DEVELOPMENT OF IMMUNE MICROPHYSIOLOGICAL SYSTEMS (IMMUNE SYSTEMS ON A CHIP) FOR MCM TESTING

Towards Multi-organ Tissue Chips For Modeling The Human Immune Response To Biothreat Agents: The Lung-brain Interface

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Deficiencies in the applicability of data derived from animal models of disease to humans are broadly recognized. This has led to a growing global effort to develop tissue chips (TCs) with human cells as disease models. To meet this need, we have been engaged in the development of several TC barrier models leveraging two key technologies. The first is a microfluidic platform termed the μSiM (Microphysiological featuring a Silicon Membrane). The ultra-thin (10's of nm) and highly porous (controllable pore diameters from 10's of nm to microns, with dual-scale porosity to better model disease states also possible) silicon nitride membrane used in the μSiM allows for unhindered transport of small molecules and proteins from one side to another, while providing a physically robust structure for cell culture. Because the membranes are completely transparent, they are also ideal for microscopy. The second key technology we employ is photonic biosensors, fabricated using the 300-mm silicon photonics platform at AIM Photonics. Placed close to the tissue under study, these enable real-time continuous detection and quantification of analytes secreted by the TC under study. We have successfully used these sensors to monitor secretion of inflammatory biomarkers from TCs for up to 55 hours (longest time tested to date). We have used this platform to develop models of the cerebrovascular barrier (μSiM-CVB; "brain chip") and the alveolar-vascular barrier (μSiM-AVB; "lung chip"). Both include the ability to observe trafficking of human leukocytes in response to stimuli. This presentation will detail development of the sensor-integrated μSiM platform, and our efforts to integrate the μSiM-AVB and μSiM-CVB into a model of respiratory virus-induced neuroinflammation.