Characterization of Interstitial Flow in Collagen Matrices

Introduction and Project Motivation

Metastasis, the spread of cancer that is responsible for over 90% of cancer related deaths, requires the complex and coordinated migration of invasive tumor cells into the surrounding tumor microenvironment (TME) containing extracellular matrix (ECM). The ECM plays a critical role in dictating cancer cell migration. Cancer cells respond to the biophysical and biochemical cues from the ECM by altering their morphology and migration mechanisms[1]. Cancer cells also secrete proteins that in-turn further remodel the ECM and promote metastasis[1]. One of the major components of the ECM is Collagen I, the realignment and remodelling of which has been shown to promote metastasis. Another pro-migratory factor in the TME is interstitial flow (IF)[2]. IF can regulate cell migration mechanisms and can also stimulate the realignment of collagen fibres in the ECM, further promoting the spread of cancer cells in the body.

Project Objective

In our previous studies, we Boukany Lab has developed a 3D microfluidic platform to build a physiologically relevant TME. In this project, we will use a collagen ECM to embed spheroids. We will combine this with IF and characterize the flow in the gel - studying how the flow modifies the collagen fibres in the chip. The hypothesis states that the collagen fibres will realign in the direction of the flow, which will in turn lead to increased tumor migration events[3].

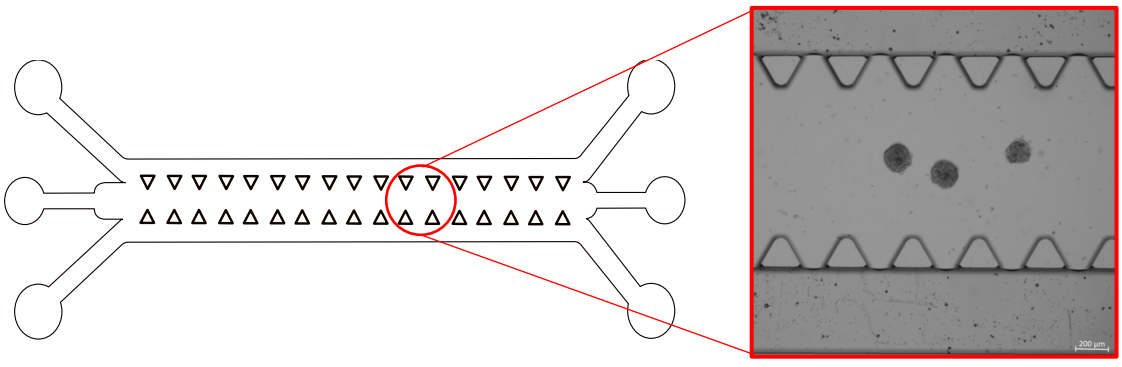

Figure 1 Schematic figure displaying the structure of the microfluidic device. On the right is a brightfield image captured at 10X with breast cancer spheroids embedded in collagen gel.

What's in it for you

The student will gain multi-disciplinary knowledge in the field of **cancer biology**, materials science, biochemical engineering, and **fluid dynamics**. Experimental skills like **soft lithography based fabrication, fluorescence microscopy, microfluidic techniques and mammalian cell cultures** will be an essential part of the project giving a complete set of skills to become an expert in the area of **microfluidics for healthcare and biological applications.**

Tentative project plan (7-8 months):

1. Literature review (1 month)
2. Project concept, problem statement and lab training (1 months)
3. Experiments (design and integration of microfluidic technology for cell migration) and data analysis/image processing (4 months)
4. Report Writing (1 month)

Contact details:

Interested students can contact Pranav Mehta (p.p.mehta@tudelft.nl) or Dr Pouyan E. Boukany (P.Boukany@tudelft.nl) at the Living Soft Matter group, Product and Process Engineering, Department of Chemical Engineering.

References

1 Winkler, J. *et al.* (2020) Concepts of extracellular matrix remodelling in tumour progression and metastasis. *Nat. Commun. 2020 111* 11, 1–19

2 Follain, G. *et al.* (2020) Fluids and their mechanics in tumour transit: shaping metastasis. *Nat. Rev. Cancer* 20, 107–124

3 Li, A. and Sun, R. (2020) Role of interstitial flow in tumor migration through 3D ECM. *Acta Mech. Sin.* 36, 768–774