

CLAIMS

1. A CAR-T cell, which comprises one or more chimeric antigen receptors (CARs) targeting one or more antigens, wherein the CAR-T cell is deficient in a subunit of the T cell receptor complex and / or is deficient in at least one or more antigens to which the one or more CARs specifically binds.
2. A CAR-T cell, which comprises one or more chimeric antigen receptors (CARs) targeting one or more antigens, wherein the CAR-T cell is deficient in one or more antigens to which the one or more CARs specifically binds.
3. The CAR-T cell as recited in claim 1, wherein the subunit of the T cell receptor complex is chosen from TCR α , TCR β , TCR δ , TCR γ , CD3 ϵ , CD3 γ , CD3 δ , and CD3 ζ .
4. The CAR-T cell as recited in any of claims 1-2, wherein the chimeric antigen receptor (CAR) specifically binds one or more antigens expressed on a malignant T cell or myeloma cell.
5. The CAR-T cell as recited in any of claims 1-4, wherein endogenous T cell receptor mediated signaling is blocked in the CAR-T cell.
6. The CAR-T cell as recited in any of claims 1-4, wherein the CAR-T cell does not induce alloreactivity or graft-versus-host disease.
7. The CAR-T cell any of claims 1-4, wherein the CAR-T cell does not induce fratricide.
8. A dual or tandem CAR-T cell as recited in any of claims 1-7.
9. The CAR-T cell as recited in claim 8, wherein the wherein the CAR(s) specifically bind(s) two different targets chosen from: CD2xCD3 ϵ , CD2xCD4, CD2xCD5, CD2xCD7, CD3 ϵ xCD4, CD3 ϵ xCD5, CD3 ϵ xCD7, CD4xCD5, CD4xCD7, CD5xCD7, TRACxCD2, TRACxCD3 ϵ , TRACxCD4, TRACxCD5, TRACxCD7, TCR β xCD2, TCR β xCD3 ϵ , TCR β xCD4, TCR β xCD7, CD2xCD3 ϵ , CD2xCD4, CD2xCD5, CD2xCD7, CD3 ϵ xCD4, CD3 ϵ xCD5, CD3 ϵ xCD7, CD4xCD5, CD4xCD7, CD5xCD7, TRACxCD2, TRACxCD3 ϵ , TRACxCD4, TRACxCD5, TRACxCD7, TCR β xCD2, TCR β xCD3 ϵ , TCR β xCD4, TCR β xCD5, TCR β xCD7, BCMAxCS1, BCMAxCD19, BCMAxCD38, CS1xCD19, CD19xCD38, APRILxCS1, APRILxBCMA, APRILxCD19, APRILxCD38, CS1xCD38, CD79AxBCMA, CD79AxCs1, CD79AxCD19, CD79AxCD38, CD79AxCD38, CD79AxApril, CD79AxCD79B, CD79BxBCMA, CD79BxCs1, CD79BxCD19, CD79BxCD38, CD79BxApril, CD79BxCD79A, CD138xBCMA, CD138xCs1,

CD138xCD19, CD138xCD38, CD138xAPRIL, CD138xCD79A, CD138xCD79B, CD138xBCMA, and CD138xCS1.

10. A tandem CAR-T cell as recited in claim 9.
11. A tandem chimeric antigen receptor (tCAR) targeting two or more plasma cell antigens.
12. The CAR as recited in claim 11, wherein the plasma cell antigen(s) is/are chosen from BCMA, CS1, CD38, CD79A, CD79B, CD138, and CD19.
13. The CAR as recited in claim 12, wherein the CAR(s) specifically bind(s) two different targets chosen from: BCMAxCS1, BCMAxCD19, BCMAxCD38, CS1xCD19, CD19xCD38, APRILxCS1, APRILxBCMA, APRILxCD19, APRILxCD38, CS1xCD38, CD79AxBCMA, CD79AxCs1, CD79AxCD19, CD79AxCD38, CD79AxCD38, CD79AxApril, CD79AxCD79B, CD79BxBCMA, CD79BxCs1, CD79BxCD19, CD79BxCD38, CD79BxApril, CD79BxCD79A, CD138xBCMA, CD138xCs1, CD138xCD19, CD138xCD38, CD138xApril, CD138xCD79A, CD138xCD79B, CD138xBCMA, and CD138xCs1.
14. A tandem chimeric antigen receptor (tCAR) targeting two or more leukemia cell antigens.
15. The CAR as recited in claim 14, wherein the leukemia cell antigen(s) is/are chosen from CD123, CLEC12A, CD117, FLT3, CD7 and Tim3.
16. The CAR as recited in claim 15, wherein the CAR(s) specifically bind(s) two different targets chosen from: CD123xCD371, CD123xCLEC12A, CD123xCD117, CD123xFLT3, CD123xCD7, CD123xTim3, CD371xCLEC12A, CD371xCD117, CD371xFLT3, CD371xCD7, CD371xTim3, CLEC12AxCD117, CLEC12AxFLT3, CLEC12AxCD7, CLEC12AxTim3, CD117xFLT3, CD117xCD7, CD117xTim3, FLT3xCD7, FLT3xTim3, and CD7xTim3.
17. A tandem chimeric antigen receptor (tCAR) targeting two or more T-cell antigens.
18. The tCAR as recited in claim 17, wherein the T-cell antigens chosen from CD5, CD7, CD2, CD4, and CD3.
19. The tCAR as recited in claim 18, targeting a pair of (i.e., two) antigens.
20. The tCAR as recited in claim 19, wherein the antigen pair is chosen from CD2xCD3 ϵ , CD2xCD4, CD2xCD5, CD2xCD7, CD3 ϵ xCD4, CD3 ϵ xCD5, CD3 ϵ xCD7, CD4xCD5, CD4xCD7, CD5xCD7, TRACxCD2, TRACxCD3 ϵ , TRACxCD4, TRACxCD5, TRACxCD7, TCR β xCD2, TCR β xCD4, TCR β xCD7, CD2xCD3 ϵ , CD2xCD4, CD2xCD5,

CD2xCD7, CD3 ϵ xCD4, CD3 ϵ xCD5, CD4xCD5, CD4xCD7, CD5xCD7, TRACxCD2, TRACxCD3 ϵ , TRACxCD4, TRACxCD5, TRACxCD7, TCR β xCD2, TCR β xCD3 ϵ , TCR β xCD4, TCR β xCD5, and TCR β xCD7.

21. The tCAR as recited in any of claims 17-20, wherein the CAR construct is a hairpin tCAR construct.
22. The tCAR as recited in any of claims 17-21, wherein each of the V_H and V_L chains is derived from an scFv that recognizes a different antigen chosen from CD5, CD7, CD2, CD4, and CD3.
23. The tCAR as recited in claim 22, wherein each of the V_H and V_L chains is different and is a sequence chosen from SEQ ID NO:12 to SEQ ID NO:31.
24. The genome-edited CAR-T cell, population of genome-edited CAR-T cells, dual CAR-T cells, or tandem CAR-T as recited in any of any of claims 1-10, or the population of CAR-T cells comprising CAR(s) as recited in any of claims 11-23, for use in the treatment of cancer.
25. Use of the genome-edited CAR-T cell, population of genome-edited CAR-T cells, dual CAR-T cells, or tandem CAR-T as recited in any of any of claims 1-10, or the population of CAR-T cells comprising CAR(s) as recited in any of claims 11-23 in the manufacture of a medicament for the treatment of cancer.
26. The use as recited in claim 25, wherein the cancer is a hematologic malignancy.
27. The use as recited in claim 26, wherein the hematologic malignancy is a T-cell malignancy.
28. The use as recited in claim 27, wherein the T cell malignancy is T-cell acute lymphoblastic leukemia (T-ALL).
29. The use as recited in claim 27, wherein the T cell malignancy is non-Hodgkin's lymphoma.
30. The use as recited in claim 27, wherein the T cell malignancy is T-cell chronic lymphocytic leukemia (T-CLL).
31. A chimeric antigen receptor (CAR)-comprising T cell (CAR-T cell) that is deficient in a subunit of the T cell receptor complex and is deficient in CD7, comprising a CAR that specifically binds to CD7 antigen, wherein the CAR comprises:
 - a CD8 α signal peptide comprising SEQ ID NO:1;
 - a light chain variable region comprising SEQ ID NO: 21;
 - a peptide linker comprising SEQ ID NO:9;
 - a heavy chain variable region comprising SEQ ID NO: 20;

- a CD8 α hinge comprising SEQ ID NO:2;
 - a CD28 transmembrane domain comprising SEQ ID NO:3;
 - a 4-1BB costimulatory domain comprising SEQ ID NO:5; and
 - a CD3 zeta signaling domain comprising SEQ ID NO:7.
32. The CAR-T cell as recited in claim 1 or 31, wherein the subunit of the T cell receptor complex is chosen from TCR α , TCR β , TCR δ , TCR γ , CD3 ϵ , CD3 γ , CD3 δ , and CD3 ζ .
 33. The CAR-T cell as recited in claim 1 or 31, wherein the chimeric antigen receptor (CAR) specifically binds one or more antigens expressed on a malignant T cell or myeloma cell.
 34. The CAR-T cell as recited in claim 1 or 31, wherein endogenous T cell receptor mediated signaling is blocked in the CAR-T cell.
 35. The CAR-T cell as recited in claim 1 or 31, wherein the CAR-T cell does not induce alloreactivity or graft-versus-host disease.
 36. The CAR-T cell as recited in claim 1 or 31, wherein the CAR-T cell does not induce fratricide.
 37. The CAR-T cell according to claim 1 or 31, further comprising hCD34.
 38. The CAR-T cell according to claim 31, wherein the hCD34 comprises SEQ ID NO. 10.
 39. The CAR-T cell according to claim 1 or 31, wherein the cell is engineered to be deficient in CD7 and TRAC by deletion or disruption of the genes encoding CD7 and TRAC using CRISPR.