What is claimed herein is:

1. A method to generate a pluripotent cell, comprising subjecting a cell to a stress.
2. The method according to claim 1, wherein the pluripotent cell is generated without introduction of an exogenous gene, a transcript, a protein, a nuclear component or cytoplasm, or without cell fusion.
3. The method of any of claims 1-2, further comprising selecting a cell exhibiting pluripotency.
4. The method of any of claims 1-3, wherein the cell is not present as part of a tissue.
5. The method of any of claims 1-4, wherein the cell is a somatic cell, a stem cell, a progenitor cell or an embryonic cell.
6. The method of any of claims 1-5, wherein the cell is an isolated cell.
7. The method of any of claims 1-6, wherein the cell is present in a heterogeneous population of cells.
8. The method of any of claims 1-7, wherein the cell is present in a homogenous population of cells.
9. The method of any of claims 1-8, wherein selecting the cell exhibiting pluripotency comprises selecting a cell expressing a stem cell marker.
10. The method of any of claim 9, wherein the stem cell marker is selected from the group consisting of :

    Oct4; Nanog; E-cadherin, and SSEA4.
11. The method of any of claims 1-10, wherein selecting the cell exhibiting pluripotency comprises selecting a cell which is not adherent.
12. The method of any of claims 1-11, wherein the stress comprises unphysiological stress in tissue or cell culture.
13. The method of any of claims 1-12, wherein the stress comprises exposure of the cell to at least one environmental stimulus selected from: trauma, mechanical stimuli, chemical exposure, ultrasonic stimulation, oxygen-deprivation, radiation, exposure to extreme temperatures, dissociation, trituration, physical stress, hyperosmosis, hypoosmosis, membrane damage, toxin, extreme ion concentration, active oxygen, UV exposure, strong visible light, deprivation of essential nutrition, or unphysiolosically acidic environment.
14. The method of any of claims 1-13, wherein the stress comprises exposing the cell to a pH of from about 3.0 to about 6.8.

15. The method of any of claims 1-4, wherein the stress comprises exposing the cell to a pH of from about 4.5 to about 6.0.
16. The method of claim 15, wherein the stress comprises exposing the cell to a pH of from about 5.4 to about 5.8.
17. The method of any of claims 12-16, wherein the cell is exposed for 2-3 days.
18. The method of any of claims 12-17, wherein the cell is exposed for 1 day or less.
19. The method of any of claims 12-18, wherein the cell is exposed for 1 hour or less.
20. The method of any of claims 12-19, wherein the cell is exposed for about 30 minutes.
21. The method of claim 13, wherein the exposure to extreme temperatures comprises exposing the cell to temperatures below 35°C or above 42°C.
22. The method of claim 21, wherein the exposure to extreme temperatures comprises exposing the cell to temperatures at, or below freezing or exposure of the cell to temperatures at least about 85°C.
23. The method of claim 13, wherein the mechanical stimulus comprises exposing the cell to shear stress or/and high pressure.
24. The method of claim 23, wherein the mechanical stimulus comprises passing the cell through at least one device with a smaller aperture than the size of the cell.
25. The method of claim 23, wherein the mechanical stimulus comprises passing the cell through several devices having progressively smaller apertures.
26. The method of any of claims 1-25, further comprising culturing the pluripotent cell to allow propagation of the pluripotent cell.
27. The method of any of claims 1-26, wherein the pluripotent cell expresses a stem cell marker.
28. The method of claim 27, wherein the stem cell marker is selected from the group consisting of:

    Oct4; Nanog; E-cadherin, and SSEA4.
29. The method of any of claims 1-28, wherein the cell is a mammalian cell.
30. The method of any of claims 1-29, wherein the cell is a human cell.
31. The method of any of claims 1-30, wherein the cell is an adult cell, a neonatal cell, a fetal cell, amniotic cell, or cord blood cell.
32. The method of any of claims 1-31, further comprising maintaining the pluripotent cell *in vitro*.

33. The method of any of claims 1-32, wherein the epigenetic state of the cell is altered to more closely resemble the epigenetic state of an embryonic stem cell.
34. The method of claim 33, wherein the epigenetic state comprises methylation patterns.
35. The method of any of claims 1-34, wherein the stress comprises removing at least about 40% of the cytoplasm from the cell.
36. The method of claim 35, wherein at least about 50% of the cytoplasm is removed from the cell.
37. The method of claim 36, wherein at least about 60% of the cytoplasm is removed from the cell.
38. The method of claim 37, wherein between 60-80% of the cytoplasm is removed from the cell.
39. The method of claim 37, wherein at least about 80% of the cytoplasm is removed from the cell.
40. The method of claim 39, wherein at least about 90% of the cytoplasm is removed from the cell.
41. The method of any of claims 1-40, wherein the stress comprises removing at least about 40% of the mitochondria from the cell.
42. The method of claim 41, wherein the removal of a portion of the cytoplasm removes at least about 50% of the mitochondria from the cytoplasm.
43. The method of claim 42, wherein the removal of cytoplasm or mitochondria removes about 50%-90% of the mitochondria from the cytoplasm.
44. The method of claim 42, wherein the removal of cytoplasm or mitochondria removes more than 90% of the mitochondria from the cytoplasm.
45. The method of any of claims 1-44, wherein the stress is sufficient to disrupt the cellular membrane of at least 10% of cells exposed to the stress.
46. An assay comprising;

    contacting a pluripotent cell produced by the method according to any of claims 1 to 45 with a candidate agent.
47. The assay of claim 46, for use to identify agents which affect one or more of the viability, differentiation, proliferation of the pluripotent cell.
48. Use of a pluripotent cell produced by the method according to any one of claims 1 to 45 in a method of cell therapy for a subject.
49. A method of preparing a cell or tissue that is compatible with cell therapy to be administered to a subject, comprising:

    generating a pluripotent cell from a cell according to any one of claims 1 to 45;

wherein the cell is an autologous cell or HLA-matched allogeneic cell.

50. The method of claim 49, further comprising differentiating the pluripotent cell along a pre-defined cell lineage prior to administering the cell or tissue to the subject.
51. A composition comprising a pluripotent cell, wherein the pluripotent cell is generated from a cell by the methods according any of claims 1 to 45.
52. A method of producing a pluripotent stem cell, the method comprising culturing a cell in the presence of adrenocorticotropic hormone (ACTH), 2i or 3i medium
53. The method of claim 52, wherein the cell is cultured in LIF medium comprising ACTH.
54. The method of claim 52 or 53, wherein the ACTH is present at a concentration of from about 0.1 μM to about 100 μM .
55. The method of any of claims 52-54, wherein the cell is a cell generated by the method of any of claims 1-45.
56. The method of any of claims 52-55, wherein the cell is a totipotent cell.
57. The method of any of claims 52-56, wherein the cell is cultured in the presence of ACTH, 2i or 3i medium for at least 3 days.
58. The method of any of claims 52-57, wherein the cell is cultured in the presence of ACTH, 2i or 3i medium for at least 5 days.
59. The method of any of claims 52-58, wherein the cell is cultured in the presence of ACTH, 21 or 3i medium for at least 7 days.
60. The method of any of claims 52-59, wherein after the culturing step, the cell expresses detectable level of a stem cell marker selected from the group consisting of:

Oct3/4; Nanog; Rex1; Klf4; Sox2; Klf2; Esrr-beta; Tbx3; and Klf5.

61. A method of increasing the self-renewal ability of a pluripotent cell, the method comprising culturing the cell in the presence of adrenocorticotropic hormone (ACTH), 2i or 3i medium.
62. The method of claim61, wherein the cell is cultured in LIF medium comprising ACTH.
63. The method of any of claims 61-62, wherein the ACTH is present at a concentration of from about 0.1 μM to about 100 μM .
64. The method of any of claims 61-63, wherein the cell is a cell generated by the method of any of claims 1-45.
65. The method of any of claims 61-64, wherein the cell is a totipotent cell.
66. The method of any of claims 61-65, wherein the cell is cultured in the presence of ACTH, 2i or 3i medium for at least 3 days.
67. The method of any of claims 61-66, wherein the cell is cultured in the presence of ACTH, 2i or 3i medium for at least 5 days.
68. The method of any of claims 61-67, wherein the cell is cultured in the presence of ACTH, 2i or 3i medium for at least 7 days.
69. The method of any of claims 61-68, wherein after the culturing step, the cell expresses detectable level of a stem cell marker selected from the group consisting of:

Oct3/4; Nanog; Rex1; Klf4; Sox2; Klf2; Esrr-beta; Tbx3; and Klf5.

70. A method of autologous cell therapy in a subject in need of cell therapy, comprising
    a. generating a pluripotent cell from a cell according to any one of claims 1 to 45, wherein the cell is obtained from the subject, and
    b. administering a composition comprising the pluripotent cell or a differentiated progeny thereof to the subject.
71. The method of claim 70, further comprising differentiating the pluripotent cell along a pre-defined cell lineage prior to administering the composition to the subject.
72. A method of producing a pluripotent cell capable of differentiating into a placental cell, the method comprising culturing the pluripotent cell generated by the method of any of claims 1-45 in the presence of FGF4.
73. The method of claim 72, wherein the concentration of FGF4 is 1 nM to 1 uM.
74. The method of claim 72 or 73, wherein the pluripotent cell is capable of differentiating into an embryonic stem cell.

CLAIMS

1. A method to generate a pluripotent cell, comprising subjecting a cell to a stress by exposing the cell to at least one stimulus selected from: trauma, mechanical stimuli, chemical exposure, ultrasonic stimulation, extreme temperatures, dissociation, trituration, physical stress, hyperosmosis, hypoosmosis, membrane damage, extreme ion concentration, active oxygen, UV exposure, strong visible light or unphysiolosically acidic environment.

2. A method according to Claim 1, in which the pluripotent cell is generated without introduction of an exogenous gene, a transcript, a protein, a nuclear component or cytoplasm, or without cell fusion.

3. A method according to Claim 1 or 2, further comprising selecting a cell exhibiting pluripotency.

4. A method according to Claim 1, 2 or 3, in which the cell is not present as part of a tissue.

5. A method according to any preceding claim, in which the cell is a somatic cell, a stem cell, a progenitor cell or an embryonic cell.

6. A method according to any preceding claim, in which the cell is an isolated cell.

7. A method according to any preceding claim, in which the cell is present in a heterogeneous population of cells.

8. A method according to any preceding claim, in which the cell is present in a homogenous population of cells.

9. A method according to any preceding claim, in which selecting the cell exhibiting pluripotency comprises selecting a cell expressing a stem cell marker.

10. A method according to Claim 9, in which the stem cell marker is selected from the group consisting of: Oct4; Nanog; E-cadherin, and SSEA4.

11. A method according to any preceding claim, in which selecting the cell exhibiting pluripotency comprises selecting a cell which is not adherent.

12. A method according to any preceding claim, in which the stress comprises exposing the cell to a pH of from about 3.0 to about 6.8.

13. A method according to any preceding claim, in which the stress comprises exposing the cell to a pH of from about 4.5 to about 6.0.

14. A method according to Claim 13, in which the stress comprises exposing the cell to a pH of from about 5.4 to about 5.8.

15. A method according to Claim 1, in which the cell is exposed for 2-3 days.

16. A method according to Claim 1, in which the cell is exposed for 1 day or less.

17. A method according to Claim 1, in which the cell is exposed for 1 hour or less.

18. A method according to Claim 1, in which the cell is exposed for about 30 minutes.

19. A method according to Claim 1, in which exposing the cell to at least one stimulus comprises exposing the cell to temperatures below 35°C or above 42°C.

20. A method according to Claim 1, in which exposing the cell to at least one stimulus comprises exposing the cell to temperatures at, or below freezing or exposing the cell to temperatures of at least about 85°C.

21. A method according to Claim 1, in which exposing the cell to at least one stimulus comprises exposing the cell to shear stress or/and high pressure.

22. A method according to Claim 1, in which exposing the cell to at least one stimulus comprises passing the cell through at least one device with a smaller aperture than the size of the cell.

23. A method according to Claim 21, in which exposing the cell to at least one stimulus comprises passing the cell through several devices having progressively smaller apertures.

24. A method according to Claim 1, further comprising culturing the pluripotent cell to allow propagation of the pluripotent cell.

25. A method according to Claim 1, in which the pluripotent cell expresses a stem cell marker.

26. A method according to Claim 25, in which the stem cell marker is selected from the group consisting of: Oct4; Nanog; E-cadherin, and SSEA4.

27. A method according to Claim 1, in which the cell is a mammalian cell.

28. A method according to Claim 1, in which the cell is a human cell.

29. A method according to Claim 1, in which the cell is an adult cell, a neonatal cell, a fetal cell, amniotic cell, or cord blood cell.

30. A method according to Claim 1, further comprising maintaining the pluripotent cell *in vitro*.

31. A method according to Claim 1, in which the epigenetic state of the cell is altered to more closely resemble the epigenetic state of an embryonic stem cell.

32. A method according to Claim 31, in which the epigenetic state comprises methylation patterns.

33. A method according to Claim 1, in which exposing the cell to at least one stimulus comprises removing at least about 40% of the cytoplasm from the cell.

34. A method according to Claim 33, in which at least about 50% of the cytoplasm is removed from the cell.

35. A method according to Claim 34, in which at least about 60% of the cytoplasm is removed from the cell.

36. A method according to Claim 35, in which between 60-80% of the cytoplasm is removed from the cell.

37. A method according to Claim 36, in which at least about 80% of the cytoplasm is removed from the cell.

38. A method according to Claim 37, in which at least about 90% of the cytoplasm is removed from the cell.

39. A method according to Claim 1, in which exposing the cell to at least one stimulus comprises removing at least about 40% of the mitochondria from the cell.

40. A method according to Claim 1, in which exposing the cell to at least one stimulus comprises removal of a portion of the cytoplasm that removes at least about 50% of the mitochondria from the cytoplasm.

41. A method according to Claim 40, in which the removal of cytoplasm or mitochondria removes about 50%-90% of the mitochondria from the cytoplasm.

42. A method according to Claim 40, in which the removal of cytoplasm or mitochondria removes more than 90% of the mitochondria from the cytoplasm.

43. A method according to Claim 1, in which the stress is sufficient to disrupt the cellular membrane of at least 10% of cells exposed to the stress.

44. An assay comprising contacting a pluripotent cell produced by a method according to Claim 1 with a candidate agent.

45. An assay according to Claim 44, for use to identify agents which affect one or more of the viability, differentiation, proliferation of the pluripotent cell.

46. A method of preparing a cell or tissue that is compatible with cell therapy to be administered to a subject, comprising generating a pluripotent cell from a cell according to Claim 1, in which the cell is an autologous cell or HLA-matched allogeneic cell.

47. A method according to Claim 46, further comprising differentiating the pluripotent cell along a pre-defined cell lineage prior to administering the cell or tissue to the subject.

48 A method of producing a pluripotent stem cell, the method comprising culturing a cell in the presence of adrenocorticotropic hormone (ACTH), 2i or 3i medium.

49. A method according to Claim 48, in which the cell is cultured in LIF medium comprising ACTH.

50. A method according to Claim 48 or 49, in which the ACTH is present at a concentration of from about 0.1 μM to about 100 μM.

51. A method according to Claim 48, 49 or 50, in which the cell is a cell generated by a method according to any of Claims 1 to 43.

52. A method according to any of Claims 48 to 51, in which the cell is a totipotent cell.

53. A method according to any of Claims 48 to 52, in which the cell is cultured in the presence of ACTH, 2i or 3i medium for at least 3 days.

54. A method according to any of Claims 48 to 53, in which the cell is cultured in the presence of ACTH, 2i or 3i medium for at least 5 days.

55. A method according to any of Claims 48 to 54, in which the cell is cultured in the presence of ACTH, 21 or 3i medium for at least 7 days.

56. A method according to any of Claims 48 to 55, in which after the culturing step, the cell expresses detectable level of a stem cell marker selected from the group consisting of: Oct3/4; Nanog; Rex1; Klf4; Sox2; Klf2; Esrr-beta; Tbx3; and Klf5.

57. A method of increasing the self-renewal ability of a pluripotent cell, the method comprising culturing the cell in the presence of adrenocorticotropic hormone (ACTH), 2i or 3i medium.

58. A method according to Claim 57, in which the cell is cultured in LIF medium comprising ACTH.

59. A method according to Claim 57 or 58, in which the ACTH is present at a concentration of from about 0.1 μM to about 100 μM.

60. A method according to any of Claims 57, 58 or 59, in which the cell is a cell generated by a method according to any of Claims 1 to 48.

61. A method according to any of Claims 57 to 60, in which the cell is a totipotent cell.

62. A method according to any of Claims 57 to 61, in which the cell is cultured in the presence of ACTH, 2i or 3i medium for at least 3 days.

63. A method according to any of Claims 57 to 62, in which the cell is cultured in the presence of ACTH, 2i or 3i medium for at least 5 days.

64. A method according to any of Claims 57 to 63, in which the cell is cultured in the presence of ACTH, 2i or 3i medium for at least 7 days.

65. A method according to any of Claims 57 to 64, in which after the culturing step, the cell expresses detectable level of a stem cell marker selected from the group consisting of: Oct3/4; Nanog; Rex1; Klf4; Sox2; Klf2; Esrr-beta; Tbx3; and Klf5.

66. A method of producing a pluripotent cell capable of differentiating into a placental cell, the method comprising culturing the pluripotent cell generated by a method according to Claim 1 in the presence of FGF4.

67. A method according to Claim 66, in which the concentration of FGF4 is 1 nM to 1 uM.

68. A method according to Claim 66 or 67, in which the pluripotent cell is capable of differentiating into an embryonic stem cell.

69. Use of a pluripotent cell produced by a method according to any of Claims 1 to 47 in the preparation of a medicament for cell therapy of a subject.

70. Use according to Claim 69, in which the cell therapy is autologous cell therapy.

71. Use according to Claim 70, in which a pluripotent cell is generated from a cell according to Claim 1, and the cell is obtained from the subject.

72. Use according to Claim 71, in which the pluripotent cell is differentiated along a pre-defined cell lineage.

73. A composition comprising a pluripotent cell, in which the pluripotent cell is generated from a cell by a method according to Claim 1.