CLAIMS

1. A method of inducing differentiation of stem cells into hepatocytes, comprising the steps of:

(a) culturing induced pluripotent stem cells as starting cells under conditions for differentiation;

(b) inducing said starting cells to exit the pluripotent state towards the mesendoderm lineage;

(c) directing the differentiating cells towards endoderm cells through culture cell transfection with first mRNAs at an effective dose and within specific time windows, wherein the first mRNAs comprise FoxA2 or Sox17 mRNAs;

(d) further directing said endoderm cells towards hepatic progenitor cells through transfection with second mRNAs, wherein the second mRNAs comprise one more of Tbx3, GATA4, GATA6, and Hex mRNAs;

(e) further maturing said hepatic progenitor cells into hepatocytes with third mRNAs, wherein the third mRNAs comprise one or more of HNF4a, HNF1a, HNF6, CEB/Pa, and CEB/Pb mRNAs; and

(f) obtaining said hepatocytes by passaging progenitor cell clusters into monolayers or collecting clusters formed from said hepatic progenitor cells and replating into monolayers.

2. The method of claim 1, wherein said first mRNAs comprise FoxA2 mRNAs.

3. The method of claim 1, wherein said first mRNAs comprise Sox17 mRNAs.

4. The method of claim 1, wherein said first mRNAs comprise FoxA2 and Sox17 mRNAs.

5. The method of claim 1, wherein said first mRNAs comprise FoxA2, Sox17, GATA4, and GATA6 mRNAs.

6. The method of claim 1, wherein said second mRNAs comprise Hex mRNAs.

7. The method of claim 1, wherein said second mRNAs comprise Tbx3 mRNAs.

8. The method of claim 1, wherein said second mRNAs comprise Tbx3 and Hex mRNAs.

9. The method of claim 1, wherein said second mRNAs comprise Tbx3, GATA4, GATA6, and Hex mRNAs.

10. The method of claim 1, wherein said third mRNAs comprise HNF1a mRNAs.

11. The method of claim 1, wherein said third mRNAs comprise HNF4a mRNAs.

12. The method of claim 1, wherein said third mRNAs comprise HNF4a, HNF1a, HNF6, CEB/Pa, and CEB/Pb mRNAs.

13. The method of claim 1, wherein said induced pluripotent stem ~~starting~~ cells are generated from a body fluid or tissue of a subject.

~~14. A footprint-free cell obtained by the method of claim 13.~~

~~15. A composition for treating a liver disease, disorder, or malformation, comprising the cell of claim 14.~~

~~16. A cell of claim 14 or a composition comprising the cell of claim 14 for use in therapy.~~

~~17. The cell or composition of claim 16 for use in therapy, wherein the cell of claim 14 is derived from the recipient of the therapy.~~

~~18. The cell or composition of claim 16 for use in therapy, wherein the cell of claim 14 is harvested from the recipient of the therapy.~~

~~19. Use of the cell of claim 14 in the manufacture of a medicament for treating a liver disease.~~

~~20. The use of claim 19, wherein the cell of claim 14 is derived from the recipient of the treatment.~~

~~21. The use of claim 19, wherein the cell of claim 14 is harvested from the recipient of the treatment.~~

~~22~~14. A method of producing differentiated hepatocytes from induced pluripotent stem cells, comprising the steps of:

(a) culturing said induced pluripotent stem cells as starting cells under conditions for differentiation;

(b) inducing said starting cells to exit the pluripotent state towards the mesendoderm lineage;

(c) directing the differentiating cells towards endoderm cells through culture cell transfection with first mRNAs at an effective dose and within specific time windows, wherein the first mRNAs comprise FoxA2 or Sox17 mRNAs;

(d) further directing said endoderm cells towards hepatic progenitor cells through transfection with second mRNAs, wherein the second mRNAs comprise one more of Tbx3, GATA4, GATA6, and Hex mRNAs;

(e) further maturing said hepatic progenitor cells into hepatocytes with third mRNAs, wherein the third mRNAs comprise one or more of HNF4a, HNF1a, HNF6, CEB/Pa, and CEB/Pb mRNAs; and

(f) obtaining said hepatocytes by passaging progenitor cell clusters into monolayers or collecting clusters formed from said hepatic progenitor cells and replating into monolayers.

~~23~~15. A method for producing endoderm cells from induced pluripotent stem cells, comprising the steps of:

(a) culturing said induced pluripotent stem cells as starting cells under conditions for differentiation;

(b) inducing said starting cells to exit the pluripotent state towards the mesendoderm lineage; and

(c) directing the differentiating cells towards endoderm through culture cell transfection with endoderm-specific mRNAs comprising FoxA2 and/or Sox17 mRNAs at an effective dose and within specific time windows.