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EDITORIAL

Love your lipids!

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The closest many of us get to considering lipids on a daily basis is in our diet or when we get a takeaway coffee and have to decide whether to have full-fat, semi-skimmed or half-and-half milk in our coffee… and what is oat milk exactly? When the average student thinks about lipids outside the context of coffee chains, they probably first think of the plasma membrane and vesicular transport. You know, those nice schematics in reviews and textbooks with proteins embedded or contained in perfectly ordered lipid bilayers. Ok, we all know that lipids are essential, but for many people, the lipid is just there, inert, not doing anything except forming membrane-bound organelles and helping to move things around in or out of cells. These are definitely important and essential cellular functions, but most of us just follow the protein, along with a generous dash of detergent to solubilize the lipids. However, for a number of enlightened people, who can follow the complex nomenclature and chemistry of lipids, it is an entirely different world. They also know those perfect lipid bilayer diagrams have been misleading the rest of us for years!

It might also come as a surprise for protein-centric researchers that the number of lipid species is on a par with that of proteins, and that the lipid composition varies greatly between organelles and cell types. However, in contrast to proteins, for the most part, our understanding of the role of this functional diversity is still severely lacking, even though lipids, as much as proteins, provide membranes and thus organelles with their cellular identities. Lipid metabolism and transport are equally complex, and are controlled by a large number of proteins that help ensure the correct lipid ends up in the right cellular location or is attached to the correct protein or sugar. As with proteins, lipids are involved in a diverse range of essential cellular processes, with important structural and signalling roles in addition to providing a source of energy. Lipid modifications, such as palmitoylation and farnesylation, are also important determinants for the cellular location of proteins. Given the above, it comes as no surprise that dysregulation of lipids and their metabolism can have dire consequences for cell homeostasis, which can lead to devastating diseases, such as Niemann–Pick, Tay–Sachs and Gaucher diseases, to name but a few.

If they are so important, why are more people not studying the regulation and cellular function of lipids? The two main issues are identification and visualization. In recent years, mass spectrometry has allowed the identification of individual lipids with exquisite sensitivity in cell extracts or purified organelles. However, this provides little or no information concerning their cellular location. Visualization of lipids *in situ* is possible but not a trivial undertaking. Lipids can be directly fluorescently labelled and individual lipid species can be detected with fluorescently tagged lipid-binding proteins or domains, such as PH domains, which are used as PIP2 lipid probes. Both approaches have technical challenges, including getting the labelled lipid to the right cellular location and the impact of any fluorescent or other chemical modification, as well as the binding of a domain on the function and biophysical properties of the lipid. The specificity of lipid-binding domains and their availability can also be problematic. Manipulation and loss-of-function experiments are essential approaches in cell biology, but how are these applied to individual lipid species? The manner in which lipids are synthesised means that RNAi approaches are largely not applicable, although it is possible to manipulate proteins involved in lipid production and transport. Small-molecule and other chemical approaches are also possible, but there is clearly an urgent need for new and improved technological advances to visualize and manipulate individual lipids that may be present as only minor species but still have essential functions. Notwithstanding this, research and interest into the function of lipids in areas such as organelle crosstalk is currently providing new fundamental insights into cell regulation and homeostasis.

James Olzmann

It is for this reason that we have decided that the sixth Journal of Cell Science special issue will focus on the cell biology of lipids. This special issue will be guest edited by James Olzmann. James received his PhD from Emory University, Georgia, USA. His postdoctoral research in the laboratory of Dr Ron Kopito at Stanford University, California, USA, focused on the organisation of endoplasmic reticulum protein quality control networks and

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connections with neutral lipid storage organelles known as lipid droplets. In 2013, James began his independent research group at the University of California, Berkeley. He is currently an Associate Professor at UC Berkeley with a joint appointment in the Departments of Nutritional Sciences and Toxicology and Molecular & Cell Biology, and an Investigator at the Chan Zuckerberg Biohub. James' current research leverages interdisciplinary approaches to understand the cell biology of lipid homeostasis, including the mechanisms that regulate lipid droplets and the pathways that govern cellular responses to lipotoxicity.

We will welcome submissions for our Special Issue on the Cell Biology of Lipids until the 15 July 2021. The Special Issue will also contain reviews and poster articles, commissioned by our in-house Reviews Editors. We look forward to working with James on this important topic. You can find out more at https://jcs.biologists.org/cell-biology-lipids, and contact us at jcs@biologists.com about any potential submissions.