CLAIMS

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

obtaining a population of CD8+ T cells from a patient or a donor,

determining a % of CD28+ CD8+ T cells in the obtained population,

activating the determined population with anti-CD3 antibody and anti-CD28 antibody, provided that the determined population comprises at least about 50% of CD28+ CD8+ T cells, or

activating the determined population with anti-CD3 antibody in the absence of anti-CD28 antibody, provided that the determined population comprises less than about 50% of CD28+ CD8+ T cells,

transducing the activated T cell population with a viral vector, and

expanding the transduced T cell population,

wherein the transducing and the expanding are carried out in the presence of IL-7 and IL-15.

2. The method of claim 1, wherein the determined population is activated with anti-CD3 antibody and anti-CD28 antibody, provided that the determined population comprises at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% of CD28+ CD8+ T cells.

3. The method of claim 1, wherein the determined population is activated with anti-CD3 antibody in the absence of anti-CD28 antibody, provided that the determined population comprises less than about 45%, less than about 40%, less than about 35%, less than about 30%, less than about 25%, less than about 20%, less than about 15%, less than about 10%, less than about 9%, less than about 8%, less than about 7%, less than about 6%, less than about 5%, less than about 4%, less than about 3%, less than about 2%, or less than about 1% of CD28+ CD8+ T cells.

4. The method of any one of claims 1-3, wherein the concentration of IL-7 is from about 1 ng/ml to 90 ng/ml, about 1 ng/ml to 80 ng/ml, about 1 ng/ml to 70 ng/ml, about 1 ng/ml to 60 ng/ml, about 1 ng/ml to 50 ng/ml, about 1 ng/ml to 40 ng/ml, about 1 ng/ml to 30 ng/ml, about 1 ng/ml to 20 ng/ml, about 1 ng/ml to 15 ng/ml, about 1 ng/ml to 10 ng/ml, about 2 ng/ml to 10 ng/ml, about 4 ng/ml to 10 ng/ml, about 6 ng/ml to 10 ng/ml, or about 5 ng/ml to 10 ng/ml.

5. The method of any one of claims 1-4, wherein the concentration of IL-15 is from about 5 ng/ml to 500 ng/ml, about 5 ng/ml to 400 ng/ml, about 5 ng/ml to 300 ng/ml, about 5 ng/ml to 200 ng/ml, about 5 ng/ml to 150 ng/ml, about 5 ng/ml to 100 ng/ml, about 10 ng/ml to 100 ng/ml, about 20 ng/ml to 100 ng/ml, about 30 ng/ml to 100 ng/ml, about 40 ng/ml to 100 ng/ml, about 50 ng/ml to 100 ng/ml, about 60 ng/ml to 100 ng/ml, about 70 ng/ml to 100 ng/ml, about 80 ng/ml to 100 ng/ml, about 90 ng/ml to 100 ng/ml, about 10 ng/ml to 50 ng/ml, about 20 ng/ml to 50 ng/ml, about 30 ng/ml to 50 ng/ml, or about 40 ng/ml to 50 ng/ml.

6. The method of any one of claims 1-5, wherein the transducing is carried out within a period of from about 1 hour to 120 hours, about 1 hour to 108 hours, about 1 hour to 96 hours, about 1 hour to 72 hours, about 1 hour to 48 hours, about 1 hour to 36 hours, about 1 hour to 24 hours, about 2 hour to 24 hours, about 4 hour to 24 hours, about 6 hour to 24 hours, about 8 hour to 24 hours, about 10 hour to 24 hours, about 12 hour to 24 hours, about 14 hour to 24 hours, about 16 hour to 24 hours, about 18 hour to 24 hours, about 20 hour to 24 hours, or about 22 hour to 24 hours.

7. The method of any one of claims 1-6, wherein the viral vector is a retroviral vector expressing a T cell receptor (TCR).

8. The method of any one of claims 1-7, wherein the viral vector is a lentiviral vector expressing a TCR.

9. The method of any one of claims 1-8, wherein the expanding is carried out within a period of from about 1 day to about 30 days, about 1 day to about 25 days, about 1 day to about 20 days, about 1 day to about 15 days, about 1 day to about 10 days, about 2 days to about 10 days, about 3 days to about 10 days, about 4 days to about 10 days, about 5 days to about 10 days, about 6 days to about 10 days, about 7 days to about 10 days, about 8 days to about 10 days, or about 9 days to about 10 days.

10. The method of any one of claims 1-9, wherein the activating comprises immobilizing the T cells with the anti-CD3 antibody and/or the anti-CD28 antibody on a solid phase support.

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

12. The method of any one of claims 1-11, wherein the activation is carried out within a period of from about 1 hour to about 120 hours, about 1 hour to about 108 hours, about 1 hour to about 96 hours, about 1 hour to about 84 hours, about 1 hour to about 72 hours, about 1 hour to about 60 hours, about 1 hour to about 48 hours, about 1 hour to about 36 hours, about 1 hour to about 24 hours, about 2 hours to about 24 hours, about 4 hours to about 24 hours, about 6 hours to about 24 hours, about 8 hours to about 24 hours, about 10 hours to about 24 hours, about 12 hours to about 24 hours, about 12 hours to about 72 hours, about 24 hours to about 72 hours, about 6 hours to about 48 hours, about 24 hours to about 48 hours, about 6 hours to about 72 hours, or about 1 hours to about 12 hours.

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

obtaining a population of CD8+ T cells from a patient or a donor,

isolating CD28+ CD8+ T cells from the obtained population,

wherein the isolated cells comprise at least 50% of CD28+ CD8+ T cells,

activating the isolated cells with anti-CD3 antibody and anti-CD28 antibody,

transducing the activated T cell population with a viral vector, and

expanding the transduced T cell population,

wherein the transducing and the expanding are carried out in the presence of IL-7 and IL-15.

14. The method of claim 13, wherein the isolated cells comprise at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% of CD28+ CD8+ T cells.

15. The method of claim 13 or 14, wherein the concentration of IL-7 is from about 1 ng/ml to 90 ng/ml, about 1 ng/ml to 80 ng/ml, about 1 ng/ml to 70 ng/ml, about 1 ng/ml to 60 ng/ml, about 1 ng/ml to 50 ng/ml, about 1 ng/ml to 40 ng/ml, about 1 ng/ml to 30 ng/ml, about 1 ng/ml to 20 ng/ml, about 1 ng/ml to 15 ng/ml, about 1 ng/ml to 10 ng/ml, about 2 ng/ml to 10 ng/ml, about 4 ng/ml to 10 ng/ml, about 6 ng/ml to 10 ng/ml, or about 5 ng/ml to 10 ng/ml.

16. The method of any one of claims 13-15, wherein the concentration of IL-15 is from about 5 ng/ml to 500 ng/ml, about 5 ng/ml to 400 ng/ml, about 5 ng/ml to 300 ng/ml, about 5 ng/ml to 200 ng/ml, about 5 ng/ml to 150 ng/ml, about 5 ng/ml to 100 ng/ml, about 10 ng/ml to 100 ng/ml, about 20 ng/ml to 100 ng/ml, about 30 ng/ml to 100 ng/ml, about 40 ng/ml to 100 ng/ml, about 50 ng/ml to 100 ng/ml, about 60 ng/ml to 100 ng/ml, about 70 ng/ml to 100 ng/ml, about 80 ng/ml to 100 ng/ml, about 90 ng/ml to 100 ng/ml,

about 10 ng/ml to 50 ng/ml, about 20 ng/ml to 50 ng/ml, about 30 ng/ml to 50 ng/ml, or about 40 ng/ml to 50 ng/ml.

17. The method of any one of claims 13-16, wherein the transducing is carried out within a period of from about 1 hour to 120 hours, about 1 hour to 108 hours, about 1 hour to 96 hours, about 1 hour to 72 hours, about 1 hour to 48 hours, about 1 hour to 36 hours, about 1 hour to 24 hours, about 2 hour to 24 hours, about 4 hour to 24 hours, about 6 hour to 24 hours, about 8 hour to 24 hours, about 10 hour to 24 hours, about 12 hour to 24 hours, about 14 hour to 24 hours, about 16 hour to 24 hours, about 18 hour to 24 hours, about 20 hour to 24 hours, or about 22 hour to 24 hours.

18. The method of any one of claims 13-17, wherein the viral vector is a retroviral vector expressing a T cell receptor (TCR).

19. The method of any one of claims 13-18, wherein the viral vector is a lentiviral vector expressing a TCR.

20. The method of any one of claims 13-19, wherein the expanding is carried out within a period of from about 1 day to about 30 days, about 1 day to about 25 days, about 1 day to about 20 days, about 1 day to about 15 days, about 1 day to about 10 days, about 2 days to about 10 days, about 3 days to about 10 days, about 4 days to about 10 days, about 5 days to about 10 days, about 6 days to about 10 days, about 7 days to about 10 days, about 8 days to about 10 days, or about 9 days to about 10 days.