

Abstract

The brain is an intricate system composed of millions of neural networks. Deciphering its overall dynamics and the underlying significance of several cues that direct neuronal development, the formation of axons, dendrites, and synapses during wiring and re-wiring remains a formidable challenge in developmental and cellular neuroscience. Although traditional *in vitro* macroscopic cell culture techniques are easy to perform, they often fail to mimic the complex phenomenon of brain microenvironments. Recent advancements in microfluidic device-based cell culture technologies have successfully overcome the limitations of conventional cell culture methods, enabling the reconstitution of neural cytoarchitecture through precise spatiotemporal regulation of compartmentalized cell culture microenvironments. These lab-on-chip technologies can aid in elucidating the fundamental principles of brain function and provide innovative platforms for screening neurotherapeutics. This thesis offers a succinct overview of the structural and functional aspects of the human nervous system by the reconstitution of the central and peripheral nervous systems on the chip. It highlights the neurological disorders associated with dysfunctions in both systems. It also reviews the several strategies researchers have adopted to mimic neurogenesis on a chip.

Additionally, we have designed and developed an economical, innovative microfluidic device utilizing a state-of-the-art Xurography technique. Thereafter, we performed on-chip cell culture studies with primary neurons and SH-SY5Y cells to validate the cytocompatibility of the device. Furthermore, we demonstrated the application of the fabricated device as a co-culture model using astrocytes and neurons. The device also served as a drug screening platform for a multi-targeted compound in the differentiated SH-SY5Y cells in the context of Alzheimer's disease. Lastly, we also developed a Ferroptosis model that can be linked to neurodegenerative disorders. In this regard, we also investigated the efficacy of a synthesized small molecule inside our fabricated microfluidic device. All these lead to the conclusion that our simple and cost-effective Xurography-based microfluidic device can open gateways to decipher neuronal events inside the human brain and serve as potential platforms for neurodegenerative disease modelling and screening novel therapeutic agents.