

WHAT IS CLAIMED IS:

1. A method of producing splanchnic mesoderm cells, comprising:
contacting lateral plate mesoderm cells with a TGF-beta signaling pathway inhibitor, a Wnt signaling pathway inhibitor, a BMP signaling pathway activator, an FGF signaling pathway activator, and a retinoic acid (RA) signaling pathway activator for a period of time sufficient to differentiate lateral plate mesoderm cells to splanchnic mesoderm cells.
2. The method of claim 1, wherein the splanchnic mesoderm cells are human splanchnic mesoderm cells.
3. The method of claim 1 or 2, wherein the lateral plate mesoderm cells have been differentiated from middle primitive stream cells.
4. The method of claim 3, wherein the lateral plate mesoderm cells have been differentiated from middle primitive streak cells by contacting the middle primitive streak cells with a TGF-beta signaling pathway inhibitor, a Wnt signaling pathway inhibitor, and a BMP signaling pathway activator.
5. The method of claim 3 or 4, wherein the middle primitive streak cells have been differentiated from pluripotent stem cells.
6. The method of claim 5, wherein the middle primitive streak cells have been differentiated from pluripotent stem cells by contacting the pluripotent stem cells with a TGF-beta signaling pathway activator, a Wnt signaling pathway activator, an FGF signaling pathway activator, a BMP signaling pathway activator, and a PI3K signaling pathway inhibitor.
7. The method of any one of claims 1 to 6, wherein the lateral plate mesoderm cells are contacted with A8301, BMP4, C59, FGF2, RA, or any combination thereof.
8. The method of any one of claims 1 to 7, wherein period of time is about 36-60 hours.
9. The method of any one of claims 1 to 8, wherein the splanchnic mesoderm cells exhibit increased expression of FOXF1, HOXA1, HOXA5, or WNT2, or any combination

thereof, and decreased expression of NKX2-5, ISL1, or TBX2, or any combination thereof, relative to cardiac mesoderm cells.

10. A method of producing septum transversum cells, comprising contacting splanchnic mesoderm cells with a retinoic acid signaling pathway activator and a BMP signaling pathway activator for a period of time sufficient to differentiate splanchnic mesoderm cells to septum transversum cells.

11. The method of claim 10, wherein the splanchnic mesoderm cells are produced by the method of any one of claims 1 to 9.

12. The method of claim 10 or 11, wherein the splanchnic mesoderm cells are contacted with RA, BMP4, or both.

13. The method of any one of claims 10 to 12, wherein the period of time is about 60-84 hours.

14. A method of producing fibroblasts, comprising contacting splanchnic mesoderm cells with a retinoic acid signaling pathway activator, a BMP signaling pathway activator, and a Wnt signaling pathway activator.

15. A method of producing respiratory mesenchyme cells, comprising a) contacting splanchnic mesoderm cells with a retinoic acid signaling pathway activator, a BMP signaling pathway activator, a hedgehog (HH) signaling pathway activator, and a Wnt signaling pathway activator for a period of time sufficient to differentiate splanchnic mesoderm cells to respiratory mesenchyme cells.

16. The method of claim 15, wherein the period of time is about 60-84 hours.

17. The method of claim 15 or 16, wherein step a) is a second step, and further comprising a first step of contacting the splanchnic mesoderm cells with a retinoic acid signaling pathway activator, a BMP signaling pathway activator, and a HH signaling pathway activator prior to the second step.

18. The method of any one of claims 15 to 17, wherein the splanchnic mesoderm cells are the splanchnic mesoderm cells produced by the method of any one of claims 1 to 9.

19. The method of any one of claims 15 to 18, wherein the splanchnic mesoderm cells are contacted with RA, BMP4, PMA, CHIR99021, or any combination thereof.

20. A method of producing esophageal/gastric mesenchyme cells, comprising contacting splanchnic mesoderm cells with a retinoic acid signaling pathway activator, a BMP signaling pathway inhibitor, and a HH signaling pathway activator.

21. An isolated splanchnic mesoderm cell produced by the method of any one of claims 1 to 9.

22. An isolated septum transversum cell produced by the method of any one of claims 10 to 13.

23. An isolated fibroblast produced by the method of claim 14.

24. An isolated respiratory mesenchyme cell produced by the method of any one of claims 15 to 19.

25. An isolated esophageal/gastric mesenchyme cell produced by the method of claim 20.