

CLAIMS

What is claimed is:

1. Use of ~~one or both of the following:~~
CD8⁺ cells that express an exogenous CD8 $\alpha\beta$ co-receptor and ~~optionally~~ express one or more exogenous engineered antigen receptors; ~~and~~
~~CD4⁺ cells that express an exogenous CD8 $\alpha\beta$ co-receptor and one or more exogenous engineered antigen receptors,~~ in the manufacture of a medicament for cancer enhancing an immune effector cell therapy for an individual;
wherein the CD8⁺ cells that express an exogenous CD8 $\alpha\beta$ co-receptor and express one or more exogenous engineered antigen receptors exhibit enhanced cytotoxicity as compared to CD8⁺ cells that express one or more exogenous engineered antigen receptors but do not express an exogenous CD8 $\alpha\beta$ co-receptor.
2. The use of claim 1, wherein the engineered antigen receptor is a T cell receptor (TCR), a chimeric antigen receptor (CAR) or both.
3. The use of claim 1 or 2, wherein the CD8⁺ cells, ~~CD4⁺ cells, or both~~ are autologous with respect to the individual.
4. The use of claim 1 or 2, wherein the CD8⁺ cells, ~~CD4⁺ cells, or both~~ are allogeneic with respect to the individual.
5. The use 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 use 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 use 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 use 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 use of any one of claims 5-8, wherein the vector is a viral vector or non-viral vector.
10. The use 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 use of any one of claims 1-10, wherein the antigen is a tumor antigen.
12. The use 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 use of any one of claims 1-12, wherein ~~the CD4⁺ T cells,~~ the CD8⁺ T cells, ~~or a mixture thereof~~ are to be further provided to the individual.
14. The use of claim 13, wherein an additional cancer therapy is to be further provided to the individual.
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 α , MUC1, MUC16, CA9, GD2, GD3, HMW-MAA, CD171,
Lewis-Y, G250/CAIX, HLA-AI MAGE-AI, HLA-A2 NY-ESO-1, PSC1, folate
receptor α , CD44v7/8, 8H9, NCAM, VEGF receptors, 5T4, Fetal AchR, NKG2D
ligands, HER2, BCMA, CD44v6, and a combination thereof.~~

~~25. Use of the CD4⁺ T cells produced by the method of any one of claims 15-24, in
the manufacture of a medicament for providing an effective amount of the CD4⁺ T
cells to an individual in need thereof.~~

~~26. The use of claim 25, wherein the individual has cancer.~~

~~27. The use of claim 25 or 26, wherein CD8⁺ T cells expressing an exogenous
CD8 $\alpha\beta$ co-receptor, an exogenous engineered antigen receptor, or both are to be
provided to the individual.~~

~~28. The use of claim 25, 26, or 27, wherein an additional cancer therapy is to be
further provided to the individual.~~

~~29~~15. 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, wherein the CD8⁺
T cells also express an exogenous engineered antigen receptor; and wherein the
transfected CD8⁺ T cells exhibit enhanced cytotoxicity as compared to CD8⁺ cells that
express one or more exogenous engineered antigen receptors but do not express an
exogenous CD8 $\alpha\beta$ co-receptor.

~~30. The method of claim 29, wherein the CD8⁺ T cells also express an exogenous
engineered antigen receptor.~~

~~31~~16. The method of claim ~~30~~15, wherein the engineered antigen receptor is a T
cell receptor (TCR), a chimeric antigen receptor (CAR) or both.

3317. The method of claim ~~30 or 31~~ 16, wherein the exogenous engineered antigen receptor and the exogenous CD8 α β co-receptor are expressed from the same vector in the cells.

3318. The method of claim 3317, wherein the vector comprises one or more expression constructs that separately express the exogenous engineered antigen receptor and the exogenous CD8 α β co-receptor.

3419. The method of claim 3318, wherein the expression construct that expresses the exogenous engineered antigen receptor and the expression construct that expresses the exogenous CD8 α β co-receptor are separated by a 2A element or an IRES element.

3520. The method of claim ~~30 or 31~~ 16, wherein the exogenous engineered antigen receptor and the exogenous CD8 α β co-receptor are expressed from different vectors in the cells.

3621. The method of any one of claims ~~3217-3520~~, wherein the vector is a viral vector or non-viral vector.

3722. The method of claim ~~3621~~, wherein the viral vector is an adenoviral vector, an adeno-associated viral vector, a retroviral vector, or a lentiviral vector.

3823. The method of any one of claims ~~3015-3722~~, wherein the antigen is a tumor antigen.

3924. The method of claim 3823, 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 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.

~~40~~25. Use of the CD8⁺ T cells whose cytotoxicity is enhanced by the method of any one of claims ~~2915-3924~~, in the manufacture of a medicament for providing an effective amount of the CD8⁺ T cells to an individual in need thereof, wherein the individual has cancer.

~~41~~26. The use of claim ~~40~~25, wherein CD4⁺ T cells are to be further provided to the individual in need thereof.

~~42~~27. The use of claim ~~40~~25, wherein the CD4⁺ T cells are engineered to express an exogenous CD8 $\alpha\beta$ co-receptor, an exogenous engineered antigen receptor, or both.

~~43~~. The use of any one of claims ~~40-42~~, wherein the individual has cancer.

~~44~~28. The use of any one of claims ~~43~~25-27, wherein an additional cancer therapy is to be further provided to the individual.

~~45~~. A composition comprising CD4⁺ T cells transgenically expressing CD8 $\alpha\beta$ co-receptor.

~~46~~. The composition of claim ~~45~~, wherein the CD4⁺ 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⁺ T cells.

~~49~~. The composition of claim ~~48~~, wherein the CD8⁺ T cells transgenically express

~~CD8 α β co-receptor, one or more exogenous engineered antigen receptors, or both.~~

5029. A composition comprising CD8⁺ T cells ~~transgenically~~ expressing exogenous CD8 α β co-receptor and optionally one or more exogenous engineered antigen receptors, wherein the CD8⁺ cells expressing exogenous CD8 α β co-receptor and one or more exogenous engineered antigen receptors exhibit enhanced cytotoxicity as compared to CD8⁺ cells that express one or more exogenous engineered antigen receptors but do not express exogenous CD8 α β co-receptor.

5130. The composition of claim 5029, 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⁺ T cells.~~

~~53. The composition of claim 52, wherein the CD4⁺ T cells transgenically express CD8 α β co-receptor, one or more exogenous engineered antigen receptors, or both.~~