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SEMINAR SERIES



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**Special
Date**

A twist in the tale of the mitotic spindle

The mitotic spindle is a fascinating and complex micro-machine made of microtubules and the accompanying proteins. Spindle microtubules attach to chromosomes via specialized protein complexes called kinetochores. We have recently shown that a bundle of antiparallel microtubules, termed “bridging fiber”, connects sister kinetochore fibers. Bridging microtubules are linked together by the protein regulator of cytokinesis 1 (PRC1). To explore the role of bridging fibers in chromosome alignment, we developed an optogenetic approach to remove PRC1 from the spindle to the plasma membrane in a fast and reversible manner by using light. PRC1 removal resulted in reduction of bridging fibers and straightening of outermost kinetochore fibers. The inter-kinetochore distance decreased, the metaphase plate widened, and lagging kinetochores appeared, suggesting that PRC1, by mechanically coupling bridging and kinetochore fibers, regulates spindle mechanics and buffers kinetochore movements in metaphase. During anaphase, bridging microtubules slide apart driven by the motor activity of kinesin-4 and kinesin-5, thereby pushing the attached kinetochore fibers poleward to segregate chromosomes. In addition to pushing and pulling forces, rotational forces (torques) may also exist in the spindle. We showed that the spindle is chiral, which is evident from our finding that bridging fibers follow a left-handed helical path, dependent on kinesin-5. This result cannot be explained by forces but rather by torques. Our theoretical model predicts that bending and twisting moments generate curved shapes of microtubule bundles. We conclude that torques, in addition to linear forces, exist in the spindle and determine its chiral architecture.

Host: Melina Schuh



Thursday / 12.03.2020 / 11:00
Max Planck Institute for Biophysical Chemistry
Large Seminar Room / Administration Building

