

CLAIMS

1. A microfluidic chip, comprising:

a planar surface;

a first channel formed on the planar surface and having a first volume defined by a first width, a first height, and a first length, the first volume extending in a first direction; and

a second channel formed on the planar surface adjacent to the first channel, the second channel having a second volume defined by a second width, a second height, and a second length, the second volume extending in the first direction, the second height being greater than the first height;

wherein the first channel is in fluid communication with the second channel through a first opening that extends along at least a portion of the first length, the first opening extending from the planar surface to the first height; and

wherein the first height and the second height are sized to generate sufficient surface tension at the first opening such that a liquid injected into the first channel or the second channel is substantially confined within the first volume or the second volume, respectively, or that flow of the liquid therebetween is controlled, the surface tension producing a non-physical microfluidic barrier that limits or selectively controls passage of the liquid.

2. The microfluidic chip of claim 1, further comprising:

a third channel formed on the planar surface adjacent to the first channel, the third channel having a third volume defined by a third width, a third height, and a third length, the third volume extending in the first direction, the third height being greater than the first height;

wherein the third channel is in fluid communication with the first channel through a second opening that extends along at least a portion of the first length, the second opening extending from the planar surface to the first height; and

wherein the first height and the third height are sized to generate sufficient surface tension at the second opening such that a liquid injected into the first channel or the third channel is substantially confined within the first volume or the third volume, respectively, or that flow of the liquid therebetween is controlled, the surface tension producing a second non-physical microfluidic barrier that limits or selectively controls passage of the liquid.

3. The microfluidic chip of claim 1, further comprising:

a third channel formed on the planar surface adjacent to the second channel, the third channel having a third volume defined by a third width, a third height, and a third length, the third volume extending in the first direction, the third height being less than the second height;

wherein the third channel is in fluid communication with the second channel through a second opening that extends along at least a portion of the second length, the second opening extending from the planar surface to the third height; and

wherein the second height and the third height are sized to generate sufficient surface tension at the second opening such that a liquid injected into the second channel or the third channel is substantially confined within the second volume or the third volume, respectively, or that flow of the liquid therebetween is controlled, the surface tension producing a second non-physical microfluidic barrier that limits or selectively controls passage of the liquid.

4. A microphysiological system, comprising:

the microfluidic chip of any one of claims 1-3; and

an extracellular matrix confined within the first volume of the first channel, a side wall of the extracellular matrix extending across the first opening and forming the non-physical microfluidic barrier between the first channel and the second channel.

5. The microphysiological system of claim 4, further comprising an epithelial barrier arranged in the first opening between the first channel and the second channel.

6. The microphysiological system of claim 5, wherein the epithelial barrier is continuous.

7. The microphysiological system of claim 5 or 6, wherein the epithelial barrier comprises endothelial cells.

8. The microphysiological system of claim 7, wherein the epithelial barrier is an endothelial barrier.

9. The microphysiological system of claim 8, wherein the endothelial barrier comprises Brain Microvascular Endothelial Cells (BMEC).

10. The microphysiological system of claim 8, wherein the endothelial barrier comprises human BMEC.

11. The microphysiological system of any one of claims 4-10, further comprising pericytes in the second channel.

12. The microphysiological system of any one of claims 4-11, further comprising first cells in the extracellular matrix in the first channel.

13. The microphysiological system of claim 12, wherein the first cells are neural cells.

14. The microphysiological system of claim 13, wherein the neural cells comprise human induced pluripotent stem cell-derived neural progenitor cells, astrocytes, microglia, or combinations thereof.

15. The microphysiological system of claim 12, wherein the first cells are cardiac cells, skeletal muscle cells, hepatic cells, renal cells, bone cells, skin cells, esophageal cells, intestinal cells, gastric cells, colon cells, lung cells, or pancreatic cells.

16. The microphysiological system of any one of claims 4-15, wherein the extracellular matrix comprises a hydrogel.

17. The microphysiological system of claim 16, wherein the hydrogel comprises basement membrane extract (BME).

18. The microphysiological system of any one of claims 4-17, further comprising a first media confined within the second volume of the second channel.

19. The microphysiological system of any one of claims 4-18, wherein the third height is greater than the first height, and the microphysiological system further comprises a second media confined within the third volume of the third channel.

20. The microphysiological system of any one of claims 4-18, wherein the third height is less than the second height, and the microphysiological system further comprises a second extracellular matrix confined within the third volume of the third channel.

21. The microphysiological system of any one of claims 4-20, wherein the microphysiological system is a vascularized tissue model.

22. The microphysiological system of claim 21, wherein the vascularized tissue model is a blood brain barrier model or a stroke model.

23. The microphysiological system of claim 21, wherein the vascularized tissue model is a cardiac model, a skeletal muscle model, a liver model, a kidney model, a bone model, a skin model, an esophageal model, a gastric model, a colon model, an intestinal model, a lung model, or a pancreatic model.

24. A method of preparing the microphysiological system of any one of claims 4-23, the method comprising:

depositing an extracellular matrix precursor into the first channel of the microfluidic chip; and

curing the extracellular matrix precursor to provide the extracellular matrix in the first channel.

25. The method of claim 24, wherein the curing the extracellular matrix precursor comprises incubating the extracellular matrix precursor, and wherein the method further comprises depositing the first media into the second channel adjacent to the extracellular matrix in the first channel.

26. The method of claim 24 or 25, further comprising culturing a continuous endothelial barrier in the first opening between the first channel and the second channel, wherein the first media further comprises pericytes.

27. A method for screening a therapeutic agent, the method comprising:
depositing the therapeutic agent in the second channel of the microfluidic chip of a microphysiological system of any one of claims 4-23; and
imaging the microfluidic chip.

28. The method of claim 27, wherein the therapeutic agent comprises a stem cell, a small molecule, or a peptide.

29. The method of claim 27 or 28, further comprising performing the method of any one of claims 24-26.