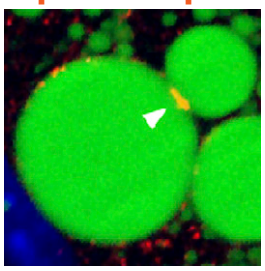
In This Issue

Text by Ben Short
bshort@rockefeller.edu

Lipid droplets fatten up with Fsp27



Fsp27 (red) localizes to the site of contact (arrowhead) between lipid droplets (green) in adipocytes.

An adipocyte protein promotes the growth of lipid droplets (LDs) by facilitating lipid transfer from smaller to larger droplets, Gong et al. report.

Consisting of a neutral lipid core surrounded by a monolayer of phospholipids and associated proteins, LDs serve as the cell's fat storage depots, particularly in adipocytes where they grow to extra large sizes. How LDs grow is unknown, but adipocytes lacking the LD-associated protein Fsp27 have many small droplets instead of a single large one.

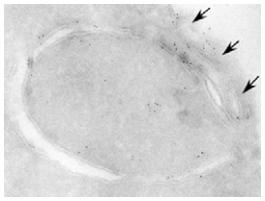
Gong et al. found that Fsp27 concentrated at the contacts between LDs and that this localization depended on the protein's C-terminal domain. Photobleaching experiments revealed that LDs in contact with each other traded neutral lipids but that this exchange was abolished in adipocytes lacking Fsp27. Moreover, the researchers identified three lysine residues—which may form part of an amphipathic helix in Fsp27's C terminus—that were required for lipid exchange and LD growth.

Although LDs exchanged lipids bidirectionally, net lipid transfer occurred from the smaller to the larger droplet of an LD pair, leading to shrinkage of the smaller droplet and growth of the larger one. This directional transfer is probably driven by the higher internal pressure within smaller droplets, which would force lipids into the larger LD.

How Fsp27 facilitates this transfer remains unclear, but senior author Peng Li thinks that the protein may help to connect LDs and form a pore to allow lipid movement. The next question, she says, is to identify additional proteins that work with Fsp27 to boost LD growth.

Gong, J., et al. 2011. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201104142.

CUPS provide a handle on Acb1 secretion



Immunoelectron microscopy reveals Grh1 (black dots) on a cup-shaped membrane structure (arrows, membrane lamellae).

Bruns et al. describe how several proteins required for an unconventional secretory pathway gather together in a novel membrane compartment.

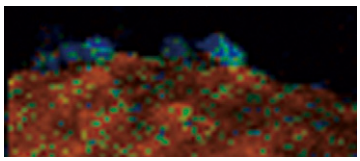
The Acyl-CoA binding protein Acb1 is secreted by starving budding yeast, but, unlike most secretory proteins, Acb1 doesn't pass through the ER and Golgi on its way to the cell surface. The details of Acb1's alternative route are unknown, but a diverse set of proteins mediate its journey. Components required for Acb1 secretion include autophagy proteins (such as Atg8 and Atg9), proteins that deliver cargo to multivesicular bodies (for example, Vps23), and Grh1, a homologue of a mammalian Golgi protein.

Bruns et al. found that, upon starvation, Grh1 concentrated in membrane compartments near ER exit sites. These structures didn't contain markers of the ER, Golgi, or endosomes, but they did contain Vps23, Atg8, and Atg9, as well as the phosphoinositide PI(3)P. Blocking PI(3)P synthesis or deleting Grh1 prevented the formation of these compartments in starving yeast.

By electron microscopy, the Grh1-containing membranes appeared cup-shaped, leading the authors to name them compartments for unconventional protein secretion or CUPS. Their shape and the presence of Atg8 and Atg9 are reminiscent of autophagosome precursors, but Bruns et al. found that CUPS weren't formed in response to the autophagy-inducing drug rapamycin, suggesting that CUPS are a novel, albeit related, compartment. Senior author Vivek Malhotra says that the identification of CUPS gives researchers a handle to uncover other steps in Acb1 secretion. CUPS may engulf Acb1 in the cytoplasm and deliver it to the plasma membrane, either directly or via fusion with secretory endosomes.

Bruns, C., et al. 2011. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201106098.

Cell death helps give closure



Several apoptotic cells (blue) persist at the edge of the neural plate as it folds to form the neural tube.

By visualizing the dynamics of apoptosis in living mouse embryos, Yamaguchi et al. reveal that cell death helps drive the morphogenetic movements required for neural tube closure (NTC).

NTC is a vital early step in the development of the central nervous system. A flat group of cells called the neural plate bends in the middle so that the sides of the plate curve around to meet and fuse with each other, forming the neural tube. Many mouse embryos lacking key apoptosis proteins, such as Apaf-1 or Caspase-3, show defects in NTC in their cranial region, but how cell death contributes to this process is unclear.

Yamaguchi et al. generated transgenic mice expressing a FRET-based apoptotic reporter whose signal is decreased when activated caspases cleave the link between two fluorescent proteins. Using this reporter, the researchers identified two types of apoptotic cells in embryonic brains undergoing NTC. Some cells died and fragmented rapidly, whereas others—particularly near the tips of the folding neural plate—persisted for longer without breaking apart.

Both types of apoptotic cells were absent from mouse embryos lacking Apaf-1 and Caspase-3. In these animals, neural plate bending was reduced, thereby delaying NTC. Senior authors Yoshifumi Yamaguchi and Masayuki Miura think that the death, and subsequent extrusion, of cells from the tips of the neural plate may generate forces that help to shape the developing tissue and facilitate cranial NTC. Alternatively, the two types of apoptotic cells may direct this developmental process by sending different signals to their surviving neighbors.

Yamaguchi, Y., et al. 2011. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201104057.