Microphysiological Systems: from lab bench to international society

Lena, Smirnova

Johns Hopkins University, Baltimore, MD, USA

The human brain represents the most complex organ of our body and thus modeling a development of functioning human brain-on-dish is an enormous challenge. Recent advances of microphysiological systems are a way to address brain development, homeostasis, functionality and diseases in more physiologically and human-relevant conditions. Already a simple brain spheroid represents higher complexity, increased cell-to-cell interactions, prolonged shelf-life than monolayer cultures, offering an opportunity to conduct longitudinal studies on chemicals affecting neural development. Brain organoids allow addressing the histoarchitecture and cellular interactions of the brain including synaptogenesis and myelination. Using CRISPR/Cas9 gene-editing technology in iPSC, we have developed multi-fluorescent brain organoids, which allowed to screen environmental chemicals and drugs in a complex brain model. To bring brain organoids closer to *in vivo*, we introduced iPSC-derived microglia, immune-cells of the brain, which allowed us to study not only the role of microglia in synaptogenesis but also neuroinflammation upon chemical exposure and viral infections. We recently developed a 3D multi-electrode array platform (organoid EEG). We use this EEGs and high-density multi-electrode arrays to develop assays for learning and memory. This should fill the gap in the functional endpoints in the *in vitro* developmental neurotoxicity testing battery. Finally, we used brain organoids with autism genetic background to address gene environmental interactions in autism and validated the findings against human data, providing a first example of *in vitro* GxE and a mechanistic validation concept.