

WHAT IS CLAIMED IS:

1. An engineered immunogen polypeptide derived from the spike (S) protein of a coronavirus, comprising an altered soluble S sequence that has modifications relative to wildtype soluble S sequence of the coronavirus that stabilize the prefusion S structure, wherein the modifications comprise (a) a mutation that inactivates the S1/S2 cleavage site, and (b) a mutation in the turn region between the heptad repeat 1 (HR1) region and the central helix (CH) region that prevents HR1 and CH to form a straight helix during fusion.
2. The immunogen polypeptide of claim 1, further comprising truncation of the heptad repeat 2 region (HR2).
3. The immunogen polypeptide of claim 1, wherein the coronavirus is SARS-CoV-2, wherein the mutation inactivating S1/S2 cleavage site comprises substitution of ⁶⁸²RRAR⁶⁸⁵ (SEQ ID NO:19) with GSAG (SEQ ID NO:20), and the mutation in the turn region comprises double mutation K986G/V987G, K986P/V987P, K986G/V987P or K986P/V987G, wherein the amino acid numbering is based on cryo-EM model PDB ID 6VSB.
4. The immunogen polypeptide of claim 3, wherein the wildtype soluble S sequence comprises SEQ ID NO:14, or a substantially identical or conservatively modified variant thereof.
5. The immunogen polypeptide of claim 4, further comprising truncation of HR2 (SEQ ID NO:9) at the C-terminus of the wildtype soluble S sequence.
6. The immunogen polypeptide of claim 5, further comprising a N-terminal leader sequence shown in SEQ ID NO:15.
7. The immunogen polypeptide of claim 5, further comprising a trimerization motif at the C-terminus.
8. The immunogen polypeptide of claim 7, wherein the trimerization motif comprises foldon (SEQ ID NO:26) or viral capsid protein SHP (SEQ ID NO:27), or a substantially identical or conservatively modified variant thereof.

9. The immunogen polypeptide of claim 5, comprising the sequence shown in any one of SEQ ID NOs:32-37, or a substantially identical or conservatively modified variant thereof.

10. The immunogen polypeptide of claim 1, further comprising the subunit sequence of a self-assembling nanoparticle that is fused to the C-terminus of the altered soluble S sequence.

11. A polynucleotide sequence that encodes the immunogen polypeptide of claim 3.

12. The polynucleotide sequence of claim 11, wherein the immunogen polypeptide further comprises a N-terminal leader.

13. The polynucleotide sequence of claim 11, encoding a fusion polypeptide comprising the immunogen polypeptide that is fused at its C-terminus to the N-terminus of the subunit sequence of a self-assembling nanoparticle.

14. A coronavirus vaccine composition, comprising the immunogen polypeptide of claim 1 that is displayed on the surface of a self-assembling nanoparticle.

15. The vaccine composition of claim 14, wherein the self-assembling nanoparticle comprises a trimeric sequence, and wherein C-terminus of the immunogen polypeptide is fused to N-terminus of the subunit sequence of the nanoparticle.

16. The vaccine composition of claim 14, wherein the self-assembling nanoparticle comprises I3-01, E2p or ferritin.

17. The vaccine composition of claim 14, further comprising a locking domain and/or a T-cell epitope that is fused to the C-terminus of the nanoparticle subunit sequence.

18. The vaccine composition of claim 14, comprising:
(1) a polypeptide sequence containing from N terminus to C terminus (a) an engineered SARS-CoV-2 spike polypeptide, a GS linker sequence, and nanoparticle sequence I3-01v9, (b) an engineered SARS-CoV-2 spike polypeptide, a GS linker sequence, and nanoparticle sequence E2p, or (c) an engineered SARS-CoV-2 spike polypeptide, a GS

linker sequence, and nanoparticle sequence ferritin; or
(2) a conservatively modified variant of the polypeptide sequence.

19. The vaccine composition of claim 18, wherein the engineered SARS-CoV-2 spike immunogen polypeptide comprises (a) substitution of the S1/S2
5 cleavage site ⁶⁸²RRAR⁶⁸⁵ (SEQ ID NO:19) with GSAG (SEQ ID NO:20), (b) double mutations K986G/V987G in the turn region, and (c) truncation of HR2 (SEQ ID NO:9) at the C-terminus of the wildtype soluble S sequence; wherein the amino acid numbering is based on cryo-EM model PDB ID 6VSB.

20. The vaccine composition of claim 18, wherein the engineered
10 SARS-CoV-2 spike immunogen polypeptide comprises SEQ ID NO:33 or 34, or a conservatively modified variant thereof.

21. The vaccine composition of claim 20, comprising (1) a polypeptide sequence containing from N terminus to C terminus (a) the engineered SARS-CoV-2 spike polypeptide shown in SEQ ID NO:33, linker sequence (G₄S)₂ (SEQ ID NO:22),
15 nanoparticle sequence shown in SEQ ID NO:23 (I3-01v9), locking domain shown in SEQ ID NO:29 (LD7), and T cell epitope shown in SEQ ID NO:30, (b) the engineered SARS-CoV-2 spike polypeptide shown in SEQ ID NO:33, linker sequence G₄S (SEQ ID NO:21), nanoparticle subunit sequence shown in SEQ ID NO:24 (E2p), locking domain shown in SEQ ID NO:28 (LD4), and T cell epitope shown in SEQ ID NO:30, or (c) the
20 engineered SARS-CoV-2 spike polypeptide shown in SEQ ID NO:33, linker sequence G₄S (SEQ ID NO:21), nanoparticle sequence shown in SEQ ID NO:25 (ferritin); or (2) a conservatively modified variant of the polypeptide sequence.

22. The vaccine composition of claim 20, comprising the sequence shown in any one of SEQ ID NOs:38-40, or a substantially identical or conservatively
25 modified variant thereof.

23. A polynucleotide sequence that encodes a polypeptide sequence, wherein the polypeptide sequence comprises subunit sequence of the vaccine composition of claim 15.

24. A pharmaceutical composition, comprising the vaccine composition of claim 14, and a pharmaceutically acceptable carrier.

25. A method for preventing or treating a SARS-CoV-2 infection in a subject, comprising administering to the subject a pharmaceutically effective amount of
5 the vaccine composition of claim 14.