Body-on-a-Chip Systems for Drug Development

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Primary CNF Tools Used: VersaLaser engraver/cutter tool, ABM contact aligner, PDMS casting station, Samco UV/Ozone stripper, hot press, ObJetPro 3D printer

Abstract:

Body-on-a-chip (BOC) microphysiological systems combine biomaterials, microfluidics, microfabrication, and stem cell technologies to recreate organ structure and functionality as well as the dynamic organ-organ interactions *in vitro* [1]. They are powerful next-generation tools for human disease modeling and drug screening [2]. Here we describe two of the BOC systems that are being developed in our lab. They are fabricated with tools at CNF and designed to be used to study cancer cell extravasation and model cancer cell metastasis, and simulate immune responses.

Summary of Research:

Liver sinusoidal vascular chip for modeling colon cancer extravasation. We have designed and constructed a gravity-driven microfluidic platform for modeling the human liver sinusoidal microenvironment and investigating the extravasation of liver metastatic colorectal cancer (CRC) cells.

The device was fabricated in poly(methyl methacrylate) (PMMA). PMMA layers of desired thickness were patterned using a CO_2 laser (VersaLaser VLS3.50), and were bond together using a hot press at CNF after a 15 min UV/Ozone (Samco UV and Ozone stripper) exposure. We have also developed an apparatus to overcome the issue of sediment and aggregation of CRC cells in the feed reservoirs by introducing a propeller stirring device driven by a small stir bar on a magnetic stirrer. The propeller stirring device was designed in Inventor and fabricated using the ObJetPro 3D printer at CNF. We have tested different combinations varying in the propeller design, the positioning in the reservoir, and the stirring speed, and formulated an optimize stirring scheme that produced minimal cell sediment while preserving maximal cell viability.

We currently focus on characterizing the phenotype of liver sinusoidal endothelial cells in our microfluidic model and comparing CRC cell interactions with human liver sinusoidal endothelial cells versus human umbilical vascular endothelial cells.

Lung-on-a-Chip:

We describe a multiorgan (lung, liver and breast cancer) microphysiological system ("Body-on-a-Chip") designed to mimic both inhalation therapy and/or intravenous therapy. Microfluidic channels, chambers and medium reservoirs were etched into a layer of PMMA with the VersaLaser VLS3.5 cutting and engraving CO_2 laser (Universal Laser Systems, Scottsdale, Arizona) at the CNF. Clear silicone gaskets were also cut/etched to help seal the device and provide support for the polycarbonate membranes. This system is "pumpless" and self-contained using a rocker platform for fluid (blood surrogate) bidirectional recirculation. Our lung compartment is constructed to maintain an air-liquid interface and contained a "breathable" component that was designed to mimic breathing by simulating gas exchange, contraction and expansion of the "lung" using a reciprocating pump.

References:

[1] Wang YI, Carmona C, Hickman JJ, Shuler ML. Multiorgan Microphysiological Systems for Drug Development: Strategies, Advances, and Challenges. Adv Healthc Mater 2018;7:1701000. https://doi.org/10.1002/adhm.201701000 (2018).

[2] Sung JH, Wang YI, Narasimhan Sriram N, Jackson M, Long C, Hickman JJ, et al. Recent Advances in Body-on-a-Chip Systems. Anal Chem 2019;91:330-51. https://doi.org/10.1021/acs.analchem.8b05293 (2019).

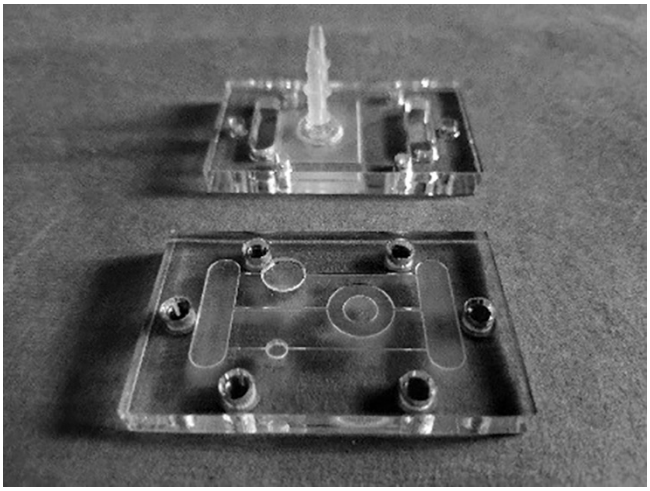

Figure 1: Actual photograph of the top and bottom frame of the microphysiological system with the breathable lung chamber.