Master End Project – Heterospheroid Dissemination under IF in Collagen Gel Matrices

Project Scope: Investigating the effect of Interstitial Flow (IF) on heterogenous CAF-MCF7 spheroid dissemination.

Background: Cancer Associated Fibroblasts (CAFs) are large spindle shaped mesenchymal cells found in the tumor stroma. Tumor cells can transform stromal fibroblasts to activated CAFs by secreting signaling molecules, and CAFs in turn will assist tumor cells in dissemination by degrading the extracellular matrix, transferring cargo to tumor cells to increase motility, and even forming heterotypic junctions to lead collective migration away from the primary tumor.

Interstitial fluid flow through the ECM is omnipresent in tissues and caused by lymphatic drainage. Because of excessive interstitial fluid pressure in tumors, interstitial flow and lymphatic drainage are increased in the tumor margin. Interstitial flow can redistribute bioactive molecules and alter gradients. This in turn may drive cancer cell invasion by skewing autologously secreted chemokines, causing chemotaxis in the flow direction. Interstitial flow can also affect stromal cells, causing cell and matrix alignment, increasing fibroblast motility via MMP-1, and inducing myofibroblast differentiation via transforming growth factor TGF-b1.

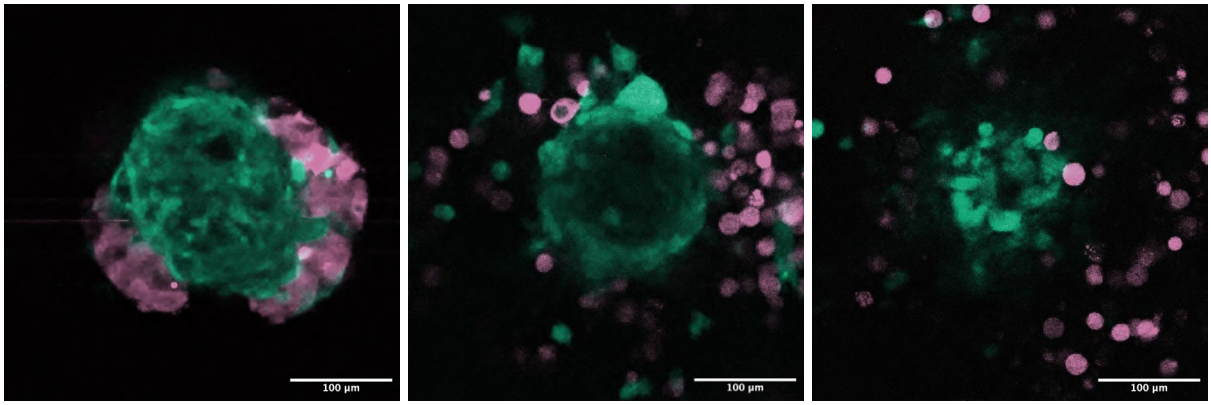

Figure 1 MCF7 (pink) and 19TT CAF (green) heterospheroid embedded in collagen gel. Counterintuitive phenomena observed, whereby tumor cells clump on the spheroid periphery and disseminate as rounded cells over a period of 48hrs. Images captured at time 0, 24hrs and, 48hrs (Left to Right).

Objective: Embedding distinct CAF and Tumor cell spheroids in collagen matrices indicate that CAFs degrade the collagen gel matrix to migrate towards the tumor cell spheroid and cause them to disseminate by contact mediated mechanisms. Upon seeding heterogenous CAF-MCF7 spheroids, we do not observe the same phenomena. The objective of this project is to investigate the effect of interstitial flow on CAF-TC heterospheroid dissemination in collagen matrices.

Experimental Parameters:

The experiments in this project will be divided into 2 parts:

1. Static Heterospheroid Experiments
    a. Embed heterospheroids in collagen matrices (3mg/ml) to run a 48-hour imaging experiment. These experiments will be compared to static MCF7 only spheroids and also be used as a baseline for future IF experiments.
    b. MCF7 mCherry and 19TT H2B GFP cells will be used. Collagen fibers will be imaged using reflection microscopy to visualize fiber remodeling.
2. Heterospheroid + Interstitial Flow Experiments
    a. Heterogenous spheroids of 19TT and MCF7 will be embedded in Collagen gels and imaged for 48hrs.
    b. Using MCF7 mCherry and 19TT H2B GFP cells, we will be able to visualize both cell types in addition to the collagen matrix via reflection microscopy.

Note: Due to regulations imposed on master's students, they will not be able to culture the CAF cells firsthand. They will be taught how to culture tumor cells and will seed their own TC spheroids, but CAF and heterospheroids will be handled by me and only handed to the student for experiments.

What's in it for you?

Working on this topic in our group allows you to:

- Deepen your knowledge on transport phenomena in the field of biology, transport phenomena, and biology
- Develop your skills at the interface between biophysics and soft matter science
- Maneuver at the Biology-Chemical Engineering Interface

Contact:

Highly motivated MSc students interested in conducting exciting and rewarding projects are encouraged to contact **Dr. Pouyan Boukany (P.Boukany@tudelft.nl)** and **Pranav Mehta (p.p.mehta@tudelft.nl)** at the Product and Process Engineering Research group in the Department of Chemical Engineering.