Journal club

THE THREE SMC SISTERS

Many tales and quests bring in the concept of three: three heirs, three suitors, three tasks. Throughout the eukaryotic kingdom, three structural maintenance of chromosomes (SMC) complexes — cohesin, condensin and SMC5–SMC6 — are crucial for chromosome reorganization events and cell viability. Each of these complexes consists of SMC heterodimers and additional non-SMC subunits, and their structures resemble a ring that embraces DNA. Cohesin and condensin are required for the establishment of physical links between sister chromatids and for chromatin compaction, respectively, but the role of SMC5–SMC6 in sustaining chromosome life is less clear. Like its ‘sister complexes’, the binding of SMC5–SMC6 to chromosomes is integral for its function, and this complex plays a part in chromosome segregation and repair. Interestingly, sister chromatid linkages are known to accumulate in *smc6* mutants during the replication

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of damaged templates, but the mechanism underlying this, and the type of DNA interactions influenced by SMC5–SMC6, are not known.

Insights into this phenomenon come from a study by Kegel *et al.* The authors discovered that the frequency of yeast Smc5–Smc6 chromosomal association sites increases in response to chromosome lengthening and sister chromatid intertwinings (SCIs), and that the replication of long chromosomes is delayed when the functionality of Smc5–Smc6 or topoisomerase 1 (Top1) is impaired. Top1 removes the superhelical tension (positive supercoils) that accumulates ahead of the advancing fork, but this can also be diminished through fork rotation along the DNA helix. One possibility is that Smc5–Smc6 facilitates supercoil release through SCI formation; indeed, aberrant Smc6 was defective in transferring supercoils to SCIs in a plasmid assay. The authors proposed that Smc5–Smc6 sequesters SCIs to reorganize the chromatids into a conformation that is friendly for fork rotation. Thus, the Smc5–Smc6 complex might sense what cohesion and condensin do not: the strength of superhelical tension on the

chromosome, which is a new possible determinant of chromosome structure organization.

These investigations open new questions about how tension is contained and organized on a chromosome scale, and how SMC5–SMC6’s topological embrace of such SCIs or specific regions might be aided by non-topological interactions or by its small ubiquitin-like modifier (SUMO)-associated activities. The relationship between precatenanes (intertwined replicated DNA duplexes) and the sister chromatid linkages that accumulate in *smc6* mutants in the presence of DNA damage is unknown. But, with the ardent quest for understanding how the three SMC sisters complementarily support chromosome organization, new insights will hopefully be forthcoming.

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