

# Department of Anatomy & Cell Biology Seminar Series

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### PP2A-dependent mechanisms of nuclear reassembly after mitosis in *Drosophila*

In animals, mitosis involves the breakdown of the nuclear envelope and the sorting of individualized, condensed chromosomes. During mitotic exit, emerging nuclei reassemble a nuclear envelope around a single mass of interconnecting chromosomes. Defects in this process can result in aberrant nuclei with abnormal structure and function. Using *Drosophila*, we are working to understand the molecular mechanisms of nuclear reassembly and the cellular and physiological consequences of defects in this process. We found that Protein Phosphatase 2A (PP2A) is required for nuclear reassembly. Two alternative regulatory subunits of PP2A, namely B55 and Ankle2, contribute to this function. Through genetic and biochemical approaches, we identified substrates of PP2A whose dephosphorylation promotes nuclear reassembly. One of them is Barrier-to-Autointegration Factor (BAF). This DNA-binding dimeric protein interconnects chromosomes in telophase to promote the formation of a single nucleus in each daughter cell. BAF also binds lamins and transmembrane nuclear envelope proteins, thereby promoting membrane recruitment around chromosomes. During mitotic entry, BAF phosphorylation disrupts its interactions with chromosomes. During mitotic exit, PP2A-Ankle2 is required for the dephosphorylation of BAF and its recruitment on reassembling nuclei. Perturbations of this mechanism in proliferative cells of the imaginal wing discs results in nuclear defects, apoptosis and smaller adult wings. We searched for signaling pathways that become critical for wing development in this context. We found that blocking apoptosis strongly enhances developmental defects. Inactivating p53 does not prevent apoptosis upon nuclear reassembly defects but it promotes tissue development through a cell cycle checkpoint. Our results suggest that apoptotic and p53-dependent responses to sporadic nuclear reassembly defects play crucial roles in safeguarding tissue development.



Wednesday, Jan. 24, 2024  
11:30am - 12:30pm

Room 1/12 - Strathcona  
Anatomy and Dentistry  
Building

Hosted by: Craig Mandato, PhD



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