M2 intership offer

Cell growth regulation under mechano-osmotic pressure

Context

In multicellular organisms, cells proliferate within a confined space, facing a spatial constraint that impacts their ability to expand. As confined cells grow, the continuous biosynthesis still occurs while cell expansion is limited. This results in an increase in intracellular crowding, defined as the accumulation of macromolecules such as proteins, nucleic acids within the cytoplasm[1,2]. In yeasts, macromolecular crowding driven by mechanical pressure relates to biomass production reduction, further leading to growth reduction[1]. This biophysical feedback might be essential for a physiologically-controlled multicellular proliferation, avoiding over-proliferation.

In solid cancer the rapid tumor growth and the environment remodeling explain their high intensity of compressive forces. One example is pancreatic ductal adenocarcinoma (PDAC) where mechanical pressure induced-macromolecular crowding interferes with multicellular aggregates growth and cell cycle progression, potentially leading to a mechanical form of chemotherapeutic resistance[3]. Investigating how cells adapt to mechanical stress in controlled experimental conditions can therefore provide fundamental insight into how compression contributes to growth regulation in physiologically and pathologically relevant settings.

An effective way to study these effects is to apply an external controlled mechano-osmotic pressure using inert macromolecules such as dextran. Dextran is a biocompatible polymer that was widely used to apply constant compressive stress on cells[4]. This creates a defined mechano-osmotic environment that allows quantitative analysis of how cells adapt to changes in volume, pressure, and turgor. Understanding these responses is essential for linking physical constraints to growth control, with potential implications for both fundamental biology and disease contexts.

Objectives of this internship

The internship will focus on three main objectives:

1. Assess the effect of dextran mechano-osmotic pressure on growth dynamics of 3D cell models.
2. Measure intracellular crowding under different dextran concentrations and over time to assess possible long-term adaptation.
3. Investigate cell adaptation under cyclic stress conditions by alternating compression (dextran exposure) and relaxation phases to evaluate whether cells adapt differently under fluctuating pressure
4. Compare these measured effects with Dextran to confined growth in agarose

How to postulate

For this essentially experimental internship, we are primarily looking for a candidate with knowledge in cell biology and/or microfluidic, imaging. The candidate must have a strong will to work at the interface between physics and biology. The student will be trained in cell culture and imaging, as well as microfabrication principles.

For more information or to apply, please send your motivation letter and a CV to mbmeksassi@laas.fr, fbaldini@laas.fr and morgan.delarue@laas.fr.

1. Alric, B., Formosa-Dague, C., Dague, E., Holt, L. & Delarue Macromolecular, M. Macromolecular crowding limits growth under pressure. *Nat Phys* (2022) doi:10.1101/2021.06.04.446859.
2. Ben Meriem, Z. *et al.* A microfluidic mechano-chemostat for tissues and organisms reveals that confined growth is accompanied with increased macromolecular crowding. *Lab Chip* 23, 4445–4455 (2023).
3. Rizzuti, I. *et al.* Mechanical Control of Cell Proliferation Increases Resistance to Chemotherapeutic Agents. *Phys Rev Lett* 125, 128103 (2020).
4. Monnier, S. *et al.* Effect of an osmotic stress on multicellular aggregates. *Methods* 94, 114–119 (2015).