

CLAIMS:

1. A method of preparing an isolated population of genetically modified T-cells having an improved engraftment fitness, comprising:
 - (a) obtaining a population of T-cells comprising a chimeric antigen receptor (CAR), wherein the population of T-cells comprises CD4+ T-cells or CD8+ T-cells;
 - (b) contacting the population of T-cells with exogenous IL-2; and
 - (c) contacting the population of T-cells with an exogenous combination of IL-7 and IL-21, wherein step (b) is performed before step (c), so as to obtain said genetically modified T-cells having an improved engraftment fitness.
2. The method of claim 1, wherein step (a) further comprises separating a CD8+ population of T-cells or a CD4+ population of T-cells from a mixed population of T-cells by affinity selection for T-cells having an epitope present on CD8 or CD4.
3. The method of claim 2, wherein the separating is performed by flow cytometry.
4. The method of claim 2, wherein the separating is performed by immuno-magnetic selection.
5. The method of claim 1, wherein the population of genetically modified T-cells comprise at least one receptor that promotes, induces, contributes to, or enhances engraftment fitness selected from CD27, CD28, or CD62L.
6. The method of claim 1, wherein step (a) further comprises stimulating the population of T-cells by contacting the population of T-cells with an antibody-bound support comprising an antibody selected from an anti-TCR antibody, an anti-CD2 antibody, an anti-CD3 antibody, an anti-CD4 antibody, or an anti-CD28 antibody.
7. The method of claim 1, wherein step (a) further comprises transducing the population of T cells with a vector comprising a first sequence encoding a leader sequence, a

second sequence encoding a ligand binding domain, a third sequence encoding a signaling domain and a fourth sequence encoding a selectable marker.

8. The method of claim 7, wherein the vector is a viral vector.
9. The method of claim 8, wherein the viral vector is derived from a simian virus 40, an adenovirus, an adeno-associated virus (AAV), a lentivirus, or a retrovirus.
10. The method of claim 8, wherein the viral vector is a lentivirus vector.
11. The method of claim 1, wherein the IL-2, IL-7 or IL-21 comprises a recombinant cytokine.
12. The method of claim 1, wherein the IL-2, IL-7, or IL-21 is provided within a range from 0.1 ng/mL to 1.0 ng/mL, or within a range from 10 U/mL to 100 U/mL.
13. The method of claim 1, wherein the IL-2, IL-7, or IL-21 is provided at 0.5 ng/mL or 50 U/mL.
14. The method of claim 1, wherein the contacting is performed for a period within a range from 1 day to 20 days.
15. The method of claim 1, wherein the method is performed with isolated, purified, or separated CD4⁺ T-cells in the absence of or substantially depleted of CD8⁺ T-cells.
16. The method of claim 1, wherein the method is performed with isolated, purified, or separated CD8⁺ T-cells in the absence of or substantially depleted of CD4⁺ T-cells.
17. The method of claim 1, wherein the CD4⁺ T-cells are propagated for a period within a range from 1 day to 20 days.

18. The method of claim 1, wherein the CD8⁺ T-cells are propagated for a period within a range from 1 day to 20 days.
19. The method of claim 1, wherein the CAR comprises a ligand binding domain comprising FMC63 or an antigen binding portion thereof.
20. The method of claim 1, wherein the CAR comprises a ligand binding domain specific for CD19.
21. The method of claim 1, wherein the method further comprises cryopreserving the genetically modified T-cells.
22. The method of claim 1, wherein the population of T-cells comprises a precursor T cell.
23. The method of claim 22, wherein the precursor T cell is a hematopoietic stem cell.
24. A population of genetically modified T-cells having improved engraftment fitness, wherein the population is prepared according to the method of any one of claims 1-22, and wherein the population of T-cells comprise at least one receptor that promotes, enhances, improves or contributes to engraftment fitness.
25. A pharmaceutical composition for human therapy, comprising:
 - a pharmaceutical excipient; and
 - the population of genetically modified T-cells of claim 24.
26. The pharmaceutical composition of claim 25 comprising a population of genetically modified CD4⁺ T-cells and a population of genetically modified CD8⁺ T-cells mixed in a 1:1 ratio.
27. The pharmaceutical composition of claim 25 for use in treatment, inhibition or amelioration of a disorder in a subject.

28. The pharmaceutical composition of claim 27 adapted for administration to said subject by adoptive cell transfer.
29. The pharmaceutical composition of claim 27, wherein the disorder comprises a leukemia.
30. The pharmaceutical composition of claim 29, wherein the leukemia is a recurrent or chemotherapy refractory CD19+ childhood acute lymphoblastic leukemia (ALL).
31. The pharmaceutical composition of claim 27, wherein the disorder comprises an autoimmune disease.
32. The pharmaceutical composition of claim 27, wherein the disorder comprises a post-HSCT relapse.
33. An *in vitro* method of making an isolated population of genetically modified T-cells having an improved engraftment fitness, comprising:
 - (a) isolating a CD8+ expressing population of T-cells or a CD4+ expressing population of T-cells from a mixed population of isolated T-cells so as to generate an isolated population of T-cells;
 - (b) stimulating the isolated population of T-cells so as to generate a stimulated population of T-cells;
 - (c) transducing the stimulated population of T-cells with a vector encoding a chimeric antigen receptor (CAR), so as to generate a transduced population of T-cells;
 - (d) contacting the transduced population of T-cells with exogenous IL-2; and
 - (e) contacting the transduced population of T-cells with an exogenous combination of IL-7 and IL-21, wherein step (e) is performed subsequent to step (d).
34. The method of claim 33, wherein the transduced population of T-cells is contacted with the exogenous IL-2 for a period of 5 days.