CLAIMS

1. A method of culturing cells, comprising:

(a) providing cells comprising stem cells under conditions of low oxygen tension for a period of time, a microfluidic device comprising a membrane having a top surface and a bottom surface;

(b) seeding the stem cells on the bottom surface; and

(c) culturing the seeded stem cells under approximately 5% oxygen in the presence of retinoic acid to support maturation and differentiation of brain microvascular endothelial cells (BMVECs), in which the BMVECs have increased expression of the glucose transporter protein GLUT1 as compared to normal oxygen conditions.

2. A method according to Claim 1, in which the stem cells, prior to step (b), are exposed to low oxygen tension for 10 days.

3. A method according to Claim 1, further comprising exposing the seeded cells to a flow of culture media.

4. A method according to Claim 1, in which the stem cells are human pluripotent stem cells.

5. A method according to Claim 4, in which the human pluripotent stem cells are induced human pluripotent stem cells.

6. A method according to Claim 1, in which the approximately 5% oxygen in step (c) is maintained for 24 hours.

7. A method according to Claim 1, in which the BMVECs are co-cultured with astrocytes and pericytes.

8. A method of culturing cells, comprising:

(a) providing cells comprising stem cells under conditions of low oxygen tension for a period of time, a microfluidic device comprising a membrane having a top surface and a bottom surface;

(b) seeding the stem cells on the bottom surface; and

(c) culturing the seeded stem cells under approximately 5% oxygen in the presence of retinoic acid to support maturation and differentiation of brain microvascular endothelial cells (BMVECs), in which the BMVECs have increased expression of the insulin receptor protein INSR as compared to normal oxygen conditions.

9. A method according to Claim 8, in which the stem cells, prior to step (b), are exposed to low oxygen tension for 10 days.

10. A method according to Claim 8, in which the increased expression of the insulin receptor protein INSR is approximately two-fold.

11. A method according to Claim 8, in which the increased expression of the insulin transporter protein INSR is approximately three-fold**.**

12. A method according to Claim 8, in which the approximately 5% oxygen in step (c) is maintained for 24 hours.

13. A method according to Claim 8, in which the BMVECs are co-cultured with astrocytes and pericytes.

14. A method of culturing cells, comprising:

(a) providing cells comprising stem cells under conditions of low oxygen tension for a period of time, a microfluidic device comprising a membrane having a top surface and a bottom surface;

(b) seeding the stem cells on the bottom surface;

(c) culturing the seeded stem cells under approximately 5% oxygen in the presence of retinoic acid to support maturation and differentiation of brain microvascular endothelial cells (BMVECs), in which the BMVECs have increased expression of a caveolin-1 protein as compared to normal oxygen conditions.

15. A method according to Claim 14, in which the stem cells, prior to step (b), are exposed to low oxygen tension for 10 days.

16. A method according to Claim 14, in which the increased expression of the caveolin-1 protein is approximately two-fold**.**

17. A method according to Claim 14, in which the approximately 5% oxygen in step (c) is maintained for 24 hours.

18. A method according to Claim 14, in which the BMVECs are co-cultured with astrocytes and pericytes.

19. A method of culturing cells, comprising:

(a) providing cells comprising stem cells under conditions of low oxygen tension for a period of time, a microfluidic device comprising a membrane having a top surface and a bottom surface;

(b) seeding the stem cells on the bottom surface; and

(c) culturing the seeded stem cells under approximately 5% oxygen in the presence of retinoic acid to support maturation and differentiation of brain microvascular endothelial cells (BMVECs), in which the BMVECs have increased expression of the clathrin heavy chain 1 protein CLTC as compared to normal oxygen conditions.

20. A method according to Claim 19, in which the stem cells, prior to step (b) are exposed to low oxygen tension for 10 days.

21. A method according to Claim 19, in which the increased expression of the clathrin heavy chain 1 protein CLTC is approximately two-fold.

22. A method according to Claim 19, in which the approximately 5% oxygen in step (c) is maintained for 24 hours.

23. A method according to Claim 19, in which the BMVECs are co-cultured with astrocytes and pericytes.

24. A method of culturing cells, comprising:

(a) providing cells comprising stem cells under conditions of low oxygen tension for a period of time, a microfluidic device comprising a membrane having a top surface and a bottom surface;

(b) seeding the stem cells on the bottom surface; and

(c) culturing the seeded stem cells under approximately 5% oxygen in the presence of retinoic acid to support maturation and differentiation of brain microvascular endothelial

cells (BMVECs), in which the BMVECs have increased expression of the multi drug resistance protein ABCC4, ABCC1 or BCRP as compared to normal oxygen conditions.

25. A method according to Claim 24, in which the stem cells, prior to step (b) are exposed to low oxygen tension for 10 days.

26. A method according to Claim 24, in which the increased expression of the ABCC4 or ABCC1 is approximately two-fold.

27. A method according to Claim 24, in which the increased expression of the BCRP is approximately twenty-two fold.

28. A method according to Claim 24, in which the approximately 5% oxygen in step (c) is maintained for 24 hours.

29. A method according to Claim 24, in which the BMVECs are co-cultured with astrocytes and pericytes.

30. A method of culturing cells, comprising:

(a) providing cells comprising stem cells under conditions of low oxygen tension for a period of time, a microfluidic device comprising a membrane having a top surface and a bottom surface;

(b) seeding the stem cells on the bottom surface; and

(c) culturing the seeded stem cells under approximately 5% oxygen in the presence of retinoic acid to support maturation and differentiation of brain microvascular endothelial cells (BMVECs), in which the BMVECs have increased expression of the transmembrane efflux pump protein ABCB as compared to normal oxygen conditions.

31. A method according to Claim 30, in which the stem cells, prior to step (b) are exposed to low oxygen tension for 10 days.

32. A method according to Claim 30, in which the increased expression of the ABCB is approximately ten-fold.

33. A method according to Claim 30, in which the approximately 5% oxygen in step (c) is maintained for 24 hours.

34. A method according to Claim 30, in which the seeded stem cells are co-cultured with astrocytes and pericytes.