SUMMARY

[0009] The present disclosure relates to immunogenic compositions comprising a varicella zoster virus surface (VZV) glycoprotein E antigen and a toll-like receptor 9 (TLR9) agonist, such as an oligonucleotide comprising an unmethylated cytidine-phospho-guanosine (CpG) motif. The immunogenic compositions are suitable for stimulating an immune response against VZV in individuals in need thereof.

In one aspect, the present disclosure refers to an immunogenic composition, comprising: a varicella zoster virus (VZV) glycoprotein E (gE) antigen and a toll-like receptor 9 (TLR9) agonist, wherein the TLR9 agonist is an oligonucleotide of from 10 to 35 nucleotides in length comprising an unmethylated cytidine-phospho-guanosine (CpG) motif, wherein the oligonucleotide comprises the sequence of 5'-TGACTGTGAA CGTTCGAGAT GA-3' (SEQ ID NO:1).

In another aspect, the present disclosure refers to use of the immunogenic composition disclosed herein in the manufacture of a medicament for preventing a varicella zoster virus (VZV) infection in a mammalian subject.

In another aspect, the present disclosure refers to an immunogenic composition, comprising: a varicella zoster virus (VZV) glycoprotein E (gE) antigen, a toll-like receptor 9 (TLR9) agonist, and an aluminum salt adjuvant; wherein the TLR9 agonist is an oligonucleotide of from 10 to 35 nucleotides in length comprising an unmethylated cytidine-phospho-guanosine (CpG) motif, wherein the oligonucleotide comprises the sequence of 5'-TGACTGTGAA CGTTCGAGAT GA-3' (SEQ ID NO:1); wherein the immunogenic composition comprises 6000 μg of the oligonucleotide; and wherein the immunogenic composition comprises 100 μg of the VZV gE antigen.

[0009a] In one example, the present disclosure refers to an immunogenic composition, comprising: a varicella zoster virus (VZV) glycoprotein E (gE) antigen and a toll-like receptor 9 (TLR9) agonist, wherein the TLR9 agonist is an oligonucleotide of from 10 to 35 nucleotides in length comprising an unmethylated cytidine-phospho-guanosine (CpG) motif.

[0009b] In one aspect, the present disclosure refers to a kit comprising: i) the immunogenic composition disclosed herein, and ii) instructions for administration of the immunogenic composition to stimulate an immune response against the VZV gE antigen in the mammalian subject.

[0009c] In one aspect, the present disclosure refers to a kit comprising: i) first composition comprising a varicella zoster virus (VZV) glycoprotein E (gE) antigen; ii) a second composition comprising a TLR9 agonist; and iii) instructions for mixing the first composition with the second composition to prepare an immunogenic composition.

[0009d] In one example, the present disclosure refers to use of the immunogenic composition disclosed herein in the manufacture of a medicament for stimulating an immune response against varicella zoster virus (VZV) in a mammalian subject.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] FIG. 1A shows the levels of anti-VZV gE-reactive IgG in sera of recipients of a first dose (prime) of a shingles vaccine and control recipients (CTL and LAV). FIG. 1B shows the levels of anti-VZV gE-reactive IgG in sera of recipients of a first dose (prime) and a second dose (boost) of a shingles vaccine and control recipients (CTL and LAV).

[0011] FIG. 2A-2C show gE-antigen induced, IL-2 and/or IFN-γ secreting CD4+ T cells of recipients of a first dose (prime) and a second dose (boost) of a shingles vaccine and control recipients (CTL and LAV).

[0012] FIG. 3A-3B show gE-antigen induced, IL-2 or IFN-γ secreting CD154+, CD4+ T cells of recipients of a first dose (prime) and a second dose (boost) of a shingles vaccine and control recipients (CTL and LAV).

General Techniques and Definitions

[0013] The practice of the present disclosure will employ, unless otherwise indicated, conventional techniques of molecular biology (including recombinant techniques), microbiology, cell biology, biochemistry and immunology, which are within the skill of the art.

[0014] As used herein and in the appended claims, the singular forms “a”, “an”, and “the” include plural references unless indicated otherwise. For example, “an” excipient includes one or more excipients.

[0015] The phrase “comprising” as used herein is open-ended, indicating that such embodiments may include additional elements. In contrast, the phrase “consisting of” is closed, indicating that such embodiments do not include additional elements (except for trace impurities). The phrase “consisting essentially of” is partially closed, indicating that such

CLAIMS

We claim:

1. An immunogenic composition, comprising: a varicella zoster virus (VZV) glycoprotein E (gE) antigen and a toll-like receptor 9 (TLR9) agonist, wherein the TLR9 agonist is an oligonucleotide of from 10 to 35 nucleotides in length comprising an unmethylated cytidine-phospho-guanosine (CpG) motif, wherein the oligonucleotide comprises the sequence of 5'-TGACTGTGAA CGTTCGAGAT GA-3' (SEQ ID NO:1).

2. The immunogenic composition of claim 1, wherein the oligonucleotide comprises a modified nucleoside selected from the group consisting of 2'-deoxy-7-deazaguanosine, 2'-deoxy-6-thioguanosine, arabinoguanosine, 2'-deoxy-2'substituted-arabinoguanosine, and 2'-O-substituted-arabinoguanosine.

3. The immunogenic composition of claim 1 or claim 2, wherein the VZV gE antigen and the oligonucleotide are present in the immunogenic composition in amounts effective to stimulate an immune response against the VZV gE antigen in a mammalian subject.

4. The immunogenic composition of any one of claims 1-3, wherein the oligonucleotide comprises at least one phosphorothioate linkage, or wherein all nucleotide linkages are phosphorothioate linkages.

5. The immunogenic composition of any one of claims 1-4, wherein the oligonucleotide is a single-stranded oligodeoxynucleotide.

6. The immunogenic composition of any one of claims 1-5, wherein the immunogenic composition comprises from 375 μg to 6000 μg of the oligonucleotide.

7. The immunogenic composition of any one of claims 1-6, wherein the immunogenic composition comprises 6000 μg of the oligonucleotide.

8. The immunogenic composition of any one of claims 1-7, wherein the VZV gE antigen is a truncated, recombinant protein devoid of signal peptide, transmembrane and cytoplasmic domains of a full-length VZV gE antigen.

9. The immunogenic composition of any one of claims 1-8, wherein the immunogenic composition comprises from 10 μg to 100 μg of the VZV gE antigen.

10. The immunogenic composition of any one of claims 1-9, wherein the immunogenic composition comprises 100 μg of the VZV gE antigen.

11. The immunogenic composition of any one of claims 1-10, further comprising an aluminum salt adjuvant.

12. The immunogenic composition of claim 11, wherein the aluminum salt adjuvant comprises one or more of the group consisting of amorphous aluminum hydroxyphosphate sulfate, aluminum hydroxide, aluminum phosphate, and potassium aluminum sulfate.

13. The immunogenic composition of claim 11, wherein the aluminum salt adjuvant comprises aluminum hydroxide.

14. The immunogenic composition of any one of claims 11-13, wherein the immunogenic composition comprises from 0.25 to 0.50 mg Al^{3+}.

15. The immunogenic composition of any one of claims 1-14, wherein the mammalian subject is a human subject.

16. A kit comprising:

i) the immunogenic composition of any one of claims 1-15, and

ii) instructions for administration of the immunogenic composition to stimulate an immune response against the VZV gE antigen in the mammalian subject.

17. A kit comprising:

i) a first composition comprising a varicella zoster virus (VZV) glycoprotein E (gE) antigen ;

ii) a second composition comprising a TLR9 agonist; and

iii) instructions for mixing the first composition with the second composition to prepare an immunogenic composition.

18. The kit of claim 17, further comprising:

iv) a further set of instructions for administration of the immunogenic composition to stimulate an immune response against the VZV gE antigen in a mammalian subject.

19. The kit of claim 18, further comprising a syringe and needle for intramuscular injection of the immunogenic composition.

20. Use of the immunogenic composition of any one of claims 1-15 in the manufacture of a medicament for preventing a varicella zoster virus (VZV) infection in a mammalian subject.

21. The use of claim 20, wherein the immunogenic composition is to be administered by intramuscular injection.

22. An immunogenic composition, comprising: a varicella zoster virus (VZV) glycoprotein E (gE) antigen, a toll-like receptor 9 (TLR9) agonist, and an aluminum salt adjuvant;

wherein the TLR9 agonist is an oligonucleotide of from 10 to 35 nucleotides in length comprising an unmethylated cytidine-phospho-guanosine (CpG) motif, wherein the oligonucleotide comprises the sequence of 5'-TGACTGTGAA CGTTCGAGAT GA-3' (SEQ ID NO:1);

wherein the immunogenic composition comprises 6000 μg of the oligonucleotide; and

wherein the immunogenic composition comprises 100 μg of the VZV gE antigen.