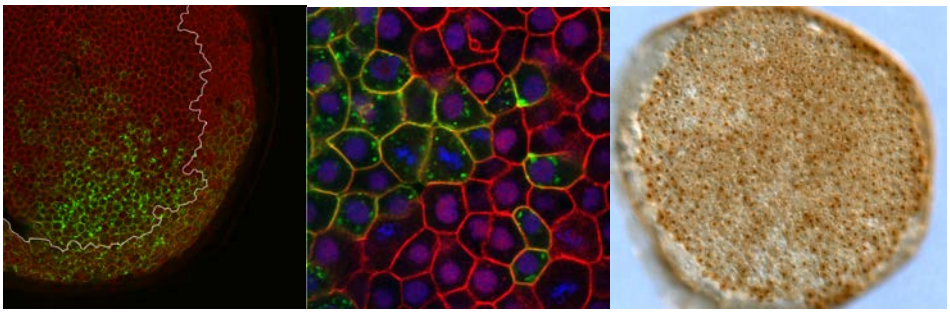
GUEST SPEAKER SEMINAR

Molecular Genetics
UNIVERSITY OF TORONTO

Regulation of Wnt signaling via negative feedback regulators



Most, if not all, signaling cascades have co-evolved feedback regulators to fine-tune the signal so that just the right amount of signal is received for just the right amount of time. Mutations in signaling pathways that usurp the feedback mechanisms are often at the core of disease. Aberrant Wnt signaling in colorectal cancer is but one example. Our lab focuses on understanding the negative feedback regulators of the Wnt pathway with the intent that this will inform us how to better control this pathway in disease. To this end we use the early zebrafish embryo as an in vivo cell model to investigate the role of Nkd1 and Axin2, two fairly constitutive and ubiquitous targets of the Wnt pathway. For this talk, I will focus on Nkd1, which is a conserved orthologue of the Drosophila Naked Cuticle gene. Our current working model for Nkd1 is as follows: Nkd1 is post-transcriptionally modified with Myristate, a reversible plasma membrane targeting molecule. Myristoylated Nkd1 interacts with the scaffolding protein Dvl, which recruits Nkd1 to the Wnt signalosome at the plasma membrane where Nkd1 becomes activated. Activated Nkd1 is released from the membrane and Dvl to interact with β-catenin where it inhibits the nuclear accumulation of β-catenin, effectively inhibiting Wnt signaling.

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Host: Dr. Brian Ciruna

Date: Friday, November 16, 2018
Time: 3:00 PM
Place: MSB 2170