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## Biography

## Project

**European Research Council Starting Grant**
Project acronym: DROPFAT
Project full title: Biogenesis of lipid droplets and lipid homeostasis

**Overview**
Organisms and cells face a myriad of environmental changes with periods of nutrient surplus and shortage. It is therefore not surprising that in all kingdoms of life, cells have evolved the means to store energy and thereby minimize the effects of environmental fluctuations. While the capability for energy storage has obvious advantages, deregulated energy accumulation can also be detrimental. Indeed, excessive energy storage is the hallmark of some of the most common diseases in the Western world such as obesity, atherosclerosis or diabetes.

In most cells energy is stored as neutral lipids, mostly triglycerides and sterol esters, in a dedicated cellular compartment, the cytoplasmic lipid droplets (LDs). LDs are found in virtually every eukaryotic cell and play a central role in cellular lipid and energy metabolism. Despite their ubiquitous presence and importance, a large number of questions regarding the physiology of LDs are poorly understood. LDs are composed of a single lipid layer and therefore distinct from all other cellular compartments. How do LDs originate at the endoplasmic reticulum (ER) and what is the machinery involved? How is the size, number and the storage capacity of the LDs regulated? How are specific proteins and lipids targeted to LDs? Addressing these questions is fundamental for understanding the “life cycle” of LDs and for a global picture of the cellular energy homeostasis.

The main goal of this proposal is to reveal the molecular mechanisms controlling neutral lipid dynamics and their storage in LDs. We will focus specifically on the role of the endoplasmic reticulum in the biogenesis of LDs. First, we will identify and functionally characterize the ER protein complexes required for LD formation and regulation. Second, we will develop an *in vivo* site specific photocrosslinking assay to dissect the mechanism by which proteins are targeted to LDs and thereby regulate the properties of this organelle. Finally, we will develop a cell-free system that recapitulates the biogenesis of LDs *in vitro*. This system will reveal the molecular mechanisms of lipid droplet biogenesis. Altogether, our strategy constitutes a systematic, in-depth analysis of LD dynamics and will lead to significant insight on the mechanisms of cellular energy storage. Our findings will likely offer a better understanding of human pathologies such as obesity and lipodistrophies, and ultimately hint at novel therapeutic avenues.