THE NEXT FIRST
IN CARDIOVASCULAR DISCOVERY

2020 Annual Report
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MAKING WOMEN’S CARDIOVASCULAR DISEASE A PRIORITY
LETTER FROM THE BOARD CHAIRMAN

Eric D. Wade
Chairman, THI Board of Trustees
For THI, 2020 proved to be a year marked by both the highest of highs and the lowest of lows. To mention one aspect on both sides of the spectrum, in October, the Texas Heart Institute successfully launched its new Texas Heart Medical Group, which now serves as a home base for twelve outstanding cardiologists with plans for future expansion. This highly anticipated debut for THMG followed the passing of Dr. James T. Willerson just a few weeks prior in September.

Dr. Willerson will be remembered as a man who lived an extraordinary life defined by curiosity and passion for the study of the human heart and its myriad complexities. In his memory, THI established the James T. Willerson, MD Editor’s Choice Awards to acknowledge and reward one physician, one fellow or resident in-training, and one researcher who publish the best original research article in the categories of cardiology and cardiovascular surgery in the Texas Heart Institute Journal. The Texas Heart Institute Journal will also become the official publication for the Texas Heart Institute Cardiac Society and the Denton A. Cooley Cardiovascular Surgical Society, as well as Texas Heart Institute’s alumni members from the Texas Children’s Pediatric Cardiology Fellowship and Anesthesiology Fellowship and the Texas Heart Institute School of Perfusion Technology Training Programs.

In a year when collaboration seemed impossible, our teams engineered new ways to work together, and internal and external partnerships reached new heights. Our researchers used small molecule drugs, gene therapy, and stem cell technologies to target an assortment of cardiovascular diseases. A promising technology invented by our scientists, which could one day enhance the effectiveness of vaccines, crossed a milestone by entering human clinical trials. The platform could be an important approach to enhancing the effectiveness of vaccines to infections like influenza, which is linked to greater risk of heart attacks.

Looking ahead to 2021, we envision a year of forward momentum. Technologies discovered at THI will be used to generate new funding mechanisms to sustain operations, attract talent and grow our portfolio of translational cardiovascular research aimed to help patients with widely known unmet needs in their cardiovascular care. From effective treatments and smaller, less invasive devices for treating patients with heart failure and life-threatening arrhythmias to molecular-based drugs for enhancing therapeutics, THI is pushing the boundaries of discovery to tackle the most challenging problems in cardiovascular medicine today.

I look forward to our community returning to in-person collaboration and celebration of this great Institute’s achievements with real hugs and handshakes. We are deeply grateful for the decades of support from our local, national, and global community. Our foundation has never been stronger as we remain steadfast in our collective commitment to push the boundaries of discovery for the millions of patients suffering from cardiovascular disease around the world today.
IN MEMORIAM

JAMES T. WILLERSON, M.D.
(1939-2020)

Dr. Willerson’s indelible legacy will live on in perpetuity through his countless achievements in cardiovascular research and philanthropy, the passion that he poured into everything he accomplished throughout his life, and the immeasurable impact he made on the evolution of a world-renowned organization recognized in all corners of the globe. Dr. Willerson lived a tremendous life defined by curiosity and an eternally burning flame for the study of the human heart and its myriad complexities.
The Texas Heart Medical Group (THMG) was launched in 2020 and represents a significant step into the future for the institution, which has played a critical role in major cardiovascular breakthroughs since its founding in 1962 by legendary heart surgeon Dr. Denton Cooley.

In October of this past year, Texas Heart Institute once again raised the bar following the long-planned official debut of Texas Heart Medical Group (THMG). THMG represents a significant step into the future for the institution, which has played a critical role in major cardiovascular breakthroughs since its founding in 1962 by legendary heart surgeon Dr. Denton Cooley.

When Dr. Cooley established THI nearly 60 years ago, his mission statement for the non-profit at Texas Medical Center was simultaneously simple and bold: namely, to reduce the devastating toll of cardiovascular disease through innovative programs in research, education, and improved patient care. Texas Heart Institute is now breathing new life into Dr. Cooley’s original vision as the Institute has set into motion its clinical practice, which specializes in cardiovascular care with the singular mission to provide the highest-quality medical care in a sophisticated and welcoming patient-oriented atmosphere.

Texas Heart Medical Group serves as a home base for twelve outstanding cardiologists who are also leaders in the subspecialty fields of Cardiac Imaging, Interventional Cardiology, Peripheral Vascular Disease, and Electrophysiology. Texas Heart Medical Group
embodies the totality of Texas Heart Institute as a fully integrated clinical cardiology practice encompassing the areas of education, research, and direct patient care.

“October 1, 2020, marked an exciting day in the history of the Texas Heart Institute. With the launch of Texas Heart Medical Group, THI ushered in a dynamic new era by venturing into the clinical care arena,” stated Texas Heart Institute Board Chair Eric Wade. He added, “Texas Heart Medical Group has tapped into Texas Heart Institute’s long-standing and relentless pursuit of excellence that began with historic breakthroughs under Dr. Cooley’s leadership and vision. I am confident in saying that he would be proud of and excited for this new chapter in THI’s dramatic story.”

To date, Texas Heart Institute has focused solely on research and education in affiliation with St. Luke’s Episcopal Health (now CHI St. Luke’s Health – Baylor St. Luke’s Medical Center). From the outset, Dr. Cooley designed an organizational structure that coordinated care at the THI-affiliated hospital partners; Texas Heart Institute did not directly treat patients under the THI umbrella, though it quickly blossomed into “the most prolific heart surgery center in the United States and possibly the world,” as the iconic surgeon wrote in his own words. “The leading physicians in the Texas Heart Medical Group, who are members of the THI Professional Staff, are eager to blaze a new trail and practice top-tier cardiovascular medicine as part of this clinical group,” emphasized Dr. Emerson Perin, Texas Heart Institute’s Medical Director. He added, “The founding physicians at THMG have upheld the same standards of excellence set forth by Dr. Cooley, spanning decades of collective experience in the practice of cardiovascular medicine and clinical investigation. In the spirit of the Cooley legacy, we are joining together as a body of clinicians, surgeons, and scientists with a unified ethos to take Dr. Cooley’s core mission far into the 21st century.”

The twelve founding members of the Texas Heart Medical Group. From left to right: Dr. R. David Fish, Dr. Zvonimir Krajcer, Dr. Alexander Postalian, Dr. Briana Costello, Dr. Paolo Angelini, Dr. Alberto Lopez, Dr. Jorge Guttin, Dr. Emerson Perin, Dr. D. Richard Leachman, Dr. Roberto Lufschanowski, Dr. Eduardo Hernandez, and Dr. Stephanie Coulter.
SHARING KNOWLEDGE GLOBALLY

THI is recognized internationally for its expertise in cardiovascular research and education, and the THI website has attracted tens of millions of people around the world since its launch. In 2020, the website grew 300%, attracting over 11 million users resulting in over 68 million page views from over 240 countries, territories, and dependencies combined. The Heart Information Center remains the most visited section of the website and covers over 200 topics in both Spanish and English. THI’s web-based features like “Frequently Asked Patient Questions” and “Straight Talk by Dr. Stephanie” are meeting a huge, previously unfilled demand for reliable information about cardiovascular disease, delivered in a way in which many people prefer to learn.

THI’s education programs are supported by a large team of publication and multimedia production experts specialized in scientific editing, library sciences, multimedia productions, graphics arts, and digital communications. Every day, these talented teams help THI’s physicians and researchers publish their findings by editing and formatting journal articles, book chapters, conference abstracts, presentations, and grants. The Scientific Publications team comprises scientific editors and writers, grants specialists, and editorial assistants. Most of the editors have advanced degrees in the sciences, and all are capable of editing papers at every level, from ensuring that research methods and results are reported properly to correcting grammar and punctuation.

In 2020, the Scientific Publications team edited hundreds of manuscripts for submission to peer-reviewed medical and scientific journals. These publications document the important basic science and clinical research being done at THI and are shared across the medical and scientific community through society meetings, online journals, the THI Journal and THI Website, and other digital media channels around the world.

"Since 1974, the Texas Heart Institute Journal has served as a valuable educational tool and resource for physician-scientists and clinical investigators around the world.”

TEXAS HEART INSTITUTE JOURNAL

The Texas Heart Institute Journal (ISSN 1526-6702) is a peer-reviewed journal published by THI as part of its medical education program. The purpose of the Journal is to educate, with emphasis on disseminating information to physicians in practice. The Journal was originally published under the name Cardiovascular Diseases from 1974 through 1981 (ISSN 0093-3546). The name was changed to Texas Heart Institute Journal in 1982, and the Journal was published in print through 2013 (ISSN 0730-2347). It is indexed by Index Medicus/MEDLINE and by other indexing and abstracting services worldwide.

Today, the Journal invites the submission of clinical and laboratory research papers, reviews, techniques papers, history of medicine pieces, case reports and series, image papers, guest editorials, and letters to the editor. Last year, the Journal accepted manuscripts from authors in over 30 different countries.

In 2020, the Texas Heart Institute Journal attracted over 1.2 million unique visitors, resulting in over 1.8 million journal page views. Dr. James T. Willerson served as the Editor-in-Chief until his passing in September of 2020. Dr. Zvonimir Krajcer is serving as the new Editor-in-Chief and is upholding the high standards Dr. Willerson established for the journal, working with the same dedicated editorial staff that includes talented production editors and consultants.

CONTINUING MEDICAL EDUCATION

For nearly 40 years, THI’s Office of Continuing Medical Education (CME) has been recognized as an accredited provider of relevant, effective, and practice-based CME activities that support the improvement of health care quality in the United States.

The mission of THI’s CME program is to provide physicians and medical professionals with comprehensive and innovative CME activities that are designed to increase medical knowledge and skills and, ultimately, to change practice behavior to improve patient
Right: Dr. Zvonimir Krajcer is the new Editor-in-Chief of the Texas Heart Institute Journal.

care. These goals are accomplished by recruiting program directors and speakers for a series of high-quality CME offerings.

In 2020 THI pivoted its program offerings during the COVID pandemic. The team accredited live CME symposia, regularly scheduled series, and journal CME activities. The focus turned to offer online programs and virtual offerings with 35 online programs and 4 virtual symposia.

A total of 1,602 physicians and 532 non-physicians participated in THI’s CME- accredited activities. The success of THI’s CME program illustrates the Institute’s extensive reach within the medical community at the local, national, and international levels.

THI continues to partner with Baylor St. Luke’s and the Catholic Health Initiatives Health System in accrediting their CME offerings across the country. THI also works with physicians at Baylor College of Medicine in accrediting and planning several of their educational offerings. This alliance strengthens and expands THI’s education efforts and scope beyond cardiology to many other subspecialties.
THI SCHOOL OF PERFUSION

THE WORK OF PERFUSIONISTS CONTINUES DURING THE COVID-19 PANDEMIC

Committed to the study of perfusion, THI School of Perfusion students voluntarily continued their clinical rotations from March to June of 2020. This team of students was the only perfusion program in the country whose students were so committed to remaining in their rotations, as most programs were closed during this timeframe. In addition, the annual THI Perfusion Conference continued but in a virtual format, with over 200 attendees able to earn CATI CEUs for recertification by the American Board for Cardiovascular Perfusion. THI graduates were also busy winning scholarships in pediatrics and medical missions in 2020.

THI’s School of Perfusion has always been a leader in their field due to their alignment with the mission of THI promoting excellence in perfusion education, training classes of knowledgeable, skilled and professional clinical perfusionists.

In support of Dr. Cooley’s vision to provide highly trained and competent perfusion technologists, the school extended the twelve-month post-baccalaureate certificate program to eighteen months, expanding the students’ clinical experience to include rotations with ECMO, Circulatory Support, and...
multiple clinical sites. In addition, the program expanded its research opportunities for perfusion students under the direction of the school’s research coordinator and in partnership with the THI Center for Clinical Research. As well, the THI School of Perfusion continues its long history of providing perfusion support for the THI Center for Preclinical Surgical and Interventional Research, which is an excellent learning opportunity for the perfusion student.

The THI School of Perfusion is not letting a global pandemic slow their efforts to impact cardiac surgery and is continuing to move forward with their studies and the production of world-class perfusionists.

PERFUSIONS STUDENTS GIVE BACK
THI Perfusion Marks THI’s First Live-stream Event

The Annual THI Perfusion Conference was broadcasted live online on June 5-6, 2020, from the historic Texas Heart Institute TV studio. The agenda for the conference included case reviews and discussions about the latest trends in the industry. Conference participants earned 16.2 CAT I Continuing Education Credits (CEUs) from the American Board of Cardiovascular Perfusion (ABCP).

Funds raised at the conference provided critical programmatic support for the School of Perfusion as they continue to train the next generation of perfusionists.

The 2020 meeting honored Terry Crane, who was involved with the perfusion school for more than four decades and who worked closely with Texas Heart Institute’s founder, Denton A. Cooley, M.D. Terry’s contributions to the success of the program are countless, and the perfusion school is currently thriving. Since its opening in 1971, more than 900 students have graduated from the program. Many of those graduates were touched by Terry’s passion for the vital role perfusionists play in operating the heart-lung machine and other ancillary devices to support patients who require cardiac surgery. The class of 2019 surprised THI with a special $2019.00 donation to honor Terry and start a tradition they hope will inspire their fellow alumni.
CARDIOLOGY AND SUBSPECIALTY FELLOWSHIPS

THE GLUE THAT HOLDS THE SYSTEM TOGETHER

“Our cardiology and subspecialty fellowships have been meticulously stewarded for over 50 years by stalwart clinical educators who take tremendous pride in creating a uniquely diverse learning matrix for our doctors in training. While the teaching faculty provide the matrix, the fellows are the real glue that holds the system together. Their curiosity and drive elevate the caliber of our program and, in turn, patient care in this complex healthcare ecosystem.” - Stephanie Coulter, MD, Cardiology Fellowship Program Director

The world-renowned research and educational center dedicated to the prevention and care of heart disease announced the 13 men and women who will comprise the prestigious THI Cardiovascular Disease Fellowship at Baylor St. Luke’s Medical Center, sponsored by Baylor College of Medicine, for the 2020-21 academic year. The program dates back to 1965 and has attracted some of the brightest clinical minds from the very best medical residencies in the country.

The new class of fellows entering the program included six first-year students who will embark upon the prestigious three-year Accreditation Council for Graduate Medical Education (ACGME) General Cardiology fellowship. The 13 fellows accepted into the highly competitive program were selected out of more than 750 worthy applicants.

“The pool of applicants is more competitive every year. Our faculty truly embraces their responsibility to provide an intellectually stimulating environment for clinical learning that includes experiences beyond the clinic, such as research, education, and outreach,” noted Dr. Stephanie Coulter, THI Fellowship Program Director.

Graduates of the three-year THI/Baylor St. Luke’s Medical Center General Cardiology fellowship are subsequently invited to continue their studies at Texas Heart Institute as part of an advanced subspecialty fellowship in electrophysiology, interventional cardiology, advanced heart failure, or cardiac imaging. This year, six graduates of the program accepted invitations to pursue additional subspecialty training. In addition to these six, THI is honored to welcome Giancarlo Acosta, who comes to THI for subspecialty training after completing a cardiology fellowship at the Joan Edwards School of Medicine at Marshall University.

These fellows stay an additional one to two years, expanding their clinical training and engaging in progressive research and education programs related to their subspecialty. Specifically, four fourth-year students will study Interventional Cardiology, two fourth-year students will study Clinical Cardiac Electrophysiology, and the aforementioned fifth-year student Gi-
ancarlo Acosta is studying Advanced Heart Failure.

**SINCE 1955**

More than 1,000 anesthesiologists have received a portion of their training in the THI program of anesthesia for cardiovascular surgery.

Cardiovascular anesthesiology training at the Texas Heart Institute (THI) originated with the association of Drs. Arthur S. Keats and Denton Cooley in 1955, before Dr. Cooley founded THI in 1962. Since then, the anesthesiologists of THI have cared for over 150,000 adult and pediatric patients undergoing cardiovascular surgery at Baylor St. Luke’s Medical Center.

Today, anesthesiologists at BSLMC provide critical perioperative care to thousands of patients undergoing coronary revascularization (including off-pump cardiac surgery, transmyocardial laser revascularization, and robotic and minimally invasive cardiac surgery), cardiac transplantation, valvular surgery, mechanical assist device placement, and electrophysiological surgery annually. Additionally, approximately 1000 thoracic and vascular cases (aortic aneurysm repair, aorta-femoral bypass, carotid endarterectomy, and A-V access grafts) are performed each year at THI and Baylor St. Luke’s Medical Center.

**INTEGRITY | RESPECT | DISCOVERY | INNOVATION**

The Texas Heart Institute/Baylor College of Medicine Thoracic Surgery Residency Program’s core values are integrity, respect for the individual, continuous commitment to excellence, dedication to discovery/innovation, and fostering leadership through education and teaching.

The program emphasizes the central role of the residents in the treatment of thoracic surgical patients. It strives to impart core values as lifelong goals for the residents and seeks to help them become educators for life. Residents obtain a large and diverse clinical experience of decision-making and hands-on operative experience at renowned institutions including M. D. Anderson Cancer Center, Harris County Hospital District/Ben Taub General Hospital, Michael E. DeBakey Veterans Administration Hospital, and Texas Heart Institute at Baylor St. Luke’s Medical Center. A large and growing program in congenital heart surgery at Texas Children’s Hospital also provides thoracic residents significant experience treating congenital heart disease.
CARDIOLOGY AND RESEARCH IN THE TIME OF COVID-19

2020 was a challenging year for us all. Nonetheless, here at the Texas Heart Institute (THI), we are always making breakthroughs in cardiovascular research. When the COVID lockdown began, we felt the need to lead efforts against the pandemic. Despite our laser focus on cardiovascular research, THI soared in COVID research as well. Cardiac involvement in many patients with COVID sparked the intellectual imagination of our clinical researchers and Professional Staff.

Our Professional Staff members and communications team made considerable strides in education about COVID-19. We updated our website with timely and accurate information about the virus and disease for the public and health care professionals. In our “Cardiology in the Time of COVID-19” series led by Dr. Zvonimir Kracjer, we focused on the disease’s impact on the population we know best—patients with cardiovascular disease.

THI also took a leadership role at Baylor St. Luke’s Medical Center (BSLMC) to make possible early and impactful inpatient treatment for COVID patients. The NIH-sponsored trial “Therapeutics for Inpatients with Covid-19” was implemented with Dr. Emerson Perin and THI taking the lead. Coordinating this hospital-wide effort across multiple specialties “engendered great optimism about the future outcomes of our hospitalized patients with COVID,” said Dr. Perin after his first Zoom call, which included all of the investigators at BSLMC.

THI has taken a leadership role against COVID-19, making available cutting-edge treatments that otherwise would not be accessible. Using our knowledge and hard work, we are here to fulfill the mission set forth by Dr. Denton A. Cooley. Alongside our COVID research and treatment, we continue to move innovative research projects and “The Next First” in cardiovascular medicine forward.

Dr. Perin serves as the Medical Director of the Texas Heart Institute. He is an alumnus of the Texas Heart Institute Cardiovascular Disease and Interventional Cardiology Fellowship programs and is an active teaching faculty member. He is honored for his pioneering clinical research in developing stem cell therapies for cardiovascular diseases and was named a McNair Scholar for his contributions to essential discoveries in the field of interventional cardiology. He holds a Clinical Professor of Medicine appointment at Baylor College of Medicine and serves as the Medical Director of the Cardiac Cath Lab at Baylor St. Luke’s Medical Center.
The Molecular Cardiology Research Laboratory (MCRL), under the leadership of Richard A. F. Dixon, Ph.D., leverages its unique expertise in small molecule therapeutics and molecular biology to treat, diagnose, and prevent cardiovascular disease. Many members of the team have pharmaceutical industry experience with track records of successful drug discovery and development. Two lead investigators in the department have been elected to the National Academy of Inventors within the past year. In keeping with Dr. Willerson’s storied history of translational research, the team has used small molecule drugs, gene therapy, and stem cell technologies to target an assortment of cardiovascular diseases. A milestone was achieved this year when a small molecule drug discovered and developed in the MCRL here at THI entered human clinical testing in October.

ATHEROSCLEROSIS AND IMAGING OF VULNERABLE PLAQUE
Atherosclerosis is an inflammatory disease, and inflammatory cells account for a high percentage of the cells that make up an atherosclerotic plaque. Indeed, the initial migration of inflammatory cells into tissue and their subsequent conversion to foam cells is considered an initial trigger of plaque development. MCRL scientists have developed small molecule drugs that can prevent inflammatory cells from entering atherosclerotic plaque. In animal models of atherosclerosis, drug treatment reduced the inflammatory plaque burden. As an extension of this work and in collaboration with investigators at Texas Children’s Hospital, MCRL scientists have modified these drugs to serve as targeting agents that selectively deliver magnetic resonance imaging (MRI) modalities to inflammatory cells in atherosclerotic plaque. This would allow the use of a noninvasive imaging modality to detect plaques at an early stage of development, thereby allowing proactive intervention with preventative treatments. The imaging agent can also be modified to deliver drugs to potentially reduce plaque burden and therefore function as both a diagnostic and targeted therapeutic. By interfering with the trafficking of inflammatory cells, these small molecule drugs and/or targeting agents potentially could be
used to treat or diagnose additional diseases, including hematologic cancers and autoimmune diseases such as multiple sclerosis and inflammatory bowel disease.

**PERIPHERAL ARTERIAL DISEASE**

Similar to coronary artery disease in the heart, atherosclerotic plaque can lead to peripheral arterial disease (PAD), which is characterized by reduced blood flow to the limbs, typically the legs. The damage to the skeletal muscles in PAD leads to pain and cramping in the legs and, if left untreated, possibly to gangrene and amputation. Despite the high incidence of PAD, current therapies are ineffective in replacing damaged tissue with new functional muscle tissue. Therefore, identifying new treatment approaches for PAD is one of the main missions of the American Heart Association. Because repair of damaged skeletal muscles requires muscle generation from stem cells, the MCRL has developed novel gene-therapy type approaches based on the seminal discoveries of Dr. James Martin, Director of the Cardiomyocyte Renewal Laboratory at THI. In animal models of PAD, treatment of injured skeletal muscle with such therapies results in activation of the muscle stem cells and dissemination of angiogenic signals to the associated blood vessels, leading to new blood vessel formation and skeletal muscle regeneration.

**BIOSYSTEMS MODELING FOR PERSONALIZED MEDICINE**

MCRL investigators have developed computer-based modeling systems to analyze the architecture of blood vessels that supply the heart and the brain. These systems can be used to create new strategies for personalized patient risk assessment and for helping to identify which therapies to use for better patient care. In a joint initiative between THI and UT Austin’s James T. Willerson Center for Cardiovascular Modeling and Simulation, investigators are using computational modeling toolsets to personalize and optimize agents that image and treat vulnerable plaque, such as those described above. In conjunction with patient-specific attributes to maximize targeting efficiency, the models will ultimately enable physicians to tailor treatment for every patient and predict with a high degree of accuracy its effects on the patient before administering it. In collaboration with researchers at Texas Children’s Hospital and UT Health Science Center, the group has also developed an image-based computational modeling toolset to noninvasively assess stroke risk in patients with cerebrovascular disease. The toolset, developed with
Texas Heart Institute support from the National Institutes of Health (NIH), can be used to help ensure that patients at risk of recurrent stroke are properly followed up and treated before strokes occur.

**VACCINE DEVELOPMENT**

Physician researchers at THI and elsewhere have established a link between respiratory infections, especially influenza, and acute myocardial infarction. Although vaccines are available to prevent the flu, the response rate among those over the age of 65 is greatly reduced due to an underactive immune system. A team of MCRL scientists has developed a small molecule drug that can “ramp up” the immune response. In animal models, the drug enhances the response to several vaccines, including the influenza vaccine. This first-in-class drug has been out-licensed to a small pharmaceutical company that has since initiated an NIH-funded phase I clinical trial in healthy volunteers to determine its safety and optimum dosing regimens. This would set the stage for future clinical trials for the treatment of geriatric influenza. In the weeks after influenza infection, patients are at an increased risk of heart attack. Improving the efficacy of influenza vaccinations in the elderly could help reduce this risk. Based on its unique mechanism of action on the immune system, the drug has also been tested in animal models of cancer in collaboration with MD Anderson Cancer Center; these studies have shown that the drug can enhance the response of checkpoint blockade antibodies against solid tumors such as melanoma.

**STEM CELL TRANSPLANT**

Umbilical cord blood has become the preferred source of stem cells for patients in need of a bone marrow transplant because a less restrictive donor match is required, and cells can be readily stored for future use. One drawback, however, is that there are significantly fewer stem cells in cord blood preparations than in other sources, which restricts their use primarily to pediatric populations. Fewer stem cells also mean it takes longer for the immune system to reconstitute itself in the recipient, resulting in a higher incidence of opportunistic infections and graft failures. Finding a means to enhance stem cell engraftment and accelerate the time to immune reconstitution is a primary goal in the transplant field. The MCRL team has developed a small molecule drug that can enhance the binding of cord blood stem cells to the bone marrow microenvironment. In animal model studies of cord blood transplant funded by the NIH, the drug enhanced engraftment of cord blood stem cells into the bone marrow and increased the rate of immune reconstitution.
CARDIOVASCULAR PATHOLOGY LAB
A CORE LAB AT THI OFFERING MANY RESEARCH SERVICES

The Cardiovascular Pathology Lab of THI has been leading the way in supporting pathology research at many public and private medical institutions and corporations across the nation.

The Lab is FDA GLP (Good Laboratory Practices) compliant because of the preclinical studies it conducts, which is essential for FDA submissions. In addition, the Lab is CLIA clear compliant, adhering to guidelines necessary for providing clinical services at THI.

SERVICES OFFERED

- Basic histopathology (the study of diseases of tissues and cells) – a core component of any pathology lab
- Necropsy support in the preclinical research lab, with a board-certified MD pathologist and a board-certified veterinary pathologist to assist
- Two types of microscopes – a scanning electron microscope and a transmission electron microscope – both providing critical data in different formats. The scanning scope looks at the surface of a sample and can also provide chemical characterizations. In contrast, the transmission scope looks deeper into the sample and reveals cellular detail; this scope is used frequently to examine biopsy tissue, which enhances the work of the histology lab and thus enhances histopathology evaluations.

STORIES OF COLLABORATION

The Cardiovascular Pathology Lab is crucial to the research of many different entities, and THI is very proud to be able to offer this type of core lab to further heart research and treatment capabilities.

- Gene therapy research for Danon disease – Clinical trial project with Rocket Pharmaceuticals to find treatments for this rare pediatric cardiomyopathy, which causes death at a young age
- Studying immune checkpoint inhibitor myocarditis in partnership with McGovern Medical School at The University of Texas Health Science Center at Houston and MD Anderson Cancer Center
- Supporting the development of the BIVACOR Total Artificial Heart at THI
- Longstanding collaboration with UT San Antonio and UT Austin in an effort to characterize coronary plaque and develop better methods of detecting it
- Catheter-based study in collaboration with UC Davis to systematically explore whether plaque autofluorescence properties assessed with intravascular fluorescence lifetime imaging (FLIm) can provide qualitative and quantitative information about intimal composition and improve the characterization of atherosclerosis lesions
- THI project utilizing a method of limited cardiac sampling that allows a thorough examination histologic examination of cardiac areas treated with biological agents by transendocardial injection
- Research project with investigators studying methods for percutaneous lung tissue resection.
Camila Hochman Mendez, PhD, Director of the Regenerative Medicine Research (RMR), has been spearheading the reorganization of the Department and merging the work of two different groups for the greater good of THI research. Dr. Hochman Mendez has a basic research lab focused on engineering cardiac tissue models by combining decellularized extracellular matrix, induced pluripotent stem cells, and advanced bioreactor technologies. She also leads the Biorepository & Cell Profiling Core facility within her multifaceted department. One of the keys to the success of the Biorepository & Cell Profiling Core is Dr. Hochman Mendez and her team’s successful maintenance of the facility’s College of American Pathologists (CAP) accreditation by guaranteeing that the equipment and environment are both controlled and Isensix monitored.

CELL PROFILING + BASIC RESEARCH

In cardiac tissue modeling, the biggest question is how to get immature cells to mature. Recently, scientists in the RMR labs developed a decellularized extracellular matrix powder that when added during differentiation enhanced cardiac lineage commitment and improved metabolic metabolism in the derived cells.

By utilizing equipment such as the multi-electrode array, researchers are able to understand how cells propagate the same electrical signal. The next step for this research will be adding electrical stimulation to this innovative differentiation protocol. The goal is to generate the most electrically and metabolically mature cardiomyocytes in the field.

Researchers in the RMR lab also produce their own decellularized extracellular matrix via two processes: perfusion decellularization and by using a turbo-less agitation device. Both processes help them to obtain the acellular extracellular matrix used in RMR lab’s clinical and basic research programs.

Demonstrating the synergy between THI Biorepository & Cell Profiling Core and basic research, Dr. Hochman Mendez developed an NHLBI R21-funded cardiac microtissue testbed using decellularized extracellular matrix and patient samples from improvers and non-improvers who participated in Cardiovascular Cell Therapy Research Network (CCTRN) clinical trials. Findings are expected to provide new insights into specific cellular and extracellular contributors to successful and unsuccessful responses to cell therapy in patients with chronic heart failure.

BIOREACTORS

The RMR lab developed a new bioreactor to have a 100% closed system in which decontamination is minimized and the incubation environment can be controlled to produce more electrically and mechanically mature engineered heart constructs repopulated with multiple cardiac cells. In this contained yet tunable environment, a microcontrolled multi-pump-driven system mimics a regular cardiac cycle in the left ventricle. This system provides mechanical and electrical stimuli to cells while simultaneously maintaining the aortic pressure needed for optimal delivery of nutrients and oxygen.

EXPLORING NEW DIRECTIONS FOR HEART FAILURE (HFpEF)

Heart failure with preserved ejection fraction (HFpEF) accounts for approximately half of all heart failure cases and for which no treatment exists.
The pathophysiology of this multifactorial syndrome is poorly understood, but recent studies suggest that alterations in cardiac titin contribute to the increased cardiomyocyte stiffness characteristic of HFpEF. Dr. Hochman Mendez is currently investigating the effects of a novel laminin polymer (PolyLM) on titin isoform expression in *in vitro* and *ex vivo* models of diastolic heart failure.

These studies are expected to provide strong preliminary data for moving to *in vivo* studies exploring the potential benefits of PolyLM delivery on titin-based cardiomyocyte stiffness, inflammation, and fibrosis in HFpEF.

**BIOREPOSITORY AND CELL PROFILING CORE FACILITY: STRATEGIES**

Sample storage is the essence of what this facility brings to RMR, THI, and our customers in the Texas Medical Center and beyond. The College of American Pathologists (CAP) accredited THI Biorepository & Cell Profiling Core of the only facilities of its kind in Texas and one of 27 nationwide. The RMR team prides itself on being a point of contact for collaborators via sample storage and analysis. This core facility is able to guarantee quality control and expert shipping of human specimens and genetic materials used in clinical research investigations.
Dr. Jim Martin, director of the Cardiomyocyte Renewal Lab (CMRL), is hard at work unraveling the genetic pathways that are involved in tissue regeneration, particularly the regeneration of heart muscle cells (cardiomyocytes). His lab is using their research findings to develop new treatments for heart disease, as heart failure is the number one cause of death in this country. Many individuals have diseased coronary blood vessels that become blocked, triggering a massive loss of cardiomyocytes, which in turn causes scar tissue to form in the heart. The result of this process is heart failure: the loss of the heart’s ability to pump.
Imagine, if you could, actually making parts of the heart regenerate? What a revolutionary shift that would cause in treatment strategies. The heart has the capacity to regrow in lower vertebrates like the zebrafish, so why not in humans?

Humans are born with half of the heart muscle cells they will ever have, and the rest are generated at a very slow rate later in life. In young people, the growth rate of cardiomyocytes is 1% per year and declines to 0.4% by the age of 75 years. This slow generation is due in large part to a critical molecular pathway called the Hippo pathway. Dr. Martin and his team believe this pathway holds the key to the genetic gate.

**HIPPO PATHWAY: GATEKEEPER TO GROWTH**

The Hippo pathway acts as a built-in “stop signal” that slows or inhibits the proliferation of heart muscle cells (cardiomyocytes) as a way to control the growth rate and size of the heart. After making this seminal discovery, Dr. Martin’s team set out to investigate what would happen if they turned this inhibitory pathway off completely.

Building on work from previous studies at the Texas Heart Institute (THI), Dr. Martin, in collaboration with Dr. Emerson Perin and the late Dr. James Willerson, have transitioned from studying the Hippo pathway in mice to larger animals. In a pig model of myocardial infarction (heart attack), they found that inhibiting the Hippo pathway substantially improved cardiac function. These impressive results have led to an early-stage biotech company called Yap Therapeutics that
THI is developing via venture capital to fund and progress the study into human clinical trials.

CARDIOMYOCYTE RENEWAL LAB AGENDA
The lab’s primary goal is to translate their studies into treatments for humans with heart failure by dissecting the Hippo pathway in greater depth. Understanding this pathway will lead to better and more specific therapies. In addition, a new exciting venture has been started called the McGill Gene Editing Laboratory. The goal of this lab is to treat heart disease by using gene editing—a cutting-edge research technique that allows investigators to alter DNA at a specific location in the genome. A Nobel Prize was awarded last year for strides made in this ground-breaking area of research.

Dr. Martin and his team are leading the way to find innovative ways to treat heart failure, from Hippo pathway research to gene editing. The future of cardiac therapy could not be more promising for THI.

Research in the cardiomyocyte renewal lab is focused on how the Hippo pathway regulates cardiac organ size. Deletion of Hippo pathway genes during prenatal development (right) produces cardiomegaly in neonatal mouse hearts. Heart from wild-type littermate mouse (left).
ELECTROPHYSIOLOGY CLINICAL RESEARCH AND INNOVATION

TRANSLATING RESEARCH INTO CUTTING-EDGE TECHNOLOGY

“We are pioneering some of the most groundbreaking cardiac arrhythmias research and management today in collaboration with institutions across the US. With a history of first-in-man devices, the next first in cardiac arrhythmia treatments is already happening at the Texas Heart Institute.”
Mehdi Razavi, MD

CLINICALLY SPEAKING: ANSWERING THE UNANSWERABLE

From a clinical perspective, the EPCRI Lab seeks to find solutions to unanswered questions in the field by performing data studies in which clinical data are entered and reviewed. Then, the statistical analysis of data and the delivery of information to physicians in a more understandable way ultimately improve patient management. Several different types of clinical studies are conducted in the EPCRI Lab, including case reports, case series, meta-analyses, and randomized controlled trials. Research currently in progress involves new catheters, as well as novel methods for ablation and mapping. Another interesting project builds upon a previous study by the Lab on the role of influenza in cardiac shock. This study is receiving a great deal of attention for its relevance to COVID-19.

The EPCRI Lab is a turn-key lab that can perform all of the steps of clinical studies from A to Z and is eager

“The ‘Triple Crown’ of treating both the most common and the most lethal cardiac arrhythmias is external powering, wireless pacing, and—far and away most importantly—cardiac defibrillation that is not only painless but is actually imperceptible to the patient. Our technology brings into sharp focus the remarkable possibility of achieving this goal.”
to collaborate with others to advance cardiac care.

A primary goal at THI is increasing physician knowledge and using state-of-the-art devices and strategies to create technologies and therapies that advance patient care. The Electrophysiology Clinical Research and Innovation (EPCRI) Lab leads the charge in this area. With Director Mehdi Razavi, MD, at the helm, the Lab’s mission is to develop, conceptualize, and validate new technologies in cardiac electrophysiology and cardiology in general.

How does this process work? Once a concept is born, iterative testing begins. If the technology is successful, clinical trials are performed. Many of the technologies developed at THI turn into startup companies or licensing deals to ensure that patients reap the benefits. By generating innovative ideas, Dr. Razavi and his team have ultimately improved patient outcomes.

ONGOING PROJECTS

The EPCRI Lab has several ongoing projects at different stages—all of which are potentially life-changing for patients.

One in 5 patients is affected by internal bleeding. The startup company Saranas (Houston, TX), which was founded on technology designed and tested at THI, has developed a modified sheath with electrodes on it that sense bioimpedance in real time and determine the rate of bleeding in a patient during a procedure. This can aid physicians in mitigating blood loss and determining postoperative care procedures.

Another large project in the works is an NIH-funded, leadless pacemaker that could prevent several common complications. Instead of requiring a battery, this device would be charged wirelessly like a smartphone. Miniature nodes would be able to pace and sense in multiple locations, which may lead to new treatment strategies that use multisite pacing.

A novel material called carbon nanotube fiber is being developed in the EPCRI Lab by using funding from the AHA. These fibers can be directly deployed onto the heart to bridge areas of scarred myocardium and reduce future arrhythmias.

Some projects do not involve new therapies but have the potential to provide physicians with better diagnostic and treatment capabilities. An example is the newly modified microfunction needle, which is a 21-gauge needle that has an electrode on it. The needle’s tip can measure bioimpedance to improve pericardial and vascular access and better differentiate tissues to avoid surgical complications.

In collaboration with Rice University, Dr. Razavi and team are developing data-driven algorithms and energy efficient hardware for their wireless, leadless pacemaker system. (Front Row L-R) Yang Zhao, Dr. Joseph Cavallaro, Dr. Yingyan Lin, Dr. Allison Post, Anton Banta (Back Row L-R) Romain Cosentino, Dr. Behnaam Aazhang, Dr. Mehdi Razavi, Mathews John, Yue Wang.
A collaboration currently in progress with Rice is the utilization of machine learning for a multitude of functions, including the detection and classification of disease. By providing the electrophysiologist with specific data obtained in a minimally invasive manner, this technology will certainly improve clinical outcomes.

LAB WORKFLOW – HOW RESEARCH GETS DONE
Projects are first evaluated against the Lab’s mission to determine feasibility. The Lab has 2 development pathways with distinct goals: the creation of new technologies or therapies and the advancement of knowledge in the field.

In the first pathway, brainstorming is the first step of creating new technologies after a clinical need is identified. Then, a decision is made as to whether a process change needs to occur or a new device needs to be designed. The other pathway of the Lab expands knowledge by testing known technologies and possibly changing operating protocols to advance techniques in the electrophysiology world. The two pathways both culminate in prototyping and engineering of solutions, intellectual property generation, and, lastly, implementation testing. To aid in this process, the Lab has the capability to design electronics and devices by using 3D printing.

Collaboration is always key at THI, and the EPCRI Lab is no exception. They have strong, productive working relationships with Rice, UCLA, UT Austin, Baylor College of Medicine, UH, and Texas A&M.

(L) Matteo Pasquali, PhD, and (R) Mehdi Razavi, MD, study the tiny carbon nanotube fibers used as conductive bridges to restore the electrical function of damaged hearts.
CENTER FOR PRECLINICAL RESEARCH

FORGING NEW PATHS IN RESEARCH

With over 45 years of innovation under its belt, the Center for Preclinical Surgical and Interventional Research and world-renowned Cullen Cardiovascular Research Laboratory is committed to harnessing the expertise of its talented team. Through its in-house work and collaborations with other institutions, it has become one of the most treasured resources in the Texas Medical Center.

FORGING NEW PATHS IN RESEARCH

The Texas Heart Institute’s Center for Preclinical Research (CPCR) is a leading research department that collaborates with teams around the world in the design, development, and testing of a range of innovative devices. Founded in 1972, the CPCR reflects the high standards of excellence established by Dr. Denton Cooley and Dr. O.H. Frazier, over the past five decades. Today, the CPCR has the resources to design and
execute translational studies that will lead to the next major advancement in cardiovascular research. The CPCR accommodates the in vivo research of interventional cardiologists, cardiovascular surgeons, cell biologists, and regenerative medicine specialists at THI in an effort to treat heart disease more effectively and provides the infrastructure for important research efforts of outside investigators and study sponsors.

The Center for Preclinical Surgical and Interventional Research (CPCR) supports Texas Heart Institute’s surgical and interventional cardiology in many ways, including medical device development and testing, pharmacological testing, efficacy testing of various regenerative treatments, and developing physician training programs for FDA-approved medical devices.

To perform a wide array of experiments, the Center encompasses a 20,000 square-foot facility with modern operating suites, a 24/7 ICU, chronic invasive and noninvasive monitoring units, necropsy and histopathology lab support, and in vitro testing capabilities.

The facility is USDA licensed, AAALAC accredited since 1994, and GLP compliant. With constant innovations to research capabilities, the CPCR team will soon have a clinical-grade cardiac catheterization laboratory, which will significantly advance research and innovation at THI through the new Phillips Azurion 7 Series technology, whose 3D imaging tool can provide real-time HD images showing complex cardiac anatomy and electrophysiology navigation mapping, and the Xper CT, which will allow head-to-toe 16 bit CT imaging capability and access to the patient from all sides.

Many surgical projects are currently underway: mechanical support device testing such as total artificial heart and ventricular assist devices, tissue-engineered vascular grafts, organ procurement with ex vivo organ perfusion and experimental heart or lung transplantation, and more. As far as interventional projects go, the CPCR has multiple efforts in this arena as well, in-
cluding catheter delivery of innovative gene and stem cell therapy products, innovative electrophysiology studies, minimally invasive heart pumps, and prototype balloons and catheters. The lab also extends the scope of work to support other research areas like urology with a total bioartificial kidney study, abdominal surgery, and many other projects throughout the Texas Medical Center.

PUMPED UP ABOUT CARDIOVASCULAR RESEARCH
Since 1972, O.H. Frazier, MD, has been studying surgical devices. For years, his research focused on pulsatile blood flow. However, in the ‘80s, when pulsatile pumps were shown to lack endurance, lasting 2 years at best, Dr. Frazier shifted his research approach to non-pulsatile blood flow. At this critical junction, Dr. Frazier went against prevailing scientific evidence and realized that continuous-flow pumps were a necessity. Out of this necessity sprung an invention: continuous-flow pump technology that has been used in more than 60,000 patients around the world, thanks to the innovation of Dr. Frazier.

At the Cullen Cardiovascular Research Laboratory at THI, Dr. Frazier currently focuses his research on another necessity: a small pump that is placed in the left atrium to decompress the heart and take the burden off the ventricles in patients with early-stage heart failure. Dr. Frazier has been working in collaboration with Yaxin Wang, PhD, to address some of the real engineering problems that must be overcome for a long-term device to be successful.

ENGINEERING CHALLENGES
To identify the optimal pump that reaches the design goal of 2 liters per minute and a pressure of 90 mmHg, Dr. Wang ran 81 different pump designs through a battery of tests, starting with animal trials and progressing to hydraulic testing. Once the selection of pump candidates was narrowed down, a collaboration was started with Catherine Fraser of Boston University to reduce the rate of hemolysis (ie, breakdown of red blood cells). In another strategy, a hydrodynamic bearing test rig is utilized to test a secondary rotor with a different bearing in the pump. A mock circulatory loop has also been created to simulate the human cardiovascular system and test pump capabilities.

Strong engineering support is driving the production of these small pumps to assist in long-term solutions that could be key to saving many children’s lives, as such equipment is not currently available for children younger than 9 years old. Dr. Frazier and his team are committed to the creation of this pump and solving more of the challenges of heart failure.
The crux of what separates Texas Heart Institute (THI) from other institutions around the world is innovation. Dr. Emerson Perin, MD, PhD, FACC, Medical Director of the Center for Clinical Research (CCR), has been leading the charge of advancing cardiovascular medicine through clinical research for several decades, with the help of Jennifer Chambers, Director of the Office of Research Administration, and Aryn Knight, Administrative Director of the CCR.

The CCR is a multifaceted arm of THI that is changing the dynamics of patient care by providing new therapies and treatments for cardiac patients and leading the way in clinical research.

THE WORK OF THE CENTER
The CCR is a unique conglomeration of clinical research experts who support all areas of cardiovascular clinical research by pushing the envelope of discovery.

The CCR team members are specialized clinical research professionals with over 200 years of research experience combined. With all this expertise comes the ability to offer many diversified services, including study development and feasibility, research operational support, regulatory consultation and support, streamlined patient recruitment, quality assurance and compliance, and trial coordination.

One element that sets this research center apart is its commitment to cutting-edge clinical research, which leads to world-class treatments.
site apart from others around the world is the clinical research recruitment division. This division is a dedicated team that identifies patients who meet the rigorous requirements for each clinical trial being performed within the CCR.

The CCR has extensive knowledge and experience in providing clinical care options to patients who are not candidates for active clinical trials through compassionate use, emergent use, and humanitarian use. The CCR team is well-versed in bringing these options to patients with critical needs.

- Compassionate Use – This involves the use of an investigational medical product outside of a clinical trial for patients who do not meet the protocol inclusion criteria for entry into the trial but who need the trial therapy.
- Emergent Use – This allows the use of a non-FDA-approved investigational product or device or the use of approved medical products in an unapproved way to diagnose, treat, or prevent serious disease in patients.
- Humanitarian Use – This pathway involves the use of a medical device that is intended to benefit patients by treating a disease that affects fewer than 8,000 individuals in the United States per year.
Texas Heart Institute Cardiology Fellow Lauren Golden, MD, with Community Ambassador Trasetta Terry at the Elnita McClain Women’s Center Go Red Luncheon and Fashion Show.
For the past 10 years, Stephanie Coulter, MD, Director of the Center for Women's Heart and Vascular Health at THI, has been prioritizing women’s health issues as a leader in her field and as co-founder of the Center with James T. Willerson, MD. The mission of the Women’s Heart Center is to reduce the devastating effect of cardiovascular disease on society and women in particular.

The Center initially started with an outreach screening program to examine the disparity in death from cardiovascular disease among women of different ethnicities, but Dr. Coulter and her team found that mortality rates were identical among women of all races. Importantly, they also found that all women are at a higher risk for death than men by almost two-fold. Therefore, the goal of the screening program shifted to the identification of risk factors for artery disease.

Houston’s diverse, multi-ethnic community allowed Dr. Coulter and her team to conduct cardiovascular biometric screenings for glucose, cholesterol, blood pressure, height, weight, abdominal circumference, and even a depression score in collaboration with trusted community partners Baker Ripley and the Lesbian Health Initiative (LHI). This relationship with LHI led to one of the largest cohorts of cardiovascular risk in the LGBT community. More work remains to be done with the follow-up data collection, which will give Dr. Coulter’s team the opportunity to compare cardiovascular risk among multiple racial groups. This registry study will allow the Center to analyze how the burden of disease...
develops and possibly spur other re-search projects.

The Center for Women’s Heart and Vascular Health at THI is prioritizing women’s cardiovascular health through education, research, and treatment and prevention strategies.

EDUCATION
The Center prides itself on providing medical education for doctors through a women’s symposium that has been attended by many notable professionals during the past 10 years, training them on the unique challenges of caring for women. There is also a definite push to increase the number of women pursuing careers in health professions.

COMMUNITY OUTREACH
Reaching more than 3,200 women with 30+ free community lectures and 1,200+ one-on-one health consultations, the Center is very proud of the impact they are having on the women’s health knowledge base.

TARGETED IMPROVEMENTS IN RESEARCH AND COLLABORATION
The Center developed robust collaborations with the School of Public Health and the University of Texas Genetic School that include research on the cardiac causes of sudden death in 11- to 15-year-olds. In 2020, the Center provided leadership to another exciting collaboration with the University Hospital at Columbia in New York City, building a registry of cardiac manifestations of COVID-19 to better assess long-term challenges.