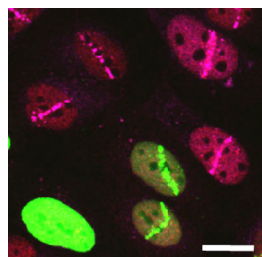


RNF169 flips the repair switch



RNF169 (green) accumulates at DNA double-strand breaks (stripes) and repels the repair enzyme 53BP1 (purple).

Poulsen et al. describe an enzyme that helps a cell determine which repair method to use on DNA double-strand breaks (DSBs).

Unrepaired DSBs can incite genomic chaos, spurring sections of chromosomes to relocate or even vanish. To ensure that doesn't happen, a cell wraps a molecular bandage around a DSB. Enzymes arrive at the injury and ubiquitylate the surrounding chromatin. In turn, the ubiquitin

attachments lure DNA repair proteins such as BRCA1 and 53BP1. By analyzing vertebrate genomic sequences, Poulsen et al. identified a previously unrecognized ubiquitylating enzyme, RNF169.

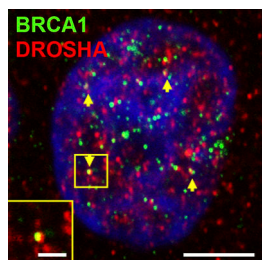
To their surprise, the researchers discovered that RNF169 has a different function from the other ubiquitylating enzymes,

including its close relative RNF168. Although RNF169 homes in on DSBs, it doesn't ubiquitylate chromatin. Instead, it rebuffs certain repair proteins by competing for binding sites on ubiquitylated chromatin. For example, the team found that boosting levels of RNF169 in cells prevented BRCA1 and 53BP1 from gathering at damaged DNA.

RNF169's role, Poulsen et al. suspect, is to favor one DNA repair mechanism. The more accurate method is homologous recombination, in which the damaged chromosome swaps sequences with a sister chromatid. However, only cells that are about to divide and have copied their DNA can perform this type of repair. By contrast, all cells can use the other mechanism, nonhomologous end joining, which involves stitching the broken DNA ends together. 53BP1 and a related repair enzyme inhibit homologous recombination, but the team found that RNF169 encourages cells to use this higher-fidelity method.

Poulsen, M., et al. 2012. *J. Cell Biol.* <http://dx.doi.org/10.1083/jcb.201109100>.

BRCA1 touches up microRNAs



BRCA1 (green) interacts with the DROSHA microRNA processing complex (red).

BRCA1, the well-known breast cancer susceptibility gene, helps control the maturation of microRNAs, Kawai and Amano show. The finding suggests another way that BRCA1 mutations promote cancer.

The BRCA1 protein helps repair damaged DNA, and mutations in the gene raise the risk of breast and ovarian cancer and other tumor types. Some evidence implies that BRCA1

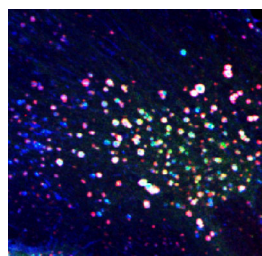
also takes part in the processing of microRNAs, the short RNA strands that modify gene expression. For example, microRNA levels are often abnormal in cells with BRCA1 mutations.

Kawai and Amano tested this idea. They found that boosting levels of the BRCA1 protein in cell lines increased the levels of several microRNAs. Deleting BRCA1 from cells had the opposite effect on the same microRNAs, all of which dwindle in cancer. BRCA1 had no impact on the levels of microRNAs whose abundance increases or remains the same in tumors, however.

BRCA1 bound to primary microRNA transcripts, Kawai and Amano found. The protein also interacted with the DROSHA processing complex and the proteins Smad3 and p53, which stimulate microRNA maturation. The results suggest that BRCA1 promotes the processing of specific microRNAs that might inhibit tumors. Whether BRCA1's effects on microRNAs contribute to its roles in DNA repair remains to be seen.

Kawai, S., and A. Amano. 2012. *J. Cell Biol.* <http://dx.doi.org/10.1083/jcb.201110008>.

Wait, save that integrin!



SNX17 (green) latches onto integrin β1 (blue), sparing it from destruction in the lysosome.

If you've ever rummaged through the trash to find something you didn't mean to toss out, you can understand one of the problems cells face. Steinberg et al. reveal that a sorting protein prevents cells from throwing away integrins.

Cells continually pluck proteins from the plasma membrane so they can be dispatched to the lysosome for destruction. But some of these proteins are still useful, so the cell diverts them back to the plasma

membrane. The nexin SNX17 helps separate the keepers from the trash.

Steinberg et al. devised a new proteomic approach to determine which proteins SNX17 rescues. They reasoned that knocking down SNX17 with RNAi should reduce the abundance of certain proteins because the cell will no longer save these molecules from destruction. Among the 15 proteins whose levels declined after RNAi treatment were the α5 and β1 integrins. Blocking lysosome activity restored the levels of these integrins, confirming that without SNX17's intervention the proteins end up in the cellular trash.

Because integrins enable cells to get a grip on the extracellular matrix, the researchers tested whether suppressing SNX17 altered cell movement. In tests of crawling speed, cells depleted of SNX17 were swifter than normal. It remains to be seen if the movement of cancer cells—which often swap integrins as they metastasize—is affected by their ability to spare integrins from lysosomal destruction.

Steinberg, F., et al. 2012. *J. Cell Biol.* <http://dx.doi.org/10.1083/jcb.201111121>.