Summary

In one example, the present disclosure refers to a nucleic acid encoding a polypeptide comprising a plurality of conserved peptide sequences, or variants thereof,

wherein the conserved sequences are conserved across one or more HPV genotypes 16, 18, 31, 52, 53, and 58; and

wherein the polypeptide comprises a conserved peptide sequence of each of the HPV proteins E1, E2, E4, E5, E6, and E7.

In one aspect, the present disclosure refers to a nucleic acid encoding a polypeptide comprising a plurality of conserved peptide sequences,

wherein the conserved sequences are conserved in one or more genotypes 16, 18, 31, 52, 53, and 58 or across two or more HPV genotypes 16, 18, 31, 52, 53, and 58; and

wherein the polypeptide comprises a conserved peptide sequence of each of the HPV proteins E1, E2, E4, E5, E6, and E7.

The disclosure advantageously provides a novel alternative and safer approach to vaccination whereby T cells can be induced to the relatively conserved antigens of the virion. The use of specially designed conserved viral segments from the non-structural proteins can provide protection against multiple important genotypes.

In one example, the polypeptide is a fusion polypeptide. The polypeptide may not be a wild-type polypeptide. The polypeptide may be synthetic/artificial, for example, the polypeptide may not exist in nature. In one example, the polypeptide may not comprise a complete gene sequence. The polypeptide may consist essentially of conserved peptide sequences. In another example, the polypeptide may consist essentially of conserved peptide sequences and a peptide adjuvant sequence. In another example, the polypeptide may consist essentially of conserved peptide sequences and one or more linkers therebetween. In another example, the polypeptide may consist essentially of conserved peptide sequences, a peptide adjuvant sequence and one or more linkers therebetween. In one example, the polypeptide is a recombinant polypeptide, such as a recombinant fusion polypeptide.

The term “fusion polypeptide” used herein is understood to mean a polypeptide comprising a combination of sequences derived from different gene products (for example different HPV proteins) or combinations of sequences from the same gene product (for example a single HPV protein), wherein the sequences are from distinct/separate regions of the wild-type gene product. For example the fusion polypeptide may comprise combinations of sequences which are normally separated by other sequence segments in wild-type, and the separating sequence(s) have been removed.

nucleic acid vaccine construct insert as provided in SEQ ID NO: 158 (underlined), or with an alternative nucleic acid vaccine construct in accordance with the disclosure herein. In another example, the nucleic acid of the disclosure (the HPV vaccine construct insert) may be inserted at the F11 locus of parental MVA virus under the control of the F11 promoter, for example through recombination with the F11 shuttle plasmid (SEQ ID NO: 159). The nucleic acid may comprise the sequence of SEQ ID NO: 159 with the nucleic acid vaccine construct insert as provided in SEQ ID NO: 159 (underlined), or with an alternative nucleic acid vaccine construct in accordance with the disclosure herein. The MVA sequence may comprise or consist of the sequence described herein (e.g. SEQ ID NOs: 69+70). The viral vector may comprise MVA when used as a vaccine boost in a prime boost regime. The viral vector may comprise Adeno-associated virus (AAV) or lentivirus. The viral vector may be an attenuated viral vector. The polypeptide sequence of the disclosure may be cloned into any suitable viral vector that is known to elicit good immune response. Suitable viral vectors have been described in Dicks et al (Vaccine. 2015 Feb 25;33(9):1121-8. doi: 10.1016/j.vaccine.2015.01.042. Epub 2015 Jan 25), Antrobus et al (Mol Ther. 2014 Mar;22(3):668-74. doi: 10.1038/mt.2013.284. Epub 2013 Dec 30.), and (Warimwe et al. (Virol J. 2013 Dec 5;10:349. doi: 10.1186/1743-422X-10-349), which are incorporated herein by reference.

According to another example of the disclosure there is provided a composition comprising one or more of:

-the polypeptide according to the disclosure;

-the nucleic acid according to the disclosure; and

-the viral vector according to the disclosure.

In another aspect, the present disclosure refers to a composition comprising one or more of:

-the nucleic acid as disclosed herein

-the polypeptide as disclosed herein; and/or

-the viral vector as disclosed herein.

The composition may be immunogenic, for example in a mammal, such as a human. The composition may comprise a pharmaceutically acceptable carrier. The composition may be a pharmaceutical composition comprising a pharmaceutically acceptable carrier. The composition may be for use in the prophylaxis or treatment of HPV infection.

In another aspect, the present disclosure refers to the nucleic acid as disclosed herein; the vaccine as disclosed herein; the polypeptide as disclosed herein; the viral vector as disclosed herein; or the composition as disclosed herein, for use in the prophylaxis or treatment of HPV infection.

According to another example of the disclosure there is provided a method of treatment or prophylaxis of HPV infection comprising the administration of:

-the polypeptide according to the disclosure;

CLAIMS

1. A nucleic acid encoding a polypeptide comprising a plurality of conserved peptide sequences,

wherein the conserved sequences are conserved in one or more genotypes 16, 18, 31, 52, 53, and 58 or across two or more HPV genotypes 16, 18, 31, 52, 53, and 58; and

wherein the polypeptide comprises a conserved peptide sequence of each of the HPV proteins E1, E2, E4, E5, E6, and E7.

2. The nucleic acid according to claim 1, wherein the polypeptide is a fusion polypeptide.

3. The nucleic acid according to claim 1 or claim 2, wherein the polypeptide does not comprise a complete gene sequence.

4. The nucleic acid according to any preceding claim, wherein the polypeptide consists essentially of conserved peptide sequences, a peptide adjuvant sequence and one or more linkers therebetween.

5. The nucleic acid according to any preceding claim, wherein the plurality of conserved peptide sequences comprises 10 or more conserved peptide sequences.

6. The nucleic acid according to any preceding claim, wherein the plurality of conserved peptide sequences comprises 40 or more conserved peptide sequences.

7. The nucleic acid according to any preceding claim, wherein the encoded polypeptide comprises at least 3 different conserved peptide sequences of each of the HPV proteins E1, E2, E4, E5, E6, and E7.

8. The nucleic acid according to any preceding claim, wherein the plurality of conserved peptide sequences are derived from distinct regions of sequence relative to each other and are not naturally concurrent in wild type.

9. The nucleic acid according to any preceding claim, wherein linker residues are provided between one or more, or all, conserved peptide sequences.

10. The nucleic acid according to claim 9, wherein the linker comprises or consists of K, G, P or S amino acid residues, or combinations thereof.

11. The nucleic acid according to any preceding claim, wherein the conserved peptide sequences are selected from any of the group comprising SEQ ID NOs: 1 to 59; or combinations thereof, in any order.

12. The nucleic acid according to any preceding claim, wherein the polypeptide comprises one or more conserved E1 sequence(s) selected from any one of SEQ ID NOs: 1-11; one or more conserved E2 sequence(s) selected from any one of SEQ ID NOs: 12-35; one or more conserved E4 sequence(s) selected from any one of SEQ ID NOs: 36-44; one or more conserved E5 sequence(s) selected from any one of SEQ ID NOs: 45-47; one or more conserved E6 sequence(s) selected from any one of SEQ ID NOs: 48-55; and one or more conserved E7 sequence(s) selected from any one of SEQ ID NOs: 56-59.

13. The nucleic acid according to any preceding claim, wherein the polypeptide comprises:

one or more conserved E1 sequence(s) selected from any one of SEQ ID NOs: 1-11, wherein each of the genotypes 16, 18, 31, 52, 53, and 58 are represented by at least one conserved E1 sequence;

one or more conserved E2 sequence(s) selected from any one of SEQ ID NOs: 12-35, wherein each of the genotypes 16, 18, 31, 52, 53, and 58 are represented by at least one conserved E2 sequence;

one or more conserved E4 sequence(s) selected from any one of SEQ ID NOs: 36-44, wherein each of the genotypes 16, 18, 31, 52, 53, and 58 are represented by at least one conserved E4 sequence;

one or more conserved E5 sequence(s) selected from any one of SEQ ID NOs: 45-47, wherein each of the genotypes 16, 18, 31, 52, 53, and 58 are represented by at least one conserved E5 sequence;

one or more conserved E6 sequence(s) selected from any one of SEQ ID NOs: 48-55, wherein each of the genotypes 16, 18, 31, 52, 53, and 58 are represented by at least one conserved E6 sequence; and

one or more conserved E7 sequence(s) selected from any one of SEQ ID NOs: 56-59, wherein each of the genotypes 16, 18, 31, 52, 53, and 58 are represented by at least one conserved E7 sequence.

14. The nucleic acid according to any preceding claim, wherein the polypeptide comprises:

one or more conserved E1 sequence(s) selected from any one of SEQ ID NOs: 1-11, wherein each of the genotypes 16, 18, 31, 52 and 58 are represented by at least one conserved E1 sequence;

one or more conserved E2 sequence(s) selected from any one of SEQ ID NOs: 12-35, wherein each of the genotypes 16, 18, 31, 52 and 58 are represented by at least one conserved E2 sequence;

one or more conserved E4 sequence(s) selected from any one of SEQ ID NOs: 36-44, wherein each of the genotypes 16, 18, 31, 52 and 58 are represented by at least one conserved E4 sequence;

one or more conserved E5 sequence(s) selected from any one of SEQ ID NOs: 45-47, wherein each of the genotypes 16, 18, 31, 52 and 58 are represented by at least one conserved E5 sequence;

one or more conserved E6 sequence(s) selected from any one of SEQ ID NOs: 48-55, wherein each of the genotypes 16, 18, 31, 52 and 58 are represented by at least one conserved E6 sequence; and

one or more conserved E7 sequence(s) selected from any one of SEQ ID NOs: 56-59, wherein each of the genotypes 16, 18, 31, 52 and 58 are represented by at least one conserved E7 sequence.

15. The nucleic acid according to any preceding claim, wherein the nucleic acid comprises or consists of the sequence of SEQ ID NO: 60; or

the nucleic acid comprises or consists of the sequence of SEQ ID NO: 60, and without encoding the TPA lead sequence; or

the nucleic acid comprises or consists of the sequence of SEQ ID NO: 60, with a different/alternative peptide adjuvant encoded than the TPA lead sequence; or

the nucleic acid comprises or consists of the sequence of SEQ ID NO: 65.

16. The nucleic acid according to any preceding claim, wherein the nucleic acid comprises or consists of the sequence of SEQ ID NO: 62; or

the nucleic acid comprises or consists of the sequence of SEQ ID NO: 62, and without encoding the TPA lead sequence; or

the nucleic acid comprises or consists of the sequence of SEQ ID NO: 62, with an alternative peptide adjuvant encoded than the TPA lead sequence.

17. The nucleic acid according to any preceding claim, wherein the nucleic acid comprises or consists of the sequence of SEQ ID NO: 71, 73 or 75; or

the nucleic acid comprises or consists of the sequence of SEQ ID NO: 71, 73 or 75, and without encoding the TPA lead sequence; or

the nucleic acid comprises or consists of the sequence of SEQ ID NO: 71, 73 or 75, with a different/alternative peptide adjuvant encoded than the TPA lead sequence.

71, 73 or 75.

18. The nucleic acid according to any preceding claim, wherein the polypeptide comprises or consists of the sequence of SEQ ID NO: 61;

the polypeptide comprises or consists of the sequence of SEQ ID NO: 61, and without the TPA lead sequence; or

the polypeptide comprises or consists of the sequence of SEQ ID NO: 61, with a different/alternative peptide adjuvant than the TPA lead sequence; or

the polypeptide comprises or consists of the sequence of SEQ ID NO: 66.

19. The nucleic acid according to any preceding claim, wherein the polypeptide comprises or consists of the sequence of SEQ ID NO: 72, 74 or 76;

the polypeptide comprises or consists of the sequence of SEQ ID NO: 72, 74 or 76, and without the TPA lead sequence; or

the polypeptide comprises or consists of the sequence of SEQ ID NO: 72, 74 or 76, with a different/alternative peptide adjuvant than the TPA lead sequence; or

the polypeptide comprises or consists of the sequence of SEQ ID NO: 72, 74 or 76.

20. The nucleic acid according to any preceding claim, wherein the conserved peptide sequences are from 7 to 250 amino acids in length, or more.

21. The nucleic acid according to any preceding claim, wherein the polypeptide further comprises a peptide adjuvant.

22. The nucleic acid according to any preceding claim, wherein the nucleic acid is a plasmid vector for vaccination.

23. The nucleic acid according to any preceding claim, wherein the nucleic acid comprises viral vector sequence.

24. A vaccine comprising a nucleic acid according to any preceding claim.

25. The vaccine according to claim 24, comprising combinations of different nucleic acids encoding different polypeptides according to any of claims 1-20.

26. The vaccine according to claim 24 or 25, further comprising another therapeutically or prophylactically active ingredient.

27. The vaccine according to any one of claims 24-26, further comprising an adjuvant.

28. A composition comprising a plurality of different nucleic acids according to any one of claims 1-23, optionally wherein the composition is a pharmaceutically acceptable composition.

29. A polypeptide encoded by the nucleic acid according to any one of claims 1-23.

30. A viral vector comprising the nucleic acid according to any one of claims 1-23.

31. The viral vector according to claim 30, wherein the virus is adenovirus.

32. A composition comprising one or more of:

-the nucleic acid according to any one of claims 1-23

-the polypeptide according to claim 29; and/or

-the viral vector according claim 30 or 31.

33. The composition according to claim 32, wherein the composition is immunogenic in a mammal.

34. The composition according to claim 32 or 33, further comprising a pharmaceutically acceptable carrier.

35. The nucleic acid according to any one of claims 1-23; the vaccine according to any one of claims 24-27; the polypeptide according to claim 29; the viral vector according claim 30 or 31; or the composition according to any one of claims 28, or 32-34, for use in the prophylaxis or treatment of HPV infection.

36. Use of the nucleic acid according to any one of claims 1-23; the vaccine according to any one of claims 24-27; the polypeptide according to claim 29; the viral vector according claim 30 or 31; or the composition according to any one of claims 28, or 32-34, in the manufacture of a medicament for the treatment or prophylaxis of HPV infection.

37. An agent for use in the prophylaxis or treatment of HPV infection, the agent comprising or consisting of the nucleic acid according to any one of claims 1-23; the polypeptide according to claim 29; the viral vector according claim 30 or 31.

38. A prime boost vaccination kit comprising:

-a prime vaccination comprising the nucleic acid according to any one of claims 1-23; the vaccine according to any one of claims 24-27; the polypeptide according to claim 29; the viral vector according claim 27 or 28; or the composition according to any one of claims 28, or 32-34; and

-a boost vaccination comprising a nucleic acid according to any one of claims 1-23; the vaccine according to any one of claims 24-27; the polypeptide according to claim 26; the viral vector according claim 30 or 31; or the composition according to any one of claims 28, or 32-34.

39. The prime boost vaccination kit according to claim 38, wherein the prime and boost vaccination are different.

40. The prime boost vaccination kit according to claim 39, wherein the prime and boost vaccination differ in the encoded polypeptide sequence and/or comprise different viral vectors.