CLAIMS

1. A method for preparing a cell population of a hematopoietic lineage, the method comprising:

preparing a pluripotent stem cell (PSC) population;

enriching for CD34+ cells to prepare a CD34-enriched population;

inducing endothelial-to-hematopoietic transition of the CD34-enriched population to prepare a population comprising hematopoietic stem cells (HSCs), and optionally harvesting cells from CD34-enriched population undergoing endothelial-to-hematopoietic transition; and

differentiating the HSC population to a hematopoietic lineage.

2. The method of claim 1, wherein the PSC population is a human iPSC population derived from lymphocytes, cord blood cells, peripheral blood mononuclear cells, CD34+ cells, or human primary tissues.

3. The method of claim 2, wherein the PSC population is derived from CD34-enriched cells isolated from peripheral blood.

4. The method of claim 2, wherein the iPSCs are homozygous for one or more HLA Class I and/or Class II genes.

5. The method of claim 2, wherein the iPSCs are gene-edited to delete one or more HLA Class I genes, delete one or more Class II genes, and/or delete one or more genes governing HLA or MHC expression or presentation capacity.

6. The method of claim 5, wherein the one or more genes governing HLA or MHC expression or presentation capacity is β2-microglobulin and/or CIITA.

7. The method of any one of claims 1 to 6, wherein CD34-enrichment and endothelial-to-hematopoietic transition is induced at Day 8 to Day 15 of iPSC differentiation.

8. The method of claim 7, wherein the endothelial-to-hematopoietic transition generates an HSC population comprising one or more of long-term hematopoietic stem cells (LT-HSCs), short-term hematopoietic stem cells, and hematopoietic stem progenitor cells.

9. The method of claim 7, wherein CD34+ cells are harvested from culture undergoing endothelial-to-hematopoietic transition, including harvesting of CD34+ floater and/or adherent cells.

10. The method of claim 7, where the induction of endothelial-to-hematopoietic transition comprises increasing the expression or activity of dnmt3b.

11. The method of claim 7, wherein the induction of endothelial-to-hematopoietic transition comprises Piezo1 activation.

12. The method of claim 11, wherein the Piezo1 activation is by contacting the CD34-enriched cells or fraction thereof with one or more Piezo1 agonists, which are optionally selected from Yoda1, Jedi1, Jedi2, or analogues or derivatives thereof.

13. The method of any one of claims 1 to 12, wherein the hematopoietic lineage is selected from progenitor-T cells, T lymphocytes, B lymphocytes, Natural Killer cells, neutrophils, monocyte, macrophages, red cells, megakaryocytes, and platelets.

14. The method of claim 13, wherein the HSC population or fraction thereof is differentiated *ex vivo* to progenitor T cells, T cells, NK cells, and/or fractions or analogous thereof.

15. The method of claim 14, wherein the HSC population or fraction thereof is cultured with a partial or full Notch ligand to produce a population comprising CD7+ progenitor T cells or a derivative cell population.

16. The method of claim 15, wherein the Notch ligand is incorporated along with a component of extracellular matrix, optionally selected from fibronectin, RetroNectin, and laminin, derivates or analogues thereof, and/or combinations thereof.

17. The method of claim 15 or 16, comprising generating a T cell lineage from the progenitor T cells.

18. The method of claim 17, comprising generating a natural killer (NK) cell population from the progenitor T cells.

19. A T cell or NK cell population, produced by the method of any one of claims 14 to 18.

20. Use of the T cell or NK cell population of claim 19 in the manufacture of a pharmaceutically acceptable composition for cell therapy to be administered to a human subject in need thereof.

21. The use of claim 20, wherein the human subject has a condition comprising one or more of lymphopenia, a cancer, an immune deficiency, an autoimmune disease, viral infection, a skeletal dysplasia, and a bone marrow failure syndrome.

22. The method of claim 13, wherein the HSC population or fraction thereof is differentiated to B lymphocytes or derivatives thereof.

23. A B lymphocyte population produced by the method of claim 22.

24. Use of the B lymphocyte population of claim 23 in the manufacture of a pharmaceutically acceptable composition for cell therapy or vaccination to be administered to a human subject in need thereof.

25. The method of claim 13, wherein the HSC population or fraction thereof is differentiated to neutrophils, monocytes or macrophages.

26. A neutrophil, monocyte, or macrophage population produced by the method of claim 25.

27. Use of the neutrophil, monocyte or macrophage population of claim 26 in the manufacture of a pharmaceutically acceptable composition for cell therapy to be administered to a human subject in need thereof.

28. The method of claim 13, wherein the HSC population or fraction thereof is differentiated to megakaryocytes, and optionally to platelets.

29. A megakaryocyte population of platelet population derived therefrom produced by the method of claim 28.

30. Use of the megakaryocyte or platelet population thereof of claim 29 in the manufacture of a pharmaceutically acceptable composition for cell therapy to be administered to a human subject in need thereof.

31. The method of claim 13, wherein the HSC population or fraction thereof is differentiated to red cells or derivatives thereof.

32. A red cell population or a population derived therefrom produced by the method of claim 31.

33. Use of the cell population thereof of claim 32 in the manufacture of a pharmaceutically acceptable composition for cell therapy to be administered to a human subject in need thereof.

34. A method comprising:

generating an HSC population comprising human long-term hematopoietic stem cells (LT-HSCs) from human pluripotent stem cells, wherein the HSC population is derived by endothelial-to-hematopoietic transition of CD34+ cells; and

culturing the HSC population or cells isolated therefrom with a partial or full Notch ligand and/or component of an extracellular matrix to produce a population comprising CD7+ progenitor T cells or a derivative cell population.

35. The method of claim 34, wherein the human pluripotent stem cells are induced pluripotent stem cells (iPSCs).

36. The method of claim 35, wherein the human pluripotent stem cells are derived from lymphocytes, cord blood cells, peripheral blood mononuclear cells, $CD34^+$ cells, or human primary tissues.

37. The method of claim 36, wherein the iPSC population is derived from CD34-enriched cells isolated from peripheral blood.

38. The method of claim 36, wherein the iPSC population is derived from T lymphocytes isolated from peripheral blood.

39. The method of any one of claims 34 to 38, wherein the iPSCs are homozygous for one or more HLA Class I and/or Class II genes.

40. The method of claim 39, wherein the iPSCs are gene-edited to delete one or more HLA Class I genes, one or more Class II genes, and/or delete one or more genes governing HLA or MHC expression or presentation capacity.

41. The method of any one of claims 34 to 40, wherein the endothelial-to-hematopoietic transition of the CD34+ cells is induced at Day 8 to Day 15 of iPSC differentiation.

42. The method of claim 41, wherein CD34+ cells are harvested from culture undergoing endothelial-to-hematopoietic transition, including harvesting of CD34+ floater and/or adherent cells.

43. The method of any one of claim 41 or 42, wherein generating the HSC population comprises increasing the expression or activity of dnmt3b in CD34+ cells.

44. The method of any one of claims 34 to 42, wherein generating the HSC population comprises Piezo1 activation.

45. The method of claim 44, wherein the cells subjected to Piezo1 activation are selected from one or more of iPSCs, EBs, CD34+ cells, ECs, HECs, and HSCs.

46. The method of claim 44 or 45, wherein the Piezo1 activation is by contacting the cells with one or more Piezo 1 agonists, which are optionally selected from Yoda1, Jedi1, Jedi2, or analogues or derivatives thereof.

47. The method of any one of claims 34 to 46, wherein the HSC population is derived from day 8 to day 17 differentiation of human iPSCs.

48. The method of any one of claims 34 to 47, wherein the $CD7^+$ progenitor T cells express CD5.

49. The method of any one of claims 34 to 48, wherein the Notch ligand comprises at least one of DLL1 and DLL4, or a functional portion thereof.

50. The method of claim 49, wherein the Notch ligand comprises a DLL1 amino acid sequence, or a functional portion thereof.

51. The method of claim 49, wherein the Notch ligand comprises a DLL4 amino acid sequence, or a functional portion thereof.

52. The method of any one of claims 34 to 51, comprising generating a derivative of the progenitor T cells or generating a T cell lineage from the progenitor T cells.