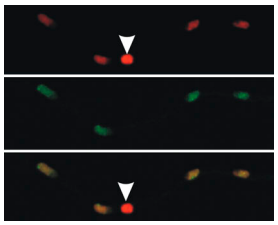
# In This Issue

Text by Ben Short
bshort@rockefeller.edu

## γ-Tubulin keeps the cell cycling



**In a γ-tubulin mutant fungal cell, cyclin B (green) doesn't accumulate in some interphase nuclei (red), preventing them from entering mitosis.**

Nayak et al. reveal that γ-tubulin, better known as a microtubule-nucleating protein, controls the cell cycle by switching off a key mitotic regulator during interphase.

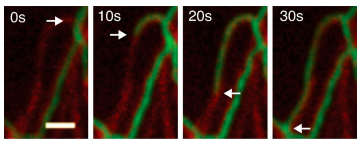
Evidence suggests that γ-tubulin has microtubule-independent functions: a γ-tubulin mutant called *mip*AD159 causes mitotic defects in *Aspergillus nidulans*, even though the fungus continues to assemble mitotic spindles and interphase microtubule arrays. *Aspergillus* cells contain multiple nuclei, which pass through the cell cycle synchronously. But *mip*AD159 blocks some nuclei from entering mitosis, or causes problems with chromosome segregation and mitotic exit.

To investigate how cell cycle regulation is disrupted in *mip*AD159 fungi, Nayak et al. followed the localization of mitotic regulatory proteins over the course of the cell cycle in strains carrying the mutation. Cyclin B, cyclin-dependent kinase 1, and the phosphatase Cdc14 all failed to accumulate in some nuclei during interphase, preventing them from entering mitosis. Other nuclei in the same cell divided, but the fraction of stalled nuclei increased with every cycle until the fungus stopped growing.

Nayak et al. traced this failure in protein accumulation to the continuous activity of the anaphase-promoting complex/cyclosome (APC/C), a ubiquitin ligase that targets mitotic proteins for destruction to help nuclei exit mitosis. The APC/C is usually inactivated during interphase to allow initiation of DNA synthesis and accumulation of mitotic proteins that drive the next round of division. This failed in many nuclei in *mip*AD159 cells, but many of the paused nuclei could re-enter the cell cycle if the APC/C was switched off with a drug. Author Berl Oakley now wants to investigate how γ-tubulin inactivates the APC/C in wild-type cells.

Nayak, T., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.201002105.

## Acetylated microtubules let the ER slide




**The ER (green) slides along a stable microtubule (red).**

The endoplasmic reticulum (ER) slides along acetylated microtubules, possibly helping it to meet up with other organelles such as mitochondria, Friedman et al. report.

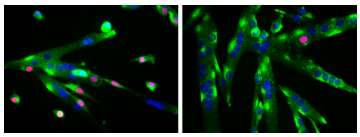
The ER constantly reorganizes, extending new tubules or retracting old ones. In some cases, tubule ends attach to the tips of dynamic microtubules as they grow or shrink but, more commonly, ER membranes slide along a stable, preexisting tubulin filament. Friedman et al. found that this second type of ER movement occurs on acetylated microtubules.

The researchers determined that acetylated microtubules are highly curved compared to unmodified filaments, and that dynamic ER tubules followed these winding tracks in living cells. The amount of ER sliding was increased by boosting microtubule acetylation. Why the ER makes these movements is still mysterious, however. One possibility is that it helps the ER contact other organelles to facilitate calcium signaling and lipid synthesis and exchange. Friedman et al. therefore looked to see if other organelles met up with the ER on acetylated microtubules.

Mitochondria were tightly associated with ER tubules sliding along stable, acetylated microtubules whereas endosomes, despite making numerous contacts with the ER, weren't preferentially localized to this modified subpopulation of the cytoskeleton. Thus, the ER might slide along acetylated microtubules to search out particular organelles. Senior author Gia Voeltz now wants to identify ER proteins specifically involved in these sliding movements so that she can disrupt the process and investigate its function.

Friedman, J.R., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.200911024.

## Syndecan-3 adds a Notch to its belt



**Satellite cell cultures lacking Syndecan-3 (right) form enlarged, multinucleate myofibers but maintain fewer satellite cells (red) in reserve.**

A component of the niche surrounding muscle stem cells regulates their differentiation by controlling the activation of Notch signaling, Pisconti et al. report.

Satellite cells—adult muscle progenitors—express Syndecan-3, a transmembrane proteoglycan that interacts with the extracellular environment to regulate the stem cells' fate. Syndecan-3 is already known to modulate HGF and FGF signaling, but Pisconti et al. found that satellite cells lacking the proteoglycan failed to activate target genes of the Notch pathway.

Mutant progenitors stalled in S phase and were therefore slower to differentiate upon stem cell activation. Nevertheless, Syndecan-3–deficient cells were more likely to terminally differentiate than return to the quiescent pool of progenitors. Mice lacking Syndecan-3 thus developed abnormally large myofibers and retained fewer satellite cells following muscle injury.

Syndecan-3–null cells contained less Notch intracellular domain (NICD), a cleavage fragment of the Notch receptor that translocates to the nucleus to induce target gene expression. Expressing the NICD fragment rescued the proliferation and self-renewal of Syndecan-3–deficient progenitors, as did Notch receptor mutants that bypassed the requirement for cleavage by the ADAM17 metalloproteinase. Syndecan-3 promotes this essential step in the generation of NICD by forming a complex that contains the Notch receptor at the satellite cell plasma membrane.

Senior author Bradley Olwin says that Syndecan-3 may recruit ADAM17 into this complex or increase the enzyme's activity in some way to permit Notch signaling and regulate the size of the muscle satellite cell pool.

Pisconti, A., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.201003081.