

## Same-same, but different: determinants of lipid droplet diversity

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Lipid droplets are organelles specialized in lipid storage and thus serve both as energy reservoir and as a source of building blocks for the cellular membrane systems. Heterogeneity within the lipid droplet pool of a single cell has been observed, but how such organelle differentiation is brought about has remained enigmatic.

Using genome-wide microscopy-based screens in yeast, we have identified the evolutionary conserved lipid droplet organization (LDO) machinery as a determinant of cellular lipid droplet identity. The LDO machinery consists of at least two components, Ldo16 and Ldo45, and cooperates with the seipin lipid droplet biogenesis machinery. The Ldo proteins are the products of two overlapping genes and thus have partially identical sequences, with Ldo16 corresponding to the C-terminal part of the longer Ldo45. The LDO machinery is enriched on a subpopulation of cellular lipid droplets located directly adjacent to the contact site between the nucleus and the vacuole, and directs their positioning in this specific cellular niche. Furthermore, the LDO machinery is required for establishing the unique surface proteome of these lipid droplets, and thus determines both characteristic features of this organelle subpopulation.

Our findings suggest a mechanistic link between lipid droplet positioning adjacent to partner organelles, and proteomic and ultimately functional lipid droplet differentiation.