

CLAIMS

1. A method for producing a CD3-positive T cell, comprising step (I) of culturing ~~a~~the CD3-positive T cell in the presence of a CD3/TCR complex agonist, fibronectin or ~~a variant thereof~~RetroNectin, and a CD30 agonist.

~~2. The method according to claim 1, further comprising, and~~ step (II) of culturing the CD3-positive T cell cultured in step (I) in the absence of a CD3/TCR complex agonist and fibronectin or RetroNectin~~a variant thereof~~, and in the presence of a CD30 agonist.

~~23.~~ The method according to claim 1 ~~or 2~~, wherein the CD3-positive T cell is derived from a pluripotent stem cell.

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~~34.~~ The method according to claim ~~23~~, wherein the pluripotent stem cell is an iPS cell.

~~45.~~ The method according to any one of claims 1 to ~~34~~, wherein the CD3-positive T cell is a chimeric antigen receptor-expressing CD3-positive T cell.

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~~56.~~ The method according to any one of claims 1 to ~~45~~, wherein the CD3-positive T cell is a CD3-positive CD8-positive T cell.

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~~67.~~ The method according to claim ~~56~~, wherein the CD3-positive CD8-positive T cell is a CD3-positive CD8-positive CD4-negative T cell.

~~78.~~ The method according to any one of claims 1 to ~~67~~, wherein the CD3-positive T cell is a γ TCR-positive and/or δ TCR-positive T cell.

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~~89.~~ The method according to any one of claims 1 to ~~78~~, wherein the CD3/TCR complex agonist is a CD3 agonist and/or a TCR agonist.

~~910.~~ The method according to claim ~~89~~, wherein the CD3 agonist is an anti-CD3 agonist antibody or a binding fragment thereof.

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~~1011.~~ The method according to claim ~~910~~, wherein the anti-CD3 agonist antibody or a binding fragment thereof is an anti-CD3 agonist antibody or a binding fragment thereof produced from UCHT1 clone.

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~~1112.~~ The method according to claim ~~89~~, wherein the TCR agonist is at least one selected from the group consisting of an anti-TCR antibody

or a binding fragment thereof, an HLA/peptide complex or a multimer thereof, and an HLA/superantigen complex or a multimer thereof.

1213. The method according to claim ~~910~~ or ~~1011~~, wherein the anti-CD3 agonist antibody or a binding fragment thereof is immobilized on a culture container.

1314. The method according to claim ~~1213~~, wherein the anti-CD3 agonist antibody or a binding fragment thereof is immobilized by contacting 1 ng/ml - 50000 ng/ml of the anti-CD3 agonist antibody or a binding fragment thereof with the culture container.

~~15. The method according to any one of claims 1 to 14, wherein the fibronectin or a variant thereof is RetroNectin (registered trade mark).~~

1416. The method according to any one of claims 1 to 13~~claim 15~~, wherein the RetroNectin ~~(registered trade mark)~~ is immobilized on the culture container.

1517. The method according to claim ~~1416~~, wherein the RetroNectin ~~(registered trade mark)~~ is immobilized by contacting 1 - 150 µg/mL of the RetroNectin ~~(registered trade mark)~~ with the culture container.

1618. The method according to any one of claims 1 to ~~1517~~, wherein the CD30 agonist is at least one selected from the group consisting of an anti-CD30 agonist antibody or a binding fragment thereof and a CD30 ligand or a binding fragment thereof.

1719. The method according to claim ~~1618~~, wherein the anti-CD30 agonist antibody or a binding fragment thereof is contained in a~~the~~ medium.

1820. The method according to claim ~~1719~~, wherein a concentration of the anti-CD30 agonist antibody or a binding fragment thereof in the medium of 1 ng/ml - 1000 ng/ml.

1921. The method according to any one of claims 1 to ~~1820~~, wherein the medium comprises at least one selected from IL-7, IL-15, IL-18 and IL-21.

2022. The method according to claim ~~1921~~, wherein the medium comprises IL-7, IL-15, IL-18 and IL-21.

~~2123~~. The method according to claim ~~1921~~ or ~~2022~~, wherein the medium further comprises TL1A and/or IL-12.

5 ~~2224~~. The method according to any one of claims 1 to ~~2123~~, wherein the CD3-positive T cell produced is further CD197-positive.

~~25. A CD3-positive cell obtained by the method according to any one of claims 1 to 24.~~

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~~2326~~. A method for expansion culture of a CD3-positive T cell, comprising a step (I) of culturing the CD3-positive T cell in the presence of a CD3/TCR complex agonist, fibronectin or RetroNectin-a-variant thereof, and a CD30 agonist, and step (II) of culturing the
15 CD3-positive T cell cultured in step (I) in the absence of a CD3/TCR complex agonist and fibronectin or RetroNectin, and in the presence of a CD30 agonist.

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~~27. A kit for expansion culture of a CD3-positive cell, comprising the following:-~~

- ~~(1) a culture container in which a CD3/TCR complex agonist, and fibronectin or a variant thereof are immobilized, and~~
- ~~(2) a medium comprising a CD30 agonist.~~

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~~28. A method for maintaining a CD3-positive cell as a CD3-positive CD197-positive cell, comprising a step of stimulating a CD30 signal in the CD3-positive cell.~~

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~~29. The method according to claim 28, wherein the CD3 positive cell is a CD3 positive CD8 positive cell.~~

~~30. The method according to claim 29, wherein the CD3 positive CD8 positive cell is a CD3 positive CD8 positive CD4 negative cell.~~

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~~31. The method according to any one of claims 28 to 30, wherein the medium used in the step of stimulation comprises at least one selected from IL-7, IL-15, IL-18 and IL-21.~~

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~~32. The method according to claim 31, wherein the medium used in the step of stimulation comprises IL-7, IL-15, IL-18 and IL-21.~~

~~33. The method according to claim 31 or 32, wherein the medium used in the step of stimulation further comprises TL1A and/or IL-12.~~

~~34. A kit for maintaining a CD3-positive cell as a CD3-positive CD197-positive cell, comprising a CD30 agonist.~~

~~35. A chimeric antigen receptor comprising an antigen binding domain, a transmembrane domain and an intracellular signal transduction domain, wherein the intracellular signal transduction domain comprises a CD30 intracellular signal transduction domain or a mutant thereof.~~

~~36. A nucleic acid comprising a polynucleotide encoding the chimeric antigen receptor according to claim 35.~~

~~37. A chimeric antigen receptor expression vector comprising the nucleic acid according to claim 36.~~

~~38. A chimeric antigen receptor-expressing cell comprising the chimeric antigen receptor expression vector according to claim 37.~~

~~39. The cell according to claim 38, wherein the chimeric antigen receptor expression cell is a CD3-positive cell.~~

~~40. A medicament comprising the cell according to claim 38 or 39.~~

~~41. The medicament according to claim 40 for use in the prophylaxis or treatment of a tumor expressing an antigen recognized by the chimeric antigen receptor according to claim 35.~~

~~42. An agent for killing a cell expressing an antigen recognized by the chimeric antigen receptor according to claim 35, wherein the agent comprises the cell according to claim 38 or 39.~~

~~43. The cell according to claim 38 or 39 for use in the prophylaxis or treatment of a tumor expressing an antigen recognized by the chimeric antigen receptor according to claim 35.~~

~~44. Use of the cell according to claim 38 or 39 in producing an agent for the prophylaxis or treatment of a tumor expressing an antigen recognized by the chimeric antigen receptor according to claim 35.~~

~~45. A method for preventing or treating a tumor expressing an antigen recognized by the chimeric antigen receptor according to claim 35, comprising administering the cell according to claim 38 or 39.~~