A novel breast-cancer model of early stage invasion

Citation for published version (APA):

Document status and date:
Published: 02/05/2017

Please check the document version of this publication:

• A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher’s website.
• The final author version and the galley proof are versions of the publication after peer review.
• The final published version features the final layout of the paper including the volume, issue and page numbers.

Link to publication

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

• Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
• You may not further distribute the material or use it for any profit-making activity or commercial gain
• You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license above, please follow below link for the End User Agreement:
www.tue.nl/taverne

Take down policy
If you believe that this document breaches copyright please contact us at:
openaccess@tue.nl

providing details and we will investigate your claim.
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.

**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.

---