

CLAIMS

1. A T cell comprising a chimeric antigen receptor (CAR-T cell), wherein the CAR-T cell is deficient in an antigen to which the chimeric antigen receptor specifically binds, and wherein the chimeric antigen receptor specifically binds an antigen expressed on a malignant T cell, wherein the antigen is selected from the group consisting of CD7, CD5, CD2, CD30, and CD4; and wherein the T cell comprises a modification of the endogenous T-cell Receptor Alpha Chain (TCR α ; TRAC) such that endogenous T cell receptor mediated signaling is blocked in the CAR-T cell.
- ~~2.~~ ~~The CAR-T cell of claim 1, wherein the antigen is selected from the group consisting of CD7, CD5, CD2, CD30, and CD4.~~
- ~~3.~~2. The CAR-T cell of claim 1, wherein the antigen is CD7.
- ~~4.~~3. The CAR-T cell of ~~any of the preceding claims~~ claim 1 or claim 2, wherein the CAR-T cell further comprises a suicide gene.
- ~~5.~~4. The CAR-T cell of claim ~~4~~3, wherein the suicide gene ~~encodes~~ comprises a genetically modified chimeric suicide gene comprising a Human-Herpes Simplex Virus-1-thymidine kinase (TK) gene fused in-frame to the extracellular and transmembrane domains of the human CD34 cDNA.
- ~~6.~~5. The CAR-T cell of claim 1, ~~further comprising a~~ wherein the modification of the endogenous T-cell Receptor Alpha Chain (TRAC) such that endogenous T cell receptor mediated signaling is blocked in the CAR-T cell, and the deficiency in the antigen to which the chimeric antigen receptor specifically binds, are effected by genome editing using CRISPR.
- ~~7.~~6. The CAR-T cell of claim 1, ~~where in the CAR-T cell comprises~~ further comprising a modification of CD7, ~~and further comprises a modification of TRAC such that the CAR-T cell no longer specifically binds the modified CD7.~~
- ~~8.~~7. A CAR-T cell of any one of the preceding claims for use in killing a malignant T cell.

~~9.8.~~ Use of a CAR-T cell of any one of claims 1 to ~~76~~ in the manufacture of a medicament for the treatment of a T-cell acute lymphoblastic leukemia (T-ALL) malignancy.

~~10.9.~~ The use of claim ~~98~~, wherein the T cell malignancy is non-Hodgkin lymphoma- or T-cell acute lymphoblastic leukemia (T-ALL).

~~11.10.~~ Use of a CAR-T cell of any one of claims 1 to ~~76~~ in the manufacture of a medicament for the treatment of myeloid and lymphoid malignancies.

~~12.11.~~ A chimeric antigen receptor T (CAR-T) cell for use in a the treatment of a mammal having a T cell malignancy, wherein a plurality of chimeric antigen receptor T (the CAR-T) cells are to be administered to the mammal, the CAR-T cells comprise the same chimeric antigen receptor, the CAR-T cells are deficient in an antigen to which the chimeric antigen receptor specifically binds, and wherein the chimeric antigen receptor specifically binds an antigen expressed on a malignant T cell—, wherein the antigen is selected from the group consisting of CD7, CD5, CD2, CD30, and CD4; and wherein the CAR-T cell comprises a modification of the endogenous T-cell Receptor Alpha Chain (TCR α ; TRAC) such that endogenous T cell receptor mediated signaling is blocked in the CAR-T cell.

~~13.12.~~ Use of a chimeric antigen receptor T (CAR-T) cell in the manufacture of a medicament for the treatment of a T cell malignancy in a mammal, wherein the medicament comprises a plurality of chimeric antigen receptor T (the CAR-T) cells to be administered to the mammal, the CAR-T cells comprise the same chimeric antigen receptor, the CAR-T cells are deficient in an antigen to which the chimeric antigen receptor specifically binds, and wherein the chimeric antigen receptor specifically binds an antigen expressed on a malignant T cell—, wherein the antigen is selected from the group consisting of CD7, CD5, CD2, CD30, and CD4; and wherein the CAR-T cell comprises a modification of the endogenous T-cell Receptor Alpha Chain (TCR α ; TRAC) such that endogenous T cell receptor mediated signaling is blocked in the CAR-T cell.

~~14.13.~~ The use of claim ~~13.12~~, wherein the antigen expressed on a malignant T cell is ~~selected from the group consisting of CD7, CD5, CD2, CD30, and CD4~~CD7.

~~15.—~~ The use of claim ~~14~~, ~~wherein the antigen expressed on a malignant T cell is CD7.~~

~~16.14.~~ ~~The use of claim 1312,~~ wherein endogenous T cell receptor mediated signaling is blocked in the CAR-T cell.

~~17.15.~~ The use of claim ~~14~~12, wherein the CAR-T cells do not induce alloreactivity or graft-versus-host disease.

~~18.16.~~ The use of claim ~~14~~12, wherein the CAR-T cells do not induce fratricide.

~~19.17.~~ The use of claim ~~13~~12, wherein the T cell malignancy is T-cell acute lymphoblastic leukemia (T-ALL) or non-Hodgkin lymphoma.

~~18. 20.~~ The use of claim ~~13~~12, wherein the CAR-T cell is to be used to treat~~to treat~~for treating myeloid and lymphoid malignancies.