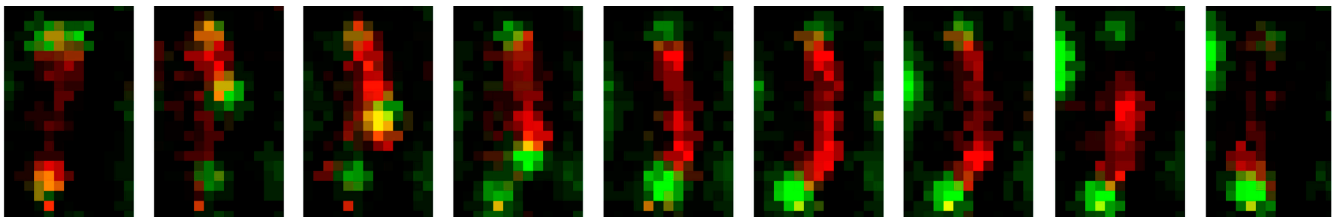
In This Issue



Plasmids (green) are pushed (left to right) around a bacterium by polymerizing filaments of ParM (red).

ParM pushes plasmids apart

A bacterial protein that looks like actin but acts like microtubules makes a Sisyphean effort to push plasmids apart, as revealed in videos by Campbell and Mullins.

The prokaryotic actin look-alike is ParM, which forms a filament that, like microtubules, is dynamically unstable. ParM is encoded by plasmid operons that also contain centromeric sequences and the gene for a DNA-binding protein that hooks plasmids to ParM. To watch ParM in action, the authors imaged bacteria containing a low-copy plasmid that is segregated to daughter cells. The videos unveiled a sloppy, dynamic segregation machinery.

When ParM protein was present, plasmids were pushed around much faster than by diffusion. In cells that had two plasmid copies, these erratic movements occasionally brought plasmids close enough together for a bundle of ParM filaments to link the two. Filaments then elongated, thereby pushing the plasmids to opposite ends of the bacterium.

Once plasmids reached the poles, the filaments rapidly collapsed, perhaps triggered by the force of the plasmids' contact on the cell membrane. The cycle then repeated: plasmids were again nudged along by new ParM filaments, found each other, and were pushed apart. This cyclic behavior continued until the cell divided, usually landing one plasmid in each daughter.

The group studied plasmid separation because it's easy to spy on in vivo, but plasmids might have pilfered the system from bacterial chromosomes. Mullins says that this DNA separation system is good enough for bacteria, whose large numbers can withstand occasional errors. It's 100-fold more efficient than no system and probably requires less energy than do high fidelity eukaryotic segregation systems. And the need for only two proteins, as opposed to the dozens eukaryotes use, helps keep the genome compact. JCB

Reference: Campbell, C.S., and R.D. Mullins. 2007. *J. Cell Biol.* 179:1059–1066.

Apoptotic inaccessibility with maturity

Mature neurons wrap up chromatin around death-sensitizing genes to prevent unwanted apoptosis, say Wright et al.

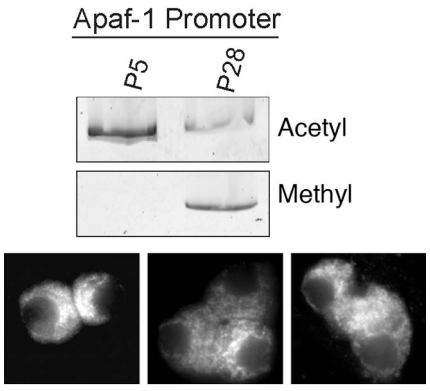
Neurons die off by the handful during development, when their proliferating brethren can easily replace them. But once neurons mature, they shut off proliferation pathways, and survival becomes precious. One way older neurons become less sensitive to apoptosis is by preventing a protein called Bax from reaching mitochondria, where it pokes holes that let out cytochrome *c* (cyt *c*). The new findings identify an additional protective step downstream of cyt *c* release.

Older sympathetic neurons survived injections of cyt *c* because they had less Apaf-1, a protein that recruits cyt *c* to the death-inducing apoptosome complex. Apoptosis, however, still killed mature neurons in response to DNA damage, the authors found. This death resulted from the return of Apaf-1.

In young neurons, *Apaf-1* expression is induced by a cell cycle–regulated transcription factor called E2F1. When neurons stop proliferating, E2F1 is shut down along with other cell cycle proteins. DNA damage restored E2F production. But the team found that giving cells E2F1 alone was not enough to force older, undamaged neurons to express *Apaf-1*. The cells also had to be prodded to open up the chromatin around the *Apaf-1* promoter.

In mature neurons, the histones at the *Apaf-1* promoter were decorated with methyl groups that signify inaccessible, silent chromatin. The same promoter in young neurons was instead tagged with acetyl groups, which indicate accessibility. When mature neurons were given both E2F1 and drugs that open chromatin by inhibiting histone deacetylases, they again made Apaf-1 and underwent apoptosis in response to cyt *c*. Since similar drugs are used in chemotherapy, oncologists might want to keep an eye out for neuronal side effects.

It is currently unclear how DNA-damaged neurons initiate pathways that unwrap chromatin around *Apaf-1* (and possibly other apoptotic genes). And whether the same thing happens under pathological conditions such as a stroke or neurodegenerative disorders is unknown. JCB



***Apaf-1* is acetylated and open in young neurons (P5) but methylated and silent in mature neurons (P28). Its derepression allows older neurons to apoptose (bottom, left to right) upon release of cyt *c* (white).**

Reference: Wright, K.M., et al. 2007. *J. Cell Biol.* 179:825–832.