CLAIMS:

1. An isolated cell composition suitable for adoptive immunotherapy, the composition comprising, in a pharmaceutically acceptable carrier: at least 10^6 CD8+ T cells specific for one or more target peptide antigens, and comprising T memory stem (T_{SCM}) cells.

2. The isolated cell composition of claim 1, wherein the CD8+ T cells are specific for from 1 to 100 target peptide antigens.

3. The isolated cell composition of claim 1, wherein T cell specificity toward a target peptide antigen in the composition is defined by MHC multimer staining.

4. The isolated cell composition of claim 1, wherein the target peptide antigens are tumor associated antigens.

5. The isolated cell composition of claim 4, wherein one or more target peptide antigens are tumor derived or tumor specific neoantigens.

6. The isolated cell composition of claim 1, wherein one or more target peptide antigens are bacterial, viral, fungal, or parasitic antigens.

7. The isolated cell composition of any one of claims 1 to 6, comprising CD8+ T cells specific for at least five target peptide antigens.

8. The isolated cell composition of claim 7, wherein at least one of the target peptide antigens is recognized by a low frequency precursor T cell.

9. The isolated cell composition of any one of claims 1 to 8, wherein the cell composition is at least 90% T cells.

10. The isolated cell composition of claim 9, wherein at least 5% of the CD8+ T cells are specific for a target peptide antigen.

11. The isolated cell composition of claim 10, wherein at least 10% of the CD8+ T cells are specific for a target peptide antigen.

12. The isolated cell composition of claim 11, wherein at least 15% of the CD8+ T cells are specific for a target peptide antigen.

13. The isolated cell composition of claim 12, wherein at least 30% of the CD8+ T cells are specific for a target peptide antigen.

14. The isolated cell composition of claim 13, wherein at least 50% of the CD8+ T cells are specific for a target peptide antigen.

15. The isolated cell composition of any one of claims 4 or 5, wherein the cell composition further comprises CD8+ T cells specific for bacterial, viral, and/or fungal pathogens.

16. The isolated cell composition of claim 15, wherein the CD8+ T cells specific for bacterial, viral, or fungal pathogens include T cells specific for antigens of influenza, CMV, EBV, and/or adenovirus.

17. The isolated cell composition of any one of claims 1 to 16, wherein the CD8+ T cells are from about 1% to about 100% T memory stem cells.

18. The isolated cell composition of claim 17, wherein the CD8+ T cells are from about 1% to about 50% T memory stem cells.

19. The isolated cell composition of claim 18, wherein the CD8+ T cells are from about 5% to about 25% T memory stem cells.

20. The isolated cell composition of claim 18, wherein the CD8+ T cells are at least 5% T memory stem cells.

21. The isolated cell composition of claim 18, wherein the CD8+ T cells are at least 20% T memory stem cells.

22. The isolated cell composition of claim 18, wherein the CD8+ T cells are at least 25% T memory stem cells.

23. The isolated cell composition of any one of claims 1 to 22, wherein the T cells specific for the one or more target antigens are at least 15% T memory stem cells.

24. The isolated cell composition of any one of claims 1 to 23, wherein greater than 95% of the CD8+ T cells comprise a memory phenotype.

25. The isolated cell composition of claim 24, wherein the CD8+ T cells comprise central memory and effector memory T cells.

26. The isolated cell composition of claim 25, wherein the CD8+ T cells are at least 30% central and effector memory T cells.

27. The isolated cell composition of claim 25, wherein the CD8+ T cells are at least 50% central and effector memory T cells.

28. The isolated cell composition of claim 25, wherein the CD8+ T cells are at least 70% central and effector memory T cells.

29. The isolated cell composition of claim 25, wherein the CD8+ T cells are at least 80% central and effector memory T cells.

30. The isolated cell composition of claim 25, wherein the CD8+ T cells are at least 90% central and effector memory T cells.

31. The isolated cell composition of claim 25, wherein the CD8+ T cells specific for the one or more target antigens are at least 50% central and effector memory T cells.

32. The isolated cell composition of claim 31, wherein the T cells specific for the one or more target antigens are at least 80% central and effector memory T cells.

33. The isolated cell composition of any one of claims 1 to 32, wherein the CD8+ T cells are less than 20% terminally differentiated.

34. The isolated cell composition of claim 33, wherein the T cells are less than 10% terminally differentiated.

35. The isolated cell composition of any one of claims 1 to 34, wherein the composition comprises less than 30% naive T cells (T_N).

36. The isolated cell composition of claim 35, wherein the composition comprises less than 15% naive cells.

37. The isolated cell composition of claim 35, wherein the composition comprises less than 5% naive cells.

38. The isolated cell composition of claim 35, wherein the composition comprises less than 1.5% naive cells.

39. The isolated cell composition of any one of claims 1 to 38, wherein at least 10% of the CD8+ T cells display a polyfunctional phenotype upon activation.

40. The isolated cell composition of any one of claims 1 to 39, wherein at least 20% of the CD8+ T cells display a polyfunctional phenotype upon activation.

41. The isolated cell composition of claim 40, wherein at least 40% of the CD8+ T cells display a polyfunctional phenotype upon activation.

42. The isolated cell composition of any one of claims 1 to 41, wherein the cell composition is less than 10% CD4+ T cells.

43. The isolated cell composition of claim 42, wherein the cell composition is less than 5% CD4+ T cells.

44. The isolated cell composition of claim 42, wherein the cell composition is less than 2% CD4+ T cells.

45. The isolated cell composition of claim 42, wherein the cell composition is less than 1.5% CD4+ T cells.

46. The isolated cell composition of claim 42, wherein the cell composition is less than 1% CD4+ T cells.

47. The isolated cell composition of any one of claims 1 to 42, wherein the composition further comprises γδ T cells.

48. The isolated cell composition of claim 47, comprising at least about 2% γδ T cells.

49. The isolated cell composition of claim 47, comprising at least about 5% γδ T cells.

50. The isolated cell composition of claim 47, comprising at least about 10% γδ T cells.

51. The isolated cell composition of claim 47, comprising at least about 20% γδ T cells.

52. The isolated cell composition of claim 47, comprising at least about 25% γδ T cells.

53. The isolated cell composition of any one of claims 47 to 52, wherein the γδ T cells comprise Vδ1 and Vδ2 cells.

54. The isolated cell composition of claim 17, wherein the composition is substantially composed of T memory stem cells, and the cells are engineered to express a chimeric antigen receptor or a recombinant TCR.

55. The isolated cell composition of any one of claims 1 to 54, wherein the composition is produced by enrichment of CD8+ T cells specific for the target peptide antigens from source cells; and/or expansion of CD8+ T cells specific for the target peptide antigens from source cells.

56. The isolated cell composition of claim 55, wherein source cells are from a patient or an HLA-matched donor.

57. The isolated cell composition of claim 56, wherein the donor cells are isolated by leukapheresis.

58. The isolated cell composition of claim 55, wherein the source cells are isolated from a patient's tumor.

59. The isolated cell composition of claim 55, wherein the source cells are a buffy coat fraction.

60. The isolated cell composition of any one of claims 55 to 59, wherein the cell source is depleted for CD4+ T cells prior to enrichment or prior to expansion.

61. The isolated cell composition of any one of claims 55 to 59, wherein the source cells are CD8+ enriched.

62. The isolated cell composition of any one of claims 55 to 59, wherein the cell source is NK cell depleted.

63. The isolated cell composition of any one of claims 55 to 62, wherein the antigen-specific T cells are enriched by aAPCs having an MHC class I ligand and optionally a co-stimulatory ligand.

64. The isolated cell composition of claim 63, wherein the aAPCs comprise a co-stimulatory ligand that is a ligand that binds CD28.

65. The isolated cell composition of claim 64, wherein the co-stimulatory ligand is a monoclonal antibody, or portion thereof, that is an agonist for CD28.

66. The isolated cell composition of any one of claims 1 to 65, wherein the enrichment is magnetic enrichment with paramagnetic aAPCs, and wherein the cells and aAPCs are optionally incubated in the presence of a magnetic field for at least one minute.

67. The isolated cell composition of claim 66, wherein the cells and aAPCs are incubated in the presence of a magnetic field for no more than about five hours.

68. The isolated cell composition of claim 67, wherein the enriched antigen-specific T cells are expanded without the use of a magnetic field.

69. The isolated cell composition of any one of claims 66 to 68, wherein the enriched cells are expanded in culture for from 1 to 4 weeks.

70. The isolated cell composition of claim 69, wherein the cells are expanded in culture in the presence of one or more cytokines or growth factors selected from MIP-1β, IL-1β, IL-2, IL-4, IL-6, IL-7, IL-10, IL-15, IL-21, and INF-γ.

71. The isolated cell composition of claim 70, wherein IL-15 is not included for expansion of the cells in culture.

72. The isolated cell composition of claim 70, wherein the cells are expanded in culture in the presence of two, three, four, or five of cytokines or growth factors selected from MIP-1β, IL-1β, IL-2, IL-4, IL-6, IL-7, IL-10, IL-15, IL-21, and INF-γ.

73. The isolated cell composition of claim 72, wherein IL-15 is not included for expansion of the cells in culture.

74. The isolated cell composition of any one of claims 70 to 73, wherein the cells are expanded in culture in the presence of at least one cytokine or growth factor selected from MIP-1β, IL-1β, IL-6, and IL-10.

75. The isolated cell composition of any one of claims 70 to 74, wherein the cells are expanded in the presence of IL-4.

76. The isolated cell composition of any one of claims 70 to 74, wherein the cells are expanded in the presence of IL-4 and IL-6.

77. The isolated cell composition of any one of claims 70 to 74, wherein the cells are expanded in the presence of IL-4 and IL-1β.

78. The isolated cell composition of any one of claims 70 to 74, wherein the cells are expanded in the presence of IL-4, IL-6, and IL-1β.

79. The isolated cell composition of any one of claims 70 to 74 wherein the cells are expanded in the presence of IL-2, IL-4, and IL-6.

80. The isolated cell composition of any one of claims 70 to 74, wherein the cells are expanded in culture in the presence of IL-2, IL-4, IL-6, INF-γ, and IL-1β.

81. The isolated cell composition of any one of claims 1 to 80, wherein one or more target peptide antigens are selected from peptide epitopes of Survivin, WT-1, PRAME, and Cyclin A1.

82. The isolated cell composition of any one of claims 1 to 81, wherein one or more target peptide antigens are selected from peptide epitopes of PR3, XBP1-US, XBP1-SP, CD138, CS1, NY-ESO1, SOX2, EBV, Influenza, CMV, RHAMM, Mart-1/Melan A, gp100, CMVpp65, and Influenza Matrix Protein M1.

83. An isolated cell composition suitable for adoptive immunotherapy, the composition comprising, in a pharmaceutically acceptable carrier:

at least 70% CD8+ T cells and less than 5% CD4+ T cells;

at least 5% of the CD8+ cells are T memory stem (T_{SCM}) cells;
at least 30% of the CD8+ cells are central and effector memory T cells;
less than 10% of the CD8+ T cells are terminally differentiated T cells; and
less than 10% of the CD8+ cells are naive cells.

84. The isolated cell composition of claim 83, wherein at least 10^6 CD8+ T cells are specific for target peptide antigens.

85. The isolated cell composition of claim 84, wherein at least 10^6 CD8+ T cells are specific for from 1 to 20 or from 1 to 10 target peptide antigens.

86. The isolated cell composition of any one of claims 83 to 85, comprising at least 10^7 or 10^8 CD8+ T cells specific for the target peptide antigens.

87. The isolated cell composition of any one of claims 83 to 86, comprising from 5% to 25% T memory stem cells.

88. The isolated cell composition of any one of claims 83 to 87, comprising less than 5% terminally differentiated T cells, and/or less than 5% naive cells.

89. The isolated cell composition of any one of claims 83 to 88, wherein the target peptide antigens are tumor or cancer associated antigens, and are optionally associated with hematological malignancy.

90. The isolated cell composition of claim 89, wherein the target peptide antigens are associated with hematological malignancy.

91. The isolated cell composition of claim 89 or 90, wherein one or more target peptide antigens are selected from peptide epitopes of Survivin, WT-1, PRAME, Cyclin A1, and PR3, wherein the peptide epitopes optionally include one or more selected from Table 1.

92. The isolated cell composition of claim 89 or 90, wherein one or more target peptide antigens are selected from peptide epitopes of XBP1-US, XBP1-SP, CD138,

CS1, NY-ESO1, and SOX2, wherein the peptide epitopes optionally include one or more from Table 2.

93. The isolated cell composition of any one of claims 83 to 92, wherein the composition further comprises γδ T cells.

94. The isolated cell composition of claim 93, comprising at least about 5% γδ T cells.

95. The isolated cell composition of claim 93, comprising at least about 10% γδ T cells.

96. The isolated cell composition of claim 93, comprising at least about 25% γδ T cells.

97. The isolated cell composition of any one of claims 93 to 96, wherein the γδ T cells comprise Vδ1 and Vδ2 cells.

98. A method for treating a patient with cancer, comprising administering the cell composition of any one of claims 1 to 97 to a patient in need.

99. The method of claim 98, wherein the patient has a hematological cancer.

100. The method of claim 99, wherein the hematological cancer has relapsed after allogeneic stem cell transplantation.

101. The method of claim 99 or 100, wherein the patient has acute myelogenous leukemia (AML) or myelodysplastic syndrome.

102. The method of any one of claims 98 to 101, wherein the patient has also undergone lympho-deleting therapy, or cyto-reductive therapy, or immunomodulatory therapy prior to administration of the cell therapy.

103. The method of any one of claims 98 to 102, wherein the cell therapy may be further provided with or without cytokine support post treatment.

104. The method of any one of claims 98 to 103, wherein antigen specific T cells persist in the patient for at least 6 months.

105. A method for producing the cell composition of any one of claims 1 to 97, comprising: expanding a population of CD4+ depleted T cells in the presence of two or more of IL-2, IL-4, IL-6, INF-γ, and IL-1β.

106. The method of claim 105, wherein the T cells are enriched for CD28+ cells.

107. The method of claim 105 or 106, wherein the cells are expanded in the presence of IL-4.

108. The method of claim 107, wherein the cells are expanded in the presence of IL-4 and IL-6.

109. The method of claim 107, wherein the cells are expanded in the presence of IL-4 and IL-1β.

110. The method of claim 107, wherein the cells are expanded in the presence of IL-4, IL-6, and IL-1β.

111. The method of claim 107, wherein the cells are expanded in the presence of IL-2, IL-4, and IL-6.

112. The method of claim 107, wherein the cells are expanded in culture in the presence of IL-2, IL-4, IL-6, INF-γ, and IL-1β.

113. The method of any one of claims 93 to 112, wherein the cells expanded in culture for from 1 to 4 weeks.

114. A method for making a population of γδ T cells, comprising, expanding a population of T cells in the presence of two or more of IL-2, IL-4, IL-6, INF-γ, and IL-1β.

115. The method of claim 114, wherein the population of T cells is CD28+ enriched.

116. The method of claim 115, wherein the population of CD28+ cells is positively selected with anti-CD28 beads or particles.

117. The method of any one of claims 114 to 116, wherein the population of T cells are CD4+ depleted.

118. The method of any one of claims 114 to 117, wherein the cells are expanded in the presence of IL-4.

119. The method of claim 118, wherein the cells are expanded in the presence of IL-4 and IL-6.

120. The method of claim 118, wherein the cells are expanded in the presence of IL-4 and IL-1β.

121. The method of claim 118, wherein the cells are expanded in the presence of IL-4, IL-6, and IL-1β.

122. The method of claim 118, wherein the cells are expanded in the presence of IL-2, IL-4, and IL-6.

123. The method of claim 118, wherein the cells are expanded in culture in the presence of IL-2, IL-4, IL-6, INF-γ, and IL-1β.

124. The method of any one of claims 117 to 123, wherein the cells expanded in culture for from 1 to 4 weeks.

125. The method of any one of claims 114 to 124, further comprising, isolating the γδ+ population of cells from γδ- cells.

126. The method of claim 125, further comprising, heterologously expressing a T cell receptor, which is an optionally an αβ TCR.

127. The method of claim 125, further comprising, heterologously expressing a chimeric antigen receptor (CAR).

CLAIMS:

1. A method for producing a cell composition comprising CD8+ cytotoxic T lymphocytes (CTLs) specific for one or more cancer-associated peptide antigens for adoptive immunotherapy, comprising:

providing a sample of T cells from whole blood or buffy coat fraction, bone marrow, lymph node tissue, spleen tissue, or tumor;

depleting the sample of CD4+ T cells;

expanding the CD4+ depleted cells ex vivo in the presence of cytokines consisting of IL-2, IL-4, IL-6, INF-γ, and IL-1β, and in the presence of artificial Antigen Presenting Cells (aAPCs) presenting one or more cancer-associated peptide antigens through association with HLA ligands, the aAPCs further presenting T lymphocyte co-stimulatory ligands;

wherein after expansion, the CD8+ T cells in the composition are predominately central memory (Tcm) and effector memory (TEM) phenotype, and comprise T memory stem cells; and at least 15% of the T cells in the composition are specific for the cancer-associated peptide antigen.

2. The method of claim 1, wherein the CD4+ depleted cells are expanded in the presence of a population of artificial Antigen Presenting Cells (aAPCs) comprising HLA ligands presenting from 1 to 10 cancer-associated peptide antigens.

3. The method of claim 2, wherein the population of aAPCs comprise HLA ligands presenting at least 3 cancer-associated peptide antigens.

4. The method of claim 2, wherein the aAPCs comprise a paramagnetic core, and the population of cells are activated in the presence of a magnetic field for a duration of from 2 to 30 minutes.

5. The method of claim 4, wherein the population of CD4+ depleted cells are enriched for T cells specific for said cancer-associated peptide antigens by magnetic enrichment with the paramagnetic aAPCs.

6. The method of claim 1, wherein the T lymphocyte co-stimulatory ligands are CD28 agonists.

7. The method of claim 1, wherein said cancer-associated peptide antigens are associated with acute myelogenous leukemia or multiple myeloma.

8. The method of claim 7, wherein said cancer-associated peptide antigens comprise epitopes derived from one or more of SURVIVIN, WT-1, PRAME, RHAMM, PR3, and CYCLIN A1.

9. The method of claim 7, wherein said cancer-associated peptide antigens comprise epitopes derived from one or more of NY-ESO-1, WT-1, SOX-2, CD138, CS1, XBP1-US, and XBP1-SP.

10. The method of claim 1, wherein the cell composition has at least 70% central and effector memory T cells.

11. The method of claim 10, wherein the cell composition has at least 80% central and effector memory T cells.

12. The method of claim 1, wherein the cell composition has less than 10% terminally differentiated T cells.

13. The method of claim 1, wherein the cell composition has less than 5% naive cells.

14. The method of claim 1, wherein the cell composition has from 1% to 25% T memory stem cells.

15. The method of claim 1, wherein at least 30% of the CD8+ T cells in the composition are specific for the cancer-associated peptide antigens.

16. The method of claim 1, wherein at least 50% of the CD8+ T cells in the composition are specific for the cancer-associated peptide antigens.

17. The method of claim 1, wherein the cell composition further comprises γδT cells.

18. The method of claim 1, wherein the cell composition comprises at least 10% γδT cells.

19. The method of claim 1, wherein the cell composition comprises at least 10^7 CD8+ T cells specific for the cancer-associated peptide antigens.

20. The method of claim 1, wherein the population of cells is expanded in culture for from 1 to 4 weeks.

21. The method of claim 20, wherein the population of cells is expanded in culture for about 2 weeks.