

Claims

1. A production method of a dopaminergic neuron(s), comprising
subjecting floor plate cells to the following step (1):
- 5 (1) a step of culturing in a medium containing (i) a cAMP
analogue and (ii) a MEK inhibitor.
2. The production method according to claim 1, wherein the
medium is a medium further containing ascorbic acid or a salt
10 thereof.
3. The production method according to claim 2, wherein the
medium is a medium further containing an activator of activin
receptor-like kinase-4,7.
- 15 4. The production method according to claim 1, wherein the cAMP
analogue is dibutyryl-cAMP.
5. The production method according to claim 1, wherein the MEK
20 inhibitor is
- (i)
N-[(2R)-2,3-dihydroxypropoxy]-3,4-difluoro-2-[(2-fluoro-4-iodo-
phenyl)amino]benzamide,
- (ii)
25 2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluor
obenzamide, or
- (iii) 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-
methyl-1H-pyrrole-3-propanoic acid.
- 30 6. The production method according to claim 3, wherein the
activator of activin receptor-like kinase-4,7 is activin.
7. The production method according to claim 3, wherein the cAMP
analogue is dibutyryl-cAMP,
- 35 the MEK inhibitor is

(i)

N-[(2R)-2,3-dihydroxypropoxy]-3,4-difluoro-2-[(2-fluoro-4-iodo-phenyl)amino]benzamide,

(ii)

5 2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide, or

(iii) 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-1H-pyrrole-3-propanoic acid, and

the activator of activin receptor-like kinase-4,7 is activin.

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8. A medicament comprising a dopaminergic neuron(s) obtained by the production method according to claim 1.

9. A reagent for producing a dopaminergic neuron(s) from floor
15 plate cells, comprising

(i) a cAMP analogue and (ii) a MEK inhibitor.

10. A kit for producing a dopaminergic neuron(s) from floor
plate cells, comprising (i) a cAMP analogue and (ii) a MEK
20 inhibitor.

11. Use of (i) a cAMP analogue and (ii) a MEK inhibitor for producing a dopaminergic neuron(s) from floor plate cells.

Claims

1. A production method of a dopaminergic neuron, comprising culturing floor plate cells in a medium containing (i) a cAMP analogue
5 and (ii) a MEK inhibitor.

2. The production method according to claim 1, wherein the medium further contains ascorbic acid or a salt thereof.

10 3. The production method according to claim 2, wherein the medium further contains an activator of activin receptor-like kinase-4,7.

4. The production method according to any one of claims 1 to 3, wherein the cAMP analogue is dibutyryl-cAMP.
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5. The production method according to any one of claims 1 to 4, wherein the MEK inhibitor is
(i)
N-[(2R)-2,3-dihydroxypropoxy]-3,4-difluoro-2-[(2-fluoro-4-iodo-phenyl)am
20 ino]benzamide,
(ii)
2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamid
e, or
(iii) 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-1H-
25 pyrrole-3-propanoic acid.

6. The production method according to any one of claims 3 to 5, wherein the activator of activin receptor-like kinase-4,7 is activin.

30 7. The production method according to claim 3, wherein the cAMP analogue is dibutyryl-cAMP,
the MEK inhibitor is
(i)
N-[(2R)-2,3-dihydroxypropoxy]-3,4-difluoro-2-[(2-fluoro-4-iodo-phenyl)am
35 ino]benzamide,

(ii)

2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide, or

(iii) 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-1H-

5 pyrrole-3-propanoic acid, and

the activator of activin receptor-like kinase-4,7 is activin.

8. A reagent for producing a dopaminergic neuron from floor plate cells, comprising

10 (i) a cAMP analogue and (ii) a MEK inhibitor.

9. The reagent according to claim 8, further comprising (iii) an activator of activin receptor-like kinase-4,7.

15 10. A kit for producing a dopaminergic neuron from floor plate cells, comprising (i) a cAMP analogue and (ii) a MEK inhibitor.

11. The kit according to claim 10, further comprising (iii) an activator of activin receptor-like kinase-4,7.

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12. Use of (i) a cAMP analogue and (ii) a MEK inhibitor for producing a dopaminergic neuron from floor plate cells.

13. Use of (i) a cAMP analogue, (ii) a MEK inhibitor and (iii)
25 an activator of activin receptor-like kinase-4,7 for producing a dopaminergic neuron from floor plate cells.