CLAIMS

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

2. A microfluidic device according to Claim 1, in which the dog hepatocytes are primary dog 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 first surface and a second surface;

(b) seeding viable dog hepatocytes on the first surface and viable dog endothelial cells on the second 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 first chamber, a second chamber, a removable top, and a membrane, the membrane comprising a first surface and a second surface,

(ii) hepatocytes and endothelial cells and

(iii) material capable of forming a gel;

(b) removing the removable top and introducing the material into the microfluidic device such that a gel forms in the first chamber, in the second chamber, or in both chambers; and

(c) introducing, in any order,

(i) the hepatocytes into the first chamber such that the hepatocytes either affix to the first surface of the membrane or the gel is between the hepatocytes and the first surface of the membrane, and

(ii) the endothelial cells such that the endothelial cells either affix to the second surface of the membrane or the gel is between the endothelial cells and the second 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 hepatocytes are selected from the group consisting of viable rat hepatocytes, viable dog hepatocytes and viable human hepatocytes.

10. A method of culturing cells, comprising

(a) providing

(i) a microfluidic device comprising a first chamber, a second chamber, one or more gels, and a membrane, the membrane comprising a first surface and a second surface,

(ii) hepatocytes, endothelial cells and Stellate cells;

(b) introducing, in any order,

(i) the hepatocytes into the first chamber such that the hepatocytes either affix to the first surface of the membrane or the gel is between the hepatocytes and the first surface of the membrane,

(ii) the endothelial cells such that the endothelial cells either affix to the second surface of the membrane or the gel is between the endothelial cells and the second surface of the membrane, and

(iii) Stellate cells within the gel, in which the gel inhibits activation and/or migration of the Stellate cells; and

(c) culturing the cells under flow conditions with media.

11. A method according to Claim 10, further comprising the step of modifying the porosity and/or stiffness of the gel.

12. A method for culturing cells, comprising:

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

(b) seeding hepatocytes in the first chamber and endothelial cells in the second chamber;

(c) perfusing at least one of the first chamber and second 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 first chamber, the second chamber, or both, so as to increase the residence time of the test compound within the fluidic device.

13. A method according to Claim 12, further comprising (f) assessing the clearance of the test compound.

14. A method according to Claim 13, in which the assessing the clearance comprises measuring the disappearance of the test compound.

15. A method for culturing cells, comprising:

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

(b) seeding dog hepatocytes in the first chamber and dog endothelial cells in the second chamber;

(c) perfusing at least one of the first chamber or second chamber with at least one fluid;

(d) disposing a test compound into the fluid such that the dog hepatocytes, dog 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.

16. A method according to Claim 15, further comprising (f) assessing the clearance of the test compound.