CLAIMS

1. A method of expanding pluripotent stem cell number, the method comprising culturing pluripotent stem cells in a culture medium comprising a basal salt nutrient solution and an ErbB3 ligand, wherein the cell medium is essentially free of serum, wherein the pluripotent stem cells expand in number and do not differentiate, wherein:

(i) the pluripotent stem cells are of human origin and the culture medium further comprises an activator of insulin like growth factor 1 receptor (IGF1R), wherein the activator of insulin like growth factor 1 receptor (IGF1R) comprises IGF-1, IGF-2, or an IGF-1 analog, wherein the IGF-1 analog comprises LongR3-IGFI, Des(1-3)IGF-1, [Arg^3]IGF-l, [Ala^{31}]IFG-1, Des(2,3)[Ala^{31}]IGF-l, [Leu^{24}]IGF-1, Des(2,3)[Leu^{24}]IGF-1, [Leu^{60}]IGF-l, [Ala^{31}][Leu^{60}]IGF-l, or [Leu^{24}][Ala^{31}]IGF-l, or

(ii) the pluripotent stem cells are of mouse origin and the culture medium further comprises leukemia inhibitory factor (LIF).

2. The method of claim 1, wherein the culture medium is free of exogenous insulin and insulin substitutes.

3. The method of any one of claims 1 or 2, wherein the ErbB3 ligand in the culture medium is selected from the group consisting of Neuregulin-β, Heregulin-β(HRG-β), Heregulin-α (HRG-α), Neu differentiation factor (NDF), acetylcholine receptor-inducing activity (ARIA), glial growth factor 2 (GGF2), motor-neuron derived factor (SMDF), Neuregulin-2, Neuregulin-2β (NRG2-β), Epiregulin, Biregulin and functional fragments thereof.

4. The method of claim 3, wherein the ErbB3 ligand is HRG-β.

5. The method of any one of claims 1-4, wherein the culture medium further comprises transforming growth factor beta (TGF-β) or a TGF-β family member.

6. The method of claim 5, wherein the TGF-β family member is selected from the group consisting of Nodal, Activin A, Activin B, bone morphogenetic protein-2 (BMP2), and bone morphogenetic protein-4 (BMP4).

7. The method of claim 6, wherein the TGF-β family member is Activin A.

8. The method of any one of claims 1-7, wherein the cell medium is free of exogenous fibroblast growth factor.

9. The method of any one of claims 1-7, wherein the cell medium further comprises at least one fibroblast growth factor (FGF) selected from the group consisting of FGF-2, FGF-7, FGF-10, and FGF-22.

10. The method of claim 9, wherein the at least one FGF is FGF-7, FGF-10 and FGF-22.

11. The method of any one of claims 1-10, wherein the culture medium comprises a serum albumin (SA).

12. The method of claim 11, wherein the SA is bovine SA (BSA) or human SA (HSA).

13. The method of claim 11, wherein the concentration of the SA is more than about 0.2%, volume to volume (v/v).

14. The method of claim 11, wherein the concentration of SA is less than about 5% v/v.

15. The method of any one of claims 1-14, wherein the pluripotent stem cells are selected from the group consisting of embryonic stem (ES) cells, early primitive ectoderm-like (EPL) cells, inner cell mass (ICM)/epiblast cells, embryonic germ (EG) cells, and pluripotent cells derived by dedifferentiation or nuclear transfer.

16. The method of claim 15, wherein the pluripotent stem cells are (ES) cells.

17. The method of any one of claims 1-16, wherein the pluripotent stem cells are of human origin and wherein the culture medium comprises an activator of insulin like growth factor 1 receptor (IGF1R).

18. The method of claim 17, wherein the activator of IGF1R comprises insulin-like growth factor 1 (IGF1) or longR3-IGF1.

19. The method of any one of claims 1-16, wherein the pluripotent stem cells are of mouse origin and the culture medium further comprises leukemia inhibitory factor (LIF).

20. The method of any one of claims 1-19, wherein the culturing comprises culturing the pluripotent stem cells on a solid surface in an adherent culture.

21. The method of any one of claims 1-19, wherein the culturing comprises culturing the pluripotent stem cells in a suspension culture.

22. A method of identifying a compound that modulates proliferation and/or differentiation of pluripotent stem cells, the method comprising:

culturing the pluripotent stem cells in a culture medium comprising a basal salt nutrient solution, an ErbB3 ligand, and a candidate compound, wherein the cell medium is essentially free of serum;

determining whether an increase or decrease in proliferation and/or differentiation occurs in the pluripotent stem cells cultured with the compound relative to a control, wherein the increase or decrease indicates that the compound modulates proliferation and/or differentiation of the pluripotent stem cells, wherein:

(i) the pluripotent stem cells are of human origin and the culture medium further comprises an activator of insulin like growth factor 1 receptor (IGF1R), wherein the activator of insulin like growth factor 1 receptor (IGF1R) comprises IGF-1, IGF-2, or an IGF-1 analog, wherein the IGF-1 analog comprises LongR3-IGFI, Des(1-3)IGF-1, [Arg^3]IGF-l, [Ala^{31}]IFG-1, Des(2,3)[Ala^{31}]IGF-l, [Leu^{24}]IGF-1, Des(2,3)[Leu^{24}]IGF-1, [Leu^{60}]IGF-l, [Ala^{31}][Leu^{60}]IGF-l, or [Leu^{24}][Ala^{31}]IGF-l, or

(ii) the pluripotent stem cells are of mouse origin and the culture medium further comprises leukemia inhibitory factor (LIF).

23. The method of claim 22, wherein the culturing comprises culturing the pluripotent stem cells on a solid surface in an adherent culture.

24. The method of claim 22, wherein the culturing comprises culturing the pluripotent stem cells in a suspension culture.

25. The method of claim any one of claims 22-24, wherein the culture medium is free of exogenous insulin and insulin substitutes.

26. The method of any one of claims 22-25, wherein the ErbB3 ligand in the culture medium is selected from the group consisting of Neuregulin-β, Heregulin-β(HRG-β), Heregulin-α (HRG-α), Neu differentiation factor (NDF), acetylcholine receptor-inducing activity (ARIA), glial growth factor 2 (GGF2), motor-neuron derived factor (SMDF), Neuregulin-2, Neuregulin-2β (NRG2-β), Epiregulin, Biregulin and functional fragments thereof.

27. The method of claim 26, wherein the ErbB3 ligand is HRG-β.

28. The method of any one of claims 22-27, wherein the culture medium further comprises transforming growth factor beta (TGF-β) or a TGF-β family member.

29. The method of claim 28, wherein the TGF-β family member is selected from the group consisting of Nodal, Activin A, Activin B, bone morphogenetic protein-2 (BMP2), and bone morphogenetic protein-4 (BMP4).

30. The method of claim 29, wherein the TGF-β family member is Activin A.

31. The method of any one of claims 22-30, wherein the cell medium is free of exogenous fibroblast growth factor.

32. The method of any one of claims 22-30, wherein the cell medium further comprises at least one fibroblast growth factor (FGF) selected from the group consisting of FGF-2, FGF-7, FGF-10, and FGF-22.

33. The method of claim 32, wherein the at least one FGF is FGF-7, FGF-10 and FGF-22.

34. The method of any one of claims 22-33, wherein the culture medium comprises a serum albumin (SA).

35. The method of claim 34, wherein the SA is bovine SA (BSA) or human SA (HSA).

36. The method of claim 34, wherein the concentration of the SA is more than about 0.2%, volume to volume (v/v).

37. The method of claim 34, wherein the concentration of SA is less than about 5% v/v.

38. The method of any one of claims 22-37, wherein the pluripotent stem cells are selected from the group consisting of embryonic stem (ES) cells, early primitive ectoderm-like (EPL) cells, inner cell mass (ICM)/epiblast cells, embryonic germ (EG) cells, and pluripotent cells derived by dedifferentiation or nuclear transfer.

39. The method of claim 38, wherein the pluripotent stem cells are (ES) cells.

40. The method of any one of claims 22-39, wherein the pluripotent stem cells are of human origin and wherein the culture medium comprises an activator of insulin like growth factor 1 receptor (IGF1R).

41. The method of claim 40, wherein the activator of IGF1R comprises insulin-like growth factor 1 (IGF1) or longR3-IGF1.

42. The method of any one of claims 22-39, wherein the pluripotent stem cells are of mouse origin and the culture medium further comprises leukemia inhibitory factor (LIF).