In this issue • The Journal of Cell Biology 187

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Unfolding chromatin nets
Spiderman doesn’t have anything on neutrophils, which snag microscopic bad guys with webs of chromatin. Wang et al. show that by unfurling chromatin, a histone-modifying protein helps the defensive cells set their traps.

During an infection or inflammation, dying neutrophils spill their DNA to form pathogen-trapping NETs (neutrophil extracellular traps). This gooey material is one of the ingredients of pus. Unlike the chromatin in cells, the extracellular chromatin comes in a loosely wrapped, decondensed form. How the cells relax their DNA for deployment was a mystery. Normally, cells alter the degree of chromatin condensation by tweaking histones, such as by adding methyl or acetyl groups. Wang et al. tested whether another histone adjustment—replacing the positively charged amino acid arginine with the electrically neutral amino acid citrulline—helps neutrophil DNA loosen up during NET formation.

The enzyme that catalyzes this exchange is PAD4, and blocking it hinders NET formation, the team found. The researchers also showed that citrulline swaps catalyzed by PAD4 prompt cells to relax their heterochromatin, the tightly wrapped form of chromatin. One way that cells cinch up their DNA is through the linker histone, which compacts chromatin by connecting neighboring nucleosomes. Wang et al.’s results suggest that citrulline replacement prevents the histone from maintaining this tight link.

Overall, the work reveals that PAD4 spurs the chromatin decondensation necessary to create neutrophil nets. An open question is whether other cell types rely on PAD4 when they need to unwind their DNA. For example, the protein’s chromatin loosening prowess might prove handy during programmed cell death.

Wang, Y., et al. 2009. J. Cell Biol. doi:10.1083/jcb.200806072.

Apoptotic cells let down their guard
Reactive oxygen species (ROS) help push suicidal cells over the edge, but the mechanism behind this has been murky. Now, Anathy et al. reveal the counterintuitive process through which ROS promote apoptosis.

The Fas receptor is a cellular grim reaper. Stimulation of the receptor sets off a molecular chain of events, including activation of caspases, which eventually triggers apoptosis. ROS seem to nudge the process along. Although ROS are best known for their destructiveness, they also perform many other cellular functions, including relaying messages. Anathy et al. wanted to nail down how ROS influence the Fas pathway.

The obvious mechanism—that Fas activation triggers a surge of ROS, amplifying the death pathway—appears to be wrong, the researchers found. Instead, upon stimulation of the receptor, the same caspases that spur the cell death program also drive the destruction of the antioxidant protein glutaredoxin 1.

The decline in glutaredoxin 1 makes an impact. High levels of ROS can trigger glutathionylation—the addition of a glutathione molecule to cysteine amino acids in a protein. The amount of glutathionylation climbed after Fas stimulation—a rise the researchers could prevent by cranking up glutaredoxin 1 production.

So ROS’s role in the cell’s demise is to spur glutathionylation. But rather than boosting ROS levels to ramp up glutathionylation, cells achieve the same effect by degrading glutaredoxin 1 and dialing down their defenses against oxidation. How glutathionylation promotes cellular suicide isn’t clear. But Fas itself is glutathionylated, and the altered receptors bunch up and slip into lipid rafts in the cell membrane, possibly strengthening signaling through the Fas pathway.

Anathy, V., et al. 2009. J. Cell Biol. doi:10.1083/jcb.200807019.