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 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 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 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 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 45%, less than 40%, less than 35%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10%, less than 9%, less than 8%, less than 7%, less than 6%, less than 5%, less than 4%, less than 3%, less than 2%, or less than 1% of CD28+ CD8+ T cells.

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

ng/ml to 15 ng/ml, 1 ng/ml to 10 ng/ml, 2 ng/ml to 10 ng/ml, 4 ng/ml to 10 ng/ml, 6 ng/ml to 10 ng/ml, or 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 5 ng/ml to 500 ng/ml, 5 ng/ml to 400 ng/ml, 5 ng/ml to 300 ng/ml, 5 ng/ml to 200 ng/ml, 5 ng/ml to 150 ng/ml, 5 ng/ml to 100 ng/ml, 10 ng/ml to 100 ng/ml, 20 ng/ml to 100 ng/ml, 30 ng/ml to 100 ng/ml, 40 ng/ml to 100 ng/ml, 50 ng/ml to 100 ng/ml, 60 ng/ml to 100 ng/ml, 70 ng/ml to 100 ng/ml, 80 ng/ml to 100 ng/ml, 90 ng/ml to 100 ng/ml, 10 ng/ml to 50 ng/ml, 20 ng/ml to 50 ng/ml, 30 ng/ml to 50 ng/ml, or 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 1 hour to 120 hours, 1 hour to 108 hours, 1 hour to 96 hours, 1 hour to 72 hours, 1 hour to 48 hours, 1 hour to 36 hours, 1 hour to 24 hours, 2 hour to 24 hours, 4 hour to 24 hours, 6 hour to 24 hours, 8 hour to 24 hours, 10 hour to 24 hours, 12 hour to 24 hours, 14 hour to 24 hours, 16 hour to 24 hours, 18 hour to 24 hours, 20 hour to 24 hours, or 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 1-6, 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 1 day to 30 days, 1 day to 25 days, 1 day to 20 days, 1 day to 15 days, 1 day to 10 days, 2 days to 10 days, 3 days to 10 days, 4 days to 10 days, 5 days to 10 days, 6 days to 10 days, 7 days to 10 days, 8 days to 10 days, or 9 days to 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 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.

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