CLAIMS

1. A recombinant SARS-CoV-2 spike protein (S protein),

(a) comprising following mutations in an extracellular domain, compared with a wild type S protein:

T19R, G142D, E156G, F157 deletion, R158 deletion, A222V, L452R, T478K, D614G, P681R and D950N; wherein the amino acid positions are numbered according to the amino acid sequence of the wild type S protein as shown in SEQ ID NO. 29; or

(b) comprising following mutations in an extracellular domain, compared with a wild type S protein:

A67V, H69 deletion, V70 deletion, T95I, G142 deletion, V143 deletion, Y144 deletion, Y145D, N211 deletion, L212I, insertion mutation of three amino acids E, P, E between R214 and D215, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K and L981F;

wherein the amino acid positions are numbered according to the amino acid sequence of the wild type S protein as shown in SEQ ID NO. 29.

2. The recombinant S protein of claim 1, wherein a S1/S2 cleavage site RRAR and/or a S2 cleavage site KR are(is) mutated to lose the ability of being cleaved by Furin-like protease and lysosomal protease; preferably, the S1/S2 cleavage site is mutated to GGSG, and/or the S2 cleavage site is mutated to AN.

3. The recombinant S protein of claim 1 or 2, further comprising K986P and V987P mutations.

4. The recombinant S protein of any one of claims 1-3, wherein in (a), the recombinant S protein does not comprise a fusion peptide (FP) domain; optionally, the recombinant S protein does not comprise a transmembrane domain and a cytoplasmic domain; optionally, the recombinant S protein further comprises a trimer domain facilitating the recombinant S protein to form a trimer, when being expressed; preferably, the trimer domain is a T4 phage fibritin trimer motif; optionally, the recombinant S protein further comprises a signal sequence, preferably, the signal sequence is a signal sequence of an immunoglobulin heavy chain variable region; or

wherein in (b), the recombinant S protein comprises, from N terminal to C terminal, an extracellular domain, a transmembrane domain and a cytoplasmic domain; preferably, the recombinant S protein further comprises a signal sequence, preferably, the signal sequence is a signal sequence of an immunoglobulin heavy chain variable region.

5. The recombinant S protein of claim 1, wherein,

in (a), the recombinant S protein has an amino acid sequence as shown in any one selected from SEQ ID NO. 1-5, preferably has an amino acid sequence as shown in any one selected from SEQ ID NO. 3-5; or

in (b), the recombinant S protein has an amino acid sequence as shown in any one selected from SEQ ID NO. 20-25, preferably has an amino acid sequence as shown in SEQ ID NO. 25.

6. A mRNA encoding the recombinant S protein of any one of claims 1-5.

7. The mRNA of claim 6, which comprises, from 5’ to 3’, a cap structure, 5’-UTR, open reading flame (ORF), 3’-UTR and a polyA tail;

preferably, wherein the 5’-UTR comprises a 5'-UTR derived from 17β-hydroxysteroid dehydrogenase 4 (HSD17B4) gene or homologs, fragments or variants thereof and/or a KOZAK sequence, preferably, the 5’-UTR comprises a sequence as shown in SEQ ID NO. 8 and/or SEQ ID NO. 9;

wherein the 3’-UTR comprises a 3'-UTR derived from albumin (ALB) gene or homologs, fragments or variants thereof, preferably, the 3’-UTR comprises a sequence as shown in SEQ ID NO. 10; and/or

wherein the polyA tail is 100-150 nucleotides in length.

8. The mRNA of claim 6, wherein the sequence of the mRNA is as shown in any one of SEQ ID NO. 14-16, or the sequence of the mRNA is as shown in SEQ ID NO. 27.

9. The mRNA of any one of claims 6-8, wherein one or more nucleotides of the mRNA each is independently replaced by naturally occurring nucleotide analogues or artificially synthesized nucleotide analogues, wherein the naturally occurring nucleotide analogues are selected from pseudouridine, 2-thiouridine, 5-methyluridine, 5-methylcytidine and N6-methyladenosine and the artificially synthesized nucleotide analogues are selected from N1-methylpseudouridine and 5-ethynyluridine;

preferably, one or more uridine triphosphate of the mRNA each is independently replaced by pseudo-uridine triphosphate, 1-methyl-pseudo-uridine triphosphate or 5-ethynyl-uridine triphosphate, and/or one or more cytidine triphosphate each is independently replaced by 5-methyl-cytidine triphosphate.

10. A composition, which comprises the recombinant S protein in (a) of any one of claims 1-5and the recombinant S protein in (b) of any one of claims1-5. or, wherein the composition comprises the mRNA encoding the recombinant S protein in (a) of any one of claims 6-9 and the mRNA encoding the recombinant S protein in (b) of any one of claims 6-9;

preferably 11. The composition of claim 10, wherein the composition comprises the mRNA having an amino sequence as shown in any one of SEQ ID NOs. 14-16 and the mRNA having an amino sequence as shown in SEQ ID NO. 27;

12. The composition of claim 10 or 11, wherein the molar ratio of the two kinds of recombinant S proteins in (a) and in (b) or the two kinds of mRNAs encoding the recombinant S protein in (a) and in (b) in the composition is 1-3:1-3, preferably 1:1.

13. The composition of any one of claims 10-12, which further comprises following recombinant S protein or mRNA encoding the same:

(a) a recombinant S protein comprising following mutations compared with a wild type S protein: K986P and V987P;

and/or

(b) a recombinant S protein comprising following mutations compared with a wild type S protein: G75V, T76I, R246 deletion, S247 deletion, Y248 deletion, L249 deletion, T250 deletion, P251 deletion, G252 deletion, D253N, L452Q, F490S, D614G, T859N; K986P; and V987P;

and/or

(c) a recombinant S protein comprising following mutations compared with a wild type S protein: mutation of a S1/S2 cleavage site to GGSG; K986P; and V987P;

and/or

(d) a recombinant S protein comprising following mutations compared with a wild type S protein: mutation of a S2 cleavage site to AN; K986P; and V987P;

and/or

(e) a recombinant S protein comprising following mutations compared with a wild type S protein: mutation of a S1/S2 cleavage site to GGSG; mutation of a S2 cleavage site to AN; K986P; and V987P;

and/or

(f) a recombinant S protein comprising following mutations compared with a wild type S protein: G75V, T76I, R246 deletion, S247 deletion, Y248 deletion, L249 deletion, T250 deletion, P251 deletion, G252 deletion, D253N, L452Q, F490S, D614G, T859N; mutation of a S1/S2 cleavage site to GGSG; K986P; and V987P;

and/or

(g) a recombinant S protein comprising following mutations compared with a wild type S protein: G75V, T76I, R246 deletion, S247 deletion, Y248 deletion, L249 deletion, T250 deletion, P251 deletion, G252 deletion, D253N, L452Q, F490S, D614G, T859N; mutation of a S2 cleavage site to AN; K986P; and V987P;

and/or

(h) a recombinant S protein comprising following mutations compared with a wild type S protein: G75V, T76I, R246 deletion, S247 deletion, Y248 deletion, L249 deletion, T250 deletion,

P251 deletion, G252 deletion, D253N, L452Q, F490S, D614G, T859N; mutation of a S1/S2 cleavage site to GGSG; mutation of a S2 cleavage site to AN; K986P; andV987P.

14. A DNA encoding the mRNA of any one of claims 6-9.

15. The DNA of claim 14, wherein the sequence of the DNA is as shown in any one of SEQ ID NOs. 11-13 and SEQ ID NO. 26.

16. A recombinant plasmid, which comprises the DNA of claim 14 or 15.

17. The recombinant plasmid of claim 16, wherein the recombinant plasmid is a pT7TS plasmid;

preferably, the recombinant plasmid further comprises an original sequence (Ori), a T7 promoter, 5'-UTR and 3'-UTR;

preferably, wherein the original sequence is of ColE1 type, preferably, the original sequence is as shown in SEQ ID NO.6;

wherein the sequence of the T7 promoter is as shown in SEQ ID NO.7;

wherein the 5'-UTR comprises a 5'-UTR derived from HSD17B4 or homologs, fragments or variants thereof, and/or a KOZAK sequence, preferably, the 5'-UTR comprises a sequences as shown in SEQ ID NO. 8 and/or SEQ ID NO. 9; and/or

wherein the 3'-UTR comprises a 3'-UTR derived from ALB or homologs, fragments or variants thereof, preferably, the 3'-UTR comprises a sequence as shown in SEQ ID NO. 10;

more preferably, wherein the recombinant plasmid further comprises a polyA, a resistance gene promoter and a resistance gene;

preferably, the polyA is 100-150 nucleotides in length; the resistance gene promoter is an ampicillin resistance gene promoter; and/or the resistance gene is a kanamycin sulfate resistance gene.

18. The recombinant plasmid of claim 16, wherein the nucleic acid sequence of the recombinant plasmid is as shown in SEQ ID NO. 28.

19. A mRNA-carrier particle, which comprises at least one of the mRNA of any one of claims 6-9, and a carrier material encapsulating the mRNA.

20. The recombinant S protein of any one of claims 1-5, the mRNA of any one of claims 6-9, the composition of any one of claims 10-13, the recombinant plasmid of any one of claims 16-17, or the mRNA-carrier particle of claim 18 for use in a method for preventing and/or treating a diseases or condition associated with SARS-CoV-2 infection in a subject; preferably, wherein the disease or condition is a disease or condition caused by infection of SARS-CoV-2 variants, such as a Delta variant, a Omicron variant or a Lambda variant.