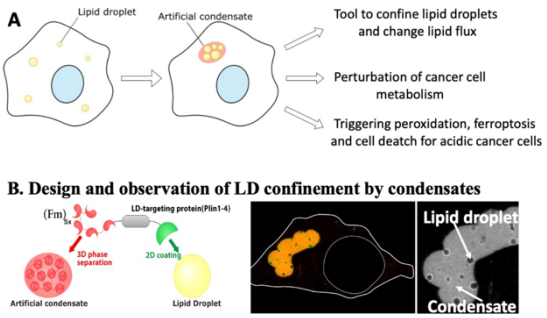
Biomolecular condensates as a tool for interfering with lipid metabolism and perturb cancer cells

1. Topics.

Summary of the Goals: Cancer cells exhibit distinct metabolic processes compared to healthy cells, fueling their malignant characteristics. Lipid droplets (LDs) play a central role in cancer cell survival by aiding in energy production, redox balance, autophagy regulation, and membrane synthesis. In this project, we propose a novel approach to interfere with cancer cell development by manipulating LD dynamics. Engineered biomolecular condensates are introduced as artificial compartments designed to disrupt with LD dynamics, redirect lipid flux, and interfere cellular metabolism. We will first assess how LD dynamics change when confined within engineered condensates and measure alterations in lipid flux, LD-organelle contacts, and cellular metabolism. Next, we will correlate LD perturbation with changes in cellular metabolism and explore potential vulnerabilities in cancer cells. This research offers a promising avenue for studying cancer cell metabolism through LD manipulation, potentially providing insights into novel strategies for interfering with cancer progression. The internship, performed within the department of Chemistry of ENS (Zoher Gueroui team at ENS), combines biophysics, synthetic biology, cell biology, and quantitative microscopy. We benefit from a collaboration with Rachid Thiam lab at LPENS.



2. Techniques: The student will learn state of the art technics in Molecular and Cell Biology (DNA cloning and human cell culture), Biochemistry (immunofluorescence, WBS), and Quantitative Imaging. To characterize the cell properties, we will time-lapse microscopy and advance imaging. For data analysis, we will use image analysis pipelines using state-of-the art approaches.

3. Expected results: The outputs of the master project are multiple and original at the international level and will bring a novel tool to modulate cell metabolism**:** This will provide a novel tool box to modulate cancer cellular metabolism and potentially open up a novel strategy to interfere with cancer cells development in complement to pharmacological approaches. The Master student will benefit from strong preliminary experiments.

4. References

DeBerardinis, R. J. & Chandel, N. S. Fundamentals of cancer metabolism. Sci. Adv. 2, e1600200 (2016).

Controlling lipid droplet dynamics via tether condensates. Amari C, Simon D, Bellon T, Plamont MA, Thiam AR, and Gueroui Z. *Nat. Chem. Biol.* (2025). https://www.nature.com/articles/s41589-025-01915-2