CLAIMS

1. A method of producing T cells comprising

(a) ~~obtaining~~ activating T cells in the presence of anti-CD3 antibody and an anti-CD28 antibody ~~from at least one individual~~,

~~activating the T cells,~~

(b) expanding a first portion of the activated T cells over a plurality of different periods of time ~~of about~~ selected from 1 days to ~~about~~ 15 days after the activating,

(c) culturing the expanded first portion of the activated T cells in (b) in the presence of at least one cytokine and in the absence of antigen presenting cells over a period of ~~over about~~ at least 21 days,

wherein the at least one cytokine is selected from the group consisting of interleukin (IL) 2, IL-7, IL-15, and a combination thereof,

(d) measuring a cytokine response in the cultured T cells in (c) in the absence of continual cytokine stimulation,

(e) comparing the cytokine response in (d) to identify a ~~identifying the~~ period of time from the plurality of different periods of time in (b) that yields a maximum cytokine response in (d), and

(f) expanding a second portion of the activated T cells in (a) for the ~~identified~~ period of time identified in (e) that yields a maximum cytokine response in (d).

2. The method of claim 1, further comprising freezing the expanded first portion of the activated T cells prior to culturing.

3. The method of claim 1 or 2, further comprising thawing the frozen expanded first portion of activated T cells prior to the culturing in (c).

4. The method of any one of claims 1-3, further comprising resting the thawed expanded first portion of the activated T cells prior to the culturing in (c).

~~5. The method of any one of claims 1-4, wherein the T cells are activated by a stimulator comprising anti-CD3 antibody and an anti-CD28 antibody.~~

~~6~~5. The method of claim 4, wherein the resting is carried out for ~~about~~ 2 hours to ~~about~~ 12 hours.

~~7. A method of decreasing cell death of T cells for use in adoptive immunotherapy comprising~~

~~obtaining T cells from at least one healthy donor, patient, or individual,~~

~~activating the T cells,~~

~~expanding the activated T cells for about 3 days to about 5 days after activation,~~

~~collecting the expanded T cells for infusing into the at least one healthy donor, patient, or individual,~~

~~wherein the cell death of the T cells expanded for about 3 to about 5 days is reduced relative to that of activated T cells expanded for about 7 days or more after activation.~~

~~8. The method of claim 7, wherein the expanded T cells are CD4+ and/or CD8+ T cells.~~

~~9. The method of claim 7 or 8, wherein the number of expanded T cells exhibiting a naïve T cells (TN) and/or stem memory T cells (Tscm)/T central memory (Tcm) phenotype is more than that of the activated T cells expanded more than about 7 days after the activation.~~

~~10. A method for producing T cells with improved efficacy for adoptive immunotherapy comprising~~

~~obtaining T cells from at least one healthy donor, patient, or individual,~~

~~activating the T cells,~~

~~expanding the activated T cells for about 3 days to about 5 days after activation,~~

~~collecting the expanded T cells for infusing into the at least one healthy donor, patient, or individual,~~

wherein the efficacy for adoptive immunotherapy of the T cells expanded for about 3 to about 5 days is improved relative to activated T cells expanded for about 7 days or more after activation.

11. The method of claim 10, wherein the T cells are expanded for about 4 days after activation and wherein the efficacy for adoptive immunotherapy of the T cells is greater than that of activated T cells expanded for about 7 days or more after activation.

12. The method of claim 10 or 11, wherein the expanded T cells are CD4+ and/or CD8+ T cells.

13. The method of any one of claims 1-12, further comprising transducing the activated T cells with a viral vector prior to the expanding, wherein the viral vector is a retroviral vector expressing a T cell receptor (TCR).

14. The method of claim 13, wherein the viral vector is a lentiviral vector expressing a TCR.

15. A T cell population produced by the method of any one of claims 1-14.

16. A method for predicting in vivo persistence of T cells in a solid tumor, comprising

thawing cryopreserved T cells expanded for a plurality of expansion times,

resting the thawed T cells in the absence of a cytokine,

seeding the rested T cells,

culturing the seeded T cells for at least one cycle of time,

wherein, at the beginning of the at least one cycle of time, one or more cytokines are added to the culture, and

wherein, at the end of the at least one cycle of time, the added one or more cytokines are depleted,

sampling the cultured T cells at a plurality of time points during the at least one cycle of time,

measuring a cytokine response of the sampled T cells,

identifying an expansion time of the sampled T cells exhibiting a maximum cytokine response from the plurality of expansion times, and

~~formulating the T cells expanded for the identified expansion time into a composition for treating the solid tumor.~~

~~17. The method of claim 16, wherein the T cells are expanded from about 1 day to about 15 days.~~

~~18. The method of claim 16 or 17, wherein the resting is carried out for about 2 hours to about 12 hours.~~

~~19. The method of any one of claims 16-18, wherein each of the at least one cycle of time is 7 days.~~

~~20. The method of claim 19, wherein the at least one cycle of time is three cycles of time.~~

6. The method of any one of claims 1-5, wherein the concentration of IL-2 is from 10 U/ml to 500 U/ml, from 10 U/ml to 450 U/ml, from 10 U/ml to 400 U/ml, from 10 U/ml to 350 U/ml, from 10 U/ml to 300 U/ml, from 10 U/ml to 250 U/ml, from 10 U/ml to 200 U/ml, from 10 U/ml to 150 U/ml, from 10 U/ml to 100 U/ml, from 10 U/ml to 50 U/ml, from 20 U/ml to 40 U/ml, from 25 U/ml to 35 U/ml, or from 30 U/ml to 35 U/ml.

7. The method of any one of claims 1-6, wherein the concentration of IL-7 is from 0.1 ng/ml to 50 ng/ml, from 0.1 ng/ml to 45 ng/ml, from 0.1 ng/ml to 40 ng/ml, from 0.1 ng/ml to 35 ng/ml, from 0.1 ng/ml to 30 ng/ml, from 0.1 ng/ml to 25 ng/ml, from 0.1 ng/ml to 20 ng/ml, from 0.1 ng/ml to 15 ng/ml, from 0.1 ng/ml to 10 ng/ml, from 0.1 ng/ml to 5 ng/ml, from 0.1 ng/ml to 4 ng/ml, from 0.1 ng/ml to 3 ng/ml, from 0.1 ng/ml to 2 ng/ml, from 0.1 ng/ml to 1 ng/ml, or from 0.1 ng/ml to 0.5 ng/ml.

8. The method of any one of claims 1-7, wherein the concentration of IL-15 is from 0.1 ng/ml to 50 ng/ml, from 0.1 ng/ml to 45 ng/ml, from 0.1 ng/ml to 40 ng/ml, from 0.1 ng/ml to 35 ng/ml, from 0.1 ng/ml to 30 ng/ml, from 0.1 ng/ml to 25 ng/ml, from 0.1 ng/ml to 20 ng/ml, from 0.1 ng/ml to 15 ng/ml, from 0.1 ng/ml to 10 ng/ml, from 0.1 ng/ml to 5 ng/ml, from 0.1 ng/ml to 4 ng/ml, from 0.1 ng/ml to 3 ng/ml, from 0.1 ng/ml to 2 ng/ml, from 0.1 ng/ml to 1 ng/ml, or from 0.1 ng/ml to 0.5 ng/ml.

9. The method of any one of claims 1-8, wherein the cytokine response is selected from one or more of increased proliferation, reduced apoptosis, increased population of naïve T cells (T_N) and/or stem memory T cells (T_{scm})/T central memory (T_{cm}), and a combination thereof.

10. The method of any one of claims 1-9, wherein the anti-CD3 antibody and the anti-CD28 antibody each have a concentration of from 0.1 μg/ml to 10.0 μg/ml, 0.1 μg/ml to 8.0 μg/ml, 0.1 μg/ml to 6.0 μg/ml, 0.1 μg/ml to 4.0 μg/ml, 0.1 μg/ml to 2.0 μg/ml, 0.1 μg/ml to 1.0 μg/ml, 0.1 μg/ml to 0.8 μg/ml, 0.1 μg/ml to 0.6 μg/ml, 0.1 μg/ml to 0.5 μg/ml, 0.1 μg/ml to 0.25 μg/ml, 0.2 μg/ml to 0.5 μg/ml, 0.2 μg/ml to 0.3 μg/ml, 0.3 μg/ml to 0.5 μg/ml, 0.3 μg/ml to 0.4 μg/ml, or 0.4 μg/ml to 0.5 μg/ml.

11. The method of any one of claims 1-10, wherein the T cell is a $CD3^+$ $CD8^+$ T cell.

12. The method of any one of claims 1-11, wherein the culturing in (c) is performed for 21 days.

13. The method of any one of claims 1-12, wherein the period of time identified in (e) is about 3 to about 5 days.

14. The method of any one of claims 1-13, wherein the at least one cytokine is IL-15.

15. The method of any one of claims 1-13, wherein the at least one cytokine is IL-2 and IL-15.

16. The method of any one of claims 1-13, wherein the at least one cytokine is IL-7 and IL-15.

17. The method of any one of claims 1-13, wherein the at least one cytokine is IL-7.

18. The method of any one of claims 1-13, wherein the at least one cytokine is IL-7 and IL-2.

19. The method of any one of claims 1-13, wherein the at least one cytokine is IL-2.

20. The method of any one of claims 1-13, wherein the at least one cytokine is IL-2, IL-7 and IL-15.