Downscaled engineered heart tissues of entirely hiPSC-derived 3-cell-type co-culture are functional and viable over several weeks

Windt, Laura; Wiendels, Maury; Dostanic, M.; Bellin, Milena; Sarro, Pasqualina M; Mastrangeli, Massimo; Mummery, Christine; van Meer, Berend

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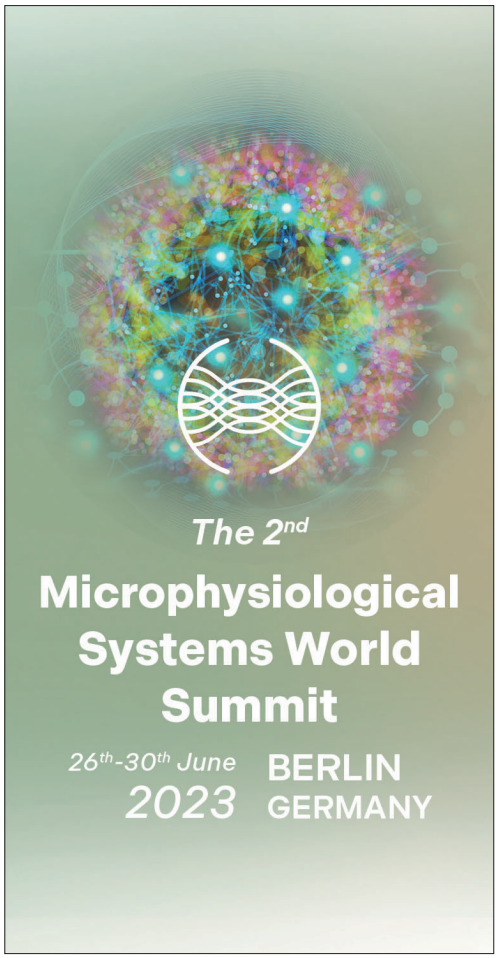
Welcome



Track 1:
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airlifted and cultured at the air liquid interface (ALI), and a differentiated mucociliary layer was achieved after approximately 21 days. Here, we present the results of characterisation studies on differentiated cultures using SEM and immunofluorescence.

Refinement of *in vitro* models is key to providing comparable infection data to that generated in animal models and may aid in demonstrating the suitability of MPS organ chip systems. This refinement may also assist in the reduction of animal use by helping to reduce our reliance on animal *in vivo* infection data.

Presentation: Poster

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Next-generation human iPSC-derived 3D brain systems to study chemical-induced myelin disruption and demyelinating diseases

Shan Wang, Marie-Gabrielle Zurich, Cendrine Repond and David Pamies

University of Lausanne, Lausanne, Switzerland

wangshan19930419@gmail.com

Growing evidence indicates that environmental toxicants contribute to the pathogenesis of neurodevelopmental disorders. However, the significance of exposure to xenobiotics during developmental stages is not fully understood. The Organization for Economic Co-operation and Development (OECD), defines toxicological test guidelines to evaluate chemicals and assure human health. However, developmental neurotoxicity (DNT) is not systematically studied due to the high costs, high number of animals, and time-consuming experiments required in the OECD test guidelines. In addition, there are rising concerns regarding the physiological relevance of extrapolating results from animal studies to humans. Together, this has resulted in a call for the development of a battery of New Approach Methodologies (NAM) assays that cover the most relevant key neurodevelopmental processes (KNDP) (e.g., proliferation, migration, myelination). Recently, an *in vitro* battery (IVB) was assembled from ten individual NAMs to investigate the effects of chemicals on various fundamental neurodevelopmental processes. However, some data gaps have been identified due to the absence of assays that address specific KNDP.

Myelination has been considered one of the most critical events during brain development and a sensible endpoint of DNT. However, the myelin assay in a human context, has not been incorporated yet in IVB of toxicity studies due to the difficulty to obtain myelin *in vitro*. Here, we used human induced pluripotent stem cells (hiPSCs) and generated a 3D model containing neurons and glial cells (also called BrainSpheres). This model presents compact myelin wrapped around axons, making it an ideal tool for myelin studies. Furthermore, it allows us to generate a reliable high amount of viable BrainSpheres, which are homogeneous in size and shape, and present reproducible percentages of the diverse cell types. To establish the myeline quantitative assay for high-throughput toxicological assessment and screening, we adapted our BrainSpheres protocol to make it suitable for High-Content analysis system. Myelin was detected by immunocytochemistry of myelin basic protein (MBP) and proteolipid protein 1 (PLP1). We aim to establish a standard operating system for automatized myelin quantification, after which a list of compounds ("training set") with either positive or negative effects on myelin will be used to validate the system.

Presentation: Poster

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Downscaled engineered heart tissues of entirely hiPSC-derived 3-cell-type co-culture are functional and viable over several weeks

Laura Windt[1], Maury Wiendels[1], Milica Dostanić[1,2], Milena Bellin[1], Lina Sarro[2], Massimo Mastrangeli[2], Christine Mummery[1] and Berend van Meer[1]

[1]LUMC, Leiden, The Netherlands; [2]TU Delft, Delft, The Netherlands

l.m.windt@lumc.nl

Microphysiological systems consisting of multiple cell types of the human heart have been shown to recapitulate certain aspects of human physiology better than conventional 2D *in vitro* models [1]. Engineered heart tissues (EHTs) that self-organise into contractile 3D structures between two flexible pillars are particularly useful to measure contraction against a force. However, conventional EHTs typically require between 50,000 and 2,000,000 cells, which makes creating many EHTs for high throughput screening costly [2]. Here, we show that downscaling EHT size, in our case to include human-induced pluripotent stem cell-derived cardiomyocytes (70%), cardiac fibroblasts (15%) and cardiac endothelial cells (15%), is feasible using as few as 16,000 cells. Tissues of three different sizes formed as expected and consistently, with 47,000, 31,000, and 16,000 cells. Moreover, while keeping the load constant relative to the size of the tissue [3], there was no difference in the viability nor functionality up to 14 days after formation. Electrical pacing of the tissues was conducted within the range of 1 to 3 Hz and with an optimal pacing frequency of 1.4 Hz, which is consistent over the three EHT sizes. Our results indicate that downscaled EHTs might be used as a cost-effective alternative to larger EHTs in drug discovery.

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Presentation: Poster