Organ-on-chip device integration and biological evaluation inside the Smart Multi-Well Plate

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Marcel Leist, Uwe Marx and Peter Loskill

Welcome

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This demonstration of inflammatory crosstalk between the two organs corresponded with alterations in tissue health (LDH, TEER), liver function (CYP, albumin) and production of APR proteins such as C-reactive protein (CRP). Furthermore, upon addition of monocytes there was enhancement of the systemic inflammatory response, demonstrating the important role of immune cells within the system. Together, this multi-organ system allows novel and data-rich insights into both local and systemic response to infection. Greater understanding of pathogens' interaction with the body can be elucidated, allowing for more rapid and targeted drug development approaches in the future to reduce severe disease and death from both current and future novel pathogens.

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Presentation: Oral

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Organ-on-chip device integration and biological evaluation inside the Smart Multi-Well Plate

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The Smart Multi-Well Plate (SMWP), an open technology platform for Organ-on-Chip (OoC) technology developed as part of the Moore4Medical (M4M) consortium, aims to showcase the advantages of standardization in design, manufacturing and assembly for OoC [1]. In previously presented work [2], we showed integration and characterization of piezoelectric micropumps for in-line perfusion of OoC devices. Here we present the integration and preliminary biological evaluation of three OoC devices in a SMWP prototype.

This prototype, a downscaled version of the full SMWP, is constructed using stacked, predefined layers. The reservoirs of a 96-well plate are fluidically connected to integrated OoC devices and micropumps through a fluidic circuit board (FCB). A printed circuit board, assembled below the FCB, enables the electrical interfacing. The following devices were integrated in the prototype: OoC devices from Bi/ond and BEOnChip, a microelectrode array (MEA) device from MultiChannel Systems, and piezoelectric micropumps from Fraunhofer EMFT. In the OoC devices, cell culture was performed on integrated on-chip membranes. On the MEA, neuronal cells were cultured directly on the surface of the chip. For initial experiments, static cultures were performed to investigate the biocompatibility of all included materials inside the prototype.

BEOnChip performed a static cell culture with skin cells (HaCaT) in their device. Normal cell viability and morphology was observed after 96 h and 21 days of culture using Calcein-AM/PI live/dead staining. MCS performed static cell culture using hiPSCs-derived neurons directly cultured on the PLO/laminin-coated MEA chips. After 14 days of culture, eGFP staining showed normal cell morphology and network formation. Bi/ond performed an endothelial cell culture (HMEC-1), showing proper cell adhesion and viability in their devices.

The biological experiments under static conditions showed normal cell morphology and viability in all integrated devices. In the next phase of the project, the full SMWP platform with integrated perfusion will be used for biological experimentation to generate an air-liquid interface with skin cells (BEOnChip), a perfusable MEA (MCS) and endothelial tube formation under unidirectional flow (Bi/ond).

References

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Presentation: Poster

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Molecular-sensitive imaging enables *in situ* monitoring of cellular dynamics at spatial and temporal resolution

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3D tissue models in Organ-on-a-Chip (OoC) systems enable to recapitulate (patho-) physiological and dynamic cellular processes such as metabolic response, phenotypic switching or tissue mechanobiology. To unravel the complex information provided by microphysiological tissue models, there is a high demand for the development of novel sensors and methods which allow for on-chip measurements.