

CLAIMS:

The invention claimed in:

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 a first combination of mRNAs at an effective dose and within specific time windows;
 - (d) further directing said endoderm cells towards hepatic progenitor cells through transfection with a second combination of mRNAs;
 - (e) further maturing said hepatic progenitor cells into hepatocytes with a third combination of 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 combination of mRNAs comprises FoxA2 mRNAs.
3. The method of claim 1, wherein said first combination of mRNAs comprises Sox17 mRNAs.
4. The method of claim 1, wherein said first combination of mRNAs comprises FoxA2 and Sox17 mRNAs.
5. The method of claim 1, wherein said first combination of mRNAs comprises FoxA2, Sox17, GATA4, and GATA6 mRNAs.
6. The method of claim 1, wherein said second combination of mRNAs comprises Hex mRNAs.
7. The method of claim 1, wherein said second combination of mRNAs comprises Tbx3 mRNAs.
8. The method of claim 1, wherein said second combination of mRNAs comprises Tbx3 and Hex mRNAs.
9. The method of claim 1, wherein said second combination of mRNAs comprises Tbx3, GATA4, GATA6, and Hex mRNAs.

10. The method of claim 1, wherein said third combination of mRNAs comprises HNF1a mRNAs.
11. The method of claim 1, wherein said third combination of mRNAs comprises HNF4a mRNAs.
12. The method of claim 1, wherein said third combination of mRNAs comprises HNF4a, HNF1a, HNF6, CEB/Pa, and CEB/Pb mRNAs.
13. The method of claim 1, wherein said starting cells are harvested from a body fluid or tissue of a subject.
14. A cell obtained by the method of claim 1.
15. A composition for treating disease, disorder, or malformation, comprising the cell of claim 14.
16. A method of treating disease, disorder, or malformation, comprising the step of administering into the subject in need thereof at least one of the cells of claim 14 and the composition of claim 15.
17. The method of claim 16, wherein said cell is derived from the recipient subject.
18. The method of claim 16, wherein said starting cells are harvested from the recipient.
19. 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 a first combination of mRNAs at an effective dose and within specific time windows;
 - (d) further directing said endoderm cells towards hepatic progenitor cells through transfection with a second combination of mRNAs;
 - (e) further maturing said hepatic progenitor cells into hepatocytes with a third combination of 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.
20. 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 at an effective dose and within specific time windows.