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A New Lecture Series Focused on Induced Pluripotent Stem Cells

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3D VESSEL-ON-CHIP TO MODEL VASCULAR DISEASE AND BEYOND

Small vessel diseases are the leading cause of disability and death worldwide. The major challenge is that they are multisystem disorders affecting different organs, such as the brain, heart and kidney. They have been difficult to model *in vitro* because high-quality vascular cells are difficult to derive from patients and the local organ microenvironment which is difficult to mimic often contributes to the disease. For this reason, human induced pluripotent stem cells (hiPSCs) have become attractive sources of patient- and organ-specific cells. We use hiPSCs to re-create blood vessels on microfluidic chips that recapitulate micro- and macrovascular networks and the local microenvironment. We developed efficient protocols to differentiate hiPSCs towards ECs, pericytes/vSMCs, and inflammatory cells (monocytes and pro- and anti-inflammatory macrophages). We have demonstrated that both micro- (10-50 µm) and macro-scale (250-300 µm) perfusable 3D vessels composed of hiPSC-derived endothelial cells, pericytes/vSMCs, and other non-vascular components, such as hiPSC- derived astrocytes, can be generated inside the microfluidic devices. Recently we also developed a microphysiological system that behaves as a human “mini-heart” using cardiomyocytes, endothelial cells, and cardiac fibroblasts all derived from hiPSCs. These mini-hearts can be produced just 5000 cells and without specialized equipment. They thus represent a low-cost, low tech platform for cardiac drug discovery and disease modeling. Using isogenic patient hiPSC lines and 3D vessels-on-chip, we recapitulated the phenotype of a genetic vascular disease called hereditary hemorrhagic telangiectasia (HHT). This patient-based hiPSC model serves as proof of principle that vascular diseases can be modeled using patient-specific hiPSCs in 3D microfluidic chips and used to identify new target cells and possible pathways for therapy.