Master 2: *Cell Physics Master*

INTERNSHIP PROPOSAL

Laboratory name: **Laboratoire de Physique de l'ENS Paris, LPENS**
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Thesis possibility after internship: **YES**
Funding: YES

Using physical approaches to study liquid crystalline lipid droplets in cells

In our lab, we are interested in elucidating the question of how lipid droplets form and grow by investigating different aspects of the lipid biogenesis pathway via biophysical and soft matter approaches. We utilize biochemical and physicochemical techniques in vitro and in vivo to get to the bottom of the mechanisms of lipid droplet biogenesis.

Lipid droplets (LDs) are cellular organelles that have a neutral lipid core consisting of neutral lipids, e.g., triglycerides, and are surrounded by a lipid monolayer. Apart from maintaining the cellular energy balance, they are also involved in protein quality control, gene expression, and development.

LDs have been described as pathological hallmarks in neurodegenerative and neuroinflammatory disorders. Therefore, LDs represent potential biomarkers and therapeutic targets. Restoring lipid balance, modulating LD biogenesis, or improving some lipid metabolic pathways could represent novel approaches to treating metabolic or even neurodegenerative disorders.

It was shown that the phase transitions and amount of cholesteryl esters (CE) in the membrane, accompanied by TAG and seipin availability, could have a major impact on lipid droplet nucleation and growth. [1]

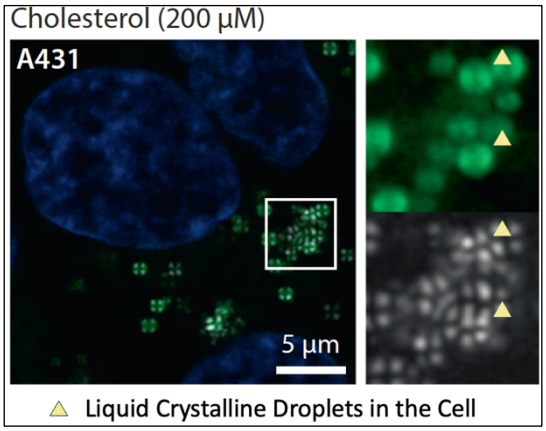

Figure 1:Figure 1: A431 cells imaged after 24 h of cholesterol (200 µM) feeding. Bodipy (green) was added upon imaging for LD labeling. [1]

During your internship, you will have the possibility to investigate the behavior and role of neutral lipids, specifically cholesterol ester, in the biophysics of lipid droplets. Different interactions/dependencies between neutral lipids, lipids and proteins can be approached in a biophysical way utilizing micromanipulation of membrane systems [2], via in vitro membrane systems like giant unilamellar vesicles or droplet-embedded vesicles.

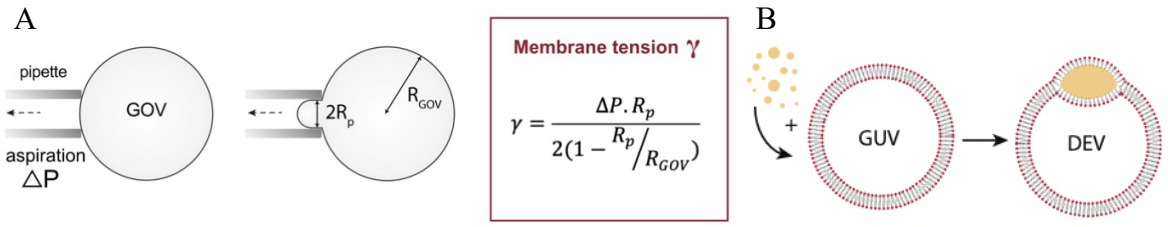

Figure 2: (A) schematic representation of membrane tension measurements via micromanipulation with glass pipettes. (B) mixing of GUVs with artificial lipid droplets to generate droplet-embedded vesicles (DEV). [2]

[1] Dumesnil, C., Vanharanta, L., Prasanna, X. *et al.* Cholesterol esters form supercooled lipid droplets whose nucleation is facilitated by triacylglycerols. *Nat Commun* **14**, 915 (2023). https://doi.org/10.1038/s41467-023-36375-6

[2] Santinho, A., Chorlay, A., Foret, L., & Thiam, A. R. Fat inclusions strongly alter membrane mechanics. *Biophysical journal*, *120*(4), 607-617 (2021).

Domains: Soft Matter and Biological Physics and a little bit of Theoretical Physics