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Micro and nanoengineering advances for the development and commercialization of Organ-on-chips

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Advances in micro and nanoengineering have permitted to implement Organ-on-chips (OOC) that mimic accurately physiological functions. OOC are multichannel 3D microfluidic cell culture bio-devices that mimic and model physiological mechanisms, activities, functions and responses of organs and tissues. These biomimetic microengineering approaches have gained significant relevance in biomedicine because they allow providing a better approximation of structure, behavior of cells and mechanisms of diseases to propose better diagnostic methods and personalized therapies [1].

OOC have been taken advantage of the semiconductor industry, like the case of Biomedical Microelectromechanical Systems (BioMEMS), because of the related semiconductor materials and the well-established micro and nanofabrication processes. Some techniques commonly employed are photolithography to create molds made of silicon, quartz or plastic, and wet or dry etching for micromachining these structures. Therefore, some modern micro and nanofabrication techniques such as soft-lithography and microcontact printing have also been used. These latter techniques employ the so-called poly(dimethylsiloxane) (PDMS) as it has advantages for 3D culture such as gas permeability [2] but it also has some drawbacks such as adsorbing small hydrophobic molecules [3].

One interesting microengineering work using PDMS consisted in the development of an OCC called lung-on-chips that mimics the alveolar-capillary interface of the human lung, to study the cytotoxicity of silica nanoparticles [4]. These with microfabricated pores that permitted it to have an air-liquid interface. However, one limitation has been that these artificial membranes are thicker than the interstitium between the alveolar epithelium and capillary endothelium in vivo (1 µm in thickness) [5]. Hence, the ultrathin porous membrane issue, which would mimic the in vivo condition, has to be overcome with novel materials and microengineering methodologies. Then, in a very recent work authors proposed the use and commercialization of 100-300 nm in vitro barriers membranes [6], which are comparable to the physiological separation distances in tissue layers and permit the transfer of cytoplasmic cargo between the co-cultured cells, being optically transparent for the fluorescence and phase image of the cells, positioned on both sizes of it. Those ultrathin membranes were made of tetraethyl-orthosilicate (TEOS)-derived SiO2 via plasma-enhanced chemical vapor deposition (PE-CVD) and the stress of the membrane was controlled by modifying the deposition parameters.

In this context, micro and nanoengineering methodologies have permitted the OOC include biosensors, with some recent advances related to the measurement of transepithelial electrical resistance (TEER), aiming to study the Blood–brain barrier (BBB) that is associated with diseases such as Alzheimer, multiple sclerosis, stroke, cancer, and vascular malformations [7]. Furthermore, some extraordinary nanomaterial as graphene are being used for live cell biosensing [8]. The development and integration of biosensors for studying cell-cell interactions and intracellular cell process will grow in near future.

On the other hand, rapid prototyping is needed to develop high-throughput microfluidic platforms as part of OOC and put them into the market. In this regard, the use of 3D bioprinting techniques such as stereolithography (SLA), Fused Deposition Modeling (FDM), Electron Beam Melting (EBM), Bioprinter and Inkjet Printing are impacting [9; 10; 11] and recently a liver-on-a-chip that used gelatin hydrogel to study protein adsorption and drug metabolism was elaborated by 3D bioprinting, in only one step [12].

The OCC have several advantages to study medical conditions in-vitro, permitting to receive drugs approvals more rapidly compared to the difficulty and the cost that represents to perform clinical studies in vivo, which has motivated some companies such as TissUse GmbH, to design Multi-Organ-Chip Platforms, having cell compartments to include different types of cells [13]. Governmental programs mainly from USA and Europe are founding projects related to OCC and large companies are are investing in the development and commercialization of this technology [14]. One commercial product is the liverchip® device, developed by C.N. Bioinnovations, it includes touchscreen controller and dynamic perfusion micro-pumps [15]. IThe development and utilization of OOC will have an enormous impact next year both in technology and economy worldwide.

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