Impact of compressive stress on pancreatic cancer evolution

Context

Cancer cells experience a wide range of mechanical stresses when tumors develop. This is notably the case for the deadly pancreatic ductal adenocarcinoma (PDAC), which account for most pancreatic cancers. In particular, confined cell growth and strong modifications of the stroma lead to the emergence of compressive mechanical stresses which is experienced by the different cells composing the tumor. We and others have found that compressive stresses can reduce cell proliferation.

Despite its importance, the sensing of compressive stress remains largely unknown. It is in particular unclear why some genotypes would be more sensitive to compressive stresses than others. This point is however crucial for a proper understanding of tumor progression: genomic instabilities favor the appearance of genotypes, which then compete mechanically for space (Fig. 1).

In this project, we wish to investigate *in vitro* the parameters leading to sensitivity to compression and the modulation of mechanical competition. To this end, we have already developed novel and original microfluidic devices which allow (i) to measure the sensitivity to compression in terms of cell proliferation and (ii) realize mechanical competitions of 3D multicellular spheroids.

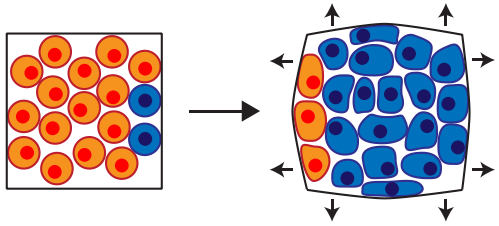

Fig. 1: Confined cell proliferation and stromal modifications lead to the emergence compressive mechanical stresses. Different genotypes compete for space in the in vivo setting of a tumor. Their sensitivity to compressive stress could guide this competition.

Objectives of the project

The objectives of this project are two-fold:

1. Measure the sensitivity to compressive stress of different genotypes, and investigate which key parameters could be associated with a differential response to compression.
2. Realize mechanical competitions for space and explore how this competition can be understood in terms of the specific cellular response to compression.

Environment

The successful candidate will be co-advised by M. Delarue, biophysicist from the LAAS-CNRS & CRCT in Toulouse (France), expert in mechano-biology and microfabrication, and J. Guillermet-Guibert, cancer biologist from the CRCT in Toulouse, expert in signaling in pancreatic cancer. The candidate will primarily conduct their research at LAAS-CNRS. The LAAS-CNRS offers 1,500m^2 of clean room with state-of-the-art microfabrication facilities, microscopy and cell culture platforms.

Application

A funded position is offered as from January 2022 for a successful candidate holding a PhD degree, with entry salary of about 2200€ / month net income. We are looking for independent researchers with a strong will for working at the interface between physics and biology. Required experience includes molecular and cell biology, and imaging. Experience in working with 3D multicellular objects or with microfluidics will be valued.

Please log-in to CNRS employment portal to candidate to this application: https://bit.ly/3CzcGV8

Additionally, please send a statement of interest, a CV, and the contact details of two references to: mdelarue@laas.fr and julie.guillermet@inserm.fr