

## CLAIMS

What is claimed is:

1. A method of enhancing an immune effector cell therapy for an individual, comprising the steps of:

providing to the individual an effective amount of one or both of the following:

CD8<sup>+</sup> cells that express an exogenous CD8 $\alpha\beta$  co-receptor and optionally express one or more exogenous engineered antigen receptors; and

CD4<sup>+</sup> cells that express an exogenous CD8 $\alpha\beta$  co-receptor and one or more exogenous engineered antigen receptors.

2. The method of claim 1, wherein the engineered antigen receptor is a T cell receptor (TCR), a chimeric antigen receptor (CAR) or both.

3. The method of claim 1 or 2, wherein the CD8<sup>+</sup> cells, CD4<sup>+</sup> cells, or both are autologous with respect to the individual.

4. The method of claim 1 or 2, wherein the CD8<sup>+</sup> cells, CD4<sup>+</sup> cells, or both are allogeneic with respect to the individual.

5. The method of any one of claims 2-4, wherein the exogenous engineered antigen receptor and the exogenous CD8 $\alpha\beta$  co-receptor are expressed from the same vector in the cells.

6. The method of claim 5, wherein the vector comprises one or more expression constructs that separately express the exogenous engineered antigen receptor and the exogenous CD8 $\alpha\beta$  co-receptor.

7. The method of claim 6, wherein the expression construct that expresses the exogenous engineered antigen receptor and the expression construct that expresses the exogenous CD8 $\alpha\beta$  co-receptor are separated by a 2A element or an IRES element.

8. The method of any one of claims 2-4, wherein the exogenous engineered antigen receptor and the exogenous CD8 $\alpha\beta$  co-receptor are expressed from different vectors in the cells.

9. The method of any one of claims 5-8, wherein the vector is a viral vector or non-viral vector.
10. The method of claim 9, wherein the viral vector is an adenoviral vector, an adeno-associated viral vector, a retroviral vector, or a lentiviral vector.
11. The method of any one of claims 1-10, wherein the antigen is a tumor antigen.
12. The method of claim 11, wherein the tumor antigen is selected from the group consisting of survivin, PRAME, CD 19, CD20, CD22, Kappa or light chain, CD30, CD33, CD 123, CD38, ROR1, ErbB2, ErbB3/4, EGFR vIII, carcinoembryonic antigen, EGP2, EGP40, mesothelin, TAG72, PSMA, NKG2D ligands, B7-H6, IL-13 receptor cc2, IL-11 receptor R a, MUC1, MUC16, CA9, GD2, GD3, HMW-MAA, CD171, Lewis Y, G250/CAIX, HLA-AI MAGE A1, HLA-A2 NY-ESO-1, PSC1, folate receptor- a, CD44v7/8, 8H9, NCAM, VEGF receptors, 5T4, Fetal AchR, NKG2D ligands, HER2, BCMA, CD44v6, and a combination thereof.
13. The method of any one of claims 1-12, further comprising the step of providing to the individual an effective amount of the CD4+ T cells, the CD8+ T cells, or a mixture thereof.
14. The method of claim 13, further comprising the step of providing to the individual an additional cancer therapy.
15. A method of producing a CD4+ T cell having cytotoxic effector cell function and helper function, comprising the step of transfecting the CD4+ T cell with an exogenous CD8 $\alpha\beta$  co-receptor and an exogenous engineered antigen receptor.
16. The method of claim 15, wherein the engineered antigen receptor is a T cell receptor (TCR), a chimeric antigen receptor (CAR) or both.
17. The method of claim 15 or 16, wherein the exogenous engineered antigen receptor and the exogenous CD8 $\alpha\beta$  co-receptor are expressed from the same vector in the cells.
18. The method of claim 17, wherein the vector comprises one or more expression constructs that separately express the exogenous engineered antigen receptor and the exogenous CD8 $\alpha\beta$  co-receptor.

19. The method of claim 18, wherein the expression construct that expresses the exogenous engineered antigen receptor and the expression construct that expresses the exogenous CD8 $\alpha$  $\beta$  co-receptor are separated by a 2A element or an IRES element.
20. The method of claim 15 or 16, wherein the exogenous engineered antigen receptor and the exogenous CD8 $\alpha$  $\beta$  co-receptor are expressed from different vectors in the cells.
21. The method of any one of claims 17-20, wherein the vector is a viral vector or non-viral vector.
22. The method of claim 21, wherein the viral vector is an adenoviral vector, an adeno-associated viral vector, a retroviral vector, or a lentiviral vector.
23. The method of any one of claims 15-22, wherein the antigen is a tumor antigen.
24. The method of claim 23, wherein the tumor antigen is selected from the group consisting of survivin, PRAME, CD 19, CD20, CD22, Kappa or light chain, CD30, CD33, CD 123, CD38, ROR1, ErbB2, ErbB3/4, EGFR vIII, carcinoembryonic antigen, EGP2, EGP40, mesothelin, TAG72, PSMA, NKG2D ligands, B7-H6, IL-13 receptor cc2, IL-11 receptor R a, MUC1, MUC16, CA9, GD2, GD3, HMW-MAA, CD171, Lewis Y, G250/CAIX, HLA-AI MAGE A1, HLA-A2 NY-ESO-1, PSC1, folate receptor- a, CD44v7/8, 8H9, NCAM, VEGF receptors, 5T4, Fetal AchR, NKG2D ligands, HER2, BCMA, CD44v6, and a combination thereof.
25. The method of any one of claims 15-24, further comprising the step of providing to the individual an effective amount of the CD4 $^{+}$  T cells to an individual in need thereof.
26. The method of claim 25, wherein the individual has cancer.
27. The method of claim 25 or 26, wherein an effective amount of CD8 $^{+}$  T cells expressing an exogenous CD8 $\alpha$  $\beta$  co-receptor, an exogenous engineered antigen receptor, or both are provided to the individual.
28. The method of claim 25, 26, or 27, further comprising the step of providing to the individual an additional cancer therapy.
29. A method of enhancing cytotoxicity of CD8 $^{+}$  T cells, comprising the step of transfecting the CD8 $^{+}$  T cell with an exogenous CD8 $\alpha$  $\beta$  co-receptor.

30. The method of claim 29, wherein the CD8<sup>+</sup> T cells also express an exogenous engineered antigen receptor.
31. The method of claim 30, wherein the engineered antigen receptor is a T cell receptor (TCR), a chimeric antigen receptor (CAR) or both.
32. The method of claim 30 or 31, wherein the exogenous engineered antigen receptor and the exogenous CD8 $\alpha$  $\beta$  co-receptor are expressed from the same vector in the cells.
33. The method of claim 32, wherein the vector comprises one or more expression constructs that separately express the exogenous engineered antigen receptor and the exogenous CD8 $\alpha$  $\beta$  co-receptor.
34. The method of claim 33, wherein the expression construct that expresses the exogenous engineered antigen receptor and the expression construct that expresses the exogenous CD8 $\alpha$  $\beta$  co-receptor are separated by a 2A element or an IRES element.
35. The method of claim 30 or 31, wherein the exogenous engineered antigen receptor and the exogenous CD8 $\alpha$  $\beta$  co-receptor are expressed from different vectors in the cells.
36. The method of any one of claims 32-35, wherein the vector is a viral vector or non-viral vector.
37. The method of claim 36, wherein the viral vector is an adenoviral vector, an adeno-associated viral vector, a retroviral vector, or a lentiviral vector.
38. The method of any one of claims 30-37, wherein the antigen is a tumor antigen.
39. The method of claim 38, wherein the tumor antigen is selected from the group consisting of CD 19, CD20, CD22, Kappa or light chain, CD30, CD33, CD 123, CD38, ROR1, ErbB2, ErbB3/4, EGFR vIII, carcinoembryonic antigen, EGP2, EGP40, mesothelin, TAG72, PSMA, NKG2D ligands, B7-H6, IL-13 receptor cc2, IL-11 receptor R a, MUC1, MUC16, CA9, GD2, GD3, HMW-MAA, CD171, Lewis Y, G250/CAIX, HLA-AI MAGE AI, HLA-A2 NY-ESO-1, PSC1, folate receptor- a, CD44v7/8, 8H9, NCAM, VEGF receptors, 5T4, Fetal AchR, NKG2D ligands, HER2, BCMA, CD44v6, and a combination thereof.

40. The method of any one of claims 29-39, further comprising the step of providing to the individual an effective amount of the CD8<sup>+</sup> T cells to an individual in need thereof.
41. The method of any one of claims 29-40, further comprising the step of providing to the individual an effective amount of CD4<sup>+</sup> T cells to an individual in need thereof.
42. The method of claim 40, wherein the CD4<sup>+</sup> T cells are engineered to express an exogenous CD8 $\alpha\beta$  co-receptor, an exogenous engineered antigen receptor, or both.
43. The method of any one of claims 40-42, wherein the individual has cancer.
44. The method of claim 43, further comprising the step of providing to the individual an additional cancer therapy.
45. A composition comprising CD4<sup>+</sup> T cells transgenically expressing CD8 $\alpha\beta$  co-receptor.
46. The composition of claim 45, wherein the CD4<sup>+</sup> T cells also transgenically express one or more exogenous engineered antigen receptors.
47. The composition of claim 46, wherein the engineered antigen receptor is a TCR, a CAR, or both.
48. The composition of any one of claims 45-47, wherein the composition further comprises CD8<sup>+</sup> T cells.
49. The composition of claim 48, wherein the CD8<sup>+</sup> T cells transgenically express CD8 $\alpha\beta$  co-receptor, one or more exogenous engineered antigen receptors, or both.
50. A composition comprising CD8<sup>+</sup> T cells transgenically expressing CD8 $\alpha\beta$  co-receptor and optionally one or more exogenous engineered antigen receptors.
51. The composition of claim 50, wherein the engineered antigen receptor is a TCR, a CAR, or both.
52. The composition of claim 50 or 51, wherein the composition further comprises CD4<sup>+</sup> T cells.

53. The composition of claim 52, wherein the CD4<sup>+</sup> T cells transgenically express CD8 $\alpha\beta$  co-receptor, one or more exogenous engineered antigen receptors, or both.