CLAIMS

We claim the following:

1. 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.

2. The use of claim 1, wherein (i) the second immunogenic composition further comprises a second adjuvant; or (ii) the first composition further comprises an adjuvant; or both (i) and (ii).

3. The use of any one of claims 1-2, wherein at least two doses of the first immunogenic composition are administered or wherein at least two doses of the second immunogenic composition are administered.

4. The use of claim 1, wherein (a) two doses; (b) three doses; (c) four doses; or (d) five doses of the first immunogenic composition are to be administered.

5. The use of claim 4, wherein two doses of the first immunogenic composition are to be administered prior to administration of the second immunogenic composition.

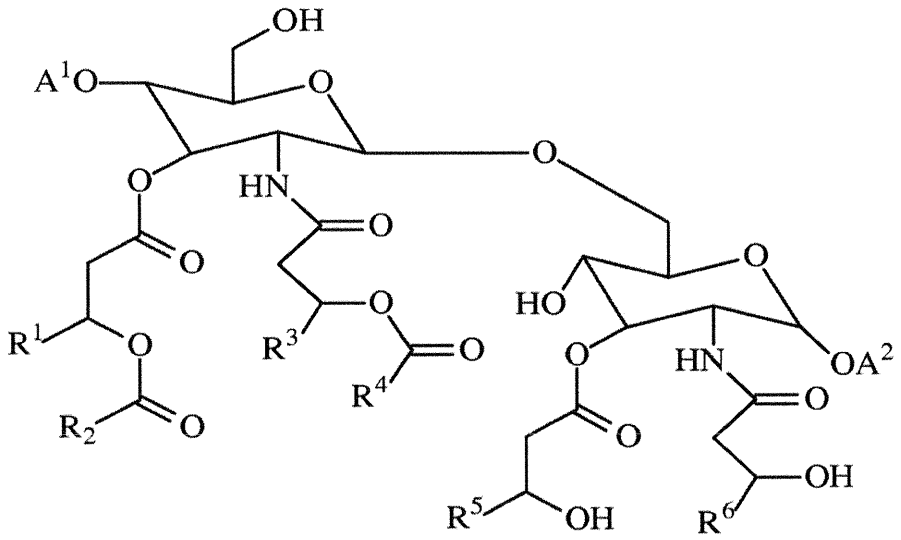
6. The use of any one of claims 1-5, wherein the immune response induced by the medicament comprises a CD4 T cell immune response specific for the first immunogen.

7. The use of any one of claims 1-6, wherein the second immunogenic composition further comprises a second immunogen, or an immunogenic fragment thereof, and wherein the lentiviral vector further comprises a nucleotide sequence that encodes the second immunogen, or

an immunogenic fragment thereof, wherein the medicament induces an immune response specific for a second immunogen.

8. The use of claim 7, wherein the immune response induced by the medicament comprises a CD4 T cell response specific for the second immunogen.

9. The use of any one of claims 1-8, wherein the TLR4 agonist is a compound of the following structure:



wherein A1 and A2 are independently selected from the group of hydrogen, phosphate, and phosphate salts and R1, R2, R3, R4, R5 and R6 are independently selected from the group of hydrocarbyl having 3 to 23 carbons, represented by C3-C23.

10. The use of claim 9, wherein A1 is phosphate or phosphate salt, A2 is hydrogen, R1, R3, R5 and R6 are undecyl and R2 and R4 are tridecyl.

11. The use of claim 10, wherein the compound is formulated in a stable oil-in-water emulsion.

12. The use of any one of claims 1-11, wherein the first immunogen is (a) a tumor-associated antigen or (b) from an infectious microorganism selected from a virus, a bacterium, a fungus, and a parasite.

13. The use of claim 12, wherein the first immunogen is from a tumor-associated antigen.

14. The use of claim 13, wherein the tumor associated antigen is selected from the group consisting of prostatic acid phosphatase, prostate specific antigen, NKX3.1, or prostate specific membrane antigen, PRAME; BAGE; RAGE, NY-ESO-1, SAGE, HAGE, Plu-1, HASH -1, HasH-2, Cripto, Criptin, MART-1/Melan-A, gp100, gp75, mda-7, tyrosinase, tyrosinase-related protein, p53, Ras, c-Myc, A-Raf, B-Raf, and C-Raf, MAGE-A1, MAGEA2, MAGE-A3, MAGE-A4, MAGE-A6, MAGE-A10, MAGE-A12, MART-1, DAM-6, -10, GAGE-1, GAGE -2, GAGE -8, GAGE-3, GAGE -4, GAGE -5, GAGE -6, GAGE -7B, NA88-A, MART-1, MC1R, Gp100, PSM, TRP-1, TRP-2, ART-4, CAMEL, CEA, Cyp-B, hTERT, hTRT, iCE, MUC1, MUC2, P15, RU1, RU2, SART-1, SART-2, SART-3, Wilms' tumor antigen (WT1), AFP, β-catenin/m, Caspase-8/m, CEA, CDK-4/m, ELF2M, GnT-V, G250, HSP70-2M, HST-2, KIAA0205, MUM-1, MUM-2, MUM-3, Myosin/m, TRP-2/INT2, 707-AP, Annexin II, CDC27/m, TPI/mbcr-abl, BCRABL, interferon regulatory factor 4 (IRF4), ETV6/AML, LDLR/FUT, Pml/RAR, Tumor associated calcium signal transducer 1 (TACSTD1) TACSTD2, Epidermal Growth Factor receptor (EGFR and EGFRvIII), platelet derived growth factor receptor (PDGFR), vascular endothelial growth factor receptor (VEGFR), integrin-linked kinase (ILK), STAT3, STAT5, STAT6, HIF-1, HIF-2, Nuclear Factor-Kappa B (NF-κB), Notch1-4, c-Met, mammalian targets of rapamycin (mTOR), WNT, PMSA, PR-3, MDM2, Mesothelin, renal cell carcinoma – 5T4, SM22-alpha, carbonic anhydrases I (CAI) and IX (CAIX) (also known as G250), STEAD, TEL/AML1, GD2, proteinase3, hTERT, sarcoma translocation breakpoints, EphA2, ML-IAP, EpCAM, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, ALK, androgen receptor, cyclin B1, polysialic acid, MYCN, RhoC, GD3, fucosyl GM1, mesothelian, PSCA, sLe, PLAC1, GM3, BORIS, Tn, GLoboH, NY-BR-1, RGs5, SART3, STn, PAX5, OY-TES1, sperm protein 17, LCK, HMWMAA, AKAP-4, SSX2, XAGE 1, B7H3, legumain, TIE2, Page4, MAD-CT-1, FAP, MAD-CT-2, and fos related antigen 1.

15. The use of claim 14, wherein the first immunogen is NY-ESO-1, MAGE A3, SSX2, or EGFRvIII.

16. The use of any one of claims 7-11, wherein each of the first immunogen and the second immunogen is a tumor associated ant.

17. The use of claim 12, wherein the infectious disease organism is a virus.

18. The use of claim 17, wherein the virus is Herpes Simplex Virus-2 (HSV-2).

19. The use of claim 16, wherein at least one of the first immunogen and the second immunogen is an NY-ESO-1 polypeptide and the other of the first immunogen and the second immunogen is a MAGE A3 polypeptide.

20. The use of claim 19, wherein the lentiviral vector particle preferentially delivers the nucleotide sequence to an antigen-presenting cell.

21. The use of claim 20, wherein the antigen-presenting cell is a dendritic cell.

22. The use of claim 1, wherein the vector particle comprises a lentiviral vector genome, and an envelope that delivers the lentiviral vector particle to a dendritic cell expressing DC-SIGN.

23. The use of claim 22, wherein the envelope comprises 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 fused to Sindbis virus E3 protein.

24. The use of claim 23, wherein the E2 glycoprotein binds to dendritic cell-specific intercellular adhesion molecule-3-grabbing non-integrin (DC-SIGN).

25. The use of claim 9 wherein R1, R3, R5 and R6 are C11-C20 alkyl; and R2 and R4 are C12-C20 hydrocarbyl.

26. The use of claim 1, wherein the first composition further comprises (i) at least the first immunogen or an immunogenic fragment thereof and (ii) a TLR4 agonist, and wherein the second composition further comprises a lentiviral vector composition a nucleotide sequence that encodes the first immunogen or an immunogenic fragment thereof, wherein the lentiviral vector is incorporated into a vector particle, wherein the vector particle comprises a lentiviral vector genome and an alpha virus envelope.

27. 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.

28. The use of claim 27, wherein two doses of the first immunogenic composition and the second immunogenic composition are to be administered.

CLAIMS

We claim the following:

1. 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 immunogeninto the subject to thereby induce an immune response specific for the first immunogen.

2. The use of claim 1, wherein (i) the first immunogenic composition further comprises a second adjuvant; or (ii) the second composition further comprises an adjuvant; orboth (i) and (ii).

3. The use of any one of claims 1-2, wherein at least two doses of the first immunogenic composition are administered or wherein at least two doses of the second immunogenic composition are administered.

4. The use of claim 1, wherein (a) two doses; (b) three doses; (c) four doses; or (d) five doses of the first immunogenic composition are to be administered.

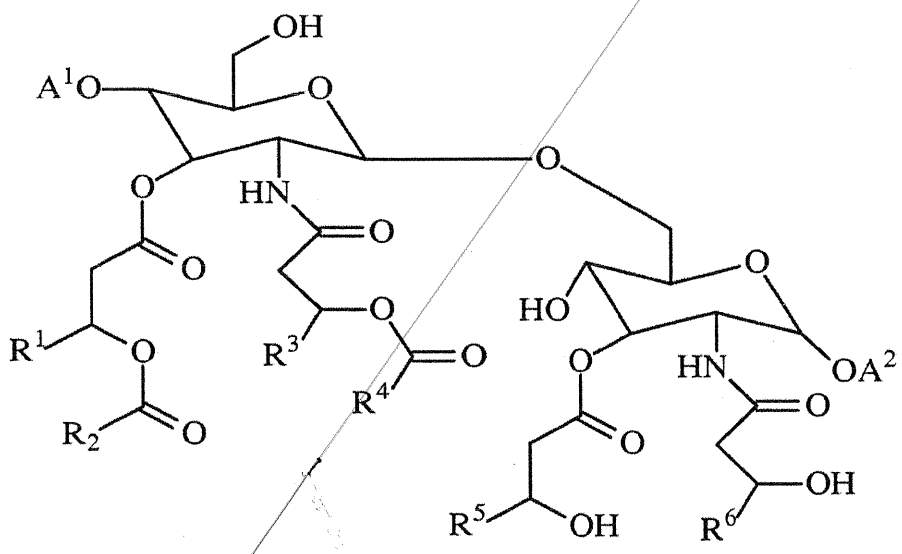
5. The use of claim 4, wherein two doses of the first immunogenic composition are to be administered prior to administration of the second immunogenic composition.

6. The use of any one of claims 1-5, wherein the immune response induced by the medicament comprises a CD4 T cell immune response specific for the first immunogen.

7. The use of any one of claims 1-6, wherein the second immunogenic composition further comprises a second immunogen, or an immunogenic fragment thereof, and wherein the lentiviral vector further comprises a nucleotide sequence that encodes the second immunogen, or an immunogenic fragment thereof, wherein the medicament induces an immune response specific for a second immunogen.

8. The use of any one of claims 7, wherein the immune response induced by the medicament comprises a CD4 T cell response specific for the second immunogen.

9. The use of any one of claims 1-8, wherein the TLR4 agonist is a compound of the following structure:



wherein A1 and A2 are independently selected from the group of hydrogen, phosphate, and phosphate salts and R1, R2, R3, R4, R5 and R6 are independently selected from the group of hydrocarbyl having 3 to 23 carbons, represented by C3-C23.

10. The use of claim 9, wherein A1 is phosphate or phosphate salt, A2 is hydrogen, R1, R3, R5 and R6 are undecyl and R2 and R4 are tridecyl.

11. The use of claim 10, wherein the compound is formulated in a stable oil-in-water emulsion.

12. The use of any one of claims 1-11, wherein the first immunogen is (a) a tumor-associated antigen or (b) from an infectious microorganism selected from a virus, a bacterium, a fungus, and a parasite.

13. The use of claim 12, wherein the first immunogen is from a virus.

14. The use of claim 13, wherein the virus is Herpes Simplex Virus-2 (HSV-2).

15. The use of claim 14, wherein the first immunogen is HSV-2 UL19 polypeptide or HSV-2 gD polypeptide.

16. The use of any one of claims 7-11, wherein each of the first immunogen and the second immunogen is an antigen from an infectious microorganism selected from a virus, a bacterium, a fungus, and a parasite.

17. The use of claim 16, wherein the infectious disease organism is a virus.

18. The use of claim 17, wherein the virus is Herpes Simplex Virus-2 (HSV-2).

19. The use of claim 18, wherein at least one of the first immunogen and the second immunogen is HSV-2 UL19 polypeptide and the other of the first immunogen and the second immunogen is HSV-2 gD polypeptide.

20. The use of claim 19, wherein the lentiviral vector particle preferentially delivers the nucleotide sequence to an antigen-presenting cell.

21. The use of claim 20, wherein the antigen-presenting cell is a dendritic cell.

22. The use of claim 1, wherein the vector particle comprises a lentiviral vector genome, and an envelope that delivers the lentiviral vector particle to a dendritic cell expressing DC-SIGN.

23. The use of claim 22, wherein the envelope comprises 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 fused to Sindbis virus E3 protein.

24. The use of claim 23, wherein the E2 glycoprotein binds to dendritic cell-specific intercellular adhesion molecule-3-grabbing non-integrin (DC-SIGN).

25. The method of claim 9 wherein R1, R3, R5 and R6 are C11-C20 alkyl; and R2 and R4 are C12-C20 hydrocarbyl.

26. The method of claim 1, wherein the first immunogenic composition and the second immunogenic composition are to be administered concurrently and two doses are to be administered.

27. The method of claim 1, wherein the first composition further comprises (i) at least the first immunogen or an immunogenic fragment thereof and (ii) a TLR4 agonist, and wherein the second composition further comprises a lentiviral vector composition a nucleotide sequence that encodes the first immunogen or an immunogenic fragment thereof, wherein the lentiviral vector is incorporated into a vector particle, wherein the vector particle comprises a lentiviral vector genome and an alpha virus envelope.

28. 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; and (b) wherein the first and second immunogenic compositions of (a) are subsequently administered; thereby priming and boosting a CD8 T cell immune response specific for the first immunogen.