Modeling Functionalized Tissues with Micro-Physiological Systems

Jin Kim

Harvard Medical School & Boston Children's Hospital

In recent years, micro-physiological system (MPS) technologies, such as organ chips, have gained prominence. Organ chips recapitulate crucial physiological features of human organs in a controlled and dynamic in vitro environment, facilitating a more *in vivo*-like *in vitro* system. However, achieving an *in vivo*-like microenvironment within a MPS involves a diverse array of choices such as architecture of the chip, tissue-mimetic material, and cell types to seed. In this presentation the focus will be on introducing two distinct models comprised of different types of cells, elaborating step by step considerations made during the development of these systems.

The first to be introduced is the human neurovascular unit (hNVU) chip with a functional blood–brain barrier (BBB) was developed to model Fungal brain infection. Functional features of the BBB could be modelled by inducing the differentiation of neural stem cells through co-culture with brain endothelial cells along with stepwise gravity-driven unidirectional flow. Utilizing the capabilities of MPS facilitating a multi-organ modeling, the hNVU chip could visualize the neurotropism of Cryptococcus neoformans —one of the most common pathogens causing fungal meningitis— and newly revealed several virulent gene that remained elusive through traditional methods such as transwell assay or animal experiments.

To achieve a more *in vivo*-like model, a diverse cell population is necessary. However, it is inefficient to co-culture all those cells individually. By inducing self-assembly through pluripotent stem cell differentiation forming organoid can solve this problem. The second model to be introduced is a human skin organoid comprising skin appendages, including neurons, sweat glands, adipocytes, and hair via co-development of mesenchymal and epithelial cells. Integrating this organoid model into the MPS facilitated live tracking of specific cell differentiation in a quantifiable format from the very early stage to the later time point which was unattainable in the conventional organoid culture.

In conclusion, by carefully considering and implementing diverse options in MPS, this system can be highly realistic models of human organs, showing great promise for drug discovery, disease modeling, and personalized medicine.