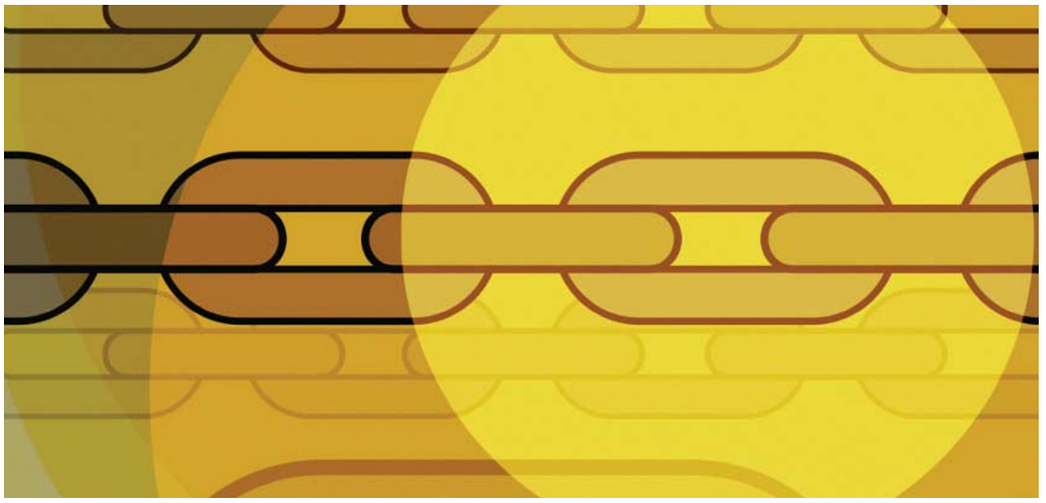

RECOMBINATION

The link between recombination and chromosome pairing

How homologues find each other during meiosis when it is time to pair remains an unresolved question. However, we do know that accurate pairing of homologous chromosomes in budding yeast requires Hop2 — a meiosis-specific recombinase. Hideo Tsubouchi and Shirleen Roeder now show that Hop2 acts in the recombination pathway, and so recombination has an important role in distinguishing between homologues and non-homologues during chromosome pairing in meiosis. In the same issue of *Developmental Cell*, Petukhova *et al.* confirm this function of Hop2 in mice, highlighting its evolutionary conservation, although their data lead them to place Hop2 in a different position in the pathway.

Previous genetic studies in budding yeast have shown that Hop2 has a role in homology searching and/or recognition. *hop2* mutants are arrested in meiosis — their double-strand breaks (DSBs), with which recombination begins, are not repaired and recombinases accumulate on meiotic chromosomes. The failure to repair DSBs could be caused by a defect in pairing — in wild-type haploid yeast cells that initiate meiosis, DSBs are stalled owing to a lack of homologue pairing. DSBs in these cells are eventually repaired by recombination between sister chromatids. Because this does not occur in haploid *hop2* strains, Hideo Tsubouchi and Shirleen Roeder suggest that a defect in meiotic recombination itself best explains the *hop2* phenotype. Double-mutant analysis showed that Hop2 acts in the same pathway as Dmc1 and Rad51 recombinases, both of which are RecA homologues, and that it lies downstream of them.

It turns out that overexpression of Rad51 suppresses defects in meiotic recombination in *dmc1* and *hop2* mutants. The authors therefore propose that there are two pathways for recombination-mediated pairing of homologues. In the first one, Rad51 alone distinguishes between homologous and non-homologous sequences during homology searches. In the other, Dmc1/Rad51 depend on Hop2 to ensure legitimacy of the pairing.

Petukhova and coworkers show that *Hop2* also interacts genetically with *Dmc1* in the mouse but that it is more likely to have an earlier role, upstream of *Dmc1*. In contrast to budding yeast, in which the double mutant had the same phenotype as the *DMC1* single mutant, $Hop2^{-/-}Dmc1^{-/-}$ mice have the same phenotype as $Hop2^{-/-}$ mice with respect to homologue pairing.

Because Rad51 is also involved in mitosis, and so its knock-out also affects the soma, it was not possible to test in mice whether it can function as a 'homology sentinel' that is independent of Hop2. So, we still do not know if the Hop2/Dmc1-independent recombination pathway also exists in mammals. Nonetheless, we do know that Hop2 is at the heart of the molecular connection between meiotic recombination and homologous pairing in both yeast and mammals, even if its precise mechanism of action might differ between these groups. In yeast, Hop2 might discriminate between homologous and non-homologous sequences after DSBs occur, either by modulating recombinase activity or by promoting disassociation of non-homologous sequences during homology search. In mice, on the other hand, Hop2 might promote strand invasion of an intact chromosome by the broken homologue, a step that would attract meiotic recombinases Dmc1 and Rad51.

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References and links

ORIGINAL RESEARCH PAPERS Tsubouchi, H. & Roeder, G. S. The importance of genetic recombination for fidelity of chromosome pairing in meiosis. *Dev. Cell* **5**, 915–925 (2003) | Petukhova, G. V. *et al.* The Hop2 protein has a direct role in promoting interhomolog interactions during mouse meiosis. *Dev. Cell* **5**, 927–936 (2003)

WEB WATCH

URLs

Saccharomyces Genome database:
http://www.yeastgenome.org

Dmc1
http://db.yeastgenome.org/cgi-bin/SGD/locus.pl?locus=Dmc1

Hop2
http://db.yeastgenome.org/cgi-bin/SGD/locus.pl?locus=Hop2

Rad51
http://db.yeastgenome.org/cgi-bin/SGD/locus.pl?locus=Rad51