

CLAIMS**We claim:**

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 the chimeric antigen receptor (CAR) displays at least 95% sequence identity to an amino acid sequence chosen from SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38 or SEQ ID NO:39.
6. The CAR-T cell as recited in any of claims 1-4, wherein the chimeric antigen receptor (CAR) displays at least 98% sequence identity to an amino acid sequence chosen from SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38 or SEQ ID NO:39.
7. The CAR-T cell as recited in any of claims 1-4, wherein the chimeric antigen receptor (CAR) is an amino acid sequence chosen from SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38 or SEQ ID NO:39.
8. The CAR-T cell as recited in any of claims 1-4, wherein the chimeric antigen receptor(s) specifically binds one or more antigen(s) chosen from BCMA, CS1, CD38, CD138, CD19, CD33, CD123, CD371, CD117, CD135, Tim-3, CD5, CD7, CD2, CD4, CD3, CD79A, CD79B, APRIL, CD56, and CD1a.
9. The CAR-T cell as recited in any of claims 1-5, wherein the chimeric antigen receptor(s) specifically binds at least one antigen expressed on a malignant T cell.

10. The CAR-T cell as recited in claim 9, wherein the antigen expressed on a malignant T cell is chosen from CD2, CD3, CD4, CD5, CD7, TCRA, and TCR β .
11. The CAR-T cell as recited in any of claims 1-5, wherein the chimeric antigen receptor specifically binds at least one antigen expressed on a malignant plasma cell.
12. The CAR-T cell as recited in claim 11, wherein the antigen expressed on a malignant plasma cell is chosen from BCMA, CS1, CD38, CD79A, CD79B, CD138, and CD19.
13. The CAR-T cell as recited in any of claims 1-5, wherein the chimeric antigen receptor(s) specifically binds at least one antigen expressed on a malignant B cell.
14. The CAR-T cell as recited in claim 13, wherein the antigen expressed on a malignant B cell is chosen from CD19, CD20, CD21, CD22, CD23, CD24, CD25, CD27, CD38, and CD45.
15. The CAR-T cell as recited in claim 14, wherein the antigen expressed on a malignant B cell is chosen from CD19 and CD20.
16. The CAR-T cell as recited in any of claims 1-15, wherein the CAR-T cell further comprises a suicide gene.
17. The CAR-T cell as recited in any of claims 1-16, wherein endogenous T cell receptor mediated signaling is blocked in the CAR-T cell.
18. The CAR-T cell as recited in any of claims 1-17, wherein the CAR-T cells do not induce alloreactivity or graft-versus-host disease.
19. The CAR-T cell as recited in any of claims 1-18, wherein the CAR-T cells do not induce fratricide.
20. A dual or tandem CAR-T cell as recited in any of claims 1-19.
21. The CAR-T cell as recited in claim 20, 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, BCMAxCD1, BCMAxCD19, BCMAxCD38, CS1xCD19, CD19xCD38, APRILxCD1, APRILxBCMA, APRILxCD19, APRILxCD38, CS1xCD38, CD79AxBCMA, CD79AxCD1, CD79AxCD19, CD79AxCD38, CD79AxCD38,

CD79A $\times$ APRIL, CD79A $\times$ CD79B, CD79B $\times$ BCMA, CD79B $\times$ CS1, CD79B $\times$ CD19, CD79B $\times$ CD38, CD79B $\times$ APRIL, CD79B $\times$ CD79A, CD138 $\times$ BCMA, CD138 $\times$ CS1, CD138 $\times$ CD19, CD138 $\times$ CD38, CD138 $\times$ APRIL, CD138 $\times$ CD79A, CD138 $\times$ CD79B, CD138 $\times$ BCMA, and CD138 $\times$ CS1.

22. The CAR-T cell as recited in claim 21, wherein the CAR(s) specifically bind(s) two different targets chosen from: CD2 $\times$ CD3 ϵ , CD2 $\times$ CD4, CD2 $\times$ CD5, CD2 $\times$ CD7, CD3 ϵ $\times$ CD4, CD3 ϵ $\times$ CD5, CD3 ϵ $\times$ CD7, CD4 $\times$ CD5, CD4 $\times$ CD7, CD5 $\times$ CD7, TRAC $\times$ CD2, TRAC $\times$ CD3 ϵ , TRAC $\times$ CD4, TRAC $\times$ CD5, TRAC $\times$ CD7, TCR β $\times$ CD2, TCR β $\times$ CD3 ϵ , TCR β $\times$ CD4, TCR β $\times$ CD7, CD2 $\times$ CD3 ϵ , CD2 $\times$ CD4, CD2 $\times$ CD5, CD2 $\times$ CD7, CD3 ϵ $\times$ CD4, CD3 ϵ $\times$ CD5, CD3 ϵ $\times$ CD7, CD4 $\times$ CD5, CD4 $\times$ CD7, CD5 $\times$ CD7, TRAC $\times$ CD2, TRAC $\times$ CD3 ϵ , TRAC $\times$ CD4, TRAC $\times$ CD5, TRAC $\times$ CD7, TCR β $\times$ CD2, TCR β $\times$ CD3 ϵ , TCR β $\times$ CD4, TCR β $\times$ CD5, and TCR β $\times$ CD7.
23. The CAR-T cell as recited in claim 21, wherein the CAR(s) specifically bind(s) two different targets chosen from: BCMA $\times$ CS1, BCMA $\times$ CD19, BCMA $\times$ CD38, CS1 $\times$ CD19, CD19 $\times$ CD38, APRIL $\times$ CS1, APRIL $\times$ BCMA, APRIL $\times$ CD19, APRIL $\times$ CD38, CS1 $\times$ CD38, CD79A $\times$ BCMA, CD79A $\times$ CS1, CD79A $\times$ CD19, CD79A $\times$ CD38, CD79A $\times$ CD38, CD79A $\times$ APRIL, CD79A $\times$ CD79B, CD79B $\times$ BCMA, CD79B $\times$ CS1, CD79B $\times$ CD19, CD79B $\times$ CD38, CD79B $\times$ APRIL, CD79B $\times$ CD79A, CD138 $\times$ BCMA, CD138 $\times$ CS1, CD138 $\times$ CD19, CD138 $\times$ CD38, CD138 $\times$ APRIL, CD138 $\times$ CD79A, CD138 $\times$ CD79B, CD138 $\times$ BCMA, and CD138 $\times$ CS1.
24. The CAR-T cell as recited in claim 21, wherein the CAR(s) specifically bind(s) two different targets chosen from: CD123 $\times$ CD371, CD123 $\times$ CLEC12A, CD123 $\times$ CD117, CD123 $\times$ FLT3, CD123 $\times$ CD7, CD123 $\times$ Tim3, CD371 $\times$ CLEC12A, CD371 $\times$ CD117, CD371 $\times$ FLT3, CD371 $\times$ CD7, CD371 $\times$ Tim3, CLEC12A $\times$ CD117, CLEC12A $\times$ FLT3, CLEC12A $\times$ CD7, CLEC12A $\times$ Tim3, CD117 $\times$ FLT3, CD117 $\times$ CD7, CD117 $\times$ Tim3, FLT3 $\times$ CD7, FLT3 $\times$ Tim3, and CD7 $\times$ Tim3.
25. A dual CAR-T cell as recited in any of claims 21-24.
26. A tandem CAR-T cell as recited in any of claims 21-34.
27. The CAR-T cell as recited in any of claims 1-26, wherein the CAR-T cell further comprises a suicide gene.

28. The CAR-T cell as recited in any of claims 1-26, wherein endogenous T cell receptor mediated signaling is blocked in the CAR-T cell.
29. The CAR-T cell as recited in any of claims 1-26, wherein the CAR-T cells do not induce alloreactivity or graft-versus-host disease.
30. The CAR-T cell as recited in any of claims 1-26, wherein the CAR-T cells do not induce fratricide.
31. A dual or tandem chimeric antigen receptor (dCAR or tCAR) targeting two or more plasma cell antigens.
32. The CAR as recited in claim 31, wherein the plasma cell antigen(s) is/are chosen from BCMA, CS1, CD38, CD79A, CD79B, CD138, and CD19.
33. The CAR as recited in claim 32, 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.
34. The CAR as recited in any of claims 31-33, wherein the CAR is a dCAR.
35. The CAR as recited in any of claims 31-33, wherein the CAR is a tCAR.
36. A dual or tandem chimeric antigen receptor (dCAR or tCAR) targeting two or more leukemia cell antigens.
37. The CAR as recited in claim 36, wherein the plasma cell antigen(s) is/are chosen from CD123, CLEC12A, CD117, FLT3, CD7 and Tim3.
38. The CAR as recited in claim 37, wherein the CAR(s) specifically bind(s) two different targets chosen from: CD123xCD371, CD123xCLEC12A, CD123xCD117, CD123xFLT3, CD123xCD7, CD123xTim3, CD371xCLEC12A, CD371xCD117, CD371xFLT3, CD371xCD7, CD371xTim3, CLEC12AxCD117, CLEC12AxFIT3, CLEC12AxCD7, CLEC12AxDim3, CD117xFLT3, CD117xCD7, CD117xDim3, FLT3xCD7, FLT3xDim3, and CD7xDim3.
39. The CAR as recited in any of claims 36-38, wherein the CAR is a dCAR.

40. The CAR as recited in any of claims 36-38, wherein the CAR is a tCAR.
41. A tandem chimeric antigen receptor (tCAR) targeting two or more T-cell antigens.
42. The tCAR as recited in claim 41, wherein the T-cell antigens chosen from CD5, CD7, CD2, CD4, and CD3.
43. The tCAR as recited in claim 42, targeting a pair of (i.e., two) antigens.
44. The tCAR as recited in claim 43, 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.
45. The tCAR as recited in claim 43, wherein the antigen pair is chosen from CD2xCD3 ϵ , CD2xCD4, CD2xCD5, CD2xCD7, CD3 ϵ xCD4, CD3 ϵ xCD5, CD3 ϵ xCD7, CD4xCD5, CD4xCD7, and CD5xCD7.
46. The tCAR as recited in any of claims 35 and 40-45, wherein the CAR construct is a linear tCAR construct.
47. The tCAR as recited in claim 46, wherein the linear tCAR construct comprises a first heavy (V_H) chain variable fragment and a first light (V_L) chain variable fragment, designated V_H1 and V_L1, joined by a (GGGGS)₂₋₆ linker to a second light (V_L) chain variable fragment and a first heavy (V_H) chain variable fragment, designated V_L2 and V_H2.
48. The tCAR as recited in claim 46, wherein the linear tCAR construct comprises a first heavy (V_H) chain variable fragment and a first light (V_L) chain variable fragment, designated V_H2 and V_L2, joined by a (GGGGS)₂₋₆ linker to a second light (V_L) chain variable fragment and a first heavy (V_H) chain variable fragment, designated V_H1 and V_L1.
49. The tCAR as recited in claim 46, wherein the linear tCAR construct comprises a first light (V_L) chain variable fragment and a first heavy (V_H) chain variable fragment, designated V_L1 and V_H1, joined by a (GGGGS)₂₋₆ linker to a second heavy (V_H) chain variable fragment and a first light (V_L) chain variable fragment, designated V_H2 and V_L2.
50. The tCAR as recited in claim 46, wherein the linear tCAR construct comprises a first light (V_L) chain variable fragment and a first heavy (V_H) chain variable fragment, designated V_L2

- and V_{H2}, joined by a (GGGGS)₂₋₆ linker to a second heavy (V_H) chain variable fragment and a first light (V_L) chain variable fragment, designated V_{H1} and V_{L1}.
51. The tCAR as recited in claim 46, wherein the linear tCAR construct comprises a structure chosen from 7-I to 7-XXXII.
52. The tCAR as recited in any of claims 35 and 40-45, wherein the CAR construct is a hairpin tCAR construct.
53. The tCAR as recited in claim 52, wherein the hairpin tCAR construct comprises a first heavy (V_H) chain variable fragment derived from a first scFv, and a second heavy (V_H) chain variable fragment derived from a second scFv, designated V_{H1} and V_{H2}, joined by a (GGGGS)₂₋₆ linker to a first light (V_L) chain variable fragment derived from the second scFv, and a second light (V_L) chain variable fragment derived from the first scFv, designated V_{L2} and V_{L1}.
54. The tCAR as recited in claim 52, wherein the hairpin tCAR construct comprises a second heavy (V_H) chain variable fragment derived from a second scFv, and a first heavy (V_H) chain variable fragment derived from a first scFv, designated V_{H2} and V_{H1}, joined by a (GGGGS)₂₋₆ linker to a first light (V_L) chain variable fragment derived from the first scFv, and a second light (V_L) chain variable fragment derived from the second scFv, designated V_{L1} and V_{L2}.
55. The tCAR as recited in claim 52, wherein the hairpin tCAR construct comprises a first light (V_L) chain variable fragment derived from a first scFv, and a second light (V_L) chain variable fragment derived from a second scFv, designated V_{L1} and V_{L2}, joined by a (GGGGS)₂₋₆ linker to a first heavy (V_H) chain variable fragment derived from the first scFv, and a second heavy (V_H) chain variable fragment derived from the second scFv, designated V_{H2} and V_{H1}.
56. The tCAR as recited in claim 52, wherein the hairpin tCAR construct comprises a second light (V_L) chain variable fragment derived from a second scFv, and a first light (V_L) chain variable fragment derived from a first scFv, designated V_{L2} and V_{L1}, joined by a (GGGGS)₂₋₆ linker to a first heavy (V_H) chain variable fragment derived from the first scFv, and a second light heavy (V_H) variable fragment derived from the second scFv, designated V_{H1} and V_{H2}.
57. The tCAR as recited in claim 52, wherein the hairpin tCAR construct comprises a structure chosen from 9-I to 9-XXXII.

58. The tCAR as recited in any of claims 35 and 40-45, wherein the CAR construct is a hairpin DSB tCAR construct with a (Cys=Cys) Double-Stranded Bond (DSB) in the linker.
59. The tCAR as recited in claim 58, wherein the hairpin tCAR construct comprises a first heavy (V_H) chain variable fragment derived from a first scFv, and a second heavy (V_H) chain variable fragment derived from a second scFv, designated V_{H1} and V_{H2} , joined by a (GGGGS)₀₋₁-(GGGGC)₁-(GGGGS)₁₋₂-(GGGGP)₁-(GGGGS)₂₋₃-(GGGGC)₁-(GGGGS)₀₋₁ linker to a first light (V_L) chain variable fragment derived from the second scFv, and a second light (V_L) chain variable fragment derived from the first scFv, designated V_{L2} and V_{L1} .
60. The tCAR as recited in claim 58, wherein the hairpin tCAR construct comprises a second heavy (V_H) chain variable fragment derived from a second scFv, and a first heavy (V_H) chain variable fragment derived from a first scFv, designated V_{H2} and V_{H1} , joined by a (GGGGS)₀₋₁-(GGGGC)₁-(GGGGS)₁₋₂-(GGGGP)₁-(GGGGS)₂₋₃-(GGGGC)₁-(GGGGS)₀₋₁ linker to a first light (V_L) chain variable fragment derived from the first scFv, and a second light (V_L) chain variable fragment derived from the second scFv, designated V_{L1} and V_{L2} .
61. The tCAR as recited in claim 58, wherein the hairpin tCAR construct comprises a first light (V_L) chain variable fragment derived from a first scFv, and a second light (V_L) chain variable fragment derived from a second scFv, designated V_{L1} and V_{L2} , joined by a (GGGGS)₀₋₁-(GGGGC)₁-(GGGGS)₁₋₂-(GGGGP)₁-(GGGGS)₂₋₃-(GGGGC)₁-(GGGGS)₀₋₁ linker to a first heavy (V_H) chain variable fragment derived from the first scFv, and a second heavy (V_H) chain variable fragment derived from the second scFv, designated V_{H2} and V_{H1} .
62. The tCAR as recited in claim 58, wherein the hairpin tCAR construct comprises a second light (V_L) chain variable fragment derived from a second scFv, and a first light (V_L) chain variable fragment derived from a first scFv, designated V_{L2} and V_{L1} , joined by a (GGGGS)₀₋₁-(GGGGC)₁-(GGGGS)₁₋₂-(GGGGP)₁-(GGGGS)₂₋₃-(GGGGC)₁-(GGGGS)₀₋₁ linker to a first heavy (V_H) chain variable fragment derived from the first scFv, and a second light heavy (V_H) variable fragment derived from the second scFv, designated V_{H1} and V_{H2} .
63. The tCAR as recited in claim 58, wherein the hairpin DSB tCAR construct comprises a structure chosen from 11-I to 11-XXXII.

64. The tCAR as recited in any of claims 41-63, 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.
65. The tCAR as recited in claim 64, wherein each of the V_H and V_L chains is different and displays at least 95% sequence identity to an amino acid sequence chosen from SEQ ID NO:12 to SEQ ID NO:31.
66. The tCAR as recited in claim 64, wherein each of the V_H and V_L chains is different and displays at least 98% sequence identity to an amino acid sequence chosen from SEQ ID NO:12 to SEQ ID NO:31.
67. The tCAR as recited in claim 64, 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.
68. The tCAR as recited in any of claims 35, 39, and 41-67, comprising at least one costimulatory domain chosen from CD28 and 4-1BB.
69. The tCAR as recited in claim 68, wherein the costimulatory domain is CD28.
70. The tCAR as recited in any of claims 35 and 40-69, comprising a CD3 ζ signaling domain.
71. The tCAR as recited in any of claims 41-63 and 68-70, wherein the each of the V_H and V_L chains is derived from an scFv recognizing CD2 or an scFv recognizing CD3.
72. The tCAR as recited in claim 64, wherein the tCAR construct is chosen from Clone 5, Clone 6, Clone 7, Clone 8, Clone 13, Clone 14, Clone 15, and Clone 16.
73. The tCAR as recited in claim 64, wherein the tCAR construct displays at least 95% sequence identity to an amino acid sequence chosen from SEQ ID NO:41 to SEQ ID NO:46.
74. A tandem chimeric antigen receptor (CAR) T cell (tCAR-T cell), which comprises a tCAR targeting two or more T-cell antigens, as recited in any of claims 35 and 40-73.
75. The tCAR-T cell as recited in claim 74, wherein the cell is deficient in one or more antigens to which the one or more CARs specifically binds.
76. The tCAR-T cell as recited in either of claims 74 and 75, wherein the tCAR-T cell is deficient in a subunit of the T cell receptor complex.
77. The tCAR-T cell as recited in claim 76, wherein the subunit of the T cell receptor complex is chosen from TCR α (TRAC), TCR β , TCR δ , TCR γ , CD3 ϵ , CD3 γ , CD3 δ , and CD3 ζ .
78. The tCAR-T cell as recited in claim 77, wherein the subunit of the T cell receptor complex is chosen from TCR α (TRAC) and CD3 ϵ .

79. The tCAR-T cell as recited in claim 78, wherein the subunit of the T cell receptor complex is TRAC.
80. The tCAR-T cell as recited in any of claims 35 and 40-79, wherein the CAR-T cell further comprises a suicide gene.
81. The tCAR-T cell as recited in any of claims 35 and 40-80, wherein endogenous T cell receptor mediated signaling is blocked in the CAR-T cell.
82. The tCAR-T cell as recited in any of claims 35 and 40-81, wherein the CAR-T cells do not induce alloreactivity or graft-versus-host disease.
83. The tCAR-T cell as recited in any of claims 35 and 40-82, wherein the CAR-T cells do not induce fratricide.
84. A tandem CAR-T cell having a CAR targeting CD2 and CD3, wherein the CAR-T cell is deficient in a subunit of the T cell receptor complex and is deficient in CD2.
85. The CAR-T cell as recited in claim 85, wherein the CAR displays at least 95% sequence identity to an amino acid sequence chosen from SEQ ID NO:41 to SEQ ID NO:44.
86. The CAR-T cell as recited in claim 85, wherein the CAR displays at least 98% sequence identity to an amino acid sequence chosen from SEQ ID NO:41 to SEQ ID NO:44.
87. The CAR-T cell as recited in claim 85, wherein the CAR is an amino acid sequence chosen from SEQ ID NO:41 to SEQ ID NO:44.
88. A tandem CAR-T cell having a CAR targeting CD2 and CD7, wherein the CAR-T cell is deficient in a subunit of the T cell receptor complex and is deficient in CD2 and CD7.
89. The CAR-T cell as recited in claim 88, wherein the CAR displays at least 95% sequence identity to an amino acid sequence chosen from SEQ ID NO:45 to SEQ ID NO:46.
90. The CAR-T cell as recited in claim 88, wherein the CAR displays at least 98% sequence identity to an amino acid sequence chosen from SEQ ID NO:45 to SEQ ID NO:46.
91. The CAR-T cell as recited in claim 88, wherein the CAR is an amino acid sequence chosen from SEQ ID NO:45 to SEQ ID NO:46.
92. A CAR-T cell, which comprises a chimeric antigen receptor (CAR) targeting CD7, wherein the CAR-T cell is deficient in TRAC and deficient in CD7, and comprises a CD28 costimulatory domain and a CD3 ζ signaling domain.
93. The CAR-T cell as recited in claim 92, wherein the CAR displays at least 95% sequence identity to an amino acid sequence chosen from SEQ ID NO:32 to SEQ ID NO:39.

94. The CAR-T cell as recited in claim 92, wherein the CAR displays at least 98% sequence identity to an amino acid sequence chosen from SEQ ID NO:32 to SEQ ID NO:39.
95. The CAR-T cell as recited in claim 92, wherein the CAR is an amino acid sequence chosen from SEQ ID NO:32 to SEQ ID NO:39.
96. A therapeutic composition comprising a population of CAR-T cells as recited in any of any of claims 1-30 and 74-95, or comprising a population of CAR-T cells comprising CAR(s) as recited in any of claims 31-73, and at least one therapeutically acceptable carrier and/or adjuvant.
97. A method of treatment of cancer in a patient comprising administering 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 1-30 and 74-95, or comprising a population of CAR-T cells comprising CAR(s) as recited in any of claims 31-73, to a patient in need thereof.
98. The method as recited in claim 97, wherein the cancer is a hematologic malignancy.
99. The method as recited in claim 98, wherein the hematologic malignancy is a T-cell malignancy.
100. The method as recited in claim 99, wherein the T cell malignancy is T-cell acute lymphoblastic leukemia (T-ALL).
101. The method as recited in claim 99, wherein the T cell malignancy is non-Hodgkin's lymphoma.
102. The method as recited in claim 99, wherein the T cell malignancy is T-cell chronic lymphocytic leukemia (T-CLL).
103. The method as recited in claim 98, wherein the hematologic malignancy is multiple myeloma.
104. The method as recited in claim 98, wherein the hematologic malignancy is acute myeloid leukemia (AML).