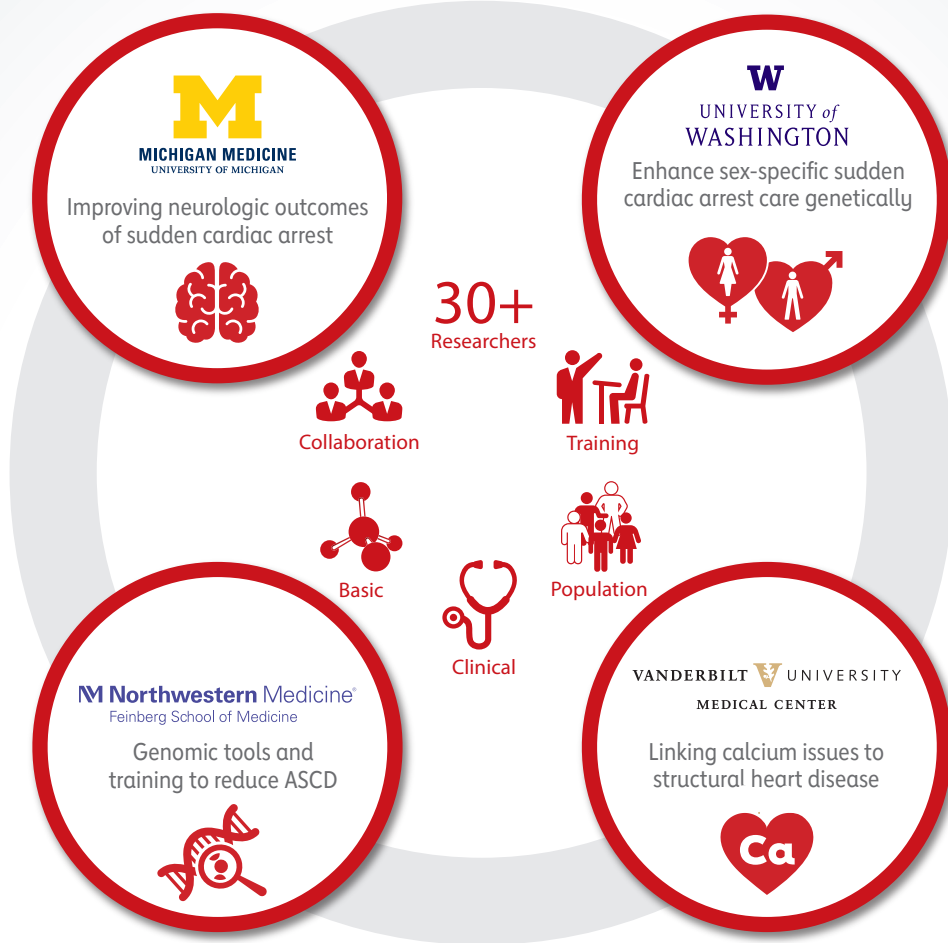




ARRHYTHMIAS AND SUDDEN CARDIAC DEATH

AHA'S INVESTMENT 2019-2023

\$15 MILLION IN RESEARCH | **\$3.7 MILLION** TO EACH CENTER

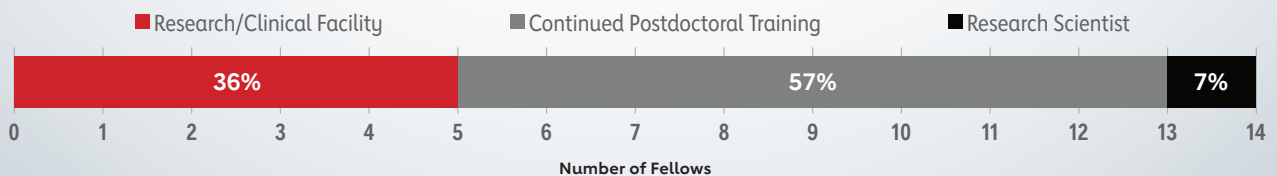


BY THE NUMBERS

- 31 subsequent grants totaling \$71.32M, one of which was awarded to a network fellow
- 40 related publications to date, including articles in *Journal of the American Heart Association*, *Circulation: Genomic and Precision Medicine*, and *JAMA Cardiology*
- Collaboration and co-authorship between awardees more than doubled over the duration of the award
- One patent application

TRAINING A NEW GENERATION OF MULTIDISCIPLINARY INVESTIGATORS

Over 90% of postdoctoral fellows transitioned into faculty positions or continued their fellowship for more advanced training.



NOTABLE PUBLICATIONS



The Selective RyR2 Inhibitor Ent-Verticilide Suppresses Atrial Fibrillation Susceptibility caused by Pitx2 Deficiency, *Journal of Molecular and Cellular Cardiology*, July 2023

Atrial fibrillation (AF) is strongly linked to genetic variants near the PITX2 gene, and Pitx2-deficient mice show increased AF susceptibility due to abnormal calcium handling. The results suggest that RyR2 hyperactivity causes abnormal calcium handling, contributing to AF in Pitx2-deficient hearts. Targeting RyR2 may offer a mechanism-based therapeutic approach for treating AF associated with PITX2 genetic variants.



Genomic Autopsy of Sudden Deaths in Young Individuals, *JAMA Cardiology*, November 2021

This study used whole-genome sequencing to investigate sudden deaths in young people and found that about 13% had harmful genetic variants linked to heart rhythm or heart muscle conditions. Many of these genetic changes were also seen in family members, though not all showed symptoms, suggesting that multiple genes may work together to increase risk. The findings highlight the value of genetic testing in understanding sudden death and identifying at-risk family members.

Rapid Treatment with Intramuscular Magnesium Sulfate During Cardiopulmonary Resuscitation Does Not Provide Neuroprotection Following Cardiac Arrest, *Molecular Neurobiology*, March 2022

Researchers tested whether giving a single dose of intramuscular magnesium sulfate during CPR could help protect the brain after cardiac arrest. The treatment successfully elevated blood magnesium levels and improved short-term (24-hour) survival. While it did not lead to improvements in long-term survival or neurological outcomes on its own, the results highlight the potential of magnesium as part of a broader treatment approach. Future research may benefit from examining repeated dosing or combining magnesium with therapies such as targeted temperature management to enhance brain protection and recovery.



Sex Hormones and Repolarization Dynamics during the Menstrual Cycle in Women with Congenital Long QT Syndrome, *Heart Rhythm*, May 2022

This study found that sex hormone levels during the menstrual cycle can influence heart rhythm patterns in women with certain types of congenital long QT syndrome (LQTS), especially type 2. In these women, changes in hormone levels, particularly progesterone and estradiol were linked to changes in ECG readings that may increase the risk of dangerous heart rhythms. These findings suggest that hormone fluctuations may play a role in the increased cardiac risk some women with LQTS face after puberty.

NOTABLE COLLABORATIONS

- Core partnership among the investigators at Northwestern with Vanderbilt University and the University of Utah led to a co-authored publication in *Genome Medicine* to better characterize genetic variation and the impact of epilepsy in sudden death in the young.
- University of Michigan fostered a strong, sustained collaboration with the Washtenaw-Livingston County Out-of-Hospital Cardiac Arrest (OHCA) Learning Health Community to create the Michigan Resuscitation Innovation and Science Enterprise to prevent brain damage and improve neurologic outcomes after sudden cardiac arrest. An important outcome was the creation of the HeartSafe Home program that works closely with local EMS leadership and key stakeholders to increase awareness and improve response to in-home cardiac arrests.
- Collaboration on the role of ryanodine receptors (RyR2) in various cardiac models at Vanderbilt University have led to several joint publications, including reports in the *Journal of Molecular and Cellular Cardiology*, *bioRxiv*, *ACS Chemical Biology*, *The Annual Review of Pharmacology and Toxicology*, *Basic Research in Cardiology*, etc.
- The University of Washington and the University of Michigan collaborated on multiple research projects to improve cardiac arrest resuscitation and deepen understanding of resuscitation science. Led by Dr. Amanda Missel, a postdoctoral fellow at the University of Michigan, new findings published in *Resuscitation* demonstrated that bystander physical limitations can delay CPR and significantly affect patient outcomes. Researchers continued their collaboration using advanced ECG waveform analysis to study the physiological effects of early bystander CPR, gaining key insights into how it improves survival by supporting heart function during cardiac arrest. These additional efforts resulted in the publication "Insights From the Ventricular Fibrillation Waveform Into the Mechanism of Survival Benefit From Bystander Cardiopulmonary Resuscitation" in the *Journal of the American Heart Association*.