Commentary

Magic with moulds: Meiotic and mitotic crossing over in Neurospora inversions and duplications

In 1982 Barbara Turner and David Perkins reported an astonishing result; from a cross between two inversion strains of *Neurospora crassa* [*In(OY348)* and *In(OY323)*] they recovered progeny of the normal sequence (Turner and Perkins 1982). If the normal sequence of loci in linkage group I is represented by ABCDEF.GHIJKL, with the dot representing the centromere, the sequence of the inversion In(OY348) can be depicted as AB**HG.FEDC**IJKL and that of the inversion In(OY323) by ABCD**JIHG.FE**KL. Note that the two inversions overlap in the sequence **HG.FE**. Note also that the recovery of the normal sequence from a cross between the two inversions is neither a trivial nor an obvious outcome. The discovery of the RNAi-based gene silencing process called meiotic silencing by unpaired DNA now provides an explanation for how normal sequence strains come to be selected. Meiotic silencing silences genes that are unpaired in meiosis, as well as their homologues, regardless of whether or not the homologues are themselves paired. This gene-silencing phenomenon was discovered in Neurospora (Shiu *et al* 2001; Shiu and Metzenberg 2002), and detected more recently also in Caenorhabditis and mouse (Lee 2005).

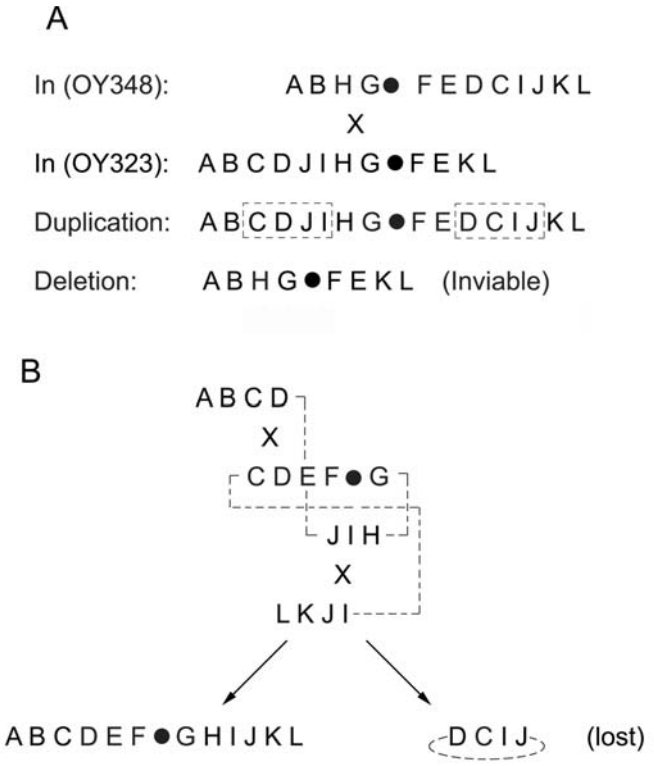

Figure 1. **(A)** Meiotic recombination in the region of overlap (shown here between the loci H and G) of the two inversions produces viable duplication progeny. The loci C, D, I, and J are duplicated and are shown in dashed boxes. The duplication causes barrenness in crosses with normal sequence, which selects for mitotic crossovers that restore fertility. **(B)** Intrachromosomal mitotic crossovers selected for in the duplication strain (shown here between C and D and between I and J) restore the normal sequence. The complementary acentric fragment bearing the other copy of C, D, I, and J is lost.

A meiotic crossover in the overlap sequence would yield duplication and deficiency progeny (figure 1A). The deficiencies are inviable, whereas the duplication progeny are viable but confer a barren phenotype in crosses. Barren crosses make normal-looking perithecia but yield very few exceptional ascospores and are a characteristic of duplication-heterozygous crosses in Neurospora. In a duplication-heterozygous cross one copy of each duplication-borne gene is unpaired in meiosis, thus all the duplication-borne genes, including any required for ascus development and meiosis, are silenced and the cross is rendered barren. Barrenness imposes a selection for mitotic crossovers that can restore normal ascospore production. Figure 1B shows the Turner/Perkins model for how such mitotic crossovers could have occurred. Note that the crossover product has the normal sequence.

The three postulated crossovers, namely, those in C-D, H-G, and I-J could, in theory, have occurred even in meiosis to directly produce a normal-sequence meiotic product. However meiotic triple crossovers are very rare. Thus one crossover must have occurred meiotically in the original inversion intercross (to produce the duplication), and the other two must have occurred premeiotically at a later time, in a testcross of the duplication. The two crossovers in the testcross must have been simultaneous in order to eliminate the duplication and produce a normal-sequence product. Progeny tests showed that the segregants from *In(OY348)* × *In(OY323)* from which the normal sequence crossover products were derived, contained both the wild-type and mutant alleles of some marker loci. Thus the normal-sequence isolates must have been mitotically derived from duplication segregants.

However, the frequency of single mitotic crossing over in Neurospora vegetative nuclei is very low, consequently it is unlikely that the double crossovers occurred during vegetative growth. Instead the double crossovers appear to have occurred during the sexual stage in the premeiotic mitoses of the dikaryon that forms between fertilization and karyogamy. It is conceivable that mitotic crossing over is more frequent during this phase than in the vegetative phase, possibly because recombination mechanisms are derepressed in the perithecium early in the sexual phase, prior to meiosis.

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References

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