Title: Organ-on-a-chip technology for multi-organ modelling of Stroke-Heart syndrome

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Abstract

The field of Organ-on-a-chip technology is moving forward to include multiple organs and their interactions within the same platform. Such multi-organ interaction is found in Stroke-Heart Syndrome (SHS), where the interactions of hypoxic brain tissue extend to the human heart. In SHS, cardiac injury markers are upregulated even though the brain is the primary organ suffering from depleted oxygen supply. [1] We have studied the key technologies that are needed to be implemented in such multiorgan model:

1. We developed a microfluidic channel structure to control oxygen concentrations in cell culture and combined it with a coculture device. This platform allows cell compartmentalization by both, cell type and oxygen microenvironment.
2. We developed a method for automatic drug supply and cell chemical stimulation.
3. We established a multitissue model with human cell-derived cortical nervous system (CNS), peripheral nervous system (PNS), and cardiac tissue, where only the compartment resembling brain (CNS) is exposed to hypoxia.

An established 2D ratiometric oxygen sensing setup was used to characterize the oxygen modulation dynamics in the organ-on-chip devices. The fluid dynamics were resolved using finite element simulations together with image-based methods. Devices were first validated to be suitable for cell culture with mouse embryonic fibroblast (MEF) cells and then followed by human induced pluripotent stem cells (hiPSC) derived cells. We established the multitissue model and with Image-iT™ Green Hypoxia Reagent showed that only the CNS cells become hypoxic.

[1] Scheitz, J. F. et al. Journal of neurology 268(6) (2021)