3(5):e2230 (2008)). Overall, the relative risk of HIV acquisition increases more than 2-fold in HSV-2-infected individuals.

[0007] The increasing prevalence of HSV-2 in the adult and pediatric populations persists despite the widespread use of pharmacological intervention. Antiviral medication given at high doses early in infection can reduce HSV transmission, but this does not prevent latent infection (see, e.g., Corey et al., Sex Transm. Dis. 12:215 (1985)). In a recent study, continuous suppressive administration with Valacyclovir reduced HSV transmission by less than 50% despite early intervention (see, e.g., Corey et al., N. Engl. J. Med. 350:11 (2004)). Alternatives to antiviral drugs, such as topical microbicides are unproven clinically. For these reasons, many leading authorities believe that vaccination is essential for diminishing the health impact of HSV-2 disease.

[0008] A need exists for vaccines, including improved vaccines, against infectious disease microorganisms, such as Human Immunodeficiency Virus (HIV) and Herpes Simplex Virus, malaria, antibiotic resistant bacteria, for which inducing a robust humoral and/or cell-mediated response is important for successful prevention and treatment of infection. In addition, considerable potential and need exists for improved cancer vaccine potency.

BRIEF SUMMARY

[0009] Provided herein are immunogenic compositions, preparations of these immunogenic compositions and, methods for using the preparations and compositions for inducing an immune response specific for one or more immunogens and related antigens.

[0009a] In one aspect, there is provided the use of (a) at least one dose of a first immunogenic composition comprising (i) a lentiviral vector comprising a nucleotide sequence that encodes a first immunogen, or an immunogenic fragment thereof, in the manufacture of a medicament for priming and boosting a CD8 T cell immune response in a subject, wherein the lentiviral vector is incorporated into a vector particle, wherein the vector particle comprises a lentiviral vector genome and an alpha virus envelope; and wherein the medicament further comprises at least one dose of a second immunogenic composition comprising (i) at least the first immunogen or an immunogenic fragment thereof and (ii) a TLR4 agonist; wherein the second immunogenic composition is to be administered subsequent to the first immunogenic composition, thereby priming and boosting a CD8 T cell immune response specific for the first immunogen into the subject to thereby induce an immune response specific for the first immunogen.

[0009b] In one ~~embodiment~~example, a method is provided for inducing an immune response in a subject, the method comprising (a) administering to the subject at least one dose of a first immunogenic composition comprising at least a first immunogen, wherein the at least one immunogen is capable of inducing an immune response specific for a first designated antigen; and (b) administering to the subject at least one dose second immunogenic composition comprising a recombinant expression vector comprising a nucleotide sequence that encodes the first immunogen, thereby inducing an immune response specific for the first designated antigen. In a particular ~~embodiment~~example, (i) the first immunogenic composition further comprises an adjuvant; (ii) the second composition further comprises an adjuvant; or (iii) each of the first composition and the second composition further comprises an adjuvant. In certain ~~embodiments~~examples, the second immunogenic composition is administered subsequent to administration of the first immunogenic composition. In other certain ~~embodiments~~examples, the

second immunogenic composition is administered prior to administration of the first immunogenic composition. In still another certain ~~embodiment~~example, the first immunogenic composition and the second immunogenic composition are administered concurrently. In specific ~~embodiments~~examples, at least two doses of the first immunogenic composition are administered or at least two doses of the second immunogenic composition are administered. In still other ~~embodiments~~examples, (a) two doses; (b) three doses; (c) four doses; or (d) five doses of the first immunogenic composition are administered. In another ~~embodiment~~example, when two or more doses are administered, (a) each dose of the first immunogenic composition is administered prior to administration of the second immunogenic composition; (b) at least one dose of the first immunogenic composition is administered subsequent to administration of the second immunogenic composition; (c) at least one dose of the first immunogenic composition is administered concurrently with administration of the second immunogenic composition; (d) at least one dose of the first immunogenic composition is administered prior to administration of the second immunogenic composition and each of any remaining doses of the first immunogenic composition is administered subsequent to administration of the second immunogenic composition; or (e) each dose of the first composition is administered concurrently with the second composition. With respect to each of these methods and ~~embodiments~~examples, the immune response induced by the first immunogen comprises a CD4 T cell immune response specific for the first designated antigen, and in certain ~~embodiments~~examples the immune response induced by the first immunogen comprises a CD8 T cell immune response specific for the first designated antigen; and in other certain ~~embodiments~~examples, the immune response induced by the first immunogen comprises a CD4 T cell immune response and a CD8 T cell immune response specific for the first designated antigen.

[0010] In certain ~~embodiments~~examples of the methods described above and herein, the first immunogenic composition further comprises a second immunogen, and the recombinant expression vector further comprises a nucleotide sequence that encodes the second immunogen, wherein the second immunogen induces an immune response specific for a second designated antigen. In certain particular ~~embodiments~~examples, the first designated antigen and the second designated antigen are the same. In other certain particular ~~embodiments~~examples, the first designated antigen and the second designated antigen are different. In certain other ~~embodiments~~examples of the methods described above and herein, the recombinant expression vector further comprises a nucleotide sequence that encodes a second immunogen capable of inducing an immune response specific for a second designated antigen. In certain particular

~~embodiments~~examples, the first designated antigen and the second designated antigen are the same. In other certain particular ~~embodiments~~examples, the first designated antigen and the second designated antigen are different. In particular ~~embodiments~~examples with respect to such methods, the immune response induced by the first immunogen comprises a CD4 T cell response specific for the first designated antigen. In particular ~~embodiments~~examples with respect to such methods, the immune response induced by the second immunogen comprises a CD8 T cell response specific for the second designated antigen.

[0011] In particular ~~embodiments~~examples of the methods described above and herein and when one or more of the immunogenic compositions comprises an adjuvant, the adjuvant is a non-toxic lipid A-related adjuvant. In certain particular ~~embodiments~~examples, the non-toxic lipid A-related adjuvant is glucopyranosyl lipid A (GLA); in more particular ~~embodiments~~examples, GLA is formulated in a stable oil-in-water emulsion.

[0012] In other particular ~~embodiments~~examples of the methods described above and herein, the first designated antigen is (a) a tumor-associated antigen or (b) from an infectious microorganism selected from a virus, a bacterium, a fungus, and a parasite. In a more specific ~~embodiment~~example, the first designated antigen is a tumor-associated antigen selected from a renal cell carcinoma antigen, a prostate cancer antigen, a mesothelioma antigen, a pancreatic cancer antigen, a melanoma antigen, a breast cancer antigen, a lung cancer antigen, and an ovarian cancer antigen. In still more specific ~~embodiments~~examples, the prostate cancer antigen is prostatic acid phosphatase, prostate specific antigen, NKX3.1, or prostate specific membrane antigen. In other particular ~~embodiments~~examples, the first designated antigen is from a virus. In a more specific ~~embodiment~~example, the virus is Herpes Simplex Virus-2 (HSV-2). In certain particular ~~embodiments~~examples, the first designated antigen is HSV-2 UL19 polypeptide or HSV-2 gD polypeptide.

[0013] In other specific ~~embodiments~~examples of the methods described above and herein when an immune response is induced specific for a first designated and a second designated antigen, each of the first designated antigen and the second designated antigen is a tumor-associated antigen. In more specific ~~embodiments~~examples, each of the first designated antigen and the second designated antigen is selected from a renal cell carcinoma antigen, a prostate cancer antigen, a mesothelioma antigen, a pancreatic cancer antigen, a melanoma antigen, a breast cancer antigen, a lung cancer antigen, and an ovarian cancer antigen. In still more specific ~~embodiments~~examples, each of the first designated antigen and the second designated antigen is a prostate cancer antigen selected from prostatic acid phosphatase, prostate specific antigen,

NKX3.1, or prostate specific membrane antigen. In other particular ~~embodiments~~examples, each of the first designated antigen and the second designated antigen is an antigen from an infectious microorganism selected from a virus, a bacterium, a fungus, and a parasite. In a more specific ~~embodiment~~example, the infectious disease organism is a virus, which in more particular ~~embodiments~~examples is Herpes Simplex Virus-2 (HSV-2). In certain ~~embodiments~~examples, at least one of the first designated antigen and the second designated antigen is HSV-2 UL19 polypeptide and the other of the first designated antigen and the second designated antigen is HSV-2 gD polypeptide.

[0014] In other specific ~~embodiments~~examples of the methods described above and herein, the recombinant expression vector is selected from a lentiviral vector genome, poxvirus vector genome, vaccinia virus vector genome, adenovirus vector genome, adenovirus-associated virus vector genome, herpes virus vector genome, and an alpha virus vector genome. In a particular ~~embodiment~~example, the recombinant expression vector is incorporated into a vector particle, which in certain specific ~~embodiments~~examples delivers the recombinant expression vector to an antigen-presenting cell. In a specific ~~embodiment~~example, the antigen-presenting cell is a dendritic cell. In particular ~~embodiments~~examples, the vector particle is a lentiviral vector particle that comprises the lentiviral vector genome; a poxvirus vector particle that comprises the poxvirus vector genome; a vaccinia virus vector particle that comprises the vaccinia virus vector genome; an adenovirus vector particle that comprises the adenovirus vector genome; an adenovirus-associated virus vector particle that comprises the adenovirus-associated virus vector genome; a herpes virus vector particle that comprises the herpes virus vector genome; or an alpha virus vector particle that comprises the alpha virus vector genome. In a more specific ~~embodiment~~example, the vector particle is a lentiviral vector particle that comprises the lentiviral vector genome. In still more specific ~~embodiments~~examples, the lentiviral vector particle further comprises an envelope comprising a Sindbis virus E2 glycoprotein comprising an amino acid sequence having at least one amino acid change compared to SEQ ID NO:1, wherein residue 160 of SEQ ID NO:1 is either absent or an amino acid other than glutamic acid, and wherein the E2 glycoprotein is not a moiety of a fusion protein that comprises Sindbis virus E3 protein. In further particular ~~embodiments~~examples, the E2 glycoprotein binds to dendritic cell-specific intercellular adhesion molecule-3-grabbing non-integrin (DC-SIGN).

[0014a] In another aspect, there is provided the use of at least one dose of a first immunogenic composition comprising (i) a lentiviral vector comprising a nucleotide sequence that encodes a first immunogen or an immunogenic fragment thereof in the manufacture of a medicament for priming and boosting a CD8 T cell immune response in a subject, said lentiviral vector is incorporated into a vector particle, wherein the vector particle comprises a lentiviral vector genome and an alpha virus envelope, and wherein the medicament is to be concurrently administered with a second immunogenic composition comprising (i) at least the first immunogen or an immunogenic fragment thereof and (ii) a TLR4 agonist; thereby priming and boosting a CD8 T cell immune response specific for the first immunogen.

[0015] Also provided herein in one ~~embodiment~~example are preparations, which in one ~~embodiment~~example, the preparation comprises (a) a first immunogenic composition that comprises at least a first immunogen capable of inducing an immune response specific for a first

designated antigen; and (b) a second immunogenic composition that comprises a recombinant expression vector that comprises a nucleotide sequence encoding the first immunogen. In a specific ~~embodiment~~example, the specific immune response induced by the first immunogen comprises a CD4 T cell response specific for the first designated antigen. In another specific ~~embodiment~~example, the specific immune response induced by the first immunogen comprises a CD8 T cell response specific for the first designated antigen. In other specific ~~embodiments~~examples, the immune response induced by the first immunogen comprises a CD4 T cell immune response and a CD8 T cell immune response specific for the first designated antigen. In another ~~embodiment~~example of the preparations described above and herein, these preparations are provided for use in inducing a cytotoxic T lymphocyte response against a tumor cell bearing (a) the first designated antigen. In other particular ~~embodiments~~examples, preparations described above and herein are provided for use in inducing a cytotoxic T lymphocyte response against an infectious disease microorganism bearing the first designated antigen. In other particular ~~embodiments~~examples, the preparations described above and herein are provided for use in reducing the likelihood of occurrence or recurrence of a tumor comprising a plurality of tumor cells that bear the tumor-associated antigen. In another ~~embodiment~~example, these preparations are provided for use in preventing or treating an infection caused by an infectious microorganism.

[0016] Additional ~~embodiments~~examples of the preparations are provided wherein the first immunogenic composition further comprises a second immunogen, and wherein the recombinant expression vector further comprises a nucleotide sequence that encodes the second immunogen, wherein the second immunogen induces an immune response specific for a second designated antigen. In one specific ~~embodiment~~example, the first designated antigen and the second designated antigen are the same. In another specific ~~embodiment~~example, the first designated antigen and the second designated antigen are different. In still other specific ~~embodiments~~examples of the preparations described above and herein, the recombinant expression vector further comprises a nucleotide sequence that encodes a second immunogen capable of inducing an immune response specific for a second designated antigen. In certain specific ~~embodiments~~examples, the first designated antigen and the second designated antigen are the same, and in other specific ~~embodiments~~examples, the first designated antigen and the second designated antigen are different. In these ~~embodiments~~examples, the immune response induced by the first immunogen comprises a CD4 T cell response specific for the first designated antigen. Also, with respect

to these ~~embodiments~~examples, of the preparations, the immune response induced by the second immunogen comprises a CD8 T cell response specific for the second designated antigen.

[0017] With respect to ~~embodiments~~examples of the preparations provided above and herein, (a) the first immunogenic composition further comprises an adjuvant (b) the second immunogenic composition further comprises an adjuvant; or (c) the first immunogenic composition and the second immunogenic composition each further comprises an adjuvant. In more specific ~~embodiments~~examples, the adjuvant is a non-toxic lipid A-related adjuvant. In still a more specific ~~embodiment~~example, the non-toxic lipid A-related adjuvant is glucopyranosyl lipid A (GLA), which in specific ~~embodiments~~examples, is formulated in a stable oil-in-water emulsion.

[0018] With respect to ~~embodiments~~examples of the preparations provided above and herein, the first designated antigen is (a) a tumor-associated antigen or (b) from an infectious microorganism selected from a virus, a bacterium, a fungus, and a parasite. In specific ~~embodiments~~examples, the first designated antigen is a tumor-associated antigen selected from a renal cell carcinoma antigen, a prostate cancer antigen, a mesothelioma antigen, a pancreatic cancer antigen, a melanoma antigen, a breast cancer antigen, a lung cancer antigen, and an ovarian cancer antigen. In more specific ~~embodiments~~examples, the prostate cancer antigen is prostatic acid phosphatase, prostate specific antigen, NKX3.1, or prostate specific membrane antigen. In other specific ~~embodiments~~examples, the first designated antigen is from a virus. In a more specific ~~embodiment~~example, the virus is Herpes Simplex Virus-2 (HSV-2). In yet another specific ~~embodiment~~example, the first designated antigen is HSV-2 UL19 polypeptide or HSV-2 gD polypeptide.

[0019] In other ~~embodiments~~examples of the preparations described above and herein, when the immune response induced by the preparations comprises an immune response specific for a first designated antigen and a second designated antigen, each of the first designated antigen and the second designated antigen is a tumor-associated antigen. In a more specific ~~embodiment~~example, each of the first designated antigen and the second designated antigen is selected from a renal cell carcinoma antigen, a prostate cancer antigen, a mesothelioma antigen, a pancreatic cancer antigen, a melanoma antigen, a breast cancer antigen, a lung cancer antigen, and an ovarian cancer antigen. In yet another more particular ~~embodiment~~example, each of the first designated antigen and the second designated antigen is a prostate cancer antigen selected from prostatic acid phosphatase, prostate specific antigen, NKX3.1, and prostate specific membrane antigen. In other specific ~~embodiments~~examples, each of the first designated antigen and the second designated antigen is an antigen from an infectious

microorganism selected from a virus, a bacterium, a fungus, and a parasite. In one particular ~~embodiment~~example, the infectious disease organism is a virus. In a particular ~~embodiment~~example, the virus is Herpes Simplex Virus-2 (HSV-2). In still another specific ~~embodiment~~example, at least one of the first designated antigen and the second designated antigen is HSV-2 UL19 polypeptide and the other of the first designated antigen and the second designated antigen is HSV-2 gD polypeptide.

[0020] In other ~~embodiments~~examples of the preparations described above and herein, the recombinant expression vector is selected from a lentiviral vector genome, poxvirus vector genome, vaccinia virus vector genome, adenovirus vector genome, adenovirus-associated virus vector genome, herpes virus vector genome, and alpha virus vector genome. In one specific ~~embodiment~~example, the recombinant expression vector is incorporated into a vector particle. In still another specific ~~embodiment~~example, the vector particle is capable of delivering the recombinant expression vector to an antigen-presenting cell. In more specific ~~embodiments~~examples, the antigen-presenting cell is a dendritic cell. In other specific ~~embodiments~~examples, the vector particle is a lentiviral vector particle that comprises the lentiviral vector genome; a poxvirus vector particle that comprises the poxvirus vector genome; a vaccinia virus vector particle that comprises the vaccinia virus vector genome; an adenovirus vector particle that comprises the adenovirus vector genome; an adenovirus-associated virus vector particle that comprises the adenovirus-associated virus vector genome; a herpes virus vector particle that comprises the herpes virus vector genome; or an alpha virus vector particle that comprises the alpha virus vector genome. In a more particular ~~embodiment~~example, the vector particle is a lentiviral vector particle that comprises the lentiviral vector genome. In yet more specific ~~embodiments~~examples, the lentiviral vector particle further comprises an envelope comprising a Sindbis virus E2 glycoprotein comprising an amino acid sequence having at least one amino acid change compared to SEQ ID NO:1, wherein residue 160 of SEQ ID NO:1 is either absent or an amino acid other than glutamic acid, and wherein the E2 glycoprotein is not a moiety of a fusion protein that comprises Sindbis virus E3 protein. In a more particular ~~embodiment~~example, the E2 glycoprotein binds to dendritic cell-specific intercellular adhesion molecule -3-grabbing non-integrin (DC-SIGN).

[0021] In another ~~embodiment~~example of the preparations described above and herein, these preparations are provided for use in inducing a cytotoxic T lymphocyte response against a tumor cell bearing (a) the first designated antigen; (b) the second designated antigen; or (c) the first designated antigen and the second designated antigen. In other particular

~~embodiments~~examples, preparations described above and herein are provided for use in inducing a cytotoxic T lymphocyte response against an infectious disease microorganism bearing (a) the first designated antigen; (b) the second designated antigen; or (c) the first designated antigen and the second designated antigen. In other particular ~~embodiments~~examples, the preparations described above and herein are provided for use in reducing the likelihood of occurrence or recurrence of a tumor comprising a plurality of tumor cells that bear the tumor-associated antigen. In another ~~embodiment~~example, these preparations are provided for use in preventing or treating an infection caused by the infectious microorganism.

[0022] As used herein, the term "isolated" means that a material is removed from its original environment (e.g., the natural environment if it is naturally occurring). For example, a naturally occurring nucleic acid or polypeptide present in a living animal is not isolated, but the same nucleic acid or polypeptide, separated from some or all of the co-existing materials in the natural system, is isolated. Such a nucleic acid could be part of a vector. A nucleic acid, which may be part of a vector, may still be isolated in that the nucleic acid is not part of the natural environment for the nucleic acid. An isolated polypeptide or protein, or fragment thereof, could be a component of a composition, and still be isolated in that the composition is not part of the natural environment for the polypeptide. The term "gene" means the segment of DNA involved in producing a polypeptide chain; a gene includes regions preceding and following the coding region "leader and trailer" as well as intervening sequences (introns) between individual coding segments (exons). Amino acids may be referred to herein according to the single letter and three letter codes, which are common textbook knowledge in the art, and therefore with which a person skilled in the art is familiar. The term "fusion polypeptide" used herein may also be used interchangeably with "fusion protein," and unless specifically indicated otherwise, the two terms are not meant to indicate molecules that have distinguishable properties or characteristics.

[0023] As used herein and in the appended claims, the singular forms "a," "and," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "an antigen" includes a plurality of such antigens, and reference to "a cell" or "the cell" includes reference to one or more cells and equivalents thereof (e.g., plurality of cells) known to those skilled in the art, and so forth. Similarly, reference to "a compound" or "a composition" includes a plurality of such compounds or compositions, and refers to one or more compounds or compositions, respectively, unless the context clearly dictates otherwise. When steps of a method are described or claimed, and the steps are described as occurring in