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CELL CYCLE

Forming healthy attachments

> an Aurora B-independent mechanism to control kinetochore–microtubule attachments

Accurate chromosome segregation during mitosis depends on the correct attachment of kinetochores to spindle microtubules. Kinetochores often first bind to the side of microtubules and then establish end-bound attachments, but how exactly this transition is regulated is unclear. Cheerambathur *et al.* now find that crosstalk between two complexes involved in kinetochore–microtubule attachments, NDC-80 (nuclear division cycle 80) and RZZ (ROD–ZW10–Zwilch), mediates this process.

STOCKBYTE

The authors visualized chromosome dynamics during the first division of *Caenorhabditis elegans* embryos to assess the formation of end-bound microtubule attachments. RZZ normally recruits dynein to kinetochores via Spindly, and together these proteins mediate initial lateral microtubule capture. The authors found that co-depletion of RZZ and Spindly allowed the formation of end-coupled attachments with only a slight delay, similar to that seen in the absence of dynein (which accelerates microtubule capture). However, if only Spindly was removed (and consequently dynein), end-bound attachments and chromosome segregation were inhibited, which suggests that RZZ inhibits the formation of end-bound attachments mediated by NDC-80.

By performing two-hybrid analysis with truncated versions of NDC-80 and ROD-1, and partially reconstituted RZZ complexes, Cheerambathur *et al.* found that RZZ directly interacts with NDC-80 via the ROD-1 amino-terminal domain and the NDC-80 N-terminal basic tail. The NDC-80 basic tail is normally phosphorylated by Aurora B, and this inhibits the interaction of NDC-80 with microtubules (which involves an adjacent CH domain). Here, the authors found that ROD-1 binding to the NDC-80 tail suppressed NDC-80 binding to microtubules *in vitro* independently of Aurora B.

To investigate the mechanisms underlying RZZ-dependent NDC-80 inhibition *in vivo*, the authors used mutant versions of NDC-80, either lacking the basic tail or bearing a mutated tail that mimics Aurora B-dependent phosphorylation (that is, a version that fails to bind to microtubules *in vitro*). NDC-80 that lacks the tail was resistant to persistent RZZ-mediated inhibition when Spindly was removed. Importantly, phosphorylation-mimicking NDC-80 responded to Spindly depletion (and thus RZZ inhibition) *in vivo* in the same way as wild-type NDC-80: it could form end-coupled microtubule attachments (although with a delay) in the absence of RZZ, but this ability was entirely suppressed when Spindly was removed. Thus, RZZ regulates NDC-80 by interacting with its N-terminal tail, but this effect is independent of the direct contribution that the tail makes to NDC-80 microtubule binding *in vitro*.

This works uncovers an Aurora B-independent mechanism to control kinetochore–microtubule attachments that depends on crosstalk between NDC-80 and RZZ. This may be a direct mechanism to prevent NDC-80-mediated end-coupled attachment during the initial phase of lateral capture and thus might minimise the risk of a kinetochore being erroneously linked to both spindle poles, leading to chromosome missegregation.

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ORIGINAL RESEARCH PAPER Cheerambathur D. K. *et al.* Crosstalk between microtubule attachment complexes ensures accurate chromosome segregation. *Science* http://dx.doi.org/10.1126/science.1246232 (2013)