In This Issue

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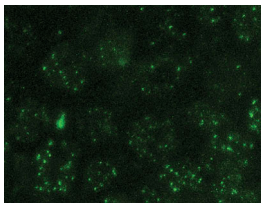
Rad54 mutant stays rooted to the spot



Multiple foci of ATPase-deficient Rad54 (green) persist more than 20 hours after radiation-induced DNA damage.

Only a small proportion of the proteins that gather around a DNA double-strand break are actively involved in repairing the damage, Agarwal et al. suggest.

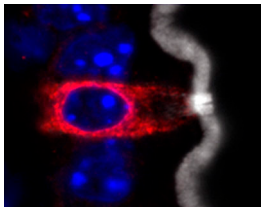
Double-strand breaks are repaired by homologous recombination, in which missing sections of DNA are replaced using sister chromatids as undamaged templates. Rad51 is the central catalyst of this process, working in combination with accessory factors like the DNA-dependent ATPase Rad54. Several functions have been proposed for Rad54, including modulating Rad51 binding on homologous DNA duplexes. But few studies have addressed Rad54's contribution to double-strand break repair in vivo.

Agarwal et al. generated cell lines expressing wild-type or ATPase-deficient Rad54 at endogenous levels. Cells that only expressed ATPase-dead Rad54 were as sensitive to DNA damage as cells that lacked Rad54 entirely, yet Rad51 accumulated rapidly at double-strand breaks as long as Rad54—even without its ATPase activity—was present. However, Rad54 remained at damage sites for longer if it lacked ATPase function, suggesting that ATP hydrolysis is required for the protein's dissociation from DNA.

The researchers estimated that between 100 and 600 Rad54 molecules normally accumulate at each spot of DNA damage. Only 10–60 of these molecules appear to be bound to the DNA, however, as photobleaching experiments revealed that mutations in Rad54's ATPase domain only immobilized 10% of the protein in each repair focus. Agarwal et al. don't yet know why so much extra Rad54 is recruited to double-strand breaks, but they plan to home in further on the molecules that actually perform the repair job by developing single-molecule imaging approaches.

Agarwal, S., et al. 2011. *J. Cell Biol.* doi:10.1083/jcb.201011025.

A fifth amendment to the intestine's constitution



A tuft cell (red) with a thick brush of microvilli (white) in the epithelium of an intestinal villus.

Gerbe et al. define a new type of secretory cell in the intestine.

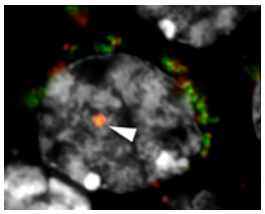
The intestinal epithelium consists of four main specialized cell lineages: absorptive enterocytes and three secretory cell types known as enteroendocrine, Paneth, and goblet cells. But a rare, fifth type of intestinal cell called tuft cells also exists. Defined by the thick brush of long microvilli that project from their apical surface, tuft cells are seen in several epithelial tissues, yet little is known about their function due to a lack of tuft cell–specific markers.

Gerbe et al. identified several proteins uniquely expressed by tuft cells, including DCLK1, a kinase that was previously thought to mark a population of quiescent intestinal stem cells. Like other intestinal cell types, tuft cells turned over rapidly and were replaced by the differentiation of proliferative stem cells' progeny in the intestinal crypts. This differentiation was blocked in the absence of ATOH1—a transcription factor required for the development of all intestinal secretory lineages. Yet tuft cell differentiation didn't require other transcription factors that specify enteroendocrine, Paneth, and goblet cells, suggesting that tuft cells represent a distinct lineage of intestinal secretory cells.

Gerbe et al. found that tuft cells secrete opioids and produce enzymes that synthesize prostaglandins. The latter observation suggests that tuft cells may promote inflammation and tumorigenesis. Indeed, the researchers identified tuft cell–like cells in several early stage intestinal tumors. To really understand tuft cells' function, however, author Philippe Jay hopes to identify transcription factors uniquely required for their development in order to generate mice that specifically lack tuft cells from their intestinal epithelium.

Gerbe, F., et al. 2011. *J. Cell Biol.* doi:10.1083/jcb.201010127.

The Tudor family produces heirs



TDRD5 (green) co-localizes with the PIWI protein MIWI (red) in a developing spermatocyte.

Yabuta et al. describe a Tudor family protein that controls multiple stages of sperm production.

Tudor domain–containing proteins (TDRDs) have several functions in germ cell development. Some family members prevent transposons from mobilizing and disrupting the germline genome during meiosis, whereas other TDRDs assemble the RNA protein granules that pack the germ cell cytoplasm and regulate the turnover and expression of mRNAs critical for spermatid maturation. Yabuta et al. found that one family member, TDRD5, is involved in both of these processes.

The LINE-1 retrotransposon was up-regulated in mouse testes lacking TDRD5, indicating that the protein works with other TDRD family members to repress transposon activation. High transposon expression can disrupt meiosis, but most germ cells lacking TDRD5 successfully formed haploid spermatids. Further development was blocked, however, as the immature sperm failed to express key maturation genes, probably because two types of RNA-processing granules, intermitochondrial cements and chromatoid bodies, were disrupted. As a result, male mice lacking TDRD5 were infertile. But their arrested spermatids could give rise to healthy offspring if they were directly injected into oocytes, suggesting that increased transposon activity doesn't damage the genome of TDRD5-null germ cells.

TDRDs work in conjunction with PIWI proteins and PIWI-interacting RNAs (piRNAs). Senior author Mitinori Saitou plans to investigate how TDRD5 represses transposons and regulates germ cell mRNAs by isolating its binding partners and examining how piRNA expression is altered in TDRD5's absence.

Yabuta, Y., et al. 2011. *J. Cell Biol.* doi:10.1083/jcb.201009043.

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