CLAIMS:

1. An isolated polypeptide comprising an HIV gp120 polypeptide or soluble gp140 polypeptide stabilized in a conformation which simultaneously exposes both CD4-bound and CD4-binding site epitopes.

2. The isolated polypeptide of claim 1, wherein the polypeptide is stabilized by inter-layer contacts between the layers of the inner domain.

3. The isolated polypeptide of claim 1 or claim 2, wherein the polypeptide is stabilized by inter-layer contacts between layers 1 and 2.

4. The isolated polypeptide of any preceding claim, wherein the polypeptide is stabilized by inter-layer contacts between layers 2 and 3.

5. The isolated polypeptide of any preceding claim, wherein the inter-layer contact is made by a disulphide bond.

6. The isolated polypeptide of claim 5, wherein the disulphide bond is formed between cysteine residues are at positions equivalent one or more pairs of amino acids: V59C & S109C, V95C & W465C, V95C & R462C, V95C & L469C, and/or H99C & R462C in SEQ ID NO: 2.

7. The isolated polypeptide of any preceding claim, wherein the stabilized HIV gp120 polypeptide or soluble gp140 polypeptide comprises an amino acid sequence with at least 90% identity to the inner domain sequence as set forth in SEQ ID NO: 2 and comprises one or more pairs of non-naturally occurring cysteine residues at positions equivalent to V59 & S109, V95 & W465, V95 & R462, V95 & L469, and/or H99 & R462 of SEQ ID NO: 2.

8. The isolated polypeptide of any preceding claim, wherein the stabilized HIV gp120 polypeptide or soluble gp140 polypeptide comprises an amino acid sequence with at least 90% identity to the sequence as set forth in SEQ ID NO: 2 and comprises one or more pairs of non-naturally occurring cysteine residues at positions equivalent to V59 & S109, V95 & W465, V95 & R462, V95 & L469 and/or H99 & R462 of SEQ ID NO: 2.

9. The isolated polypeptide of any preceding claim, wherein the stabilized HIV gp120 polypeptide or soluble gp140 polypeptide comprises one or more non-naturally encoded cysteine pairs at positions corresponding to W90 & E268, I103 & Q413 in SEQ ID NO: 2.

10. The isolated polypeptide of claim 7 or claim 8, wherein the stabilized HIV gp120 polypeptide comprises an amino acid sequence as set forth in SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20 or 22.

11. An immunogenic fragment of the isolated polypeptide of any preceding claim, wherein the immunogenic fragment comprises and exposes both CD4-bound and CD4-binding site epitopes of HIV gp120.

12. A fusion protein comprising an isolated polypeptide according to any one of claims 1 to 10 or an immunogenic fragment according to claim 11 and a further polypeptide.

13. The fusion protein of claim 12, wherein the further polypeptide is the HA polypeptide from influenza.

14. A trimeric polypeptide comprising three subunits, wherein each subunit is independently selected from the group consisting of an isolated polypeptide according to any one of claims 1 to 10, an immunogenic fragment according to claim 11 and a fusion protein according to claim 12 or claim 13.

15. A isolated polynucleotide encoding an isolated polypeptide according to any one of claims 1 to 10, an immunogenic fragment according to claim 11 or a fusion protein according to claim 12 or claim 13.

16. The polynucleotide of claim 15, wherein the polynucleotide comprises a nucleic acid sequence with at least 90% identity to the sequence as set forth in SEQ ID NOs: 3, 5, 7, 9, 11, 13, 15, 17, 19 or 21.

17. An immunogenic composition comprising an isolated polypeptide according to any one of claims 1 to 10, an immunogenic fragment according to claim 11, a fusion protein according to claim 12 or claim 13, a trimer according to claim 14, and/ or a polynucleotide according to claim 15 or claim 16.

18. The immunogenic composition of claim 17, further comprising an adjuvant.

19. The immunogenic composition of claim 17 or claim 18 for use as a vaccine for treating or preventing infection by HIV and/or AIDS.

20. A method for generating an immune response in a subject, comprising administering an isolated polypeptide according to any one of claims 1 to 10, an immunogenic fragment according to claim 11, a fusion protein according to claim 12 or claim 13, a trimer according to claim 14, a polynucleotide according to claim 15 or claim 16 or an immunogenic composition according to claims 17 or claim 18 to the subject.

21. An isolated polypeptide according to any one of claims 1 to 10, an immunogenic fragment according to claim 11, a fusion protein according to claim 12 or claim 13, a trimer according to claim 14, a polynucleotide according to claim 15 or claim 16 and/or an immunogenic composition according to claims 17 or claim 18, for use in treating or preventing infection with HIV and/or AIDS in a subject.

22. A method of treating or preventing infection with HIV and/or AIDS in a subject, comprising administering an isolated polypeptide according to any one of claims 1 to 10, an immunogenic fragment according to claim 11, a fusion protein according to claim 12 or claim 13, a trimer according to claim 14, a polynucleotide according to claim 15 or claim 16 and/or an immunogenic composition according to claims 17 or claim 18 to the subject.

23. An isolated polypeptide, an immunogenic fragment, a fusion protein, a trimer, a polynucleotide or an immunogenic composition according to claim 21 or a method according to claim 20 or 22, wherein the subject is human.

CLAIMS:

1. An isolated polypeptide comprising an HIV gp120 polypeptide or soluble gp140 polypeptide stabilized in a conformation which simultaneously exposes both CD4-bound and CD4-binding site epitopes.

2. The isolated polypeptide of claim 1, wherein the polypeptide is stabilized by inter-layer contacts between the layers of the inner domain.

3. The isolated polypeptide of claim 1 or claim 2, wherein the polypeptide is stabilized by inter-layer contacts between layers 1 and 2.

4. The isolated polypeptide of any preceding claim, wherein the polypeptide is stabilized by inter-layer contacts between layers 2 and 3.

5. The isolated polypeptide of any preceding claim, wherein the inter-layer contact is made by a disulphide bond.

6. The isolated polypeptide of claim 5, wherein the disulphide bond is formed between cysteine residues at positions equivalent to one or more pairs of amino acids: V59C & S109C, V95C & W465C, V95C & R462C, V95C & L469C, and/or H99C & R462C in SEQ ID NO: 2.

7. The isolated polypeptide of any preceding claim, wherein the stabilized HIV gp120 polypeptide or soluble gp140 polypeptide comprises an amino acid sequence with at least 90% identity to the inner domain sequence as set forth in SEQ ID NO: 2 and comprises one or more pairs of non-naturally occurring cysteine residues at positions equivalent to V59 & S109, V95 & W465, V95 & R462, V95 & L469, and/or H99 & R462 of SEQ ID NO: 2.

8. The isolated polypeptide of any preceding claim, wherein the stabilized HIV gp120 polypeptide or soluble gp140 polypeptide comprises an amino acid sequence with at least 90% identity to the sequence as set forth in SEQ ID NO: 2 and comprises one or more pairs of non-naturally occurring cysteine residues at positions equivalent to V59 & S109, V95 & W465, V95 & R462, V95 & L469, and/or H99 & R462 of SEQ ID NO: 2.

9. The isolated polypeptide of any preceding claim, wherein the stabilized HIV gp120 polypeptide or soluble gp140 polypeptide comprises one or more non-naturally encoded cysteine pairs at positions corresponding to W90 & E268, I103 & Q413 in SEQ ID NO: 2.

10. The isolated polypeptide of claim 7 or claim 8, wherein the stabilized HIV gp120 polypeptide comprises an amino acid sequence as set forth in SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20 or 22.

11. An immunogenic fragment of the isolated polypeptide of any preceding claim, wherein the immunogenic fragment comprises and exposes both CD4-bound and CD4-binding site epitopes of HIV gp120.

12. A fusion protein comprising an isolated polypeptide according to any one of claims 1 to 10 or an immunogenic fragment according to claim 11 and a further polypeptide.

13. A trimeric polypeptide comprising three subunits, wherein each subunit is independently selected from the group consisting of an isolated polypeptide according to any one of claims 1 to 10, an immunogenic fragment according to claim 11 and a fusion protein according to claim 12.

14. A isolated polynucleotide encoding an isolated polypeptide according to any one of claims 1 to 10, an immunogenic fragment according to claim 11 or a fusion protein according to claim 12.

15. The polynucleotide of claim 14, wherein the polynucleotide comprises a nucleic acid sequence with at least 90% identity to the sequence as set forth in SEQ ID NOs: 3, 5, 7, 9, 11, 13, 15, 17, 19 or 21.

16. An immunogenic composition comprising an isolated polypeptide according to any one of claims 1 to 10, an immunogenic fragment according to claim 11, a fusion protein according to claim 12, a trimer according to claim 13, and/ or a polynucleotide according to claim 14 or claim 15.

17. The immunogenic composition of claim 16, further comprising an adjuvant.

18. The immunogenic composition of claim 16 or claim 17 for use as a vaccine for treating or preventing infection by HIV and/or AIDS.

19. An isolated polypeptide according to any one of claims 1 to 10, an immunogenic fragment according to claim 11, a fusion protein according to claim 12, a trimer according to claim 13, a polynucleotide according to claim 14 or claim 15 and/or an immunogenic composition according to claim 16 or claim 17, for use in treating or preventing infection with HIV and/or AIDS in a subject.