The role and influence of shear flow in wound healing application using in-vitro 3D cell culture techniques

(Master End project, Living Soft Matter group, PPE, TU Delft)

Introduction:

During embryonic morphogenesis, wound repair and cancer invasion, cells often migrate collectively via tight cell-cell junctions, a process named collective migration[1]. In the framework of cellular locomotion, the migratory mode of a cell is determined by adhesion to the substrate, forward actin protrusion and actomyosin contraction[2]. In collective cell migration, the cells exhibiting a "multicellular structure" enables them to better respond to chemical and physical cues, as compared with isolated cells (Figure 1). The migratory mode is influenced by cell-intrinsic factors and signaling from external or environment factors. As cells respond to physical shear stress or interstitial fluid flow through mechanotransduction pathways (conversion of biophysical to biochemical cues), it is fundamental to understand the underlying mechanism on how cells adapt to such dynamic environment[3]. From previous studies, it is shown that fluid flow creates a biochemical gradient across the cell that promotes directional migration[4].

Project description:

Previous research has focused on 2D migration on glass substrates that shows a preferential directional migration. In this study, we will use relevant hydrogel matrices mimicking the native ECM architecture as patterned surfaces to see the effect of external environments on migration strategies adopted by A549 lung cancer cells. Furthermore, we would also like to visually observe and quantify how shear flows affect collective cell migration behavior for wound healing application in a microfluidic chip (Figure 2). With real-time imaging techniques and image analysis software, we can carefully observe the wound healing progression events under various stimuli such as substrate stiffness and shear flow.

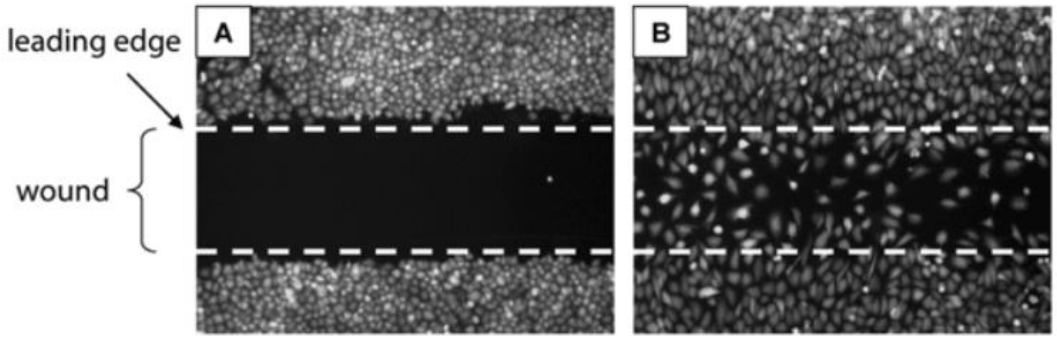

Figure 1: (A)Confluent monolayer of cells wounded by a scratch assay separated by a void. Cells at the leading edge adopt polarized morphology into the direction of the void. (B) Over the period of time, cells migrate into the void and completely close the wound.
Ref:https://www.europeanpharmaceuticalreview.com/article/4346/advances-in-two-dimensional-cell-migration-assay-technologies/

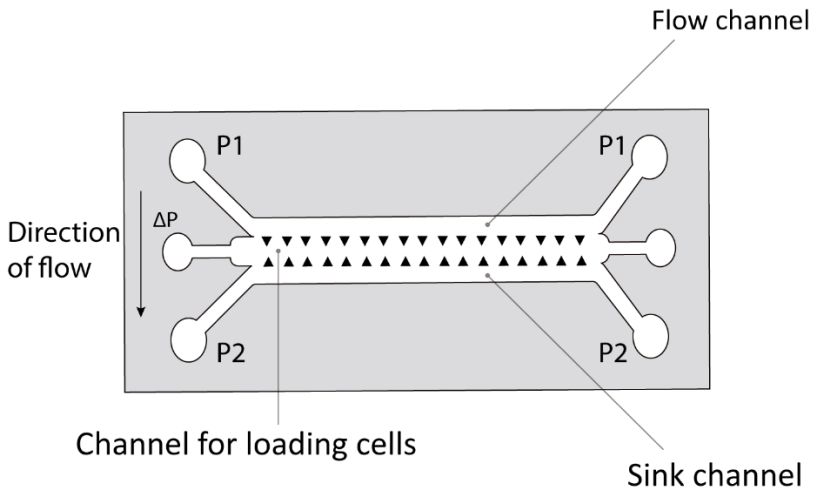

Figure 2: Design for shear flow microfluidic device. The middle channel allows to seed cells and create a wound healing assay. The top and bottom channels can be operated at different pressures to drive a shear flow across the device.

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 and data analysis/image processing (4 months)
4. Report Writing (1 month)

Contact details:

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References:

1 Lintz, M. *et al.* (2017) The Mechanics of Single Cell and Collective Migration of Tumor Cells. *J. Biomech. Eng.* 139, 1–9

2 Mayor, R. and Etienne-Manneville, S. (2016) The front and rear of collective cell migration. *Nat. Rev. Mol. Cell Biol.* 17, 97–109

3 Liu, Q. *et al.* (2020) Role of the mechanical microenvironment in cancer development and progression. *Cancer Biol. Med.* 17, 282–292

4 Polacheck, W.J. *et al.* (2011) Interstitial flow influences direction of tumor cell migration through competing mechanisms. *Proc. Natl. Acad. Sci. U. S. A.* 108, 11115–11120