CLAIMS

1. A process in which a cell of a first type is reprogrammed to a desired cell of a different type that is multipotent or unipotent, the process comprising:

(1) transiently applying at least one reprogramming agent to the cell of a first type, in which the reprogramming agent induces a direct or indirect remodelling of the chromatin and/or DNA and endogenous expression of at least one gene regulator, in which said endogenous expression of the gene regulator is necessary for the existence of the desired cell of a different type;

(2) permitting the stable expression of the gene regulator; and

(3) permitting the stable expression of a plurality of secondary genes, in which the stable expression of the secondary genes is the result of the stable expression of the gene regulator(s), and in which: (i) the stable expression of the plurality of secondary genes is characteristic of the phenotypical and/or functional properties of the desired cell, and (ii) the stable expression of at least one of said secondary genes is not characteristic of phenotypical and functional properties of a totipotent or pluripotent stem cell.

2. A process according to Claim 1, in which:

step (1) comprises placing the cell in conditions for supporting the transformation of the desired cell and maintaining intracellular levels of the reprogramming agent for a sufficient period of time to allow stable expression of the gene regulator in the absence of the reprogramming agent; and

step (3) comprises maintaining the cell in culture conditions supporting the transformation of the desired cell for a sufficient period of time to allow a stable expression of the plurality of secondary genes, whereby at the end of said period of time the cell of the first type has been transformed into the desired cell of a different type.

3. A process according to Claim 1 or 2, further comprising contacting the chromatin and/or DNA of the cell of the first type with an agent capable of remodeling chromatin and/or DNA of said cell, in which the agent capable of remodeling chromatin and/or DNA is selected from the group consisting of histone acetylators, inhibitors of histone deacetylation, DNA demethylators, inhibitors of DNA methylation and combinations thereof.

4. A process according to Claim 1 or 2 in which the desired cell of a different type is then differentiated into a somatic cell.

5. A process according to Claim 1 or 2 in which the unipotent cell is a differentiated cell.

6. A process according to any preceding claim, in which the desired cell of a different type obtained is characterized by a stable repression of a plurality of genes expressed in the first cell type.

7. A process according to any preceding claim, in which the reprogramming agent is selected from the group consisting of Musashi1 (Msi1); Msi1 and Neurogenin 2 (Ngn2); Msi1 and methyl-CpG binding domain protein 2 (MBD2); Ngn2 and MBD2; Msi1, Ngn2 and MBD2; Ascl1; Sox2; Mesp1; T; Sox17; Pdx1; Ngn3; Oct4; FoxD3; Mixl1; nanog; Rex1; Klf4; FoxD3 and Mixl1; Sall4, Oct4, Klf4 and nanog; and Oct4, Klf4 and Sall4.

8. A process according to any preceding claim, in which the reprogramming agent is delivered intracellularly.

9. A process according to any of Claims 2 to 8, in which the desired cell of a different type is selected from the group consisting of: a neural stem-like cell expressing one or more of Nestin, Sox2, GFAP and Msi1; a neural-like cell expressing one or more of βIII-tubulin, Map2b, Synapsin, and ACHE; an ectoderm-like cell expressing one or more of Sox2, Sox1, Zic1, Nestin, Notch 1, FoxJ3, Olx2, Cripto1 and Vimentin; a mesendoderm-like cell expressing one or more of Sox17, FoxA2, CXCR4, GATA4, Mix1 and Eomesodermin; and a pluripotent-like cell expressing one or more of Oct4, SSEA4, TRA-1-60, TRA-1-81 and AP.

10. A process according to any preceding claim, in which the cell of a first type is selected from the group consisting of: germ cells, embryonic stem cells and derivations thereof, adult stem cells and derivatives thereof, progenitor cells and derivatives thereof, cells derived from mesoderm, endoderm or ectoderm, and a cell of mesoderm, endoderm or ectoderm lineage, adipose-derived stem cell, mesenchymal stem cell, hematopoietic stem cell, skin derived precursor cell, hair follicle cell, fibroblast, keratinocyte, epidermal cell, endothelial cell, epithelial cell, granulosa epithelial cell, melanocyte, adipocyte, chondrocyte, hepatocyte, B lymphocyte, T lymphocyte, granulocyte, macrophage, monocyte, mononuclear cell, pancreatic islet cell, sertoli cell, neuron, glial cell, cardiac muscle cell, and other muscle cell.

11. A process according to any preceding claim, in which the desired multipotent or unipotent cell is neural , and in which the reprogramming agent is an expression vector allowing expression of a Musashi1 (Msi1) polypeptide; Musashi1 (Msi1) and Neurogenin 2 (Ngn2) polypeptides; Musashi1 (Msi1) and methyl-CpG binding domain protein 2 (MBD2) polypeptides; Neurogenin 2 (Ngn2) and methyl-CpG binding domain protein 2 (MBD2) polypeptides; or Musashi1 (Msi1), Neurogenin 2 (Ngn2) and methyl-CpG binding domain protein 2 (MBD2) polypeptides.

12. A process according to Claim 11, in which the neural multipotent or unipotent cell so obtained possesses all of the following characteristics:

(i) ability to self-renew or proliferate, except in the case of a terminally differentiated somatic cell;

(ii) is not a cancerous cell;

(iii) is stable and not artificially maintained by forced gene expression or by similar means;

(iv) can differentiate to at least one of a progenitor cell, a precursor cell, a somatic cell and another more differentiated cell type of the same lineage, except if the cell is a terminally differentiated somatic cell;

(v) does not exhibit uncontrolled growth, teratoma formation, and tumour formation *in vivo*.

13. A process according to Claim 11 or 12 in which the cell of the first type is a somatic cell, a progenitor cell or a stem cell.

14. An isolated neural multipotent or unipotent cell obtainable by a process according to any preceding claim in which the reprogramming agent is an expression vector allowing expression of Musashi1 (Msi1), Neurogenin 2 (Ngn2) and methyl-CpG binding domain protein 2 (MBD2) polypeptides, and in which the cell expresses one or more neural stem cell markers selected from the group consisting of Sox2, Nestin, GFAP, Msi1, and Ngn2; expresses at least one neural-specific antigen selected from the group consisting of neural-specific tubulin, microtubule associated protein 2, NCAM, and marker for a neurotransmitter; is not of a totipotent or pluripotent lineage; and does not exhibit tumor or teratoma formation *in vivo*.

15. An isolated multipotent cell obtainable by the process a process according to any of Claims 1 to 13, possessing all of the following characteristics:

(i) expression of at least one marker that is characteristic of a first multipotent cell phenotype and at least one marker that is characteristic of another multipotent or unipotent cell phenotype;

(ii) ability to self-renew for at least two months;

(iii) is not a cancerous cell;

(iv) is stable and not artificially maintained by forced gene expression or by similar means;

(v) can differentiate to at least one of a progenitor, precursor, somatic cell or to another more differentiated cell type of the same lineage; and

(vi) does not exhibit uncontrolled growth, teratoma formation, and tumor formation *in vivo*; and

(vii) is negative for teratoma growth in SCID mice.

16. A cell according to Claim 14 or 15 for use in a method of treatment of disease or to effect regeneration or repair of a tissue or organ or a desired therapeutic characteristic in a patient.

CLAIMS

1. A process for reprogramming a cell of a first type to a desired cell of a different type that is multipotent or unipotent, the cell of a first type being a fibroblast cell, keratinocyte, blood cell or bone marrow cell, the process comprising:

(1) introducing into the cell of a first type an agent capable of remodelling the chromatin and/or DNA of the cells, in which the agent capable of remodelling the chromatin and/or DNA is a histone acetylator, an inhibitor of histone deacetylation, a DNA demethylator, and/or chemical inhibitor of DNA methylation;

(2) transiently increasing intracellular levels of at least one reprogramming agent in the cell of a first type, in which the at least one reprogramming agent increases directly or indirectly the endogenous expression of at least one multipotent or unipotent gene regulator to a level at which the gene regulator is capable of driving transformation of the cell of a first type into the multipotent or unipotent cell;

(3) in which the cell of a first type is maintained in culture conditions supporting the transformation of the cell of a first type to the multipotent or unipotent cell for a sufficient period of time to allow a stable expression of a plurality of secondary genes characteristic of the phenotypical and/or functional properties of the multipotent or unipotent cell, where one or more of the secondary genes is not characteristic of phenotypical and functional properties of an embryonic stem cell and in which stable expression of the plurality of secondary genes occurs in the absence of the reprogramming agent, whereby at the end of said period of time the cell of a first type has been transformed into the multipotent or unipotent cell.

2. A process according to Claim 1, in which step (2) comprises placing the cell in conditions for supporting the transformation of the multipotent or unipotent cell and maintaining intracellular levels of the reprogramming agent for a sufficient period of time to allow stable expression of the gene regulator in the absence of the reprogramming agent.

3. A process according to Claim 1, in which the desired cell is a multipotent or unipotent neural cell.

4. A process according to Claim 1 or 2 in which the desired unipotent or multipotent cell is then differentiated into a somatic cell.

5. A process according to Claim 1, 2 or 3 in which the unipotent cell is a differentiated cell.

6. A process according to any preceding claim, in which the desired unipotent or multipotent cell is characterized by a stable repression of a plurality of genes expressed in the first cell type.

7. A process according to any preceding claim, in which the reprogramming agent is at least one of Musashi1 (Msi1), Neurogenin 2 (Ngn2), Ascl1, Sox2, Mesp1, T, Sox17, Pdx1, Ngn3, Oct4, FoxD3, Mixl1, nanog, Rex1 and Klf4.

8. A process according to any preceding claim, in which the reprogramming agent is delivered intracellularly.

9. A process according to any of Claims 1 to 8, in which the unipotent or multipotent cell is selected from the group consisting of: a neural stem-like cell expressing one or more of Nestin, Sox2, GFAP and Msi1; a neural-like cell expressing one or more of βIII-tubulin, Map2b, Synapsin, and ACHE; an ectoderm-like cell expressing one or more of Sox2, Sox1, Zic1, Nestin, Notch 1, FoxJ3, Olx2, Cripto1 and Vimentin; a mesendoderm-like cell expressing one or more of Sox17, FoxA2, CXCR4, GATA4, Mix1 and Eomesodermin; and a cell expressing one or more of Oct4, SSEA4, TRA-1-60, TRA-1-81 and AP.

10. A process according to any preceding claim, in which the multipotent or unipotent cell so obtained possesses all of the following characteristics:

(i) ability to self-renew or proliferate, except in the case of a terminally differentiated somatic cell;

(ii) is not a cancerous cell;

(iii) is stable and not artificially maintained by forced gene expression or by similar means and may be maintained in standard neural stem cell media;

(iv) can differentiate to at least one of a progenitor cell, a precursor cell, a somatic cell and another more differentiated cell type of the same lineage, except if the cell is a terminally differentiated somatic cell;

(v) does not exhibit uncontrolled growth, teratoma formation, and tumour formation *in vivo*.

11. An isolated neural multipotent or unipotent cell obtainable by a process according to any preceding claim in which the reprogramming agent is an expression vector allowing expression of Musashi1 (Msi1) and/or Neurogenin 2 (Ngn2), and optionally with expression of methyl-CpG binding domain protein 2 (MBD2); and in which the cell expresses one or more neural stem cell markers selected from the group consisting of Sox2, Nestin, GFAP, Msi1, and Ngn2; expresses at least one neural-specific antigen selected from the group consisting of neural-specific tubulin, microtubule associated protein 2, NCAM, and marker for a neurotransmitter; is not of a totipotent or pluripotent lineage; and does not exhibit tumor or teratoma formation *in vivo*; and expresses at least one market characteristic of the cell of a first type.

12. A neural stem-like cell obtainable by a process according to any of Claims 1 to 10, possessing all of the following characteristics:

(i) expression of at least one marker that is characteristic of a first multipotent cell phenotype and at least one marker that is characteristic of another multipotent or unipotent cell phenotype;

(ii) ability to self-renew for at least two months;

(iii) is not a cancerous cell;

(iv) is stable and not artificially maintained by forced gene expression or by similar means;

(v) can differentiate to at least one of a progenitor, precursor, somatic cell or to another more differentiated cell type of the same lineage; and

(vi) does not exhibit uncontrolled growth, teratoma formation, and tumor formation *in vivo*; and

(vii) is negative for teratoma growth in SCID mice.

13. A cell according to Claim 11 or 12 for use in a method of treatment of disease or to effect regeneration or repair of a tissue or organ or a desired therapeutic characteristic in a patient.