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CHROMOSOME SEGREGATION

Tension rules

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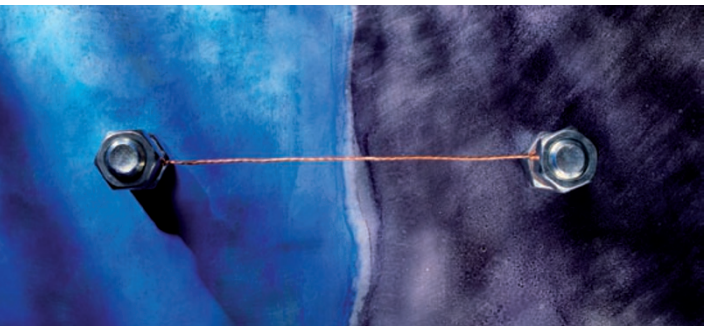
How sister chromatids are protected from being prematurely segregated at the first meiotic division in mammals has remained elusive. New research by Yoshinori Watanabe and colleagues shows that, in mammals, a family of proteins called shugoshins regulate centromeric cohesion in mitosis and meiosis in a tension-dependent manner.

Meiosis is a specialized type of cell division that generates non-identical haploid gametes from diploid progenitor cells. This is achieved by a single round of DNA replication followed by two chromosome segregation phases: segregation of the homologues (meiosis I) is followed by the dissolution of centromere cohesion and the segregation of sister chromatids (meiosis II). Previous studies in yeast have shown that shugoshin associates with protein phosphatase-2A (PP2A) throughout meiosis I and prevents phosphorylation of centromeric cohesin — a multiprotein complex that maintains tight association of sister chromatids. This prevents cleavage of cohesin by the protease separase and subsequent sister chromatid separation.

> “…shugoshins are involved in all instances of centromeric cohesion protection…”



To investigate the role of mammalian shugoshins SGO1 and SGO2 during meiosis, the team led by Watanabe used mouse oocytes that were cultured *in vitro*. First, the authors showed that SGO1 and SGO2 localize to the centromeres during the two chromosome segregation phases of meiosis as well as during mitosis, but SGO2 is much more abundant than SGO1 in oocytes. Furthermore, REC8, a meiosis-specific cohesin component, colocalizes with SGO2 during meiosis I and is protected from cleavage by the PP2A pathway.

Next, they depleted oocytes of either one or both shugoshins by RNA interference and found that SGO2, but not SGO1, is important for protecting centromeric cohesion in meiosis I. By contrast, SGO1 appears to be more important during mitosis than SGO2.

So, why are centromeric cohesins not protected from cleavage during meiosis II and mitosis despite the presence of SGO2? The authors proposed that the tension generated by the spindle microtubules when they pull the kinetochores to opposite directions — which occurs in mitosis and meiosis II but not in meiosis I — could affect the localization of SGO2, and thereby affect the protection of centromeric cohesin.

To test this hypothesis, Watanabe and colleagues first confirmed previous observations that SGO2 relocates from the centromeres towards the kinetochores during metaphase II. At this stage, REC8 is retained at its original centromeric position and can be cleaved, thereby triggering sister chromatid separation. Next, by artificially removing tension from the centromeres at the metaphase–anaphase transition in mitosis, the colocalization of shugoshin and cohesin was preserved and centromeric cohesin was protected from separase cleavage.

Together, these observations suggest that shugoshins are involved in all instances of centromeric cohesion protection, both during mitosis and meiosis. In addition, the relocalization of SGO2 (due to the tension generated by the spindle microtubules when sister kinetochores are pulled to opposite poles) triggers the events that lead to sister chromatid separation in mitosis and meiosis II. How tension causes the relocation of shugoshins has yet to be determined.

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ORIGINAL RESEARCH PAPER Lee, J. *et al.* Unified mode of centromeric protection by shugoshin in mammalian oocytes and somatic cells. *Nature Cell Biol.* 16 Dec 2007 (doi:10.1038/ncb1667)
FURTHER READING Marston, A. L. & Amon, A. Meiosis: cell-cycle controls shuffle and deal. *Nature Rev. Mol. Cell Biol.* **5**, 983–997 (2004)