

WHAT IS CLAIMED IS:

1. Use of a therapeutically effective amount of an engineered T cell having substantially suppressed surface expression of endogenous CD7 and expressing an anti-CD7 chimeric antigen receptor (CAR) in the preparation of a medicament for the treatment of T-cell acute lymphoblastic leukemia (T-ALL) or early T-cell progenitor acute lymphoblastic leukemia (ETP-ALL) in a patient in need thereof, wherein the medicament is to be administered to said patient, thereby treating T-ALL or ETP-ALL in the patient in need thereof,

wherein said engineered T cell comprises:

i) a nucleic acid comprising a nucleotide sequence encoding a first single chain variable fragment (scFv) that specifically binds to CD7 linked to an intracellular localizing domain,

wherein said first scFv comprises:

a heavy chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:1 and a light chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:2,

a heavy chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:14 and a light chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:15, or

a heavy chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:16 and a light chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:17, and

wherein said localizing domain comprises an endoplasmic reticulum (ER) retention sequence comprising an amino acid sequence of SEQ ID NO:8; and

wherein said first scFv linked to said intracellular localizing domain intracellularly retains endogenous CD7 in said engineered T cell; and

ii) a nucleic acid comprising a nucleotide sequence encoding said anti-CD7 chimeric antigen receptor (CAR), wherein said CAR comprises a 4-1BB intracellular signaling domain, a CD3 ζ intracellular signaling domain, and a second scFv that specifically binds to CD7.

2. The use of claim 1, wherein said 4-1BB intracellular signaling domain comprises an amino acid sequence of SEQ ID NO:3 and wherein the CD3 ζ intracellular signaling domain comprises an amino acid sequence of SEQ ID NO:4.

3. The use of claim 1 or 2, wherein said CAR further comprises a hinge and transmembrane domain.
4. The use of claim 3, wherein said hinge and transmembrane domain comprises an amino acid sequence of SEQ ID NO:10.
5. The use of any one of claims 1 to 4, wherein said second scFv comprises a heavy chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:1 and a light chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:2; said second scFv comprises a heavy chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:14 and a light chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:15; or said second scFv comprises a heavy chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:16 and a light chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:17.
6. The use of any one of claims 1 to 5, wherein said engineered T cell is to be administered to said patient by intravenous infusion, intra-arterial infusion, intraperitoneal infusion, direct injection into tumor and/or perfusion of tumor bed after surgery, implantation at a tumor site in an artificial scaffold, or intrathecal administration.
7. An engineered immune cell comprising
 - i) a target-binding molecule linked to a localizing domain, wherein said target-binding molecule is a first antibody that specifically binds to CD7; and
 - ii) a chimeric antigen receptor (CAR), wherein said CAR comprises a 4-1BB intracellular signaling domain, a CD3 ζ intracellular signaling domain, and a second antibody that specifically binds to CD7.
8. The engineered immune cell of claim 7, wherein said first antibody that specifically binds to CD7 is a first single chain variable fragment (scFv) and/or wherein said second antibody that specifically binds to CD7 is a second single chain variable fragment (scFv).

9. The engineered immune cell of claim 7 or 8, wherein said first and/or second single chain variable fragment (scFv) comprises a heavy chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:1 and a light chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:2.
10. The engineered immune cell of any one of claims 7 to 9, wherein said first and/or second single chain variable fragment (scFv) comprises a heavy chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:14 and a light chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:15.
11. The engineered immune cell of any one of claims 7 to 10, wherein said first and/or second single chain variable fragment (scFv) comprises a heavy chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:16 and a light chain variable domain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:17.
12. The engineered immune cell of any one of claims 7 to 11, wherein said localizing domain comprising an amino acid sequence selected from the group consisting of an endoplasmic reticulum (ER) retention sequence, a Golgi retention sequence, a proteasome localizing sequence, and a transmembrane domain sequence derived from CD8 α , CD8 β , 4-1BB, CD28, CD34, CD4, Fc ϵ RI γ , CD16, OX40, CD3 ζ , CD3 ϵ , CD3 γ , CD3 δ , TCR α , CD32, CD64, VEGFR2, FAS, or FGFR2B.
13. The engineered immune cell of claim 12, wherein said localizing domain comprises an endoplasmic reticulum (ER) retention sequence comprising an amino acid sequence of SEQ ID NO:8 or SEQ ID NO:9.
14. The engineered immune cell of claim 12 or 13, wherein said localizing domain comprises transmembrane domain sequence derived from CD8 α hinge and transmembrane domain sequence comprising an amino acid sequence of SEQ ID NO:13.

15. The engineered immune cell of any one of claims 7 to 14, wherein the 4-1BB intracellular signaling domain comprises an amino acid sequence of SEQ ID NO:3 and wherein the CD3 ζ intracellular signaling domain comprises an amino acid sequence of SEQ ID NO:4.
16. The engineered immune cell of any one of claims 7 to 15, wherein said CAR further comprises a hinge and transmembrane domain, preferably said hinge and transmembrane domain comprises an amino acid sequence of SEQ ID NO:10.
17. The engineered immune cell of claim 16, wherein said hinge and transmembrane domain comprises an amino acid sequence of SEQ ID NO:10.
18. The engineered immune cell of any one of claims 7 to 17, wherein the engineered cell is an engineered T cell, an engineered natural killer (NK) cell, an engineered NK/T cell, an engineered monocyte, an engineered macrophage, or an engineered dendritic cell.
19. A pharmaceutical composition comprising the engineered immune cell of any one of claims 7 to 18 and a pharmaceutically acceptable carrier.
20. A method of producing the engineered immune cell of any one of claims 7 to 18, the method comprising:
- i) introducing into an immune cell
 - a) a first nucleic acid comprising a nucleotide sequence encoding a target-binding molecule linked to a localizing domain, wherein said target-binding molecule is a first antibody that specifically binds to CD7; and
 - b) a second nucleic acid comprises a nucleotide sequence encoding a CAR, wherein said CAR comprises a 4-1BB intracellular signaling domain, a CD3 ζ intracellular signaling domain, and a second antibody that specifically binds to CD7; and
 - ii) isolating the engineered immune cell comprising said target-binding molecule linked to said localizing domain and said CAR, thereby producing said engineered immune cell.