strains and subtypes investigated, strongly suggests that the globular domains which will work as vaccines can be predicted for future emerging influenza strains and subtypes.

**Table 13:**

| Antigen | Mice per group | Coating used for ELISA | Anti-HA IgG titers d21 |
|---|---|---|---|
| Qβ_gdHA_AB5907_42_310 | 5 | rHA_A/Brisbane/59/2007 | 394 |
| AP205_gdHA_AB5907_42_310 | | | 30 |
| gdHA_AB5907_42_310 | | | 0 |
| AP205_gdHA_AU71607_42_310 | | ecHA-Uruguay | 26 |
| gdHA_AU71607_42_310 | | | 0 |
| AP205_gdHA_BB307_42_310 | | rHA_B/Florida/04/2006 | 476 |
| gdHA_BB307_42_310 | | | 33 |
| Qβ_gdHA_AV120304_42_310 | | rHA_A/Vietnam/1203/2004 | 92 |
| gdHA_AV120304_42_310 | | | 0 |
| Qβ_gdHA_AI505_42_310 | | rHA_A/Indonesia/05/2005 | 1058 |
| AP205_gdHA_AI505_42_310 | | | 49 |
| gdHA_AI505_42_310 | | | 0 |
| Qβ_gdHA_AC0709_42_310 | 3 | rHA_A/California/04/2009 | 1334 |
| gdHA_AC0709_42_310 | | | 20 |

## EXAMPLE ~~34~~ 33 CB5

### A) Coupling of gdHA_PR8_42_310 (H1N1) to Cb5 virus-like particles

**[00140]** A solution of 2 ml of 1 mg/ml Cb5 VLPs protein (SEQ ID NO:92) in PBS/10 % glycerol pH 7.2 was reacted for 60 min at room temperature with 42.6 µl of a SMPH solution (50 mM in DMSO). The reaction solution was dialyzed at 4 °C against two 2 l changes of 20 mM HEPES/10 % glycerol pH 7.2 over 12 and 4 hours. 1.4 ml of the derivatized and dialyzed Cb5 solution was mixed with 2 ml of a solution containing 1 mg/ml of the purified gdHA_PR8_42_310 protein obtained in EXAMPLE 16 in PBS pH 7.2 and incubated 4h at room temperature for chemical cross linking, resulting in Cb5-gdHA_PR8_42_310. Uncoupled protein was removed by size exclusion chromatography using a Sepharose CL4B column. The coupled product was analyzed on a 12 % Bis-Tris-polyacrylamide gel under reducing conditions. A band of increased molecular weight with respect to the Cb5 capsid monomer was visible, clearly demonstrating the successful cross-linking of the influenza gdHA_PR8_42_310 protein to the Cb5 VLP.

**B) Immunization of mice with gdHA-PR8 (H1N1) protein coupled to Cb5 capsids (Cb5-gdHA(PR8)**

**[00141]** The efficacy of Cb5-gdHA(PR8) immunization was tested in a murine model of influenza infection as described in EXAMPLE 8. Briefly four female balb/c mice per group were immunized with 15 µg of Cb5-gdHA_PR8_42_310 vaccine or 15 µg of Cb5 VLPs formulated in 200 µl PBS and injected subcutaneously on day 0. Mice were bled retro-orbitally on day 34 and sera were analyzed using ecHA_PR8-specific and Cb5-specific ELISA. Mice were then challenged at day 41 with a lethal dose (4xLD50) of mouse adapted influenza A/PR/8/34. The result of this experiment is shown in Table 14. The result shown in Table 14 demonstrates that coupling of gdHA(PR8) to Cb5 VLPs allows the induction of a high anti-ecHA(PR8) antibody response. Morover a single immunization of mice with Cb5-gdHA(PR8) vaccine induces of a protective antibody response against a lethal challenge with mouse adapted influenza A/PR/8/34 demonstrating that Cb5 is a good carrier for influenza vaccines based on the globular domain of HA.

**Table 14:**

| Antigen | Amount [µg] | Anti-ecHA(PR8) d34 | Anti-Cb5 | Survival [%] 20d p.I |
|---|---|---|---|---|
| Cb5-gdHA(PR8) | 15 | 3'560 | 13'044 | 100 |
| Cb5 | 15 | n.d. | 10'510 | 0 |

**EXAMPLE ~~35~~34: Hemagglutination Assay**

**[00142]** In order to test if the gdHA fragments produced as described in Example 24 and coupled to Qβ or AP205 as described in Example 25 are structurally similar to native HA protein, a hemagglutination assay was performed with gdHA_PR8_42_310 or gdHA_PR8_46_310 conjugated to Qβ or AP205. Native HA proteins present on influenza viruses are able to agglutinate red blood cells as a consequence of their binding to their receptor on red blood cells (RBCs). This agglutination of chicken RBCs by influenza virus is inhibited in the hemagglutination inhibition assay by neutralizing antibodies as described in Example 7. To test if the gdHA fragments coupled to Qβ or AP205 had a similar structure as native HA protein on the surface of influenza viruses and therefore were able to bind to the receptor on RBCs and as consequence were inducing agglutination of chicken RBCs, Qβ-gdHA_PR8_42_310, Qβ-gdHA_PR8_46_310, AP205-gdHA_PR8_42_310 and AP205-gdHA_PR8_46_310 solutions were serially diluted in PBS and mixed with 50 µl of 1 %

## CLAIMS

1. A composition comprising:
   (a) a virus-like particle (VLP) with at least one first attachment site, wherein said virus-like particle is a virus-like particle of an RNA bacteriophage; and
   (b) at least one antigen with at least one second attachment site, wherein said at least one antigen is an ectodomain of an influenza virus hemagglutinin protein or a fragment of said ectodomain of an influenza virus hemagglutinin protein, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises at least 80 contiguous amino acids of said ectodomain of an influenza virus hemagglutinin protein;
   wherein (a) and (b) are linked through said at least one first and said at least one second attachment site.

2. The composition of claim 1, wherein said ectodomain of an influenza virus hemagglutinin protein is a protein, wherein said protein is composed of (a) the HA1 subunit comprising or preferably consisting of amino acid position 11 to amino acid position 328 of SEQ ID NO:75 and (b) the HA2 subunit consisting of position 1 to 176 of SEQ ID NO:76.

3. The composition of any one of the preceding claims, wherein said ectodomain of an influenza virus hemagglutinin protein is an ectodomain of an influenza A virus hemagglutinin protein.

4. The composition of any one of the preceding claims, wherein said ectodomain of said influenza A virus hemagglutinin protein is an ectodomain of an influenza A virus hemagglutinin protein subtype selected from the group consisting of influenza A virus hemagglutinin protein subtype H1, H2, H3, H4, H5, H6, H7, H8, H9, H10, H11, H12, H13, H14, H15, and H16, and wherein preferably said ectodomain of said influenza A virus hemagglutinin protein is an ectodomain of an influenza A virus hemagglutinin protein subtype selected from the group consisting of influenza A virus hemagglutinin protein subtype H1, H2, and H3.

5. The composition of any one of the preceding claims, wherein said ectodomain of an influenza virus hemagglutinin protein is a naturally occurring ectodomain of an influenza virus hemagglutinin protein.

6. The composition of any one of the preceding claims, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:39; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:39.

7. The composition of any one of claims 1 to 5, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:40; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:40.

8. The composition of any one of claims 1 to 5, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:41; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:41.

9. The composition of any one of claims 1 to 5, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:42; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:42.

10. The composition of any one of claims 1 to 5, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:43; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:43.

11. The composition of any one of claims 1 to 5, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:73; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:73.

12. The composition of any one of claims 1 to 5, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:74; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:74.

13. The composition of claim 1, wherein said ectodomain of an influenza virus hemagglutinin protein is an ectodomain of an influenza B virus hemagglutinin protein.

14. The composition of any one of the preceding claims, wherein said antigen is an ectodomain of an influenza virus hemagglutinin protein, and wherein preferably said ectodomain of an influenza virus hemagglutinin protein is in a trimeric form.

15. The composition of any one of claims 1 to 13, wherein said antigen is a fragment of said ectodomain of an influenza virus hemagglutinin protein, wherein preferably said fragment of said ectodomain of an influenza virus hemagglutinin protein is the HA1 subunit of said ectodomain of an influenza virus hemagglutinin protein or a fragment of said HA1 subunit of said ectodomain of an influenza virus hemagglutinin protein.

16. The composition of claim 15, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises at least one eight-stranded Jelly roll barrel and at least one α-helix of the influenza virus hemagglutinin protein.

17. The composition of any one of claims 15 or 16, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises, or preferably consists of, a receptor binding domain.

18. The composition of any one of claims 15 to 17, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein further comprises a vestigial esterase domain.

19. The composition of any one of the claims 15 to 18, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises the amino acid residues tyrosine corresponding to the positions 98 and 195 of SEQ ID NO:75,

tryptophan corresponding to the position 153 of SEQ ID NO:75, and histidine corresponding to of SEQ ID NO:75.

20. The composition of any one of the claims 15 to 19, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises a cysteine residue corresponding to of SEQ ID NO:75, preferably said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises a cysteine residue corresponding to positions 64, 76, 97, 139 of SEQ ID NO:75, more preferably said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises a cysteine residue corresponding to positions 52, 64, 76, 97, 139, 277, 281, 305 of SEQ ID NO:75.

21. The composition of any one of the claims 15 to 20, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises, or preferably consists of, an amino acid sequence corresponding to position 57 to position 276 of SEQ ID NO:75.

22. The composition of any one of the claims 15 to 21, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises, or preferably consists of, an amino acid sequence corresponding to position 46 to position 310 of SEQ ID NO:75.

23. The composition of any one of the claims 15 to 22, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises, or preferably consists of, an amino acid sequence corresponding to position 42 to position 310 of SEQ ID NO:75.

24. The composition of any one of the claims 15 to 23, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises, or preferably consists of, an amino acid sequence corresponding to position 54 to position 276 of SEQ ID NO:75.

25. The composition of any one of the claims 15 to 24, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises, or preferably

consists of, an amino acid sequence corresponding to position 54 to position 270 of SEQ ID NO:75.

26. The composition of any one of the claims 15 to 25, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises, or preferably consists of, an amino acid sequence corresponding to position 54a to position 276 of SEQ ID NO:75.

27. The composition of any one of the claims 15 to 26, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises, or preferably consists of, an amino acid sequence corresponding to position 54a to position 270 of SEQ ID NO:75.

28. The composition of any one of claims 15 to 27, wherein said ectodomain of an influenza virus hemagglutinin protein has an amino acid sequence identity of at least 70 % with the HA ectodomain of influenza A virus strain A/California/07/2009 (H1N1) (Genebank Accession No: ACP44189.1) or A/Perth/16/2009 (H3N2) (Genebank Accession No: ACS71642.1), and wherein preferably said ectodomain of an influenza virus hemagglutinin protein is a naturally occurring said ectodomain of an influenza virus hemagglutinin protein.

29. The composition of any one of claims 15 to 27, wherein said ectodomain of an influenza virus hemagglutinin protein has an amino acid sequence identity of at least 70 % with the HA ectodomain of influenza B virus strain B/Brisbane/33/2008 (Genbank Accession No: ACN29387.1), B/Guangzhou/01/2007 (Genbank Accession No: ABX71684.1), or B/Brisbane/60/2008 (Genbank Accession No: ACN29383.1) and wherein preferably said ectodomain of an influenza virus hemagglutinin protein is a naturally occurring said ectodomain of an influenza virus hemagglutinin protein.

30. The composition of any one of the preceding claims, wherein said virus-like particle comprises, consists essentially of, or alternatively consists of, recombinant coat proteins of an RNA bacteriophage.

31. The composition of any one of the preceding claims, wherein said virus-like particle comprises, consists essentially of, or alternatively consists of, recombinant coat proteins of RNA bacteriophage Qβ, of RNA bacteriophage AP205, or of RNA bacteriophage φCb5.

32. The composition of any one of the preceding claims, wherein said virus-like particle comprises, consists essentially of, or alternatively consists of, recombinant coat proteins comprising or preferably consisting of an amino acid sequence selected from the group consisting of: (a) SEQ ID NO:1; (b) a mixture of SEQ ID NO:1 and SEQ ID NO:2; (c) SEQ ID NO:19; (d) SEQ ID NO:92; (e) SEQ ID NO:93; and (f) SEQ ID NO:94.

33. The composition of any one of the preceding claims, wherein said VLP is a VLP of RNA bacteriophage Qβ.

34. The composition of any one of the preceding claims, wherein said virus-like particle comprises, consists essentially of, or alternatively consists of, recombinant coat proteins of RNA bacteriophage Qβ.

35. The composition of any one of the preceding claims, wherein said virus-like particle comprises, consists essentially of, or alternatively consists of, recombinant coat proteins comprising or preferably consisting of SEQ ID NO:1.

36. The composition of any of the preceding claims, wherein said first attachment site and said second attachment site are linked via at least one non-peptide covalent bond.

37. The composition of any of the preceding claims, wherein said first attachment site comprises, or preferably is, an amino group, preferably an amino group of a lysine residue.

38. The composition of any of the preceding claims, wherein said second attachment site comprises, or preferably is, a sulfhydryl group, preferably a sulfhydryl group of a cysteine residue.

39. A vaccine composition comprising an effective amount of the composition of any one of the preceding claims, wherein preferably said vaccine composition further comprises an adjuvant.

40. A pharmaceutical composition comprising:
    (a) the composition of any one of the claims 1 to 38 or the vaccine composition of claim 39; and
    (b) a pharmaceutically acceptable carrier.

41. Use of the composition of any one of claims 1 to 38, the vaccine composition of claim 39, or the pharmaceutical composition of claim 40 in the manufacture of a medicament for immunizing an animal, preferably a human.

42. The composition of any one of claims 1 to 38, the vaccine composition of claim 39, or the pharmaceutical composition of claim 40 for use as a medicament.

43. The composition of any one of claims 1 to 38, or the vaccine composition of claim 39, or the pharmaceutical composition of claim 40 for use in a method of the treatment of influenza.

44. Use of an immunologically effective amount of the composition of any one of claims 1 to 38, of the vaccine composition of claim 39, and / or of the pharmaceutical composition of claim 40 in the manufacture of a medicament for treatment, amelioration and / or prevention of influenza in an animal, preferably a human.

**CLAIMS**

1. A composition comprising:

   (a) a virus-like particle (VLP) with at least one first attachment site, wherein said virus-like particle is a virus-like particle of an RNA bacteriophage; and

   (b) at least one antigen with at least one second attachment site, wherein said at least one antigen is a fragment of an ectodomain of an influenza virus hemagglutinin protein, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises at least 80 contiguous amino acids of said ectodomain of an influenza virus hemagglutinin protein, and wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein is a fragment of the HA1 subunit of said ectodomain of an influenza virus hemagglutinin protein, and wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises at least two and at most four pairs of cysteine residues which are capable of forming intramolecular disulfide bonds;

   wherein (a) and (b) are linked through said at least one first and said at least one second attachment site.

2. The composition of any one of the preceding claims, wherein said ectodomain of an influenza virus hemagglutinin protein is an ectodomain of an influenza A virus hemagglutinin protein.

3. The composition of any one of the preceding claims, wherein said ectodomain of said influenza A virus hemagglutinin protein is an ectodomain of an influenza A virus hemagglutinin protein subtype selected from the group consisting of influenza A virus hemagglutinin protein subtype H1, H2, H3, H4, H5, H6, H7, H8, H9, H10, H11, H12, H13, H14, H15, and H16.

4. The composition of any one of the preceding claims, wherein said ectodomain of said influenza A virus hemagglutinin protein is an ectodomain of an influenza A virus hemagglutinin protein subtype selected from the group consisting of influenza A virus hemagglutinin protein subtype H1, H2, and H3.

5. The composition of any one of the preceding claims, wherein said ectodomain of an influenza virus hemagglutinin protein is a naturally occurring ectodomain of an influenza virus hemagglutinin protein.

6. The composition of any one of the preceding claims, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:39; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:39.

7. The composition of any one of claims 1 to 5, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:40; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:40.

8. The composition of any one of claims 1 to 5, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:41; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:41.

9. The composition of any one of claims 1 to 5, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:42; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:42.

10. The composition of any one of claims 1 to 5, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:43; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:43.

11. The composition of any one of claims 1 to 5, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:73; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:73.

12. The composition of any one of claims 1 to 5, wherein the amino acid sequence of said ectodomain of said influenza A virus hemagglutinin protein is selected from the group consisting of: (i) the amino acid sequence as set forth in SEQ ID NO:74; and (ii) an amino acid sequence of at least 70 % amino acid sequence identity with SEQ ID NO:74.

13. The composition of claim 1, wherein said ectodomain of an influenza virus hemagglutinin protein is an ectodomain of an influenza B virus hemagglutinin protein.

14. The composition of any one of claims 1 to 13, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises at least one eight-stranded Jelly roll barrel and at least one α-helix of the influenza virus hemagglutinin protein.

15. The composition of any one of claims 1 or 14, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises a receptor binding domain.

16. The composition of any one of claims 1 or 14, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein consists of a receptor binding domain.

17. The composition of any one of claims 1 to 16, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein further comprises a vestigial esterase domain.

18. The composition of any one of the claims 1 to 18, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises the amino acid residues tyrosine corresponding to the positions 98 and 195 of SEQ ID NO:75, tryptophan corresponding to the position 153 of SEQ ID NO:75, and histidine corresponding to of SEQ ID NO:75.

19. The composition of any one of the claims 1 to 19, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises a cysteine residue corresponding to of SEQ ID NO:75.

20. The composition of any one of the claims 1 to 19, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises a cysteine residue corresponding to positions 64, 76, 97, 139 of SEQ ID NO:75.

21. The composition of any one of the claims 1 to 19, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises a cysteine residue corresponding to positions 52, 64, 76, 97, 139, 277, 281, 305 of SEQ ID NO:75.

22. The composition of any one of the claims 1 to 21, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises an amino acid sequence corresponding to position 57 to position 276 of SEQ ID NO:75.

23. The composition of any one of the claims 1 to 21, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein consists of an amino acid sequence corresponding to position 57 to position 276 of SEQ ID NO:75.

24. The composition of any one of the claims 1 to 23, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises an amino acid sequence corresponding to position 46 to position 310 of SEQ ID NO:75.

25. The composition of any one of the claims 1 to 23, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein consists of an amino acid sequence corresponding to position 46 to position 310 of SEQ ID NO:75.

26. The composition of any one of the claims 1 to 25, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises an amino acid sequence corresponding to position 42 to position 310 of SEQ ID NO:75.

27. The composition of any one of the claims 1 to 25, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein consists of an amino acid sequence corresponding to position 42 to position 310 of SEQ ID NO:75.

28. The composition of any one of the claims 1 to 27, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises an amino acid sequence corresponding to position 54 to position 276 of SEQ ID NO:75.

29. The composition of any one of the claims 1 to 27, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein consists of an amino acid sequence corresponding to position 54 to position 276 of SEQ ID NO:75.

30. The composition of any one of the claims 1 to 29, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises an amino acid sequence corresponding to position 54 to position 270 of SEQ ID NO:75.

31. The composition of any one of the claims 1 to 29, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein consists of an amino acid sequence corresponding to position 54 to position 270 of SEQ ID NO:75.

32. The composition of any one of the claims 1 to 31, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises an amino acid sequence corresponding to position 54a to position 276 of SEQ ID NO:75.

33. The composition of any one of the claims 1 to 31, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein consists of an amino acid sequence corresponding to position 54a to position 276 of SEQ ID NO:75.

34. The composition of any one of the claims 1 to 33, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein comprises an amino acid sequence corresponding to position 54a to position 270 of SEQ ID NO:75.

35. The composition of any one of the claims 1 to 33, wherein said fragment of said ectodomain of an influenza virus hemagglutinin protein consists of an amino acid sequence corresponding to position 54a to position 270 of SEQ ID NO:75.

36. The composition of any one of claims 1 to 35, wherein said ectodomain of an influenza virus hemagglutinin protein has an amino acid sequence identity of at least 70 % with the HA ectodomain of influenza A virus strain A/California/07/2009 (H1N1) (Genebank Accession No: ACP44189.1) or A/Perth/16/2009 (H3N2) (Genebank Accession No: ACS71642.1).

37. The composition of claim 36, wherein said ectodomain of an influenza virus hemagglutinin protein is a naturally occurring said ectodomain of an influenza virus hemagglutinin protein.

38. The composition of any one of claims 1 to 37, wherein said ectodomain of an influenza virus hemagglutinin protein has an amino acid sequence identity of at least 70 % with the HA ectodomain of influenza B virus strain B/Brisbane/33/2008 (Genbank Accession No: ACN29387.1), B/Guangzhou/01/2007 (Genbank Accession No: ABX71684.1), or B/Brisbane/60/2008 (Genbank Accession No: ACN29383.1).

39. The composition of any one of claims 1 to 37, wherein said ectodomain of an influenza virus hemagglutinin protein is a naturally occurring said ectodomain of an influenza virus hemagglutinin protein.

40. The composition of any one of the preceding claims, wherein said virus-like particle comprises, consists essentially of, or alternatively consists of, recombinant coat proteins of an RNA bacteriophage.

41. The composition of any one of the preceding claims, wherein said virus-like particle comprises, consists essentially of, or alternatively consists of, recombinant coat proteins of RNA bacteriophage Qβ, of RNA bacteriophage AP205, or of RNA bacteriophage φCb5.

42. The composition of any one of the preceding claims, wherein said virus-like particle comprises, consists essentially of, or alternatively consists of, recombinant coat proteins comprising an amino acid sequence selected from the group consisting of: (a) SEQ ID NO:1; (b) a mixture of SEQ ID NO:1 and SEQ ID NO:2; (c) SEQ ID NO:19; (d) SEQ ID NO:92; (e) SEQ ID NO:93; and (f) SEQ ID NO:94.

43. The composition of any one of the preceding claims, wherein said virus-like particle comprises, consists essentially of, or alternatively consists of, recombinant coat proteins consisting of an amino acid sequence selected from the group consisting of: (a) SEQ ID NO:1; (b) a mixture of SEQ ID NO:1 and SEQ ID NO:2; (c) SEQ ID NO:19; (d) SEQ ID NO:92; (e) SEQ ID NO:93; and (f) SEQ ID NO:94.

44. The composition of any one of the preceding claims, wherein said VLP is a VLP of RNA bacteriophage Qβ.

45. The composition of any one of the preceding claims, wherein said virus-like particle comprises, consists essentially of, or alternatively consists of, recombinant coat proteins of RNA bacteriophage Qβ.

46. The composition of any one of the preceding claims, wherein said virus-like particle comprises, consists essentially of, or alternatively consists of, recombinant coat proteins comprising SEQ ID NO:1.

47. The composition of any one of the preceding claims, wherein said virus-like particle comprises, consists essentially of, or alternatively consists of, recombinant coat proteins consisting of SEQ ID NO:1.

48. The composition of any of the preceding claims, wherein said first attachment site and said second attachment site are linked via at least one non-peptide covalent bond.

49. The composition of any of the preceding claims, wherein said first attachment site comprises an amino group.

50. The composition of any of the preceding claims, wherein said first attachment site comprises an amino group of a lysine residue.

51. The composition of any of the preceding claims, wherein said first attachment site is an amino group.

52. The composition of any of the preceding claims, wherein said first attachment site is an amino group of a lysine residue.

53. The composition of any of the preceding claims, wherein said second attachment site comprises a sulfhydryl group.

54. The composition of any of the preceding claims, wherein said second attachment site comprises a sulfhydryl group of a cysteine residue.

55. The composition of any of the preceding claims, wherein said second attachment site is a sulfhydryl group.

56. The composition of any of the preceding claims, wherein said second attachment site is a sulfhydryl group of a cysteine residue.

57. A vaccine composition comprising an effective amount of the composition of any one of the preceding claims.

58. A vaccine composition of claim 57 further comprising an adjuvant.

59. A pharmaceutical composition comprising:
    (a) the composition of any one of the claims 1 to 56 or the vaccine composition of claim 57 or 58; and
    (b) a pharmaceutically acceptable carrier.

60. Use of the composition of any one of claims 1 to 56, the vaccine composition of claim 57 or 58, or the pharmaceutical composition of claim 59 in the manufacture of a medicament for immunizing an animal.

61. The use of claim 60, wherein said animal is a human.

62. The composition of any one of claims 1 to 56, the vaccine composition of claim 57 or 58, or the pharmaceutical composition of claim 59 for use as a medicament.

63. The composition of any one of claims 1 to 56, or the vaccine composition of claim 57 or 58, or the pharmaceutical composition of claim 59 for use in a method of the treatment of influenza.

64. Use of an immunologically effective amount of the composition of any one of claims 1 to 56, of the vaccine composition of claim 57 or 58, and / or of the pharmaceutical composition of claim 59 in the manufacture of a medicament for the treatment, amelioration and / or prevention of influenza in an animal.

65. The use of claim 64, wherein said animal is a human.