Growing spheroids in a continuous perfusion microfluidic chip

*Amani Ghassan, Sarah Sahloul, Ajymurat Orozaliev, Piergiorgio Percipalle and Yong-Ak Song**

New York University Abu Dhabi (NYUAD)
Abu Dhabi, UAE
New York University, Tandon School of Engineering
Brooklyn, NY, USA
rafael.song@nyu.edu

A spheroid is a self-organizing 3D tissue derived from human cells or pluripotent stem cells with a cellular composition and structural organization representative of the developing human organ[1]. For this reason, spheroids have become an excellent 3D tissue model for investigating various diseases. Still, there are many unsolved challenges when it comes to the spheroid culture such as the uniformity of spheroids in terms of size and shape. Also, the throughput remains relatively low due to manual handling. We propose a microfluidic device design that allows multiplexing as well as its opening and closing in a reversible manner. In this way, the main advantage of facile access for cell loading in each well can seamlessly be combined with that of closed microchannel for subsequent continuous cell perfusion in a single device. This hybrid microfluidic chip contains 6 wells with a diameter of 4 mm. Once each open well was loaded with ~9000 cells in 40 μL, it was centrifuged at 100 g for 3 min. to accelerate the formation of spheroids at the bottom of each well. Finally, the wells were covered with a hydrophilic film on top using an adhesive layer and the cell culture media were continuously perfused with a syringe pump at various flow rates between 2 μL/min -10 μL/min without leakage. The spheroids obtained after 7 days of continuous perfusion had a uniform size distribution of ~400 μm. We foresee that this integrated microfluidic spheroid on-a-chip platform could become a high-throughput next-generation platform in the study of 3D disease models and in screening of novel drug candidates.

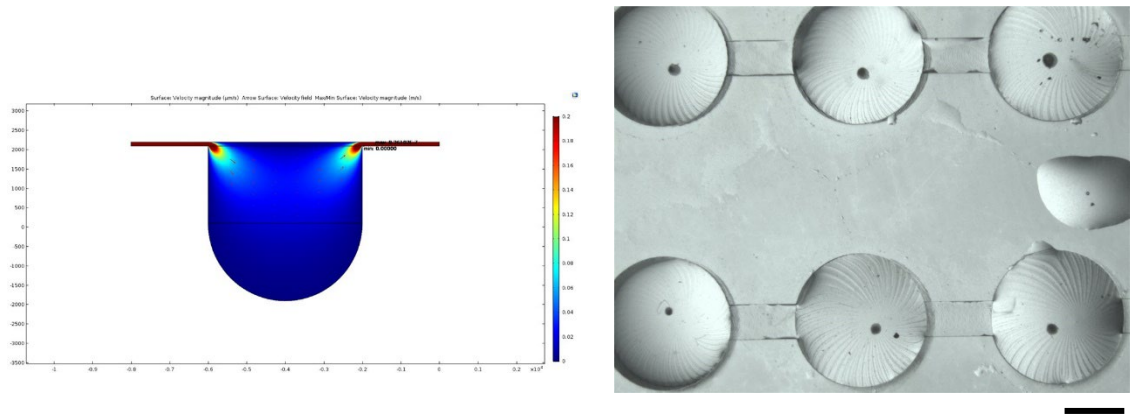

Figure 1: A continuous perfusion microfluidic chip with a reversibly bonded hydrophilic cover that can be opened and closed. a) The COMSOL simulation shows the flow profile at a flow rate of 2 μL/min inside a 4mm well. The channel height was 100 μm. b) The spheroids were grown from fibroblasts in each well under continuous perfusion for 4 days. The size of the spheroids was approximately ~400 μm (the scale bar is 2 mm).

References:

[1] Park, E. S.; Georgescu, A., Huh, D. *Science* **2019**, *364*, 960-965.