which results in an expanded follicle — but this was not the case in these mutants. In fact, the only detected defect in *Gpr3*$^{-/-}$ follicles was the failure to maintain meiotic arrest. This phenotype could be reversed by injecting *Gpr3* RNA into oocytes from *Gpr3*$^{-/-}$ pre-antral or very early antral follicles and letting the follicles grow in culture. Only 11% of the injected oocytes had resumed meiosis after a 4-day culture period, compared with about half of the non-injected oocytes.

Together, these data indicate that GPR3 is a negative regulator of meiotic progression in mouse oocytes. Future studies will undoubtedly look into how LH might relieve the arrest and reinitiate meiosis as well as try to identify the ligands that interact with GPR3.

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DNA REPAIR

Breaking up is hard to do

Two new papers in *Current Biology* have helped to clarify the mechanism by which DNA double-strand breaks (DSBs) are held together during DNA repair.

DSB formation is a significant event for a cell as, if a DSB remains unrepaired, it could result in a chromosomal break and the potentially lethal loss of genetic information. Cell-cycle checkpoints and various DSB-repair mechanisms exist to prevent this from occurring. But how exactly are DSBs held together during DNA repair, and which factors contribute to chromosome fragmentation when it does occur?

Kaye *et al*. and Lobachev *et al*. both employed systems in which an inducible endonuclease was used to generate DSBs at an engineered recognition site in budding yeast chromosomes. Recognition sites for fluorescent fusion proteins were also engineered into the chromosome arms close to the DSB site, so that the chromosome ends could then be visualized under a microscope. Both groups found that, in wild-type cells, DSB formation did not immediately result in chromosome fragmentation. But what was holding the ends together?

Kaye *et al*. induced DSB formation in G1-arrested cells and investigated what happened to the chromosomes after passage through S phase. They found that there was an intrachromosomal association between centric and acentric fragments of the broken chromosome, which was not permanently disrupted by DNA replication. Furthermore, such intrachromosomal association depended on the homologous-recombination proteins Rad50 and Rad52, which both helped to maintain this association. If mitosis was allowed to occur, Kaye *et al*. found that, in 95% of cases, the acentric fragments co-segregated into either the mother or the daughter cell. Similarly, rejoining of the acentric and centric fragments post-mitosis occurred in the mother cell or in the daughter cell, but almost never in both, which indicates that the broken sister-chromatid fragments are passaged into the same nucleus.

The authors propose that two mechanisms contribute to the segregation of broken chromosomes. First, intrachromosomal association holds the two halves of a single, broken sister chromatid together. Second, interchromosomal association tethers the homologous fragments of broken sister chromatids to each other, which, in fact, promotes the missegregation of the chromosome fragments, particularly the acentic fragment.

Lobachev *et al*. investigated the behaviour of DSB-induced chromosome ends in cells that lacked components of the RMX complex, which comprises Rad50, Mre11 and Xrs2, and is involved in non-homologous end-joning (NHEJ)-mediated DSB repair. They showed that DNA ends moved apart in cells that lacked any of these three proteins, and that mutations in the zinc-hook domain of Rad50 also caused significant increases in the separation of DNA ends. By contrast, mutations in Ku70, Ku80 and DNA ligase IV (Dnl4), which are specifically required for DNA end-joining, did not caused separation of DNA ends. Chromosome fragmentation was also shown to require microtubule-based forces.

So, it seems that broken chromosomes are harder to split up than might be imagined. The RMX complex and Rad52 contribute to the continued association of chromosome ends; whereas inter-chromatid forces — which are probably mediated by residual cohesins — promote the continued association of chromosome fragments with their sister chromatids.

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