Master End Project – Effect of Altered Collagen Matrix Density on Heterospheroid Dissemination

Project Scope: Investigating the effect of varying collagen matrix density 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.

Extracellular Matrix (ECM) density and mechanical properties play a very influential role in tumor dissemination. Denser matrices are tougher to traverse through compared to loosely bound matrices. High energy requirements often result in altered motility mechanisms. Understanding how hetero CAF-TC clusters interact upon altering the collagen density will provide insight into underlying dissemination mechanisms.

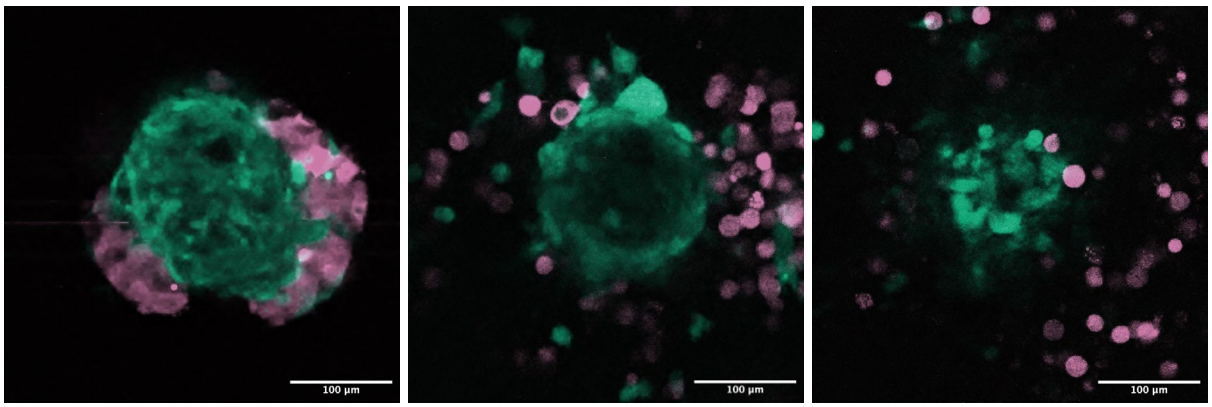

Figure 1 MCF7 (pink) and 19TT CAF (green) heterospheroid embedded in collagen gel. Counterintuitive phenomena observed, whereby tumor cells clump on the spheroid periphery and disseminate as rounded cells over a period of 48hrs. Images captured at time 0, 24hrs and, 48hrs (Left to Right).

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 varying collagen density on CAF-TC heterospheroid dissemination in collagen matrices.

Experimental Parameters:

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

1. Heterospheroid Experiments in 3mg/ml Collagen matrices
    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 + Dense Collagen Matrices
   a. Heterogenous spheroids of 19TT and MCF7 will be embedded in Collagen gels with a density of 8mg/ml 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 metastasis of cancer cells, migration, and transport phenomena in living systems.

Develop your technical skills in cell culture, fluorescence microscopy, Image analysis, and more.

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.