In This Issue

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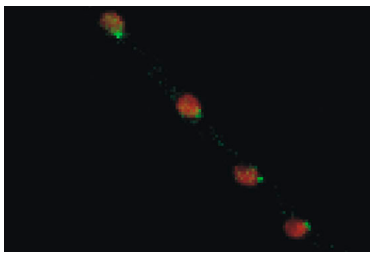
γ-Tubulin flips the G1/S switch



During its active period in G1, Cdh1 (green) localizes to the spindle pole bodies of an *Aspergillus* cell containing multiple nuclei (red).

Edgerton-Morgan and Oakley reveal that γ-tubulin promotes cells' entry into S phase by controlling the localization of a key cell cycle regulator.

γ-Tubulin is best known for nucleating microtubules at microtubule-organizing centers such as centrosomes or fungal spindle pole bodies, but γ-tubulin also regulates the cell cycle. *Aspergillus nidulans* strains expressing the γ-tubulin mutant *mipA*-D159 fail to inactivate a ubiquitin ligase called the anaphase-promoting complex/cyclosome (APC/C) during interphase. This prevents the accumulation of proteins such as cyclin B and cyclin-dependent kinase 1 that would normally initiate DNA synthesis and cell cycle progression.

In many species, a protein called Cdh1 activates the APC/C during G1 to prevent premature entry into S phase. Edgerton-Morgan and Oakley found that *Aspergillus* Cdh1 delays S phase by targeting cyclin B for destruction and that *mipA*-D159 strains lacking Cdh1 were once more able to accumulate cyclin B and progress through the cell cycle. Cdh1 localized to spindle pole bodies while it was active in G1 but disappeared as the cells entered S phase. In *mipA*-D159 mutants, however, Cdh1 remained at the spindle pole bodies for longer, suggesting that γ-tubulin normally inactivates the APC/C by promoting Cdh1's displacement from these structures.

Senior author Berl Oakley now wants to investigate how γ-tubulin regulates Cdh1's localization and to understand why this is compromised in *mipA*-D159 mutants. The most likely explanation, Oakley says, is that wild-type γ-tubulin binds to a protein that promotes Cdh1's destruction or dissociation from the spindle pole body.

Edgerton-Morgan, H., and B.R. Oakley. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201203115.

Rad53 keeps watch over mitochondrial DNA

A kinase that arrests cells in response to nuclear DNA damage also safeguards the inheritance of mitochondrial DNA (mtDNA), Crider et al. report.

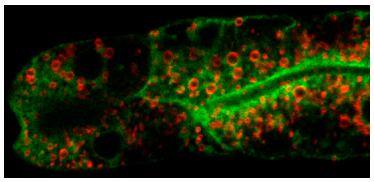
mtDNA encodes many of the proteins required for mitochondrial respiration. Budding yeast lacking mtDNA can still survive, but Crider et al. found that these cells arrested during the cell cycle, often failing to progress from G1 into S phase.

This arrest wasn't due to defects in the electron transport chain or ATP synthesis, because deleting a subunit of cytochrome *c* oxidase or inhibiting ATP synthase had no effect on the cell cycle. Yeast also entered S phase promptly if their mtDNA was replaced by junk, noncoding sequences, suggesting that arrest is triggered by the absence of DNA from mitochondria rather than the loss of any specific gene.

Rad53 is a protein kinase that delays S phase entry when nuclear DNA is damaged and is also required for mtDNA maintenance in yeast and mammalian cells. Crider et al. found that Rad53 was activated by the loss of mtDNA and that yeast lacking the kinase no longer arrested in G1/S. The researchers now want to investigate how mitochondria sense the absence of mtDNA and signal to Rad53 to initiate what senior author Liza Pon calls a "mtDNA inheritance checkpoint." Pon is also intrigued by the idea that mutations in the Rad53 pathway may cause the changes in mtDNA copy number that are often seen in tumor samples, which may, in turn, lead to alterations in cancer cell metabolism.

Crider, D.G., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201205193.

An enzyme complex helps fatten up lipid droplets



FATP1 (green) localizes to the ER and forms a complex with DGAT2 (red) on lipid droplets.

Xu et al. describe how two lipid-modifying enzymes form a complex that links the endoplasmic reticulum (ER) to lipid droplets in order to promote triglyceride synthesis and storage.

Cells store excess fatty acids inside lipid droplets. These organelles consist of a neutral triglyceride core surrounded by a phospholipid monolayer and are closely associated with ER cisternae. How and why the ER contacts lipid droplets is unclear, however.

Xu et al. screened for *C. elegans* mutants that suppressed the formation of large lipid droplets in a strain with elevated fatty acid levels. Two enzymes involved in triglyceride synthesis were required for lipid droplet expansion: an acyl-CoA synthetase called FATP1 and the diacylglycerol acyl-transferase DGAT2. FATP1 localized to the ER, whereas DGAT2 resided on lipid droplets. Nevertheless, the two enzymes formed a complex in vivo that concentrated at the interface between their respective organelles, and mislocalizing DGAT2 to the ER prevented it from promoting lipid droplet expansion.

The two proteins behaved similarly in mammalian cells loaded with excess fatty acids, suggesting that they have a conserved function in linking the ER to lipid droplets and channeling newly synthesized triglycerides to the lipid droplet core. Senior author Ho Yi Mak now wants to investigate whether the FATP1–DGAT2 complex contains additional enzymes involved in triglyceride synthesis and to determine whether formation of the complex is regulated by nutrient availability.

Xu, N., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201201139.