CLAIMS

WHAT IS CLAIMED IS:

1. A method of inducing a trophoblast stem (TS) cell to differentiate into an induced hepatocyte *in vitro*, comprising:

contacting the trophoblast stem cell with a conditioned medium to induce differentiation of the trophoblast stem cell into an induced hepatocyte,

wherein the conditioned medium comprises a fibroblast growth factor (FGF), a steroid, and a cytokine.

2. The method of claim 1, further comprising contacting the trophoblast stem cell with the FGF prior to addition of the steroid and the cytokine to the conditioned medium.

3. The method of claim 2, wherein the trophoblast stem cell is contacted with the FGF for at least 2 hours, at least 4 hours, at least 6 hours, 8 hours, at least 12 hours, at least 16 hours, at least 20 hours, or at least 24 hours prior to addition of the steroid and the cytokine to the conditioned medium.

4. The method of any preceding claim, further comprising incubating the trophoblast stem cell for at least 1 day, at least 2 days, at least 3 days, at least 4 days, at least 5 days, at least 6 days, or at least 7 days.

5. The method of any preceding claim, wherein the induced hepatocyte is a hepatic progenitor cell.

6. The method of any preceding claim, wherein the differentiation comprises one or more of four stages: primitive streak to definitive endoderm (DE) stage, hepatic specified endoderm stage, hepatoblastic stage, and the fetal and adult hepatocyte cell stage.

7. The method of claim 6, wherein one or more biomarkers selected from the group consisting of CXCR4, FOXA2, SOX17, HHEX, TTR, ALB, TAT, CYP7A1, BSEP, SERPINA1, G6PC, ABCC2, C/EBPβ, HNF1α, HNF4α, and any combination thereof express in one or more of the four stages.

8. The method of claim 6 or 7, wherein one or more biomarkers selected from the group consisting of CXCR4, FOXA2, SOX17, HHEX, and any combination thereof, express at the primitive streak to DE stage.

9. The method of claim 8, wherein an expression level of CXCR4, FOXA2, SOX17, and/or HHEX increases at the primitive streak to DE stage, relative to that before the primitive streak to DE stage.

10. The method of claim 9, wherein the increased expression level is an increased level of gene expression.

11. The method of claim 9 or 10, wherein the expression level of CXCR4, FOXA2, SOX17 and/or HHEX increases by about 1 fold and about 10,000 fold higher than that before the primitive streak to DE stage.

12. The method of claim 9 or 10, wherein the expression level of CXCR4, FOXA2, SOX17 and/or HHEX increases by about 10 fold and about 1000 fold higher than that before the primitive streak to DE stage.

13. The method of any one of claims 6-12, wherein one or more biomarkers selected from the group consisting of SOX17, TTR, ALB, TAT, SERPINA1, CYP7A1, and any combination thereof express in the hepatic specified endoderm stage.

14. The method of claim 13, wherein an expression level of SOX17, TTR, ALB, TAT, SERPINA1, and/or CYP7A1 increases at the hepatic specified endoderm stage, relative to that before the hepatic specified endoderm stage.

15. The method of claim 14, wherein the increased expression level is an increased level of gene expression.

16. The method of claim 14 or 15, wherein the expression level of SOX17, TTR, ALB, TAT, SERPINA1, and/or CYP7A1 increases by about 1 fold and about 1000 fold higher than that before the hepatic specified endoderm stage.

17. The method of claim 14 or 15, wherein the expression level of SOX17, TTR, ALB, TAT, SERPINA1, and/or CYP7A1 increases by about 10 fold and about 100 fold higher than that before the hepatic specified endoderm stage.

18. The method of any one of claims 5-17, wherein one or more biomarkers selected from the group consisting of TTR, ALB, TAT, CYP7A1, SERPINA1, BSEP, and any combination thereof express at the hepatoblastic stage.

19. The method of claim 18, wherein an expression level of TTR, ALB, TAT, CYP7A1, SERPINA1, and/or BSEP increases at the hepatoblastic stage, relative to that before the hepatoblastic stage.

20. The method of claim 19, wherein the increased expression level is an increased level of gene expression.

21. The method of claim 19 or 20, wherein the expression level of TTR, ALB, TAT, CYP7A1, SERPINA1, and/or BSEP increases by about 1 fold and about 1000 fold higher than that before the hepatoblastic stage.

22. The method of claim 19 or 20, wherein the expression level of TTR, ALB, TAT, CYP7A1, SERPINA1, and/or BSEP increases by about 10 fold and about 100 fold higher than that before the hepatoblastic stage.

23. The method of any one of claims 6-22, wherein one or more biomarkers selected from the group consisting of HHEX, BSEP, TTR, ALB, TAT, SERPINA1, G6PC, ABCC2, C/EBPβ, HNF1α, HNF4α, and any combination thereof express at the fetal and adult hepatocyte-like cell stage.

24. The method of claim 23, wherein an expression level of HHEX, BSEP, TTR, ALB, TAT, SERPINA1, G6PC, ABCC2, C/EBPβ, HNF1α, and/or HNF4α increases at the fetal and adult hepatocyte-like cell stage, relative to that before the fetal and adult hepatocyte-like cell stage.

25. The method of claim 24, wherein the increased expression level is an increased level of gene expression.

26. The method of claim 24 or 25, wherein the expression level of HHEX, BSEP, TTR, ALB, TAT, SERPINA1, G6PC, ABCC2, C/EBPβ, HNF1α, and/or HNF4α increases by about 10 fold and about 1000 fold higher than that before the fetal and adult hepatocyte cell stage.

27. The method of claim 24 or 25, wherein the expression level of HHEX, BSEP, TTR, ALB, TAT, SERPINA1, G6PC, ABCC2, C/EBPβ, HNF1α, and/or HNF4α increases by at least 100 fold higher than that before the fetal and adult hepatocyte cell stage.

28. The method of any preceding claim, wherein the TS cell is a human TS cell.

29. The method of any preceding claim, wherein the steroid is dexamethasone.

30. The method of any preceding claim, wherein the cytokine is oncostatin M.

31. The method of claim 30, wherein the oncostatin M is a human oncostatin M.

32. The method of claim 31, wherein the human oncostatin M is a recombinant human oncostatin M.

33. The method of any preceding claim, wherein the conditioned medium further comprises a bone morphogenetic protein (BMP).

34. The method of claim 33, wherein the BMP is present in a concentration of about 1-100 ng/ml.

35. The method of claim 33, wherein the BMP is present in a concentration of about 1-50 ng/ml.

36. The method of claim 33, wherein the BMP is present in a concentration of about 20 ng/ml.

37. The method of any one of claims 33-36, wherein the BMP is BMP1, BMP2, BMP3, BMP4, BMP5, BMP6, BMP7, BMP8a, BMP8b, BMP10, or BMP15.

38. The method of claim 37, wherein the BMP is BMP4.

39. The method of any preceding claim, wherein the conditioned medium further comprises a hepatic growth factor (HGF).

40. The method of claim 39, wherein the HGF is present in a concentration of about 0.1-50 ng/ml.

41. The method of claim 39, wherein the HGF is present in a concentration of about 0.1-25 ng/ml.

42. The method of claim 39, wherein the HGF is present in a concentration of about 5 ng/ml.

43. The method of any preceding claim, wherein the induced hepatocyte is immune privileged.

44. The method of any preceding claim, wherein the induced hepatocyte expresses TGFβ1.

45. The method of any preceding claim, wherein the induced hepatocyte expresses TGFβ1, fibronectin, and collagen IV in extracellular matrix (ECM).

46. The method of any preceding claim, wherein the induced hepatocyte expresses HLA-G.

47. The method of any preceding claim, wherein the induced hepatocyte expresses HLA-G and stem-121.

48. The method of any preceding claim, wherein the induced hepatocytes recruit $CD4^+Foxp3^+$ Treg cells.

49. The method of any preceding claim, wherein the induced hepatocytes form tissue of a 3-dimensional structure.

50. The method of any preceding claim, wherein the induced hepatocytes cluster or aggregate.

51. The method of any preceding claim, wherein the induced hepatocytes form a crescent cell mass.

52. The method of any preceding claim, wherein the induced hepatocytes comprise a peripheral compartment and a central compartment.

53. The method of claim 52, wherein the induced hepatocytes distribute irregularly along ECM beyond basement membrane in the peripheral compartment.

54. The method of claim 52 or 53, wherein the induced hepatocytes distribute from basal towards central areas in the central compartment.

55. The method of any preceding claim, wherein the induced hepatocyte expresses one or more markers selected from the group consisting of TGFβ1, HLA-G, stem-121, C-kit,

CK19, CK18, ALB, α-AFP, betatrophin, ADH1, APOF, CPS1, GATA4, CYP1A1, CYP2B6, ASGR1, CXCR4, BSEP, MRP2, Cx32, and any combination thereof.

56. The method of claim 55, wherein the induced hepatocyte expresses one or more markers selected from the group consisting of TGFβ1, HLA-G, stem 121, C-kit, betatrophin, ADH1, APOF, CPS1, CYP2B6, ASGR1, CXCR4, Cx32, and any combination thereof.

57. The method of claim 56, wherein the induced hepatocyte expresses one or more markers selected from the group consisting of CPS1, CYP2B6, and a combination thereof.

58. An induced hepatocyte produced by the method of any preceding claim.

59.1. An isolated induced hepatocyte derived from a trophoblast stem cell, wherein the hepatocyte expresses one or more biomarkers selected from the group consisting of human leukocyte antigen G (HLA-G), transforming growth factor beta 1 (TGFβ1), cluster of differentiation 4 (CD4), forkhead box P3 (Foxp3), human cytoplasmic marker stem 121 (stem 121), mast/stem cell growth factor receptor C-kit (C-kit), betatrophin, apolipoprotein F (APOF), alcohol dehydrogenase 1 (ADH1), carbamoyl phosphate synthase 1 (CPS1), GATA transcription factor 4 (GATA4), cytochrome P450 family 1 subfamily A polypeptide 1 (CYP1A1), cytochrome P450 2B6 (CYP2B6), asialoglycoprotein receptor 1 (ASGR1), C-X-C chemokine receptor type 4 (CXCR4), bile salt export pump (BSEP), multi-drug resistance protein 2 (MRP2), connexin 32 (CX32), forkhead box protein A2 (FOXA2), SRY-box 17 (SOX17), hexosaminidase A alpha polypeptide (HEXA), hematopoietically expressed homeobox (HHEX), transthyretin (TTR), albumin (ALB), tyrosine aminotransferase (TAT), cytochrome P450 7A1 (CYP7A1), glucose-6-phosphatase (G6PC), serpin peptidase inhibitor clade A (alpha-1 antiproteinase, antitrypsin) member 1 (SERPINA1), ATP-binding cassette sub-family C (ABCC2), CCAAT-enhancer-binding protein beta (C/EBPβ), and hepatocyte nuclear factor 1-alpha (HNF1α)., hepatocyte nuclear factor 4-alpha (HNF4α), alpha-1-fetoprotein (AFP), cytokeratin 8 (CK8), phosphoenolpyruvate carboxykinase 2 mitochondrial (PCK2), glycogen synthase 2 (GYS2), hepatocyte nuclear factor 6 (HNF6), alcohol dehydrogenase 1C (class I) gamma polypeptide (ADH1C), cytochrome P450 3A4 (CYP3A4), prospero homeobox 1 (PROX1), tryptophan 2,3-dioxygenase (TDO2), cytokeratin 18 (CK18), and cytokeratin 19 (CK19).

60. The hepatocyte of any preceding claim, wherein the hepatocyte is a hepatic progenitor cell.

61. The hepatocyte of any preceding claim, wherein the hepatocyte is at one of four stages: primitive streak to definitive endoderm (DE) stage, hepatic specified endoderm stage, hepatoblastic stage, and the fetal and adult hepatocyte cell stage.

62. The hepatocyte of claim 61, wherein one or more biomarkers selected from the group consisting of CXCR4, FOXA2, SOX17, HHEX, TTR, ALB, TAT, CYP7A1, BSEP, SERPINA1, G6PC, ABCC2, C/EBPβ, HNF1α, HNF4α, and any combination thereof express in one or more of the four stages.

63. The hepatocyte of claim 61 or 62, wherein one or more biomarkers selected from the group consisting of CXCR4, FOXA2, SOX17, HHEX, and any combination thereof, express at the primitive streak to DE stage.

64. The hepatocyte of claim 63, wherein an expression level of CXCR4, FOXA2, SOX17, and/or HHEX increases at the primitive streak to DE stage, relative to that before the primitive streak to DE stage.

65. The hepatocyte of claim 64, wherein the increased expression level is an increased level of gene expression.

66. The hepatocyte of claim 64 or 65, wherein the expression level of CXCR4, FOXA2, SOX17 and/or HHEX increases by about 1 fold and about 10,000 fold higher than that before the primitive streak to DE stage.

67. The hepatocyte of claim 64 or 65, wherein the expression level of CXCR4, FOXA2, SOX17 and/or HHEX increases by about 10 fold and about 1000 fold higher than that before the primitive streak to DE stage.

68. The hepatocyte of any one of claims 60-67, wherein one or more biomarkers selected from the group consisting of SOX17, TTR, ALB, TAT, SERPINA1, CYP7A1, and any combination thereof express in the hepatic specified endoderm stage.

69. The hepatocyte of claim 68, wherein an expression level of SOX17, TTR, ALB, TAT, SERPINA1, and/or CYP7A1 increases at the hepatic specified endoderm stage, relative to that before the hepatic specified endoderm stage.

70. The hepatocyte of claim 69, wherein the increased expression level is an increased level of gene expression.

71. The hepatocyte of claim 69 or 70, wherein the expression level of SOX17, TTR, ALB, TAT, SERPINA1, and/or CYP7A1 increases by about 1 fold and about 1000 fold higher than that before the hepatic specified endoderm stage.

72. The hepatocyte of claim 69 or 70, wherein the expression level of SOX17, TTR, ALB, TAT, SERPINA1, and/or CYP7A1 increases by about 10 fold and about 100 fold higher than that before the hepatic specified endoderm stage.

73. The hepatocyte of any one of claims 60-72, wherein one or more biomarkers selected from the group consisting of TTR, ALB, TAT, CYP7A1, SERPINA1, bile salts excretion pump (BSEP), and any combination thereof express at the hepatoblastic stage.

74. The hepatocyte of claim 73, wherein an expression level of TTR, ALB, TAT, CYP7A1, SERPINA1, and/or BSEP increases at the hepatoblastic stage, relative to that before the hepatoblastic stage.

75. The hepatocyte of claim 74, wherein the increased expression level is an increased level of gene expression.

76. The hepatocyte of claim 74 or 75, wherein the expression level of TTR, ALB, TAT, CYP7A1, SERPINA1, and/or BSEP increases by about 1 fold and about 1000 fold higher than that before the hepatoblastic stage.

77. The hepatocyte of claim 74 or 75, wherein the expression level of TTR, ALB, TAT, CYP7A1, SERPINA1, and/or BSEP increases by about 10 fold and about 100 fold higher than that before the hepatoblastic stage.

78. The hepatocyte of any one of claims 60-77, wherein one or more biomarkers selected from the group consisting of HHEX, BSEP, TTR, ALB, TAT, SERPINA1, G6PC, ABCC2, C/EBPβ, HNF1α, HNF4α, and any combination thereof express at the fetal and adult hepatocyte-like cell stage.

79. The hepatocyte of claim 78, wherein an expression level of HHEX, BSEP, TTR, ALB, TAT, SERPINA1, G6PC, ABCC2, C/EBPβ, HNF1α, and/or HNF4α increases at the fetal and adult hepatocyte-like cell stage, relative to that before the fetal and adult hepatocyte-like cell stage.

80. The hepatocyte of claim 79, wherein the increased expression level is an increased level of gene expression.

81. The hepatocyte of claim 79 or 80, wherein the expression level of HHEX, BSEP, TTR, ALB, TAT, SERPINA1, G6PC, ABCC2, C/EBPβ, HNF1α, and/or HNF4α increases by about 10 fold and about 1000 fold higher than that before the fetal and adult hepatocyte cell stage.

82. The hepatocyte of claim 79 or 80, wherein the expression level of HHEX, BSEP, TTR, ALB, TAT, SERPINA1, G6PC, ABCC2, C/EBPβ, HNF1α, and/or HNF4α increases by at least 100 fold higher than that before the fetal and adult hepatocyte cell stage.

~~83. The hepatocyte of any one of claims 59-82, wherein the trophoblast stem cell is a human trophoblast stem cell.~~

~~84. The hepatocyte of any preceding claim, wherein the hepatocyte is immune privileged.~~

~~85. The hepatocyte of any preceding claim, wherein the hepatocyte expresses TGFβ1.~~

~~86. The hepatocyte of any preceding claim, wherein the hepatocyte expresses TGFβ1, fibronectin, and collagen IV in extracellular matrix (ECM).~~

~~87. The hepatocyte of any preceding claim, wherein the hepatocyte expresses HLA-G.~~

~~88. The hepatocyte of any preceding claim, wherein the hepatocyte expresses HLA-G and stem-121.~~

~~89.~~2. The hepatocyte of ~~any preceding~~ claim 1, wherein the hepatocyte recruits $CD4^+Foxp3^+$ Treg cells.

~~90.~~3. The hepatocyte of ~~any preceding~~ claim 1, wherein the hepatocytes form tissue of a 3-dimensional structure.

~~91.~~4. The hepatocyte of ~~any preceding~~ claim 1, wherein the hepatocytes cluster or aggregate.

~~92.~~5. The hepatocyte of ~~any preceding~~ claim 1, wherein the hepatocytes form a crescent cell mass.

~~93. The hepatocyte of any preceding claim, wherein the hepatocytes comprise a peripheral compartment and a central compartment.~~

~~94. The hepatocyte of claim 93, wherein the hepatocytes distribute irregularly along ECM beyond basement membrane in the peripheral compartment.~~

~~95. The hepatocyte of claim 93 or 94, wherein the hepatocytes distribute from basal towards central areas in the central compartment.~~

~~96.~~6. The hepatocyte of ~~any preceding~~ claim 1 or 2, wherein the hepatocyte expresses one or more markers selected from the group consisting of ~~TGFβ1, HLA-G, stem-121,~~ C-kit, CK19, CK18, ALB, α-AFP, betatrophin, ADH1, APOF, CPS1, GATA4, CYP1A1, CYP2B6, ASGR1, ~~CXCR4, BSEP,~~ MRP2, Cx32, G6PC, HNF4α, SOX17, TTR, TAT, and any combination thereof.

~~97. The hepatocyte of claim 96, wherein the hepatocyte expresses one or more markers selected from the group consisting of TGFβ1, HLA-G, stem-121, C-kit, betatrophin, ADH1, APOF, CPS1, CYP2B6, ASGR1, CXCR4, Cx32, and any combination thereof.~~

~~98. The hepatocyte of claim 97, wherein the hepatocyte expresses one or more markers selected from the group consisting of CPS1, CYP2B6, and a combination thereof.~~

99. The hepatocyte of claim 96, wherein the hepatocyte expresses one or more markers selected from the group consisting of stem 121, C-kit, CK19, CK18, and any combination thereof.

100. The hepatocyte of claim 96, wherein the hepatocyte expresses one or more markers selected from the group consisting of ALB, AFP, betatrophin, ADH1, APOF, CPS1, GATA4, CYP1A1, CYP2B6, and any combination thereof.

101. The hepatocyte of claim 96, wherein the hepatocyte expresses one or more markers selected from the group consisting of ASGR1, CXCR4, BSEP, MRP2, Cx32, and any combination thereof.

102. A method of screening a therapeutic compound for use in treatment or prevention of a condition, comprising:

a) contacting the isolated hepatocyte of any one of claims 55-101 with the therapeutic compound; and

b) detecting an expression level of a biomarker in the isolated hepatocyte.

103. The method of claim 102, wherein the expression level of a biomarker in the isolated hepatocyte increases as compared to an equivalent isolated hepatocyte not contacted with the therapeutic compound.

104. The method of claim 102, wherein the expression level of a biomarker in the isolated hepatocyte decreases as compared to an equivalent isolated hepatocyte not contacted with the therapeutic compound.

105. The method of any one of claims 102-104, wherein the expression level is a gene expression level.

106. The method of any one of claims 102-105, wherein the biomarker comprises CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2D6, CYP2E1, CYP3A4, or CYP7A1.

107. The method of any one of claims 102-106, wherein the therapeutic compound is a small molecule drug, a peptide, or a protein.

108. The method of any one of claims 102-106, wherein the therapeutic compound is a synthetic chemical drug.

109. The method of any one of claims 102-108, wherein the condition is a liver failure.

110. The method of any one of claims 102-109, wherein the condition is a liver-associated disease or disorder.

111. The method of claim 110, wherein the liver-associated disease or disorder comprises alagille syndrome, alpha-1 anti-trypsin deficiency, autoimmune hepatitis, benign liver tumors, biliary atresia, cirrhosis, cystic disease of the liver, fatty liver disease including

alcohol-related liver disease and non-alcohol fatty liver disease (NAFLD), galactosemia, gallstones, Gilbert's Syndrome, hemochromatosis, liver cysts, liver cancer, liver disease in pregnancy (optionally acute fatty liver of pregnancy, intrahepatic cholestasis of pregnancy, preeclampsia, or HELLP Syndrome (hemolysis, elevated liver tests, low platelets)), neonatal hepatitis, primary billary cirrhosis, primary sclerosing cholangitis, porphyria, Reye's Syndrome, sarcoidosis, toxic hepatitis, type 1 glocogen storage disease, tyrosinemia, viral hepatitis, Wilson disease, or any combination thereof.

112.7. A composition comprising the isolated hepatocyte of any one of claims 55-1011.

113.8. A pharmaceutical composition comprising the isolated hepatocyte of any of claims 55-101claim 1.

114.9. Use of the isolated hepatocyte of claim 1 in the manufacture of a medicament for the treatment of A method of treating a condition a liver-associated disease or disorder in a subject, comprising administering to a subject a pharmaceutical composition that comprises the isolated hepatocyte of any one of claims 55-101, in an amount effective for the hepatocytes to engraft to the subject.

115.10. The method use of claim 1149, wherein the medicament comprises the isolated hepatocytes are administered of claim 1 in a pharmaceutically acceptable carrier.

116.11. The method use of claim 11410, wherein the pharmaceutically acceptable carrier comprises a phosphate buffer saline.

117. The method of any one of claims 114-116, wherein the hepatocytes are administered in a suspension containing about $10x10^6$ to about $40x10^6$ cells per ml.

118. The method of any one of claims 114-117, wherein the hepatocytes are administered in a volume of about 10 ml to about 150 ml.

119. The method of any one of claims 114-118, wherein the subject is a human.

120. The method of any one of claims 114-119, wherein the administering comprises an injection.

121.12. The method use of claim 12011, wherein the injection medicament is formulated for administration as is an intravenous injection.

122. The method of claim 120, wherein the injection is administered at a hepatic vein.

123. The method of claim 120, wherein the injection is administered at a hepatic artery.

124. The method of any one of claims 114-123, wherein the condition is a liver-associated disease or disorder.

125.13. The method use of claim 1249, wherein the condition disease or disorder is a liver failure.

126. The method of claim 124, wherein the liver-associated disease or disorder comprises alagille syndrome, alpha-1 anti-trypsin deficiency, autoimmune hepatitis, benign liver tumors, biliary atresia, cirrhosis, cystic disease of the liver, fatty liver disease including alcohol-related liver disease and non-alcohol fatty liver disease (NAFLD), galactosemia, gallstones, Gilbert's Syndrome, hemochromatosis, liver cysts, liver cancer, liver disease in pregnancy (optionally, acute fatty liver of pregnancy, intrahepatic cholestasis of pregnancy, preeclampsia, or HELLP Syndrome (hemolysis, elevated liver tests, low platelets)), neonatal hepatitis, primary billary cirrhosis, primary sclerosing cholangitis, porphyria, Reye's Syndrome, sarcoidosis, toxic hepatitis, type 1 glocogen storage disease, tyrosinemia, viral hepatitis, Wilson disease, or any combination thereof.

127. Use of a composition comprising the isolated hepatocyte of any one of claims 55-101 for the production of therapeutic proteins.

128. The use of claim 127, wherein the therapeutic proteins comprise major plasma proteins such as human serum albumin, soluble plasma fibronectin, α-fetoprotein, C-reactive protein, and several globulins; proteins involved in hemostasis and fibrinolysis such as coagulation factors involved in the coagulation cascade, α2-macroglobulin, α1-antitrypsin, antithrombin III, protein S, protein C, plasminogen, α2-antiplasmin, and complement component 3; carrier proteins such as albumin, ceruloplasmin, transcortin, haptoglobin, hemopexin, IGF-binding rotein, major urinary proteins, retinol binding protein, sex hormone-binding globulin, transthyretin, transferrin, and Vitamin D-binding protein; hormones such as insulin-like growth factor 1, thrombopoietin, hepcidin, and betatrophin; prohormones such as angiotensinogen; or apolipoproteins.

129.14. Use of a composition comprising the hepatocyte of any one of claims 55-101claim 1 in the manufacture of a medicament for liver regeneration.

130.15. The use of claim 12914, wherein the liver regeneration is an *ex vivo* liver regeneration.

131. The use of claim 130, wherein the *ex vivo* liver regeneration is a bioprinting method.

132. The use of claim 131, wherein the bioprinting method is a 3-dimensional bioprinting method.

133. Use of a composition comprising the hepatocyte of any one of claims 55-101 for bioprinting.

134. The use of claim 133, wherein the bioprinting is a 3-dimensional bioprinting.

135. Use of the hepatocyte of any one of claims 55-101 for tissue scaffold generation.

136. The use of claim 135, wherein the tissue scaffold is a 3-dimensional tissue scaffold.

~~137. Use of a composition comprising the hepatocyte of any one of claims 55-101 for gene therapy.~~

~~138. The use of claim 137, wherein the gene therapy is an *ex vivo* gene therapy.~~

~~139. An artificial tissue generated from the hepatocytes of any one of claims 55-101.~~

~~140. The tissue of claim 139, wherein the tissue is three-dimensional.~~

~~141. The tissue of claim 139 or 140, wherein the issue is vascularized.~~

~~142. An artificial organ generated from the hepatocytes of any one of claims 55-101.~~

~~143. The hepatocyte, tissue, or organ of any preceding claim, wherein the hepatocyte, tissue, or organ produces AFP, ALB, alpha-1-antitrypsin, glucose, or glycogen.~~

~~144. The hepatocyte, tissue, or organ of any preceding claim, wherein the hepatocyte, tissue, or organ metabolizes a lipid, cholesterol, or carbohydrate.~~

~~145. The hepatocyte, tissue, or organ of any preceding claim, wherein the hepatocyte, tissue, or organ metabolizes a pharmaceutical drug or toxic substance.~~

~~146. The hepatocyte, tissue, or organ of any preceding claim, wherein the hepatocyte, tissue, or organ uptakes ammonia or bile acid.~~