# A novel breast cancer model of early stage invasion

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## Using microfluidic methods to mimic a heterogeneous physical tumor microenvironment


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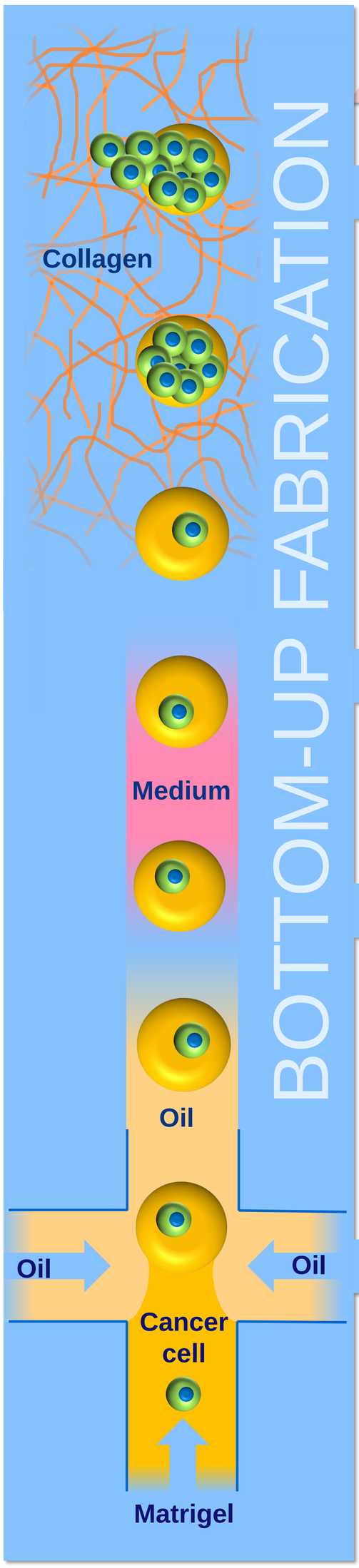
**The majority of breast cancer deaths are not caused by the primary tumor, but by metastasis to other organs [1]. However, the mechanisms that underlie the first stage of metastasis, the invasion of cancer cells into surrounding tissue remain elusive, due to the complexity of the cellular, biochemical,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

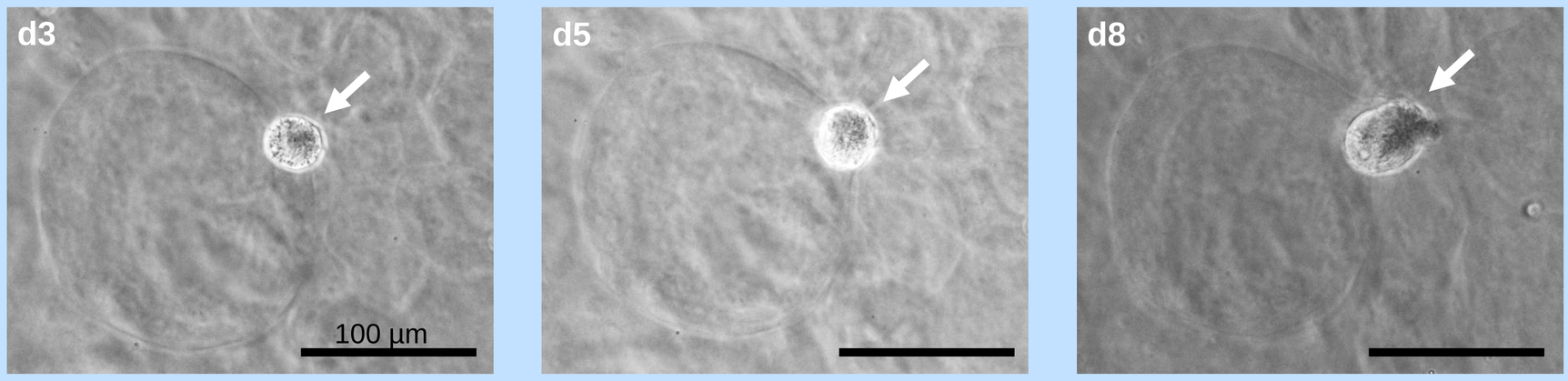
BOTTOM-UP FABRICATION




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.

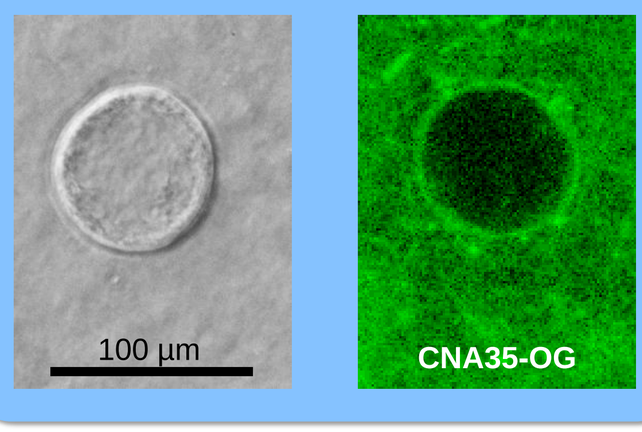
**4**

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.



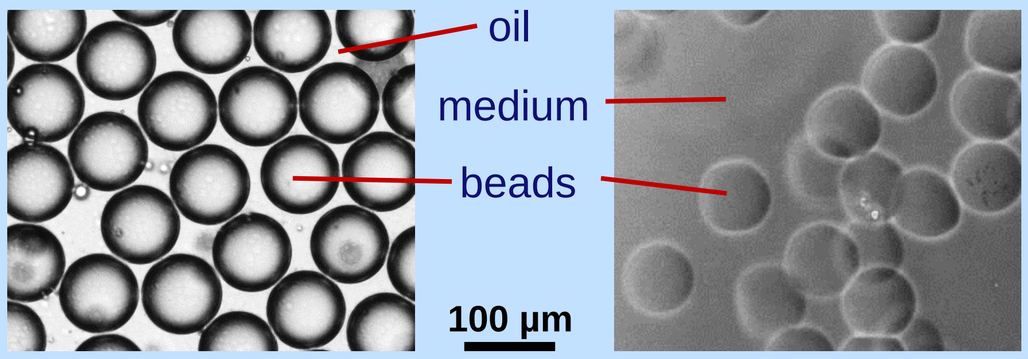

**3**

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



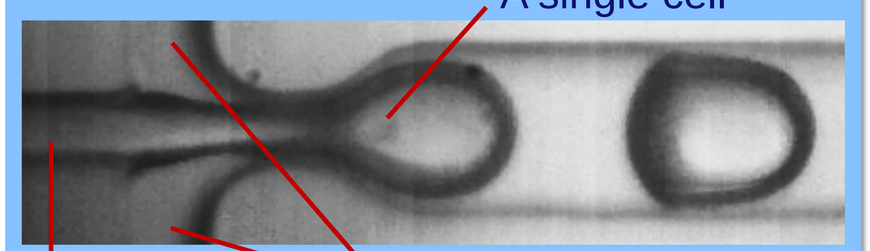

**2**

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




**1**

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




**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**


[1] Aceto, N., et al. (2014). Circulating tumor cell clusters are precursors of breast cancer metastasis. Cell, *158*(5), 1110–1122.
[2] Yu, H., et al. (2011). Forcing form and function: Biomechanical regulation of tumor evolution. Trends in Cell Biology, 21(1), 47–56.