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Towards a Biologically Relevant Tumor-on-a-Chip: Multiplex Microfluidic Platform to Study Breast Cancer Drug Response

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Abstract : Microfluidics integrated with 3D cell culture is a powerful technology to mimic cellular environment, and can be used to study cell activities such as proliferation, migration and response to drugs. This technology has gained more attention in cancer studies over the past years, and many organ-on-a-chip systems have been developed to study cancer cell behaviors in an ex-vivo tumor microenvironment. However, there are still some barriers to adoption which include low throughput, complexity in 3D cell culture integration and limitations on non-optical analysis of cells. In this study, a user-friendly microfluidic multi-well plate was developed to mimic the in vivo tumor microenvironment. The microfluidic platform feeds multiple 3D cell culture sites at the same time which enhances the throughput of the system. The platform uses hydrophobic Cassie-Baxter surfaces created by microchannels to enable convenient loading of hydrogel/cell suspensions into the device, while providing barrier free placement of the hydrogel and cells adjacent to the fluidic path. The microchannels support convective flow and diffusion of nutrients to the cells and a removable lid is used to enable further chemical and physiological analysis on the cells. Different breast cancer cell lines were cultured in the device and then monitored to characterize nutrient delivery to the cells as well as cell invasion and proliferation. In addition, the drug response of breast cancer cell lines cultured in the device was compared to the response in xenograft models to the same drugs to analyze relevance of this platform for use in future drug-response studies.

Keywords : microfluidics, multi-well 3d cell culture, tumor microenvironment, tumor-on-a-chip
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