SUMMARY

[0010] The disclosure provides composition comprising virus-like particles (VLPs) of at least one type of human papillomavirus (HPV) selected from the group consisting of HPV types: 6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 55, 56, 58, 59, 66, 68, 69, 70, 73, and 82 adsorbed on an aluminum adjuvant and a squalene nanoemulsion (SNE) adjuvant, wherein the SNE adjuvant comprises sorbitan trioleate (SPAN-85); polysorbate-20 (PS-20) or polysorbate-80 (PS-80); and squalene.

[0011] The disclosure, in one aspect, provides compositions comprising virus-like particles (VLPs) of at least one type of human papillomavirus (HPV) selected from the group consisting of HPV types: 6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 55, 56, 58, 59, 66, 68, 69, 70, 73, and 82 and a squalene nanoemulsion (SNE) adjuvant, wherein the SNE adjuvant comprises sorbitan trioleate (SPAN-85); polysorbate-20 (PS-20) or polysorbate-80 (PS-80); and squalene. In some examples, the composition also includes an aluminum adjuvant. In some examples, the VLPs are adsorbed on an aluminum adjuvant.

[0012] The disclosure further provides a method of inducing an immune response to a human papillomavirus (HPV) in a human patient comprising administering to the patient a pharmaceutical composition comprising virus-like particles (VLPs) of at least one type of human papillomavirus (HPV) selected from the group consisting of HPV types: 6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 55, 56, 58, 59, 66, 68, 69, 70, 73, and 82 and a squalene nanoemulsion (SNE) adjuvant, wherein the SNE adjuvant comprises sorbitan trioleate (SPAN-85); polysorbate-20 (PS-20) or polysorbate-80 (PS-80); and squalene, and an optionally an aluminum adjuvant.

[0012a] The disclosure, in another aspect, provides a composition as defined herein for use in inducing an immune response to a human papillomavirus (HPV) in a human patient.

[0013] The disclosure further provides, among other things, a method of preventing infection of or reducing the likelihood of infection of a human patient by a human papillomavirus (HPV) comprising administration to the patient the pharmaceutical composition comprising virus-like particles (VLPs) of at least one type of human papillomavirus (HPV) selected from the group consisting of HPV types: 6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 55, 56, 58, 59, 66, 68, 69, 70, 73, and 82 adsorbed on an aluminum adjuvant and a squalene nanoemulsion (SNE) adjuvant, wherein the SNE adjuvant comprises sorbitan trioleate (SPAN-85); polysorbate-20 (PS-20) or polysorbate-80 (PS-80); and squalene.

[0014] The disclosure further provides the use of comprising virus-like particles (VLPs) of at least one type of human papillomavirus (HPV) selected from the group consisting of HPV types: 6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 55, 56, 58, 59, 66, 68, 69, 70, 73, and 82 adsorbed on an aluminum adjuvant and a squalene nanoemulsion (SNE) adjuvant, wherein the SNE

adjuvant comprises sorbitan trioleate (SPAN-85); polysorbate-20 (PS-20) or polysorbate-80 (PS-80); and squalene for preventing infection of or reducing the likelihood of infection of a human patient by a human papillomavirus (HPV).

[0014a] The disclosure, in another aspect, provides use of the composition as defined herein in the manufacture of a medicament for preventing infection of or reducing the likelihood of infection of a human patient by a human papillomavirus (HPV).

[0014b] The disclosure, in another aspect, provides a composition as defined herein for use in therapy.

[0015] The disclosure, in another aspect, provides a kit comprising: (1) a human papillomavirus (HPV) vaccine; and (2) a squalene nanoemulsion (SNE) adjuvant, wherein the SNE adjuvant comprises sorbitan trioleate (SPAN-85); polysorbate-20 (PS-20) or polysorbate-80 (PS-80); and squalene. The kit optionally comprises an aluminum adjuvant.

DEFINITIONS

[0016] As used throughout the specification and in the appended claims, the singular forms "a," "an," and "the" include the plural reference unless the context clearly dictates otherwise.

[0017] As used throughout the specification and appended claims, the following abbreviations and definitions apply:

CLA	((13Z,16Z)-N,N-dimethyl-3-nonyldocosa-13,16-dien-1-amine)
HPV	human papillomavirus
ID	intradermal
IM	intramuscular
ME	microemulsion
MNS	microfluidic nanoemulsion self-assembly
Mw	molecular weight
NE	nanoemulsion
NMWCO	nominal molecular weight cut off
PHE	pre-homogenized emulsion
PS-20	polysorbate-20
PS-80	polysorbate-80
SNE	squalene nanoemulsion
SPAN-85	sorbitan-trioleate
VPL(s)	virus-like particle(s) (VLPs)
w/v	weight per volume

[0018] As used throughout the specification and appended claims, the following definitions and abbreviations apply:

[0019] ***AAHS****:* As used herein, the term "AAHS" refers to an amorphous aluminum hydroxyphosphate sulfate adjuvant.

WHAT IS CLAIMED IS:

1. A composition comprising virus-like particles (VLPs) of at least one type of human papillomavirus (HPV) selected from the group consisting of HPV types: 6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 55, 56, 58, 59, 66, 68, 69, 70, 73, and 82 and a squalene nanoemulsion (SNE) adjuvant, wherein the SNE adjuvant comprises sorbitan trioleate (SPAN-85); polysorbate-20 (PS-20) or polysorbate-80 (PS-80); and squalene.

2. The composition of claim 1, wherein the composition is made by mixing an HPV vaccine and an SNE adjuvant; wherein the HPV vaccine comprises HPV VLPs and a pharmaceutically acceptable carrier and the SNE adjuvant comprises SPAN-85, PS-20 or PS-80, and squalene.

3. The composition of claim 1 or claim 2 wherein the SNE adjuvant comprises 6 μg/mL - 14 mg/mL SPAN-85, 6 μg/mL - 14 mg/mL PS-20 or PS-80, and 20 μg/mL - 240 mg/mL of squalene.

4. The composition of any of claims 1-3 wherein the SNE adjuvant further comprises a cationic lipid.

5. The composition of claim 4 wherein the cationic lipid is (13Z,16Z)-N,N-dimethyl-3-nonyldocosa-13,16-dien-1-amine.

6. The composition of claim 4 or 5 comprising 30 μg/mL - 4.8 mg/mL of cationic lipid.

7. The composition of any of claims 1-6 wherein the SNE comprises PS-20.

8. The composition of any of claims 1-7 wherein the composition further comprises a buffer.

9. The composition of claim 8, wherein the buffer is selected from the group consisting of: acetic acid, histidine, citrate, Bis-Tris, HEPES, phosphate, MES, sodium chloride, succinate, Tris, and combinations thereof.

10. The composition of any of claims 8 and 9, wherein the buffer is present in the amount of about 1mMol to about 100mMol.

11. The composition of any of claims 1-10 wherein the composition further comprises a salt.

12. The composition of claim 11 wherein the salt is NaCl.

13. The composition of any of claims 1-12 wherein the composition comprises 5 mM - 40 mM histidine at pH 5.1 - 7.0 and 25 mM - 300 mM NaCl.

14. The composition of any of claims 1-12 wherein the composition comprises about 20 mM histidine at about pH 5.8 and about 75 mM NaCl.

15. The composition of any of claims 1-14, wherein the composition comprises VLPs of HPV types 16 and 18.

16. The composition of any of claims 1-15, wherein the composition comprises VLPs of HPV types 6, 11, 16, and 18.

17. The composition of any of claims 1-16, wherein the composition comprises VLPs of HPV types 31, 45, 52, and 58.

18. The composition of any of claims 1-17, wherein the composition comprises VLPs of HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58.

19. The composition of any of claims 1-17, wherein the composition comprises VLPs of HPV types 6, 11, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59.

20. The composition of any of claims 1-17, wherein the composition comprises VLPs of HPV types 6, 11, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 73.

21. The composition of any of claims 1-17, wherein the composition comprises VLPs of HPV types 6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 69, and 70.

22. The composition of any of claims 1-21, wherein the composition further comprises aluminum.

23. The composition of any of claims 1-22, wherein the HPV VLPs comprise recombinant HPV Ll or recombinant HPV Ll + L2 protein.

24. The composition of any of claims 1-22, wherein the HPV VLPs comprise HPV L1 protein and do not comprise HPV L2 protein.

25. The composition of any of claims 1-22, wherein the HPV VLPs consist of HPV L1 protein.

26. A composition of any of claims 1-25 for use in inducing an immune response to a human papillomavirus (HPV) in a human patient.

27. Use of the composition of any of claims 1-25 in the manufacture of a medicament for preventing infection of or reducing the likelihood of infection of a human patient by a human papillomavirus (HPV).

28. A composition of any of claims 1-25 for use in therapy.

29. A kit comprising:

(a) a human papillomavirus (HPV) vaccine; and

(b) a squalene nanoemulsion (SNE) adjuvant, wherein the SNE adjuvant comprises sorbitan trioleate (SPAN-85); polysorbate-20 (PS-20) or polysorbate-80 (PS-80); and squalene.

30. The kit of claim 29, further comprising instructions for administering to a human patient the HPV vaccine and the SNE adjuvant.

31. The kit of claim 29 or claim 30, wherein the HPV vaccine comprises virus-like particles (VLPs) of at least one type of human papillomavirus (HPV) selected from the group consisting of HPV types: 6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 55, 56, 58, 59, 66, 68, 69, 70, 73, and 82.