Porous membrane electrical cell-substrate impedance sensing for barrier-on-chip modeling

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Microfluidic organ-on-chip (OOC) systems that recapitulate specific human organ structures and functions hold great promise as advanced culture models for biological research, disease modeling, and drug development. OOCs are particularly well-suited for modeling biological barriers (e.g., vascular, epithelial) as they can mimic key aspects of the barrier microenvironment, including multiple interacting cell types, extracellular matrix, and fluid shear stresses. However, broad adoption of barrier-on-chip models has been hindered by their operational complexity, low throughput, and limited incorporation of biosensors for on-chip assays.

To facilitate adoption and translation of barrier-on-chip models, we have developed VitroFlo, a microfluidic system that enables co-culture and incorporation of 3D biomaterials in a simple-to-use membrane-based, 12-well configuration [1]. Of particular relevance to barrier modeling, unidirectional physiological shear stresses can be applied without the complexity of pumps, enabling long-term dynamic culture. In this talk, I will briefly discuss how we recently used VitroFlo to reveal insights into the role of perfusion on blood-brain barrier function in stem cell-derived models of Alzheimer's disease.

A persistent challenge with barrier-on-chip models is measuring barrier integrity within the complex culture set ups, where geometry, biomaterials, and fluid shear can confound measurements. To this end, I will discuss our work developing methods to adapt electrical cell-substrate impedance sensing (ECIS) to our membrane-based OOCs [2-4]. Using a simple, cost-effective prototyping method, gold electrodes can be embossed on to polyethylene terephthalate porous membranes with high fidelity. Porous membrane ECIS (PM-ECIS) performs similarly to solid-substrate ECIS, enabling sensitive, real-time measurement of endothelial cell barrier impedance with cell growth, barrier disruption, and fluid shear responses, with expected sensitivities to electrode size. Importantly for barrier modeling, PM-ECIS measurements are not confounded by 3D biomaterials typical of OOC models. In on-going work, we are incorporating PM-ECIS into VitroFlo as an integrated user-friendly, scalable, and cost-effective system that we expect will enable new insights into barrier function across a range of fields.

References:

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