Claims

1 A method for preparing an induced pluripotent stem cell by nuclear reprogramming of a somatic cell, which comprises a step of contacting the somatic cell with a nuclear reprogramming factor NRF, the factor comprising one or more of:

(i) a gene product from a retinoic acid receptor (RAR/RXR) family member, or an agonist or antagonist thereof;
(ii) a gene product from an Lrh1 family member; or an agonist thereof;
(iii) retinoic acid or a gene product involved in synthesizing or metabolizing retinoic acid; or an agonist or antagonist thereof ;
(iv) a gene product that is involved in transporting a retinoic acid family member
(v) a polynucleic acid encoding a gene product of any of (i) to (iv) above.

2 A method according to claim 1 wherein the NRF comprises a gene product or a polynucleotide encoding a gene product from a retinoic acid receptor RAR family member and a gene product or a polynucleotide encoding a gene product from an Lrh1 family member.

3 A method according to claim 1 or 2 wherein the NRF comprises the Rarg and Lrh1 gene products or polynucleotides encoding such gene products.

4 A method according to claim 1 comprising a Rarg protein having a C terminal truncation.

5 A method according to any preceding claim wherein the NRF comprises a gene product or a polynucleotide encoding a gene product of an Oct family gene and a Myc family gene or equivalents or substitutes thereof.

6 A method according to claim 5 wherein the NRF additionally comprises a gene product or a polynucleotide encoding a gene product of a Klf family gene.

7 A method according to claim 5 or 6 wherein the NRF additionally includes a gene product or a polynucleotide encoding a gene product of the Sox family.

8 A method according to any preceding claim comprising:

(a) contacting a somatic cell with a NRF which is one or more of:
(i) a gene product from a retinoic acid receptor (RAR/RXR) family member, or an agonist thereof ;

(ii) a gene product from an Lrh1 family member; or an agonist thereof ;

(iii) retinoic acid or a gene product involved in synthesizing or metabolizing a retinoic acid family member; or an agonist or antagonist thereof;

(iv) a gene product that is involved in transporting a retinoic acid family member;

(v) a polynucleic acid encoding a gene product of any of (i) to (iv) above;

; and then

(b) optionally checking to determine if the somatic cell has been reprogrammed, and

(c) contacting the product from step (a) with an antagonist of RA or RAR/RXR family member, or removing contact with the NRF, to maintain pluripotency.

9 A NRF comprising one or more of:

(i) a gene product from a retinoic acid receptor RAR/RXR family member, or an agonist or antagonist thereof ;

(ii) a gene product from an Lrh1 family member; or an agonist or antagonist thereof;

(iii) a gene product of an Lrh1 family member;

(iv) retinoic acid or a gene product involved in synthesizing or metabolizing retinoic acid; or an agonist thereof ;

(v) a gene product that is involved in transporting a retinoic acid family member

(vi) a polynucleic acid encoding a gene product of any of (i) to (iv) above.

10 An NRF according to claim 9 for reprogramming somatic cells into induced pluripotent cells.

11 An NRF according to claim 9 or 10 comprising or encoding at least 2 gene products.

12 An NRF according to claim 11 comprising, or encoding, a gene product from an RAR family member and an Lrh1 family member

13 An NRF according to claim 12 comprising or encoding a gene product from RARG and Lrh1.

14 An NRF according to claims 9 -13 additionally comprising or encoding a gene product from an Oct family gene and a Myc family gene

15 An NRF according to claim 14 additionally comprising or encoding a gene product from a Klf family gene.

16 An NRF according to claim 14 or 15 additionally comprising or encoding a gene product of the Sox family

17 An induced pluripotent stem cell obtained or obtainable by the methods of claim 1- 8.

18. An induced human pluripotent cell characterised by at least one of the following:

- expression of one or more pluripotency markers such as Oct4, Nanog, Rex1
- growth independent of FGF;
- retain a normal karyotype as measured by using spectral karyotyping analysis after passaging;
- capable of forming teratomas when injected into mice;
- demethylation of promoter regions for one, or more of, oct4, nanog or rex1;
- Cells can be dissociated to viable single cells capable of forming secondary colonies;
- proliferation in M15 +hLIF media and/or 2i+LIF media
- Absent or insignificant exogenous reprogramming factor expression.

19 An induced pluripotent stem cell according to claim 17 or 18 wherein the iPS cell comprises an exogenous DNA sequence.

20. An induced pluripotent stem cell according to claim 19 wherein when the exogenous DNA sequence is the sequence of an exogneous reprogramming factor, the exogenous sequence is not expressed.

21 An induced pluripotent stem cell according to claim 17 or 18 wherein the iPS cell does not comprise an exogenous reprogramming factor.

22. An induced pluripotent stem cell according to claim 17 or 18 produced by using an NRF as claimed in claim 15 or claim 16 wherein the iPS cell produced does not have KLF-4 and/ or SOX2 insertion in the chromosome.

23 A somatic cell derived by differentiation of the induced pluripotent stem cell according to any of claims 17 - 22.

24 A tissue, organ or non-human animal comprising a somatic cell derived by differentiation of the induced pluripotent stem cell of claim 17-22.

25 A pharmaceutical composition comprising a nuclear reprogramming factor of claims 9-16, or iPS cell or cell derived therefrom or tissue or organ of claims 17-24, in combination with a pharmaceutically acceptable excipient.

26 Use of a nuclear reprogramming factor of claims 9-16, or iPS cell or cell derived therefrom, or tissue or organ of claims 17-24 in medicine.

27 A method of preventing a disease or treating a disease in a patient in need thereof, the method comprising delivery to the patient a pharmaceutically acceptable amount of one of : a reprogramming factor according to claims 9-16, cell according to claims 17- 23, or tissue or organ according to claim 24, optionally in the form of a pharmaceutical composition according to claim 25.

28 Use of a nuclear reprogramming factor according to claims 9- 16, cell according to claims 17- 23, or tissue or organ according to claim 24, optionally in the form of a pharmaceutical composition according to claim 25, in the preparation of a medicament for the treatment of a patient in need thereof.

29 Method or use of a somatic cell according to claims 27 or claim 28 wherein the somatic cell for reprogramming is obtained from the patient who is intended to be treated.

CLAIMS

1. A thing.