Technology Licensing Opportunity

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Blood Brain Barrier Model in a 3D Co-culture Microfluidic System

Technology overview

Blood brain barrier (BBB) is a selective barrier that restricts compounds entering the central nervous system (CNS). This tight regulation is important for maintaining homeostasis of the neural microenvironment and protecting the CNS from chemical insults and damage. However, this protective barrier may also hinder drug delivery. The *in-vivo* BBB consists of brain endothelial cells (EC), astrocytes, pericytes, smooth muscle cells, and glial cells. EC forms the wall of capillaries and astrocytes form a complex network surrounding the capillaries. This close cell association between neurons, astrocytes and EC is important in induction and maintenance of the barrier properties. An efficient in vitro BBB model consisting of these key cells is required to recapitulate the i*n vivo* BBB and to shed light on contributions from each individual cell type.

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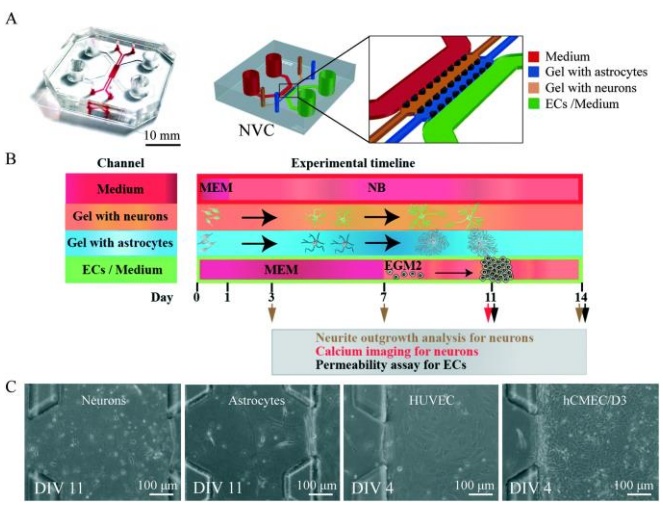
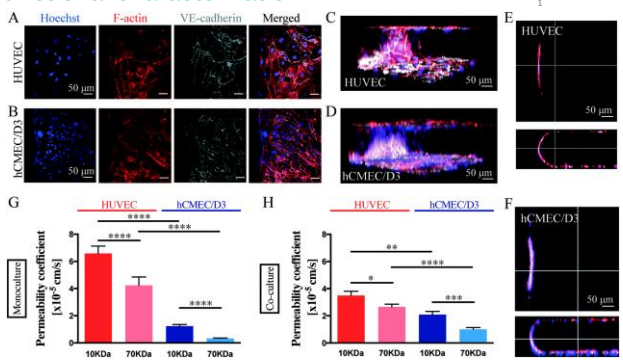
Our current design of the microfluidic device consists of two central gel regions flanked by two media channels. We use rat primary neurons and astrocytes together with human endothelial cell lines (HUVECs and hCMEC/D3) to develop a 3D *in-vitro* BBB model within a microfluidic device, but other cell types such as those derived from induced pluripotent stem cells are currently been used in our experiments. Initially, to model the neurovascular unit, we have incorporated into the device the walls of the brain vasculature by culturing endothelial cells in a triple co-culturing system with astrocytes and neurons. However, more recently we have also added a fourth type of cell to the system: human pericytes.

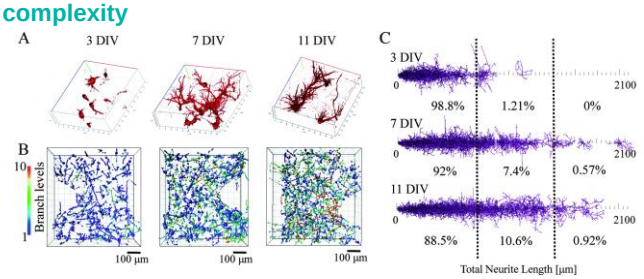
Schematic layout of the 3D microfluidic BBB device



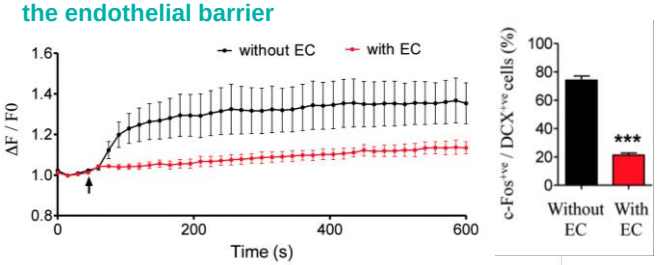
Endothelial barrier formation: morphological and functional characterization



Possibility to quantify neurons growth and network complexity



Compound testing: reduced glutamate transport across the endothelial barrier



Main advantages

- Address the 3D cellular organization of BBB that is crucial to many cellular processes *in vivo*.
- Allow specific manipulation and real-time monitoring of BBB integrity or function in drug delivery studies.
- Allow studies on drug screening through the BBB and on neuronal growth on one single platform.
- 3D microfluidic platform allows a reduction in sample volumes and cost, as well as the capabilities to precisely control media flow and reagent delivery and to regulate spatiotemporal parameters of the microenvironment.
- The use of hiPSCs increase the relevance of the system and reduces the interspecies differences.

➢ **A neurovascular chip (NVC) for comparative therapeutic studies with the opportunity to assess drug effects on neural function**

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