the activating and/or inhibiting of one or more signaling pathways within a precursor cell. Also disclosed are methods for using the disclosed gastric cells, gastric tissues, and or gastric organoids derived from precursor cells.

[0006a] In one aspect provided herein is an *in vitro* method of inducing formation of a gastric tissue, comprising the steps of: a) contacting a definitive endoderm cell with a WNT signaling pathway activator, an FGF signaling pathway activator, and a BMP signaling pathway inhibitor for a period of time sufficient to form SOX2+ foregut cells; b) contacting the SOX2+ foregut cells with retinoic acid for a period of time sufficient to form posterior foregut spheroids; and either c1) contacting the posterior foregut spheroids with retinoic acid, EGF, and a BMP signaling pathway inhibitor for a period of time sufficient to form the gastric tissue, wherein the gastric tissue is antrum gastric tissue; or c2) contacting the posterior foregut spheroids with retinoic acid, EGF, a BMP signaling pathway inhibitor and a WNT signaling pathway activator for a period of time sufficient to form the gastric tissue, wherein the gastric tissue is fundus gastric tissue.

[0006b] In one aspect provided herein is a gastric tissue produced by the method as described herein.

[0006c] In one aspect provided herein is an *in vitro* method for identifying the absorption effect of a gastric tissue, comprising the steps of: a) contacting the gastric tissue with a compound, wherein said gastric tissue is produced *in vitro* by the method as described herein; and b) detecting a level of absorption of said compound by said gastric tissue.

Brief Description of the Drawings

[0007] Those of skill in the art will understand that the drawings, described below, are for illustrative purposes only. The drawings are not intended to limit the scope of the present teachings in any way.

[0008] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

[0009] **FIG 1** depicts expression of Sox2/Cdx2/B-catenin in gastric spheroids and the effect of RA.

[0010] **FIG 2A-2E** depicts schematic representation of the *in vitro* culture system used to direct the differentiation of hPSCs into three-dimensional gastric organoids (FIG 2A), the defining markers of developing posterior foregut organs by wholemount immunofluorescent staining of mouse E10.5 embryos with Sox2, Pdx1 and Cdx2 (FIG 2B), PDX1 expression in the presence and absence of RA (FIG 2C), stereomicrographs showing morphological changes during growth of posterior foregut spheroids into hGOs (FIG 2D), and a comparison of developing mouse antrum at E14.5 and E18.5 and comparable stages of hGO development (FIG 2E).

[0011] **FIG 3A-3D** depictsMuc5AC, TFF2, GSII UEAI, and CHGA expression in P12 Antrum, E18.5 Antrum and d34 Organoid (FIG

Claims

What is claimed is:

1. An *in vitro* method of inducing formation of a gastric tissue, comprising the steps of:
a) contacting a definitive endoderm cell with a WNT signaling pathway activator, an FGF signaling pathway activator, and a BMP signaling pathway inhibitor for a period of time sufficient to form SOX2+ foregut cells;
b) contacting the SOX2+ foregut cells with retinoic acid for a period of time sufficient to form posterior foregut spheroids; and either
c1) contacting the posterior foregut spheroids with retinoic acid, EGF, and a BMP signaling pathway inhibitor for a period of time sufficient to form the gastric tissue, wherein the gastric tissue is antrum gastric tissue; or
c2) contacting the posterior foregut spheroids with retinoic acid, EGF, a BMP signaling pathway inhibitor and a WNT signaling pathway activator for a period of time sufficient to form the gastric tissue, wherein the gastric tissue is fundus gastric tissue.

2. The method of claim 1, wherein the gastric tissue is a gastric organoid.

3. The method of claim 2, wherein the definitive endoderm cell is derived from a pluripotent stem cell.

4. The method of any one of claims 1 through 3, wherein said definitive endoderm cell is derived from contacting a pluripotent stem cell with one or more molecules selected from Activin, the BMP subgroups of the TGF-beta superfamily of growth factors; Nodal, Activin A, Activin B, BMP4, Wnt3a, and combinations thereof.

5. The method of any one of claims 1 through 4, wherein said FGF signaling pathway activator is selected from one or more molecules selected from the group consisting of FGF1, FGF2, FGF3, FGF4, FGF10, FGF11, FGF12, FGF13, FGF14, FGF15, FGF16, FGF17, FGF18, FGF19, FGF20, FGF21, FGF22, and FGF23.

6. The method of any one of claims 1 through 5, wherein said FGF signaling pathway activator is FGF4.

7. The method of claim 6, wherein FGF4 is at a concentration between about 50 to about 1500 ng/mL.

8. The method of any one of claims 1 through 7, wherein said WNT signaling pathway activator is selected from one or more molecules selected from the group consisting of Wnt1, Wnt2, Wnt2b, Wnt3, Wnt3a, Wnt4, Wnt5a, Wnt5b, Wnt6, Wnt7a, Wnt7b, Wnt8a, Wnt8b, Wnt9a, Wnt9b, Wnt10a, Wnt10b, Wnt11, Wnt16, and a small molecule activator of the WNT signaling pathway.

9. The method of claim 8, wherein said small molecule activator of the WNT signaling pathway is selected from the group consisting of: Lithium Chloride; 2-amino-4,6-disubstituted pyrimidine (hetero) arylpyrimidines; IQ1; QS11; DCA; beta-catenin; 2-amino-4-[3,4-(methylenedioxy)-benzyl-amino]-6-(3-methoxyphenyl) pyrimidine; a GSK inhibitor; CHIR99021; WAY-316606; SB-216763 and BIO (6-bromoindirubin-3'-oxime).

10. The method of any one of claims 1 through 9, wherein said WNT signaling pathway activator is Wnt3a or CHIR99021.

11. The method of claim 10, wherein Wnt3 is at a concentration between about 50 and about 1500 ng/mL, or CHIR99021 is at a concentration of about 2 μM.

12. The method of any one of claims 1 through 11, wherein the WNT signaling pathway activator is Wnt3a or CHIR99021 and the FGF pathway activator is FGF4.

13. The method of any one of claims 1 through 12, wherein the BMP signaling pathway inhibitor is selected from Noggin, Dorsomorphin, LDN189, DMH-1, and combinations thereof.

14. The method of claim 13, wherein the BMP signaling pathway inhibitor is Noggin.

15. The method of claim 14, wherein Noggin is at a concentration between about 50 and about 1500 ng/mL.

16. The method of any one of claims 1 through 15, wherein the posterior foregut spheroids express PDX1, SOX2, HNF1beta, and HNF6.

17. The method of any one of claims 1 through 16 wherein the retinoic acid is contacted in an amount of between about 0.2 uM to about 20 uM.

18. The method of any one of claims 1 through 17, wherein step a) is carried out for a period of about 1 to about 4 days, and wherein step b) is carried out for about 1 to about 2 days .

19. The method of any one of claims 1 through 18, wherein the gastric tissue is greater than 1 mm in diameter, or greater than 2 mm in diameter, or greater than 3 mm in diameter, or greater than 4 mm in diameter.

20. The method of any one of claims 1 through 19, wherein the antrum gastric tissue is characterized by expression of MUC5AC, gastrin, ghrelin, 5-HT, and ChrA.

21. The method of any one of claims 1 through 20, wherein the fundus gastric tissue is characterized by expression of IRX3 and IRX5, and repression of PDX1.

22. A gastric tissue produced by the method of any one of claims 1-21.

23. The method of any one of claims 1-21, wherein step c1) is performed.

24. The method of any one of claims 1-21, wherein step c2) is performed.

25. An *in vitro* method for identifying the absorption effect of a gastric tissue, comprising the steps of:

a) contacting the gastric tissue with a compound, wherein said gastric tissue is produced *in vitro* by the method of any one of claims 1-21; and

b) detecting a level of absorption of said compound by said gastric tissue.