CLAIMS

1. A microfluidic device comprising a membrane, the membrane comprising a top surface and a bottom surface, the top surface comprising hepatocytes and the bottom surface comprising endothelial cells and a gel, in which the gel is between the hepatocytes and the top surface of the membrane, between the endothelial cells and the bottom surface of the membrane, or both.

2. A microfluidic device according to Claim 1, in which the hepatocytes are primary hepatocytes.

3. A microfluidic device according to Claim 1, further comprising additional cell types over, under or within the gel, the additional cell types selected from the group consisting of Stellate cells and Kupffer cells.

4. A method of culturing cells, comprising: (a) providing a microfluidic device comprising a membrane, the membrane comprising a top surface and a bottom surface; (b) seeding viable dog hepatocytes on the top surface and viable dog endothelial cells on the bottom surface; and (c) culturing the seeded cells under flow conditions such that the cells remain viable for at least 28 days.

5. A method according to Claim 4, in which the dog hepatocytes are primary dog hepatocytes.

6. A method of culturing cells, comprising (a) providing (i) a microfluidic device comprising a top chamber, a bottom chamber, and a membrane, the membrane comprising a top surface and a bottom surface, (ii) hepatocytes and endothelial cells and (iii) material capable of forming a gel; (b) introducing the material into the microfluidic device such that a gel forms in the top chamber, in the bottom chamber, or in both chambers; and (c) introducing, in any order, (i) the hepatocytes into the top chamber such that the hepatocytes either affix to the top surface of the membrane or the gel is between the hepatocytes and the top surface of the membrane, and (ii) the endothelial cells such that the endothelial cells either affix to the bottom surface of the membrane or the gel is between the endothelial cells and the bottom surface of the membrane; and (d) culturing the cells under flow conditions with media.

7. A method according to Claim 6, further comprising (e) adding additional cell types over, under or within the gel, the additional cell types selected from the group consisting of Kupffer cells and stellate cells.

8. A method according to Claim 6, in which the microfluidic device further comprises a removable top and the method further comprises, prior to step (b), removing the removable top so that the material can be introduced in step (b).

9. A method according to Claim 6, in which the microfluidic device further comprises a removable top and the method further comprises, prior to step (c), removing the removable top so that the hepatocytes can be introduced in step (c).

10. A method according to Claim 6, in which the hepatocytes are selected from the group consisting of viable rat hepatocytes, viable dog hepatocytes and viable human hepatocytes.

11. A method of culturing cells, comprising (a) providing (i) a microfluidic device comprising a top chamber, a bottom chamber, one or more gels, and a membrane, the membrane comprising a top surface and a bottom surface, (ii) hepatocytes and endothelial cells; (b) introducing, in any order, (i) the hepatocytes into the top chamber such that the hepatocytes either affix to the top surface of the membrane or the gel is between the hepatocytes and the top surface of the membrane, and (ii) the endothelial cells such that the endothelial cells either affix to the bottom surface of the membrane or the gel is between the endothelial cells and the bottom surface of the membrane; and (c) culturing the cells under flow conditions with media.

12. A method according to Claim 11, further comprising (d) adding additional cell types over, under or within the gel, the additional cell types selected from the group consisting of Kupffer cells and stellate cells.

13. A method for culturing cells, comprising:

(a) providing a fluidic device comprising a first structure defining a top chamber, a second structure defining a bottom chamber, and a membrane located at an interface region between the top chamber and the bottom chamber, the membrane including a top side facing toward the top chamber and a bottom side facing toward the bottom chamber;

(b) seeding hepatocytes in the top chamber and endothelial cells in the bottom chamber;

(c) perfusing at least one of the top chamber and bottom chamber with at least one fluid;

(d) disposing a test compound into the fluid, or introducing a second fluid comprising the test compound, such that hepatocytes, endothelial cells or both come in contact with the test compound; and

(e) stopping the perfusing in the top chamber, the bottom chamber, or both, so as to increase the residence time of the test compound within the fluidic device.

14. A method according to Claim 13, further comprising (f) assessing the clearance of the test compound.

15. A method according to Claim 14, in which the assessing the clearance comprises measuring the disappearance of the test compound.

16. A method for culturing cells, comprising:

(a) providing a fluidic device comprising a first structure defining a top chamber, a second structure defining a bottom chamber, and a membrane located at an interface region between the top chamber and the bottom chamber, the membrane including a top side facing toward the top chamber and a bottom side facing toward the bottom chamber;

(b) seeding hepatocytes in the top chamber and endothelial cells in the bottom chamber;

(c) perfusing at least one of the top chamber or bottom chamber with at least one fluid;

(d) disposing a test compound into the fluid such that hepatocytes, endothelial cells or both come in contact with the test compound; and

(e) recirculating the fluid so as to increase the interaction time of the test compound with the cells.

17. A method according to Claim 16, further comprising (f) assessing the clearance of the test compound.