Claims:

1. A method of producing hepatocytes comprising;

(i) providing a population of iPSCs

(ii) introducing a set of transcription factors comprising HNF1A; HNF6; a FOXA family protein; RORc and optionally ERα and/or NR1I3 into the population of iPSCs, and

(iii) culturing the population, such that one or more cells in the population are programmed into hepatocytes.

2. A method according to claim 1 wherein the set of transcription factors consists of HNF1A; HNF6; a FOXA family protein; RORc and ERα.

3. A method according to claim 1 wherein the set of transcription factors consists of HNF1A; HNF6; a FOXA family protein; and RORc.

4. A method according to claim 1 wherein the set of transcription factors consists of HNF1A; HNF6; a FOXA family protein; RORc and NR1I3.

5. A method according to any one of the preceding claims wherein the hepatocytes are functionally mature.

6. A method according to any one of the preceding claims wherein the pluripotent stem cells are human pluripotent stem cells (hPSCs).

7. A method according to any one of the preceding claims wherein the transcription factors are human transcription factors.

8. A method according to any one of the preceding claims wherein the population of cells is cultured under suitable conditions and for a sufficient period of time to allow one or more cells to display a hepatocyte phenotype.

9. A method according to any one of the preceding claims wherein during step (iii) the cells of said population do not display endoderm and hepatic progenitor phenotypes.

10. A method according to any one of the preceding claims wherein the set of transcription factors is introduced into the PSCs by:

(a) expressing nucleic acid encoding the combination of transcription factors in the PSCs;

(b) contacting the PSCs with the combination of transcription factor mRNAs or proteins; or

(c) activating endogenous expression of genes encoding the combination of transcription factors in the PSCs.

11. A method according to claim 10 wherein nucleic acid encoding the set of transcription factors is expressed in the PSCs by transfecting the PSCs with one or more vectors, optionally wherein the vectors are lentiviral vectors, comprising said nucleic acids operably linked to one or more regulatory elements for expression of the nucleic acids in the PSCs, optionally wherein the one or more regulatory elements are inducible regulatory elements.

12. A method according to any one of the preceding claims wherein the population of PSCs is cultured for at least 7 days.

13. A method according to any one of the preceding claims wherein at least 5% of said population are forward programmed into hepatocytes following step (iii).

14. A method according to any one of the preceding claims comprising:
isolating and/or purifying hepatocytes;
expanding the population of hepatocytes; and/or
storing the population of hepatocytes.

15. A population of PSCs or hepatocytes programmed to express heterologous nucleic acids encoding a set of transcription factors comprising HNF1A; HNF6; a FOXA family protein; RORc and optionally ERα and/or NR1I3.

16. A pharmaceutical composition comprising a population of hepatocytes according to claim 15, and a pharmaceutically acceptable excipient.

17. Use of a population of hepatocytes according to claim 15 in the manufacture of a medicament for the treatment of a liver disorder.

18. Use of a set of transcription factors comprising HNF1A; HNF6; a FOXA family protein; RORc and optionally ERα and/or NR1I3; or one or more nucleic acids encoding the set of transcription factors; to produce hepatocytes.

19. A method of screening for a compound useful in the treatment of a liver disorder comprising;
contacting a population of hepatocytes according to claim 15 with a test compound, and;
determining the effect of the test compound on said hepatocytes or the effect of the hepatocytes on the test compound.

20. A method of determining the hepatotoxicity of a compound comprising;
contacting isolated hepatocyte cells according to claim 15 with a test compound, and;
determining the effect of the test compound on said hepatocytes.