Jae-Hoon Chung
PhD Candidate

“Regulation of Human Cardiac Muscle Contraction and Relaxation in Health and Disease”

February 26, 2018
Hamilton 302C
10:00 am
VITA

July 25, 1989. ................. Born – Pupyeong, South Korea

2012 .................. B.A. Chemistry, Northwestern University

2012-Present. . . . MD/PhD Candidate, The Ohio State University

COMMITTEE MEMBERS

Paul M.L. Janssen, PhD, Advisor

Jonathan Davis, PhD

Noah Weisleder, PhD

Bryan Whitson, MD/PhD
ABSTRACT

Heart disease is the leading cause of death in the United States. Heart failure is a disease in which the heart fails to pump sufficient amount of blood to the body. It is a serious health burden that claims the lives of 58,000 Americans per year with a grim 5-year mortality rate of 50%. Over the years, the field of cardiovascular medicine has produced improved treatment options for patients with heart failure, such as beta blockers and angiotensin converting enzyme (ACE) inhibitors. However, the field has not yet been able to produce treatments to reverse the pathophysiology of heart failure, as the mechanism of disease has not been fully elucidated.

We have obtained human non-failing and failing hearts and isolated intact trabeculae from left and right ventricle. We first utilized right ventricular intact trabeculae to characterize baseline twitch force and kinetics and found that non-failing and failing trabeculae do not have different developed force or contraction kinetics. However, failing trabeculae had slower relaxation kinetics. In addition, we found evidence that suggests trabeculae from males trend towards having greater developed force compared to trabeculae from females. After baseline twitch characterization, we investigated changes in their contractile and relaxation capacities at different lengths, stimulation frequencies, and beta-adrenergic activation levels. We found that length-dependent activation is present in both non-failing and failing trabeculae. Moreover, the slowing of contraction and relaxation kinetics at longer lengths was observed in both non-failing and failing trabeculae. Non-failing trabeculae exhibited positive force-frequency relationship, meaning that their developed force increases as stimulation frequency is increased. On the other hand, failing trabeculae displayed negative force-frequency. Upon maximal beta-adrenergic stimulation, developed force was increased by ~5 fold in non-failing trabeculae and ~3 fold in failing trabeculae. Kinetics of contraction and relaxation were
accelerated in both non-failing and failing trabeculae upon beta-adrenergic stimulation, but these kinetics were slower in failing trabeculae compared to non-failing trabeculae.

We further investigated the mechanism of force-frequency relationship by inhibiting the sarcoplasmic reticulum (SR) in human right ventricular trabeculae via cyclopiazonic acid (CPA) and ryanodine. Upon SR blockade, force-frequency relationship was preserved and contraction kinetics slowed down. In addition, early relaxation kinetics was not affected by SR blockade, but total twitch time was slower at low frequencies after SR blockade. We also studied the role of cross-bridge cycling kinetics in force-frequency relationship. We measured ktr, an index of rate of cross-bridge cycling, in non-failing and failing left ventricular trabeculae and found that ktr does not change at different frequencies but failing trabeculae had slower ktr and lower potassium contracture at 3 Hz stimulation frequency. Across the frequencies we tested, contraction kinetics was not different between non-failing and failing trabeculae, but relaxation kinetics were slower. The maximal rate of force decay was significantly slower in failing trabeculae at 3 Hz stimulation frequency.

Chung JH., Milani-Nejad N., Karaze T., Kilic A., Mohler PJ., and Janssen PML. Effect of Frequency Modification on Kinetic Parameters of Explanted Human Myocardium with Non-ischemic and Ischemic Cardiomyopathy. Myofilament Meeting: Local and Global Regulatory Networks in Muscle, Madison, Wisconsin. (June 2016).


RECENT PUBLICATIONS

Milani-Nejad N.*, **Chung JH.***, Canan BD., Fedorov VV., Whitson BA., Kilic A., Mohler PJ., Janssen PML. Increased cross-bridge recruitment contributes to transient increase in force generation beyond maximal capacity in human myocardium. Journal of Molecular Cellular Cardiology. 2017.


(* denotes equal contribution to the project)
AWARDS AND HONORS

University Fellowship: 2014 – 2015
Ohio Physiological Society Research Award: 2016
Margaret T. Nishikawara Scholarship: 2017
American Heart Association Predoctoral Fellowship: 2017-2019

FUTURE PLANS

I am returning to medical school to complete the last two years of my medical training. My current goal is to pursue residency in internal medicine followed by a fellowship. I would like to become an expert and leader in my chosen medical field to make significant contribution to patient care and solve medical problems through translational research.