Effect of biochemical cues on tumor cell migration in a microfluidic chip (MEP)

Introduction & Project motivation

Cancer cell migration is a series of fundamental, multistage succession of physico-chemical events that results in the transformation of a locally growing tumor to disseminate individual tumor cells to distant sites within the human body. This develops into a secondary tumor, hence coining the term metastasis, as a major life-threatening disease. Many biochemical and biophysical factors contribute to tumor progression. One of the most important being TGFβ, a well-known biochemical signal that is responsible for tumor progression[1]. When cancer cells and fibroblasts are cultured together, cancer cell invasion enhances in response to interstitial flow(IF)[2]. This response is mediated by TGFβ. IF upregulate TGFβ inside the microenvironment of tumor causing ECM remodeling and stiffening[3].

Project objective

In our previous studies, we have developed a 3D microfluidic platform to build a physiologically relevant tumor microenvironment (TME). This model is used to study the effect of interstitial flow (fluid stresses) on A549 lung cancer spheroids embedded in a hydrogel mimicking the ECM (Figure 1). We show the effect of IF to promote tumor spheroid dissociation takes place as a result of genetic and morphological changes (Figure 2). In this project, we would like to combine IF with TGFβ signaling as an added stimuli to study the response in cell migration events. The hypothesis states that IF upregulate TGFβ in cancer cells, which in turn leads to several physical changes in the ECM promoting tumor migration events[4].

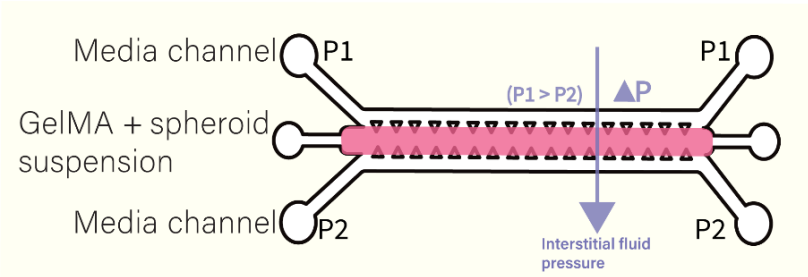

Figure 1: Schematic of 3D-matrix based microfluidic device. Pressure gradient across the middle channel results in Interstitial flow through the porous structure of the hydrogel.

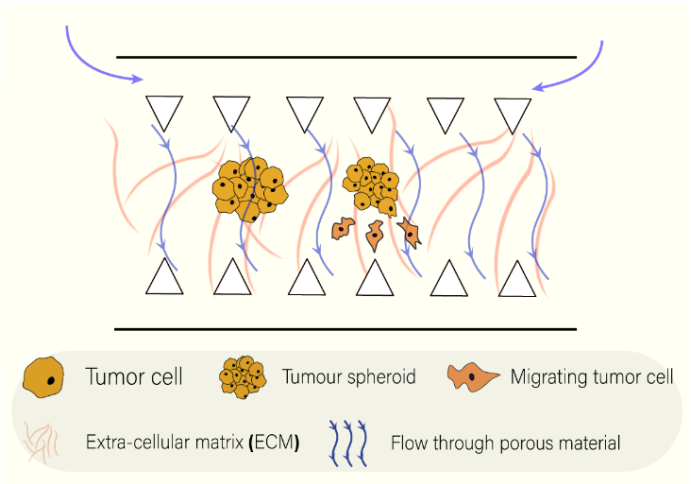

Figure 2: Schematic of the tumor spheroid dissociation upon application of an interstitial flow. Cells change their morphology and become more aggressive disseminating from the primary tumor and travel through the ECM material.

What's in it for you

The student will gain multi-disciplinary knowledge in the field of **cancer invasion**, 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:

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References:

1 Colak, S. and ten Dijke, P. (2017) Targeting TGF-β Signaling in Cancer. *Trends in Cancer* 3, 56–71

2 Jain, R.K. *et al.* (2014) The role of mechanical forces in tumor growth and therapy. *Annu. Rev. Biomed. Eng.* 16, 321–346

3 Pandya, P. *et al.* (2017) Modes of invasion during tumour dissemination. *Mol. Oncol.* 11, 5–27

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