Cancer metastasis on chip

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CANCER METASTASIS ON A CHIP

Mohammad Jouybar$_P$[12], Jelle J.F. Sleeboom[12], Andreas Pollet[12], Jaap M.J. den Toonder[12]
[1] *Microsystems, TU/e, Eindhoven, NL*
[2] *Institute for Complex Molecular Systems, TU/e, Eindhoven, NL*
Corresponding author's e-mail: m.jouy.bar@tue.nl

Most breast cancer related deaths are not caused directly by the primary tumor, but by secondary tumors formed through metastasis to other organs [1]. Current in-vitro models rarely mimic the initial phase of metastasis: invasion. Hence, we focus on modeling breast cancer invasion and the relevant microenvironment on a chip. We develop microfluidic Cancer-on-a-Chip (CoC) devices to recapitulate essential cues in cancer microenvironment, namely (1) Extracellular Matrix (ECM) heterogeneity and (2) microvasculature. To generate the cancer niche, we use cell-embedded hydrogel encapsulation [2]. A water in oil flow-focusing device was used to encapsulate cancer cells in Matrigel beads. Next, Matrigel beads were cultured in collagen I hydrogel, mimicking the stromal ECM. This way we recapitulate the pre-invasive condition where cancer cells initially reside in a soft basement membrane before invading the fibrous and stiffer stromal ECM. Beside encapsulation method, we use alternative techniques like sugar-printing in CoC models to create the interface between two different materials. The model of ECM heterogeneity can potentially lead to better understanding of pre-invasive and invasive breast cancer.
Moreover, we use sugar-printing technology to create perfusion lumens, cast directly in ECM [3]. When seeded with endothelial cells, these form the (micro) vasculature. Combined with a neighboring channel for cancer cell culture, the process of cancer invasion, migration through ECM, and intravasation can be studied. This way we avoid using artificial materials like Polydimethylsiloxane (PDMS) which usually have drawbacks for cellular experiments.

Keywords
Cancer on Chip; Organ on Chip; Vasculature

References
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