CLAIMS

1. A method of reprogramming human non-pluripotent cells comprising:

introducing into the non-pluripotent cells a plurality of polypeptides, or polynucleotides encoding the plurality of polypeptides, in which the plurality of polypeptides comprise

(i) an OCT4 polypeptide;

(ii) one or more of SOX2, NANOG, KLF, LIN28, MYC, ECAT1, UTF1, ESRRB, and SV40LT; and

(iii) a plurality of different polypeptides selected from the group consisting of HESRG, CDH1, TDGF1, DPPA4, ZIC3, and L1TD1;

thereby reprogramming the non-pluripotent cells to produce pluripotent cells.

2. A method according to Claim 1, in which the one or more polynucleotides are comprised in one or more constructs; and in which the one or more constructs are introduced to the non-pluripotent cells by a vector.

3. A method according to Claim 2, in which the one or more constructs comprises at least one of the following:

(i) at least two OCT4 encoding polynucleotides;

(ii) at least one OCT4 encoding polynucleotide and at least one NANOG encoding polynucleotide;

(iii) at least one OCT4 encoding polynucleotide and at least one ESRRB encoding polynucleotide;

(iv) at least one ECAT1 encoding polynucleotide and at least one UTF1 encoding polynucleotide;

(v) at least one OCT4 encoding polynucleotide, at least one ESRRB encoding polynucleotide, and at least one NANOG encoding polynucleotide;

(vi) one or more polynucleotides encoding at least one of CDH1, ZIC3, and HESRG;

(vii) one or more polynucleotides encoding at least one of L1TD1, DPPA4, and TDGF1; and

(viii) at least one DNMT3B encoding polynucleotide.

4. A method according to Claim 3, in which the one or more constructs comprises:

(a) at least one construct comprising at least one of the following:

(i) at least two OCT4 encoding polynucleotides;

(ii) at least one OCT4 encoding polynucleotide and at least one NANOG encoding polynucleotide;

(iii) at least one OCT4 encoding polynucleotide and at least one ESRRB encoding polynucleotide;

(iv) at least one ECAT1 encoding polynucleotide and at least one UTF1 encoding polynucleotide; or

(v) at least one OCT4 encoding polynucleotide, at least one ESRRB encoding polynucleotide, and at least one NANOG encoding polynucleotide; and

(b) one or more additional constructs comprising at least one of the following:

(i) at least one CDH1 encoding polynucleotide, at least one ZIC3 encoding polynucleotide, and at least one HESRG encoding polynucleotide;

(ii) at least one L1TD1 encoding polynucleotide, at least one DPPA4 encoding polynucleotide, and at least one TDGF1 encoding polynucleotide; or

(iii) at least one DNMT3B encoding polynucleotide.

5. A method according to Claim 4, in which the one or more constructs comprises at least one of the following:

(a) one or more polynucleotides encoding one or more of Nanog, ESRRB and OCT4;

(b) one or more polynucleotides encoding one or both of ECAT1 and UTF1;

(c) one or more polynucleotides encoding one or more of L1TD1, DPPA4 and TDGF1; or

(d) one or more polynucleotides encoding one or more of CDH1, ZIC3, and HESRG.

6. A method according to Claim 4, in which the one or more constructs comprises one or more polynucleotides encoding OCT4, and at least another construct comprises at least one of the following:

(a) polynucleotides encoding L1TD1, DPPA4 and TDGF1; and

(b) polynucleotides encoding CDH1, ZIC3, and HESRG.

7. A method according to Claim 2, in which the vector is a retrovirus, a Sendai virus, an adenovirus, an episome, a plasmid, a mini-circle, a vector system with expression cassette, or an mRNA.

8. A method according to Claim 7, in which the vector is a Sendai virus.

9. A method according to Claim 2, in which the one or more polynucleotides comprised in a construct are linked by at least one self-cleaving polypeptide.

10. A method according to Claim 1, in which the method has at least one of the following characteristics: (i) the non-pluripotent cell is a somatic cell; or (ii) the one or more polypeptides excludes at least one of SOX2, KLF4 and c-Myc.

11. A composition comprising

(i) an OCT4 polypeptide or a polynucleotide encoding the same;

(ii) one or more polypeptides, or exogenous polynucleotides encoding the polypeptides, selected from the group consisting of SOX2, NANOG, KLF, LIN28, MYC, ECAT1, UTF1, ESRRB, SV40LT; and

(iii) a plurality of different polypeptides, or one or more exogenous polynucleotides encoding the plurality of different polypeptides, in which the plurality of different polypeptides is selected from the group consisting of HESRG, CDH1, TDGF1, DPPA4, ZIC3, and L1TD1.

12. A composition according to Claim 11, further comprising a population of human non-pluripotent cells.

13. A composition according to Claim 11, in which the one or more exogenous polynucleotides are comprised in one or more constructs.

14. A composition according to Claim 13, in which the one or more constructs comprise at least one of the following:

(i) one or more polynucleotides encoding one or more polypeptides selected from the group consisting of OCT4, ESRRB, ECAT1, UTF1, and NANOG; and one or more

additional polynucleotides encoding one or more polypeptides selected from the group consisting of CDH1, ZIC3, HESRG, L1TD1, DPPA4, TDGF1, and DNMT3B;

(ii) at least two polynucleotides encoding OCT4;

(iii) at least one OCT4 encoding polynucleotide and at least one NANOG encoding polynucleotide;

(iv) at least one OCT4 encoding polynucleotide and at least one ESRRB encoding polynucleotide;

(v) at least one ECAT1 encoding polynucleotide and at least one UTF1 encoding polynucleotide; and/or

(vi) at least one OCT4 encoding polynucleotide, at least one ESRRB encoding polynucleotide, and at least one NANOG encoding polynucleotide,

in which the one or more constructs optionally do not comprise one or more of SOX2, KLF and c-Myc.

15. A composition according to Claim 13, in which the one or more constructs comprise at least one of the following:

(i) at least one CDH1 encoding polynucleotide, at least one ZIC3 encoding polynucleotide, and at least one HESRG encoding polynucleotide;

(ii) at least one L1TD1 encoding polynucleotide, at least one DPPA4 encoding polynucleotide, and at least one TDGF1 encoding polynucleotide; and/or

(iii) at least one DNMT3B encoding polynucleotide.

16. A composition according to Claim 13, in which the one or more constructs comprise at least one of the following:

(i) at least two OCT4 encoding polynucleotides;

(ii) at least one OCT4 encoding polynucleotide and at least one NANOG encoding polynucleotide;

(iii) at least one OCT4 encoding polynucleotide and at least one ESRRB encoding polynucleotide;

(iv) at least one ECAT1 encoding polynucleotide and at least one UTF1 encoding polynucleotide;

(v) at least one OCT4 encoding polynucleotide, at least one ESRRB encoding polynucleotide, and at least one NANOG encoding polynucleotide;

(vi) one or more polynucleotides encoding at least one of CDH1, ZIC3, and HESRG;

(vii) one or more polynucleotides encoding at least one of L1TD1, DPPA4, and TDGF1; or

(viii) at least one DNMT3B encoding polynucleotide.

17. A composition according to Claim 13, in which the one or more constructs comprise at least one combination from group (a) and at least one combination from group (b):

(a):

(i) at least two OCT4 encoding polynucleotides;

(ii) at least one OCT4 encoding polynucleotide and at least one NANOG encoding polynucleotide;

(iii) at least one OCT4 encoding polynucleotide and at least one ESRRB encoding polynucleotide;

(iv) at least one ECAT1 encoding polynucleotide and at least one UTF1 encoding polynucleotide; or

(v) at least one OCT4 encoding polynucleotide, at least one ESRRB encoding polynucleotide, and at least one NANOG encoding polynucleotide; and,

(b):

(i) at least one CDH1 encoding polynucleotide, at least one ZIC3 encoding polynucleotide, and at least one HESRG encoding polynucleotide;

(ii) at least one L1TD1 encoding polynucleotide, at least one DPPA4 encoding polynucleotide, and at least one TDGF1 encoding polynucleotide; or

(iii) at least one DNMT3B encoding polynucleotide.

18. A composition according to Claim 12, in which the human non-pluripotent cells comprise at least one of the following combinations:

(a) one or more polynucleotides encoding one or more of Nanog, ESRRB and OCT4;

(b) one or more polynucleotides encoding one or more of ECAT1 and UTF1;

(c) one or more polynucleotides encoding one or more of L1TD1, DPPA4 and TDGF1; or

(d) one or more polynucleotides encoding one or more of CDH1, ZIC3, and HESRG.

19. A composition according to Claim 13, in which at least one of the one or more constructs is (i) in a retrovirus, a Sendai virus or an adenovirus; or (ii) in the form of an episome, a plasmid, a mini-circle or an mRNA.

20. A method of reprogramming human non-pluripotent cells comprising:

(a) introducing into the non-pluripotent cells one or more polynucleotides encoding OCT4, and one or more of KLF, SOX2, MYC, NANOG, ECAT1, UTF1, LIN28, SV40LT and ESRRB; and

(b) introducing into the non-pluripotent cells one or more polynucleotides encoding a plurality of different polypeptides selected from the group consisting of L1TD1, DPPA4, TDGF1, CDH1, ZIC3, and HESRG;

thereby obtaining pluripotent cells.

21. A method according to Claim 20, in which the one or more polynucleotides of (a) and (b) are comprised in one or more constructs.

22. A method according to Claim 21, in which the one or more constructs comprise at least one of the following:

(a) one or more polynucleotides encoding one or more of NANOG, ESRRB and OCT4;

(b) one or more polynucleotides encoding one or more of ECAT1 and UTF1;

(c) one or more polynucleotides encoding one or more of L1TD1, DPPA4 and TDGF1; or

(d) one or more polynucleotides encoding one or more of CDH1, ZIC3, and HESRG.

23. A method according to Claim 21, in which at least one construct of the one or more constructs comprises at least two polynucleotides encoding OCT4.

24. A method according to Claim 21, in which the one or more constructs are introduced to the non-pluripotent cells by retrovirus, Sendai virus, adenovirus, episome, plasmid, mini-circle, or mRNA.

25. A method according to Claim 24, in which at least one construct of the one or more constructs is carried by a Sendai virus.

26. A method of reprogramming human non-pluripotent cells using Sendai virus comprising:

(a) introducing into the non-pluripotent cells one or more polynucleotides encoding OCT4, and one or more of KLF, SOX2, MYC, NANOG, , ECAT1, UTF1, LIN28, SV40LT and ESRRB; and

(b) introducing into the non-pluripotent cells one or more polynucleotide encoding a plurality of different polypeptides selected from the group consisting of L1TD1, DPPA4, TDGF1, CDH1, ZIC3, and HESRG;

thereby obtaining pluripotent cells.

27. A method according to Claim 26, in which the one or more polynucleotides of (a) and (b) are introduced by one or more vectors.

28. A method according to Claim 27, in which the one or more vectors comprises a construct comprising:

(a) one or more polynucleotides encoding one or more of Nanog, ESRRB and OCT4;

(b) one or more polynucleotides encoding one or more of ECAT1 and UTF1;

(c) one or more polynucleotides encoding one or more of L1TD1, DPPA4 and TDGF1; or

(d) one or more polynucleotides encoding one or more of CDH1, ZIC3, and HESRG.

29. A method according to Claim 26, in which the one or more polynucleotides of (a) and (b) are introduced via a vector comprising one or more polynucleotides encoding OCT4, and at least one of:

(a) a vector comprising polynucleotides encoding Nanog, ESRRB and OCT4;

(b) a vector comprising polynucleotides encoding ECAT1 and UTF1;

(c) a vector comprising polynucleotides encoding L1TD1, DPPA4 and TDGF1; and

(d) a vector comprising polynucleotides encoding CDH1, ZIC3, and HESRG;

in which the vectors are carried by Sendai virus.

30. A method of reprogramming human non-pluripotent cells using Sendai virus comprising:

(a) introducing into the non-pluripotent cells a polynucleotide encoding OCT4, and one or more of KLF, SOX2, MYC, NANOG, ECAT1, UTF1, LIN28, SV40LT and ESRRB; and

(b) introducing into the non-pluripotent cells one or more constructs comprising

(i) polynucleotides encoding L1TD1, DPPA4 and TDGF1; or

(ii) polynucleotides encoding CDH1, ZIC3, and HESRG;

thereby obtaining pluripotent cells.

31. A method according to Claim 30, comprising introducing into the non-pluripotent cells and at least one of:

(a) a vector comprising polynucleotides encoding Nanog, ESRRB and OCT4;

(b) a vector comprising polynucleotides encoding ECAT1 and UTF1;

(c) a vector comprising polynucleotides encoding L1TD1, DPPA4 and TDGF1; and

(d) a vector comprising polynucleotides encoding CDH1, ZIC3, and HESRG;

in which the vectors are carried by Sendai virus.