

WHAT IS CLAIMED IS:

1. A vaccine composition, comprising a polypeptide immunogen that is displayed on the surface of a self-assembling nanoparticle, wherein a locking domain is embedded inside the nanoparticle and is linked to subunit of the self-assembling
5 nanoparticle, and wherein the locking domain is a protein subunit that can naturally form a dimer with another locking domain attached to a nearby nanoparticle subunit in solution through non-covalent interactions at the interface.
2. The vaccine composition of claim 1, wherein the locking domain is a protein domain that forms a homodimer with another identical protein domain.
- 10 3. The vaccine composition of claim 2, wherein subunit of the locking domain comprises the amino acid sequence as shown in any one of SEQ ID NOs: 1-9, a conservatively modified variant or a substantially identical sequence thereof.
4. The vaccine composition of claim 1, wherein the locking domain is covalently linked to subunit of the nanoparticle.
- 15 5. The vaccine composition of claim 4, wherein N-terminus of the locking domain is fused to C-terminus of the nanoparticle subunit via a linker sequence.
6. The vaccine composition of claim 1, further comprising a pan-reactive T-cell epitope.
7. The vaccine composition of claim 6, wherein N-terminus of the T-cell
20 epitope is fused to the C-terminus of the locking domain.
8. The vaccine composition of claim 1, further comprising a neck region inserted between the immunogen and the nanoparticle subunit, wherein the neck region comprises a 3-helix protein domain that elevates the immunogen further away from the surface of the nanoparticle.
- 25 9. The vaccine composition of claim 1, further comprising a protein domain inserted between the immunogen and the nanoparticle subunit, wherein the protein domain stabilizes the immunogen polypeptide.

10. The vaccine composition of claim 1, wherein the nanoparticle is a ball-shaped nanoparticle with rotational symmetry.

11. The vaccine composition of claim 11, wherein the rotational symmetry has 3-fold axis and/or 5-fold axis.

5 12. The vaccine composition of claim 11, wherein the nanoparticle is of an icosahedral structure.

13. The vaccine composition of claim 1, wherein the polypeptide immunogen is a viral immunogen.

10 14. The vaccine composition of claim 13, wherein the polypeptide immunogen is a viral immunogen from a virus utilizing class-I fusion mechanism.

15 15. The vaccine composition of claim 14, wherein the virus is selected from the group consisting of HIV-1 virus, Ebola virus, Marburg virus, Arenaviruses, respiratory syncytial viruses (RSV), and coronaviruses.

16 16. The vaccine composition of claim 13, wherein the polypeptide immunogen is a viral immunogen from a virus utilizing class-II fusion mechanism.

17. The vaccine composition of claim 16, wherein the virus is HCV or Zika virus.

18. The vaccine composition of claim 13, wherein the polypeptide immunogen is a non-viral immunogen.

20 19. The vaccine composition of claim 18, wherein the polypeptide immunogen is an antigen from Plasmodium falciparum, an antigen from Mycobacterium tuberculosis (TB), or human protein proprotein convertase subtilisin/kexin type 9 (PCSK9).

25 20. The vaccine composition of claim 1, wherein the polypeptide immunogen is an HIV-1 Env-derived trimer protein.

21. The vaccine composition of claim 20, wherein N-terminus of the locking domain is fused to C-terminus of the nanoparticle subunit via a linker sequence that comprises one or more tandem copies of GGGGS (SEQ ID NO:17).

22. The vaccine composition of claim 20, further comprising a pan-reactive T-cell epitope.
23. The vaccine composition of claim 22, wherein N-terminus of the T-cell epitope is fused to the C-terminus of the locking domain.
- 5 24. The vaccine composition of claim 22, wherein the T-cell epitope comprises the sequence AKFVAAWTLKAAA (SEQ ID NO:18).
25. The vaccine composition of claim 20, wherein C-terminus of subunit of the HIV-1 trimer protein is covalently linked to N-terminus of subunit of the nanoparticle.
- 10 26. The vaccine composition of claim 20, wherein the HIV-1 trimer protein subunit is fused to the nanoparticle subunit via a linker sequence.
27. The vaccine composition of claim 26, wherein the linker sequence comprises the sequence (GaSb)_n, wherein a is an integer of 1 to 5, b is an integer of 1 to 2, and n is an integer of 1 to 5.
- 15 28. The vaccine composition of claim 20, wherein the self-assembling nanoparticle comprises a trimeric sequence.
29. The vaccine composition of claim 20, wherein subunit of the self-assembling nanoparticle comprises the polypeptide as shown in SEQ ID NO:21 (E2p), SEQ ID NO:22 (I3-01), SEQ ID NO:25 (I3-01 variant) or SEQ ID NO:26 (ferritin), a
20 conservatively modified variant or a substantially identical sequence thereof.
30. The vaccine composition of claim 20, wherein the HIV-1 Env-derived trimer protein is derived from gp140.
31. The vaccine composition of claim 20, wherein the HIV-1 Env-derived trimer protein is an uncleaved prefusion-optimized (UFO) gp140 trimer.
- 25 32. The vaccine composition of claim 31, wherein the UFO gp140 trimer is a chimeric trimer comprising a modified gp41_{ECTO} domain from HIV-1 strain BG505.

33. The vaccine composition of claim 31, wherein subunit of the UFO gp140 trimer comprises the sequence shown in SEQ ID NO:23, a conservatively modified variant or a substantially identical sequence thereof.

34. The vaccine composition of claim 31, having a subunit sequence that
5 comprises from the N-terminus to the C-terminus: HIV-1 Env-derived UFO gp140 trimer subunit as shown in SEQ ID NO:23, self-assembling nanoparticle subunit as shown in SEQ ID NO:21 (E2p), the locking domain as shown in SEQ ID NO:1 (LD4), and T-cell epitope AKFVAAWTLKAAA (SEQ ID NO:18).

35. The vaccine composition of claim 34, further comprising a first linker
10 sequence (GGGGS)₂ (SEQ ID NO:24) between the gp140 trimer subunit and the nanoparticle subunit, and/or a second linker sequence GGGGS (SEQ ID NO:17) between the nanoparticle subunit and the locking domain.

36. The vaccine composition of claim 31, having a subunit sequence that
comprises from the N-terminus to the C-terminus: HIV-1 Env-derived UFO gp140 trimer
15 as shown in SEQ ID NO:23, self-assembling nanoparticle subunit as shown in SEQ ID NO:22 or 25 (I3-01), the locking domain as shown in SEQ ID NO:2 (LD7), and T-cell epitope AKFVAAWTLKAAA (SEQ ID NO:18).

37. The vaccine composition of claim 36, further comprising a first linker
sequence (GGGGS)₂ (SEQ ID NO:24) between the gp140 trimer subunit and the
20 nanoparticle subunit, and/or a second linker sequence GGGGS (SEQ ID NO:17) between the nanoparticle subunit and the locking domain.

38. A pharmaceutical composition, comprising the vaccine composition of claim 1, and a pharmaceutically acceptable carrier.

39. A polynucleotide, encoding a fusion protein comprising an
25 immunogen polypeptide at the N-terminus, a self-assembling nanoparticle subunit, and subunit of a locking domain; wherein the locking domain is a protein subunit that can naturally form a dimer with another locking domain attached to a nearby nanoparticle subunit in solution through non-covalent interactions at the interface.

40. A method of treating or preventing HIV-1 infection in a subject, comprising administering to the subject a pharmaceutical composition comprising a therapeutically effective amount of the HIV-1 vaccine composition of claim 20, thereby treating or preventing HIV-1 infection in the subject.