developed by Chiron and the other by GlaxoSmithKline, were both halted due to insufficient efficacy. Chiron's vaccine comprised truncated forms of two HSV-2 glycoproteins, gD2 and gB2, in combination with the adjuvant MF59. The vaccine at best provided transient protection against HSV-2 although high titers of antibodies to HSV-2 were generated (Stanberry, ibid). GlaxoSmithKline (GSK) developed and tested a similar vaccine; however it contained only a single glycoprotein, gD2, and alum and MPL as adjuvants. Following eight years of studies and clinical trials, GSK pronounced it as a failure in October 2010. The vaccine was unsuccessful in preventing infection in seronegative women, the only group in early clinical trials that had seemed to benefit.

SUMMARY

In one aspect of the disclosure, an immunogenic, pharmaceutical composition comprising: (i) an immunogenic fragment of an HSV-2 UL19 polypeptide, wherein the immunogenic fragment of the UL19 has the amino acid sequence set forth in SEQ ID NO: 12, and wherein the immunogenic fragment is a fragment of the UL19 polypeptide lacking at least 75% of amino acids 1-450 of SEQ ID NO: 4 and lacks at least 75% of amino acids of 1055-1374 of SEQ ID NO: 4; or an immunogenic variant thereof that retains at least 90% amino acid identity over the full length of the immunogenic fragment; (ii) glycoprotein D of HSV-2 (gD2), wherein gD2 comprises the amino acid sequence set fort in SEQ ID NO: 2 or 3, or an immunogenic fragment thereof comprising at least 15 contiguous amino acids of SEQ ID NO: 2 or 3; (iii) UL25, wherein the UL25 comprises the amino acid sequence set forth in SEQ ID NO: 5, or an immunogenic fragment thereof comprising at least 15 contiguous amino acids of SEQ ID NO: 5; (iv) Glucopyranosyl Lipid Adjuvant (GLA); and (v) a pharmaceutically acceptable carrier.

In another aspect of the disclosure, use of an immunogenic pharmaceutical composition comprising: (i) an immunogenic fragment of an HSV-2 UL19 polypeptide, wherein the immunogenic fragment has the amino acid sequence set forth in SEQ ID NO: 12, and wherein the immunogenic fragment is a fragment of the UL19 polypeptide that lacks at least 75% of amino acids 1-450 of SEQ ID NO: 4 and lacks at least 75% of amino acids of 1055-1374 of SEQ ID NO: 4; or an immunogenic variant thereof that retains at least 90% amino acid identity over the full length of the immunogenic fragment; (ii) glycoprotein D of HSV-2 (gD2), wherein gD2 comprises the amino acid sequence set fort in SEQ ID NO: 2 or 3, or an

immunogenic fragment thereof comprising at least 15 contiguous amino acids of SEQ ID NO: 2 or 3; and (iii) UL25, wherein the UL25 comprises the amino acid sequence set forth in SEQ ID NO: 5, or an immunogenic fragment thereof comprising at least 15 contiguous amino acids of SEQ ID NO: 5; (iv) Glucopyranosyl Lipid Adjuvant (GLA); and (v) a pharmaceutically acceptable carrier in the manufacture of a medicament for the treatment of an Herpes Simplex virus type 2 infection (HSV-2 infection) in a subject.

In another aspect of the disclosure, use of an immunogenic pharmaceutical composition comprising: (i) an immunogenic fragment of an HSV-2 UL19 polypeptide wherein the immunogenic fragment has the amino acid sequence set forth in SEQ ID NO: 12, and wherein the immunogenic fragment is a fragment of the UL19 polypeptide that lacks at least 75% of amino acids 1-450 of SEQ ID NO: 4 and lacks at least 75% of amino acids of 1055-1374 of SEQ ID NO: 4, or an immunogenic fragment thereof that retains at least 90% amino acid identity over the full length of the immunogenic fragment; (ii) gD2, wherein gD2 comprises the amino acid sequence set fort in SEQ ID NO: 2 or 3, or an immunogenic fragment thereof comprising at least 15 contiguous amino acids of SEQ ID NO: 2 or 3; and (iii) UL25, wherein the UL25 comprises the amino acid sequence set forth in SEQ ID NO: 5, or an immunogenic fragment thereof comprising at least 15 contiguous amino acids of SEQ ID NO: 5; (iv) Glucopyranosyl Lipid Adjuvant (GLA); (v) a pharmaceutically acceptable carrier in the manufacture of a medicament for generating an immune response to HSV-2 in a subject.

In one ~~aspect~~ example of the disclosure, an immunogenic fragment of an HSV-2 polypeptide is provided selected from the group consisting of: (a) an immunogenic fragment of UL19 polypeptide lacking at least 75% of amino acids 1-450 of SEQ ID NO: 4 and lacking at least 75% of amino acids of 1055-1374 of SEQ ID NO: 4; (b) the sequence set out in SEQ ID NO: 12; (c) an immunogenic variant of (a) or (b) that retains at least 85% amino acid identity over at least 15 contiguous amino acids; (d) an immunogenic fragment of (a) or (b); and (e) a chimeric fusion of (a), (b), (c) or (d). In another embodiment an isolated polynucleotide encoding the aforementioned polypeptide is provided.

[0009] Pharmaceutical compositions are also provided by the instant disclosure. In one ~~aspect~~example, an immunogenic, pharmaceutical composition is provided comprising: (i) an immunogenic fragment of an HSV-2 polypeptide selected from the group consisting of: (a) an immunogenic fragment of UL19 polypeptide lacking at least 75% of amino acids 1-450 of SEQ ID NO: 4 and lacking at least 75% of amino acids of

1055-1374 of SEQ ID NO: 4; (b) the sequence set out in SEQ ID NO: 12; (c) an immunogenic variant of (a) or (b) that retains at least 85% amino acid identity over at least 15 contiguous amino acids; (d) an immunogenic fragment of (a) or (b); and (e) a chimeric fusion of (a), (b), (c) or (d); (ii) optionally, an agent that activates innate immunity; and (iii) a pharmaceutically acceptable carrier.

CLAIMS

What is claimed is:

1. An immunogenic, pharmaceutical composition comprising:

(i) an immunogenic fragment of an HSV-2 UL19 polypeptide, wherein the immunogenic fragment is:

a fragment of the UL19 polypeptide lacking at least 75% of amino acids 1-450 of SEQ ID NO: 4 and lacks at least 75% of amino acids of 1055-1374 of SEQ ID NO: 4; or an immunogenic variant thereof that retains at least 85% amino acid identity thereto, and comprising at least 100 amino acids;

glycoprotein D of HSV-2 (gD2), or an immunogenic fragment thereof; and

UL25, or an immunogenic fragment thereof; and

(ii) Glucopyranosyl Lipid Adjuvant (GLA); and

(iii) a pharmaceutically acceptable carrier.

2. The composition of claim 1 wherein the GLA is in the form of an oil-in-water emulsion or is in an aqueous form.

3. Use of an immunogenic pharmaceutical composition comprising:

(i) an immunogenic fragment of an HSV-2 UL19 polypeptide, wherein the immunogenic fragment is

a fragment of the UL19 polypeptide that lacks at least 75% of amino acids 1-450 of SEQ ID NO: 4 and lacks at least 75% of amino acids of 1055-1374 of SEQ ID NO: 4; or an immunogenic variant thereof that retains at least 85% amino acid identity thereto, and comprising at least 100 amino acids;

glycoprotein D of HSV-2 (gD2), or an immunogenic fragment thereof; and

UL25, or an immunogenic fragment thereof; and

(ii) Glucopyranosyl Lipid Adjuvant (GLA),

in the manufacture of a medicament for the treatment of an Herpes Simplex virus type 2 infection (HSV-2 infection) in a subject.

4. Use of an immunogenic pharmaceutical composition comprising:

(i) an immunogenic fragment of an HSV-2 UL19 polypeptide wherein the immunogenic fragment is

a fragment of the UL19 polypeptide that lacks at least 75% of amino acids 1-450 of SEQ ID NO: 4 and lacks at least 75% of amino acids of 1055-1374 of SEQ ID NO: 4, or an immunogenic fragment thereof that retains at least 85% amino acid identity thereto and comprising at least 100 amino acids;

gD2, or an immunogenic fragment thereof; and

UL25, or an immunogenic fragment thereof; and

(ii) Glucopyranosyl Lipid Adjuvant (GLA)

in the manufacture of a medicament for generating an immune response to HSV-2 in a subject.

5. The use of claim 3, wherein the immunogenic fragment of an HSV-2 UL19 polypeptide has the amino acid sequence set forth in SEQ ID NO:12.

6. The use of claim 3, wherein the immunogenic pharmaceutical composition further comprises one or more HSV-2 proteins, or an immunogenic fragment thereof, selected from the group consisting of UL47, ICP0, UL25, UL46, UL39, UL7 and UL26.

7. The use of claim 3, wherein the GLA is in the form of an oil-in-water emulsion or is in an aqueous form.

8. The use of claim 3, wherein the immunogenic pharmaceutical composition further comprises a second adjuvant.

9. The use of claim 8, wherein the second adjuvant is selected from the group consisting of a TLR7 agonist, a TLR9 agonist, alum; an emulsion; a saponin; a cytokine; an unmethylated CpG dinucleotide; and a modified saponin.

10. The use of claim 8 or 9, wherein the second adjuvant is an oil-in-water emulsion.

11. The use of claim 4, wherein the immunogenic fragment of an HSV-2 UL19 polypeptide has the amino acid sequence set forth in SEQ ID NO:12.

12. The use of claim 4, wherein the immunogenic pharmaceutical composition further comprises one or more HSV-2 proteins, or an immunogenic fragment thereof, selected from the group consisting of UL47, ICP0, UL25, UL46, UL39, UL7 and UL26.

13. The use of claim 4, wherein the GLA is in the form of an oil-in-water emulsion or is in an aqueous form.

14. The use of claim 4, wherein the immunogenic pharmaceutical composition further comprises a second adjuvant.

15. The use of claim 14, wherein the second adjuvant is selected from the group consisting of a TLR7 agonist, a TLR9 agonist, alum; an emulsion; a saponin; a cytokine; an unmethylated CpG dinucleotide; and a modified saponin.

16. The use of claim 14 or 15, wherein the second adjuvant is an oil-in-water emulsion.

CLAIMS

What is claimed is:

1. An immunogenic, pharmaceutical composition comprising:

(i) an immunogenic fragment of an HSV-2 UL19 polypeptide, wherein the immunogenic fragment

of the UL19 has the amino acid sequence set forth in SEQ ID NO: 12, and wherein the immunogenic fragment is a fragment of the UL19 polypeptide lacking at least 75% of amino acids 1-450 of SEQ ID NO: 4 and lacks at least 75% of amino acids of 1055-1374 of SEQ ID NO: 4; or an immunogenic variant thereof that retains at least 90% amino acid identity over the full length of the immunogenic fragment;

(ii) glycoprotein D of HSV-2 (gD2), wherein gD2 comprises the amino acid sequence set fort in SEQ ID NO: 2 or 3, or an immunogenic fragment thereof comprising at least 15 contiguous amino acids of SEQ ID NO: 2 or 3;

(iii) UL25, wherein the UL25 comprises the amino acid sequence set forth in SEQ ID NO: 5, or an immunogenic fragment thereof comprising at least 15 contiguous amino acids of SEQ ID NO: 5;

(iv) Glucopyranosyl Lipid Adjuvant (GLA); and

(v) a pharmaceutically acceptable carrier.

2. The composition of claim 1 wherein the GLA is in the form of an oil-in-water emulsion or is in an aqueous form.

3. Use of an immunogenic pharmaceutical composition comprising:

(i) an immunogenic fragment of an HSV-2 UL19 polypeptide, wherein the immunogenic fragment has the amino acid sequence set forth in SEQ ID NO: 12, and wherein the immunogenic fragment is

a fragment of the UL19 polypeptide that lacks at least 75% of amino acids 1-450 of SEQ ID NO: 4 and lacks at least 75% of amino acids of 1055-1374 of SEQ ID NO: 4; or an immunogenic variant thereof that retains at least 90% amino acid identity over the full length of the immunogenic fragment;

(ii) glycoprotein D of HSV-2 (gD2), wherein gD2 comprises the amino acid sequence set fort in SEQ ID NO: 2 or 3, or an immunogenic fragment thereof comprising at least 15 contiguous amino acids of SEQ ID NO: 2 or 3; and

(iii) UL25, wherein the UL25 comprises the amino acid sequence set forth in SEQ ID NO: 5, or an immunogenic fragment thereof comprising at least 15 contiguous amino acids of SEQ ID NO: 5;

(iv) Glucopyranosyl Lipid Adjuvant (GLA); and

(v) a pharmaceutically acceptable carrier

in the manufacture of a medicament for the treatment of an Herpes Simplex virus type 2 infection (HSV-2 infection) in a subject.

4. Use of an immunogenic pharmaceutical composition comprising:

(i) an immunogenic fragment of an HSV-2 UL19 polypeptide wherein the immunogenic fragment has the amino acid sequence set forth in SEQ ID NO: 12, and wherein the immunogenic fragment is

a fragment of the UL19 polypeptide that lacks at least 75% of amino acids 1-450 of SEQ ID NO: 4 and lacks at least 75% of amino acids of 1055-1374 of SEQ ID NO: 4, or an immunogenic fragment thereof that retains at least 90% amino acid identity over the full length of the immunogenic fragment;

(ii) gD2, wherein gD2 comprises the amino acid sequence set fort in SEQ ID NO: 2 or 3, or an immunogenic fragment thereof comprising at least 15 contiguous amino acids of SEQ ID NO: 2 or 3; and

(iii) UL25, wherein the UL25 comprises the amino acid sequence set forth in SEQ ID NO: 5, or an immunogenic fragment thereof comprising at least 15 contiguous amino acids of SEQ ID NO: 5;

(iv) Glucopyranosyl Lipid Adjuvant (GLA);

(v) a pharmaceutically acceptable carrier

in the manufacture of a medicament for generating an immune response to HSV-2 in a subject.

5. The use of claim 3, wherein the immunogenic pharmaceutical composition further comprises one or more HSV-2 proteins, or an immunogenic fragment thereof, selected from the group consisting of UL47, ICP0, UL46, UL39, UL7 and UL26.

6. The use of claim 3, wherein the GLA is in the form of an oil-in-water emulsion or is in an aqueous form.

7. The use of claim 3, wherein the immunogenic pharmaceutical composition further comprises a second adjuvant.

8. The use of claim 7, wherein the second adjuvant is selected from the group consisting of a TLR7 agonist, a TLR9 agonist, alum; an emulsion; a saponin; a cytokine; an unmethylated CpG dinucleotide;

and a modified saponin.

9. The use of claim 7 or 8, wherein the second adjuvant is an oil-in-water emulsion.

10. The use of claim 4, wherein the immunogenic pharmaceutical composition further comprises one or more HSV-2 proteins, or an immunogenic fragment thereof, selected from the group consisting of UL47, ICP0, UL46, UL39, UL7 and UL26.

11. The use of claim 4, wherein the GLA is in the form of an oil-in-water emulsion or is in an aqueous form.

12. The use of claim 4, wherein the immunogenic pharmaceutical composition further comprises a second adjuvant.

13. The use of claim 12, wherein the second adjuvant is selected from the group consisting of a TLR7 agonist, a TLR9 agonist, alum; an emulsion; a saponin; a cytokine; an unmethylated CpG dinucleotide; and a modified saponin.

14. The use of claim 12 or 13, wherein the second adjuvant is an oil-in-water emulsion.