CLAIMS

WHAT IS CLAIMED IS:

1. A pluripotent stem cell (PSC) engineered to express a nucleic acid comprising one or more transcription factors, wherein the PSC expresses at least three hepatocyte markers in a time period of 96 hours or less after induction of the one or more transcription factors.

2. The PSC of claim 1, wherein the one or more transcription factors comprise (a) one or more hepatocyte nuclear factor ("HNF") family members, (b) one or more forkhead box ("FOX") family members, or both.

3. The PSC of claim 2, wherein said one or more transcription factors comprises 2 or more HNF family members.

4. The PSC of claim 2 or 3, further comprising one or more additional transcription factors, wherein the one or more additional transcription factors comprises one or more of a CEBP, FOS, JUN, FOX, PROX, GATA, HHEX, HIF, HNF, MYC, CEBP, NFE, NFI, NR, RBPJ, RXR, SMAD, SOX, SPI, TBX, TP, PPAR, SALL, EGR, ONECUT, SKI or HLF family member.

5. The PSC of any one of claims 2-4, further comprising one or more additional transcription factors from Table 12.

6. The PSC of any one of claims 2-5, wherein said one or more HNF family members comprises HNF4A, HNF1A, ONECUT1/HNF6, or any combination thereof.

7. The PSC of any one of claims 2-6, wherein said one or more FOX family members comprises FOXA1, FOXA2, or both.

8. The PSC of any one of the preceding claims, wherein said one or more transcription factors comprises HNF4A, HNF1A, and FOXA1.

9. The PSC of any one of the preceding claims, wherein said one or more transcription factors comprises HNF4A, HNF1A, ONECUT1/HNF6, and FOXA1.

10. The PSC of any one of the preceding claims, wherein said one or more transcription factors comprises FOXA1, HNF1A, FOXA2, CEBPA, ONECUT1, HNF4A, and RBPJ.

11. The PSC of any one of the preceding claims, wherein said one or more transcription factors comprises CEBPA, FOXA1, HNF1A, HNF4A, ONECUT1/HNF6, and RBPJ.

12. The PSC of any one of the preceding claims, wherein said one or more transcription factors comprises GATA6.

13. The PSC of any one of the preceding claims, wherein said one or more transcription factors comprises HNF4A, HNF1A, CEBPA, FOXA1, and GATA6.

14. The PSC of any one of the preceding claims, wherein said one or more transcription factors comprises HNF4A, HNF1A, CEBPA, FOXA1, GATA6, and FOXA2.

15. The PSC of any one of the preceding claims, wherein the at least three hepatocyte markers comprise one or more of: CK18, Albumin, ASGR-1, and CXCR4.

16. A method of generating a population of hepatocytes or hepatic cells comprising:

(a) providing one or more pluripotent stem cells (PSCs);

(b) delivering to said one or more PSCs at least one nucleic acid comprising one or more transcription factors;

(c) generating said population of hepatocytes or hepatic cells from said one or more PSCs, wherein the PSCs express at least three hepatocyte markers in a time period of 96 hours or less after induction of the one or more transcription factors.

17. The method of claim 16, wherein the one or more transcription factors comprise (i) one or more hepatocyte nuclear factor ("HNF") family members, (ii) one or more forkhead box ("FOX") family members, or both.

18. The method of claim 17, wherein the one or more transcription factors comprises 2 or more HNF family members.

19. The method of claim 17 or 18, further comprising one or more additional transcription factors, wherein the one or more additional transcription factors comprises one or more of a CEBP, FOS, JUN, FOX, PROX, GATA, HHEX, HIF, HNF, MYC, CEBP, NFE, NFI, NR, RBPJ, RXR, SMAD, SOX, SPI, TBX, TP, PPAR, SALL, EGR, ONECUT, SKI or HLF family member.

20. The method of any one of claims 17-19, further comprising one or more additional transcription factors from Table 12.

21. The method of any one of claims 17-19, wherein said one or more HNF family members comprises HNF4A, HNF1A, ONECUT1/HNF6, or any combination thereof.

22. The method of any one of claims 17-21, wherein said one or more FOX family members comprises FOXA1, FOXA2, or both.

23. The method of any one of claims 16-22, wherein said one or more transcription factors comprises HNF4A, HNF1A, and FOXA1.

24. The method of any one of claims 16-22, wherein said one or more transcription factors comprises HNF4A, HNF1A, ONECUT1/HNF6, and FOXA1.

25. The method of any one of claims 16-22, wherein said one or more transcription factors comprises FOXA1, HNF1A, FOXA2, CEBPA, ONECUT1, HNF4A, and RBPJ.

26. The method of any one of claims 16-22, wherein said one or more transcription factors comprises CEBPA, FOXA1, HNF1A, HNF4A, ONECUT1/HNF6, and RBPJ.

27. The method of any one of claims 16-22, wherein said one or more transcription factors comprises GATA6.

28. The method of claim 27, wherein said one or more transcription factors comprises HNF4A, HNF1A, CEBPA, FOXA1, and GATA6.

29. The method of claim 27, wherein said one or more transcription factors comprises HNF4A, HNF1A, CEBPA, FOXA1, GATA6, and FOXA2.

30. The method of any one of claims 16-29, wherein the at least three hepatocyte markers comprise one or more of: CK18, Albumin, ASGR-1, and CXCR4.

31. The method of claim 30, wherein 4% or more of the PSCs express CK18.

32. The method of claim 30, wherein 2% or more of the PSCs express Albumin.

33. The method of claim 30, wherein a portion of the PSCs expressing Albumin also express CK18.

34. The method of claim 30, wherein 2% or more of the PSCs express ASGR-1.

35. The method of claim 30, wherein 2% or more of the PSCs express CXCR-4.

36. The method of any one of claims 16-35, wherein at least one of said one or more hepatocytes or said hepatic cells of said population of hepatocytes or hepatic cells expresses ASGR-1.

37. The method of any one of claims 16-36, wherein at least one of said one or more hepatocytes or said hepatic cells of said population of hepatocytes or hepatic cells expresses CXCR-4.

38. The method of any one of claims 16-37, wherein at least 2% of said population of hepatocytes or hepatic cells express ASGR-1.

39. The method of any one of claims 16-38, wherein at least 10% of said population of hepatocytes or hepatic cells express CXCR-4.

40. An exogenous expression cassette that induces differentiation of a pluripotent stem cell (PSC) into a hepatocyte or a hepatic cell, wherein the PSC expresses at least three hepatocyte markers in a time period of 96 hours or less after induction of the exogenous expression cassette comprising one or more transcription factor genes.

41. The exogenous expression cassette of claim 40, wherein the exogenous expression cassette comprises: (a) one or more hepatocyte nuclear factor (“HNF”) family member genes; (b) one or more forkhead box (“FOX”) family member genes; or both.

42. The exogenous expression cassette of claim 41, wherein the exogenous expression cassette comprises 2 or more HNF family members.

43. The exogenous expression cassette of claims 41 or 42, further comprising one or more additional transcription factor genes, wherein the one or more additional transcription factor genes comprises one or more genes of a CEBP, FOS, JUN, FOX, PROX, GATA, HHEX, HIF, HNF, MYC, CEBP, NFE, NFI, NR, RBPJ, RXR, SMAD, SOX, SPI, TBX, TP, PPAR, SALL, EGR, ONECUT, SKI or HLF family member.

44. The exogenous expression cassette of any one of claims 41-43, further comprising one or more gene of a transcription factor from Table 12.

45. The exogenous expression cassette of any one of claims 41-44, wherein said one or more HNF family members comprises HNF4A, HNF1A, ONECUT1/HNF6, or any combination thereof.

46. The exogenous expression cassette of any one of claims 41-45, wherein said one or more FOX family members comprises FOXA1, FOXA2, FOXA3, or any combination thereof.

47. The exogenous expression cassette of any one of claims 40-46, wherein said one or more transcription factors comprises HNF4A, HNF1A, and FOXA1.

48. The exogenous expression cassette of any one of claims 40-46, wherein said one or more transcription factors comprises HNF4A, HNF1A, ONECUT1/HNF6, and FOXA1.

49. The exogenous expression cassette of any one of claims 40-46, wherein said one or more transcription factors comprises FOXA1, HNF1A, FOXA2, CEBPA, ONECUT1, HNF4A, and RBPJ.

50. The exogenous expression cassette of any one of claims 40-46, wherein said one or more transcription factors comprises CEBPA, FOXA1, HNF1A, HNF4A, ONECUT1/HNF6, and RBPJ.

51. The exogenous expression cassette of any one of claims 40-46, wherein said one or more transcription factors comprises GATA6.

52. The exogenous expression cassette of any one of claim 51, wherein said one or more transcription factors comprises HNF4A, HNF1A, CEBPA, FOXA1, and GATA6.

53. The exogenous expression cassette of any one of claim 51, wherein said one or more transcription factors comprises HNF4A, HNF1A, CEBPA, FOXA1, GATA6, and FOXA2.

54. The exogenous expression cassette of any one of claims 40-53, wherein the at least three hepatocyte markers comprise one or more of: CK18, Albumin, ASGR-1, and CXCR4.

55. A pluripotent stem cell (PSC) comprising a nucleic acid comprising an open reading frame encoding one or more transcription factors, one or more transcription factors, or activator

of transcription of the open reading frame encoding one or more transcription factors, wherein said one or more transcription factors comprise: FOXA1, HNF1A, FOXA2, CEBPA, ONECUT1/HNF6, HNF4A, and RBPJ.

56. A pluripotent stem cell (PSC) comprising a nucleic acid comprising an open reading frame encoding one or more transcription factors, one or more transcription factors, or activator of transcription of the open reading frame encoding one or more transcription factors, wherein said one or more transcription factors comprise: HNF4A, HNF1A, ONECUT1/HNF6, and FOXA1.

57. A pluripotent stem cell (PSC) comprising a nucleic acid comprising an open reading frame encoding one or more transcription factors, one or more transcription factors, or activator of transcription of the open reading frame encoding one or more transcription factors, wherein said one or more transcription factors comprise: FOXA1, HNF1A, CEBPA, ONECUT1/HNF6, and HNF4A.

58. A pluripotent stem cell (PSC) comprising a nucleic acid comprising an open reading frame encoding one or more transcription factors, one or more transcription factors, or activator of transcription of the open reading frame encoding one or more transcription factors, wherein said one or more transcription factors comprise: CEBPA, FOXA1, HNF1A, HNF4A, ONECUT1/HNF6, and RBPJ.

59. A pluripotent stem cell (PSC) comprising a nucleic acid comprising an open reading frame encoding one or more transcription factors, one or more transcription factors, or activator of transcription of the open reading frame encoding one or more transcription factors, wherein said one or more transcription factors comprise: CEBPA, FOXA1, HNF1A, and HNF4A.

60. A kit for inducing differentiation of a pluripotent stem cell (PSC) into a hepatocyte or a hepatic cell, the kit comprising one or more transcription factors, wherein the PSC expresses at least three hepatocyte markers in a time period of 96 hours or less after induction of the one or more transcription factors.

61. The kit of claim 60, wherein the one or more transcription factors comprise (a) one or more hepatocyte nuclear factor (“HNF”) family members; (b) one or more forkhead box (“FOX”) family members; or both.

62. The kit of claim 61, wherein the one or more transcription factors comprises 2 or more HNF family members.

63. The kit of claim 61 or 62, further comprising one or more additional transcription factors, wherein the one or more additional transcription factors comprises one or more of a CEBP, FOS, JUN, FOX, PROX, GATA, HHEX, HIF, HNF, MYC, CEBP, NFE, NFI, NR,

RBPJ, RXR, SMAD, SOX, SPI, TBX, TP, PPAR, SALL, EGR, ONECUT, SKI or HLF family member.

64. The kit of any one of claims 61-63, further comprising one or more additional transcription factors from Table 12.

65. The kit of any one of claims 61-64, wherein said one or more HNF family members comprise HNF4A, HNF1A, ONECUT1/HNF6, or any combination thereof.

66. The kit of any one of claims 61-65, wherein said one or more FOX family members comprise FOXA1, FOXA2, or FOXA3, or any combination thereof.

67. The kit of any one of claims 60-66, wherein said one or more transcription factors comprises HNF4A, HNF1A, and FOXA1.

68. The kit of any one of claims 60-66, wherein said one or more transcription factors comprise HNF4A, HNF1A, ONECUT1/HNF6, and FOXA1.

69. The kit of any one of claims 60-66, wherein said one or more transcription factors comprises FOXA1, HNF1A, FOXA2, CEBPA, ONECUT1, HNF4A, and RBPJ.

70. The kit of any one of claims 60-66, wherein said one or more transcription factors comprise CEBPA, FOXA1, HNF1A, HNF4A, ONECUT1/HNF6, and RBPJ.

71. The kit of any one of claims 60-66, wherein said one or more transcription factors comprises GATA6.

72. The kit of claim 71, wherein said one or more transcription factors comprises HNF4A, HNF1A, CEBPA, FOXA1, and GATA6.

73. The kit of claim 71, wherein said one or more transcription factors comprises HNF4A, HNF1A, CEBPA, FOXA1, GATA6, and FOXA2.