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CHROMOSOME BIOLOGY

Spindle asymmetry drives selfish segregation

> "tyrosination asymmetry in meiotic spindles can be directly linked to biased segregation of chromosomes"

Certain genetic elements known as selfish elements can violate Mendel's law of inheritance by promoting their own transmission to the germ line. This phenomenon is known as meiotic drive and can have a large impact on organismal fitness and, in consequence, on evolution. The mechanisms responsible for meiotic drive are largely unknown. Akera *et al.* now show that the asymmetry in spindle microtubules supports meiotic drive during female meiosis.

During oogenesis meiotic spindles are positioned near the cell cortex and are oriented perpendicular to the cortex, allowing asymmetric division with the formation of a large egg cell and the expulsion of a small polar body from the cortical side. Thus, to increase their inheritance, selfish elements need to bias their attachment towards the non-cortical half of the spindle. The authors hypothesized that asymmetry of microtubules between the two halves of the spindle may favour this biased attachment. Interestingly, they found that in mouse meiotic oocytes microtubules at the cortical side are more extensively tyrosinated than microtubules at the egg side of the spindle. The asymmetrical tyrosination was induced when spindles were prematurely targeted to the cortex early in mitosis. This suggested that microtubules in the meiotic spindle are modified by cortical factors. Further experiments identified the small GTPase CDC42 as a cortical factor responsible for mediating this asymmetrical tyrosination.

Spindle–chromatin interactions are established at centromeres, which can be classified as strong or weak, depending on their protein composition. Imaging of hybrid oocytes derived from crossing mouse strains harbouring centromeres of differing strengths revealed that in meiotic pairs chromosomes with stronger centromeres were preferentially oriented towards the future egg. Importantly, this bias was abolished when tyrosination asymmetry was perturbed by expressing a dominant-negative variant of CDC42. This showed that tyrosination asymmetry in meiotic spindles can be directly linked to biased segregation of chromosomes.

As tyrosination asymmetry arises after the establishment of chromatin–spindle microtubule interactions, biased distribution of chromosomes must involve some degree of chromosome reorientation once spindle asymmetry was established, for example, flipping of chromosomes with strong centromeres from the cortical to the egg side of the spindle. Indeed, such flipping was observed in hybrid oocytes. Notably, attachments between strong centromeres and spindle microtubules were found to be unstable, in particular at the cortical side of the spindle. Such attachment instability at the cortical side can be expected to facilitate chromosome flipping to the opposite, egg side of the spindle and in consequence to promote segregation to the future egg.

In summary, this study revealed that during meiosis in oocytes asymmetric tyrosination of spindle microtubules promotes germline transmission of selfish genomic elements — in this case, strong centromeres. It would be interesting to study whether similar mechanisms involving spindle asymmetry drive biased segregation of selfish elements in other contexts.

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ORIGINAL ARTICLE Akera, T. *et al.* Spindle asymmetry drives non-Mendelian chromosome segregation. *Science* **358**, 668–672 (2017)
FURTHER READING McKinley, K. L. & Cheeseman, I. M. The molecular basis for centromere identity and function. *Nat. Rev. Mol. Cell Biol.* **17**, 16–29 (2016)