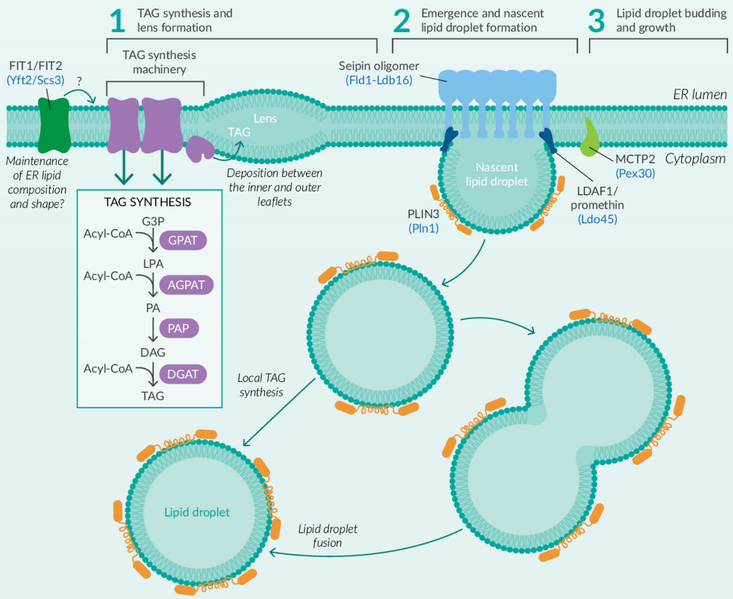
LIPID DROPLET BIOLOGY

BIOGENESIS

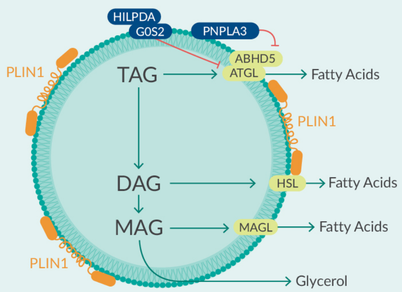
Lipid droplets are endoplasmic reticulum (ER)-derived organelles. Neutral lipids such as triacylglycerol (TAG) are synthesized and deposited between the leaflets of the ER bilayer. Above a certain concentration, the neutral lipids phase separate and form a lens in the membrane. The lipid droplet then emerges from the outer leaflet of the ER through a process facilitated by assembly factors and asymmetric membrane tension. Lipid droplets continue to grow through local neutral lipid synthesis and lipid droplet-lipid droplet fusion.



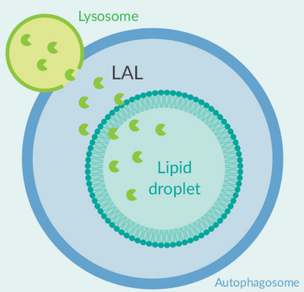
LIPOLYSIS & LIPOPHAGY

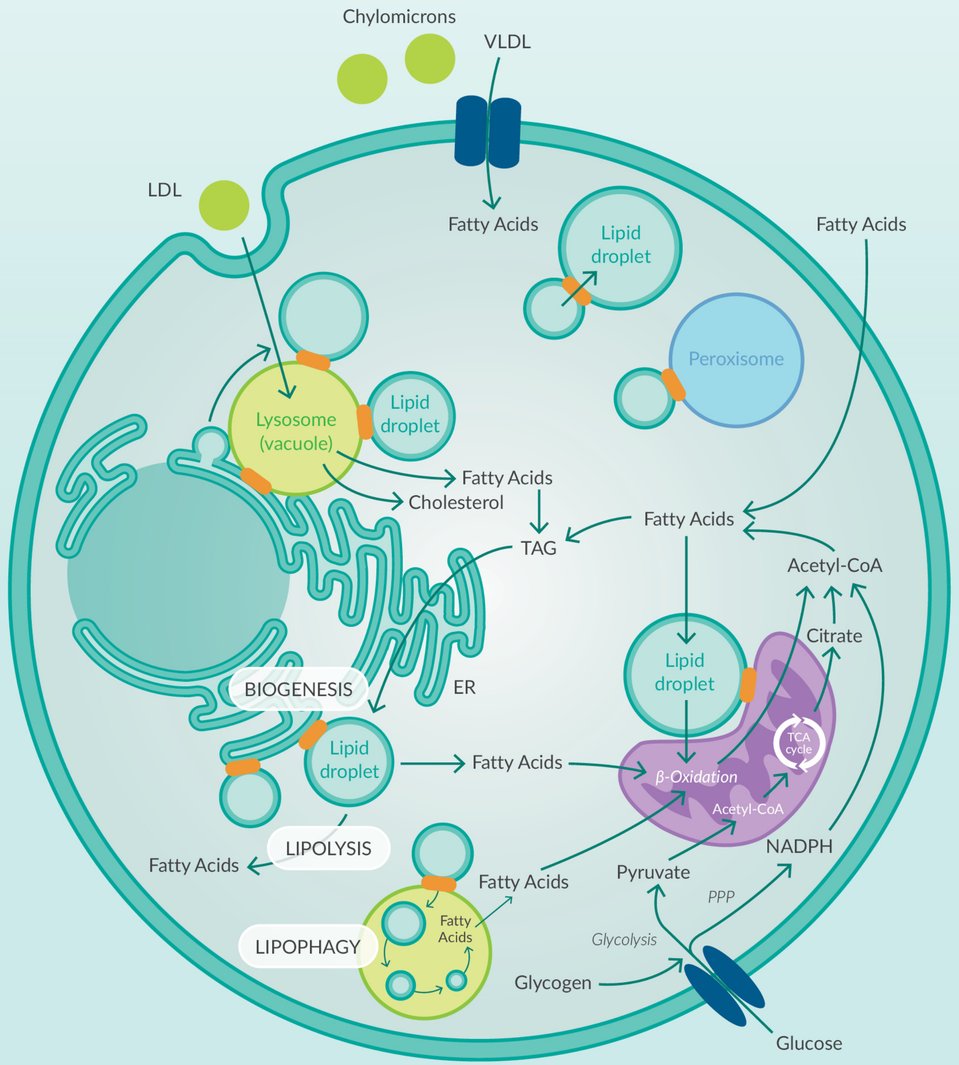
Lipid droplet breakdown is mediated by two catabolic processes, lipolysis and lipophagy. During lipolysis, stored TAG is broken down by a series of lipolytic reactions catalyzed by lipid droplet-associated lipases. During lipophagy, lipid droplets are engulfed within a double-membrane autophagosome that fuses with lysosomes to generate an autolysosome, allowing the entire lipid droplet to be degraded by lysosomal hydrolases.

Lipolysis



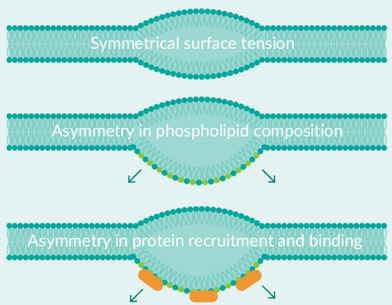
Lipophagy





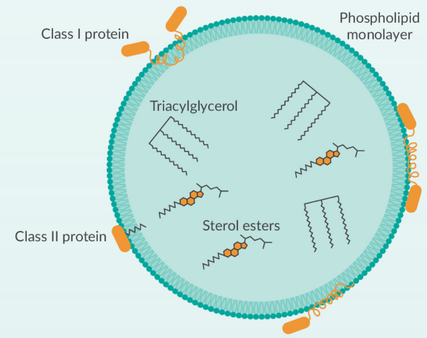
HOW DO LIPID DROPLETS EMERGE?

Proteins and lipids are surfactants that mask the interface of the hydrophobic oil droplet and the surrounding hydrophilic milieu. Differential compositions of proteins and lipids within the inner and outer leaflets of the ER membrane induce asymmetries in surface tension that drive directional lipid droplet emergence. Lipid droplets commonly bud into the cytosol, suggesting that the ER membrane surface tension is tightly regulated.



COMPOSITION & PROTEOME

Lipid droplets consist of a neutral lipid core surrounded by a phospholipid monolayer decorated with a set of ~150 integral and peripheral proteins in human cells (for more information visit dropletproteome.org) and ~30-40 proteins in yeast. Triacylglycerol and cholesterol esters are the most common lipids found in the core of the lipid droplet, but retinyl esters, ether lipids, acylceramides, squalene, fat-soluble vitamins and drugs, and waxes can also be present.

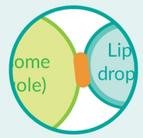


ORGANELLE INTERACTIONS

Membrane contact sites are regions in which the membranes of organelles are held in close apposition. Lipid droplets form membrane contacts with a variety of organelles, providing sites for the exchange of lipids or other molecules. Protein-based tethering complexes establish and maintain these sites. For some lipid droplet membrane contact sites tethering complexes have been identified.

Nucleus:Vacuole Junction
Nvj1:Vac8
Mdm1

Mitochondrion:Lipid Droplet
MFN2:PLIN1
MIGA2
Unknown:PLIN5



Lysosome:Lipid Droplet
LAMP2A:PLIN2
Hsc70

Plasma Membrane:Lipid Droplet
BTN
XDH
PLIN2
Caveolae proteins
EHD2
Snazarus

Lipid Droplet:Lipid Droplet
CIDE-A
CIDE-B
CIDE-C (FSP27)
Ubiquitinated AUP1

ER:Lipid Droplet
Seipin (Fld1-Ldb16)
NRZ-SNARE:RAB18
FATP1:DGAT2
SNX14
DFCP1
Promethin (LDAF1)
Ice2:Unknown
VPS13A/C

Peroxisome:Lipid Droplet
ABCD1:M1-spastin

yeast
human
Drosophila

Special thanks to Dr. James Olzmann from the University of California, Berkeley for consultation on this diagram.