

CLAIMS

1. A coronavirus (CoV) Spike (S) glycoprotein comprising
 - (i) an S1 subunit with an inactivated furin cleavage site, wherein the S1 subunit comprises an N-terminal domain (NTD), a receptor binding domain (RBD), subdomains 1 and 2 (SD1/2), wherein the inactivated furin cleavage site has an amino acid sequence of QQAQ;
wherein the NTD optionally comprises one or more modifications selected from the group consisting of:
 - (a) deletion of one or more amino acids selected from the group consisting of amino acid 56, 57, 131, 132, 229, 230, 231, and combinations thereof; and
 - (b) mutation of one or more amino acids selected from the group consisting of amino acid 67, 229, 202, 139, 5, 233, 7, 13, 125, 177, and combinations thereof;
wherein the RBD optionally comprises mutation of one or more amino acids selected from the group consisting of amino acid 488, 404, 471, 439, 426, 440, and combinations thereof;
wherein the SD1/2 domain optionally comprises mutation of one or more amino acids selected from the group consisting of 601, 557, 668, 642, and combinations thereof; and
 - (ii) an S2 subunit, wherein amino acids 973 and 974 are proline,
wherein the S2 subunit optionally comprises one or more modifications selected from the group consisting of:
 - (a) deletion of one or more amino acids from 676-702, 702-711, 775-793, 806-815 and combinations thereof;
 - (b) mutation of one or more amino acids selected from the group consisting of 703, 1105, 688, 969, and 1014, and combinations thereof; and
 - (c) deletion of one or more amino acids from the TMCT.
2. The coronavirus S glycoprotein of claim 1, comprising deletion of amino acids 676-685.
3. The coronavirus S glycoprotein of claim 1, comprising deletion of amino acids 702-711.
4. The coronavirus S glycoprotein of claim 1, comprising a deletion of amino acids 806-815.

5. The coronavirus S glycoprotein of claim 1, comprising a deletion of amino acids 775-793.
6. The coronavirus S glycoprotein of claim 1, comprising deletion of amino acids 1-292 of the NTD.
7. The coronavirus S glycoprotein of claim 1, comprising deletion of amino acids 1201-1260 of the transmembrane and cytoplasmic tail (TMCT).
8. The coronavirus S glycoprotein of claim 1 comprising or consisting of an amino acid sequence selected from the group consisting of SEQ ID NOS: 85-89, 105, 106, and 112-115.
9. The coronavirus S glycoprotein of any one of claims 1 to 8 comprising a signal peptide, optionally wherein the signal peptide comprises an amino acid sequence of SEQ ID NO: 5 or SEQ ID NO: 117.
10. The coronavirus S glycoprotein of any one of claims 1 to 9 comprising a C-terminal fusion protein.
11. The coronavirus S glycoprotein of claim 10, wherein the C-terminal fusion protein is a hexahistidine tag.
12. The coronavirus S glycoprotein of claim 10, wherein the C-terminal fusion protein is a foldon.
13. The coronavirus S glycoprotein of claim 12, wherein the foldon has an amino acid sequence corresponding to SEQ ID NO: 68.

14. The coronavirus S glycoprotein of any one of claims 1-13, wherein the ΔH_{cal} is at least 2-fold greater than the ΔH_{cal} of the wild-type CoV S glycoprotein (SEQ ID NO: 2).
15. The coronavirus S glycoprotein of any one of claims 1-14, wherein each of the S2 subunit, NTD, RBD, and SD1/2 is 95 % identical to the corresponding subunit or domain of the CoV S glycoprotein having an amino acid sequence of SEQ ID NO: 2.
16. The coronavirus S glycoprotein of any one of claims 1-14, wherein each of the S2 subunit, NTD, RBD, and SD1/2 is 97 % identical to the corresponding subunit or domain of the CoV S glycoprotein having an amino acid sequence of SEQ ID NO: 2.
17. The coronavirus S glycoprotein of any one of claims 1-14, wherein each of the S2 subunit, NTD, RBD, and SD1/2 is 99 % identical to the corresponding subunit or domain of the CoV S glycoprotein having an amino acid sequence of SEQ ID NO: 2.
18. The coronavirus S glycoprotein of any one of claims 1-14, wherein each of the S2 subunit, NTD, RBD, and SD1/2 is 99.5 % identical to the corresponding subunit or domain of the CoV S glycoprotein having an amino acid sequence of SEQ ID NO: 2.
19. An isolated nucleic acid encoding the S glycoprotein of any of claims 1-18.
20. A vector comprising the nucleic acid of claim 19.
21. A nanoparticle comprising the coronavirus S glycoprotein of any one of claims 1-18.
22. The nanoparticle of claim 21, wherein the nanoparticle has a Z_{avg} diameter of between about 20 nm and about 35 nm.
23. The nanoparticle of claim 21, wherein the nanoparticle has a polydispersity index from about 0.2 to about 0.45.

24. A cell expressing the coronavirus S glycoprotein of any of claims 1-18.
25. A vaccine composition comprising the coronavirus S glycoprotein of any one of claims 1-18 and a pharmaceutically acceptable buffer.
26. The vaccine composition of claim 25, comprising an adjuvant.
27. The vaccine composition of claim 26, wherein the 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.
28. The vaccine composition of claim 27, 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 weights of fraction A of *Quillaja Saponaria* Molina and fraction C of *Quillaja Saponaria* Molina in the adjuvant.
29. The vaccine composition of claim 26, wherein the adjuvant is administered at a dose of about 50 µg.
30. A method of stimulating an immune response against SARS-CoV-2 in a subject comprising administering the vaccine composition of any one of claims 25-29.
31. The method of claim 30, wherein the subject is administered a first dose at day 0 and a boost dose at day 21.
32. The method of claim 30, wherein the subject is administered between about 5 µg and about 25 µg of coronavirus S glycoprotein.

33. The method of claim 30, wherein the subject is administered about 5 µg of coronavirus S glycoprotein.
34. The method of any one of claims 30-33, wherein the vaccine composition is administered intramuscularly.
35. The method of any one of claims 30, 32, 33, and 34, wherein a single dose of the vaccine composition is administered.
36. The method of any one of claims 30-34, wherein multiple doses of the vaccine composition are administered.
37. The method of any one of claims 30-36, wherein the vaccine composition is coadministered with an influenza glycoprotein.
38. An immunogenic composition comprising:
 (i) a nanoparticle comprising a coronavirus S (CoV S) glycoprotein having the amino acid sequence of SEQ ID NO: 87, and a non-ionic detergent core;
 (ii) a pharmaceutically acceptable buffer, and
 (iii) a saponin adjuvant.
39. The immunogenic composition of claim 38, comprising between about 5 µg and about 25 µg of CoV S glycoprotein.
40. The immunogenic composition of claim 39, comprising about 5 µg of CoV S glycoprotein.
41. The immunogenic composition of claim 38, 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.

42. The immunogenic composition of claim 41, 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.
43. The immunogenic composition of claim 41, 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.
44. The immunogenic composition of claim 38, comprising about 50 µg of saponin adjuvant.
45. The immunogenic composition of claim 38, wherein the non-ionic detergent core is selected from the group consisting of polysorbate-20 (PS20), polysorbate-40 (PS40), polysorbate-60 (PS60), polysorbate-65 (PS65), and polysorbate-80 (PS80).
46. A method of stimulating an immune response against SARS-CoV-2 in a subject comprising administering the immunogenic composition of claim 38.
47. The method of claim 46, comprising between about 5 µg and about 25 µg of CoV S glycoprotein.
48. The method of claim 47, comprising 5 µg of CoV S glycoprotein.
49. The method of claim 46, 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.

50. The method of claim 49, 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.

51. The method of claim 49, 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.

52. The method of claim 46, comprising about 50 µg of saponin adjuvant.

53. The method of claim 46, wherein the non-ionic detergent core is selected from the group consisting of polysorbate-20 (PS20), polysorbate-40 (PS40), polysorbate-60 (PS60), polysorbate-65 (PS65), and polysorbate-80 (PS80).

54. The method of claim 46, wherein the subject is administered a first dose at day 0 and a boost dose at day 21.

55. The method of claim 46, wherein a single dose of the immunogenic composition is administered.

56. The method of claim 46, comprising administering a second immunogenic composition different from the first immunogenic composition.

57. The method of claim 56, 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.