

WHAT IS CLAIMED IS:

1. A recombinant HCMV vector comprising a nucleic acid sequence encoding heterologous antigen, wherein the recombinant HCMV vector does not express UL18, UL128, and UL130.
- ~~2. The recombinant HCMV vector of claim 1, wherein the recombinant HCMV vector does not express UL128.~~
- ~~3. The recombinant HCMV vector of claims 1 or 2, wherein the recombinant HCMV vector does not express UL130.~~
- ~~4. The recombinant HCMV vector of any one of claims 1-3, wherein the recombinant HCMV vector does not express UL128 and UL130.~~
- ~~5~~2. The recombinant HCMV vector of claim ~~4~~1, wherein the recombinant HCMV vector does not express UL146 and UL147.
- ~~6~~3. The recombinant HCMV vector of ~~any one of claims 1-5~~ claim 2, wherein the recombinant HCMV vector does not express a UL18 protein, UL128 protein, UL130 protein, UL146 protein, and UL147 protein, or orthologs thereof, due to the presence of one or more mutations in the nucleic acid sequence encoding UL18, UL128, UL130, UL146, ~~or~~ and UL147.
- ~~7~~4. The recombinant HCMV vector of claim ~~6~~3, wherein the mutations in the nucleic acid sequence encoding UL18, UL128, UL130, UL146, ~~or~~ and UL147 are selected from the group consisting of point mutations, frameshift mutations, truncation mutations, and deletion of all of the nucleic acid sequence encoding the viral protein.

~~85~~. The recombinant HCMV vector of any one of claims 1-~~74~~, wherein the recombinant HCMV vector further comprises a nucleic acid sequence encoding UL40, or an ortholog thereof.

~~96~~. The recombinant HCMV vector of any one of claims 1-~~85~~, wherein the recombinant HCMV vector further comprises a nucleic acid sequence encoding US28, or an ortholog thereof.

~~107~~. The recombinant HCMV vector of any one of claims 1-~~96~~, wherein the recombinant HCMV vector does not express UL82 (pp71), or an ortholog thereof.

~~118~~. The recombinant HCMV vector of any one of claims 1-~~107~~, wherein the recombinant HCMV vector does not express US11, or an ortholog thereof.

~~129~~. The recombinant HCMV vector of any one of claims 1-~~107~~, wherein the recombinant HCMV vector further comprises a nucleic acid sequence encoding a microRNA (miRNA) recognition element (MRE), wherein the MRE contains a target site for a miRNA expressed in endothelial cells.

~~1310~~. The recombinant HCMV vector of claim ~~129~~, wherein the miRNA expressed in endothelial cells is miR126, miR-126-3p, miR-130a, miR-210, miR-221/222, miR-378, miR-296, or miR-328.

~~1411~~. The recombinant HCMV vector of any one of claims 1-~~118~~, wherein the recombinant HCMV vector further comprises a nucleic acid sequence encoding a MRE, wherein the MRE contains a target site for a miRNA expressed in myeloid cells.

~~1512~~. The recombinant HCMV vector of claim ~~1411~~, wherein the miRNA expressed in myeloid cells is miR-142-3p, miR-223, miR-27a, miR-652, miR-155, miR-146a, miR-132, miR-21, or miR-125.

~~14~~13. The recombinant HCMV vector of any one of claims 1-~~15~~12, wherein the heterologous antigen is a pathogen-specific antigen, a tumor antigen, a tissue-specific antigen, or a host self-antigen.

~~17~~14. The recombinant HCMV vector of claim ~~16~~13, wherein the pathogen-specific antigen is human immunodeficiency virus (HIV), herpes simplex virus type 1, herpes simplex virus type 2, hepatitis B virus, hepatitis C virus, papillomavirus, *Plasmodium* parasites, or *Mycobacterium tuberculosis*.

~~18~~15. The recombinant HCMV vector of any one of claims ~~5-10~~2-7 and ~~12-13~~9-10, wherein the pathogen-specific antigen is an MHC-E supertope.

~~19~~16. The recombinant HCMV vector of claim ~~18~~15, wherein pathogen-specific antigen comprises a HIV epitope.

~~20~~17. The recombinant HCMV vector of claim ~~19~~16, wherein the HIV epitope is at least 80%, at least 85%, at least 90%, at least 95%, or 100% identical to LDAWEKIRLRPGGKK (SEQ ID NO: 13); DAW EKIRLR (SEQ ID NO: 14); KKAQQAAADTGNSSQ (SEQ ID NO: 15); KAQQAAADT (SEQ ID NO: 16); QMVHQAI SPRTLNAW (SEQ ID NO: 17); HQAI SPRTL (SEQ ID NO: 18); NTMLNTVGGHQAAMQ (SEQ ID NO: 19); VGGHQAAMQ (SEQ ID NO: 20); STLQEQIGWMTNNPP (SEQ ID NO: 21); STLQEQIGW (SEQ ID NO: 22); IVRMYS PVSILDIRQ (SEQ ID NO: 23); RMYSPVSIL (SEQ ID NO: 24); QKQEPIDKELYPLAS (SEQ ID NO: 25); KQEPIDKEL (SEQ ID NO: 26); SFSFPQITLWQRPLV (SEQ ID NO: 27); VRQYDQILIEICGKK (SEQ ID NO: 28); EPFRKQNPDI VIYQL (SEQ ID NO: 29); YVDGAANRETKLGKA (SEQ ID NO: 30); EEHEKYSNWRAMAS (SEQ ID NO: 31); or ILDLWVYHTQGYFPD (SEQ ID NO: 32).

~~21~~18. The recombinant HCMV vector of claim ~~16~~13, wherein the tumor antigen is related to acute myelogenous leukemia, chronic myelogenous leukemia, myelodysplastic syndrome, acute

lymphoblastic leukemia, chronic lymphoblastic leukemia, non-Hodgkin's lymphoma, multiple myeloma, malignant melanoma, breast cancer, lung cancer, ovarian cancer, prostate cancer, pancreatic cancer, colon cancer, renal cell carcinoma (RCC), or germ cell tumors.

2219. The recombinant HCMV vector of claim ~~16~~13, wherein the host self-antigen is an antigen derived from the variable region of a T cell receptor (TCR) or an antigen derived from the variable region of a B cell receptor.

2320. A pharmaceutical composition comprising the recombinant HCMV vector of any one of claims 1-~~22~~19 and a pharmaceutically acceptable carrier.

2421. An immunogenic composition comprising the recombinant HCMV vector of any one of claims 1-~~22~~19 and a pharmaceutically acceptable carrier.

~~25. — A method of generating an immune response in a subject to the at least one heterologous antigen, comprising administering to the subject the recombinant HCMV vector of any one of claims 1-22 in an amount effective to elicit a CD8+ T cell response to the at least one heterologous antigen.~~

2622. Use of the recombinant HCMV vector of any one of claims 1-~~22~~19 in the manufacture of a medicament for use in generating an immune response in a subject.

2723. The recombinant HCMV vector of any of claims 1-~~22~~19 for use in generating an immune response in a subject.

~~28. — A method of treating or preventing cancer in a subject, comprising administering the recombinant HCMV vector of any one of claims 1-22 in an amount effective to elicit a CD8+ T cell response to the at least one heterologous antigen.~~

~~29~~24. Use of the recombinant HCMV vector of ~~any one of claims 1-22~~claim 13 or claim 18 in the manufacture of a medicament for use in treating or preventing cancer in a subject.

~~30~~25. The recombinant HCMV vector of ~~any one of claims 1-22~~claim 13 or claim 18 for use in treating or preventing cancer in a subject.

~~31~~—. A method of treating or preventing a pathogenic infection in a subject, comprising administering to the subject the recombinant HCMV vector of any one of claims 1-22 in an amount effective to elicit a CD8+ T cell response to the at least one heterologous antigen.

~~32~~26. Use of the recombinant HCMV vector of any one of claims ~~1-22~~13-17 in the manufacture of a medicament for use in treating or preventing a pathogenic infection in a subject.

~~33~~27. The recombinant HCMV vector of any one of claims ~~1-22~~13-17 for use in treating or preventing a pathogenic infection in a subject.

~~34~~—. A method of treating an autoimmune disease or disorder in a subject, comprising administering to the subject the recombinant HCMV vector of any one of claims 1-22 in an amount effective to elicit a CD8+ T cell response to the at least one heterologous antigen.

~~35~~28. Use of the recombinant HCMV vector of ~~claims 1-22~~claim 13 or claim 19 in the manufacture of a medicament for use in treating an autoimmune disease or disorder in a subject.

~~36~~29. The recombinant HCMV vector of ~~any one of claims 1-22~~claim 13 or claim 19 for use in treating an autoimmune disease or disorder in a subject.

~~37~~30. The ~~method~~, CMV vector for ~~use~~use, or use in manufacture, of any one of claims ~~25-36~~22-29, wherein at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% of the CD8+ T cells elicited by the recombinant HCMV vector are restricted by MHC-E or an ortholog thereof.

~~38. The method, CMV vector for use, or use in manufacture of claim 37, wherein at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% of the CD8+ T cells elicited by the recombinant HCMV vector are restricted by MHC E or an ortholog thereof.~~

~~3931. The method, CMV vector for use, or use in manufacture, of any one of claims 25-3622-29, wherein at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60% or at least 75% of the CD8+ T cells elicited by the recombinant HCMV vector are restricted by MHC-II or an ortholog thereof.~~

~~40. The method, CMV vector for use, or use in manufacture of claim 39, wherein at least 20%, at least 30%, at least 40%, at least 50%, at least 60% or at least 75% of the CD8+ T cells elicited by the recombinant HCMV vector are restricted by MHC II or an ortholog thereof.~~

~~4132. The method, CMV vector for use, or use in manufacture, of any one of claims 25-3622-29, wherein fewer than 10%, fewer than 20%, fewer than 30%, fewer than 40%, or fewer than 50% of the CD8+ T cells elicited by the recombinant HCMV vector are restricted by MHC-class Ia or an ortholog thereof.~~

~~4233. The method, CMV vector for use, or use in manufacture of any one of claims 25-3622-29, wherein at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% of the CD8+ T cells elicited by the recombinant HCMV vector are restricted by MHC-class Ia or an ortholog thereof.~~

~~43. The method, CMV vector for use, or use in manufacture of claim 42, wherein at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or the CD8+ T cells elicited by the recombinant HCMV vector are restricted by MHC class Ia or an ortholog thereof.~~

44. — ~~The method, CMV vector for us, or use in manufacture of any one of claims 25-36, further comprising identifying a CD8+ TCR from the CD8+ T cells elicited by the recombinant HCMV vector, wherein the CD8+ TCR recognizes a MHC II/heterologous antigen-derived peptide complex.~~

45. — ~~The method, CMV vector for us, or use in manufacture of any one of claims 25-36, further comprising identifying a CD8+ TCR from the CD8+ T cells elicited by the HCMV vector, wherein the CD8+ TCR recognizes a MHC E/heterologous antigen-derived peptide complex.~~

46. — ~~The method, CMV vector for us, or use in manufacture of any one of claims 25-36, further comprising identifying a CD8+ TCR from the CD8+ T cells elicited by the HCMV vector, wherein the CD8+ TCR recognizes a MHC class Ia/heterologous antigen-derived peptide complex.~~

47. — ~~The method, CMV vector for us, or use in manufacture of claim 44-46, wherein the CD8+ TCR is identified by DNA or RNA sequencing.~~

48. — ~~The method, CMV vector for us, or use in manufacture of claim 44, wherein the CD8+ TCR recognizes MHC II supertopes.~~

49. — ~~The method, CMV vector for us, or use in manufacture of claim 45, wherein the CD8+ TCR recognizes MHC E supertopes.~~

50. — ~~The method, CMV vector for us, or use in manufacture of claim 49, wherein the MHC E supertope is an human immunodeficiency virus epitope.~~

51. — ~~The method, CMV vector for us, or use in manufacture of claim 50, wherein the MHC E supertope is at least 80%, at least 85%, at least 90%, at least 95%, or is 100% identical to the amino acid sequence of LDAWEKIRLRPGGKK (SEQ ID NO: 13); DAW EKIRLR (SEQ ID NO: 14); KKAQQAAADTGNSSQ (SEQ ID NO: 15); KAQQAAADT (SEQ ID NO: 16);~~

QMVHQAISPRTLNAW (SEQ ID NO: 17); HQAISPRTL (SEQ ID NO: 18);
NTMLNTVGGHQAAMQ (SEQ ID NO: 19); VGGHQAAMQ (SEQ ID NO: 20);
STLQEQIGWMTNNPP (SEQ ID NO: 21); STLQEQIGW (SEQ ID NO: 22); IVRMYSPPVSILDIRQ
(SEQ ID NO: 23); RMYSPVSIL (SEQ ID NO: 24); QKQEPIDKELYPLAS (SEQ ID NO: 25);
KQEPIDKEL (SEQ ID NO: 26); SFSFPQITLWQRPLV (SEQ ID NO: 27); VRQYDQILIEICGKK
(SEQ ID NO: 28); EPFRKQNPDIVIYQL (SEQ ID NO: 29); YVDGAANRETKLGKA (SEQ ID
NO: 30); EEHEKYSNWRAMAS (SEQ ID NO: 31); or ILDLWVYHTQGYFPD (SEQ ID NO: 32).

52. — A method of generating CD8+ T cells that recognize MHC E-peptide complexes, the method comprising:

- a. — administering to a first subject the recombinant HCMV vector of any one of claims 5-10, 12-13, or 16-17 in an amount effective to generate a set of CD8+ T cells that recognize MHC E-peptide complexes;
- b. — identifying a first CD8+ TCR from the set of CD8+ T cells, wherein the first CD8+ TCR recognizes a MHC E/heterologous antigen-derived peptide complex;
- c. — isolating one or more CD8+ T cells from a second subject; and
- d. — transfecting the one or more CD8+ T cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8+ TCR and a promoter operably linked to the nucleic acid sequence encoding the second CD8+ TCR, wherein the second CD8+ TCR comprises CDR3 α and CDR3 β of the first CD8+ TCR, thereby generating one or more CD8+ T cells that recognize MHC E-peptide complexes.

5334. A method of generating CD8+ T cells that recognize MHC-E-peptide complexes, the method comprising:

- a. identifying a first CD8+ TCR from a set of CD8+ T cells, wherein the set of CD8+ T cells are generated from the recombinant HCMV vector of any one of claims 5-10, 12-13, or 16-17;

7, 9, 10, 13, or 14, wherein the first CD8+ TCR recognizes a MHC-E/heterologous antigen-derived peptide complex;

- b. isolating one or more CD8+ T cells from a second subject; and
- c. transfecting the one or more CD8+ T cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8+ TCR and a promoter operably linked to the nucleic acid sequence encoding the second CD8+ TCR, wherein the second CD8+ TCR comprises CDR3 α and CDR3 β of the first CD8+ TCR, thereby generating one or more TCR-transgenic CD8+ T cells that recognize MHC-E-peptide complexes.

~~54. The method of claims 52 or 53, wherein the first CD8+ T cell recognizes MHC E supertopes.~~

~~55. The method of claim 54, wherein the MHC E supertopes comprise human immunodeficiency virus epitopes.~~

~~56. The method of any one of claims 54-55, wherein the MHC E supertope is at least 80%, at least 85%, at least 90%, at least 95%, or is 100% identical to the amino acid sequence of LDAWEKIRLRPGGKK (SEQ ID NO: 13); DAW EKIRLR (SEQ ID NO: 14); KKAQQAAADTGNSSQ (SEQ ID NO: 15); KAQQAAADT (SEQ ID NO: 16); QMVHQAISPRTLNAW (SEQ ID NO: 17); HQAISPRTL (SEQ ID NO: 18); NTMLNTVGGHQAAMQ (SEQ ID NO: 19); VGGHQAAMQ (SEQ ID NO: 20); STLQEQIGWMTNNPP (SEQ ID NO: 21); STLQEQIGW (SEQ ID NO: 22); IVRMYSPVSILDIRQ (SEQ ID NO: 23); RMYSPVSIL (SEQ ID NO: 24); QKQEPIDKELYPLAS (SEQ ID NO: 25); KQEPIDKEL (SEQ ID NO: 26); SFSFPQITLWQRPLV (SEQ ID NO: 27); VRQYDQILIEICGKK (SEQ ID NO: 28); EPFRKQNPDIVIYQL (SEQ ID NO: 29); YVDGAANRETKLGKA (SEQ ID NO: 30); EEHEKYSNWRAMAS (SEQ ID NO: 31); or ILDLWVYHTQGYFPD (SEQ ID NO: 32).~~

~~57. The method of any one of claims 52-56, wherein the second CD8+ T cell recognizes MHC E supertopes.~~

58. — ~~The method of claim 57, wherein the MHC E supertopes comprise human immunodeficiency virus epitopes.~~

59. — ~~The method of any one of claims 57-58, wherein the MHC E supertope is at least 80%, at least 85%, at least 90%, at least 95%, or is 100% identical to the amino acid sequence of LDAWEKIRLRPGGKK (SEQ ID NO: 13); DAW EKIRLR (SEQ ID NO: 14); KKAQQAAADTGNSSQ (SEQ ID NO: 15); KAQQAAADT (SEQ ID NO: 16); QMVHQ AISPRTLNAW (SEQ ID NO: 17); HQAISPRTL (SEQ ID NO: 18); NTMLNTVGGHQ AAMQ (SEQ ID NO: 19); VGGHQ AAMQ (SEQ ID NO: 20); STLQEQIGWMTNNPP (SEQ ID NO: 21); STLQEQIGW (SEQ ID NO: 22); IVRMYSPVSILDIRQ (SEQ ID NO: 23); RMYSPVSIL (SEQ ID NO: 24); QKQEPIDKELYPLAS (SEQ ID NO: 25); KQEPIDKEL (SEQ ID NO: 26); SFSFPQITLWQRPLV (SEQ ID NO: 27); VRQYDQILIEICGKK (SEQ ID NO: 28); EPFRKQNPDIYIYQL (SEQ ID NO: 29); YVDGAANRETKLGKA (SEQ ID NO: 30); EEHEKYSNWRAMAS (SEQ ID NO: 31); or ILDLWVYHTQGYFPD (SEQ ID NO: 32).~~

60. — ~~The method of any one of claims 52-59, wherein the first CD8⁺ TCR is identified by DNA or RNA sequencing.~~

61. — ~~The method of any one of claims 52-60, wherein the nucleic acid sequence encoding the second CD8⁺ TCR is identical to the nucleic acid sequence encoding the first CD8⁺ TCR.~~

62. — ~~The method of any one of claims 52-61, wherein the first subject is a human.~~

63. — ~~The method of any one of claims 52-62, wherein the second subject is a human.~~

64. — ~~A method of generating CD8⁺ T cells that recognize MHC E peptide complexes, the method comprising:~~

a. ~~administering to a non human primate a recombinant rhesus CMV (RhCMV) or cynomolgus CMV (CyCMV) vector deficient for orthologs of UL128, UL130, UL146, and UL147 and expressing HIV antigens in an amount effective to generate a set of CD8⁺ T cells that recognize MHC-E in complex with HIV supertope peptides of claims 18-20;~~

b. ~~identifying a first CD8⁺ TCR from the set of CD8⁺ T cells, wherein the first recognizes a MHC-E/supertope peptide complex;~~

c. ~~isolating one or more CD8⁺ T cells from a second subject; and~~

d. ~~transfecting the one or more CD8⁺ T cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8⁺ TCR and a promoter operably linked to the nucleic acid sequence encoding the second CD8⁺ TCR, wherein the second CD8⁺ TCR comprises CDR3 α and CDR3 β of the first CD8⁺ TCR, thereby generating one or more CD8⁺ T cells that recognize MHC-E peptide complexes.~~

65. ~~A method of generating CD8⁺ T cells that recognize MHC-E peptide complexes, the method comprising:~~

a. ~~identifying a first CD8⁺ TCR that recognizes a MHC-E/supertope peptide complex from a set of CD8⁺ T cells that recognize MHC-E in complex with the HIV supertope peptides of claims 18-20, wherein the set of CD8⁺ T cells are generated from a recombinant rhesus (RhCMV) or cynomolgus CMV (CyCCMV) vector deficient for orthologs of UL128, UL130, UL146, and UL147 and expressing HIV antigens in an amount effective to generate the set of CD8⁺ T cells;~~

b. ~~isolating one or more CD8⁺ T cells from a second subject; and~~

c. ~~transfecting the one or more CD8⁺ T cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8⁺ TCR and a promoter operably~~

linked to the nucleic acid sequence encoding the second CD8⁺ TCR, wherein the second CD8⁺ TCR comprises CDR3 α and CDR3 β of the first CD8⁺ TCR, thereby generating one or more CD8⁺ T cells that recognize MHC-E peptide complexes.

66. — The method of claim 64 or 65, wherein the first subject is a nonhuman primate and the second subject is a human, and wherein the second CD8⁺ TCR is a chimeric nonhuman primate-human CD8⁺ TCR comprising the non-human primate CDR3 α and CDR3 β of the first CD8⁺ TCR.

67. — The method of any one of claims 64-66, wherein the second CD8⁺ TCR comprises the non-human primate CDR1 α , CDR2 α , CDR3 α , CDR1 β , CDR2 β , and CDR3 β of the first CD8⁺ TCR.

68. — The method of any one of claims 64-67, wherein the second CD8⁺ TCR comprises CDR1 α , CDR2 α , CDR3 α , CDR1 β , CDR2 β , and CDR3 β of the first CD8⁺ TCR.

69. — The method of any one of claims 64-68, wherein the second CD8⁺ TCR is a chimeric CD8⁺ TCR.

70. — The method of any one of claims 64-69, wherein administering the recombinant HCMV vector to the first subject comprises intravenous, intramuscular, intraperitoneal, or oral administration of the recombinant HCMV vector to the first subject.

71. — The method of any one of claims 52-70, further comprising administering the transfected CD8⁺ T cells to the second subject to treat or prevent cancer.

72. — The method of claim 71, wherein the cancer is acute myelogenous leukemia, chronic myelogenous leukemia, myelodysplastic syndrome, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, non-Hodgkin's lymphoma, multiple myeloma, malignant melanoma, breast cancer, lung cancer, ovarian cancer, prostate cancer, pancreatic cancer, colon cancer, renal cell carcinoma (RCC), or germ cell tumors.

~~73. — The method of any one of claims 52-70, further comprising administering the transfected CD8+ T cells to the second subject to treat or prevent a pathogenic infection.~~

~~74. — The method of claim 73, wherein the pathogenic infection is caused by human immunodeficiency virus, herpes simplex virus type 1, herpes simplex virus type 2, hepatitis B virus, hepatitis C virus, papillomavirus, Plasmodium parasites, or *Mycobacterium tuberculosis*.~~

~~75. — The method of any one of claims 52-70, further comprising administering the transfected CD8+ T cells to the subject to induce an autoimmune response to the host self-antigen.~~

~~76. — A method of generating CD8+ T cells that recognize MHC-II-peptide complexes, the method comprising:~~

~~a. — administering to a first subject the recombinant HCMV vector of any one of claims 1-11, 14, or 15 in an amount effective to generate a set of CD8+ T cells that recognize MHC-II/peptide complexes;~~

~~b. — identifying a first CD8+ TCR from the set of CD8+ T cells, wherein the first CD8+ TCR recognizes a MHC-II/heterologous antigen-derived peptide complex;~~

~~c. — isolating one or more CD8+ T cells from a second subject; and~~

~~d. — transfecting the one or more CD8+ T cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8+ TCR and a promoter operably linked to the nucleic acid sequence encoding the second CD8+ TCR, wherein the second CD8+ TCR comprises CDR3 α and CDR3 β of the first CD8+ TCR, thereby generating one or more CD8+ T cells that recognize a MHC-II-peptide complexes.~~

7735. A method of generating CD8+ T cells that recognize MHC-II-peptide complexes, the method comprising:

a. identifying a first CD8+ TCR that recognizes a MHC-II/heterologous antigen-derived peptide complex from a set of CD8+ T cells that recognize MHC-II/peptide complexes, wherein the set of CD8+ T cells are generated from the recombinant HCMV vector of any one of claims ~~1-11, 14,~~ ~~or 15~~1-8, 11, or 12;

b. isolating one or more CD8+ T cells from a second subject; and

c. transfecting the one or more CD8+ T cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8+ TCR and a promoter operably linked to the nucleic acid sequence encoding the second CD8+ TCR, wherein the second CD8+ TCR comprises CDR3 α and CDR3 β of the first CD8+ TCR, thereby generating one or more CD8+ T cells that recognize a MHC-II peptide complexes.

~~78. The method of any one of claims 76-77, wherein the first CD8+ T cell recognizes MHC-II supertopes.~~

~~79. The method of any one of claims 76-78, wherein the second CD8+ T cell recognizes MHC-II supertopes.~~

~~80. The method of any one of claims 76-79, wherein the first CD8+ TCR is identified by DNA or RNA sequencing.~~

~~81. The method of any one of claims 76-80, wherein the nucleic acid sequence encoding the second CD8+ TCR is identical to the nucleic acid sequence encoding the first CD8+ TCR.~~

~~82. The method of any one of claims 76-81, wherein the first subject is a human.~~

~~83. The method of any one of claims 76-82, wherein the second subject is a human.~~

84. — ~~The method of claim 76-83, wherein administering the HCMV vector to the first subject comprises intravenous, intramuscular, intraperitoneal, or oral administration of the HCMV vector to the first subject.~~

85. — ~~The method of any one of claims 76-84, further comprising administering the transfected CD8+ T cells to the second subject to treat or prevent cancer.~~

86. — ~~The method of claim 85, wherein the cancer is selected from the group consisting of acute myelogenous leukemia, chronic myelogenous leukemia, myelodysplastic syndrome, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, non-Hodgkin's lymphoma, multiple myeloma, malignant melanoma, breast cancer, lung cancer, ovarian cancer, prostate cancer, pancreatic cancer, colon cancer, renal cell carcinoma (RCC), and germ cell tumors.~~

87. — ~~The method of any one of claims 76-84, further comprising administering the transfected CD8+ T cells to the second subject to treat or prevent a pathogenic infection.~~

88. — ~~The method of claim 87 wherein the pathogenic infection is caused by a pathogen selected from the group consisting of human immunodeficiency virus, herpes simplex virus type 1, herpes simplex virus type 2, hepatitis B virus, hepatitis C virus, papillomavirus, Plasmodium parasites, and *Mycobacterium tuberculosis*.~~

89. — ~~The method of any one of claims 76-84, further comprising administering the transfected CD8+ T cells to the subject to induce an autoimmune response to the host self-antigen.~~

90. — ~~A method of generating CD8+ T cells that recognize MHC-I-peptide complexes, the method comprising:~~

a. — ~~administering to a first subject the recombinant HCMV vector of any one of claims 1-11 in an amount effective to generate a set of CD8+ T cells that recognize MHC-I-peptide complexes;~~

b. ~~identifying a first CD8+ TCR from the set of CD8+ T cells, wherein the first CD8+ TCR recognizes a MHC-I/heterologous antigen-derived peptide complex;~~

e. ~~isolating one or more CD8+ T cells from a second subject; and~~

d. ~~transfecting the one or more CD8+ T cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8+ TCR and a promoter operably linked to the nucleic acid sequence encoding the second CD8+ TCR, wherein the second CD8+ TCR comprises CDR3 α and CDR3 β of the first CD8+ TCR, thereby generating one or more CD8+ T cells that recognize MHC-I peptide complexes.~~

9136. A method of generating CD8+ T cells that recognize MHC-I-peptide complexes, the method comprising:

a. identifying a first CD8+ TCR that recognizes a MHC-I/heterologous antigen-derived peptide complex from a set of CD8+ T cells that recognize a MHC-I/heterologous antigen-derived peptide complex, wherein the set of CD8+ T cells are generated from the recombinant HCMV vector of any one of claims ~~1-11~~1-8;

b. isolating one or more CD8+ T cells from a second subject; and

c. transfecting the one or more CD8+ T cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8+ TCR and a promoter operably linked to the nucleic acid sequence encoding the second CD8+ TCR, wherein the second CD8+ TCR comprises CDR3 α and CDR3 β of the first CD8+ TCR, thereby generating one or more CD8+ T cells that recognize MHC-I peptide complexes.

92. ~~The method of any one of claims 90-91, wherein the first CD8+ TCR is identified by DNA or RNA sequencing.~~

93. ~~The method of any one of claims 90-92, wherein the nucleic acid sequence encoding the second CD8+ TCR is identical to the nucleic acid sequence encoding the first CD8+ TCR.~~

94. — ~~The method of any one of claims 90-93, wherein the first subject is a human.~~

95. — ~~The method of any one of claims 90-94, wherein the second subject is a human.~~

96. — ~~The method of any one of claims 90-95, wherein administering the HCMV vector to the first subject comprises intravenous, intramuscular, intraperitoneal, or oral administration of the HCMV vector to the first subject.~~

97. — ~~The method of any one of claims 90-96, further comprising administering the transfected CD8⁺ T cells to the second subject to treat or prevent cancer.~~

98. — ~~The method of claim 97, wherein the cancer is selected from the group consisting of acute myelogenous leukemia, chronic myelogenous leukemia, myelodysplastic syndrome, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, non-Hodgkin's lymphoma, multiple myeloma, malignant melanoma, breast cancer, lung cancer, ovarian cancer, prostate cancer, pancreatic cancer, colon cancer, renal cell carcinoma (RCC), and germ cell tumors.~~

99. — ~~The method of any one of claims 90-96, further comprising administering the transfected CD8⁺ T cells to the second subject to treat or prevent a pathogenic infection.~~

100. — ~~The method of claim 99, wherein the pathogenic infection is caused by a pathogen selected from the group consisting of human immunodeficiency virus, herpes simplex virus type 1, herpes simplex virus type 2, hepatitis B virus, hepatitis C virus, papillomavirus, Plasmodium parasites, and Mycobacterium tuberculosis.~~

101. — ~~The method of any one of claims 90-96, further comprising administering the transfected CD8⁺ T cells to the subject to induce an autoimmune response to the host self antigen.~~

102. — ~~A CD8⁺ T cell generated by the method of claims 25-101.~~

~~103. — The CD8+ T cell of claim 102, wherein the pathogen specific antigen is human immunodeficiency virus, simian immunodeficiency virus, herpes simplex virus type 1, herpes simplex virus type 2, hepatitis B virus, hepatitis C virus, papillomavirus, Plasmodium parasites, or *Mycobacterium tuberculosis*.~~

~~104. — The CD8+ T cell of claim 102, wherein the tumor antigen is related acute myelogenous leukemia, chronic myelogenous leukemia, myelodysplastic syndrome, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, non-Hodgkin's lymphoma, multiple myeloma, malignant melanoma, breast cancer, lung cancer, ovarian cancer, prostate cancer, pancreatic cancer, colon cancer, renal cell carcinoma (RCC), or germ cell tumors.~~

~~105. — The CD8+ T cell of claim 102, wherein the host self antigen is an antigen derived from the variable region of a T cell receptor (TCR) or an antigen derived from the variable region of a B cell receptor.~~

~~106. — A method of treating or preventing a pathogenic infection in a subject, the method comprising administering the CD8+ T cell of claim 102 or 103 to the subject.~~

~~107. — Use of the CD8+ T cell of claim 102 or 103 in the manufacture of a medicament for use in treating or preventing a pathogenic infection in a subject.~~

~~108. — The CD8+ T cell of claim 102 or 103 for use in treating or preventing a pathogenic infection in a subject.~~

~~109. — A method of treating or preventing cancer in a subject, the method comprising administering the CD8+ T cell of claim 102 or 104 to the subject.~~

~~110. — Use of the CD8+ T cell of claim 102 or 104 in the manufacture of a medicament for use in treating or preventing cancer in a subject.~~

~~111. The CD8+ T cell of claim 102 or 104 for use in treating or preventing cancer in a subject.~~

~~112. A method of treating an autoimmune disease or disorder, the method comprising administering the CD8+ T cell of claim 102 or 105 to the subject.~~

~~113. Use of the CD8+ T cell of claim 102 or 105 in the manufacture of a medicament for use in treating an autoimmune disease or disorder.~~

~~114. The CD8+ T cell of claim 102 or 105 for use in treating an autoimmune disease or disorder.~~

~~115. A method of inducing an autoimmune response to a host self antigen, the method comprising administering the CD8+ T cell of claim 102 or 105 to the subject.~~

~~116~~37. A recombinant HCMV vector comprising a nucleic acid encoding one or more A human immunodeficiency virus antigens, wherein the human immunodeficiency virus antigen is between 9 and 15 amino acids in length and that is at least 90%, at least 95%, or 100% identical to the amino acid sequence of LDAWEKIRLRPGGKK (SEQ ID NO: 13); DAW EKIRLR (SEQ ID NO: 14); KKAQQAAADTGNSSQ (SEQ ID NO: 15); KAQQAAADT (SEQ ID NO: 16); QMVHQAISPRTLNAW (SEQ ID NO: 17); HQAISPRTL (SEQ ID NO: 18); NTMLNTVGGHQAAMQ (SEQ ID NO: 19); VGGHQAAMQ (SEQ ID NO: 20); STLQEQIGWMTNNPP (SEQ ID NO: 21); STLQEQIGW (SEQ ID NO: 22); IVRMYSPPVSILDIRQ (SEQ ID NO: 23); RMYSPVSIL (SEQ ID NO: 24); QKQEPIDKELYPLAS (SEQ ID NO: 25); KQEPIDKEL (SEQ ID NO: 26); SFSFPQITLWQRPLV (SEQ ID NO: 27); VRQYDQILIEICGKK (SEQ ID NO: 28); EPFRKQNPDIVIYQL (SEQ ID NO: 29); YVDGAANRETKLGKA (SEQ ID NO: 30); EEHEKYSNWRAMAS (SEQ ID NO: 31); or ILDLWVYHTQGYPFD (SEQ ID NO: 32).

~~117. — A recombinant HCMV vector comprising a nucleic acid encoding one or more of the human immunodeficiency virus antigens of claim 116.~~

~~118. — The recombinant HCMV vector of claim 117, wherein the recombinant HCMV vector does not express UL18.~~

~~119. — The recombinant HCMV vector of claim 117 or 118, wherein the recombinant HCMV vector does not express UL128.~~

~~120. — The recombinant HCMV vector of any one of claims 117–119, wherein the recombinant HCMV vector does not express UL130.~~

~~121. — The recombinant HCMV vector of any one of claims 117–120, wherein the recombinant HCMV vector does not express UL128 and UL130.~~

~~122. — The recombinant HCMV vector of claim 121, wherein the recombinant HCMV vector does not express UL146 and UL147.~~

~~123. — The recombinant HCMV vector of any one of claims 117–122, wherein the recombinant HCMV vector does not express UL18 protein, UL128 protein, UL130 protein, UL146 protein, and UL147 protein, or orthologs thereof, due to the presence of one or more mutations in the nucleic acid sequence encoding UL18, UL128, UL130, UL146, or UL147.~~

~~124. — The recombinant HCMV vector of claim 123, wherein the mutations in the nucleic acid sequence encoding UL18, UL128, UL130, UL146, or UL147 are selected from the group consisting of point mutations, frameshift mutations, truncation mutations, and deletion of all of the nucleic acid sequence encoding the viral protein.~~

~~125.—The recombinant HCMV vector of any one of claims 117-124, wherein the recombinant HCMV vector further comprises a nucleic acid sequence encoding UL40, or an ortholog thereof.~~

~~126.—The recombinant HCMV vector of any one of claims 117-125, wherein the recombinant HCMV vector further comprises a nucleic acid sequence encoding US28, or an ortholog thereof.~~

~~127.—The recombinant HCMV vector of any one of claims 117-126, wherein the recombinant HCMV vector does not express UL82 (pp71), or an ortholog thereof.~~

~~128.—The recombinant HCMV vector of any one of claims 117-127, wherein the recombinant HCMV vector does not express US11, or an ortholog thereof.~~

~~129.—The recombinant HCMV vector of any one of claims 117-128, wherein the recombinant HCMV vector further comprises a nucleic acid sequence encoding a microRNA (miRNA) recognition element (MRE), wherein the MRE contains a target site for a miRNA expressed in endothelial cells.~~

~~130.—The recombinant HCMV vector of claim 129, wherein the miRNA expressed in endothelial cells is miR126, miR-126-3p, miR-130a, miR-210, miR-221/222, miR-378, miR-296, or miR-328.~~

~~131.—The recombinant HCMV vector of any one of claims 117-130, wherein the recombinant HCMV vector further comprises a nucleic acid sequence encoding a MRE, wherein the MRE contains a target site for a miRNA expressed in myeloid cells.~~

~~132. The recombinant HCMV vector of claim 131, wherein the miRNA expressed in myeloid cells is miR 142 3p, miR 223, miR 27a, miR 652, miR 155, miR 146a, miR 132, miR 21, or miR 125.~~