



**Announcement:**

All interested members of the university community are invited to attend the Final Oral Examination for the degree of **Master of Science** of

**EVAN DESPOND**

on Tuesday, November 27, 2018 at 9:30 a.m. in SSC 1511

**Thesis Title:** The hypertrophic cardiomyopathy-linked alpha-cardiac actin variant A331P

**Examination Committee:**

Dr. G. van der Merwe, Dept. of Molecular and Cellular Biology (Exam Chair)

Dr. J. Dawson, Dept. of Molecular and Cellular Biology

Dr. D. Josephy, Dept. of Molecular and Cellular Biology

Dr. S. Graether, Dept. of Molecular and Cellular Biology

**Advisory Committee:**

Dr. J. Dawson (Adv)

Dr. G. Pyle

Dr. D. Josephy

**Abstract:** Hypertrophic cardiomyopathy (HCM) is a common inherited cardiovascular disease that has been linked to proteins of the cardiac sarcomere. Over many years of research, a common hypothesis for this disease has emerged: protein variants cause an increase in calcium ( $\text{Ca}^{2+}$ ) sensitivity that leads to greater sarcomere contractility, eventually resulting in the hypertrophy that is characteristic of HCM. Studies of many proteins have supported this hypothesis, but only one is inconsistent. The  $\alpha$ -cardiac actin (ACTC) variant A331P has shown a decrease in  $\text{Ca}^{2+}$  sensitivity. In this thesis, A331P-ACTC was compared to wild-type recombinant- (WTrec-) ACTC and again found to have a slight decrease in  $\text{Ca}^{2+}$  sensitivity, based on the actin-activated myosin ATPase and *in vitro* motility assays. These findings are in agreement with previous research and suggest that the properties of A331P-ACTC are inconsistent with the global hypothesis of HCM. My research also raises the question of whether  $\text{Ca}^{2+}$  sensitivity should be the absolute point of comparison used in cardiomyopathy research, or merely one aspect of a larger picture of the disease.

**Curriculum Vitae:** Evan obtained his Bachelor of Science (Hons), Biological and Pharmaceutical Chemistry, at the University of Guelph in spring of 2016, and then began his M.Sc. program in the lab of Dr. John Dawson in the fall of the same year.

**Publication:** Despond EA and Dawson JF (2018). Classifying cardiac actin variants associated with hypertrophic cardiomyopathy. *Front Physiol* **9**:1-6.