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. 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.

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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.