Claims

1. A method of determining a potency state of an embryonic stem cell (ESC) in culture comprising:

   a) detecting the expression level of Negative Elongation Factor Complex Member A (Nelfa) in said embryonic stem cell; and

   b) correlating the expression level of Nelfa in said embryonic stem cell with that of a reference sample to determine the potency state of said embryonic stem cell.

2. The method of claim 1 wherein the ESC is a mammalian ESC.

3. The method of claim 2, wherein the mammalian ESC is a human ESC.

4. The method as claimed in any one of claims 1 to 3, wherein the potency state is a totipotent-like state.

5. The method as claimed in any one of claims 1 to 4, wherein an increased level of Nelfa expression relative to the reference sample indicates that said embryonic stem cell has a totipotent-like state.

6. The method as claimed in any one of claims 1 to 5, wherein the expression level of Nelfa is gene expression level, protein expression level or combinations thereof.

7. The method of claim 6, wherein the step of detecting the protein expression level of Nelfa is by immunohistochemistry or flow cytometry.

8. The method of claim 6, wherein the step of detecting the gene expression level of Nelfa comprises:

   a) contacting a nucleic acid sequence obtained or derived from said embryonic stem cell with at least one primer and/or at least one probe for amplification of the Nelfa sequence;

b) amplifying said nucleic acid sequence using said at least one primer and/or said at least one probe, and

c) detecting the gene expression level of Nelfa.

9. The method of claim 8 wherein said amplification step is performed by polymerase chain reaction (PCR).

10. The method of claim 9 wherein said PCR is quantitative RT-PCR.

11. The method as claimed in any one of claims 4 to 10, wherein the totipotent-like state is characterized by the Nelfa induced expression of Zscan4, Tcstv3, Gm4340, MERVL/HERVL family of retrotransposons, gsat_mm, Dux or combinations thereof in said ESC.

12. The method of claim 11, wherein the totipotent-like state is further characterized in that Nelfa acts upstream of Zscan4 and MERVL/HERVL family of retrotransposons in said ESC.

13. The method of claim 11 or 12, wherein the Nelfa induced expression of MERVL/HERVL family of retrotransposons comprises the retrotransposons mt2_mm, Mervl-b4-int, MERVL_gag and Mervl-int.

14. The method as claimed in any one of claims 4 to 13, wherein the totipotent-like state is further characterized by transient nuclear import of NAP1 in said ESC.

15. The method as claimed in any one of claims 4 to 14, wherein the totipotent-like state is further characterized by chromatin decondensation and expression of MERVL/HERVL family of retrotransposons and Zscan4 in said ESC.

16. A method of selecting totipotent-like embryonic stem cells (ESCs) from a population of embryonic stem cells in culture, comprising:

a) providing a population of ESCs that displays a predetermined phenotype when Nelfa is expressed;
b) identifying the ESCs that express the predetermined phenotype; and
c) selecting the ESCs that express the predetermined phenotype.

17. The method of claim 16, wherein the predetermined phenotype is expression of a reporter gene.
18. The method of claim 17, wherein the reporter gene is green fluorescent protein (GFP).

19. A method of selecting totipotent-like embryonic stem cells (ESCs) from a population of embryonic stem cells in culture, comprising:
a) contacting said population of ESCs with an anti-Nelfa antigen binding protein;
b) selecting the ESCs binding to said anti-Nelfa antigen binding protein; and
c) optionally isolating the ESCs from said anti-Nelfa antigen binding protein.

20. The method as claimed in any one of claims 16 to 19, wherein said cells are selected using single cell sorting, fluorescent activated cell sorting or magnetic cell sorting.

21. The method as claimed in any one of claims 19 or 20, wherein the antigen binding protein is selected from the group consisting of a monoclonal antibody, a recombinant antibody, a polyclonal antibody, chimeric, a humanised antibody, a bispecific antibody, a heteroconjugate antibody, a single variable domain, a domain antibody, an antigen binding fragment, an immunologically effective fragment, a single chain Fv, a single chain antibody, a univalent antibody lacking a hinge region, a minibody, a diabody, and a tandem antibody.

22. A method of inducing totipotency in an embryonic stem cell (ESC) in culture, comprising contacting and incubating said ESC with one or more of a metabolic regulator, a small molecule compound, a chemical, a virus, a nucleic acid or a polypeptide, to induce expression of Nelfa.

23. The method of claim 22, wherein the metabolic regulator is selected from the group consisting of metabolites, metabolic intermediates, purines and pyrimidines, fatty acids, metabolic enzyme activators and inhibitors, glycolytic inhibitors, FDA approved drugs, dehydroepiandrosterone, L-buthionine sulfoximine, 3-bromopyruvate, 2-deoxy-D-glucose, dichloroacetate, GW9662, acetate, lactate, glucose, pyruvate, imatinib and amino acids.

24. The method of claim 23, wherein the metabolic regulator is selected from the group consisting of 2-deoxy-D-glucose, 3-bromopyruvate and imatinib.

25. The method of claim 22, wherein the nucleic acid is selected from the group consisting of microRNA, siRNA, RNA and cDNA.

26. Use of a metabolic regulator, a nucleic acid, a small molecule, a chemical, a virus or a polypeptide for inducing totipotency in an embryonic stem cell.

27. A cell comprising an expression vector encoding Nelfa operably linked to a promoter.

28. The cell of claim 27, wherein the cell is an ESC.

29. The cell of claim 28 wherein the ESC is a mammalian ESC.

30. The cell of claim 29, wherein the mammalian ESC is a human ESC.

31. The cell as claimed in any one of claims 27 to 30, wherein the promoter is an inducible promoter.

32. The cell as claimed in any one of claims 27 to 31, wherein the vector further comprises a reporter gene.

33. The cell of claim 32, wherein the reporter gene is selected from streptavidin or green fluorescent protein.

34. A kit comprising at least one of a metabolic regulator, a nucleic acid, a polypeptide, a small molecule, a virus or a chemical when used in the method as claimed in any one of claims 22 to 25.

35. A method of improving the reprogramming efficiency of a somatic cell into an induced pluripotent stem cell (iPSC), comprising contacting and incubating said somatic cell with one or more of a metabolic regulator, a small molecule compound, a chemical, a nucleic acid, a virus or a polypeptide to induce expression of Nelfa.

36. The method of claim 35, wherein the somatic cell is a mouse or human cell.

37. The method of claim 36, wherein the mouse or human cell is selected from the group consisting of an embryonic fibroblast cell, a neonatal foreskin fibroblast cell, a neuronal progenitor and a B-cell.

38. The method as claimed in claims 35 to 37, wherein the improvement of reprogramming efficiency is determined by comparing a preselected phenotype in an iPSC where Nelfa expression was induced to an iPSC where Nelfa expression was not induced, wherein an increased level of expression or increased rate of expression of the preselected phenotype indicates an improvement in reprogramming efficiency.

39. The method of claim 38, wherein the preselected phenotype is selected from the group consisting of pluripotent marker gene expression, surface marker expression, alkaline phosphatase staining and teratoma formation.

40. The method of claim 39, wherein the pluripotent marker gene is Oct4 and/or Nanog.

41. The method of claim 39, wherein the surface marker is selected from the group consisting of SSEA-1, SSEA-4, TRA-1-60, TRA-1-81, CD73, CD49d, CD54 and CD326.

42. A method of reprogramming a somatic cell into a totipotent stem cell comprising contacting and incubating said somatic cell with one or more of a metabolic regulator,

a small molecule compound, a chemical, a nucleic acid, a virus or a polypeptide to induce expression of Nelfa.

5