Claims:

1. A method for interconversion of cellular phenotypes to desired, multipotent, pluripotent, self-renewing or differentiating cell types, said method comprising selecting a fixed, differentiated or somatic cell and introducing or overexpressing one or more specific transcription factors and/or cell fate determinants.
2. The method of claim 1 comprising introduction of short PRR- Numb and/or Numblike.
3. The method of claim 1 wherein the one or more transcription factors are selected from

    a) Mash1 (Ascl1), or a portion thereof;

    b) MyoD, myogenin, Myf5, Myf6, Mef2, myocardin, Ifrd1, a muscle transcription factor and/or a muscle type specific bHLH-encoding sequence, or a portion thereof;

    c) Foxa2, Sox17, HLXB9, and/or Pdx1, or a portion thereof;

    d) hepatic nuclear factor (HNF)-1, HNF-3, HNF-4, HNF-6, and/or CREB-binding protein, or a portion thereof;

    e) Runx1/AML1 and/or NOV (CCN3), or a portion thereof;

    f) Sox9, CREB-binding protein, Gata6 and/or Runx2, or a portion thereof;

    g) OLIG1, OLIG2, and/or Zfp488, or a portion thereof;

    h) MyoD, myogenin, myocardin, Myf5, Myf6, Mef2A, Gata4, Gata5, and Gata6, or portions thereof;

    i) Gata4, Gata5 and/or Gata6, or a portion thereof;

    j) Myocardin, or a portion thereof;

    k) Myogenin and MyoD, or portions thereof;

    l) Runx2, or a portion thereof;

    m) Mash1 (Ascl1), Ngn2, Nurr1, Lmx1b, and/or Ptx-3, or a portion thereof;

    n) Mash1 (Ascl1), Phox2b, Lmx1b, Nkx2.2, Pet1, Gata2, Gata3, and/or Pet1 or a portion thereof;

    o) Mash1 (Ascl1), Phox2a and/or REST4, or a portion thereof;

p) Mash1 (Ascl1), PITX2, Dlx2, Dlx5, HES1 targeting synthetic oligonucleotides, Phox2a and/or REST4, or portions thereof;

q) Mash1 (Ascl1), Phox2a, Phox2b, dHand, Gata2 and/or Gata3, or portions thereof;

r) Mash1 (Ascl1), Nurr1, REN, neurogenin1, neurogenin2, neurogenin3, Mash1, Phox2b, Phox2a, dHand, Shh, FGF8, Lmx1b, Nkx2.2, Pet1, Lbx1, Rnx, Gata3, and/or anti-sense Hes1 RNA or portions thereof;

s) PRR- Numb or a portion thereof; or

t) Numblike or a portion thereof.

4. The method of claim 1, characterized in that said cells and/or their progeny are incubated in a differentiation medium.

5. The method of claim 1, characterized in that said cells and/or their progeny are incubated in a differentiation medium comprising one or more agents selected from the group comprising:

a) retinoic acid, neurotrophin 3 (NT3), nerve growth factor (NGF), glial cell-line derived growth factor (GDNF), and/or interferon-γ (IFN-γ), hexamethylene bis acrylamide, dimethylsulfoxide (DMSO), fetal bovine serum (FBS), normal bovine serum (NBS), retinoic acid, cardiomyocyte conditioned medium, vascular endothelial growth factor (VEGF), LIF, thrombopoietin, a colony stimulating factor, M-CSF (CSF-1), GMCSF, IL-7, a cytokine promoting CD4+ T cell differentiation, sodium butyrate, activin A, epidermal growth factor, basic fibroblast growth factor, noggin, insulin-like growth factor and nicotinamide;

b) retinoic acid, neurotrophin 3 (NT3), nerve growth factor (NGF), glial cell-line derived growth factor (GDNF) and/or interferon-γ (IFNγ);

c) hexamethylene bis acrylamide or dimethylsulfoxide;

d) fetal bovine serum (FBS);

e) normal bovine serum (NBS), dimethylsulfoxide, retinoic acid and/or cardiomyocyte conditioned medium;

f) vascular endothelial growth factor (VEGF), thrombopoietin, and colony stimulating factors appropriate to the desired cell type; and

g) LIF, neurotrophin 3 (NT3), and/or nerve growth factor (NGF);

6. The vector comprising the transcription factors of claim 1.

7. The method claim 1 wherein the cells are cultured in a 2D or 3D format, grown in association with three-dimensional or two-dimensional scaffoldings, cultured in hanging drops, or utilized in an ink jet-style, printer.

8. The method claim 1 wherein the cells are utilized for tissue engineering or organ production.

9. The method of claim 1 wherein the selected cells are genetically-modified cells.

10. The method of claim 9 wherein the genetically-modified cells express gene products deficient in a patient.

11. The method of claim 9 wherein the cells are rendered disease-resistant.

12. The method of claim 9 wherein the cells are rendered less susceptible to viral infection.

13. The method of claim 1 wherein the cells further express siRNA, miRNA, shRNA, a decoy sequence or a synthetic oligonucleotide sequence.

14. The method of claim 1 wherein the cells are provided to an animal or patient in need thereof.

15. The method of claim 1 further comprising the use of electroporation, chemically mediated transfection, fusogenic or non-fusogenic liposomes, nanocapsules, nanovaults other standard transfection techniques, or an approach avoiding viral integration or other random alteration of the cell's genome.

16. The method of claims 1 or 2 wherein proliferation, self-renewal, or stem/progenitor cell behavior is blocked in cells aberrantly displaying such behavior.

17. The vector comprising the transcription factors and cell fate determinants of claim 1.

18. The vector comprising the cell fate determinants of claim 2.

19. The vector comprising the cell fate determinants of claim 3.

20. The method of claim 1 for production of pluripotent cells comprising the steps of:

    i. selecting non-pluripotent, somatic cells;

    ii. introducing or overexpressing proteins or sequences comprising one or more of a “long” (Prr+) numb isoform, Oct4, Sox2, and Nanog;

    iii. growing the selected cells in a growth medium comprising cytokines; and

    iv. maintaining the cells under these culture conditions until the desired number of pluripotent cells is achieved.

21. The method of claim 20, characterized in that nucleic acid(s) or protein(s) utilized comprise:

    a. a Prr+ Numb isoform;

    b. a Prr+ Numb isoform and one of LIF, a gene with LIF activity, LIFR, oncostatin M, oncostatin M Receptor, cardiotrophin-1 and CNTF;

    c. a Prr+ Numb isoform and Notch;

    d. a Prr+ Numb isoform, OCT3/4, SOX2 and Notch;

    e. a Prr+ Numb isoform, OCT3/4, SOX2, NANOG, and Notch;

    f. a Prr+ Numb isoform, OCT3/4, SOX2, NANOG, and a transgene with LIF activity;

g. a Prr+ Numb isoform, OCT3/4, SOX2, NANOG, and multiple transgenes with LIF activity;

h. ones selected from those encoding a long Prr+ Numb isoform, NANOG, OCT3/4, SOX2, transgenes with Notch activity, Hoxb4, FGF-4, LIF, LIFR, CNTF, oncostatin, oncostatin receptor, cardiotrophin-1, IL-6, IL6R, hyper IL-6, IL-11, gp130 and other transgenes with LIF activity;

i. a Prr+ Numb isoform and ones selected from LIF, LIFR, oncostatin-M, cardiotrophin-1, IL-11, IL-6, IL6R, hyper IL-6, LIFR, gp130 and FGF-4; and one or more of OCT3/4, SOX2, NANOG, and FGF-4;

j. ones selected from LIF, LIFR, oncostatin-M, cardiotrophin-1, IL-11, IL-6, IL6R, hyper IL-6, LIFR, gp130 and FGF-4; and one or more of OCT3/4, SOX2, NANOG, and FGF-4;

k. a Prr+ Numb isoform and FGF-4;

l. FGF-4.

22. The method of claim 21, characterized in that “a long” (PRR+) numb isoform encoding nucleic acid sequence or protein is:

a. accompanied by other nucleic acid sequences or proteins including ones selected from a group consisting of those encoding human LIF, oncostatin-M, cardiotrophin-1, IL-11, IL-6, IL6R, hyper IL-6, LIFR, gp130, OCT3 (OCT4), NANOG, SOX2, and/or FGF-4; or

b. replaced by transfection with other nucleic acid sequences or proteins including ones selected from a group consisting of those encoding human LIF, oncostatin M, cardiotrophin-1, IL-11, IL-6, IL6R, hyper IL-6, LIFR, gp130, OCT3 (OCT4), NANOG, SOX2, and/or FGF-4.

23. The method of claim 20, characterized in that the selected cell is modified to express:

a. telomerase altering the cell’s life span;

b. a gene product deficient in a patient;

c. a nucleic acid sequence encoding a protein selected from aspartoacyclase (ASP), HRPT, HTT, NPC1, GBA, PARK2, VHL, beta-glucuronidase, hexosaminidase A (HEXA), hexosaminidase B (HEXB), HRPT, HTT, galactosidase alpha (GLA), glucosidase beta acid (GBA), von Hippel Lindau tumor suppressor (VHL), beta globin (HBB), NPC1, PARK2.

24. The method of claim 20, characterized in that the selected cell or its progeny is modified to expresses:

a. a beneficial nucleic acid sequence;

b. a synthetic oligonucleotide, complementary RNA (siRNA), microRNA, forming pegs (shRNA), interfering microRNA, antisense RNA;

c. a nucleic acid sequence or protein retarding infection by a virus;

d. a. nucleic acid sequence or protein rendering said cells and/or their progeny less capable of sustaining viral replication;

e. a. nucleic acid sequence or protein rendering said cells and/or their progeny less capable of sustaining viral transcription;

f. a synthetic oligonucleotide directed against an immunodeficiency virus co-receptor;

g. a decoy RNA;

h. an HIV psi sequence;

i. a. nucleic acid or protein sequence rendering said cells and/or their progeny disease resistant.

25. The method of claim 20, characterized in that said selected cell and/or its progeny are incubated in a growth medium comprising cytokines selected from a group consisting of EGF, bFGF, LIF, steel factor, IL-6, hyper IL-6, IL-7, oncostatin M, cardiotrophin-1 and other growth enhancing cytokines.

26. The method of claim 20, characterized in that said selected cell and/or its progeny are differentiated by overexpression or introduction of nucleic acid(s) or protein(s) corresponding to one or more transcription factors normally present in the desired cells.

27. The method of claim 20, characterized in that said cells and/or their progeny further overexpress transcription factor proteins or nucleic acids selected from the group consisting of:

a. Mash1 (Ascl1), or a portion thereof;

b. MyoD, myogenin, Myf5, Myf6, Mef2, myocardin, Ifrd1, a muscle transcription factor and/or a muscle type specific bHLH-encoding sequence, or a portion thereof;

c. Foxa2, Sox17, HLXB9, and/or Pdx1, or a portion thereof;

d. hepatic nuclear factor (HNF)-1, HNF-3, HNF-4, HNF-6, and/or CREB-binding protein, or a portion thereof;

e. Runx1/AML1 and/or NOV (CCN3), or a portion thereof;

f. Sox9, CREB-binding protein, Gata6 and/or Runx2, or a portion thereof;

g. OLIG1, OLIG2, and/or Zfp488, or a portion thereof;

h. MyoD, myogenin, myocardin, Myf5, Myf6, Mef2A, Gata4, Gata5, and Gata6, or portions thereof;

i. Gata4, Gata5 and/or Gata6, or a portion thereof;

j. Myocardin, or a portion thereof;

k. Myogenin and MyoD, or portions thereof;

l. Runx2, or a portion thereof;

m. Mash1 (Ascl1), Ngn2, Nurr1, Lmx1b, and/or Ptx-3, or a portion thereof;

n. Mash1 (Ascl1), Phox2b, Lmx1b, Nkx2.2, Pet1, Gata2, Gata3, and/or Pet1 or a portion thereof;

o. Mash1 (Ascl1), Phox2a and/or REST4, or a portion thereof;

p. Mash1 (Ascl1), PITX2, Dlx2, Dlx5, HES1 targeting synthetic oligonucleotides, Phox2a and/or REST4, or portions thereof;

q. Mash1 (Ascl1), Phox2a, Phox2b, dHand, Gata2 and/or Gata3, or portions thereof;

r. Mash1 (Ascl1), Nurr1, REN, neurogenin1, neurogenin2, neurogenin3, Mash1, Phox2b, Phox2a, dHand, Shh, FGF8, Lmx1b, Nkx2.2, Pet1, Lbx1, Rnx, Gata3, and/or anti-sense Hes1 RNA or portions thereof;

s. PRR- Numb or a portion thereof; or

t. Numblike or a portion thereof.

28. The method of claim 20, characterized in that said cells and/or their progeny are incubated in a differentiation medium.

29. The method of claim 20, characterized in that said cells and/or their progeny are incubated in a differentiation medium comprising one or more agents selected from the group comprising:

a. retinoic acid, neurotrophin 3 (NT3), nerve growth factor (NGF), glial cell-line derived growth factor (GDNF), and/or interferon-γ (IFN-γ), hexamethylene bis acrylamide, dimethylsulfoxide (DMSO), fetal bovine serum (FBS), normal bovine serum (NBS), retinoic acid, cardiomyocyte conditioned medium, vascular endothelial growth factor (VEGF), LIF, thrombopoietin, a colony stimulating factor, M-CSF (CSF-1), GMCSF, IL-7, a cytokine promoting CD4+ T cell differentiation, sodium butyrate, activin A, epidermal growth factor, basic fibroblast growth factor, noggin, insulin-like growth factor and nicotinamide;

b. retinoic acid, neurotrophin 3 (NT3), nerve growth factor (NGF), glial cell-line derived growth factor (GDNF) and/or interferon-γ (IFNγ);

c. hexamethylene bis acrylamide or dimethylsulfoxide;

d. fetal bovine serum (FBS);

e. normal bovine serum (NBS), dimethylsulfoxide, retinoic acid and/or cardiomyocyte conditioned medium;

f. vascular endothelial growth factor (VEGF), thrombopoietin, and colony stimulating factors appropriate to the desired cell type;

g. LIF, neurotrophin 3 (NT3), and/or nerve growth factor (NGF);

h. a colony stimulating factor, optionally M-CSF (CSF-1), GM-CSF, IL-7, or a cytokine promoting CD4+ T cell differentiation; and

i. sodium butyrate, activin A, retinoic acid, epidermal growth factor, basic fibroblast growth factor, noggin, insulin-like growth factor II and nicotinamide.

30. The method of claim 20, characterized in that wherein a protein, nucleic acid or agent is present in order to screen for its ability to induce phenotypic changes or differentiation of the selected cells into desired cell populations.

31. The method of any of claims 20 to 30, characterized in that said cell and/or its progeny are cultured in a three-dimensional or two-dimensional scaffolding, said cells and/or its progeny are grown in a de-cellularized organ or on de-cellularized tissue, or said cells or its progeny are utilized in conjunction with

inkjet printing technology for tissue engineering.

32. The method of claim 20, characterized in that is performed in vivo.

33. The method of claim 20, characterized in that electroporation, liposomes, nanocapsules, nanovaults, and/or another approach avoiding retroviral/lentiviral integration or other random alteration of said cell's genome is utilized, including site- directed mutagenesis.

34. The multipotent, pluripotent, self-renewing or differentiated cell, derived from the patient or a donor, for use in fields utilizing cellular therapies, gene therapy, or animal husbandry produced by the recombinant methods of claims 1 to 33.

35. Use of the cell population of claim 34 in screening based on cell type specific markers; transgenic marker expression under the control of cell type specific promoters; or transgenic marker expression under the control of neurotransmitter related promoters.

36. A method of treating a patient with a condition or disease

a) ameliorated by correction of a genetic deficiency;

b) dependent upon expression of genes producing susceptibility;

c) ameliorated by renewed cell proliferation; or

d) characterized by dysplasia, cancer or aberrant cell behavior, comprising introducing into said patient a therapeutically effective amount of the cells of claim 34.

37. The method of claims 1, 2, 3, or 20 performed in vivo.

38. The cells provided by claims 1-37.

Claims:

1. A method for producing multipotent, pluripotent, and/or self-renewing cells from the selected cells, comprising;

transfecting selected cells obtained by selecting cells from the group of somatic cells with nucleotide sequences encoding the "long" (PRR insert +) isoform(s) of the mammalian numb protein and with an additional nucleotide sequence encoding Notch; and

growing the selected cells in a growth medium comprising cytokines selected from EGF, bFGF, LIF, steel factor, IL-6, hyper IL-6, IL-7, oncostatin-M, cardiotrophin-1 and other growth enhancing cytokines effective that the selected cells expand at a rate, wherein said rate is determined from the doubling times of the selected cells in said growth culture medium; and maintaining the cells under these culture conditions until the desired cell number is achieved.