Title: Towards BBB-on-Chip to study vascular defects in Multiple Sclerosis

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Abstract
Vascularization is an essential component of all living tissues and plays a critical role in several pathological conditions. The blood-brain barrier (BBB) is specialized vasculature structure of the central nervous system, which dysfunction has been reported in multiple sclerosis (MS). To understand pathogenetic mechanisms of BBB dysfunction, differentiating the BBB cell types from MS patient-derived induced pluripotent stem cell(hiPS) has become attractive approach. In this study, we develop hiPSC-based BBB model to study key vascular defects in MS.
First, we focused on differentiating brain microvascular endothelial (BMVECs) and smooth muscle cells from healthy-hiPSC derived cells and studied their ability to produce vascular structures. To produce vascular structures, BMVECs were cocultured with three different human mural cell types (fat stem/stromal cells (HFSC), bone marrow stem/stromal cells (BMSC), WI-38 lung fibroblasts) in two different endothelial growth media (EGM-2, hESCR) for seven days. BMVEC monocultures by immunostaining were also characterized with tight junction markers ZO-1, claudin-5, and occludin to show brain-specific endothelial phenotype.
Differentiated hiPS-BMVEC expressed functional phenotype in coculture with all three murine cell types as shown with robust vascular network formation. In addition, BMVEC monocultures were positive for tight junction markers. These results suggest that hiPS-derived BMVECs can be used to model brain microvasculature and provide a promising new platform to study BBB-related vascular defects in vitro.