

## CLAIMS

1. A non-naturally occurring sudden acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike (CoV S) glycoprotein, wherein the CoV S glycoprotein comprises modifications compared to a native CoV S glycoprotein, wherein:
  - (i) the first modification is an inactivated furin cleavage site; and
  - (ii) the second modification is mutation of amino acids 973 and 974 to proline;wherein the amino acids are numbered according to SEQ ID NO: 2.
2. The non-naturally occurring SARS-CoV-2 CoV S glycoprotein of claim 1, wherein the inactivated furin cleavage site comprises a polypeptide sequence selected from any one of SEQ ID NOS: 7-34, 97, and 111.
3. The non-naturally occurring SARS-CoV-2 S glycoprotein of claim 1 or 2, wherein the inactivated furin cleavage site comprises the amino acid sequence of QQAQ (SEQ ID NO: 7).
4. The non-naturally occurring SARS-CoV-2 CoV S glycoprotein of claim 1, wherein the CoV S glycoprotein consists of two modifications compared to a native CoV S glycoprotein, wherein:
  - (i) the first modification is an inactivated furin cleavage site, wherein the inactivated furin cleavage site comprises the amino acids QQAQ (SEQ ID NO: 7); and
  - (ii) the second modification is mutation of amino acids 973 and 974 to proline;wherein the amino acids are numbered according to SEQ ID NO: 2.
5. The non-naturally occurring SARS-CoV-2 CoV S glycoprotein of any one of claims 1-4, wherein the CoV S glycoprotein is at least 80 %, at least 90 %, at least 95 %, at least 97 %, or at least 99 % identical to a SARS-CoV-2 S glycoprotein comprising the sequence of SEQ ID NO: 2.

6. The non-naturally occurring SARS-CoV-2 CoV S glycoprotein of any one of claims 1-4, wherein the CoV S glycoprotein is at least 95 %, at least 96 %, at least 97 %, at least 98 %, at least 99 %, at least 99.5 %, or 100 % identical to a SARS-CoV-2 S glycoprotein comprising the sequence of SEQ ID NO: 87.
7. A nucleic acid encoding the CoV S glycoprotein of any one of claims 1-6.
8. A host cell comprising the SARS-CoV-2 CoV S glycoprotein of any one of claims 1-6.
9. A host cell expressing the nucleic acid of claim 7.
10. The host cell of claim 8 or 9, wherein the cell is an insect cell.
11. The host cell of claim 10, wherein the insect cell is selected from the group consisting of a *Spodoptera frugiperda* 9 (Sf9) cell, a *Spodoptera frugiperda* 21 (Sf21) cell, a *Trichoplusia ni* cell, and a *Drosophila* S2 cell.
12. The host cell of claim 10 or 11, wherein the insect cell is a Sf9 cell.
13. An immunogenic composition comprising:
  - (a) a non-naturally occurring SARS-CoV-2 CoV S glycoprotein of any one of claims 1-6;
  - (b) an adjuvant; and
  - (c) a pharmaceutically acceptable buffer.
14. An immunogenic composition comprising:
  - (a) a nanoparticle comprising a non-naturally occurring SARS-CoV-2 CoV S glycoprotein of any one of claims 1-6 and a non-ionic detergent core;
  - (b) an adjuvant; and
  - (c) a pharmaceutically acceptable buffer.
15. An immunogenic composition comprising:

(a) a non-naturally occurring SARS-CoV-2 CoV S glycoprotein comprising the polypeptide sequence of SEQ ID NO: 87;

(b) a saponin adjuvant; and

(c) a pharmaceutically acceptable buffer;

wherein the saponin adjuvant comprises at least two iscom particles, wherein:

the first iscom particle comprises fraction A of *Quillaja Saponaria* Molina and not fraction C of *Quillaja Saponaria* Molina; and

the second iscom particle comprises fraction C of *Quillaja Saponaria* Molina and not fraction A of *Quillaja Saponaria* Molina;

wherein fraction A of *Quillaja Saponaria* Molina accounts for 50-96% by weight and fraction C of *Quillaja Saponaria* Molina accounts for the remainder, respectively, of the sum of the weights of fraction A of *Quillaja Saponaria* Molina and fraction C of *Quillaja Saponaria* Molina in the adjuvant.

16. The immunogenic composition of any one of claims 13-15, comprising from 3 µg to 25 µg of CoV S glycoprotein.

17. The immunogenic composition of claim 16 comprising from 5 µg to 25 µg of CoV S glycoprotein.

18. The immunogenic composition of any one of claims 13-17, comprising about 5 µg of CoV S glycoprotein.

19. The immunogenic composition of any one of claims 13-18, wherein the adjuvant is selected from alum, incomplete Freund's adjuvant; aluminum hydroxide adjuvant; a paucilamellar lipid vesicle; monophosphoryl lipid A; MF-59; or a saponin adjuvant.

20. The immunogenic composition of any one of claims 13, 14, 16-19, wherein the adjuvant is a saponin adjuvant.

21. The immunogenic composition of claim 20, wherein the saponin adjuvant comprises at least two iscom particles, wherein:
- the first iscom particle comprises fraction A of *Quillaja Saponaria* Molina and not fraction C of *Quillaja Saponaria* Molina; and
- the second iscom particle comprises fraction C of *Quillaja Saponaria* Molina and not fraction A of *Quillaja Saponaria* Molina.
22. The immunogenic composition of claim 21, wherein fraction A of *Quillaja Saponaria* Molina accounts for 50-96% by weight and fraction C of *Quillaja Saponaria* Molina accounts for the remainder, respectively, of the sum of the weights of fraction A of *Quillaja Saponaria* Molina and fraction C of *Quillaja Saponaria* Molina in the adjuvant.
23. The immunogenic composition of claim 21 or claim 15, wherein fraction A of *Quillaja Saponaria* Molina and fraction C of *Quillaja Saponaria* Molina account for about 85 % by weight and about 15 % by weight, respectively, of the sum of the weights of fraction A of *Quillaja Saponaria* Molina and fraction C of *Quillaja Saponaria* Molina in the adjuvant.
24. The immunogenic composition of any one of claims 14-23; wherein the non-ionic detergent is selected from the group consisting of polysorbate-20 (PS20), polysorbate-40 (PS40), polysorbate-60 (PS60), polysorbate-65 (PS65), and polysorbate-80 (PS80).
25. The immunogenic composition of any one of claims 14-23; wherein the non-ionic detergent is PS80.
26. The immunogenic composition of any one of claims 20-23; wherein the composition comprises 50 µg of saponin adjuvant.

27. Use of the immunogenic composition of any one of claims 13-26 or the SARS-CoV-2 CoV S glycoprotein of any one of claims 1-6 in the preparation of a medicament for stimulating an immune response against SARS-CoV-2 in a subject.
28. The use of claim 27, wherein the immunogenic composition comprises from 3 µg to 25 µg of CoV S glycoprotein.
29. The use of claim 28, wherein the immunogenic composition comprises from 5 µg to 25 µg of CoV S glycoprotein.
30. The use of any one of claims 27-29, wherein the immunogenic composition comprises about 5 µg of CoV S glycoprotein.
31. The use of any one of claims 27-30, wherein the immunogenic composition comprises about 50 µg of adjuvant.
32. The use of any one of claims 27-31, wherein the adjuvant is saponin adjuvant.
33. The use of claim 32, wherein the saponin adjuvant comprises at least two iscom particles, wherein:
  - the first iscom particle comprises fraction A of *Quillaja Saponaria* Molina and not fraction C of *Quillaja Saponaria* Molina; and
  - the second iscom particle comprises fraction C of *Quillaja Saponaria* Molina and not fraction A of *Quillaja Saponaria* Molina.
34. The use of claim 33, wherein fraction A of *Quillaja Saponaria* Molina accounts for 50-96% by weight and fraction C of *Quillaja Saponaria* Molina accounts for the remainder, respectively, of the sum of the weights of fraction A of *Quillaja Saponaria* Molina and fraction C of *Quillaja Saponaria* Molina in the adjuvant.

35. The use of claim 33, wherein fraction A of *Quillaja Saponaria* Molina and fraction C of *Quillaja Saponaria* Molina account for about 85 % by weight and about 15 % by weight, respectively, of the sum of the weights of fraction A of *Quillaja Saponaria* Molina and fraction C of *Quillaja Saponaria* Molina in the adjuvant.
36. The use of claim 33, wherein fraction A of *Quillaja Saponaria* Molina and fraction C of *Quillaja Saponaria* Molina account for about 92 % by weight and about 8 % by weight, respectively, of the sum of the weights of fraction A of *Quillaja Saponaria* Molina and fraction C of *Quillaja Saponaria* Molina in the adjuvant.
37. The use of any one of claims 27-36, wherein a single dose of the immunogenic composition is to be administered to the subject.
38. The use of any one of claims 27-36, wherein the subject is to be administered a first dose of the immunogenic composition at day 0 and a boost dose at day 21.
39. The use of any one of claims 27-38, comprising a second immunogenic composition to be administered to the subject, wherein the second immunogenic composition is different from the immunogenic composition of claims 13-26 or the SARS-CoV-2 CoV S glycoprotein of claims 1-6.
40. The use of claim 39, wherein the second immunogenic composition comprises an mRNA encoding a SARS-Cov-2 Spike glycoprotein, a plasmid DNA encoding a SARS-Cov-2 Spike glycoprotein, a viral vector encoding a SARS-Cov-2 Spike glycoprotein, or an inactivated SARS-CoV-2 virus.
41. The use of claim 39 or claim 40, wherein the second immunogenic composition is to be administered before or after the immunogenic composition of claims 13-26 or the SARS-CoV-2 CoV S glycoprotein of claims 1-6.