BIOGRAPHICAL SKETCH

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NAME: Kristin Shirey Edwards

eRA COMMONS USER NAME (credential, e.g., agency login): KRISTINEDWARDS

POSITION TITLE: Postdoctoral Research Fellow

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Jacksonville State University, Jacksonville, AL	BS	04/2011	Biology and Chemistry
University of Mississippi Medical Center	PhD	05/2017	Biochemistry

A. Personal Statement

My long-term research interests involve understanding how alterations in mitochondrial bioenergetics contribute to human disease, in particular cardiovascular disease associated with diabetes and obesity. My academic training and research experience have provided me with a broad background in multiple biological disciplines including mitochondrial bioenergetics, molecular biology, genetics, biochemistry and developmental toxicology. As an undergraduate, I participated in two summer undergraduate research programs at The University of Alabama and the Georgia Institute of Technology. I also participated in research at my undergraduate institution leading to three publications. As a predoctoral student, I was responsible for establishing protocols for isolating mitochondria from various tissues, assays for measuring coupled respiration in intact mitochondria, assays for whole chain electron transfer in broken mitochondria and assays of the individual electron transfer complexes of oxidative phosphorylation. My investigations led to the discovery of novel inhibitors/stimulators of the individual complex activities of mitochondrial oxidative phosphorylation. Through collaborative work at the University of Mississippi Medical Center, I also explored alterations of mitochondrial bioenergetics in various disease models. As an undergraduate and graduate student, I received several awards for academics, research and leadership. Along with research, I also participated in the Teachers in Training Program at the University of Mississippi Medical Center that has allowed me to gain teaching experience at the undergraduate and graduate levels. For my postdoctoral training, I will continue to build on my previous training in mitochondrial bioenergetics by exploring alterations that arise from cardiovascular disease induced by diabetes and obesity. In March 2017, I initiated my postdoctoral training in the laboratory of Dr. Romain Harmancey in the Department of Physiology and Biophysics at the University of Mississippi Medical Center. Dr. Harmancey has a strong research background investigating the molecular mechanisms by which diabetes and obesity increase the risk to develop cardiovascular disease. With the guidance of Dr. Harmancey, I will identify the impact of mitochondrial uncoupling protein 3 (UCP3) deficiency induced by diabetes on cardiac myocytes survival, mitochondrial fatty acid oxidation and mitochondrial ROS generation following myocardial ischemia and reperfusion. This project will be successfully carried out by combining my previous experience in mitochondrial bioenergetics with physiological techniques learned in the Harmancey lab. The education and research training I will acquire during this project will allow me to become a more skillful independent investigator and to develop a unique area of research that will expand our knowledge of cardiac metabolism and therapeutic strategies for diabetic patients. In summary, I expect my postdoctoral fellowship will provide the necessary foundation to build my research, teaching, oral communication, and grant writing skills, which will allow me to reach my ultimate goal, which is to create my own research program in the area cardiovascular disease and to be an effective educator.

B. Positions and Honors

Positions and Employment

2009	Summer Undergraduate Research Program Participant, The University of Alabama, Tuscaloosa, AL
2010	Summer Undergraduate Research Program Participant, Georgia Institute of Technology, Atlanta, GA
2009-2011	Chemistry, Biology and Mathematics Tutor, Academic Center of Excellence, Jacksonville State University, Jacksonville, AL
2011-2017	Graduate Assistant, Department of Biochemistry, University of Mississippi Medical Center, Jackson, MS
2017-present	Postdoctoral Research Fellow, Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, MS

Professional Memberships

2007 – Present	American Chemical Society
2015 – Present	American Society of Biochemistry and Molecular Biology
2017 – Present	American Physiological Society
2017 – Present	American Heart Association

Honors

2007	Phi Eta Sigma inductee
2008	Beta Beta Beta inductee
2009	Jacksonville State University College of Arts and Sciences Symposium Best Biology Presentation
2009	Alabama Academy of Sciences 3rd Place Biology Presentation
2009	Alabama Academy of Sciences 2nd Place Chemistry Presentation
2009	National Society of Environmental Toxicology and Chemistry 3rd Place Poster Presentation
2009	Phi Kappa Phi inductee
2010	Omicron Delta Kappa inductee
2010	Beta Beta Beta Southeastern Region Frank Brooks Award
2010	Jacksonville State University Department of Physical and Earth Sciences Richard J. Beschi Leadership Award
2011	Jacksonville State University College of Arts and Sciences Symposium Best Biology Presentation
2011	Kappa Mu Epsilon inductee
2011	Biology Outstanding Academic Award
2011	Biology Outstanding Undergraduate Research Award
2015	Research Day Graduate Student Poster Winner
2017	Regions Outstanding Graduate Research Award
2017	SGSHS Research Day Postdoctoral Poster Award

C. Contribution to Science

1. Novel membrane bound effectors of the proton pumps of oxidative phosphorylation:

My PhD project focused on a group of cyclic lipopeptides, the echioncandins, as effectors of mitochondrial function. A cyclic lipopeptide (CLP) is an amphipathic molecule with a small cyclic peptide as the polar end and a fatty acid-like chain as the non-polar end, which can insert into biological membranes, placing the cyclic peptide near the membrane surface. Little is known about the effect of these molecules on membrane protein activity, particularly integral membrane pumps and ion channels, where 'substrates' and 'products' are taken up and released near the membrane surface. Although the echinocandin CLPs are structurally similar, some carry positive or negative charge in their peptide headgroup. These charges may alter the uptake or release of charged molecules by the mitochondrial oxidative phosphorylation complexes. Remarkably, I discovered that the CLPs altered the activities of all three of the proton pumps of oxidative phosphorylation (complexes I, III and IV) in isolated mitochondria. However, the activities of these complexes were altered in different ways, indicating specificity for each CLP-protein interaction. For example, low micromolar concentrations of the positively charged CLP caspofungin inhibit complex IV from the outer surface of the complex, by preventing the release of pumped protons. In contrast, negatively charged micafungin causes a three-fold stimulation of

complex IV, by promoting proton uptake from the inner surface of the complex. Each of these interactions provides new opportunities for understanding and manipulating the molecular functions of complexes I, III and IV.

Shirey, K., Stover, K. R., Cleary, J., Hoang, N., and Hosler, J. (2016) Membrane-anchored cyclic peptides as effectors of mitochondrial oxidative phosphorylation, Biochemistry 55: 2100-11, doi: 10.1021/acs.biochem.5b01368, PMID: 26985698

2. A negatively charged CLP reprograms an anion channel in the inner mitochondrial membrane:

In the second part of my PhD project, I found that the addition of negatively charged micafungin led to the rapid release of essentially all soluble cytochrome *c* from the intermembrane space of intact mitochondria. The release of cytochrome *c* was induced by rapid swelling and the complete rupture of the mitochondria. Further, micafungin-induced mitochondrial swelling was traced to a strong alteration in ion transport across the inner mitochondrial membrane. Our hypothesis is that micafungin interacts with the inner membrane anion channel (IMAC), and alters its activity such that it rapidly transfers both cations and anions. In the presence of micafungin, IMAC rapidly transfers a wide variety of anions and cations into the mitochondrial matrix, causing swelling, membrane rupture and cytochrome *c* release. A CLP with a headgroup identical to that of micafungin, but lacking the negative charge, fails to activate IMAC. Hence, a simple electrostatic interaction between micafungin and the outer surface of IMAC completely alters the activity of this anion channel, but the negative charge must be anchored in the membrane for the effect to be observed. A manuscript describing these results (Shirey et al, 2017) is in final preparation.

Shirey, K., Hoang, N, and Hosler, J. Micafungin induces large scale mitochondrial swelling. 2016 UMMC Graduate School Research Day.

Other relevant publications:

Lawson, W. J.*, Shirey, K.*, Spann, R.A., Zamarripa, A., Hosler, J.P., Grayson, B.E. (2016) Vertical sleeve gastrectomy improves indices of metabolic disease in a rodent model of surgical menopause. The Journal of The North American Menopause Society 24 (4): 426–436

Puskarich, M. A., Kline, J. A., Watts, J. A., Shirey, K., Hosler, J., and Jones, A. E. (2016) Early alterations in platelet mitochondrial function are associated with survival and organ failure in patients with septic shock, J. Crit. Care 31, 63-67 PMID: 26511963

Zouein, F., Duhé, R., Arany, I., Shirey, K., Hosler, J.P., Liu, H., Iman Saad, I., Kurdi, M., and Booz, G. (2014) Loss of STAT3 in mouse embryonic fibroblasts reveals its Janus-like actions on mitochondrial function and cell viability. Cytokine 66: 7-16 PMID: 24548419

Shirey, K. and Rayburn, J. (2013) Old World vs. New World: a preliminary comparison of the developmental toxicity of venom from two tarantula species, Grammostola rosea and Haplopelma lividium, using frog embryos from Xenopus laevis. BIOS 84(3):127-135.

Vasumathi, N., Zettili, M., and Shirey, K. (2009) Bromination of dimethyl maleate using bromoform as catalyst under different energy sources: A case study for its role in biotransformations. Journal of the Alabama Academy of Science. 80 (3-4): 220-232.

Vasumathi, N., Zettili, M., and Shirey, K. (2009) Effects of concentration, temperature, and varied energy conditions on the specific rotations of isoborneol and (s)-(-)-endo borneol. Journal of Undergraduate Chemistry Research. 8 (4):115-121

D. Additional Information: Research Support and/or Scholastic Performance

Research Support

2017 – Present NIH Ruth L. Kirschtein Institutional National Research Service Award (T32HL105324-07)
University of Mississippi Medical Center, Role: Research Fellow
PI: Joey P. Granger, Ph.D.
This grant provides support to acquire methodological research and mentored research with established investigators of the Cardiovascular-Renal Research Center at UMMC.

Scholastic Performance

YEAR	SCIENCE COURSE TITLE	GRADE
	Jacksonville State University (BS)	
2007	Genetics	A
2007	Cell Biology	A
2008	Comparative Vertebrate Anatomy	A
2008	Biochemistry I	A
2009	Biochemistry II	A
2009	Animal Behavior	A
2010	Animal Systems Physiology	A
2010	Evolutionary Biology	A
	University of Mississippi Medical Center (PhD)	
2011	Biochemistry	A
2011	Seminar	P
2011	Biochemical Methods	A
2012	Mechanisms of Enzyme Action	A
2012	Physical Biochemistry	A
2012	Cellular Biochemistry I	A
2013	Research Tools in Molecular Biology	A
2013	Cellular Biochemistry II	A

YEAR	OTHER COURSE TITLE	GRADE
	Univerisity of Mississippi Medical Center (PhD)	
2012	Research Ethics	A
2013	Professional Skills	A