

NORA ECCLES HARRISON CARDIOVASCULAR RESEARCH & TRAINING INSTITUTE (CVRTI)


Annual Newsletter | Volume 3 | 2023-2024





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**NORA ECCLES HARRISON
CARDIOVASCULAR RESEARCH
& TRAINING INSTITUTE**

Building Hours
9:00 AM to 5:00 PM
Monday thru Friday

LETTER FROM THE DIRECTOR

Welcome to the 2023-2024 Nora Eccles Harrison Cardiovascular Research and Training Institute (CVRTI) Newsletter!

Established in 1967, the CVRTI is a freestanding 40,000 square foot cardiovascular research institute on The University of Utah Health Sciences campus that provides a highly integrated approach to the study of basic and translational cardiac biology. CVRTI personnel include 16 full-time faculty Investigators (PhDs, MDs, MD/PhDs, and DVM/PhDs), with 120 early career investigators (postdocs, graduate students, undergraduates) and dedicated research staff. Our faculty investigators are presently drawn from three colleges and six departments across The University of Utah.

Featured events of this past academic year include the grand opening of our new Eccles Research Wing for which recruitment of new Investigators is underway, the creation of four CVRTI research programs organized by research themes within the larger institute, continued growth in our extramural funding with a 27% increase in funding compared to last fiscal year, and an increasing list of awards won by our early career investigators and faculty.

Aside from individual lab achievements, in the past year, the CVRTI successfully engaged the Food and Drug Administration to advance cBIN1 gene therapy for chronic heart failure. The CVRTI is on the cusp of changing the paradigm of treating heart failure in the United States and the world over.

Thank you for taking a moment to review this 2023-2024 annual progress report.



A handwritten signature in black ink that reads "(Robin Shaw)". The signature is stylized and includes a long horizontal line extending to the right.

Robin Shaw, MD, PhD

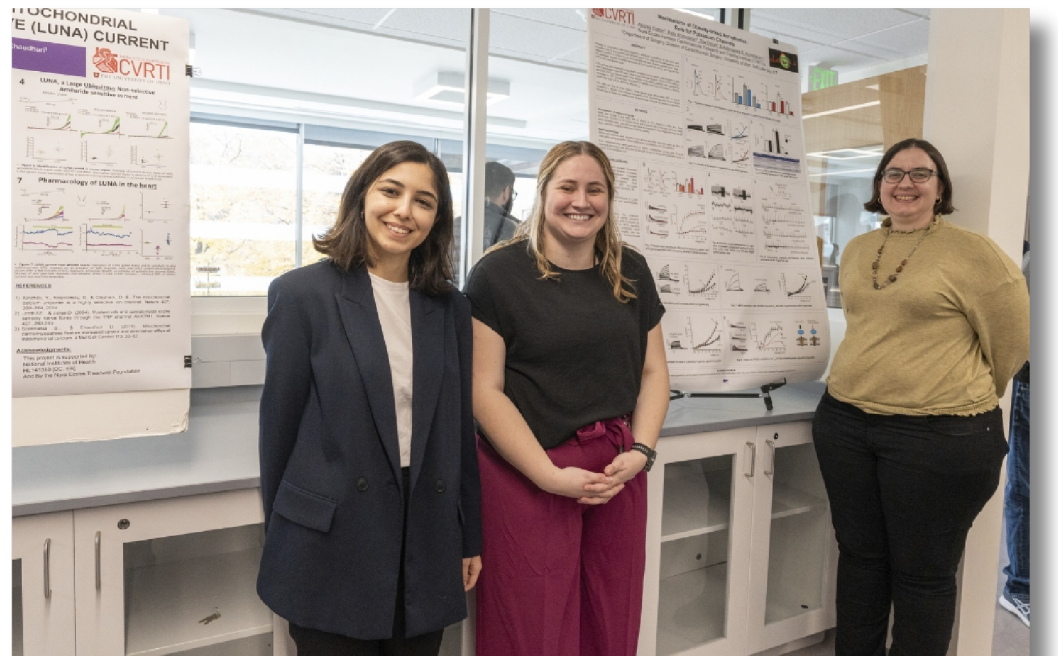
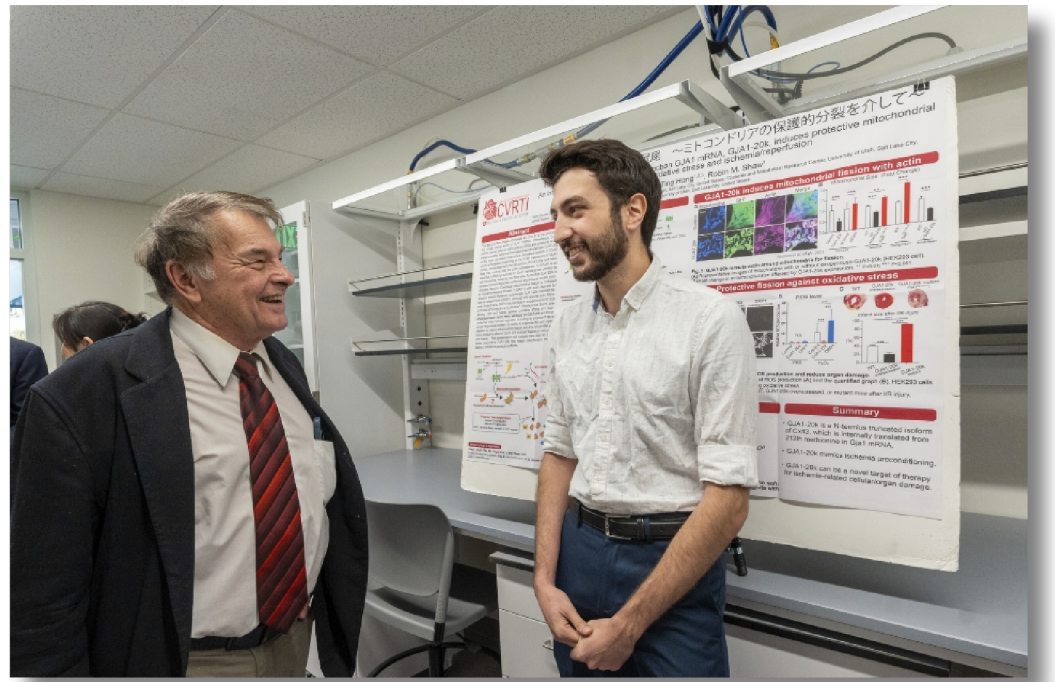
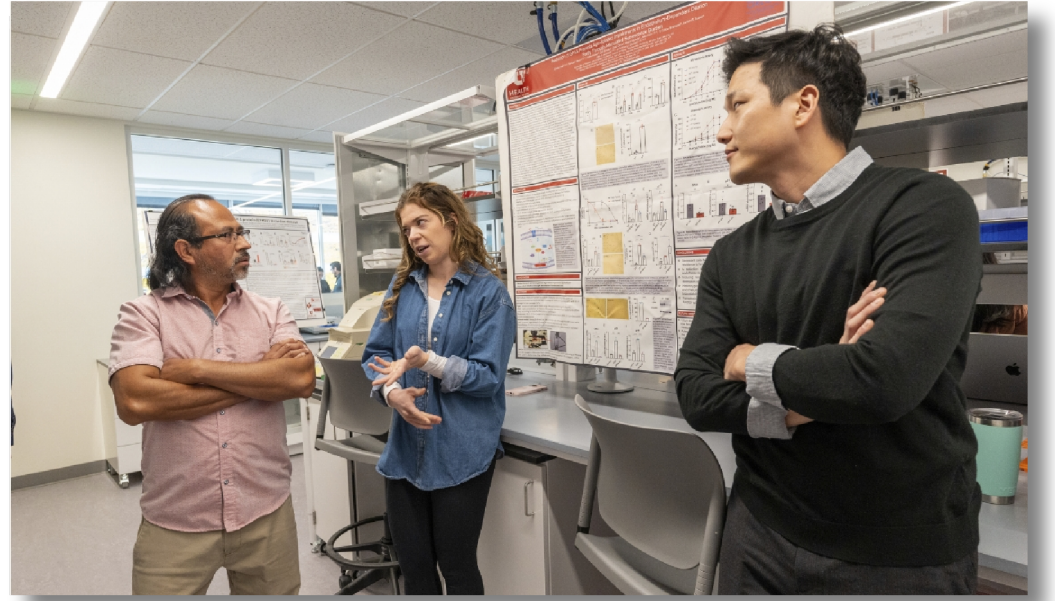
Director, Nora Eccles Harrison Cardiovascular Research and Training Institute
Nora Eccles Harrison Presidential Endowed Chair
Professor of Medicine, Adjunct Professor of Biomedical Engineering

ECCLLES RESEARCH WING



Pictured from left to right: Robin M. Shaw, MD, PhD; President Taylor Randall; Kenneth W. Spitzer, PhD; Lawrence Harrison; Katie Eccles; Spencer F. Eccles; Kathryn Econome, MD; Robert Graham; & Michael Good, MD

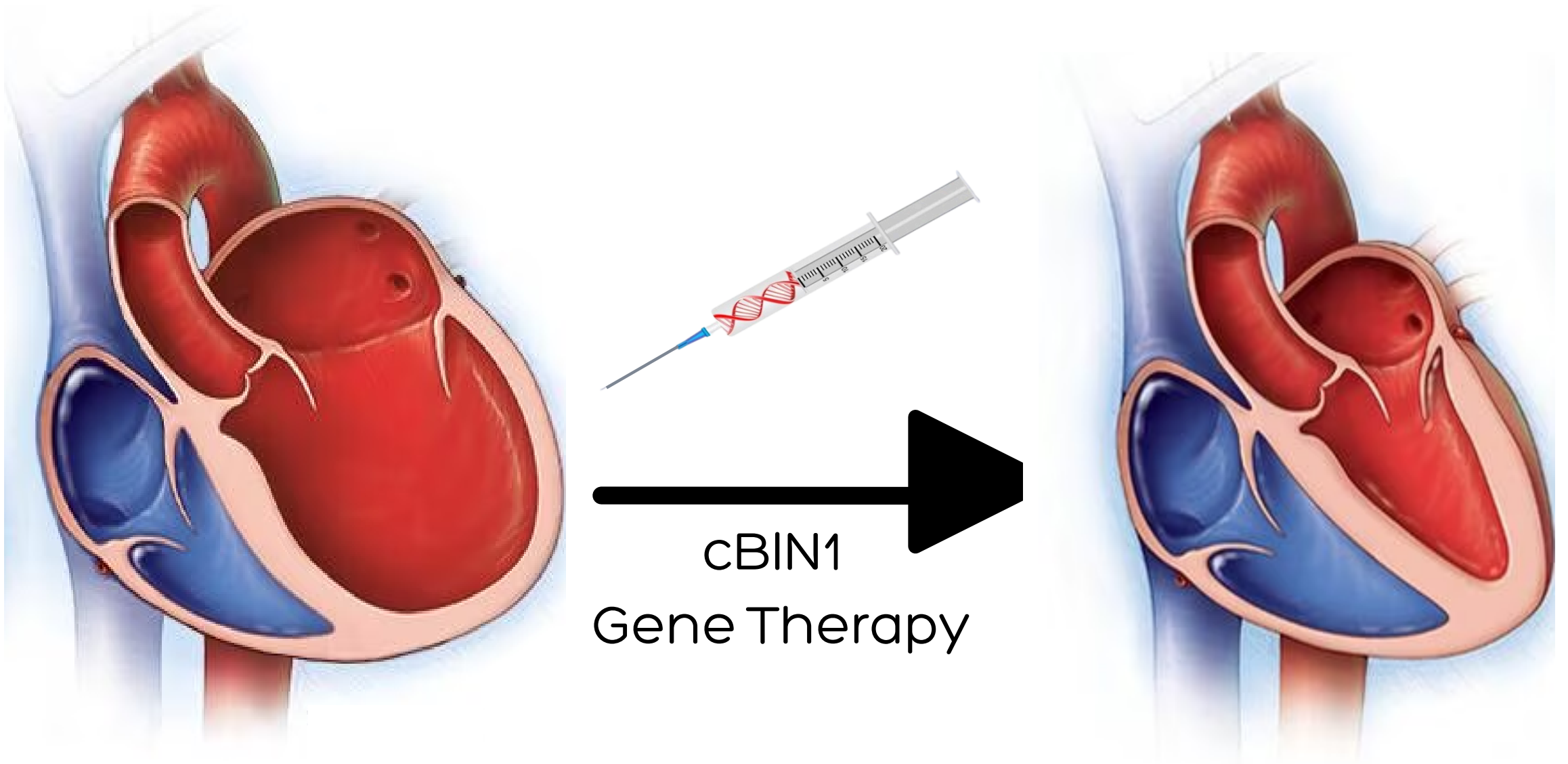
The CVRTI and University of Utah community commemorated the grand opening of our new 10,000 square foot research wing on November 13th, 2023. The space is comprised of new biochemical lab research space, private offices for Investigators, shared trainee workspaces, and a 1,300 square foot freezer farm. The research wing was made possible by the Nora Eccles Treadwell Foundation (NETF), University of Utah President Randall, and Senior Vice President of Health Sciences Dr. Michael Good. The NETF Board Members (Mr. Spencer Eccles, Ms. Katie Eccles, Mr. Lawrence Harrison, Mr. Robert Graham, Dr. Kathryn Econome, and Dr. Kenneth Spitzer) joined President Randall, Dr. Good, and University of Utah dignitaries in celebrating the completion of the new wing.



cBIN1 GENE THERAPY

Failing Heart

Healthy Heart



The CVRTI is on the cusp of changing the paradigm of treating heart failure in the United States and the world over through its cBIN1 gene therapy.

Current medical therapy for heart failure only limits the body's stress response to failing hearts. cBIN1 gene therapy is able to recover failing heart muscle cells and failing hearts, and can reduce the complex systemic syndrome of heart failure to that of a treatable disease.

This past year, we had a successful pre-IND FDA meeting, and have commenced our IND enabling safety and toxicity studies. In parallel, we are manufacturing the gene therapy under clinical grade guidelines. We expect to be able to commence First-in-Human studies in the 2025-2026 academic year.

CVRTI LEADERSHIP



Robin Shaw, MD, PhD
Director, CVRTI

Administration



Tara Hitzeman, MPH
Associate Director

Research



Ademuyiwa
Aromolaran, PhD
Electrophysiology



Dipayan
Chaudhuri, MD, PhD
Metabolism



Stavros Drakos, MD,
PhD
Muscle Biology



Lisa Lesniewski,
PhD
Vascular & Genetics

CVRTI ELECTROPHYSIOLOGY PROGRAM

The CVRTI Electrophysiology Program consists of laboratories that explore the formation of electrical activity in the heart, understanding how the electrical system coordinates every heartbeat, the mechanisms of dangerous arrhythmias (which are disturbances of the electrical system), and how the electrical system can be used as a diagnostic for acute cardiac events.

The Investigators of the program are Ademuyiwa Aromolaran, PhD (Director), Derek Dossdall, PhD, Rob MacLeod, PhD, and Ravi Ranjan, MD, PhD. The Aromolaran Lab focuses on sudden cardiac death and arrhythmias with a goal of arrhythmia therapy to normalize sinus rhythm and help promote longevity and quality of life in patients. To advance this objective, the Aromolaran Lab utilizes individual or multiple combinations of state-of-the-art approaches (including cellular and clinical electrophysiology, optical imaging, and computer simulations), in both preclinical small and large animal models to address fundamental questions in ion channel biology/electrophysiology and how this relates to acquired arrhythmias with implications for the identification and validation of novel druggable targets. The Dossdall Lab uses different mapping techniques to understand arrhythmia mechanisms and also develop novel therapies for failing hearts. The Ranjan Lab has extensive experience in clinical electrophysiology and advanced models of disease to investigate arrhythmia mechanisms. The MacLeod lab focuses on the electrocardiographic mapping of the heart and body surface, cardiac electrophysiology, and computational electrophysiology.



Ademuyiwa Aromolaran, PhD
Director, CVRTI Electrophysiology



Derek Dossdall, PhD
Investigator, CVRTI



Rob Macleod, PhD
Investigator, CVRTI



Ravi Ranjan, MD, PhD
Investigator, CVRTI

CVRTI METABOLISM PROGRAM

Laboratories in the CVRTI Metabolism Program investigate how alterations in bioenergetics contribute to various adult, congenital, and inherited forms of heart failure, using a combination of cutting-edge imaging, proteomic, metabolomic, and electrophysiological techniques.

The program consists of Dipayan Chaudhuri, MD, PhD (Director), Sarah Franklin, PhD, Guillaume Hoareau, DVM, PhD, and Joseph Palatinus, MD, PhD. The Chaudhuri Lab is exploring how altering mitochondrial ion transport may be a potential therapy for heart failure and metabolic diseases. The Franklin Lab's research provides deep insights into how the control of transcription alters the progression of cardiac disease, partly via the control of metabolic pathways. The Hoareau Lab is focused on mitochondria-targeting therapies that prevent hemorrhagic shock and cardiac ischemia-reperfusion injury, particularly in military warfighters. The Palatinus Lab is focused on understanding how metabolic dysfunction triggers inflammation in arrhythmogenic cardiomyopathy, a genetic heart disease with no treatments available, where healthy cardiac tissue is slowly replaced by scar and fat. These groups with complementary skills share a common goal of developing potential therapies by identifying new pathways at the intersection of metabolism and heart failure.



Dipayan Chaudhuri, MD, PhD
Director, CVRTI Metabolism



Sarah Franklin, PhD
Investigator, CVRTI



Guillaume Hoareau, DVM, PhD
Investigator, CVRTI



Joseph Palatinus, MD, PhD
Investigator, CVRTI

CVRTI MUSCLE BIOLOGY PROGRAM

The CVRTI Muscle Biology Program is focused on advancing our understanding of the biology of cardiac muscle in health and disease. The program consists of Stavros Drakos, MD, PhD (Director), TingTing Hong, MD, PhD, and Craig Selzman, MD.

The Drakos Lab is focused on myocardial recovery. To investigate cardiac recovery mechanisms, the lab is using human myocardial tissue from cardiac recovery patients to guide their basic science investigations which include knockout, inhibition or overexpression strategies in vitro and in vivo. With this approach they identified novel therapeutic targets for myocardial recovery in chronic heart failure: MCT4 inhibition, (b) VDAC2 activation, (c) the glucose accessory pathways pentose-phosphate and 1-carbon metabolism and (d) RUNX1 inhibition. The Hong Lab focuses on studying how heart muscle cells organize and remodel in normal and failing hearts. The ultimate research goal is to identify, at the bench, new molecular and cellular targets that can be translated to develop new therapeutic tools for clinical management of heart failure. The Selzman lab focuses on the basic, translational, and clinical aspects of ischemia reperfusion injury as well as the study of mechanisms and treatments for heart failure and myocardial recovery. Several models have been historically utilized to better define the transcriptional regulation and pathologic events associated with pressure overload, ischemic injury, and cardiac remodeling. More recently, attention has been directed at the role of human amniotic products in modifying the inflammatory response and its impact on cardiac remodeling.



Stavros Drakos, MD, PhD
Director, CVRTI Muscle Biology



TingTing Hong, MD, PhD
Investigator, CVRTI



Craig Selzman, MD
Investigator, CVRTI

CVRTI VASCULAR AND GENETICS PROGRAM

The CVRTI Vascular and Genetics Program brings together investigators interested in elucidating genetic influences and vascular mechanisms underlying cardiovascular diseases.

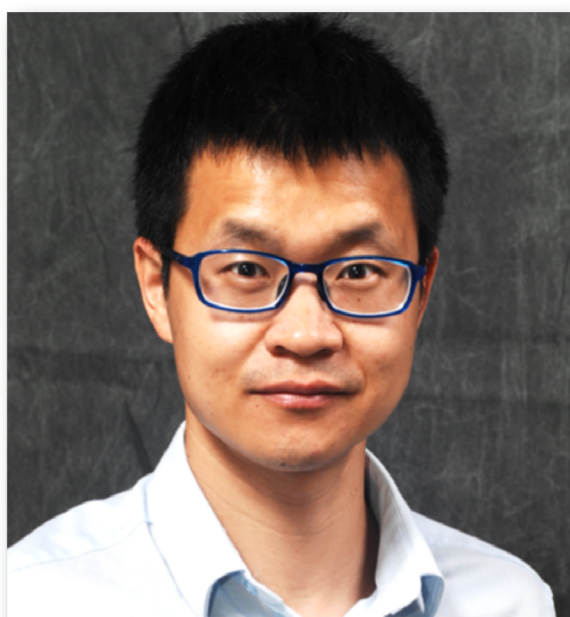
The program consists of Lisa Lesniewski, PhD (Director), Anthony Donato, PhD, Hongchao Guo, PhD, Martin Tristani-Firouzi, MD. Dr. Guo's Lab seeks to advance precision medicine by increasing our understanding of the genetic and epigenetic mechanisms underlying cardiovascular development and disease. Dr. Tristani-Firouzi's Lab utilizes the Utah population database, as well as cellular and zebra fish models to explore the mechanisms of cardiac arrhythmias. Dr. Donato's Lab explores the mechanisms of age-associated vascular dysfunction and seeks to discover novel therapeutics to reduce cardiovascular disease in aged populations. Dr. Lesniewski's Lab seeks to understand the mechanisms underlying both vascular and metabolic dysfunction and disease in aging and obesity.



Lisa Lesniewski, PhD
Director, CVRTI Vascular and Genetics



Anthony Donato, PhD
Investigator, CVRTI



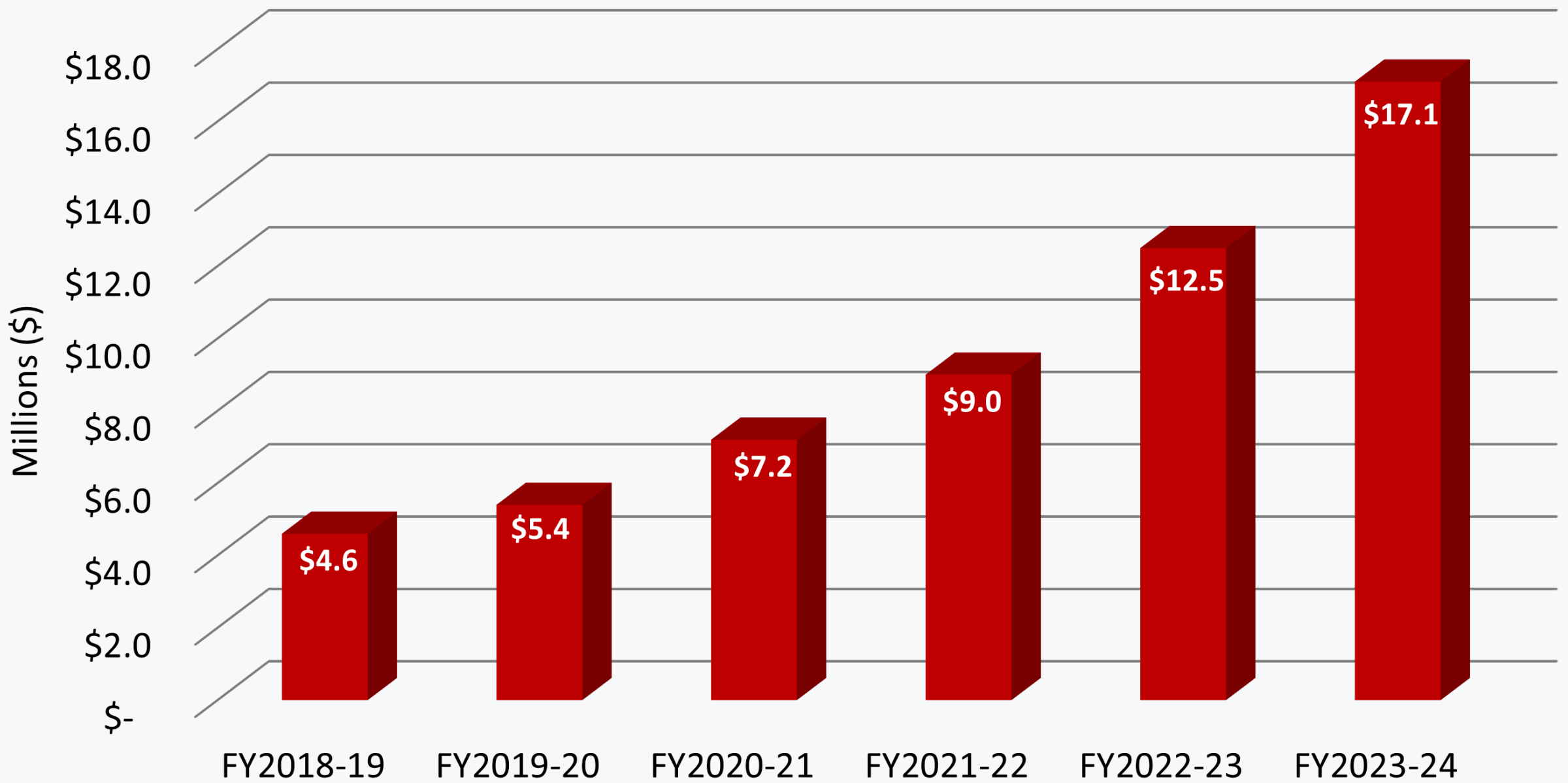
Hongchao Guo, PhD
Investigator, CVRTI



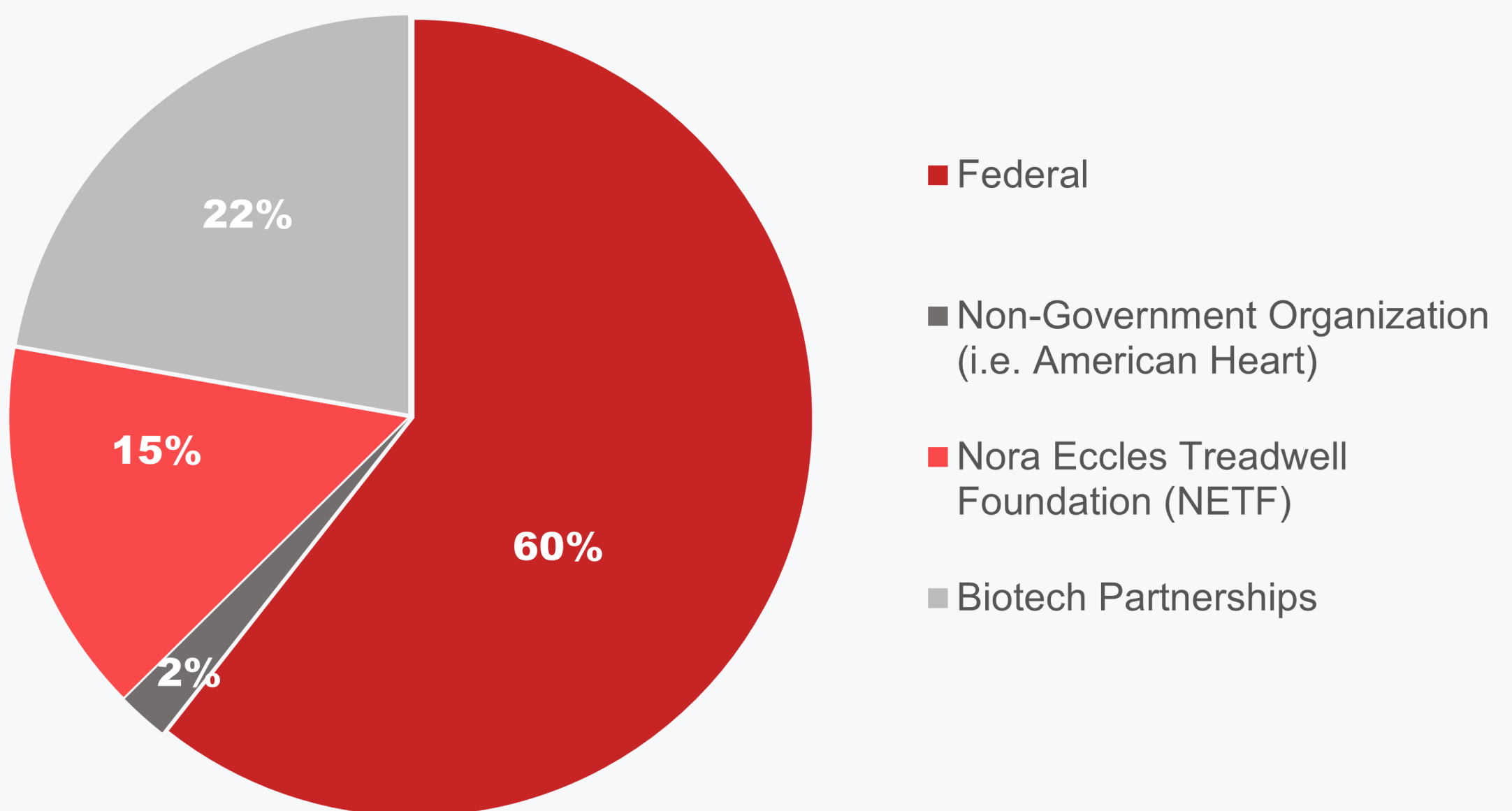
Martin Tristani-Firouzi, MD
Investigator, CVRTI

ANNUAL EXTRAMURAL FUNDING

Annual Grant Income



FY2023-2024 Extramural Funding Agency



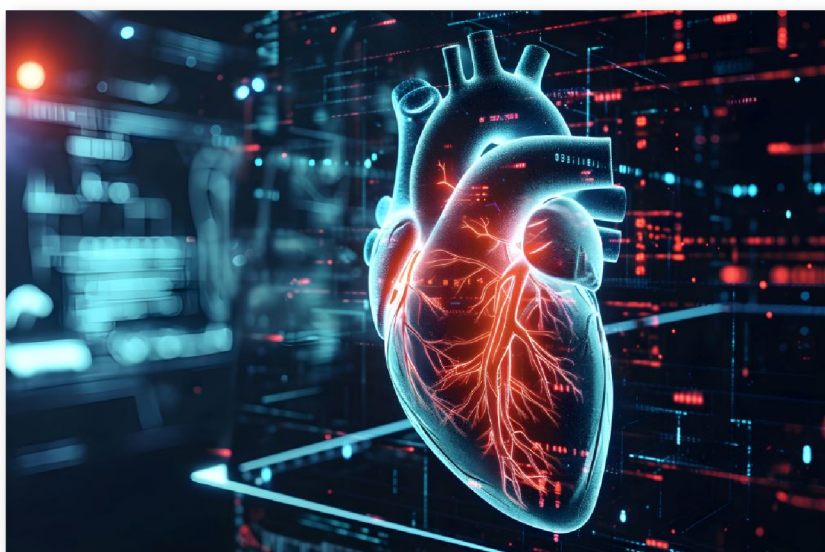
RECENT PUBLICATIONS

Drakos Lab, JAMA Cardiol, 2023

Machine Learning Multicenter Risk Model to Predict Right Ventricular Failure After Mechanical Circulatory Support: The STOP-RVF Score

Late-stage left heart failure often leads to death and affects hundreds of thousands in the U.S. A mechanical heart pump can save lives, but this intervention is also associated with risks, particularly due to the possibility of right heart failure. Predicting which patients are at high risk has been challenging, as past efforts often failed when the created predictive models were tried outside the hospitals that created them. To create a more reliable risk calculator, we used data from 1,125 patients across six health centers, including U of U Health. We applied machine learning to analyze various factors like pre-existing conditions, medications, and demographics. This helped us identify key variables that predict right heart failure after the surgery.

We developed an easy-to-use online tool called STOP-RVF to calculate a patient's risk of right heart failure. This new tool is more accurate and versatile than earlier models. We validated its accuracy by testing it on patients from another hospital system and comparing the predictions to actual outcomes. Many clinical teams are now using this risk calculator (easily accessible on the [CVRTI website](#)) to better prepare and care for patients undergoing implantation of heart pumps.

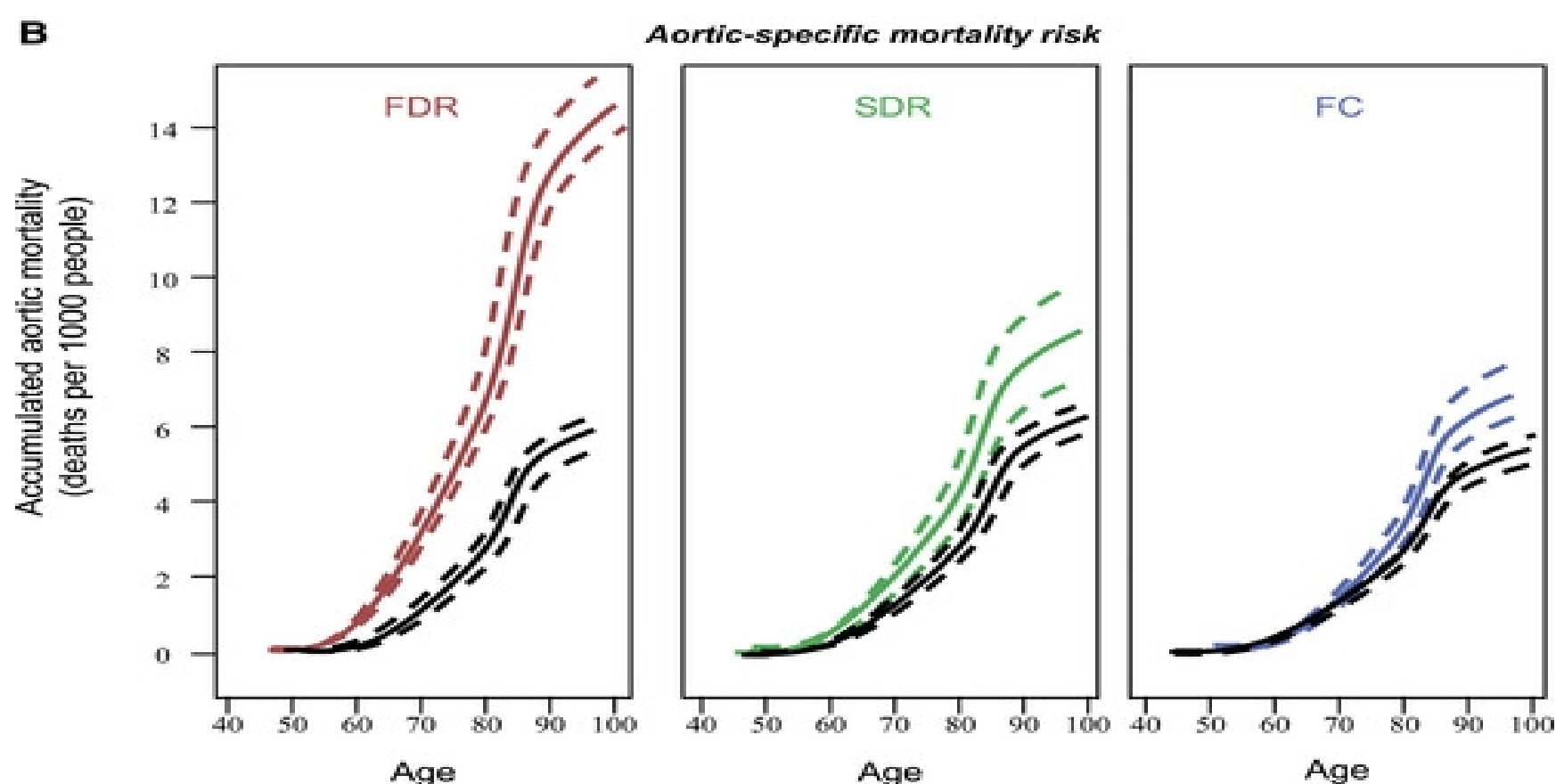


RECENT PUBLICATIONS

Sezman Lab, Circulation, 2023

Familial Associations of Prevalence and Cause-Specific Mortality for Thoracic Aortic Disease and Bicuspid Aortic Valve in a Large-Population Database

Researchers at the University of Utah led by Dr. Jason Glotzbach, used the Utah Population Database to investigate the likelihood that family members of people with bicuspid aortic valve or thoracic aortic disease also have these conditions. Bicuspid aortic valve is the most common congenital cardiovascular abnormality, when the aortic valve has two leaflets rather than the usual three. This can cause a heart murmur and can lead to valve dysfunction, which may require valve replacement. In addition, people with a bicuspid aortic valve have an increased risk of developing dilation of the aortic wall, called an aortic aneurysm, and aortic dissection, which is a life-threatening emergency caused when blood flow creates a tear in the lining of the aortic wall and splits the layers of the aorta.

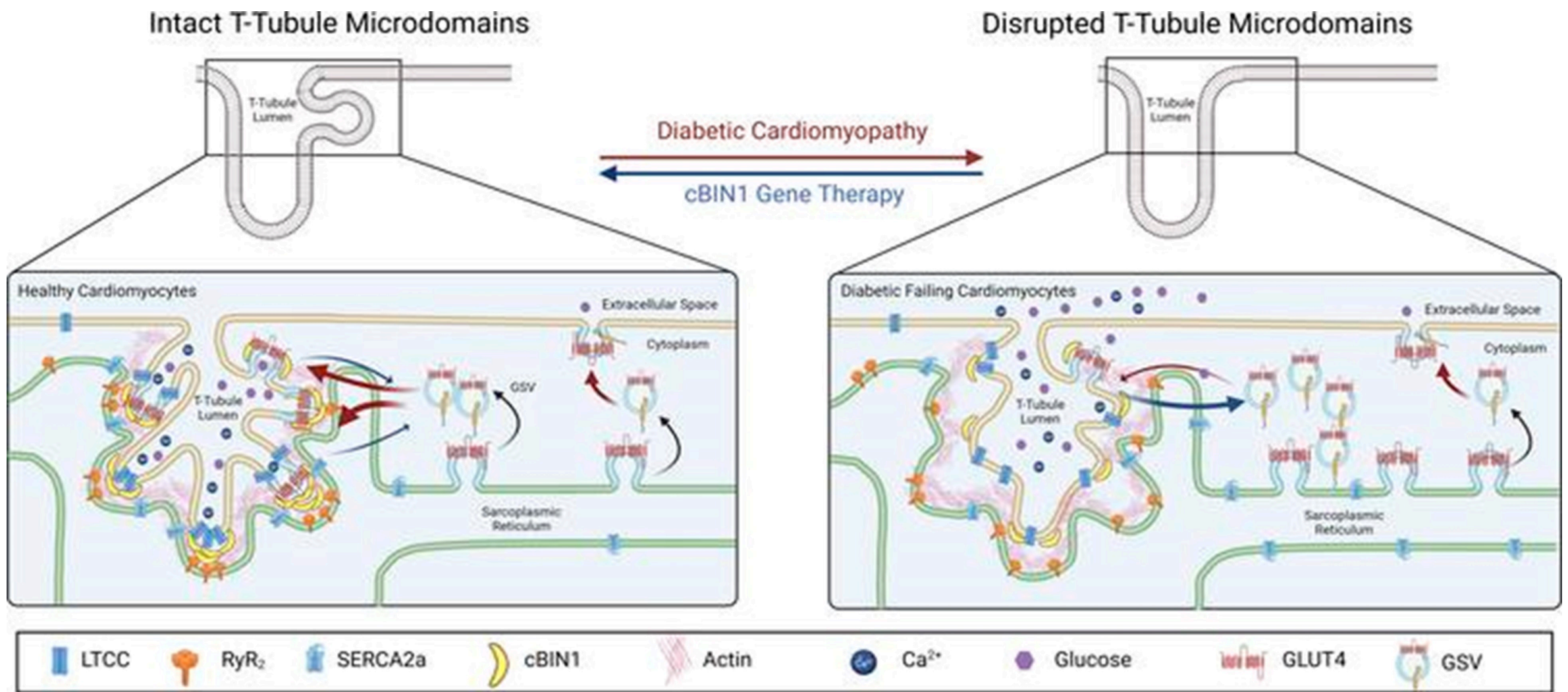


This study provides important new information regarding these conditions. It is the largest study performed to date on this topic, with over 3 million individuals included in the cohort. The research team demonstrated that relatives of patients with bicuspid aortic valve, thoracic aortic aneurysm, and aortic dissection are much more likely to develop these conditions as compared to non-related people in the control group. Importantly, this risk also translated to an increased risk of aortic-specific mortality in relatives with these conditions. While this study is an observational study and must be confirmed with future research, it does provide strong evidence in support of rigorous screening of family members with these conditions. Dr. Glotzbach and his team are currently using the results of this study to inform ongoing research into the genetic causes of these diseases in order to help patients and families better understand their risk. This research will eventually help physicians provide more accurate and effective prognosis and treatment for patients with bicuspid aortic valve and thoracic aortic disease to improve outcomes for these common cardiovascular conditions.

RECENT PUBLICATIONS

Hong Lab, JCI Insight, 2023

Cardiac Gene Therapy Treats Diabetic Cardiomyopathy and Lowers Blood Glucose



In this publication (JCI Insight, 2023, PMID: 37639557), our team reported that a cardiac gene therapy can rescue not only the heart function but also systemic glucose control and insulin sensitivity in a mouse model of obesity and type 2 diabetes. We previously found that a heart muscle cell membrane protein, known as cardiac bridging integrator 1 (cBIN1), is critical to normal heart contraction and relaxation, and that cBIN1 expression is decreased in failing hearts from animals and humans with acquired heart failure. Importantly, our prior research also identified that cBIN1 gene therapy mediated by an adeno-associated virus (AAV)-based approach can rescue heart failure in rodents. In this study, we revealed a novel function of the cBIN1-organized structure in heart muscle cells: mobilization of the cellular machinery required for insulin-stimulated glucose utilization (see below for the Graphic Abstract, JCI Insight, 2023). As a result, the therapeutic effect of cBIN1 gene therapy can be extended to improve systemic glucose control and insulin resistance in patients with type 2 diabetes and diabetic heart failure. Given the increasing global epidemic of diabetes and its major comorbidity heart failure, the proposed cBIN1 gene therapy has a tremendous translational impact by benefiting billions of patients worldwide with insulin-resistant diabetes and diabetic heart failure.

DISSERTATION DEFENSES



SMYD Remarks: Non-Histone Interactions of a Histone Methyltransferase

Andrea Corbin, MS

Aromolaran Lab,
Department of Biomedical Engineering



Protein Phosphatase 2A and Obesity-Linked Atrial Remodeling

Magnus Creed, PhD

Franklin Lab,
Department of Biochemistry



Epigenetics is a Key Mechanism Regulating Cardiac Morphology and Function

Kathryn Davis, PhD

Franklin Lab,
Department of Biochemistry



Epigenetic Modification of Histone H4K20 Methylation in Heart During Disease

Sam Hickenlooper, PhD

Franklin Lab,
Department of Biochemistry

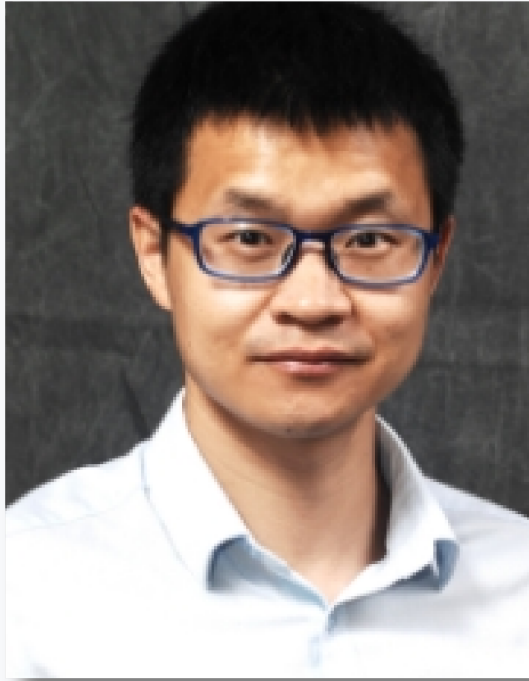


Complex I Assembly Produces Reactive Oxygen Species (ROS), Triggering Baseline Inflammation

Sandra Lee, PhD, MD Candidate

Chaudhuri Lab,
Department of Biochemistry

EARLY CAREER INVESTIGATOR AWARDS & HONORS



Targeting Acetaldehyde Dehydrogenase 2 in Smoking-induced Coronary Artery Disease

Geneen Foundation Award

Hongchao Guo, PhD

Guo Lab



Exogeneous cBIN1 Gene Therapy Rescues Myocardium in Ischemic Heart Failure

AHA 2023 Career Development Award

Muhammad S. Khan, PhD

Dosdall Lab



A Novel Mechanism of Mitochondrial Protein Turnover in Complex I Deficient Mitochondrial Cardiomyopathy

Ruth L. Kirschstein NIH NRSA F30 Predoctoral Fellowship

Sandra Lee, MD, PhD Student

Chaudhuri Lab



Adipocyte Enhancer Binding Protein 1 (AEBP1) as a Potential Therapeutic Target to Combat Cardiac Fibrosis

AHA Predoctoral Fellowship

Thirupura S. Shankar, PhD

Drakos Lab

EARLY CAREER INVESTIGATOR AWARDS & HONORS



*A Novel Regulator of Ca²⁺ Homeostasis and
Arrhythmia Susceptibility*

K01 Award

Natalia Torres, PhD
Tristani-Firouzi Lab



*The Role of Glycosyl Ceramides in Heart Failure
and Recovery*

K08 Award

Eleni Tseliou, MD, PhD
Tseliou-Drakos Labs



*Effects of Cardiac Bridging Integrator 1 Gene
Therapy on Atrial Remodeling in Canine
Ischemic Cardiomyopathy*

Eli S. Gang Most Innovative Abstract Award

Kyoichiro Yazaki, MD, PhD
Doddall Lab

**NIH RUTH L. KIRSCHSTEIN
CARDIOVASCULAR TRAINING GRANT
(T32) FELLOWSHIP
2023-2024**



Computational Modeling of Atypical Left Atrial Flutter to Improve Clinical Outcomes

Jake Bergquist, PhD

Ranjan Lab



Interactions Between Fetal Cerebrovascular Autoregulation, Neonatal Neurobehavior, and Genetic Variants in Critical Congenital Heart Disease

Marlayna Despres, MD

Hogan and Tristani-Firouzi Labs



The Role of Hypertension in Heart Failure with Preserved Ejection Fraction (HFpEF) in Veterans with Type 2 Diabetes Mellitus and Chronic Kidney Disease

Sydney Hartsell, MD, MPH

Beddhu Lab

T32 FELLOWSHIP

Global Myocardial Ischemia and the Protective Capacity of Human Amniotic Fluid

Ian Nickel, MD

Selzman Lab



Predicting and Understanding Myocardial Recovery in Advanced Heart Failure Patients Undergoing Mechanical Unloading and Circulatory Support

Christos Kyriakopoulos, MD

Drakos Lab



Pyruvate & Lactate Metabolism in Myocardial Ischemic Reperfusion Injury

Joseph R. Visker, PhD, RCEP

Drakos Lab



Investigating the Cellular Response to Changes in Phospholipid Saturation

Sara Wong, PhD

Hughes Lab



RUUTES: SUMMER UNDERGRADUATE RESEARCH EXPERIENCE (SURE) FOR MINORITIES



Sarah Franklin, PhD



Ademuyiwa Aromolaran, PhD

Drs. Sarah Franklin and Ademuyiwa Aromolaran are Co-Investigators of CVRTI's five-year NIH R25 Research Education Award: Summer Undergraduate Research Experience (SURE) for Minorities, affiliated with The Rural & Underserved Utah Training Experience (RUUTE) at the University of Utah. The program is a 10-week research opportunity for minority undergraduate students from rural and underserved areas throughout Utah, Idaho, Wyoming, and Montana. RUUTE provides opportunities for students to work on projects emphasizing rural and underserved health. Dr. Franklin is Assistant Director of RUUTE. Students conclude their experience by presenting at the University of Utah Undergraduates Research Symposium.

Summer 2023



Click [here](#) to learn more about SURE, RUUTE, and their lead supporters!

2023/24 CVRTI SEMINAR SERIES

CVRTI was honored to host several extraordinary external speakers for our 2023-2024 Seminar Series. Watch past seminars on our [YouTube](#) channel and check out CVRTI's [website](#) to stay up to date on upcoming speakers and events for the 2024-2025 year.

- Nipavan Chiamvimonvat, MD, University of California, Davis
- Adrian Hernandez, MD, MHS, Duke University
- Priscilla Hsue, MD, University of California, San Francisco
- Fady I. Malik, MD, PhD, Cytokinetics, University of California, San Francisco
- Eduardo Marbán, MD, PhD, Cedars-Sinai Medical Center
- Zian H. Tseng, MD, MAS, FHRS, University of California, San Francisco



CVRTI Investigators enjoying dinner with Seminar Speaker Eduardo Marbán, MD, PhD

UTAH CARDIAC RECOVERY SYMPOSIUM (U-CARS)

2024 Keynote Speaker:

Eric N. Olson, PhD



Annie and Willie Nelson Professorship in Stem Cell Research
Pogue Distinguished Chair in Research on Cardiac Birth Defects
Robert A. Welch Distinguished Chair in Science
University of Texas Southwestern Medical Center

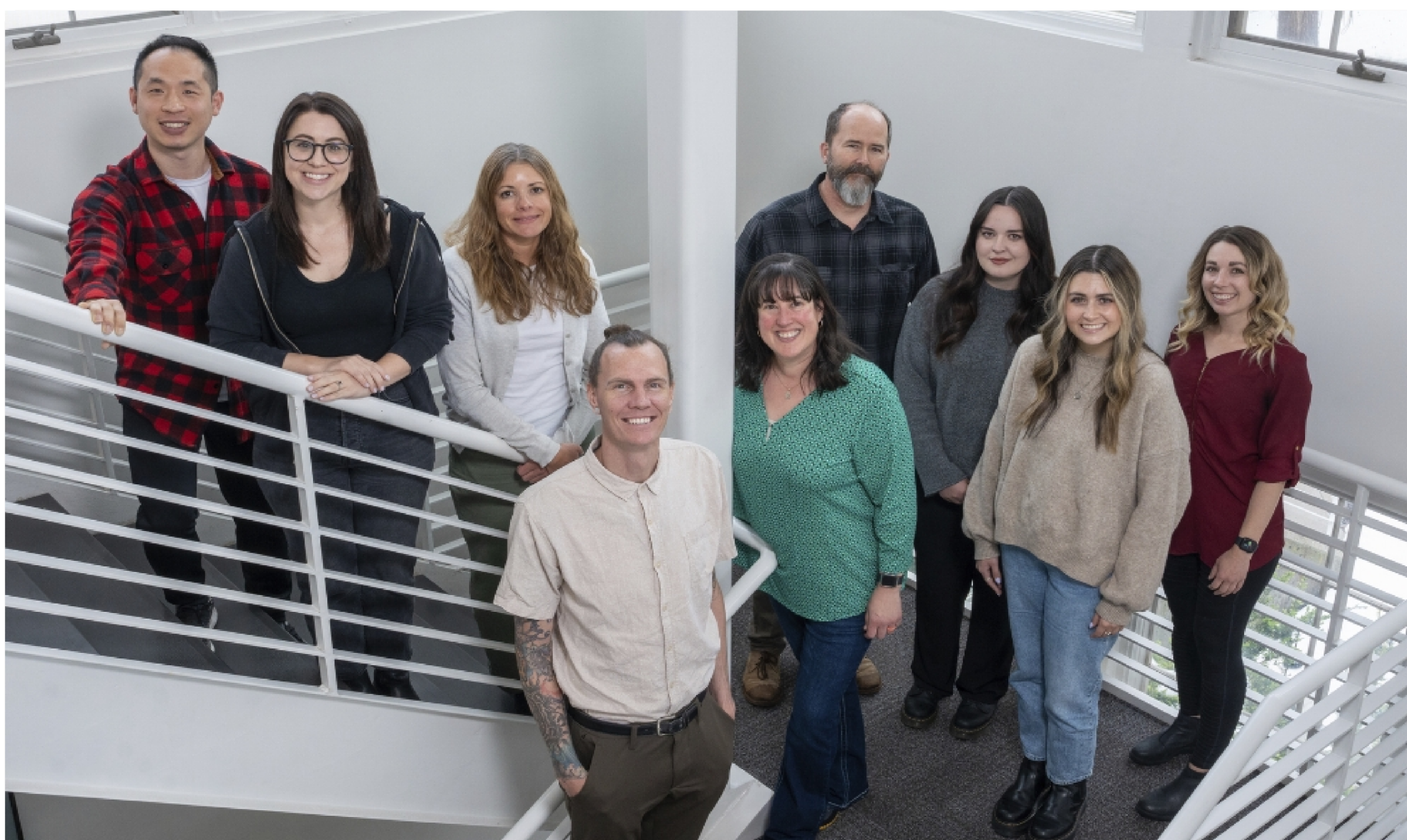
The symposium planning committee had the honor of hosting the 12th annual Utah Cardiac Recovery Symposium (U-CARS) in February 2024. The U-CARS symposium was held in person with a livestream option to over 800 registered participants.

CLICK [HERE](#) TO VIEW THE 2024
UCARS Virtual Exhibit Hall

Save the Date! The 13th Annual Utah Cardiac Recovery
Symposium will be held February 20th & 21st, 2025

MEET THE CVRTI CORE STAFF

The CVRTI Core Staff is the operational backbone of the CVRTI, contributing to our productivity and uniquely attractive research environment. It is made up of outstanding individuals, including a facilities specialist who supports the research laboratories and coordinates larger projects with The University of Utah's facilities team; a laboratory specialist, dedicated to the management of CVRTI's operating room, and an IT specialist. Additionally, we have six individuals responsible for administration including pre-award and post-award grants management, accounting, human resources, and coordination of seminar series and events.



From top left:

Haonan Yang, MS- IT Specialist | Tara Hitzeman, MPH- Associate Director
Kat Cannon- Administrative Manager | Coby Leavett- Lab Specialist
Nuria Anderson- Executive Assistant | Greg Brown- Facilities Specialist
Anja Petrovic- Grants Specialist | Megan Woodard- Administrative Assistant
Stefanie Lehman- Administrative Project Specialist

Learn more about the Core Staff [here](#)

CVRTI EVENTS

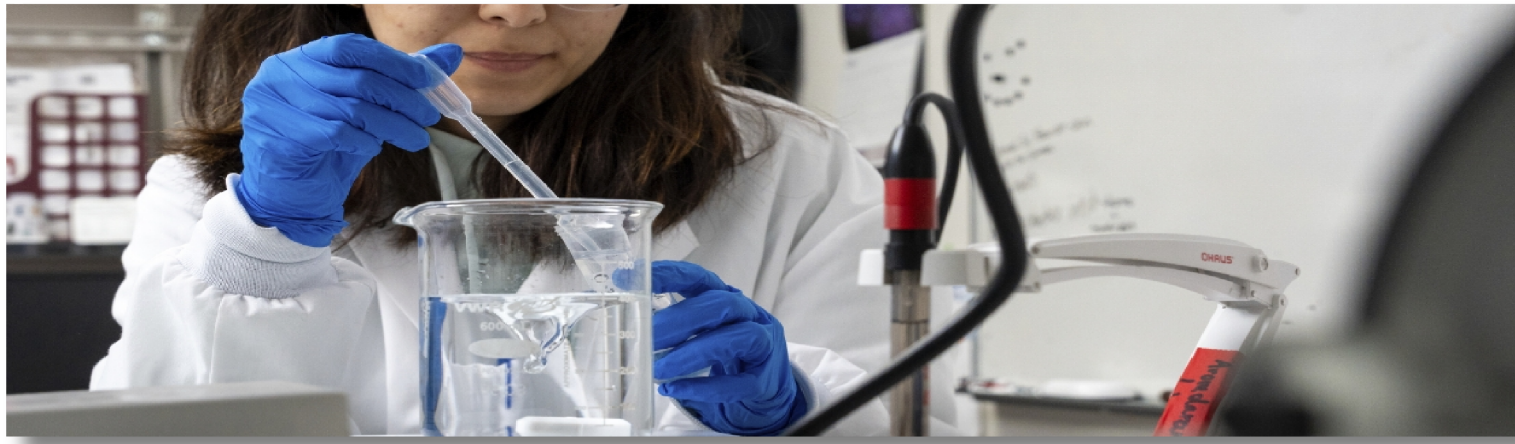
CVRTI community enjoying the annual holiday party



Faculty and staff participating in the Annual American Heart Association Walk



CAREERS AT CVRTI



WE'RE HIRING!

To explore specific opportunities, click [here](#). For additional inquiries, please contact CVRTI's Administrative Manager, Kat Cannon at kat.cannon@utah.edu.



THANK YOU!

These word clouds highlight the entities and individuals who make the CVRTI possible.

Faculty Home Departments

Pharmacology & Toxicology Pediatrics
Internal Medicine
Emergency Medicine **Surgery** Biomedical Engineering

Extramural Funding

Biosense Webster
Geneen Foundation **Department of Defense** Novartis
American Heart Association
National Institutes Of Health
Tikkunlev Therapeutics **Nora Eccles Treadwell Foundation**

Birthplace of Our Research Community

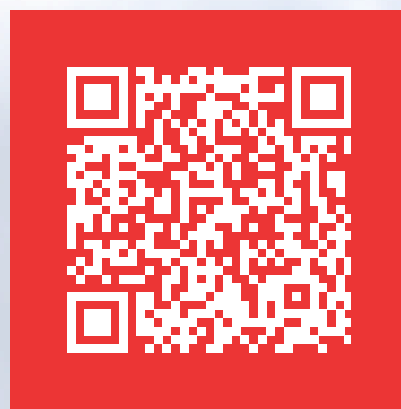
Australia Peru **England** Cuba Bosnia Philippines
Greece Mexico **Reunion** Singapore Lebanon Iran Canada Argentina
United States Of America Korea
South Africa Nigeria **China** Suriname Japan Ghana Vietnam
Colombia Poland **India** Pakistan Thailand Turkey
Tanzania

FIND & FOLLOW US ONLINE

Website: <https://cvrti.utah.edu/>

X (Twitter): [@NEH_CVRTI](https://twitter.com/NEH_CVRTI)

YouTube: <https://tinyurl.com/YouTubeCVRTI>



NORA ECCLES HARRISON
CARDIOVASCULAR RESEARCH
& TRAINING INSTITUTE

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