Homolog pairing during meiosis: Dyneins on the move

Meiosis is a specialized form of cell division that generates haploid gametes from diploid cells. This is achieved by having 1 round of DNA replication followed by 2 rounds of nuclear division. A unique aspect of meiosis is that homologous chromosomes undergo recombination that can result in formation of chiasmata. This is essential for bi-orientation of bivalents on the meiosis I spindle. But how a chromosome pairs with its homolog and engages in recombination is poorly understood.

Meiotic chromosome pairing is though to occur in 3 steps: a) Alignment of the chromosome axes of the homologs b) recombination c) formation of SC (synaptonemal complex) a proteinaceous structure that connects the homologs along their entire lengths.

An insight into how the homologs might be aligned with each other came from cytological observations in multiple organisms that meiotic chromosomes in prophase adopt a 'bouquet' configuration wherein telomeres from different chromosomes cluster together(*1*). The fission yeast *Schizosaccharomyces pombe* has served as an excellent system to study the mechanism of homolog pairing. During meiotic prophase in *S. pombe*, the nucleus moves back and forth between the cell poles for several hours. During these nuclear oscillations, the telomeres remain clustered to Spindle Pole Bodies (SPB's- fungal equivalent of centrosomes) and localize to the leading edge of the nucleus, which is elongated and shaped like a horse-tail(*2*). Horsetail nuclear movement in *S. pombe* is thought to occur due to the pulling force exerted on astral microtubules that connect SPB to cortical attachment sites(*3*). A meiosis-specific SPB component Hrs1/Mcp6 organizes the astral microtubules into a horse-tail-astral array(*4*). Pulling force is generated by the cytoplasmic dynein(*5, 6*) and associated dynactin complex(*7*) bound to a cortical anchor protein Mcp5(*8*) Mutations in genes encoding Hrs1/Mcp6, Dynein heavy chain (Dhc1), Dynein light chain (Dlc1) and p150-Glued (Ssm4) and Mcp5, severely affect nuclear oscillations during meiotic prophase and reduce recombination frequencies(*4-8*). This is consistent with the hypothesis that horsetail nuclear movements help the aligned chromosomes to 'mix and match' rapidly until they pair with the right partner.

In this issue of *Cell Cycle*, Rumpf et al. report the identification of a novel Dynein intermediate chain length (Dil1) related protein, which is also required for efficient nuclear oscillations during meiosis in *S. pombe(9)*. Dil1 was isolated in a high-throughput knockout screen which targeted 87 meiotically upregulated genes and assayed for mutants that had an elevated rate of chromosome missegregation during meiosis. A more careful characterization using synchronous meiotic cultures revealed that *dil1Δ* cells had an increased level of lagging chromosomes and homolog non-disjunction during anaphase I.

Missegregation of chromosomes during meiosis I could be attributed to either defective cohesion along chromosome arms or due to reduced crossing-over. Rumpf et al. ruled out the former possibility since cohesion along chromosome arms was unaffected in the *dil1Δ* strain. However *dil1Δ* strains had a 2-3 fold reduction in both intragenic and intergenic recombination frequencies suggesting that homolog non-disjunction phenotype could be due to reduced crossing over.

Although Dil1 had been annotated as an orphan sequence with no obvious orthologs in the *S. pombe* genome database, a detailed bioinformatic analysis revealed that Dil1 was similar to dynein light intermediate chain proteins (DLIC). Since dyneins have been previously implicated in nuclear oscillations that assists pairing and recombination between homologs (see above), Rumpf et al. assayed horsetail movement and homolog pairing in *dil1Δ* cells. Indeed *dil1Δ* cells were defective for pairing of homologous centromeres and displayed abnormal horsetail nuclear movement.

Do Dil1 and Dhc1 work in the same pathway? The nuclear morphology and rates of homolog non-disjunction were similar in *dil1Δ*, *dhc1Δ* and *dil1Δdhc1Δ* strains suggesting this to be the case. Like Dhc1, Dil1 also localized to the leading edge of horsetail nuclei and to the leading microtubules strongly suggesting a direct interaction between Dil1 and Dhc1. However Rumpf et al. failed to detect any physical interaction between Dhc1 and Dil1 by mass spectrometric analysis of TAP-purified Dil1 protein complexes from mitotically grown cells. This means either, Dhc1 and Dil1 do not interact with each other, or they interact weakly or in a meiosis–specific manner.

Is Dil1 required for Dhc1's interaction with Ssm4 and localization to the cortex? Does Dil1 regulate the formation of horsetail-astral-arrays and control microtubule dynamics? Future research will reveal how Dil1 and other dyneins collaborate to orchestrate oscillations of meiotic nuclei that promote pairing of homologs.

References

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