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Thematic Minireview Series on the Lipid Droplet, a Dynamic Organelle of Biomedical and Commercial Importance

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The lipid droplet (also known as lipid particle and oil body) is a dynamic organelle whose boundary is surrounded by a phospholipid monolayer and whose inner core is composed mainly of triacylglycerol (TAG) and steryl esters. The monolayer surface is coated with an assortment of proteins that serve structural and metabolic functions. Although the existence of lipid droplets in mammalian cells, plants, yeast, and bacteria has been known for many years, a great deal of attention is currently being paid to the mechanisms of its formation and growth and the metabolism of its core components. Indeed, the lipid droplet is now appreciated because it plays important roles in lipid-based diseases and has commercial importance with respect to production of cooking oils and biofuels.

The first minireview by Dawn L. Brasaemle and Nathan E. Wolins, "Packaging of Fat: An Evolving Model of Lipid Droplet Assembly and Expansion," summarizes evidence supporting the following model of lipid droplet assembly. Nucleation initiates in the endoplasmic reticulum (ER) when diacylglycerol accumulates and attracts members of the perilipin family of structural lipid droplet proteins to patches of the ER where lipid droplets begin to emerge. Resident proteins of the ER, including seipin and fat storage-inducing transmembrane proteins FIT1 and FIT2, contribute to early assembly through as yet uncharacterized mechanisms. After the nascent lipid droplet emerges, other organelles, including mitochondria and peroxisomes, contribute additional lipids. Changes in protein composition accompany droplet maturation. In most cells, lipid droplets are few and small, but in adipocytes ("professional" fat storing cells), the droplets enlarge to 100 μm or larger. Adipocyte lipid droplets grow, in part, by fusion of smaller droplets; however, the mechanism of fusion is also poorly understood. Observations suggesting that the fat-specific protein FSP27 plays a role in lipid droplet expansion and perhaps fusion are discussed.

Proteins associated with lipid droplets serve a vital role in mobilizing lipids at times of need; perilipins function to coordinate access of lipases to substrate lipids. Pathways of lipase delivery to lipid droplets share features with well characterized mechanisms of vesicular trafficking. Changes in the phospholipid monolayer surrounding the neutral lipid core accompany attrition of lipid droplets during lipolysis and also the expansion and maturation of the droplets. Recent studies show that several steps in phospholipid biosynthesis occur in the immediate proximity of lipid droplets, either by recruitment of enzymes to lipid droplets or through increased association of ER membranes harboring enzymes with lipid droplets. Brasaemle and Wolins integrate current data on lipid droplet assembly into the framework of our understanding of basic cellular processes.

The second minireview by Eva Herker and Melanie Ott, "Emerging Role of Lipid Droplets in Host/Pathogen Interactions," highlights recent findings on how viruses, bacteria, and parasites hijack lipid droplets to support their own replication. The tight physical and functional interaction of lipid droplets with pathogens has only recently become apparent. On one side, these interactions provide important new insights into the life cycles of the pathogens and might lead to new therapeutic interventions. On the other side, they increase our mechanistic understanding of lipid droplet biology by spotlighting unique aspects exploited by pathogens. Hepatitis C and dengue viruses need lipid droplets to produce infectious particles, and rotaviruses rely on them to form viroplasms, which contain the active viral RNA replication complexes. Bacteria such as *Chlamydia trachomatis* and diverse mycobacteria utilize lipid droplets as a source for energy substrates or phospholipids to support bacterial replication. Some pathogens have evolved strategies to evade the immune system involving lipid droplets or to support their own survival by using these organelles as dumping grounds for toxic metabolites or proteins, as in the case of infections with *Plasmodium falciparum* or Reoviridae μ1.

There is considerable and increasing interest in the health consequences of diets rich in fat content. A large proportion of fat calories in Western diets are derived from plant TAGs, or vegetable oils, which are mostly enriched in seed or oleaginous fruit tissues. Although TAGs are assembled and packaged in plant tissues into lipid droplets by mechanisms that resemble those found in other eukaryotes, there are important differences in factors that regulate the supply of TAGs for lipid droplet biogenesis. In the third minireview by Kent D. Chapman and John B. Ohlrogge, "Compartmentation of Triacylglycerol Accumulation in Plants," the multitude of pathways and recently discovered features of TAG accumulation in plants are reviewed, with an eye toward identifying gaps in knowledge that will be important to the general cell biology of storage lipid metabolism. New ideas about fatty acid biosynthesis, acyl-CoA incorporation into phosphatidylcholine, and several acyl-CoA-independent pathways for TAG synthesis all indicate that the accumulation of oils into lipid droplets in different plant tissues is far more complex than the well known stepwise acylation of glycerol by enzymes of the Kennedy pathway. Genetic engineering approaches to alter the fatty acid composition of oilseeds for nutritional and industrial purposes have met with limited success. It is certain that the future design of strategies to enhance the accumulation of TAGs in plant-derived tissues for food and biofuels will depend on improved appreciation for the metabolic complexity and flexibility of TAG formation and packaging.

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