# Heart Failure Translational Research Laboratory

## History

The Heart Failure Translational Research Laboratory at Houston Methodist Hospital was founded in the 1990s by an endowment from Eugene and Judith Campbell to fund research in the field of Heart Failure and Cardiac Transplantation. Dr. Guillermo Torre-Amione, Director of the Laboratory, has continuously been a champion for this program since its inception, enabling this program to service as both a training ground for postdoctoral fellows while providing cutting edge research in heart failure and cardiac transplantation. Dr. Keith Youker, Associate Professor, joined in 2006 and has been providing day to day oversight of the scientific studies and mentorship for the research fellows.

Drs. Torre and Youker created a mouse model that provides a unique opportunity to study heart failure focused in the setting of heart failure without heart attacks. Fifty percent of Americans who have congestive heart failure have it without any myocardial infarction (heart attack issues) and the mechanisms leading to and progressing to worse symptoms are poorly understood. They have also established a world class repository of human heart tissue (hearts that are taken out during a heart transplant) from patients who have congestive heart failure providing a mechanism to expand studies from mice to humans. Creating such logistics that expand from research in mice to opportunities to work with human samples is a unique strength of this laboratory.

The culture of our research has the sole objective of identifying ways to implement new technologies and treatments to benefit the health of patients as early as feasible. With the expansion of the division of heart failure in the last few years, the laboratory has now become a house for three more heart failure faculty members (listed below) pursuing their translational research careers. With this growth and expansion, Dr. Arvind Bhimaraj took helm as the Co-Director of the laboratory to provide an ongoing vision and expansion of the operations of the laboratory. Dr. Bhimaraj, along with Dr. Youker, has added a biorepository of samples (heart tissue and blood) from heart transplant patients to promote research in this area. With the addition of new faculty members, the research focus has in fact expanded into various areas of heart failure as listed below.

The laboratory is designed to provide a medium for collaboration with the clinical faculty within the division to test new hypotheses and create an arena for new mechanistic, therapeutic and innovative discovery focused on treating patients with cardiac disorders. Our cutting edge technology allows us to perform everything from physiological measurements to cell culture to gene chips to nanotechnology. The Heart Failure Translational Research Laboratory actively collaborates with many researchers within the Houston Methodist Research Institute and provides the infrastructure to aid the research studies.

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## Faculty Members & Areas of Focus

**Dr. Guillermo Torre-Amione** is the Director of the Heart Failure Research Laboratory at Houston Methodist, and is a world renowned researcher examining the mechanisms of immune activation and inflammation in congestive heart failure. With his background doctorate in immunology, he is uniquely positioned to explore this innovative mechanism contributing to heart failure. He has proposed, validated and conducted mice experiments showing that B-cells (certain kinds of white blood cells in the blood), which were unsuspected in the past, contribute significantly to causing fibrosis (scarring) in the heart. Dr. Torre-Amione has also led the first two FDA-approved trials exploring the impact of suppressing T-cells (a different kind of white blood cell). Currently, he is exploring novel strategies of combining nanotechnology to create a vaccine to prevent the progression in heart failure.

**Dr. Arvind Bhimaraj** is the Co – Director of the Heart Failure Research Laboratory. He has been in this position since 2016 and has taken up a leadership role in guiding the trajectory of the laboratory to promote a collaborative translational work for all the laboratory faculty members. He also presides over the weekly laboratory meeting and guides the research fellows on their work. His area of focus is anti-fibrotic mechanisms and how to promote recovery of a heart. He has developed a unique mouse model to study such mechanisms. He actively collaborates with researchers in the institute of nanotechnology and regenerative medicine with a focus to create a nano-RNA therapy to promote recovery (healing) of damaged hearts. He is also working actively to explore similar mechanisms in heart tissue (biopsy sample) from heart transplant patients to identify mechanisms of fibrosis and hypertrophy (damage) in these hearts in an effort to create a genetic test to identify these mechanisms from blood tests. He actively collaborates with researchers in the institute of informatics at the Houston Methodist Research Institute. His ultimate goal in this area is to identify mechanisms and create treatment strategies to decrease damage to a transplanted heart and hence prolong longevity in this population.

**Dr. Barry H. Trachtenberg** is a cardiologist specializing in heart failure and cardiac transplantation. He is also the director of the Michael Debakey Cardiology Associates Cardio-Oncology program, an evolving field devoted to prevention and management of cardiovascular complications of cancer therapies such as chemotherapy and radiation.

He is conducting research studying novel genomic biomarkers, nanopeptide biomarkers, and wearable fitness devices to detect heart damage earlier, and thus prevent clinical heart failure in patients receiving life-saving chemotherapy. In addition, he is interested in the genetic predisposition of chemotherapy induced cardiomyopathy, as well as other types of cardiomyopathy. He has contributed to many publications related to advanced heart failure, cardiac transplantation, regenerative therapies, and ventricular assist devices. Dr. Trachtenberg is a member of the American Heart Association, the International Society for Heart and Lung Transplantation Association, Heart Failure Society of America, and the International CardiOncology Society of North America.

**Dr. Ashrith Guha** is cardiologist with a specialization in the care of patients with advanced heart failure, mechanical circulatory support, and cardiac transplants. He has a special interest to treat patients with pulmonary hypertension and has used this passion in the research laboratory to develop a nanoparticle delivery system for treatment of pulmonary arterial hypertension. Using a rapamycin (a medication that decreases arterial wall thickening) laden polymeric nanoparticle, it was successfully demonstrated in mice (a monocrotaline model of pulmonary arterial hypertension) to have a beneficial effect on pulmonary artery changes and have less toxic side effects. Using this context, he is currently collaborating with nano-researchers to develop nanoparticles for mRNA delivery for treatment of pulmonary hypertension. He is also studying pulmonary vascular remodeling in our heart failure model and the role of hyaluron in the development of pulmonary hypertension in heart failure patients to better describe these mechanisms. In line with this area of interest, he also focuses on the right ventricle, which is the chamber that pumps blood into the pulmonary vasculature and therefore often gets effected by high pulmonary pressures. A unique pathway alternate, polyadenylation, can affect the genetic material in a cell and hence cause disease. Dr. Guha is studying the contribution of this mechanism in the right ventricle when there is pulmonary hypertension apart from heart failure. In this area of work, he has secured funding from the National Institute of Health in collaboration with Dr. Karmouty-Quintana's group at UT –Houston. Apart from working with the mice model, he has established collections of serum and heart tissue samples in patients with pulmonary hypertension and heart failure.

**Dr. Keith Youker** earned his Ph.D. in Cardiovascular Sciences from Baylor College of Medicine and was the first graduate from this program. The program used a broad knowledge approach to training including course work from medical school, graduate school, and cardiovascular core courses designed for basic scientists to work in clinical cardiovascular research. His dissertation work earned him a nomination for the Sigma Xi "Excellence in Science Dissertation Award." Since graduation, Dr. Youker has been a faculty member in both the departments of Medicine and Surgery at Baylor College

of Medicine prior to joining Houston Methodist Hospital. Dr. Youker's primary focus has been in heart failure with a particular interest in inflammation and its role in the progression of heart failure. Dr. Youker prefers a hands-on approach in the laboratory and is expert in many areas from electron microscopy to molecular biology techniques and has earned a reputation of excellence in cardiovascular immunopathology research. He has trained over 20 postdoctoral students in laboratory methods and the scientific method of research and has published over 90 peer-reviewed articles in the cardiovascular field. His current laboratory Postdoctoral Trainees include: Ana Sofia Cruz Solbes, MD, and Areeba Ali, MD.

## Current & Past Research Trainees:

Areeba Ali, MBBS

Javier Amione Guerra, MBBS

Raquel Araujo Gutierrez, MBBS

Ana Sofia Cruz Solbes, MBBS

Andrea Cordero Reyes, MBBS

Cesar Uribe, MBBS