

CLAIMS

1. A modified HIV-1 envelope gp140 protein, comprising a gp120 polypeptide and a gp41 polypeptide, wherein amino acid residues 548-568 of the N-terminus of heptad 1 region (HR1) of the gp41 polypeptide is replaced with a loop sequence of 6 to 14 amino acid residues in length that stabilizes the pre-fusion gp140 structure, wherein the numbering of the amino acid residues corresponds to HxB2 nomenclature.
2. The modified HIV-1 gp140 protein of claim 1, wherein the gp41 polypeptide is gp41_{ECTO}.
3. The modified HIV-1 gp140 protein of claim 1, wherein the gp120 and gp41 polypeptides are from different HIV-1 strains.
4. The modified HIV-1 gp140 protein of claim 1, which is derived from HIV-1 strain BG505.
5. The modified HIV-1 gp140 protein of claim 1, wherein the loop sequence comprises (GS)_n (SEQ ID NO:23), wherein n is any integer between 3 and 7, inclusive.
6. The modified HIV-1 gp140 protein of claim 1, wherein the loop sequence comprises (GS)₄ (SEQ ID NO:24).
7. The modified HIV-1 gp140 protein of claim 1, wherein the loop sequence comprises 10 amino acid residues.
8. The modified HIV-1 gp140 protein of claim 7, wherein the loop sequence comprises any one of SEQ ID NOs:1-5.
9. The modified HIV-1 gp140 protein of claim 1, wherein the loop sequence comprises 8 amino acid residues.
10. The modified HIV-1 gp140 protein of claim 9, wherein the loop sequence comprises any one of SEQ ID NOs:6-10.
11. The modified HIV-1 gp140 protein of claim 1, further comprising a flexible linker sequence that substitutes for the cleavage site sequence between gp120 and gp41.

12. The modified HIV-1 gp140 protein of claim 11, wherein the linker sequence comprises (G₄S)₂ (SEQ ID NO:22) or SGS and substitutes for residues 508-511 at the cleavage site.

13. The modified HIV-1 gp140 protein of claim 11, wherein the linker sequence comprises 8 amino acid residues and substitutes for residues 501-518 at the cleavage site, and wherein numbering of the amino acid residues corresponds to that of HIV-1 strain BG505.SOSIP.664 gp140.

14. The modified HIV-1 gp140 protein of claim 13, wherein the linker sequence comprises the sequence shown in any one of SEQ ID NOs:16-20.

15. The modified HIV-1 gp140 protein of claim 1, further comprising an engineered disulfide bond between gp120 and gp41.

16. The modified HIV-1 gp140 protein of claim 15, wherein the engineered disulfide bond is between residues A501C and T605C.

17. The modified HIV-1 gp140 protein of claim 1, comprising a gp140 trimer with each monomer comprising a gp120 polypeptide and a gp41_{ECTO} polypeptide, wherein the gp41_{ECTO} polypeptide is derived from HIV-1 strain BG505, and wherein the N-terminus of heptad 1 region (HR1) (SEQ ID NO:28) in the gp41_{ECTO} polypeptide is replaced with a loop sequence shown in SEQ ID NO:6.

18. The modified HIV-1 gp140 protein of claim 17, further comprising (a) a linker sequence (G₄S)₂ (SEQ ID NO:22) that substitutes for residues 508-511 at the cleavage site, and (b) an engineered disulfide bond between residues A501C and T605C.

19. A HIV-1 vaccine composition, comprising an HIV-1 Env-derived trimer immunogen presented on a self-assembling nanoparticle or a virus-like particle (VLP), wherein the HIV-1 Env-derived trimer immunogen is a modified gp140 protein of claim 1.

20. The HIV-1 vaccine composition of claim 19, wherein the nanoparticle platform comprises dihydrolipoyl acyltransferase (E2P), ferritin, or lumazine synthase (LS).

21. A pharmaceutical composition comprising a therapeutically effective amount of the HIV-1 vaccine composition of claim 19 for the treatment or prevention of HIV-1 infection in the subject.

22. Use of the modified HIV-1 envelope gp140 protein of claim 1 in the manufacture of a medicament for use in the treatment or prevention of HIV-1 infection.