Spindle mechanics and chromosome segregation

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The Minisymposium "Spindle Mechanics and Chromosome Segregation" featured new and exciting findings related to the spindle and chromosomes during mitosis and meiosis. It covered a range of topics including spindle architecture and mechanics, kinetochore–microtubule interactions, chromosome dynamics at mitotic entry and exit, as well as mitotic errors and mechanisms preventing them.

The session started with talks on the organization of microtubules in the spindle. **Iva Tolić** (Ruđer Bošković Institute, Zagreb) used expansion microscopy on human spindles and showed that a bundle of antiparallel microtubules, termed "bridging fiber," connects sister kinetochore fibers. Optogenetic experiments revealed that bridging fibers regulate tension on kinetochores. On the basis of the finding that the spindle is chiral due to the helical twist of bridging fibers, she concluded that rotational forces (torques) exist in the spindle in addition to pulling and pushing forces (Novak *et al.*, 2018). **Dick McIntosh** (University of Colorado, Boulder) presented elegant electron tomographic reconstructions of mammalian spindles. He and Eileen O'Toole have tracked individual microtubules and identified associations between microtubules of different classes. Exploring the concept of "bridging fibers," he found that nonkinetochore microtubules that overlap near the spindle equator approach close to kinetochore-associated microtubules and fan out as they pass the kinetochore, some of them connecting with the sister kinetochore fibers and others with neighboring spindle microtubules. **Sophie Dumont** (University of California, San Francisco), the recipient of the ASCB Women in Cell Biology (WICB) Junior Award for Excellence in Research, discussed how the spindle reaches a steady-state shape. She showed that knockout of NuMA or dynein, proteins required for microtubule end clustering, results in turbulent spindles with impressive dynamics driven by kinesin-5. Thus, microtubule end clustering is essential for the spindle network to achieve a defined geometry.

The program then turned to the interactions between kinetochores and spindle microtubules. **Vladimir Volkov** (Dogterom lab, Delft University of Technology) focused on the kinetochore–microtubule interface and how it generates force. By attaching a glass bead to the Ndc80 trimers bound to a depolymerizing microtubule and letting the microtubule pull against the optical tweezers, he found that the microtubule stalls and may subsequently switch to growth, depending on the number of interacting Ndc80s and the amount of force. Phosphorylation of Ndc80 resulted in shorter stalls and fewer rescues. **Takashi Akera** (Lampson lab, University of Pennsylvania) discovered how centromeres cheat in meiosis by preferentially attaching to the egg side of the spindle. Larger centromeres detach more easily from microtubules oriented toward the polar body, due to a surplus of the microtubule depolymerizer MCAK. In an interspecies hybrid, centromeres with more MCAK win irrespective of their kinetochore size, demonstrating that the microtubule-destabilizing activity is decisive for non-Mendelian segregation of selfish centromeres to the egg (Akera *et al.*, 2018).

The session subsequently covered research on chromosome dynamics at mitotic exit and entry. **Daniel Gerlich** (IMBA–Institute of Molecular Biotechnology, Vienna) revealed how during nuclear assembly after mitosis chromosomes remove cytoplasmic components. By using genetically encoded multimeric nanoparticles (GEMs) as microrheology probes, he found that chromosomes coalesce into a cluster that sequesters cytoplasm, and that this is regulated by the chromosome surface protein Ki-67. **Alexander Booth** (Tanaka lab, University of Dundee) discovered how chromosomes move to the region between centrosomes at the onset of mitosis, to be captured by microtubules. He showed that the chromosome scattering volume is reduced quickly after the nuclear envelope breakdown. This process is independent of microtubules but requires contraction of the actomyosin network assembled on the nuclear envelope (Booth *et al.*, 2018).

The last three talks explored the causes of mitotic errors and mechanisms that prevent them. **Kristin Knouse** (Amon lab, Massachusetts Institute of Technology; now principal investigator at Whitehead, MIT) explored the difference in chromosome segregation fidelity in two-dimensional cell cultures and three-dimensional tissues. She found almost no segregation errors in epithelial tissues, but many errors in dissociated cells from these tissues. Similarly, mature spheroids had fewer errors than immature ones. Integrin was required for correct segregation, suggesting that tissue architecture is crucial to prevent aneuploidy (Knouse *et al.*, 2018). **Renata Basto** (Institut Curie, Paris) explored two in vivo polyploid systems based on cytokinesis inhibition of *Drosophila* and mouse neural stem cells. She found high levels of DNA damage generated during mitosis, in addition to chromosome segregation errors. In binucleated or multinucleated cells, mitosis is asynchronous and the delayed nucleus accumulates DNA damage due to its premature exposure to a mitotic cytoplasm, thereby contributing to cancer genome evolution. **Christian Zierhut** (Funabiki lab, Rockefeller University) discussed cGAS, a cytoplasmic DNA sensor, which counteracts infections. He discovered that in mitosis,

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nucleosomes prevent the inappropriate activation of cGAS by acting as a signature of self-DNA. However, during mitotic arrest, cGAS signaling is eventually activated and promotes cell death, thereby guarding against mitotic errors (Zierhut and Funabiki, 2017).

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