CLAIMS

We claim:

1. An *in vitro* blood-brain barrier (BBB) system comprising E4ORF1+ endothelial cells.

2. The system of claim 1, wherein the endothelial cells are mouse endothelial cells.

3. The system of claim 1, wherein the endothelial cells are human endothelial cells.

4. The system of claim 1, wherein the endothelial cells are brain endothelial cells.

5. The system of claim 4, wherein the brain endothelial cells are brain microvascular endothelial cells.

6. The system of claim 4, wherein the brain endothelial cells are derived from a brain tumor.

7. The system of claim 4, wherein the brain endothelial cells are derived from a glioma.

8. The system of claim 4, wherein the brain endothelial cells are derived from a glioblastoma (GBM).

9. The system of claim 1, wherein the E4ORF1+ endothelial cells are disposed upon a permeable solid support.

10. The system of claim 9, wherein the permeable solid support is a membrane or filter.

11. The system of claim 9, wherein the permeable solid support comprises polyester, polycarbonate, nitrocellulose, cellulose, or fiberglass.

12. The system of claim 9, wherein the permeable solid support is coated with one or more extracellular matrix components.

13. The system of claim 12, wherein the extracellular matrix components are selected from the group consisting of astrocyte extracellular matrix, laminin, vitronectin, fibronectin, collagen, and Matrigel.

14. The system of claim 1, further comprising an additional cell type selected from the group consisting of astrocytes, pericytes, and neural stem/progenitor cells (NSPCs).

15. The system of claim 14, wherein the astrocytes are mouse astrocytes.

16. The system of claim 14, wherein the astrocytes are human astrocytes.

17. The system of claim 14, wherein the astrocytes are in in direct contact with the endothelial cells.

18. The system of claim 1, wherein the endothelial cells are present in an essentially confluent endothelial monolayer.

19. The system of claim 1, comprising an essentially confluent monolayer of astrocytes.

20. The system according to claim 18, wherein the endothelial cell monolayer has a trans endothelial electrical resistance (TEER) of greater than about 25 $\Omega \cdot cm^2$, or greater than about 50 $\Omega \cdot cm^2$, or greater than about 75 $\Omega \cdot cm^2$, or greater than about 100 $\Omega \cdot cm^2$, or greater than about 125 $\Omega \cdot cm^2$, or greater than about 150 $\Omega \cdot cm^2$, or greater than about 175 $\Omega \cdot cm^2$, or greater than about 200 $\Omega \cdot cm^2$.

21. The system according to claim 18 wherein the endothelial cell monolayer has a Lucifer Yellow permeability coefficient (Pc) of less than about 2.5×10^{-6} cm/s.

22. A method for assessing the blood-brain barrier permeability of a candidate agent, the method comprising contacting the endothelial cells in the system of claim 1 with a candidate agent.

23. A method for assessing the blood-brain barrier permeability of a candidate agent, the method comprising: (a) contacting one side of an endothelial cell monolayer in a BBB system according to claim 1 with a candidate agent, and (b) determining whether the candidate agent is present on the other side of the endothelial cell monolayer, wherein if

the candidate agent is present on the other side of the endothelial cell monolayer the agent is blood-brain-barrier permeable, and wherein if the candidate agent is not present on the other side of the endothelial cell monolayer the agent is not blood-brain-barrier permeable.

24. A method for assessing the effect of an agent on the permeability of the blood-brain barrier, the method comprising: contacting the endothelial cells in a system according to claim 1 with a candidate agent.

25. A method for assessing the effect of an agent on the permeability of the blood-brain barrier, the method comprising: (a) contacting the endothelial cells in a BBB system according to claim 1 with a candidate agent, and (b) determining the trans endothelial electrical resistance (TEER) of the BBB system, wherein if the candidate agent decreases the TEER value of the BBB system as compared to the TEER value in the absence of the candidate agent, then the candidate agent increases the permeability of the BBB, and if the candidate agent increases the TEER value of the BBB system as compared to the TEER value in the absence of the candidate agent, then the candidate agent reduces the permeability of the BBB.

26. A method for assessing the effect of an agent on the permeability of the blood-brain barrier, the method comprising: contacting the endothelial cells in a BBB system according to claim 1 with a candidate agent, and determining the permeability coefficient (Pc) of the BBB system, wherein if the candidate agent decreases the Pc value of the BBB system as compared to the Pc value in the absence of the candidate agent, then the candidate agent decreases the permeability of the BBB, and if the candidate agent increases the Pc value of the BBB system as compared to the Pc value in the absence of the candidate agent, then the candidate agent increases the permeability of the BBB.

27. A composition comprising E4ORF1+ endothelial cells and astrocytes, and optionally also comprising (a) pericytes and/or (b) neural stem/progenitor cells (NSPCs).

28. The composition of claim 27, wherein the endothelial cells are mouse E4ORF1+ endothelial cells.

29. The composition of claim 27, wherein the E4ORF1+ endothelial cells are human E4ORF1+ endothelial cells.

30. The composition of claim 27, wherein the E4ORF1+ endothelial cells are brain endothelial cells.

31. The composition of claim 30, wherein the brain endothelial cells are brain microvascular endothelial cells.

32. The composition of claim 30, wherein the brain endothelial cells are derived from a brain tumor.

33. The composition of claim 30, wherein the brain endothelial cells are derived from a glioma.

34. The composition of claim 30, wherein the brain endothelial cells are derived from a glioblastoma.

35. The composition of claim 27, wherein the astrocytes are mouse astrocytes.

36. The composition of claim 27, wherein the astrocytes are human astrocytes.

37. The composition of claim 27, wherein the astrocytes are in in direct contact with the endothelial cells.

38. The composition according to any of claims 27 to 37, wherein the endothelial cells are present in an essentially confluent endothelial monolayer.