NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

VIRTUAL BIOLOGY COLLOQUIUM

Friday, 21 May 2021 | 4pm | Online Zoom Session

Hosted by A/P Liou Yih-Cherng

Mechanobiology of the mitotic spindle

By **Iva Tolić**

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At the onset of division the cell forms a spindle, a micro-machine made of microtubules, which divide the chromosomes by pulling on kinetochores, protein complexes on the chromosome. The central question in the field is how accurate chromosome segregation results from the interactions between kinetochores, microtubules and the associated proteins. We have shown that a bundle of antiparallel microtubules, termed "bridging fiber", connects sister kinetochore fibers in human spindles. Bridging microtubules are linked together by the protein regulator of cytokinesis 1 (PRC1). To explore the role of bridging fibers in chromosome movements, we developed an optogenetic approach to remove PRC1 from the spindle to the plasma membrane in a fast and reversible manner. These experiments showed that bridging fibers promote chromosome alignment at the metaphase plate by forces that depend on the microtubule overlap within the bridging fiber. By combining a theoretical model with superresolution imaging of the bridging fibers, we discovered that they are twisted in the shape of a left-handed helix, making the spindle a chiral object. This finding suggests that torques exist in the spindle in addition to linear (pushing and pulling) forces. During anaphase, bridging microtubules promote chromosome segregation by sliding apart, which is driven by the motor activity of kinesin-4 and kinesin-5. Understanding the role of bridging microtubules in force generation and chromosome movements not only sheds light on the mechanobiology of a well-functioning spindle, but will also help to understand the origins of errors in chromosome segregation.

About the Speaker

Iva Tolić is a Professor of Biology and Senior Research Group Leader with tenure at the Ruđer Bošković Institute in Zagreb, Croatia. She graduated in molecular biology from the University of Zagreb. Her PhD work on cell mechanics was done with Prof. Ning Wang at Harvard. Afterwards, she did a postdoc in cell biophysics with Prof. Kirstine Berg-Sørensen at the Niels Bohr Institute in Copenhagen, Denmark, and later with Prof. Francesco Pavone at LENS - European Laboratory for Non-Linear Spectroscopy, in Florence, Italy. From 2004 until 2014 she worked as a Research Group Leader at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden, Germany. In 2015, she returned to her hometown Zagreb. Her research areas are biophysics of the spindle in mitosis and meiosis, microtubules and motor proteins. Iva is a recipient of the prestigious grants funded by the European Research Council (ERC), Consolidator and Synergy. She has been elected to EMBO membership. In 2014, she was chosen by the journal Cell as one of 40 scientists from around the world and working in diverse biological fields, "40 under 40". She received numerous awards such as the Ignaz Lieben Award of the Austrian Academy of Sciences, European Biophysical Societies Association (EBSA) Young Investigators' Medal and Prize, European Life Science Award in the category Investigator of the Year, Croatian Women of Influence Award, and National Science Award of the Republic of Croatia.

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