

CLAIMS

1. An *in vitro* or *ex vivo* method of activating/proliferating T cells, and delivering a nucleic acid into T cells, comprising a
5 step of contacting a cell population containing T cells non-treated for activation 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.
- 15 3. The method according to claim 1, wherein the aforementioned 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
20 nucleic acid delivery carrier is a lipid nanoparticle or a liposome.
5. The method according to claim 1, wherein the aforementioned nucleic acid delivery carrier comprises, in its inside, a
25 nucleic acid that suppresses 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),
30 CD160, Cbl-b and endogenous TCR, and
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
5 CAR or TCR.

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.

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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.

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

11. The method according to claim 7, wherein the aforementioned
nucleic acid delivery carrier comprises a nucleic acid
25 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),
30 CD160, Cbl-b and endogenous TCR, and

wherein the T cell activation promoting factor is selected from
CD28, ICOS, CD137, OX40, CD27, GITR, BAFTR, 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
5 containing T cells non-treated for activation 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.

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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.

15 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
20 nanoparticle or a liposome.

16. The method according to claim 12, wherein the aforementioned nucleic acid delivery carrier includes a nucleic acid suppressing expression of a T cell activation inhibitory
25 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.

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17. The method according to claim 12, wherein the
aforementioned nucleic acid delivery carrier comprises a
5 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 non-treated for activation
10 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.

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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 20. The method according to claim 18, wherein two or more kinds
of T cell activating ligands are contacted.

21. The method according to claim 18, wherein the
aforementioned nucleic acid delivery carrier is a lipid
25 nanoparticle or a liposome.

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
30 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
35 wherein the T cell activation promoting factor is selected from

CD28, ICOS, CD137, OX40, CD27, GITR, BAFFR, TACI, BCMA and CD40L.

23. The method according to claim 18, wherein the
5 aforementioned nucleic acid delivery carrier comprises a
nucleic acid encoding 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
10 cells non-treated for activation, 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
15 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
20 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.