Department of Anatomy & Cell Biology Seminar Series

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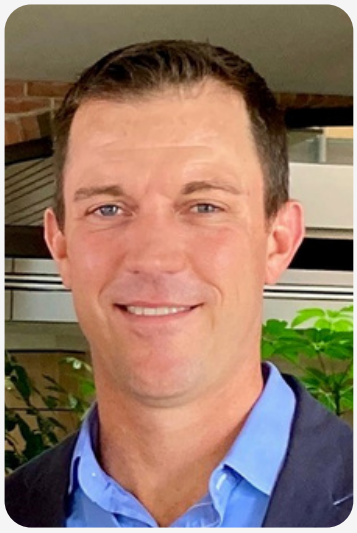
Powering on and off the forces that move mitotic chromosomes



KIF22 (or Kid) is a kinesin motor that binds directly to chromosomes and moves them directionally toward the center of the mitotic spindle during mitosis. Point mutations in the motor domain of KIF22 dominantly cause a skeletal developmental disorder characterized by short limb bones and short stature, and we recently identified a patient carrying a point mutation in the coiled-coil domain of KIF22 with similar phenotypes. However, the effects of these pathogenic mutations on KIF22 function are not known. We discovered that cells expressing patient-derived KIF22 mutants exhibit a dramatic chromosome recongression phenotype, where chromosomes begin to segregate in anaphase, then reverse direction to move back toward the center of the spindle rather than continuing toward the spindle poles. This defect leads to reduced proliferation, abnormal daughter cell nuclear morphology, and cytokinesis failure. Interestingly, a phosphomimetic mutation within the tail of KIF22 (T463D), which constitutively activates the motor, phenocopies the effects of pathogenic mutations. Thus, we propose that pathogenic mutations in KIF22 constitutively activate the motor. This, in turn, could lead to the continued generation of forces toward the center of the spindle during anaphase and the disruption of chromosome segregation. We are currently working to further test this model and determine whether or how this defect preferentially affects skeletal development.

Wednesday, Apr. 5, 2023
11:30am - 12:30pm

Room 1/12 - Strathcona Anatomy and Dentistry Building

Join us in room 1/53 after the seminar for an opportunity to meet the speaker over a pizza lunch!

Hosted by: Susanne Bechstedt, PhD

McGill