Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, Feb. 9, 2018 in SSC 1511 @ 12 noon

presented by:

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(Advisor: J. Dawson)

"The Impact of ACTC Mutations Causing Hypertrophic Cardiomyopathy in Zebrafish"

It is estimated that 600,000 Canadians live with heart failure. Heart failure can result from cardiomyopathy, a disease of the heart muscle. Hypertrophic (HCM) and dilated cardiomyopathy (DCM) are the two main types, and their development has been linked to mutations in genes that encode proteins of muscle sarcomeres. One of these proteins is cardiac actin (ACTC), which is essential for proper contraction of the heart. Although mutations in sarcomere genes are the main cause of cardiomyopathy, the cellular changes that bring about the diseased state of the heart is unclear. *In vitro* and *in vivo* studies have been used to study cardiomyopathy-linked mutations in *ACTC*. These studies have revealed that ACTC variants may have altered interactions with the binding proteins needed for muscle contraction. I will study HCM-associated mutations that cause changes in subdomain 1 of the ACTC protein, which is close to the myosin binding site. I hypothesize that *ACTC* mutations causing changes in subdomain 1 of the ACTC protein will have detrimental effects on the morphology and function of the heart due to altered interactions with myosin. To test my hypothesis, I will study an *in vivo* system of transgenic zebrafish carrying human ACTC gene variants generated using the *Tol2* transposon system. Phenotype characterization will then be conducted on the zebrafish, and the histology of the zebrafish hearts will be studied to deduce the structure and tissue arrangement. My study will provide insight into how *ACTC* mutations cause cardiomyopathy and further increase knowledge in the cardiovascular field.