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Integration of electro-spun scaffolds inside microfluidic chips : towards 3D migration assays on a chip

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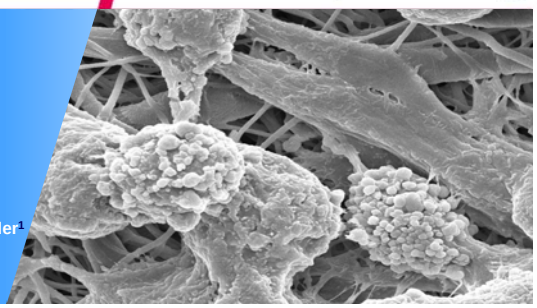
Integration of electro-spun scaffolds inside microfluidic chips:
Towards 3D migration assays on a chip



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Introduction

Extracellular matrix (ECM), as a bio-chemical and -physical support for cells, is of great importance in cell migration studies. 3D migration studies, compared to 2D cultures, have proven to best represent the in vivo conditions[1]. Hydrogels are usually used in *in vitro* studies as the 3D ECM. However, the relevance of the architecture and controllability of gels are debatable[2]. Self standing fibrous scaffolds, which more closely mimic the *in vivo* condition, can be fabricated (by electro-spinning) with different fiber sizes and architecture and from different materials. In addition, microfluidic chips can intrinsically control the biochemical content of the cell micro-environment which is also important for the cell migration. In this project, we have developed a *new micro-fabrication method* to integrate *fibrous scaffolds* inside a *microfluidic device* to study cell migration on a chip.

Materials and Methods

Figure 1 shows the fabrication method called "*selective curing*" which integrates a piece of Poly-caprolactone (PCL) electro-spun scaffold in a microfluidic device.

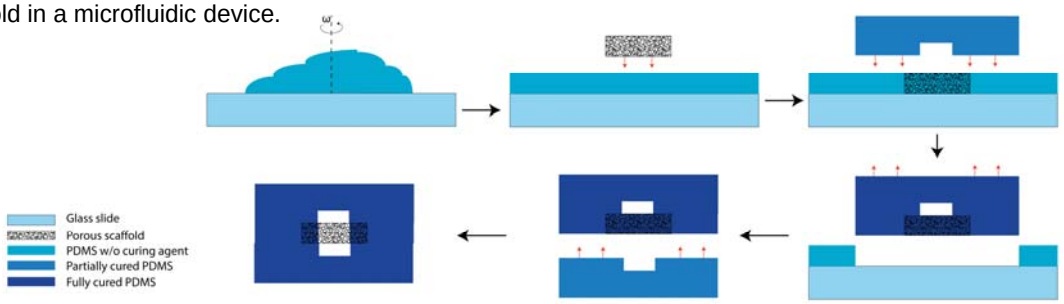

Figure 1 – *Selective curing* process; a piece of electro-spun scaffold is sandwiched between two microchannels. Where the channels overlay, PDMS is removed and there is a direct connection between the microchannels through the scaffold.

Results and Discussion

Figure 2 shows the complete chip. The fabrication method is robust and suitable for porous membranes from different materials with thickness smaller than 500µm. One of the features of the method is the reversible bonding of the layers. After the biological experiments, the layers can be separated and further analysis can be done with direct access to the cells and the ECM (figure 3).

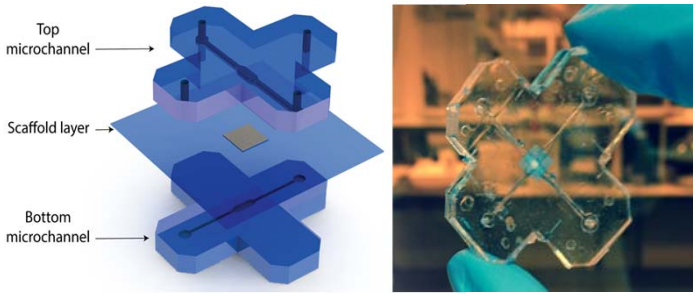

Figure 2 – Exploded view (left) and assembled version (right) of the chip.

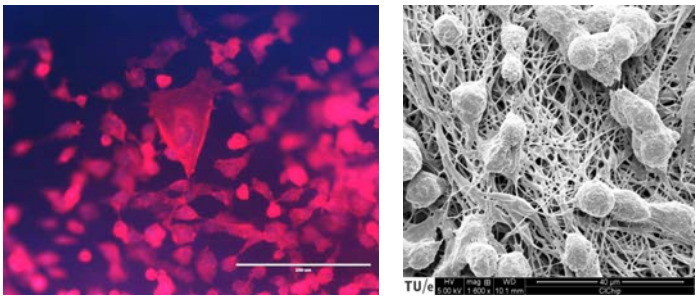

Figure 3 – Fluorescent image (left) and scanning electron microscopy image (right) of breast cancer cells in the chip.

Conclusion and Outlook

We have developed a new method to integrate self standing fibrous scaffolds representing ECM inside a microfluidic chip. The method is robust and reproducible. The next step is to do the chemotaxis assay across the fibrous scaffold to study how the geometry and stiffness of the extracellular matrix affects the intravasation of cancer cells into the blood (figure 4).

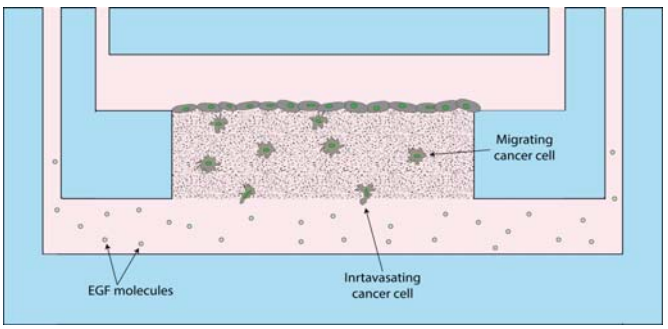

Figure 4 – Overview of intravasation on a chip. Breast cancer cells are cultured on top of the scaffold and attracted to the bottom chamber by a chemoattractant (e.g. EGF). In this way, cell migration through the 3D matrix can be studied.

[1] Stevens, Molly M., and Julian H. George. "Exploring and engineering the cell surface interface." *Science* 310.5751 (2005): 1135-1138.
[2] Cukierman, Edna, et al. "Taking cell-matrix adhesions to the third dimension. "*Science* 294.5547 (2001): 1708-1712.

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