CHROMOSOME BIOLOGY

Pairing up for the genetic exchange

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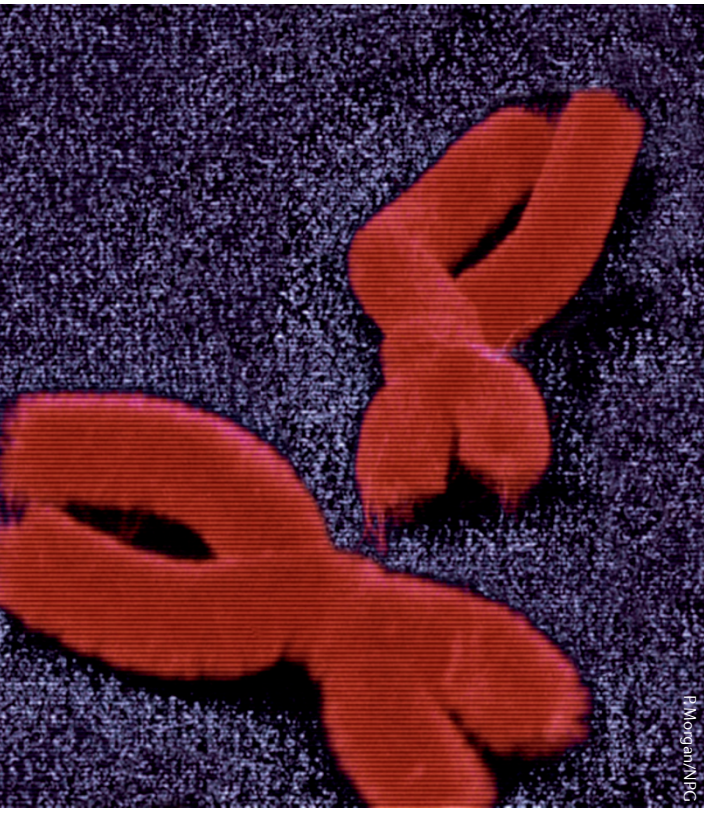
For recombination to occur, chromosomes must find their homologous partner and then determine the sites of genetic recombination. Two new studies have shed some light onto how homologous chromosomes find and identify one another; one study was conducted in fission yeast and the other in budding yeast. Another group has improved the understanding of the subsequent step in mice — the determination of double-stranded break sites.

In *Saccharomyces cerevisiae*, chromosome pairing is accompanied by rapid meiotic prophase chromosome movements (RPMs). During these movements, telomeres cluster on the nuclear envelope, resulting in the formation of the 'chromosome bouquet' that has been hypothesized to stimulate chromosome pairing. Using a novel 'collision trap' system, Lee *et al.* studied chromosome pairing in *S. cerevisiae.* They generated strains in which the different chromosomes could be cross-linked by tetrameric lacI–GFP binding to *lacO* concatamers. This 'trapped' transient interactions of chromosomes, and the trapping could be observed as single fluorescent foci. Using strains mutant for RPM-mediating proteins, they showed that RPMs foster the interaction of homologous and heterologous chromosomes and that the kinetics of homologous pairing correlates with RPM activity. Bouquet formation, however, is poorly correlated with homologous pairing rates, hence homologous pairing is likely to be dependent on RPMs that stir the nuclear contents independently of bouquet formation.



P. Morgan/NPG

Following pairing, chromosomes must recognize whether they are homologous. In *Schizosaccharomyces pombe*, telomeric clustering accompanied by horsetail movements in meiotic prophase promotes homologous chromosome pairing alignment. Ding *et al.* show that the *sme2* gene on chromosome II produces a non-coding RNA (namely, *meiRNA-L)* that mediates the subsequent recognition step. The authors visualized robust pairing at the *sme2* locus using inserted *lacO* arrays and lacI–GFP proteins. Deletion of the *sme2* locus indicated its necessity for the pairing event, and translocation of the *sme2* locus showed that it is sufficient for transient ectopic pairing. Transcription of *meiRNA-L* was necessary for pairing. Fluorescent detection showed that this RNA localizes to the *sme2* locus to mediate recognition in combination with RNA-binding proteins. However, the viability of *sme2* mutants indicates that other pairing sites may exist on chromosome II.

The next step is for recombination to be initiated by the production of double-stranded breaks. The histone H3 lysine 4 methyl transferase protein PR domain containing 9 (PRDM9) that is present in most vertebrates is thought to be involved in the determination of these sites at recombination hotspots. Brick *et al.* identified recombination hotspots in mice with different *Prdm9* alleles and in *Prdm9* knockouts using chromatin immunoprecipitation and single-stranded sequencing. They found that although these strains have a similar number of recombination sites, in the absence of PRDM9 they occur at regions of high H3K4 trimethylation (H3K4me3), which are regions that include important regulatory elements. Thus the authors conclude that the function of PRDM9 is to sequester the recombination machinery away from functional genomic elements.

Together, these three studies improve our mechanistic understating of the initial stages of recombination.

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ORIGINAL RESEARCH PAPERS Lee, C.-H., Conrad, M. N. & Dresser, M. E. Meiotic chromosome pairing is promoted by telomere-led chromosome movements independent of bouquet formation. *PLoS Genet.* **8**, e1002730 (2012) | Ding, D.-Q. Meiosis-specific noncoding RNA mediates robust pairing of homologous chromosomes in meiosis. *Science* **336**, 732–736 (2012) | Brick, K. *et al.* Genetic recombination is directed away from functional genomic elements in mice. *Nature* 13 May 2012 (doi:10.1038/nature11089)