

Department of Molecular and Cellular Biology
Graduate Seminar MCB*6500



Friday, March 10, 2017 in SSC 1511 @ 12 noon

presented by:

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Phenotypic classification of cardiac actin knockouts in zebrafish using the CRISPR-Cas9 system

Cardiomyopathy is a common cause of heart failure, a growing epidemic in Canada. Two prevalent forms of cardiomyopathy are hypertrophic cardiomyopathy (HCM) and dilated cardiomyopathy (DCM), which are characterized by changes to the heart muscle (myocardium). The development of HCM and DCM has been associated with mutations found in genes encoding muscle proteins, including cardiac actin (*ACTC1*). Anatomical and histological descriptions of cardiomyopathy are largely determined, but our understanding of the molecular basis of cardiomyopathy development remains incomplete. To address this gap in understanding, an *in vivo* model is required to study the underlying molecular mechanisms leading to the development of cardiomyopathy. Generating a model for cardiovascular disease will allow scientists to target the associated dysfunctions with precision therapies leading to improved treatments and reducing the global burden of heart failure. I will take the first step toward our overall goal of using zebrafish to determine connections between cardiac actin mutations and cardiomyopathy development by using CRISPR-Cas9 system to produce and characterize *zfactc* knockout lines. This work will clarify which *zfactc* gene(s) is a cardiac isoform and will be the first characterization of the putative *actc1c* gene. I hypothesize that a cardiac phenotype should be observed if the knocked out zebrafish gene encodes for cardiac actin. This work will provide a *zfactc* knockout background for future human *ACTC* rescue experiments, including the characterization of cardiomyopathy-related *ACTC* mutants.