In This Issue

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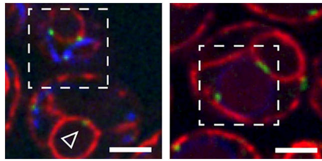
Ltc1 gets added to the ER's contacts



Ltc1 (green) localizes to sites where the ER (red) contacts either mitochondria (blue, left) or vacuoles (blue, right).

Murley et al. identify a yeast protein that might coordinate the function of vacuoles and mitochondria by transferring sterols at the sites where these organelles are contacted by the ER.

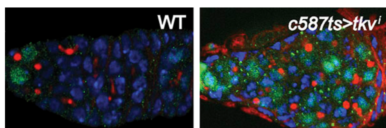
The ERMES complex connects the yeast ER to mitochondria, promoting the exchange of lipids between these organelles and marking the sites of mitochondrial division. Murley et al. looked for proteins that interact with the ERMES complex and identified a previously uncharacterized ER protein called Ylr072w. The protein localized to ER–vacuole as well as ER–mitochondria contacts and was recruited to these sites by Vac8 and Tom70/71, respectively. Because Ylr072w could transfer sterols between artificial membranes in vitro, the researchers renamed it Lipid transfer at contact site 1, or Ltc1. The researchers also identified a family of related proteins, conserved from yeast to humans.

Certain environmental stresses induce the formation of ergosterol-rich domains in vacuolar membranes. Cells required Ltc1 to form these domains and, when Murley et al. increased the proportion of Ltc1 at ER–vacuole contacts, cells formed ergosterol-rich vacuole domains even in the absence of stress. The function of these membrane domains is unknown, but, because they contain components of the TORC1 signaling complex, they may control the activity of this key metabolic regulator.

Whether Ltc1 senses or alters the lipid content of mitochondria remains unclear, but the protein was required for cell viability in the absence of the ERMES complex protein Mdm34, indicating that Ltc1 separately regulates mitochondrial function. Indeed, by contacting both mitochondria and vacuoles, Ltc1 might coordinate the metabolic activities of the two organelles.

Murley, A., et al. 2015. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201502033

A stem cell niche shows self-restraint



Compared with a wild-type germarium (left), a germarium whose escort cells lack Tkv (right) displays extensive Dpp signaling activity (green), and a large number of undifferentiated germ cells marked by a spherical structure containing α-Spectrin (red). DNA is labeled blue.

Luo et al. describe how the *Drosophila* ovarian niche limits its own ability to maintain germline stem cells (GSCs) in an undifferentiated state.

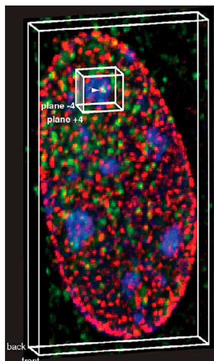
Stem cells reside in specialized microenvironments, or niches, that prevent them from differentiating prematurely. In the germaria of *Drosophila* ovaries, GSCs reside next to cap cells that inhibit differentiation by secreting the TGFβ-like molecule Dpp. In other tissues, Dpp can influence cell fate over long distances, but, in the ovary, its range is spatially restricted such that, when a GSC divides, one of its daughters is positioned too far away from the cap cells to receive the Dpp signal, and therefore starts to differentiate into an egg. Luo et al. were interested in how escort cells—another component of the ovarian niche—help to limit Dpp's sphere of influence.

The researchers found that escort cells express the Dpp receptor Tkv so that they can mop up excess Dpp secreted from the cap cells. Depleting Tkv from the escort cells extended Dpp's range, resulting in an increased number of undifferentiated germ cells. Tkv's expression in escort cells was stimulated by several Wnt ligands released from the cap cells. The ovarian niche therefore limits its own ability to maintain GSCs, ensuring that the stem cells' progeny can undergo differentiation.

Tkv's function in escort cells does not require canonical Dpp signaling. Senior author Yu Cai now wants to investigate whether the receptor activates noncanonical signaling pathways instead.

Luo, L., et al. 2015. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201409142

A SMRTer way to track molecules



A 3D projection of a nucleus shows the distribution of β-actin mRNA (green), nuclear pores (red), and heterochromatin (blue).

Smith et al. describe a microscopy technique that instantaneously captures 3D images of live cells, allowing them to track the movement of single mRNAs in the nucleus.

3D microscopy images are usually obtained by capturing a series of 2D images at different focal planes, but this process is often too slow to follow the rapid movements of individual molecules within a particular region of the cell. One potential solution is to use multifocus microscopy, in which the detection light is split into nine different focal planes that can be imaged simultaneously. However, the acquired images need to be carefully realigned with each other in order to generate an accurate 3D snapshot of the region of interest.

Smith et al. developed a way to achieve this realignment that they called 3D single-molecule real-time (3D-SMRT) microscopy. The researchers used multifocus microscopy to image the nuclei of cultured fibroblasts expressing fluorescent proteins labeling the nuclear pores and β-actin mRNA. The nuclei were also stained with a vital DNA dye that emits light across a broad spectral range, allowing the researchers to precisely align the images obtained in each focal plane and color channel. The entire nucleus could thus be imaged 10 times per second, fast enough to track the diffusion of individual β-actin transcripts.

The researchers found that β-actin mRNAs could freely access every part of the nucleus; the transcripts weren't excluded from heterochromatin-rich regions, for example. Nevertheless, because of the nucleus's disc-like shape, most mRNAs were located within 0.5 µm of a nuclear pore. Senior author David Grunwald says that such precise spatiotemporal localization studies are just the beginning of what 3D microscopy will eventually be capable of.

Smith, C.S., et al. 2015. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201411032

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