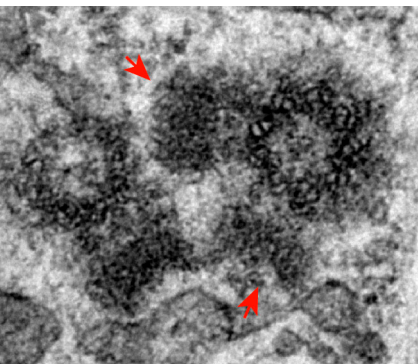


Hitched to lipids, glowing proteins advance into a bleached area of the cell membrane.



Cells unable to break down Plk4 manufacture extra centrioles (arrows).

## Membrane proteins stick around

You wouldn't call it a long-term relationship, but the interaction between proteins and certain membrane lipids is not just a one-millisecond stand. As [Hammond et al.](#) discovered, the proteins remain attached to the lipids longer than researchers expected. The findings explain how these lipids localize their effects.

By temporarily hooking up with various proteins, inositol lipids in the plasma membrane help cells do everything from transmit signals to move. The lipids can confine their influence to a specific section of the membrane. For example, a crawling cell cranks up inositol levels at its leading edge and destroys the lipids at its tail end. But inositol-bound proteins face a dilemma. As the inositols wander around the cell membrane, the proteins need to hang on long enough to encounter other proteins and thereby transmit the inositol signal. But if the proteins cling on too long, they risk spreading their effects beyond the target area. How the proteins resolve this dilemma wasn't clear because nobody had measured how long the molecules stay attached.

Using photobleaching, Hammond et al. estimated how fast protein-lipid couples moved within the membrane and how long they remained together. Riding the inositol molecules, the proteins traveled at a brisk pace of around  $1 \mu\text{m}^2$  per second, about the same speed as other researchers had measured for the lipids alone. To the team's surprise, the proteins could stick to the inositols for several seconds. As a result, a protein-inositol duo has time to search its neighborhood for potential interaction partners, but it can spread its influence over a few microns at the most. The researchers are now working to determine how interactions with other proteins affect the mobility of the pairs.

Hammond, G.R., et al. 2009. *J. Cell Biol.* doi:[10.1083/jcb.200809073](#).

## Birth control for centrioles

Like DNA, centrioles need to duplicate only once per cell cycle. [Rogers et al.](#) uncover a long-sought mechanism that limits centriole copying, showing that it depends on the timely demolition of a protein that spurs the organelles' replication.

Centrioles start reproducing themselves during G1 or S phase. What prevents the organelles from xeroxing themselves again and again has puzzled researchers for more than a decade. The process could be analogous to the mechanism for controlling DNA replication. There, a licensing factor preps the DNA for duplication. During DNA synthesis, the factor gets tagged with ubiquitin molecules that prompt its destruction, thus preventing another round of copying.

To determine whether a similar mechanism keeps centrioles in check, Rogers et al. blocked *Drosophila* cells' production of different proteins that combine to form a ubiquitin-adding complex. Loss of one of these proteins, Slimb, allowed cells to fashion extra centrioles, the researchers found.

Slimb's target, the team showed, is the enzyme Plk4, which sports a Slimb-binding motif. Plk4 levels on the centrioles peaked during mitosis, and the enzyme vanished from the organelles by S phase. However, a mutant form of Plk4 that Slimb couldn't latch onto clung to the centrioles throughout the cell cycle and caused their over-duplication.

Plk4 serves as a licensing factor for centriole copying, Rogers et al. suggest. During mitosis, it sets the stage for the next cell division by phosphorylating an unidentified protein (or proteins) that will later instigate centriole duplication. Slimb and its protein partners then ubiquitinate Plk4, so that no enzyme remains on the centrioles by the time they are ready for copying. Thus, the organelles are duplicated once only. Tumor cells often bypass the limit on centriole duplication, and the work suggests that drugs to restrict the organelles' replication might hold promise as cancer treatments.

Rogers, G.C., et al. 2009. *J. Cell Biol.* doi:[10.1083/jcb.200808049](#).

## 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](#).

## Unfolding chromatin nets

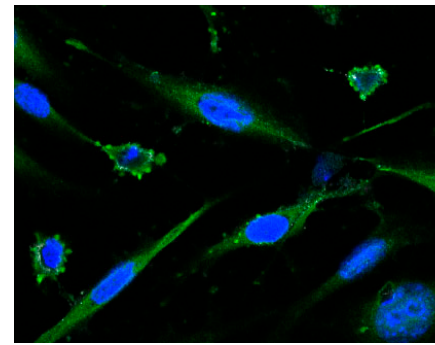
Spiderman doesn't have anything on neutrophils, which snag microscopic bad guys with webs of chromatin. [Wang et al.](#) show that by unfurling chromatin, a histone-modifying protein helps the defensive cells set their traps.

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.

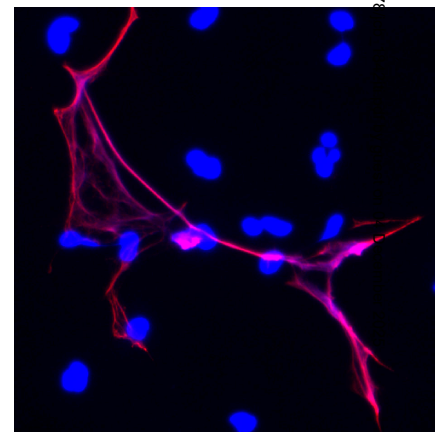
The enzyme that catalyzes this exchange is PAD4, and blocking it hinders NET formation, the team found. The researchers also showed that citrulline swaps catalyzed by PAD4 prompt cells to relax their heterochromatin, the tightly wrapped form of chromatin. One way that cells cinch up their DNA is through 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](#).



Glutathionylated proteins (green) show up in cells after stimulation of Fas.



A neutrophil extracellular trap (red) is ready to snare passing microbes.