

St. Catherine University
SOPHIA

Sr. Seraphim Gibbons Undergraduate Symposium

2014 Sr. Seraphim Gibbons Undergraduate
Research Symposium

Building a Better Phospholamban: Using Structure and Dynamics-Based Design to Engineer Therapeutic Mutants for Treating Heart Failure

Adedolapo moyinoluwa ojoawo
St. Catherine University

Choua Xiong
St. Catherine University

Follow this and additional works at: https://sophia.stkate.edu/undergraduate_research_symposium

ojoawo, Adedolapo moyinoluwa and Xiong, Choua, "Building a Better Phospholamban: Using Structure and Dynamics-Based Design to Engineer Therapeutic Mutants for Treating Heart Failure" (2014). *Sr. Seraphim Gibbons Undergraduate Symposium*. 12.
https://sophia.stkate.edu/undergraduate_research_symposium/2014/natural_sciences/12

This Event is brought to you for free and open access by the Conferences and Events at SOPHIA. It has been accepted for inclusion in Sr. Seraphim Gibbons Undergraduate Symposium by an authorized administrator of SOPHIA. For more information, please contact amshaw@stkate.edu.

Abstract

Building a Better Phospholamban: Using Structure and Dynamics-Based Design to Engineer Therapeutic Mutants for Treating Heart Failure

Choua Xiong, Adedolapo Ojoawo, Dr. Kim N. Ha

Heart disease is the leading cause of death in the United States. Heart failure, one of the chronic conditions of heart disease, is marked by a loss of strength in muscle contractility. Impairment in calcium signaling in cardiac muscle cells has a direct impact on the development of heart failure. Interactions between an enzyme, the sarcoplasmic reticulum Ca^{2+} ATPase (SERCA), and its regulatory inhibitor, the membrane protein phospholamban (PLN), play an important role in the regulation of cardiac muscle relaxation and contraction. PLN is a membrane protein that inhibits SERCA, an enzyme that facilitates transport of calcium ions into the sarcoplasmic reticulum to allow relaxation to occur. Several naturally occurring mutations in PLN lead to inherited heart diseases. In order to augment SERCA activity and increase cardiac relaxation, we are designing PLN mutants which will be able to selectively increase SERCA activity by down-regulating PLN inhibition. The ultimate goal is to identify the most promising PLN mutants, deliver them into animal models using gene therapy, and test whether they improve cardiac relaxation. Based on the known structure of PLN, we have designed, cloned, and isolated new generation of PLN mutants for study and explored the interactions between PLN mutants and protein phosphatase 1 (PP1), one of the main enzymes that dephosphorylates PLN and controls PLN inhibition activity. We have successfully completed preparation of PLN mutant samples for activity assays. These interactions will eventually be correlated to changes in SERCA activity to determine if the therapeutic mutants can deliver expected results.

Keywords: Phospholamban, Therapeutic, Dynamics, Inhibition, Dephosphorylation, contractility, cloning, Regulation, SERCA2A