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Bridging microtubules promote centering of the kinetochores by length-dependent pulling forces

Chromosome positioning to the equatorial plane of the mitotic spindle is necessary to prevent lagging chromosomes and abnormal nuclear envelope reformation [1,2]. It has been proposed that two centering mechanisms play a key role here, microtubule (MT) catastrophe promoted by kinesin-8 motors and pushing forces exerted by chromokinesins. Surprisingly, our experiments suggest that removal of PRC1 molecules from the antiparallel overlaps of the bridging MTs [3] disrupts alignment of the kinetochores. Here we show, by introducing a theoretical model, that kinetochore MTs cross-linked by bridging MTs exert centering pulling forces. Our model also shows that length-dependent catastrophe and rescue regulated by motor proteins and passive cross-linkers are necessary for well defined length of MTs and their antiparallel overlap, respectively [4]. We predict that stable antiparallel overlaps subsequently navigate positioning of the kinetochores in the center of the metaphase plate. These predictions were confirmed in experiments with overexpression of PRC1 proteins and silencing of Kif18A motors.

[1] Fonseca et al. 2019 J Cell Biol [2] Stumpff et al. 2012 Cell [3] Vukušić, Buđa, Bosilj et al. 2017 Dev Cell [4] Klemm, Bosilj et al. 2018 Mol Biol Cell

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