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A chromosome's guide to the spindle equator

> "detyrosinated microtubules form preferential tracks ... along which CENP-E transports chromosomes"

Accurate chromosome segregation during mitosis requires that chromosomes bi-orient; that is, that their centromeres attach to microtubules that emanate from opposite ends of a bipolar spindle. Bi-orientation is achieved more efficiently if chromosomes are aligned at the spindle equator. For this alignment to occur, chromosomes are transported from near spindle poles to the equator through a process known as chromosome congression.

How chromosomes are guided specifically to the equator during congression has been unclear. Barisic *et al.* now report that transport by the kinesin motor centromere-associated protein E (CENP-E; also known as kinesin 7) to the spindle equator of human cells depends on microtubule detyrosination, which consists of the removal of the carboxy-terminal tyrosine from α-tubulin.

During congression, chromosomes are first transported along microtubules to the spindle poles by dynein and then to the equator by CENP-E, which is a motor that walks towards microtubule plus ends. As the plus ends of microtubules that emanate from the poles point in different directions, including towards the cell cortex, the cause of the directionality of CENP-E-mediated transport towards the equator remained unclear.

Tubulin acetylation and detyrosination, which are known to regulate transport in neurons, are found on stable spindle microtubules that point to the equator. Whereas acetylation had no effect on chromosome congression in human U2OS cells, the authors found that overexpression of the enzyme responsible for α-tubulin tyrosination, combined with a treatment that prevents detyrosination of polymerized α-tubulin, resulted in delayed mitotic progression and the misalignment of pole-proximal chromosomes. This phenotype was similar to that observed following inhibition of CENP-E, indicating that spindle microtubule detyrosination is required for transport to the cell equator.

Moreover, inhibition of detyrosination induced dissociation of CENP-E from microtubules, suggesting that detyrosination promotes CENP-E–microtubule interactions *in vivo*.

To test whether detyrosination affects CENP-E directly, the authors reconstituted CENP-E motility *in vitro* using purified tubulin from HeLa cells. Although CENP-E bound and moved processively on both tyrosinated and detyrosinated microtubules, it was faster and achieved longer runs on detyrosinated microtubules. Moreover, by measuring the force produced by single CENP-E motors using a stationary optical trap, the authors found that CENP-E generated greater forces on detyrosinated microtubules. Furthermore, CENP-E was seen to detach less frequently from detyrosinated microtubules, indicating that it can carry larger cargoes on detyrosinated microtubule tracks.

Together, these results suggest that detyrosinated microtubules form preferential tracks from the poles to the cell equator, along which CENP-E transports chromosomes. Consistent with this model, the authors found that abnormal detyrosination of microtubules, other than those pointing to the equator, caused delivery of pole-proximal chromosomes to inappropriate locations.

This work adds to the growing body of evidence that post-translational modifications can contribute to the subcellular differentiation of microtubules.

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