

Department of Molecular and Cellular Biology



Graduate Seminar MCB*6500

Friday, Feb. 3, 2017 in SSC 1511 @ 12:45 p.m.

presented by:

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Investigation of the effect of the ACTC variants A295S and A331P on interactions with tropomyosin in hypertrophic cardiomyopathy (HCM)

Heart disease has been an issue in human civilization for centuries, and is the leading cause of death worldwide. One commonly inherited heart disease is known as hypertrophic cardiomyopathy, or HCM. It is typified by a thickening of the left ventricular muscle, and can cause sudden cardiac death especially among young athletes. Although no definitive single cause has been discovered, there have been many genes implicated in the pathogenesis of HCM. This includes the gene encoding α -cardiac actin, known as *ACTC1*, an integral part of cardiac muscle tissue. To date, 12 mutations in *ACTC1* have been linked to HCM, encoding variant proteins that contribute to the disease state. Of these, the ACTC variants A295S and A331P are of particular interest for their proposed interaction with the regulatory protein tropomyosin. Recombinant protein variants will be tested to determine their binding affinity with tropomyosin using a fluorescence-based assay, their influence on the enzymatic activity of myosin using an ATPase assay, and their effect on filament velocity and movement in an *in vitro* motility assay. This research aims to investigate the altered interactions of these ACTC variants with tropomyosin and other sarcomeric proteins in a biologically relevant system. The information generated will provide a better understanding of how HCM develops for individuals with these variant proteins, and may eventually lead to the development of more personalized treatments for individuals with this disease.