In This Issue

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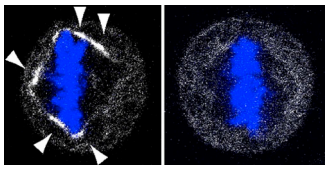
Lipins cause a lamina breakdown



Even in metaphase, much of the lamina (gray, arrowheads) remains in a cell lacking PKC and CDK1 (left), but the structure has disappeared at that stage in a normal cell (right).

Mall et al. reveal how lipid-making enzymes spur the demolition of the nuclear lamina in mitotic cells.

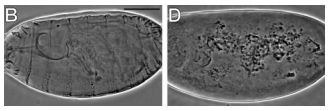
Before a cell divides, it takes apart the lamina, the protein backing for the nuclear envelope. Cells remove the individual lamin proteins from the structure and save them for later reuse. At least two lamin-phosphorylating kinases, protein kinase C (PKC) and cyclin-dependent kinase 1 (CDK1), stimulate lamina breakdown. Lipid-manufacturing enzymes called lipins are necessary for lamina disassembly, but the mechanics of the process remain unclear.

To tease out the roles of PKC and CDK1, Mall et al. mutated lamin B1 molecules so that they carried fewer phosphorylation sites for the two enzymes. Mutating only the CDK1 sites or a combination of CDK1 and PKC sites progressively slowed lamina breakdown. Blocking both kinases with inhibitors enhanced the delay, indicating that the two enzymes collaborate to take apart the lamina. Relying on more than one enzyme to stimulate lamina disassembly could ensure that cells complete the process promptly, the researchers suggest.

PKC's involvement suggests a link with lipins because the product of these enzymes, diacylglycerol (DAG), switches on PKC. To determine whether lipins activate PKC during lamina breakdown, the researchers knocked down all three mammalian lipins with RNAi or applied inhibitors. Lamina disassembly slowed dramatically in these cells. But adding DAG to the lipin-depleted cells restored lamina breakdown. The findings suggest that lipins prompt lamina deconstruction by spawning DAG that activates PKC.

Mall, M., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201205103.

Crumbs stands united against ROS



The epithelium has visibly broken down in a fly embryo lacking Crb (right) compared to a control embryo (left).

Light triggers formation of damaging reactive oxygen species (ROS) in photoreceptor cells. Chartier et al. show that a membrane protein protects cells in the eye and elsewhere in the body by quashing ROS production.

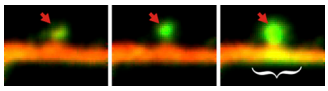
The *Drosophila* protein Crumbs (Crb) helps polarize epithelial cells, boosting the amount of membrane with apical characteristics. Crb also seems to serve as a cellular guardian. Mutations in one of its human versions cause diseases such as retinitis pigmentosa, which results in tunnel vision and poor night vision. Researchers have reported previously that Crb blocks Rac1, a protein that teams up with the enzyme NADPH oxidase to generate the ROS superoxide. Although cells use superoxide for signaling, in large quantities it can be destructive.

To determine whether Crb provides protection by curtailing ROS, the researchers gauged levels of these damaging molecules in fruit fly epithelial cells. They found that cells without Crb carried more ROS than did control cells. Inhibiting Rac1 or NADPH oxidase in the mutant cells restored their ROS levels to normal. Previous studies showed that loss of Crb causes epithelial layers in the embryo to disintegrate. Chartier et al. discovered that they could prevent this degeneration by engineering the embryos to produce extra amounts of the ROS-neutralizing enzyme Sod1.

The researchers also showed that Crb shields photoreceptor cells in the fly eye. Earlier work revealed that, if Crb is absent, photoreceptor cells die if exposed to light. This team found large quantities of ROS in eyes from flies that lacked Crb only in their eye cells. Feeding these flies compounds that suppress Rac1, NADPH oxidase, or ROS prevented their retinas from degenerating after exposure to light, Chartier et al. reported.

Chartier, F.J.-M., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201203083.

CaMKII points the way



Over time, CaMKII (green) accumulates in a dendrite's spine (arrow) and adjacent regions of the shaft (bracket).

Synapses that receive high levels of stimulation typically grow stronger. Lemieux et al. show that a protein complex that lands on microtubules near these active synapses permits them to be remodeled.

Neurons need a way to mark high-use synapses so they can attract the molecular raw material necessary to enhance the connections, which is manufactured far away in the body of the cell. One explanation, the so-called "synaptic tag and capture" hypothesis, suggests that the cell adds a label to the synapses that hooks passing raw material. What researchers don't know is whether some factor also guides this material into active synapses. The CaMKII complex is a leading candidate for the synaptic tag. The complex is necessary for synaptic plasticity—mice lacking one of the four complex genes are slow learners—and CaMKII accumulates at active synapses, where calcium levels climb. But nobody had determined whether it also gathers inside nearby areas of the dendritic shaft, where calcium also increases.

Lemieux et al. found that CaMKII builds up in these neighboring portions of the dendrite. The complex adheres to microtubules in the dendrite and actively signals from there. CaMKII triggered nearby synapses to attract more receptors for the neurotransmitter glutamate, thus boosting synaptic sensitivity. Sections of the dendrite where CaMKII accumulated also sprouted more dendritic spines, the team revealed. Neurons carrying a version of CaMKII that can't bind to microtubules didn't show these changes. These results suggest that CaMKII fosters synaptic plasticity not only from its synaptic location but also from its position on dendritic microtubules. How CaMKII helps direct molecular cargoes to active synapses remains unclear.

Lemieux, M., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201202058.