WHAT IS CLAIMED IS:

1. An in vitro or ex vivo method of producing induced pluripotent stem cells from mammalian non-pluripotent cells, the method comprising, contacting the cells with at least one of: an agent that inhibits H3K9 methylation or promotes H3K9 demethylation; an L-type Ca channel agonist; an activator of the cAMP pathway; DNA methyltransferase (DNMT) inhibitor; a nuclear receptor ligand; a GSK3 inhibitor; a MEK inhibitor; a TGFβ receptor/ALK5 inhibitor; a HDAC inhibitor; and an erk inhibitor, thereby producing induced pluripotent stem cells.

2. The method of claim 1, comprising introducing one or more exogenous polypeptides selected from the group consisting of: a Klf polypeptide, an Oct polypeptide, a Myc polypeptide, and/or a Sox polypeptide into the non-pluripotent cells.

3. An in vitro or ex vivo method of producing induced pluripotent stem cells from mammalian non-pluripotent cells, the method comprising, a) introducing one or more exogenous polypeptides selected from the group consisting of: an Oct polypeptide, a Klf polypeptide, a Myc polypeptide, and a Sox polypeptide into the non-pluripotent cells; b) contacting the non-pluripotent cells with an agent that inhibits H3K9 methylation or promotes H3K9 demethylation, thereby producing induced pluripotent stem cells.

4. The method of claim 3, wherein step a) comprises:

(i) at least two cycles of contacting the non-pluripotent cells with one or more exogenous polypeptides selected from the group consisting of: a Klf polypeptide, an Oct polypeptide, a Myc polypeptide, and a Sox polypeptide; followed by culturing the cells in the absence of the exogenous polypeptides; or

(ii) contacting the non-pluripotent cells with an exogenous Oct polypeptide and an exogenous Sox polypeptide.

5. The method of claim 3, wherein the non-pluripotent cells are somatic cells.

6. The method of claim 3, wherein the non-pluripotent cells are progenitor cells.

7. The method of claim 3, wherein the induced pluripotent stem cells are differentiated into a desired cell type.

8. The method of claim 3, wherein the agent that inhibits H3K9 methylation is BIX-01294.

9. A method for screening for agents that induce reprogramming or dedifferentiation of non-pluripotent mammalian cells into pluripotent stem cells, the method comprising,

a) introducing at least one of, but not all of, an exogenous Oct polypeptide, an exogenous Klf polypeptide, an exogenous Myc polypeptide, and an exogenous Sox polypeptide into the non-pluripotent cells;

b) contacting the non-pluripotent cells to a library of different agents;

c) screening the contacted cells for pluripotent stem cell characteristics; and

d) correlating the development of stem cell characteristics with a particular agent from the library, thereby identifying an agent that stimulates dedifferentiation of cells into pluripotent stem cells.

10. The method of claim 9, wherein step (b) comprises contacting cells with a MAPK/ERK kinase (MEK) inhibitor such that growth of non-pluripotent cells is inhibited and growth of pluripotent stem cells is promoted.

11. The method of claim 10, wherein the MEK inhibitor is PD0325901.

12. An in vitro or ex vivo mixture of non-pluripotent mammalian cells and an agent that inhibits H3K9 methylation or promotes H3K9 demethylation, wherein the cells: are in contact with at least one or more of an exogenous Oct polypeptide, an exogenous Klf polypeptide, an exogenous Sox polypeptide, and an exogenous Myc polypeptide.

13. The mixture of claim 12, wherein the agent that inhibits H3K9 methylation is BIX-01294.

14. An in vitro or ex vivo mixture of non-pluripotent mammalian cells and at least one of an agent that inhibits H3K9 methylation or promotes H3K9 demethylation, an L-type Ca channel agonist; an activator of the cAMP pathway; DNA methyltransferase (DNMT) inhibitor; a nuclear receptor ligand; a GSK3 inhibitor; a MEK inhibitor; a TGFβ receptor/ALK5 inhibitor; a HDAC inhibitor; and an erk inhibitor.

15. The mixture of claim 14, wherein one or more exogenous polypeptides selected from the group consisting of: a Klf polypeptide, an Oct polypeptide, a Myc polypeptide, and a Sox polypeptide have been introduced into the non-pluripotent cells.

16. A composition comprising:

(a) at least one of: an agent that inhibits H3K9 methylation; an L-type Ca channel agonist; an activator of the cAMP pathway; DNA methyltransferase (DNMT) inhibitor; a nuclear receptor ligand; a GSK3 inhibitor; a MEK inhibitor; a TGFβ receptor/ALK5 inhibitor; a HDAC inhibitor; and an erk inhibitor; and

(b) one or more polypeptides selected from the group consisting of: a Klf polypeptide, an Oct polypeptide, a Myc polypeptide, and a Sox polypeptide.

17. A kit comprising at least two of: (i) an agent that inhibits H3K9 methylation and (ii) an agent selected from the group consisting of an L-type Ca channel agonist; an activator of the cAMP pathway; DNA methyltransferase (DNMT) inhibitor; a nuclear receptor ligand; a GSK3 inhibitor; a MEK inhibitor; a TGFβ receptor/ ALK5 inhibitor; a HDAC inhibitor; and an erk inhibitor.

THE CLAIMS

1. A method of producing induced pluripotent stem cells from mammalian non-pluripotent cells, the method comprising:

(a) introducing into the mammalian non-pluripotent cells one or more expression cassettes comprising a polynucleotide encoding at least one reprogramming factor polypeptide; and

(b) contacting the mammalian non-pluripotent cells with a GSK3 inhibitor, a MEK inhibitor, and a TGFβ receptor/ALK5 inhibitor;

thereby producing induced pluripotent stem cells.

2. The method of claim 1, wherein the at least one reprogramming factor polypeptide is an Oct polypeptide, a Klf polypeptide, a Sox polypeptide, or a Myc polypeptide.

3. The method of claim 1 or claim 2, wherein the mammalian non-pluripotent cells are somatic cells, or are fibroblast cells.

4. The method of any one of claims 1 to 3, wherein the introducing step is performed *in vitro*.

5. The method of any one of claims 1 to 4, further comprising,

(c) selecting cells that exhibit pluripotent stem cell characteristics.

6. The method of any one of claims 1 to 5, wherein the mammalian non-pluripotent cells are obtained from an animal; and

the induced pluripotent stem cells are differentiated into a desired cell type.

7. The method of any one of claims 1 to 6, wherein the mammalian non-pluripotent cells are human cells, or are progenitor cells.

8. The method of claim 7, wherein the progenitor cells are neural progenitor cells, skin progenitor cells or hair follicle progenitor cells.

9. The method of any one of claims 1 to 8, wherein the at least one reprogramming factor polypeptide is an Oct polypeptide, a Klf polypeptide, and optionally, a Sox polypeptide, or a Myc polypeptide.

10. A method of inducing endogenous Oct4 expression in a cell, the method comprising,

introducing one or more expression cassettes comprising a polynucleotide encoding one or more reprogramming factor polypeptides into the cell and contacting the cell with a GSK3 inhibitor, a MEK inhibitor, and a TGFβ receptor/ALK5 inhibitor, thereby inducing endogenous Oct4 expression in the cell.

11. The method of claim 10, wherein the cell does not endogenously express Oct4 immediately prior to the contacting step.

12. The method of claim 10 or claim 11, wherein the one or more expression cassettes are introduced into a cell that is not a pluripotent cell.

13. The method of any one of claims 10 to 12, wherein the cell is induced to pluripotency after the contacting step.

14. The method of any one of claims 10 to 13, wherein the one or more reprogramming factor polypeptides are selected from an Oct polypeptide, a Klf polypeptide, and a Sox polypeptide.

15. A mixture of mammalian cells and a GSK3 inhibitor, a MEK inhibitor, and a TGFβ receptor/ALK5 inhibitor, wherein one or more expression cassettes comprising a polynucleotide encoding at least one reprogramming factor polypeptide selected from the group consisting of: an Oct polypeptide, a Klf polypeptide, and a Sox polypeptide, are introduced into the cells.

16. The mixture of claim 15, wherein the cells are human cells, or comprise progenitor cells.

17. The mixture of claim 16, wherein the progenitor cells are neural progenitor cells, skin progenitor cells or hair follicle progenitor cells.

18. The mixture of any one of claims 15 to 17, wherein the cells are non-pluripotent cells, or are fibroblast cells.

19. The method of any one of claims 1 to 14, or the mixture of any one of claims 15 to 18, wherein the Klf polypeptide is Klf4.

20. The method of any one of claims 1 to 14 and 19, or the mixture of any one of claims 15 to 19, wherein the Oct polypeptide is Oct4.

21. The method of any one of claims 1 to 14, 19 and 20, or the mixture of any one of claims 15 to 20, wherein the Sox polypeptide is Sox2.

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