

CLAIMS

1. An *in vitro* or *ex vivo* method of activating/proliferating T cells, comprising a step of contacting a cell population
5 containing T cells with a nucleic acid delivery carrier and at least one kind of T cell activating ligand, wherein the nucleic acid delivery carrier has the T cell activating ligand added to a surface thereof.
- 10 2. The method according to claim 1, wherein the aforementioned T cell activating ligand includes an antibody to CD3 and/or an antibody to CD28.
3. The method according to claim 1, wherein the aforementioned
15 nucleic acid delivery carrier has two or more kinds of T cell activating ligands added to the surface thereof.
4. The method according to claim 1, wherein the aforementioned nucleic acid delivery carrier is a lipid nanoparticle or a
20 liposome.
5. The method according to claim 1, wherein the aforementioned nucleic acid delivery carrier comprises, in its inside, a nucleic acid that suppresses expression of a T cell activation
25 inhibitory factor and/or a nucleic acid encoding a T cell activation promoting factor,
wherein the T cell activation inhibitory factor is selected from CTLA-4, PD-1, TIM-3, LAG-3, TIGIT, BTLA, VISTA(PD-1H), CD160, Cbl-b and endogenous TCR, and
30 wherein the T cell activation promoting factor is selected from CD28, ICOS, CD137, OX40, CD27, GITR, BAFR, TACI, BCMA and CD40L.

6. The method according to claim 1, wherein the aforementioned nucleic acid delivery carrier comprises a nucleic acid encoding CAR or TCR.

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7. The method according to claim 1, wherein the nucleic acid delivery carrier contains a nucleic acid inside, and wherein the nucleic acid is delivered into T cells.

10 8. The method according to claim 7, wherein the aforementioned T cell activating ligand includes an antibody to CD3 and/or an antibody to CD28.

9. The method according to claim 7, wherein the aforementioned
15 nucleic acid delivery carrier has two or more kinds of T cell activating ligands added to a surface thereof.

10. The method according to claim 7, wherein the aforementioned nucleic acid delivery carrier is a lipid nanoparticle or a
20 liposome.

11. The method according to claim 7, wherein the aforementioned nucleic acid comprises a nucleic acid suppressing expression of a T cell activation inhibitory factor and/or a nucleic acid
25 encoding a T cell activation promoting factor,
wherein the T cell activation inhibitory factor is selected from CTLA-4, PD-1, TIM-3, LAG-3, TIGIT, BTLA, VISTA(PD-1H), CD160, Cbl-b and endogenous TCR, and
wherein the T cell activation promoting factor is selected from
30 CD28, ICOS, CD137, OX40, CD27, GITR, BAFFR, TACI, BCMA and CD40L.

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12. An *in vitro* or *ex vivo* method of delivering a nucleic acid into T cells, comprising a step of contacting a cell population containing T cells simultaneously with at least one kind of T cell activating ligand, and a nucleic acid delivery carrier containing a nucleic acid inside, wherein the nucleic acid delivery carrier is free of a T cell activating ligand added to a surface thereof.
13. The method according to claim 12, wherein the aforementioned T cell activating ligand includes an antibody to CD3 and/or an antibody to CD28.
14. The method according to claim 12, wherein two or more kinds of T cell activating ligands are contacted.
15. The method according to claim 12, wherein the aforementioned nucleic acid delivery carrier is a lipid nanoparticle or a liposome.
16. The method according to claim 12, wherein the aforementioned nucleic acid includes a nucleic acid suppressing expression of a T cell activation inhibitory factor and/or a nucleic acid encoding a T cell activation promoting factor, wherein the T cell activation inhibitory factor is selected from CTLA-4, PD-1, TIM-3, LAG-3, TIGIT, BTLA, VISTA(PD-1H), CD160, Cbl-b and endogenous TCR, and wherein the T cell activation promoting factor is selected from CD28, ICOS, CD137, OX40, CD27, GITR, BAFFR, TACI, BCMA and CD40L.
17. The method according to claim 12, wherein the aforementioned nucleic acid comprises a nucleic acid encoding CAR or TCR.

18. An *in vitro* or *ex vivo* method of producing a medicament comprising T cells, comprising a step of contacting a cell population containing T cells simultaneously with at least one
5 kind of T cell activating ligand, and a nucleic acid delivery carrier containing a nucleic acid inside, wherein the nucleic acid delivery carrier is free of a T cell activating ligand added to a surface thereof.
- 10 19. The method according to claim 18, wherein the aforementioned T cell activating ligand includes an antibody to CD3 and/or an antibody to CD28.
20. The method according to claim 18, wherein two or more kinds
15 of T cell activating ligands are contacted.
21. The method according to claim 18, wherein the aforementioned nucleic acid delivery carrier is a lipid nanoparticle or a liposome.
- 20 22. The method according to claim 18, wherein the aforementioned nucleic acid delivery carrier comprises a nucleic acid suppressing expression of a T cell activation inhibitory factor and/or a nucleic acid encoding a T cell
25 activation promoting factor,
wherein the T cell activation inhibitory factor is selected from CTLA-4, PD-1, TIM-3, LAG-3, TIGIT, BTLA, VISTA(PD-1H), CD160, Cbl-b and endogenous TCR, and
wherein the T cell activation promoting factor is selected from
30 CD28, ICOS, CD137, OX40, CD27, GITR, BAFFR, TACI, BCMA and CD40L.
23. The method according to claim 18, wherein the aforementioned nucleic acid comprises a nucleic acid encoding
35 CAR or TCR.

24. A cell culture when used in a method according to any one of claims 12 to 23, comprising a cell population containing T cells, at least one kind of T cell activating ligand, a nucleic acid delivery carrier without a T cell activating ligand added to a surface thereof, and a medium.

25. A composition when used in a method according to any one of claims 12 to 23, comprising at least one kind of T cell activating ligand, and a nucleic acid delivery carrier without a T cell activating ligand added to a surface thereof.

26. A kit when used in a method according to any one of claims 12 to 23, comprising at least one kind of T cell activating ligand, and a nucleic acid delivery carrier without a T cell activating ligand added to a surface thereof.