In This Issue

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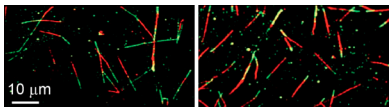
FANCJ lets chromatin stay true



After a treatment that stalls replication forks, cells lacking FANCJ (right) show shorter tracts of newly synthesized DNA (green) than do controls (left).

Schwab et al. show how a protein that unkinks DNA might help cells to maintain chromatin organization during DNA replication.

The DNA replication machinery can run into roadblocks. For instance, a DNA stretch with multiple guanines can develop a kink—known as a G4 quadruplex—that halts copying. The protein FANCJ helps cells overcome these blockages. Faulty FANCJ is one cause of the rare genetic disease Fanconi anemia, which leaves patients prone to leukemia as children, and the gene is often mutated in breast cancers. Researchers have found that FANCJ unwinds G4 quadruplexes in vitro, but they weren't sure how it promotes DNA replication.

To find out how DNA copying proceeds past obstacles, Schwab et al. monitored individual replication forks. In the presence of a molecule that stabilizes G4 quadruplexes, genome duplication slowed dramatically in cells lacking FANCJ. On the lagging strands of the forks, cells missing FANCJ often showed single-strand gaps where the nucleotides hadn't been filled in. Although cells with FANCJ can unravel G4 kinks and other blockages, allowing replication complexes to move forward, cells lacking the protein skip over these blockages, leaving unduplicated DNA.

After replicating their DNA, cells normally re-compress the strands to produce the original balance of tightly wound heterochromatin and more relaxed euchromatin. But Schwab et al. discovered that heterochromatin spreads in cells that have lost functional FANCJ. So by enabling DNA duplication to proceed efficiently through obstacles like G4 quadruplexes, FANCJ might help cells regain the correct organization of chromatin domains.

Schwab, R.A., et al. 2013. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201208009.

STT3B gets the tip

To glycosylate the C-terminal tail of a protein, cells turn to a little understood enzyme subunit, Shrimal et al. reveal.

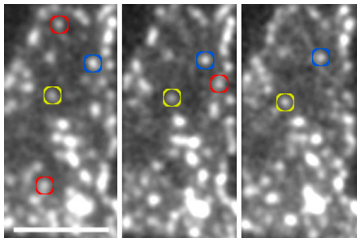
Affixing oligosaccharides to asparagine residues in a protein, a process known as N-linked glycosylation, can change how that protein folds and works and whether it gets secreted. Some proteins require these added groups at their C terminus. The protein complex responsible for glycosylation is oligosaccharyltransferase (OST). The OST subunit that catalyzes the modification is STT3, which comes in two isoforms, STT3A and STT3B. However, STT3A might skip sites at the C terminus of a protein.

Shrimal et al. found that STT3B picks up the slack. Sex hormone–binding globulin, for example, has two glycosylation sites near its C terminus. The researchers showed that siRNA that targeted STT3A had no effect on glycosylation of the protein, whereas siRNA targeting STT3B often left the C-terminal sites bare.

By adding amino acids to transferrin, which harbors two glycosylation sites, the team determined that STT3A can glycosylate acceptor sites that are more than 50 to 55 amino acids from the end of the protein. That makes sense, given its location. OST is embedded in the ER membrane, and STT3A glycosylates a growing protein strand as it feeds into the ER. However, STT3A can't modify the C-terminal tip before translation finishes and the new protein is released from the ribosome. That's when STT3B steps in and glycosylates the remaining sites on the completed protein, although how STT3B finds its targets in the ER remains a mystery.

Shrimal, S., et al. 2013. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201301031.

Actin draws a cadherin crowd



This time series shows that some clusters of cadherin lacking its actin-binding tail (red circles) quickly disperse.

The actin cytoskeleton helps stabilize the cadherin clusters that connect adjacent cells, Hong et al. reveal.

Despite cadherin's reputation as an adhesion molecule, an individual cadherin molecule isn't very sticky. Instead, cadherins team up to create adherens junctions that fasten cells together. The process begins when an individual cadherin on the surface of one cell grabs a cadherin on a neighboring cell. This interaction enables each of the cadherin molecules to cling to other cadherins on the same cell, forming adhesive clusters that hold the cells together. Although researchers knew that adherens junctions connect to the actin cytoskeleton, they haven't been able to demonstrate actin's role in cadherin-based adhesion.

Hong et al. found that tailless cadherin molecules that couldn't link to actin formed ephemeral clumps that sped around within cell–cell contacts. The team then put the tailless cadherins on a leash, adding to them a fragment of α-catenin that ties them to actin filaments. These attached cadherins gathered in long-lasting groups that moved toward the apical surface of the cell. The cadherin clusters dispersed when the researchers treated the cells with the actin-depolymerizing drug latrunculin A, confirming that the actin cytoskeleton helps maintain the clusters. Actin and cadherin turnover were also required for the clusters' movement to the apical surface.

Overall, the study shows that actin promotes clustering by limiting cadherin diffusion within intercellular junctions. Thus, cells might be able to adjust the strength and dynamics of adherens junctions by changing the number and strength of the bonds between the actin cytoskeleton and cadherin clusters.

Hong, S., et al. 2013. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201211054.