Further provided are compositions that include the optimized influenza HA polypeptides, fusion proteins or VLPs disclosed herein in a pharmaceutically acceptable carrier. Methods of eliciting an immune response against influenza virus in a subject by administering the disclosed compositions, fusion proteins or VLPs are also provided by the present disclosure.

Also provided are methods of immunizing a subject against influenza virus by administering to the subject a composition comprising a VLP that contains an optimized HA polypeptide.

The foregoing and other objects, features, and advantages of the invention will become more apparent from the following detailed description, which proceeds with reference to the accompanying figures.

Further provided is the use of the influenza HA polypeptide as disclosed herein, the VLP as disclosed herein, the fusion protein as disclosed herein, or the composition as disclosed herein in the manufacture of a medicament for eliciting an immune response to influenza virus in a subject. Further provided is the use of a composition comprising the VLP as disclosed herein and pharmaceutically acceptable carrier in the manufacture of a medicament for immunizing a subject against influenza virus.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic summarizing the process for generating a COBRA HA sequence using 1989 human and avian H5N1 influenza virus isolates, referred to herein as "All H5 COBRA" HA.

FIG. 2 is a schematic summarizing the process for generating a COBRA HA sequence using 1213 human and avian H5N1 clade 2 isolates, referred to herein as "Human-Avian COBRA-2" HA.

FIG. 3 is a graph showing HAI titers against clade 1, clade 2 and clade 7 challenge strains following vaccination with VLPs containing the All H5 COBRA HA sequence (SEQ ID NO: 1), VLPs containing the Human-Avian COBRA-2 HA sequence (SEQ ID NO: 3), VLPs containing a human clade 2 influenza virus COBRA HA sequence (Human COBRA-2), or VLPs containing Whooper Swan (A/Whooper Swan/Mongolia/244/2005) influenza virus HA. Vaccinations (3 μg) were performed at 0 and 3 weeks with adjuvant (Imject™).

FIG. 4 is a graph showing body weight of animals vaccinated with VLPs containing the All H5 COBRA HA sequence (SEQ ID NO: 1), VLPs containing the Human-Avian COBRA-2 HA sequence (SEQ ID NO: 3), VLPs containing the Human COBRA-2 HA sequence, or Whooper Swan VLPs and subsequently challenged with Indonesia clade 2.1 virus (A/Indonesia/5/2005). Vaccinations (3

19. A fusion protein comprising the influenza HA polypeptide of any one of claims 1-7.

20. A composition comprising the influenza HA polypeptide of any one of claims 1-7, the VLP of any one of claims 16-18 or the fusion protein of claim 19, and a pharmaceutically acceptable carrier.

21. ~~A method of eliciting an immune response to influenza virus in a subject, comprising administering~~Use of the influenza HA polypeptide of any one of claims 1-7, the VLP of any one of claims 16-18, the fusion protein of claim 19, or the composition of claim 20 in the manufacture of a medicament for eliciting an immune response to influenza virus in a subject.

22. ~~A method of immunizing a subject against influenza virus, comprising administering to the subject~~Use of a composition comprising the VLP of any one of claims 16-18 and pharmaceutically acceptable carrier in the manufacture of a medicament for immunizing a subject against influenza virus.

23. The ~~method~~ use of claim 22, wherein the composition further comprises an adjuvant.

24. The ~~method~~ use of claim 22 or claim 23, wherein the composition is to be administered intramuscularly.

25. The ~~method~~ use of any one of claims 22-24, wherein the composition comprises about 1 to about 25 μg of the VLP.

26. The ~~method~~ use of claim 25, wherein the composition comprises about 15 μg of the VLP.