Doctoral Dissertation Defense Announcement

“Cardiomyocyte Ploidy Dynamics in Development and Repair”

Samantha K. Swift
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Cell and Developmental Biology
School of Graduate Studies
Medical College of Wisconsin

Committee in Charge:
Michaela Patterson, PhD (Mentor)
Brian Link, PhD
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Matt Veldman, PhD
Sridhar Rao, PhD
Lu Han, PhD

Date: Thursday, October 12, 2023
Time: 10:00 AM (CST)
Defense Location: HUB A7520/A7628
Zoom: Contact sswift@mcw.edu for Zoom link
Graduate Studies:
Introduction to Biomedical Research
Biochemistry of the Cell
Techniques in Molecular and Cellular Biology
Molecular and Cellular Biology
Mechanisms in Cellular Signaling
Classical and Molecular Genetics
Ethics and Integrity in Science
Biostatistics I
Research Ethics Discussion Series
Reading and Research
Advanced Cell Biology
Functional Genomics
Boundaries of Science and Medical Practices
Doctoral Dissertation
Somatic polyploidization, an adaptation by which cells increase their DNA content to support growth, is observed in many cell types, including cardiomyocytes. Although polyploidization is believed to be beneficial, progression to a polyploid state is often accompanied by loss of proliferative capacity, leading many in the field to hypothesize that polyploidization is linked to cell cycle exit. However, much of our understanding surrounding the progression to polyploidization stems from work that was done on a very limited number of mouse strains. Recent studies have shown that genetic background influences levels of cardiomyocyte polyploidization and also regenerative capacity of the heart. These studies have even gone on to suggest the two phenomena are linked, demonstrating a need for a deeper understanding of the progression to polyploidization, especially when considering the role of genetic variability. Further, studies which further investigate the lingering blind spots of cardiomyocyte polyploidization may also inform us of genetic regulators of the process and ultimately, provide insight into mechanisms that drive regeneration.

In order to address the aforementioned gaps in knowledge, the fields of cardiac biology and regeneration are in need of easily implemented tools to discern proliferation from polyploidization during times of growth and tissue expansion. Traditional markers of proliferation are insufficient to distinguish the two processes, and current genetic models which can differentiate cardiomyocyte proliferation from polyploidization require intensive and potentially even prohibitive breeding strategies. In this dissertation, we improve upon one such tool designed to evaluate cardiomyocyte cell division and present a comprehensive methodology that any lab can implement to study cardiomyocyte growth and proliferation in vivo. This novel method is presented in chapter 2. We then utilized this new methodology to investigate many lingering questions in the fields of cardiomyocyte development and regeneration. For example, in chapter 2 we investigate the potentially
regenerative window post myocardial infarction in two diverse inbred mouse strains using thymidine analogs to ask if the number of cardiomyocytes that enter and complete the cell cycle is consistent throughout the weeks following injury. We discovered that genetic background does play a role in the timing, degree, and completion of cardiomyocyte cell cycle activity after injury. In chapter 3 we asked how the developmental progression to polyploidy can differ between genetically diverse strains of mice, and which genes regulate this process. Similar to the injury context, we found that genetic background significantly influenced the timing and degree of polyploidization, as well as general expansion and establishment of cardiomyocyte numbers. This also led us to identify novel cardiomyocyte ploidy reversal in one strain, and both pinpoint and validate two genetic regulators of this process. At the end of chapter 3 and throughout chapter 4 we investigated the role of these two genes in the regenerative context using multiple strain backgrounds and confirmed that the same genes which regulate developmental ploidy progression and novel ploidy reversal regulate cardiomyocyte proliferation after a myocardial infarction.

This dissertation provides novel insights regarding the developmental path to cardiomyocyte polyploidization and challenges the paradigm that cardiomyocyte hypertrophy is the only mechanism for growth and tissue expansion in the postnatal heart. These data also highlight the importance of utilizing diverse genetic backgrounds in the study of cardiac regeneration and development.
Samantha K. Swift  
Curriculum Vitae  
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EDUCATION
Medical College of Wisconsin  Ph.D. Cell and Developmental Biology  
Wisconsin with a certificated concentration in Basic and Translational Science  
Milwaukee, WI  August 2018 – Present, expected defense: October 2023

Iowa State University  B. Sc. Biology, (College of Agriculture and Life Sciences)  
Ames, IA  Minor in Animal Science  
August 2014 – May 2018

EMPLOYMENT
Aug 2018 – Present  Graduate Student  
Medical College of Wisconsin, Milwaukee, WI 53226

Jan 2017 – August 2018  Laboratory Technician  
MG Biologics, Ames, IA 50014

Dec 2015 – May 2017  Undergraduate Research Assistant  
Iowa State University, Ames, IA 50011

PEER-REVIEWED PUBLICATIONS
A.L. Purdy*, S.K. Swift*, H.M. Sucov, M. Patterson. Tnni3k Influences Cardiomyocyte S-Phase Activity and Proliferation. JMCC. PMID: 37597489  
* Co-first authors


FUNDING
Feb 2022 - Jan 2025* Ruth L. Kirschstein National Research Service Award (NRSA) National Heart Lung and Blood Institute (NHLBI), Grant number: F31HL162468 The Role of Runx1 in Cardiomyocyte Cell Cycle and Ploidy

AWARDS
July 2023 Paper of the Season Award Winner, Medical College of WI
Mar 2022 Chicago Regional Cardiovascular Symposium Best Poster Award
Aug 2021 MCW Graduate Student Travel Award
Mar 2021 MCW Grad Student Association Symposium Oral Presentation Award

SELECT PRESENTATIONS
➢ Presentation Award


➢ Presentation Award


➢ Best Poster Award


S.K. Swift, K.A. Akins, K. Andresen, M. Patterson. The Role of Runx1 in Cardiomyocyte Cell Cycle and Ploidy. Poster presentation delivered at the Basic Cardiovascular Sciences Scientific Sessions, Virtual, August, 2021.


➢ Presentation Award

SERVICE

June 2020- May 2021 Vice President
Medical College of Wisconsin Graduate Student Association

May 2019- May 2020 Student Representative
MENTORSHIP & TEACHING EXPERIENCE

Fall 2022  
**Teaching Assistant**, Mount Mary University, Milwaukee, WI  
Undergraduate elective on Biodiversity  
Course Instructor: Dr. Kathleen Boyle  
Led bi-weekly small group discussions deconstructing scientific lectures

Fall 2019 – Fall 2023  
**Graduate Student Mentor**, Patterson Lab, MCW, Milwaukee  
*Undergraduate Students*: Kaitlyn Andresen (Previous SPUR participant, now pursuing a PhD); Jeovannee Castillo, Shawna Butler, and Carmen Lopez (American Heart Association, SURE Recipients)  
*Graduate (rotation) Students*: Kaelin Akins (joined Patterson lab), Christina Mecca, Donovan Drouillard

Fall 2017 – Spring 2018  
**Teaching Assistant**, Iowa State University, Ames  
*General Chemistry* (Basic Chemistry for Engineers),  
Led 3 groups of 24 students in recitation-style lecture

Fall 2016  
**Teaching Assistant**, Iowa State University, Ames  
*General Chemistry* (Basic Chemistry for Science Majors)  
Led 2 sections in laboratory exercises, one section in recitation style lecture