

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 CD7.
3. The CAR-T cell of claim 1 or claim 2, wherein the CAR-T cell further comprises a suicide gene.
4. The CAR-T cell of claim 3, wherein the suicide gene 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.
5. The CAR-T cell of claim 1, 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.
6. The CAR-T cell of claim 1, further comprising a modification of CD7 such that the CAR-T cell no longer specifically binds the modified CD7.
7. A CAR-T cell of any one of the preceding claims for use in killing a malignant T cell.
8. Use of a CAR-T cell of any one of claims 1 to 6 in the manufacture of a medicament for the treatment of a T-cell malignancy.
9. The use of claim 8, wherein the T cell malignancy is non-Hodgkin lymphoma or T-cell acute lymphoblastic leukemia (T-ALL).

10. Use of a CAR-T cell of any one of claims 1 to 6 in the manufacture of a medicament for the treatment of myeloid and lymphoid malignancies.
11. A chimeric antigen receptor T (CAR-T) cell for use in the treatment of a mammal having a T cell malignancy, wherein a plurality of 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.
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 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.
13. The use of claim 12, wherein the antigen expressed on a malignant T cell is CD7.
14. The use of claim 12, wherein endogenous T cell receptor mediated signaling is blocked in the CAR-T cell.
15. The use of claim 12, wherein the CAR-T cells do not induce alloreactivity or graft-versus-host disease.
16. The use of claim 12, wherein the CAR-T cells do not induce fratricide.

17. The use of claim 12, wherein the T cell malignancy is T-cell acute lymphoblastic leukemia (T-ALL) or non-Hodgkin lymphoma.
18. The use of claim 12, wherein the CAR-T cell is to be used for treating myeloid and lymphoid malignancies.