GDCB Seminar

4:10 p.m. • Tuesday, Sept. 14, 2021 • 1414 Molecular Biology Building

"Deciphering the mechanics of complex microtubule networks"

Abstract: Cells organize cytoskeletal networks to perform complex physical tasks such as segregating chromosomes during mitosis and building axons and dendrites in neurons. For example, the dynamic mitotic spindle network is built from microtubules that are organized, bundled, and transported by motor and non-motor proteins that produce 'active' pushing and 'passive' frictional forces. How these mesoscale forces are regulated at the micron-scale by ensembles of nanometer-sized proteins in order to properly move chromosomes has been unclear. We are addressing this knowledge gap by characterizing crosslinked microtubule bundles under load using optical tweezers and single molecule fluorescence microscopy. We have found that ensembles of PRC1, an essential non-motor crosslinking protein needed both to assemble bridging fibers during metaphase and build the central spindle in anaphase, operate in two distinct modes to control microtubule sliding. In the first mode, PRC1 forms high-density clustered aggregates at microtubule tips to significantly impede kinesin-driven microtubule sliding activity. In the second mode, PRC1 ensembles behave as viscous frictional elements whose resistance to motor-driven microtubule sliding scales linearly with velocity and local protein concentration. Our direct experimental measurements and computational simulations describe how PRC1 ensembles can adopt multiple states that differentially regulate microtubule motions to establish stable rates of both chromosome and pole separation during cell division. These results set the groundwork for understanding higher-order microtubule networks in diverse cellular contexts as "machines" that use simple rules to modulate their force production and control the spatiotemporal organization of the dynamic cytoskeleton.

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