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A novel breast-cancer model of early stage invasion

Using microfluidic methods to mimic a heterogeneous physical tumor microenvironment

The majority of breast cancer deaths are not caused by the primary tumor, but by metastasis to other organs [1]. However, the mechanisms that underlie the first stage of metastasis, the invasion of cancer cells into surrounding tissue remain elusive, due to the complexity of the cellular, biochemical, and biophysical interactions in cancer tissue.

In this work, we propose a novel in vitro breast cancer model that focuses on dissecting the influence of the biophysical properties of the extracellular matrix (ECM) on the onset of cancer invasion. Based on microfluidic technology, it will provide us with the necessary tools to independently vary different material and cell properties, while it provides the cells with a physiologically relevant environment.

The key biophysical property this model captures is the heterogeneous ECM composition before invasion: Initially, cancer cells reside in a soft basement membrane before invading the fibrous and stiffer stromal ECM [2]. A microfluidic bottom-up fabrication approach enables the generation of this environment.

Model fabrication

First, MDA-MB-231 cells are encapsulated in Matrigel beads that mimic the basement membrane. Next, the beads are embedded in a collagen I hydrogel, mimicking the stromal extracellular matrix.

By generating these micro-tissues using droplet microfluidics, many controlled cancer models can be generated in a high throughput fashion, while systematically changing parameters like ECM structure and composition, tumor size, and inclusion of different cell types.

Cancer invasion

We observe different types of invasion into the stromal ECM compartment: clusters of cancer cells invading the stromal collagen matrix, and complete invasion by proliferating cancer cells.

Further development is aimed towards integration of control over physical parameters such as the stiffness, and development of quantitative analyses of the cell invasion process.

References: