CLAIMS

What is claimed is:

1. A liver organoid derived from pluripotent stem cells (PSCs), said liver organoid comprising mesenchymal cells and a luminal structure comprising internalized microvilli, wherein said luminal structure is surrounded by polarized hepatocytes.

2. The liver organoid of claim 1 wherein said pluripotent stem cells (PSCs) are human induced pluripotent stem cells (iPSCs) or embryonic stem cells (ESCs).

3. The liver organoid of claim 1 or claim 2 wherein said liver organoid comprises functional stellate cells and functional Kupffer cells.

4. The liver organoid of any one of claims 1-3, wherein said liver organoid is characterized by having one or more of the following: bile production capacity, bile transport activity, Complement factor H expression of at least 50 ng/mL/1xe^6 cells/24hr, Complement factor B of at least 40 ng/mL/1xe^6 cells/24hr, C3 expression of at least 1000 ng/mL/1xe^6 cells/24hr, C4 expression of at least 1000 ng/mL/1xe^6 cells/24hr, fibrinogen production of at least 1,000 ng/mL/1xe^6 cells/24hr and albumin production of at least 1,000 ng/mL/1xe^6 cells/24hr.

5. The liver organoid of any one of claims 1-4, wherein said liver organoid is characterized by having total hepatic protein expression of at least 10,000 ng/mL 1xe^6 cells/24 hours.

6. The liver organoid of any one of claims 1-5, wherein said liver organoid expresses one or more genes selected from PROX1, RBP4, CYP2C9, CYP3A4, ABCC11, CFH, C3, C5, ALB, FBG, MRP2, ALCAM, CD68, CD34, CD31.

7. The liver organoid of any one of claims 1-6, wherein said liver organoid comprises a drug metabolism cytochrome variant, preferably a CY2C9*2 variant.

8. The liver organoid of any one of claims 1-7, wherein said liver organoid does not comprise inflammatory cells, for example T-cells or other inflammatory secreted proteins.

9. An *in vitro* method of screening for a serious adverse event (SAE), preferably liver failure and/or drug induced liver injury (DILI), comprising the step of contacting a drug of interest with the liver organoid of any one of claims 1-8.

10. The method of claim 9, wherein said method comprises the step of measuring intake and/or efflux of fluorescein diacetate (FD), wherein impaired efflux indicates that said drug is likely to induce a serious adverse event.

11. The method of claim 9 or 10, wherein the toxicity of said drug of interest is determined by measurement of a parameter selected from mitochondria membrane potential, measurement of ROS, swelling of liver mitochondria, and combinations thereof, wherein injury to said mitochondria indicates that said drug is likely to induce a serious adverse event.

12. The method of any one of claims 9-11, wherein said method comprises the step of assaying organoid viability, wherein an impaired organoid viability determination indicates that said drug is likely to induce a serious adverse event.

13. Use of the liver organoid of any one of claims 1-8 in treating an individual having liver damage.

14. Use of the liver organoid of claim 13, wherein said liver damage is selected from metabolic liver disease, end stage liver disease, or both.

15. An *in vitro* method of testing a candidate compound for an individual, comprising contacting the liver organoid of any one of claims 1-8 with a candidate compound.

16. The method of claim 15, wherein said liver organoid comprises one or more mutations found in said individual.

17. The method of claim 15 or 16, wherein said liver organoid is derived from the same ethic background of said individual.

18. The method of any one of claims 15-17, wherein said organoid is derived from said individual.