, a mutation of the amino acid at position 614, a mutation at position 572, a mutation at position 532, a disulfide bridge between residues 880 and 888, and a disulfide bridge between residues 884 and 893, wherein the numbering of the amino acid positions is according to the numbering of the amino acid positions in SEQ ID NO: 1.
2. The protein, or fragment thereof, according to claim 1, comprising an amino acid sequence wherein the amino acid at position 892 is not alanine (A), the amino acid at position 614 is not aspartic acid (D), the amino acid at position 532 is not Asparagine (N) and/or amino acid at position 572 is not threonine (T).
3. The protein, or fragment thereof, according to claim 1, or 2, comprising a mutation of at least one amino acid in the loop region corresponding to amino acid residues 941 – 945 into P, and a mutation selected from the group consisting of a mutation of the amino acid at position 892, a mutation of the amino acid at position 614, a mutation at position 572, a mutation at position 532, a disulfide bridge between residues 880 and 888 and a disulfide bridge between residues 884 and 893.
4. The protein, or fragment thereof, according to claim 3, comprising a mutation of at least one amino acid in the loop region corresponding to amino acid residues 941 – 945

into P, and a mutation selected from the group consisting of a mutation of the amino acid at position 892, a mutation of the amino acid at position 614, a mutation at position 572, a mutation at position 532, a disulfide bridge between residues 880 and 888 and a disulfide bridge between residues 884 and 893, provided that the proteins do not comprise both the disulfide bridge between residues 880 and 888 and the disulfide bridge between residues 884 and 893.

5. The protein, or fragment thereof, according to any one of the preceding claims, wherein the disulfide bridge is a disulfide bridge between residues 880 and 888.
6. The protein, or fragment thereof, according to any one of the preceding claims, wherein at least one mutation in the loop region corresponding to amino acid residues 941 – 945 is a mutation of the amino acid at position 942 into P.
7. The protein, or fragment thereof, according to any one of the preceding claims, wherein the at least one mutation in the loop region corresponding to amino acid residues 941 – 945 is a mutation of the amino acid at position 941 into P.
8. The protein, or fragment thereof, according to any one of the preceding claims, wherein the at least one mutation in the loop region corresponding to amino acid residues 941 – 945 is a mutation of the amino acid at position 944 into P.
9. The protein, or fragment thereof, according to any one of the preceding claims, wherein the mutation at position 892 is a mutation into P.

10. The protein, or fragment thereof, according to any one of the preceding claims, wherein the mutation at position 614 is a mutation into N or G.
11. The protein, or fragment thereof, according to any one of the preceding claims, wherein the mutation at position 532 is a mutation into P.
12. The protein, or fragment thereof, according to any one of the preceding claims, wherein the mutation at position 572 is a mutation into I.
13. The protein, or fragment thereof, according to any one of the preceding claims, comprising an amino acid sequence wherein the amino acid at position 892 is proline (P), the amino acid at position 614 is glycine (G), the amino acid at position 942 is proline (P) and/or the amino acid at position 944 is proline (P).
14. The protein, or fragment thereof, according to any one of the preceding claims, further comprising a deletion of the furin cleavage site.
15. The protein, or fragment thereof, according to claim 14, wherein the deletion of the furin cleavage site comprises a mutation of the amino acid at position 682 into S and/or a mutation of the amino acid at position 685 into G.
16. The protein, or fragment thereof, according to any one of the preceding claims, further comprising a mutation of the amino acids at position 986 and/or 987 into P.

17. The protein according to any of the preceding claims, comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 5-194 and SEQ ID NO: 197-418, SEQ ID NO: 420 and SEQ ID NO: 421, or a fragment thereof.
18. The protein, or fragment thereof, according to anyone of the preceding claims, wherein the protein, or fragment thereof, does not comprise a signal peptide or a tag sequence.
19. The protein, or fragment thereof, according to any one of the preceding claims, comprising a truncated S2 domain.
20. The protein, or fragment thereof, according to claim 18 wherein the transmembrane and cytoplasmic domain have been removed.
21. The protein, or fragment thereof, according to claim 18 or 19, wherein a heterologous trimerization domain has been linked to the truncated S2 domain.
22. The protein, or fragment thereof, according to claim 21, wherein the heterologous trimerization domain is a foldon domain comprising the amino acid sequence of SEQ ID NO:4.
23. Nucleic acid molecule encoding a protein, or fragment thereof, according to any one of the preceding claims 1-22.

24. Nucleic acid according to claim 23, wherein the nucleic acid molecule is DNA or RNA.
25. Vector comprising a nucleic acid according to claim 23 or 24.
26. Vector according to claim 25, wherein the vector is a human recombinant adenoviral vector.
27. A composition comprising a protein according to any one of the claims 1-22, a nucleic acid according to claim 23 or 24 and/or vector according to claim 25 or 26.
28. A vaccine against COVID-19 comprising a protein, or fragment thereof, according to any one of the claims 1-22, a nucleic acid according to claim 23 or 24 and/or vector according to claim 25 or 26.
29. Use of the vaccine according to claim 28 in the manufacture of a medicament for vaccinating a subject against COVID-19, wherein the vaccine is to be administered to the subject.
30. Use of the composition according to claim 27 or the vaccine according to claim 28 in the manufacture of a medicament for reducing infection and/or replication of SARS-CoV-2 in a subject, wherein the composition or vaccine is to be administered to the subject.
31. An isolated host cell comprising a nucleic acid according to claim 23.

32. An isolated host cell comprising a recombinant human adenovirus of serotype 26 comprising a nucleic acid according to claim 23.
33. The vaccine according to claim 28 for use in vaccinating a subject against COVID-19.
34. The composition according to claim 27 or the vaccine according to claim 28 for use in reducing infection and/or replication of SARS-CoV-2 in a subject.