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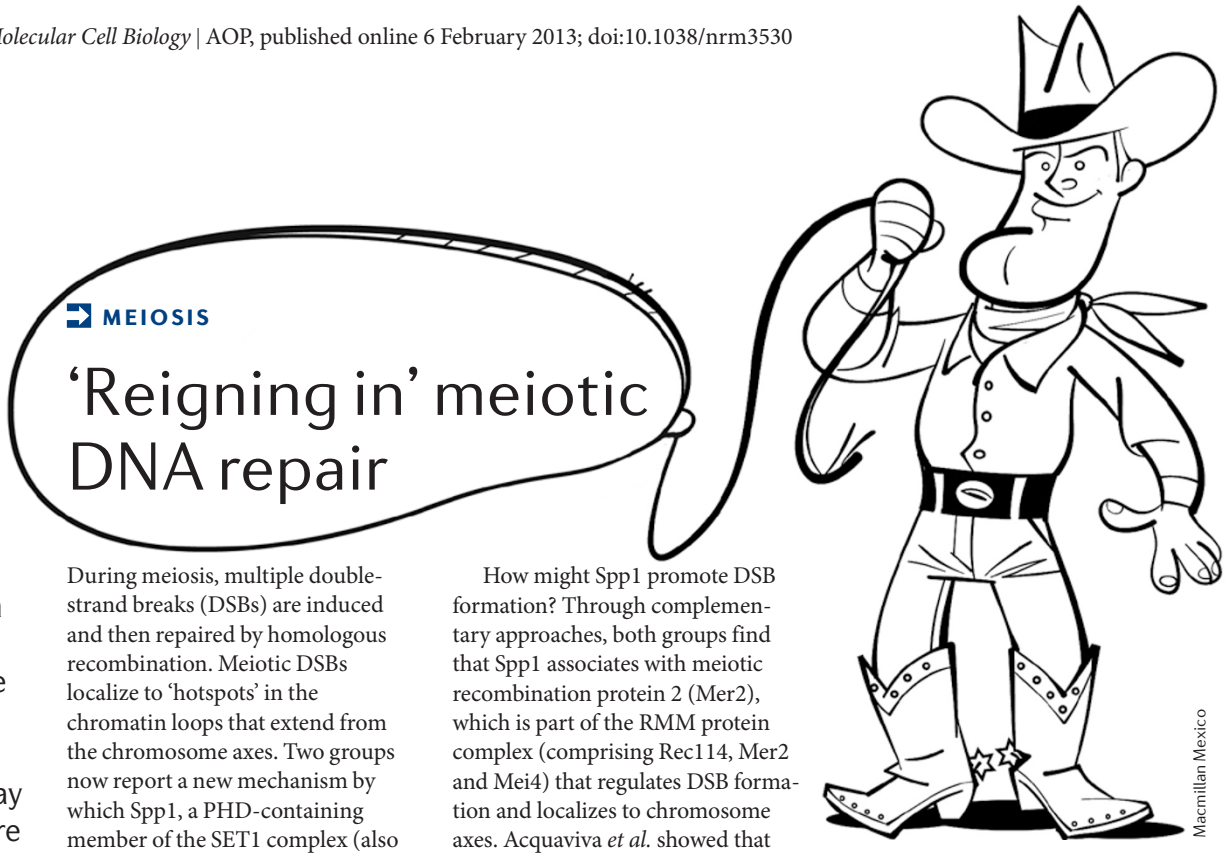

'Reigning in' meiotic DNA repair

> coordination between chromosome structure and DSB induction may in turn ensure a healthy number of crossover events

During meiosis, multiple double-strand breaks (DSBs) are induced and then repaired by homologous recombination. Meiotic DSBs localize to 'hotspots' in the chromatin loops that extend from the chromosome axes. Two groups now report a new mechanism by which Spp1, a PHD-containing member of the SET1 complex (also known as COMPASS), might recruit sites of potential DSBs towards the chromosomal axes for subsequent break induction and repair by the DSB machinery.

Several features of the chromatin environment have been correlated to some extent with the induction of meiotic DSBs, including nucleosome-depleted regions and sites of histone H3 trimethylation at Lys 4 (H3K4me3). To better understand how the chromatin state might influence meiotic DSB induction, both groups set out to determine the functions of COMPASS, which mediates H3K4me3 and is also important for meiotic DSB formation.

Both laboratories homed in on the Spp1 subunit of COMPASS and showed that it is required for DSB formation during meiosis. Acquaviva *et al.* also demonstrated that targeting of Spp1 to regions that do not normally undergo recombination was sufficient to induce DSBs.

How might Spp1 promote DSB formation? Through complementary approaches, both groups find that Spp1 associates with meiotic recombination protein 2 (Mer2), which is part of the RMM protein complex (comprising Rec114, Mer2 and Mei4) that regulates DSB formation and localizes to chromosome axes. Acquaviva *et al.* showed that Mer2 associated with full-length Spp1 in a yeast two-hybrid screen, and then confirmed this interaction both *in vitro* and *in vivo* during meiosis. Sommermeyer *et al.* also found that Spp1 and Mer2 co-immunoprecipitate and used genome-wide analysis to show that, during meiosis, endogenous Spp1 associates with the chromosome axes in a Mer2-dependent manner.

If Spp1 localizes to chromosome axes, how might it promote induction of DSBs in the loop regions? The authors showed that this might be through its known ability to recognize the H3K4me3 mark that is enriched in the loop regions. Although Spp1 was not observed to bind potential DSB sites, mutation of its PHD finger (which recognizes di- and trimethylated H3K4) disrupted DSB formation. On the basis of this, both groups propose that the ability of Spp1 to 'read' H3K4me3 is important for subsequent DSB formation. Furthermore, Sommermeyer *et al.* showed that the recruitment of Spo11, the transesterase that induces DSB breaks, was reduced in Spp1 mutants.

Both groups propose that the interaction between Spp1 and Mer2 is important for providing spatial control over where DSBs are induced, by increasing contact between the DNA loops and the chromosome axes where repair factors are enriched. This coordination between chromosome structure and DSB induction may in turn ensure a healthy number of crossover events and normal chromosome segregation during meiosis.

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ORIGINAL RESEARCH PAPERS Sommermeyer, V. *et al.* Spp1, a member of the Set1 complex, promotes meiotic DSB formation in promoters by tethering histone H3K4 methylation sites to chromosome axes. *Mol. Cell* **49**, 43–54 (2013) | Acquaviva, L. *et al.* The COMPASS subunit Spp1 links histone methylation to initiation of meiotic recombination. *Science* **339**, 215–218 (2013)