A novel breast cancer model of early stage invasion

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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.

Matrigel is employed as a model for the basement membrane, and collagen I is used as a model for the stromal ECM. Preliminary data shows a spherical micro-tumor invading the collagen that surrounds the Matrigel environment between day 3 and 8.

The beads are retrieved from the oil and transferred to cell culture medium. Not all beads contain cells.

Microfluidic high-throughput encapsulation of single MDA-MB-231 breast cancer cells in Matrigel droplets.

The beads are embedded in a collagen I hydrogel without loss of material or mixing, as shown by a CNA35-OG probe for collagen.

Future work will focus on developing and optimizing the shown fabrication methods to increase yield and control. Including:

- Microfluidic bead retrieval
- Microfluidic encapsulated cell sorting
- Microfluidic embedding in collagen

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