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Funded Ph.D. Project: Biophysical study of lipid exchanges between organelles

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During energy-rich conditions, cells fabricate lipid droplets (LDs) made of a neutral lipid oil core, surrounded by a phospholipid monolayer containing proteins (Figure 1). LDs represent organelles that are the energy storage of cells. They play multiple biological functions amongst which is the regulation of cellular energy metabolism. Excessive accumulation of lipid droplets leads to obesity and major metabolic disorders.
A dysregulation of LD formation and maintenance is responsible for several metabolic disorders affecting the liver, brain, heart, etc. Regulation of LDs relies on the control of their oil composition, phospholipid, and protein content, which are acquired from the endoplasmic reticulum (ER) bilayer during their formation (Figure 1).
How LDs exchange lipids with the endoplasmic reticulum and other organelles are unknown. Addressing this question is critical to understanding how cells reach their homeostasis.

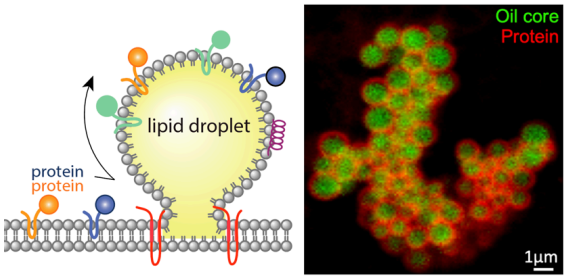

Figure 1: Left. A lipid droplet is being formed from at the endoplasmic reticulum bilayer and proteins relocalize to the droplet surface. Right. Image of lipid droplets in a liver cell. The oil core is in green and one protein type is labeled in red

In essence, LDs represent intracellular oil-in-water emulsion droplets. Thus, the physics of emulsions rules out their behavior and fate. Our lab has developed these past years emulsion tools now enabling us to study LDs and how lipids and proteins are exchanged between the ER phospholipid bilayer and the LD phospholipid monolayer (Figure 1).

The present project aims at developing semi-in vivo emulsion droplets to study how LDs interact with bilayers in their environment and how lipid transfers happen. The work of the Ph.D. student will be to use cell extracts and reconstitute organelle bilayer, which will contain all endogenous proteins. The student will decipher how model LDs exchange lipids with the reconstituted bilayer and how proteins mediate such transfer. To achieve such, the student will combine soft matter science and biophysical approaches to study by fluorescence the contribution of selected proteins. Mechanisms controlling the lipid transfers between the bilayer and the LD will be deciphered.

The Ph.D. candidate will benefit from a multidisciplinary environment in the lab where biologists and physicists collaborate on different but interrelated topics.

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