IN BRIEF

Crossover Guard: MEICA1 Prevents Meiotic Mishaps

During meiosis, recombination between allelic sequences on pairs of homologous chromosomes forms crossovers; these crossovers help make sure that the homologs segregate accurately (reviewed in Zhang et al., 2014). However, cells must suppress recombination between non-allelic sequences, as ectopic recombination can create massive chromosomal rearrangements. Eukaryotes have evolved mechanisms to prevent non-allelic recombination, including suppressing the formation of double-stranded breaks in repetitive DNA, promoting allelic recombination by chromosome pairing, and producing non-crossover events from inappropriate recombination events. Mismatch repair proteins function with some helicases to resolve inappropriate recombination and can stop the formation of a heteroduplex if the region contains too many mismatches.

Based on a genetic screen for sterile mutants in rice (Oryza sativa). Hu et al. (2017) identified MEICA1 (meiotic chromosome association 1), a novel protein that functions to regulate crossover formation and limit aberrant crossovers. Sequence analysis showed that MEICA1 has a domain of unknown function (DUF4487), but lacks other known domains. Also, MEICA1 has been conserved in eukaryotes. The meica1 mutants show normal vegetative growth, but produce non-viable pollen. Staining and immunohistochemistry showed that the meica1 mutants underwent normal synapsis, including formation of the synaptonemal complex. However, staining of meiotic chromosomes showed the formation of abnormal connections between chromosomes in meica1 mutants during pachytene and chromosome bridges and fragments at anaphase I in meica1 mutants (see figure) and MEICA1 RNA interference plants.

The authors next used a genetic analysis to examine the pathways involved in MEICA1 function. First, they found that double mutants with a mutant that fails to produce DNA double-stranded breaks (and thus fails to initiate crossovers) suppressed the meica1 mutant phenotype. However, a mutant defective in non-homologous end-joining did not suppress meica1. Genetic analysis showed that the recombinase Disrupted Meiotic cDNA1 (DMC1) functions upstream in the same pathway as MEICA1: the dmc1 meica1 mutants have a phenotype similar to dmc1 and DMC1 localization does not require MEICA1. Immunolocalization showed that MEICA1 associates with chromatin during early meiosis. Moreover, MEICA1 localization was disrupted in dmc1 mutants, and in other mutants that affect early steps of recombination. Finally, a yeast two-hybrid screen (confirmed by split-luciferase assays) identified the mismatch repair protein MSH7 and the type IA topoisomerase (TOP3α) as interacting with MEICA1.

The genetic and immunolocalization assays showed that MEICA1 acts in recombination after strand invasion and work in yeast and humans showed that TOP3α forms a complex (including the RecQ helicase) that suppresses crossovers by disassembling an early intermediate, the D-loop. Indeed, the meica1 mutants showed increased numbers of foci of proteins involved in late crossover events, indicating an increased number of crossovers. How MEICA1 functions to guard genomic integrity by preventing aberrant crossovers from proceeding, remains an intriguing subject for future research.

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REFERENCES


The meica1 mutants form chromosome bridges and fragments during meiosis. Chromosome spreads of wild type (A–F) and the meica1 mutant (G–N) in, from left to right: pachytene, diakinesis, metaphase I, and anaphase I, anaphase II, and tetrads. [Reprinted from Hu et al., 2017; Figure 2] ©2017 American Society of Plant Biologists. All Rights Reserved