Study of the impact of compression on cancer cell growth with microfluidics

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), accounting for most pancreatic cancers. In particular, confined cell growth and modifications of the stroma lead to the emergence of compressive mechanical stresses which are experienced by the different cells composing the tumor. We and others have found that compressive stresses can reduce cell proliferation (see for instance Rizzuti *el al., Phys. Rev. Lett*, 2020).

Despite their importance, the sensing of compressive stress alongside some of its key consequences remains understudied. This is partly due to the lack of tools available to perfectly control the mechanical and chemical environment. We have developed original microfluidic devices that allow us to confine multicellular spheroids, and study how compressive stress can impact their proliferation. These devices retain high-resolution imaging, and allow for mechanical competitions by caging multiple spheroids (Fig. 1).

In this project, we wish to investigate *in vitro* the parameters leading to sensitivity to compression, and understand how they can shape mechanical competitions of spheroids. We wish to test novel hypotheses of sensing of compressive stress based on the modification of a key biophysical parameter: macromolecular crowding, which we have recently shown to impact yeast proliferation under pressure (Alric *et al., Nature Physics*, 2022).

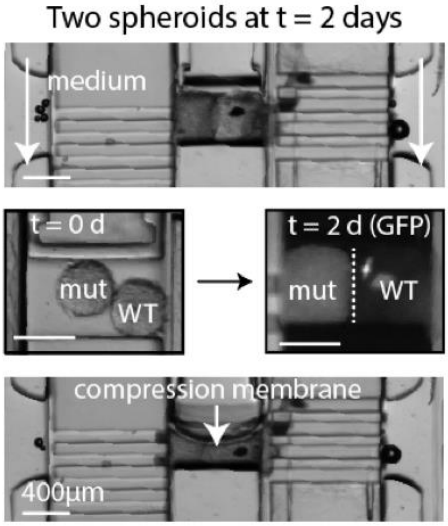

Fig. 1: Microfluidic device which allow to confine multicellular spheroids, to study their proliferation and build-up of growth-induced pressure.

Objectives of the project

Using the microfluidic devices, the objectives of this project are two-fold:

1. Test the hypothesis that macromolecular crowding could be a key parameter controlling cancer cell proliferation under mechanical pressure.
2. Explore how genetic perturbations can affect the sensitivity to pressure and perform mechanical competitions for space.

Environment

The successful candidate will be co-advised by M. Delarue, biophysicist from the LAAS-CNRS 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 conduct their research at LAAS-CNRS, which 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 starting April 2022 for a successful candidate holding a PhD degree, with entry salary at 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 microfabrication, microfluidic, and mammalian cell culture.

Please log-in to CNRS employment portal to apply to this offer: https://bit.ly/3HAUYTk

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