



COLLEGE of  
BIOLOGICAL SCIENCE

DEPARTMENT OF MOLECULAR  
AND CELLULAR BIOLOGY

**Announcement:**

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

**ZI (GRACE) TENG**

on Tuesday, March 24, 2020 at 9:30 a.m. in SSC 2315

**Thesis Title:** The dark side of actin: Characterization of hypertrophic cardiomyopathy linked S271F ACTC variant and dilated cardiomyopathy linked T126I ACTC variant.

**Examination Committee:**

Dr. M. Kimber, Dept. of Molecular and Cellular Biology (Exam Chair)

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

Dr. J. Simpson, Dept. of Human Health and Nutritional Science

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

**Advisory Committee:**

Dr. John Dawson (Adv)

Dr. Tami Martino

**Abstract:** Cardiomyopathy is a commonly inherited cardiovascular disease that affect the heart muscle. Two types of cardiomyopathy include hypertrophic cardiomyopathy (HCM), where the left ventricle is thickened, and dilated cardiomyopathy (DCM), where left ventricle is thinned out. Mutations in genes that code for contractile proteins, such as  $\alpha$ -cardiac actin (ACTC), were identified in patients who suffer from HCM or DCM. This thesis investigates two ACTC variants that have never been studied before: S271F, an HCM-linked ACTC variant and T126I, an DCM-linked ACTC variant. Both variants are located on the backside of the traditional ribbon diagram of actin; what I call the “dark side” of actin. A systematic approach was used to characterize these two variants. This approach included testing protein stability, actomyosin interactions and investigating calcium sensitivity when regulated with troponin and tropomyosin. The S271F ACTC variant showed significant intrinsic changes and no deviation in calcium sensitivity when compared to recombinant WTrec ACTC. On the other hand, the T126I ACTC variant exhibited few changes in its intrinsic properties but displayed a decrease in calcium sensitivity. Furthermore, this is the first study to test a cardiac troponin complex binding calcium sensitizer to reverse the decreased calcium sensitivity observed with an ACTC variant. This research contributes to the understanding on disease mechanism of these ACTC variants in the development of cardiomyopathy.

**Curriculum Vitae:** Grace completed her Bachelor of Science (Hons.), majoring in Biomedical Sciences with a minor in Microbiology, at the University of Guelph in April 2018. She then began her M.Sc. in the lab of Dr. John Dawson in May 2018.

**Publication:** Teng, G. Z., Shaikh, Z., Liu, H., and Dawson, J. F. (2019). M-class hypertrophic cardiomyopathy cardiac actin mutations increase calcium sensitivity of regulated thin filaments. *Biochem. Biophys. Res. Commun.* doi:10.1016/j.bbrc.2019.08.151.