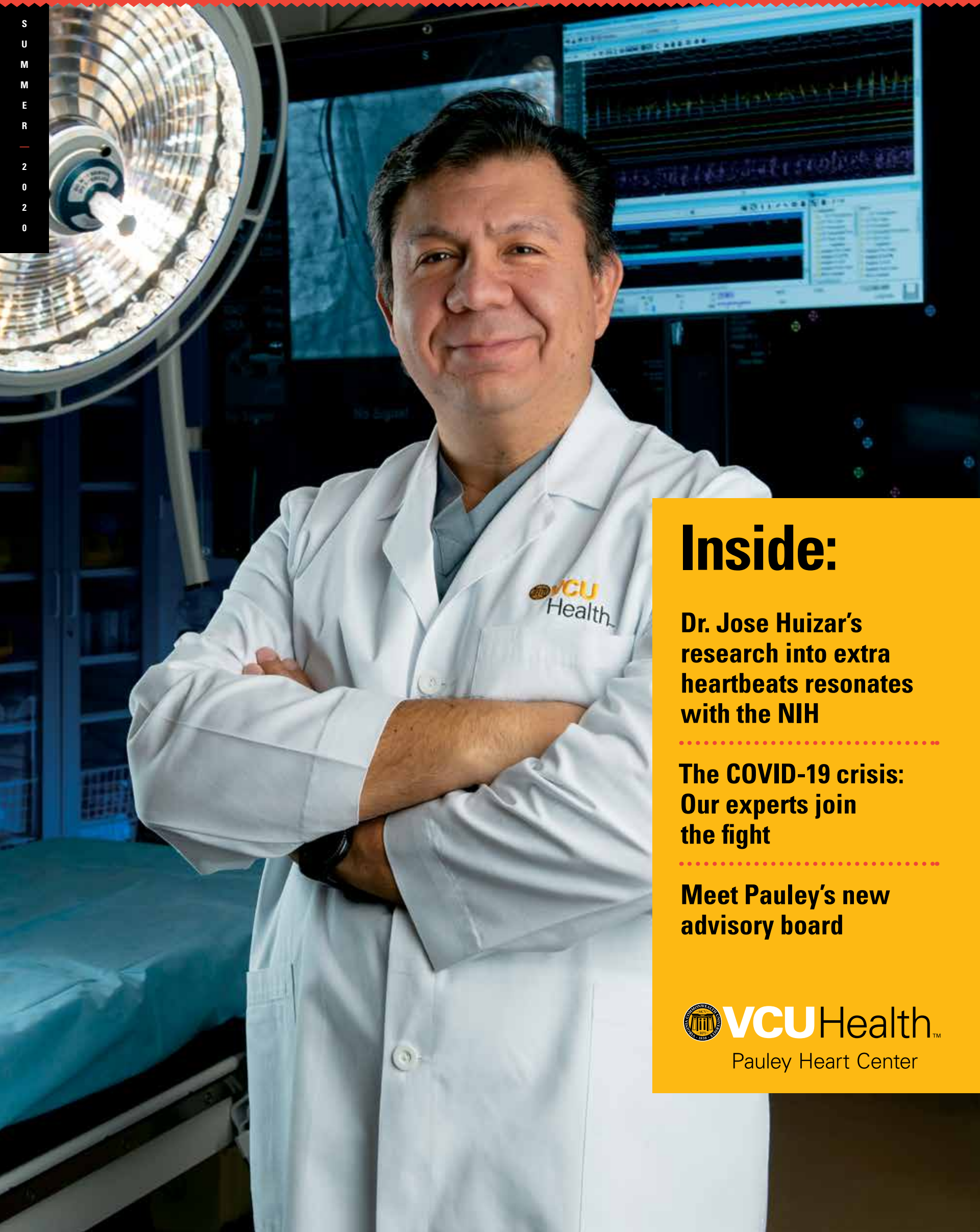


# The Beat

A publication of  
VCU Health  
Pauley Heart Center



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## Inside:

**Dr. Jose Huizar's research into extra heartbeats resonates with the NIH**

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**The COVID-19 crisis: Our experts join the fight**

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**Meet Pauley's new advisory board**



**VCU**Health™

Pauley Heart Center





## The \$2 million man

### Research into extra heartbeats resonates with grant-making agencies

**Early in his career, Dr. Jose Huizar became increasingly intrigued by extra heartbeats in his cardiac patients.**

It was the mid-2000s, and Huizar was providing clinical care to veterans at Hunter Holmes McGuire VA Medical Center, where he is co-affiliated with Pauley Heart Center. At the time, the medical literature was divided on the phenomenon of extra heartbeats, which present as a fluttering or flip-flop feeling in the chest. Some researchers suggested that these extra beats, called premature ventricular contractions, or PVCs, weaken the heart. Others argued that, no, a weak heart causes the extra beats.

The common treatments to eradicate PVCs were medication or ablation — treatments that Huizar and his colleagues routinely provided. But Huizar, who'd become keenly interested in electrophysiological unknowns since completing his post-residency fellowship, was compelled to ask: Were these actions medically necessary? Did the PVCs, in fact, weaken the heart?

The pursuit of answers set Huizar's career on its current trajectory — and to date has resulted in more than \$2 million in research grants.

Huizar, associate professor in the VCU Department of Internal of Medicine, Division of Cardiology, and director of the Arrhythmia and Device Clinic at McGuire,

has devoted more than a decade to expanding his understanding and knowledge of the chronic effects of PVCs. He has done so while concurrently caring for patients in his field of cardiac electrophysiology. "I believe this gives me the advantage to better understand and try to answer critical clinical questions," he explained.

**Huizar's highly successful record of attracting both public and private funding comes as no surprise to Pauley Heart Center Director Dr. Greg Hundley.**

Last July, Huizar received a VA Merit Grant from the Department of Veterans Affairs to continue his work exploring the mechanisms behind a type of cardiomyopathy, or disease of the heart muscle, caused by PVCs. The grant builds on a three-year National Institutes of Health R01 grant he received that runs until April 2021. He is also principal investigator for a three-year R34 study, funded by the NIH, that runs until June 2020.

Huizar's highly successful record of attracting both public and private funding comes as no surprise to Pauley Heart Center Director Dr. Greg Hundley. "[PVC-related cardiomyopathy] is a significant

health problem," he said. "Dr. Huizar brings innovation and a great plan to help solve the problem. He is a rapidly emerging, important investigator in the field."

#### **Understanding PVCs**

Premature ventricular contractions are extra, abnormal heartbeats that begin in one of the heart's two lower pumping chambers, called ventricles. They occur when ventricle contractions beat sooner than the next expected regular heartbeat, often interrupting the normal order of pumping. The extra beat is followed by a stronger heartbeat, which creates the feeling of a skipped beat or a flutter. These extra beats are usually less effective in pumping blood throughout the body.

PVCs can be triggered by heart disease or injury, which can interfere with the normal electrical impulses. Occasional extra beats are common, and usually no cause can be found. Often, they go away on their own. PVCs are diagnosed with an electrocardiogram test or by analyzing data from a Holter monitor, a portable device that captures heart rhythms over a period of time. Frequently, extra beats coexist in patients with cardiomyopathy, a condition characterized by heart failure and weak heart function. Cardiomyopathy impacts not only quality of life, but also the patient's health and life expectancy.

"As a junior faculty, I realized the lack of understanding of the chronic effects of PVCs, and of how to identify patients at risk

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Left: Dr. Jose Huizar in his lab  
on the MCV Campus

to develop PVC-induced cardiomyopathy," Huizar said. "At that time, there were skeptics that believed that PVCs were the result of the cardiomyopathy. I took this as a challenge."

Devising a way to reproduce PVCs for a preclinical study required original thinking and ingenuity. Huizar brought both to the task. He conceived the idea to reprogram a pacemaker to reproduce PVCs. Dr. Kenneth Ellenbogen, chair of VCU's Division of Cardiology and director of clinical cardiac electrophysiology and pacing, supported the plan and connected him with a pacemaker company. "I thought it was a great idea and a very important line of research," Ellenbogen said. "I encouraged him to pursue this method to create a clinically relevant model."

Huizar developed a novel premature pacing algorithm that delivered extra beats on command, allowing him to reproduce chronic states of PVCs and study their lasting effects. "This will not only allow us to understand the mechanism associated with left-ventricular dysfunction and increased sudden cardiac death in patients with frequent PVCs, but, most importantly, will help us find targets to prevent and treat the effects of frequent PVCs," he said.

From the three years of preclinical research that followed, Huizar proved that a normal heart exposed to "a lot" of extra beats induces a weak heart. In 2012 he was awarded a five-year American Heart Association Scientist Development Grant to study in detail how many extra beats were needed to debilitate the heart and cause heart failure.

In 2016, the American Heart Association published a scientific statement recognizing PVC-induced cardiomyopathy (PVC-CM) as a unique clinical entity — citing Huizar's published research as establishing proof of concept. "It validated my work," he said.

### R34 and R01 studies

Huizar's research into PVCs represents a major advance in the field of cardiac electrophysiology as we understand the mechanisms of disease progression and regression, Ellenbogen said.

Two NIH grants — an R34 and an R01 — are enabling Huizar to further distinguish himself in the field and advance his understanding of PVCs on heart function. The studies made possible by

these grants support the National Heart, Lung and Blood Institute's mission of advancing translational research and are Huizar's current research focus.

The R34 clinical pilot study is testing the hypothesis that the prevalence of PVC-CM is underestimated and that conducting a large, randomized clinical trial to test treatments is possible. Twenty thousand ambulatory ECG Holter monitors collected from health care centers around the country are being screened to identify patients with probable diagnosis of PVC-CM. Thirty-six patients with frequent PVCs and cardiomyopathy are being enrolled into the pilot study and randomized to receive either ablation or medication.

Generally, patients identified with PVC-CM are offered radiofrequency ablation, antiarrhythmic drugs or no treatment. "There is clear need for a large clinical trial comparing these strategies," said Huizar, the study director working alongside co-investigators Ellenbogen, Dr. Adam Sima at VCU Medical Center, and Dr. Alex Tan and Dr. Karoly Kazsala at McGuire VA. "Yet, we need to better understand the prevalence of PVC-CM, and the feasibility and limitations of such a trial."

VCU Medical Center and McGuire VA are two of the nine patient recruitment sites. All participants are receiving baseline cardiac imaging and are being observed for a three-month period before receiving treatment.

If successful, the R34 study will pave the way for a large, full-scale randomized trial to identify the best treatment strategy for patients with PVC-CM. "The pilot study is to get a sense of how many patients we can recruit and what are going to be the restrictions of recruiting," Huizar explained.

Concurrent with the pilot study, Huizar and co-investigators Dr. Montserrat Samsó, associate professor, and Drs. Jose Eltit and Rafael Ramirez, assistant professors in the Department of Physiology and Biophysics, are conducting an NIH R01 translational study to understand what changes PVCs cause on a molecular level that trigger weakening of the heart. The mechanism responsible for PVCs is unclear.

Some patients have a lot of PVCs but a normal heart, while other patients have a weak heart whose function improves when

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Huizar continues on Page 14

## Grants at a glance

Funding for scientific research is highly competitive. In the last decade, Dr. Jose Huizar has received the following grants:

### ACTIVE FUNDING:

- **"Contraction-induced Cardiomyopathy on a Swine Model"**  
Veterans Affairs Merit Grant  
June 2021 – July 2025  
BX004861-01 (Huizar JF, PI)
- **"Mechanistic Insight of PVC-induced Cardiomyopathy"**  
National Institutes of Health/NHLBI – R01  
May 2018 – July 2021  
1R01HL139874-01 (Huizar JF, PI)
- **"Prospective Assessment of Premature Ventricular Contractions Suppression in Cardiomyopathy (PAPS): A Pilot Study"**  
National Institutes of Health/NHLBI – R34 Clinical Pilot Studies  
August 2017 – July 2020  
1R34HL138110-01 (Huizar JF, PI)

### PAST / COMPLETED FUNDING:

- **"Mechanistic Insight of PVC-induced Cardiomyopathy"**  
National Institutes of Health – R56 Bridging Funds  
September 2016 – August 2017  
1R56HL133182-01 (Huizar JF, PI)
- **"Injection of Nanoparticle for Ablation of Ganglionated Autonomic Plexi to Prevent Atrial Fibrillation"**  
Center for Innovative Technology – Commonwealth Research Commercialization Funds  
July 2016 – June 2018  
Matching Funds Program (Tan, A, PI, Huizar JF, co-PI)
- **"Autonomic Mechanisms of Premature Ventricular Contraction-induced Cardiomyopathy"**  
American Heart Association – Scientist Development Grant  
July 2016 – June 2018  
16SDG31260012 (Tan, A, PI, Huizar JF, co-PI)
- **"LV Systolic Dysfunction Induced by Ventricular Ectopy: A Novel Model for PVC-induced Cardiomyopathy"**  
American Heart Association – Scientist Development Grant. National Award  
January 2012 – December 2015  
12SDG9310032 (Huizar JF, PI)
- **"LV Systolic Dysfunction Induced by Premature Ventricular Contractions: A Novel Model"**  
A.D. Williams Award - Virginia Commonwealth University  
July 2010 – December 2011  
Huizar, JF (PI)



# Decades-long determination

## VCUART3 proves there's a light at the end of the tunnel for IL-1 blockers and prevention of heart failure

**Thanks to advancements in cardiac medicine, the most dangerous phases of heart attack these days aren't in the attack itself. Instead, they're in the months and years that follow.**

Treatment of ST-segment elevation myocardial infarction (STEMI) has improved drastically over the past 30 to 40 years, said Dr. Antonio Abbate, the James C. Roberts Esq. Professor of Cardiology at VCU. "Someone who had a large event used to have a 1-in-3 or 1-in-4 chance of dying during the hospital admission," a time period that may have lasted three to four weeks. These days, the chances of survival are more like 90% to 95%.

With those odds, however, come a larger number of patients leaving hospitals alive but less than well. Instead, they're leaving with damaged hearts that are at high risk for disease and failure in the days ahead.

Following every STEMI are intense inflammatory responses brought on in part by Interleukin-1 (IL-1), a key mediator, and systemic inflammatory reaction to injury. Inflammatory responses begin within hours, bringing with them the possibility for future heart failure and increased risk of death. Traditionally, steroids have been used as a "blunt instrument" for treating inflammation, Abbate said, but they also come with short-term results and steep side effects.



From left: Dr. Benjamin Van Tassell, Charlotte Roberts and Dr. Antonio Abbate

Could existing drug treatments used for blocking IL-1 in patients with rheumatoid arthritis help to prevent — or even undo — heart damage?

That's the question Abbate pondered during his studies as a medical student at the University Campus Bio-Medico in Rome. A native of Fondi, Italy, Abbate

### Heading into its fourth phase, already the project's findings have worked to save lives.

worked to determine correlations between broad-based biomarkers and the risk of heart attack, eventually theorizing that immunomodulatory drugs could serve the novel purpose of preventing heart disease and failure. In 2007, he brought that hunch to VCU, where there was a collective experience of doing clinical trials in STEMI, he said. "That creates a fertile environment, one that's ready to test and accept new ideas, which can be translated to the benefit of patients. That's why I'm here."

In the years that followed, the project grew from an idea to a small protocol, supported by the generosity of the donors of VCU Health Pauley Heart Center, Abbate said. Thanks to them, "VCUART was born."

Twenty years ago, Abbate started working on this project, and when he joined VCU he assembled a team of researchers around a comparative study, examining IL-1 blockade with the drug Anakinra, an FDA-approved treatment for blocking IL-1 in patients with rheumatoid arthritis. The drug can also be used to treat neonatal-onset multisystem inflammatory disease. "Anakinra had been around for many years, but no one had given it to patients with heart attack," he said.

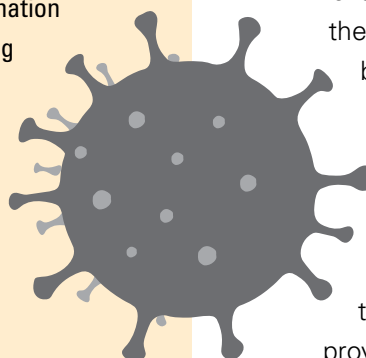
Dubbed VCUART for Virginia Commonwealth University Anakinra Remodeling Trial, the project began as a preclinical study. Then, 11 years ago, the team began testing on patients with STEMI, initially assigning them into two groups — one receiving the drug, the other a placebo. When test data showed improvements and no adverse events among inflammatory biomarkers among those receiving Anakinra, Abbate's idea began to show promise — enough to warrant a second phase and sponsorship from the American Heart Association.

Going steps further to see if Anakinra would not only prevent biomarkers, but also prevent heart failure, VCUART2 enlisted 30 patients. Enrolled within 12 hours of presentation at three locations across the U.S., this second study compared the use of Anakinra given once daily (the standard dose) and twice daily against placebos — and again showed that the drug significantly inhibited inflammatory responses.

Next, the team needed to pinpoint the impacts of dosage. Sponsored by the National Institutes of Health's National Heart, Lung and Blood Institute and including 99 patients, VCUART3 utilized two doses of Anakinra — once daily and twice daily — both of which proved equally effective.

## COVID-19 and inflammatory response

In the midst of this COVID-19 pandemic emergency, Abbate's knowledge of inflammation and cytokines comes in handy as new therapies for SARS-CoV-2 infection are being explored. According to Abbate's interpretation of the currently available data, the severe hypoxemia seen in the later phase of COVID-19 pneumonia in some patients is not related to the virus itself but more to an overwhelming inflammatory response (hyperinflammation). In his role as medical director of the Clinical Research Unit and associate director of the C. Kenneth and Dianne Wright Center for Clinical and Translational Center, Abbate has now embarked on clinical trials with cytokine inhibitors in patients with severe COVID-19 pneumonia.



# Better than blood?

## Promising crystalloid solution may improve survival time of patients

**The new crystalloid IV solution developed by Martin Mangino, Ph.D., is getting national attention because it revolutionizes resuscitation for hemorrhage shock. The PEG-20k solution can save the lives of patients.**



Karl Steimbrenner photo

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**Martin Mangino, Ph.D.**

In the summer of 2019, Abbate and a team of researchers presented their findings at the European Society of Cardiology Congress. Billed as “the world’s largest and most influential cardiovascular event,” ESC Congress brings together more than 30,000 health professionals from 150 countries to raise global awareness for the latest and most promising clinical trials.

Over the course of two decades and by leaning on the involvement of hundreds of people across Pauley and VCU, “I think we’re succeeding in showing that reducing inflammation [post heart attack] is an important target,” Abbate said. Meanwhile, the program has drawn on collaborations with medicinal chemists, pharmacists and molecular scientists to produce numerous breakthroughs, including new, patentable molecules, helping to advance the field of inflammasome inhibitors. While there are many that Dr. Abbate would like to recognize, a special note is for Benjamin Van Tassell, Pharm.D., professor of pharmacotherapy and outcome sciences, VCU School of Pharmacy, who has co-led the clinical trials.

Heading into its fourth phase, already the project’s findings have worked to save lives. Data suggests that the treatment of approximately 300 patients has left them “better off today,” Abbate said, even in cases that include symptoms of heart failure. For instance, one patient, who was in her 60s and preparing to enter hospice, “wasn’t ready to go,” he said. After opting for the trial program, 3 1/2 years later, she’s doing much better and back to enjoying life.

“It’s an incredible story,” Abbate said. And was her recovery due to the drug?

Abbate isn’t 100% sure. But in its next phase, the program aims to enroll a larger number of patients to help lay that question to rest. ❤️

Mangino, professor of surgery and associate chair for basic research in the Department of Surgery, and research director of the VCU Trauma Center started working on the project in 2010 when the military asked him to develop a new, low-volume crystalloid for use by the armed forces. “I put into practice what I learned in previous research to develop new solutions to preserve donor organs for transplantation,” he said.

Preclinical trials of the solution showed increases in survival even when compared to resuscitation with fresh whole blood. “It took the survival time from minutes to days,” Mangino said.

Take for example a soldier who is bleeding on a mountaintop in Afghanistan and needs immediate transport. The more stable that soldier is in the field, the better they will be in the hospital, Mangino said. “This new IV solution helps prolong a soldier’s stay in the field, which allows medics to take the time needed to transport the soldier to more definitive care at the forward field hospital.”

The research is funded by grants from the U.S. Department of Defense and the National Institutes of Health. The product is awaiting FDA approval for use in trauma patients with hemorrhagic shock and sepsis, and intensive care unit patients with critical illness. The solution can additionally be used in patients with sudden-death heart failure undergoing CPR.

This approach may improve patient survival, as well as normalize cardiac and brain functions after resuscitation from CPR. Currently only about 8% of patients survive out-of-hospital cardiac arrest and leave the hospital with normal brain function.

“We have a lot of applications we haven’t explored yet,” Mangino said. “We are going to put in the application with the FDA this year.”

First trials will be conducted in randomized testing at VCU when the solution receives an FDA exemption this year. Some patients will get PEG-20k, and some will receive the standard-of-care solution. “The military will probably get involved in trials, as well,” Mangino said.

Mangino is also studying applications of the IV solution in polytrauma, where someone suffers both a traumatic head or spinal cord injury and is losing large amounts of blood. “What this solution does is move water out of the cells and prevents swelling in the brain,” he explained. “It works by preventing cell swelling, which then opens capillaries and allows the body to exchange oxygen better.”

The trauma resuscitation fluid is “a game changer,” said Mangino, who is licensing the technology from VCU to his new company (Perfusion Medical LLC) to commercialize it. “It has such a dramatic effect when you compare it with the gold standard, whole blood. This is a big deal. We think we can save a lot of lives in the field and in the ICU. It’s a huge advancement.” ❤️

**Pre-clinical trials of the solution showed increases in survival even when compared to resuscitation with fresh whole blood.**





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From left: Dr. Greg Hundley, Stanley Pauley and Dr. Kenneth Ellenbogen

## Mapping the future for cardiac arrhythmia

### Pauley family's \$5 million gift will support research and clinical care

**A generous donation from the Pauley Family Foundation will help the VCU Health Pauley Heart Center address urgent, unmet needs in the management of cardiac arrhythmia.**

The \$5 million gift, announced in November, will support the next evolution of the most comprehensive treatments for patients with harmful irregular heart rhythms.

"The gift will fund the equipment necessary to diagnose and treat arrhythmia disorders, one of the major adverse consequences of cardiovascular disease," said Dr. Greg Hundley, director of the center.

"It pleases me to support the center's research and innovation in the area of cardiac arrhythmia, whereby their discoveries will continue to improve lives in our community," said Stanley Pauley, a former heart center patient who oversees the Pauley Family Foundation, along with his wife, Dorothy, and daughters, Katharine Pauley Hickok and Lorna Pauley Jordan. In 2006, the foundation gave its first \$5 million gift to the heart center, which was later renamed the Pauley Heart Center.

Under the direction of Dr. Kenneth A. Ellenbogen, VCU Health has gained international recognition in the management of heart disease related to harmful heart rhythms. Those that are irregular, too slow or too fast can increase mortality, reduce

quality of life and limit one's ability to perform activities of daily living.

As the population ages, atrial fibrillation, an irregular and often rapid heart rate, is increasingly common. Ventricular dysrhythmia, a disturbance in the electrical activity of the heart's lower chambers, is an additional health care concern for those with existing heart disease.

The \$5 million gift will be used to help VCU Health researchers and clinicians

### Specifically, the funds will help expand imaging into the field of electrophysiology

perfect their diagnoses, and develop and deliver innovative therapies to cure adverse heart rhythms in an effective, cost-efficient manner. Specifically, the funds will help expand imaging into the field of electrophysiology, Hundley said. The new imaging devices will allow physicians to see precisely where — and, most importantly, why — the electrical issues in the heart are originating, so that they can be most accurately ablated or defibrillated.

Plans include acquiring state-of-the-art clinical and noninvasive blood pressure monitoring equipment with advanced technology that will enable Ellenbogen and his team to tackle a range of cardiac

procedures. The gift will also permit the purchase of four handheld echo machines that will help clinicians make bedside diagnoses.

Additionally, the gift will allow the center to build out a research operating room in the Cottrell Surgical Innovation Suite and outfit the Pauley Heart Center Imaging Clinic with an advanced 1.5 Tesla MRI scanner and state-of-the-art CT scanner, expanding non-ionizing radiation (or X-ray) imaging capabilities. The ability to provide cardiac imaging to patients with implanted devices will allow VCU Health to more efficiently and effectively diagnose and treat diseases like atherosclerosis, cardiomyopathy, heart failure, aorta aneurysm, heart valve disease and cardiac tumors.

Previous gifts from the Pauley Family Foundation are helping VCU Health stay at the forefront of cardiac care nationally. The recent purchase of a 3T MRI scanner brought the latest technology to VCU Medical Center and filled a critical need in cardiac imaging regarding management of patients with coronary heart disease and heart failure. From this investment, Pauley has increased the number of cardiac MRIs by 95% in the first year and prevented at least 87 heart attacks. Additionally, five researchers were recruited to develop and test innovations toward management of patients with coronary heart disease and heart failure. ❤️

# Listening to her body

## With help from VCU Health cardiologists, busy mom recovers from aortic stenosis

**Suzanne Spivey is a typical, busy working mom. A 56-year-old mother of four, Spivey holds close ties to her family, has maintained a steady workout routine for most of her life, and works full time at Children’s Hospital of Richmond at VCU as a program coordinator for physical medicine and rehabilitation.**

But in April 2019, Spivey was struck with the news that her older sister had unexpectedly passed away. She was in shock and grieving, and in the subsequent days, she felt a horrible, fatigued feeling throughout her body. “I was dizzy. I was short of breath,” Spivey said. “I wasn’t able to lay down because I’d have trouble breathing. I was starting to just push through the days.”

Spivey had no idea what was going on but knew it had to be more than grief. Just two weeks prior she was taking Zumba. Now she couldn’t raise her arms above her

**“Dr. Kasirajan and Dr. Ashley saved my life, and I can’t thank them enough.”**

head without feeling faint. “It was just horrible how I felt,” Spivey said. “I told myself, don’t ignore this because you’re upset — it could be something else.”

In fact, what Spivey was experiencing were the symptoms of severe aortic stenosis, a potentially fatal condition in which the valve transmitting blood from the heart to the main artery of her body



Suzanne Spivey (left) with her cardiologist, Dr. Phoebe Ashley

had narrowed, decreasing blood flow to the rest of her body. Spivey and her family have a history of heart conditions, including a valve abnormality she had monitored since she was 18 and knew she’d have to address eventually. But as an otherwise healthy woman, she didn’t expect to get this daunting diagnosis.

Last May, Spivey met with Pauley cardiologist Dr. Phoebe Ashley, who sat with her for nearly two hours, comforting Spivey as she informed her of her full diagnosis — severe aortic stenosis due to a congenital aortic valve with two cusps instead of three, and an aortic aneurysm resulting from a weak artery wall.

Ashley prepared Spivey for what was ahead, walking her through the tests she required before open-heart surgery. Dr. Vigneshwar Kasirajan, chair of the Department of Surgery at VCU Medical Center, led the surgery. Dutifully repairing Spivey’s aorta, Kasirajan and his surgical team removed her heavily calcified aortic

valve, replaced it with an artificial prosthetic valve, and took several measures to strengthen the artery.

Three days later — and only two months after her original diagnosis — Spivey went home to her family with her heart repaired.

“Her quick post-operative recovery speaks to her level of fitness heading to the operating room. Often post-operative cardiac patients spend a week or longer in recovery,” Ashley said, emphasizing how healthy living can aid in preventing, mitigating and recovering from heart diseases.

Spivey, however, also credits her instinct and the high-level, compassionate care she received at VCU Health. “Dr. Kasirajan and Dr. Ashley saved my life, and I can’t thank them enough,” Spivey said. “I had an amazing team. My doctors, the nurses, the X-ray techs, those in transportation, my cardiac rehab facilitators — everyone is just incredible here.” ❤️

## Congratulations to our Pauley 2020 Richmond Magazine Top Docs winners!

Each year in Richmond Magazine’s Top Docs survey, Richmond’s medical community shares the doctors they would visit themselves or recommend to family and friends.

### Cardiac electrophysiology

- Kenneth A. Ellenbogen\*
- Jordana Kron
- Richard K. Shepard

### Cardiology

- Antonio Abbate
- Phoebe Ashley

### Cardiology (interventional)

- Richard Cooke
- Zachary Gertz\*
- Barbara Lawson

### Surgery (cardiac)

- Vigneshwar Kasirajan
- Mohammed Quader

### Surgery (thoracic)

- Anthony Cassano\*
- Rachit Shah

### Surgery (vascular)

- Mark M. Levy\*

\* Top vote-getter in the category





# VCU researchers begin clinical trials on investigational drug therapy for COVID-19



**Virginia Commonwealth University researchers began two clinical trials in late March on a potential, experimental treatment for COVID-19, the novel coronavirus that has spread across the globe.**

Dr. Arun Sanyal, a liver specialist and gastroenterologist at VCU Health, is leading clinical trials of an investigational drug for patients with moderate and severe symptoms of COVID-19 and the virus responsible for the disease, SARS-CoV-2.

The investigational antiviral drug remdesivir was developed by Gilead Sciences, Inc. and used experimentally to treat Ebola. Earlier this year, its use on a man hospitalized with coronavirus in Washington state piqued the interest of researchers globally. Remdesivir is an investigational agent; it is not approved anywhere globally and has not been demonstrated to be safe or effective for any use.

“We feel it is extremely important that drugs to be used for this potentially life-threatening disease be tested rigorously so we have good evidence of their efficacy, as well as their safety,” Sanyal said. “We are delighted to work with Gilead on this trial, and we look forward to generating the data that hopefully will help lots of people who have this condition.”

VCU Health is one of the handful of institutions in the United States to make these clinical trials available to patients who meet the criteria for this investigational drug.

“The selection of VCU as a site for this global trial reflects our ability to bring multidisciplinary care to clinical trials and in having the capacity, the breadth and the depth of expertise needed to manage these patients,” said Sanyal, a professor of internal medicine in the VCU School of Medicine.

Remdesivir has previously shown antiviral activity against other coronaviruses like Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) in vitro and in animal models. But clinical trials were never completed due to the lack of available study participants, and the investigational drug is not currently publicly available.

Remdesivir acts by mimicking the appearance of part of the virus and infiltrating the enzyme that viruses can use to replicate themselves. It is designed to slow the



**Dr. Arun Sanyal**

infection of healthy cells in a patient’s body. The trials are a chance not only to provide access to remdesivir, Sanyal said, but also to generate data on the investigational drug’s safety and effectiveness.

## **The trials represent a first-of-its-kind partnership among hepatology, infectious disease, critical care-pulmonology and cardiology departments at VCU.**

VCU’s trials are enrolling participants with documented COVID-19 infection who have fever and symptoms warranting hospitalization. Doctors at VCU Health are administering the investigational drug intravenously in five- or 10-day regimens and following up 28 days later. There are two levels of acuteness being tested: moderate and severe, the latter defined as “someone whose symptoms require them to be on supplemental oxygen,” Sanyal said.

All patients and researchers know whether the patient is receiving the investigational drug therapy, and the majority

of patients are receiving the drug. All participants in the trial for severe COVID-19 will receive the active drug. In the moderate COVID-19 trial, two-thirds will get the drug therapy for different durations of time.

One-third — a control group — will receive standard-of-care treatment, not a placebo.

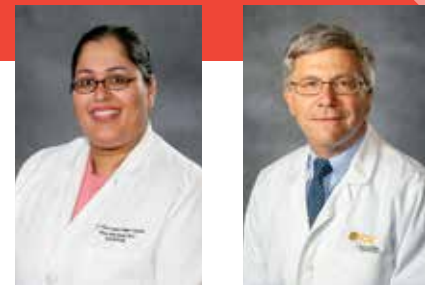
The trials represent a first-of-its-kind partnership among hepatology, infectious disease, critical care-pulmonology and cardiology departments at VCU. Sanyal leads the trials with a team of infectious disease doctors (Gonzalo M. Bearman, M.D., Michael P. Stevens, M.D., and Michelle E. Doll, M.D.), pulmonary critical care doctors (Marjolein de Wit, M.D., Lisa Brath, M.D., and Curtis N. Sessler, M.D.), researchers in inflammation

**Covid Trials continues on Page 14**



# COVID-19: Questions and answers with Drs. Kontos and Bhardwaj

COVID-19 can have a serious cardiovascular impact on patients. To learn more about the relationship between the novel coronavirus and heart health, we spoke with Pauley faculty Dr. Michael Kontos, medical director of the Coronary Intensive Care Unit and president of the Virginia chapter of the American College of Cardiology, and Dr. Hem Bhardwaj, director of echocardiography and inpatient care. They share their expertise and insight below.



Dr. Hem Bhardwaj and Dr. Michael Kontos

**Q Individuals with existing health conditions, including cardiovascular disease, appear to be most at risk for severe complications from COVID-19. Can you elaborate?**

**A** Studies have shown that patients infected with COVID-19 who have underlying cardiovascular disease are at increased risk for mortality. In addition, cardiac risk factors, specifically hypertension and diabetes, have also been associated with higher risk. It is unclear if this higher risk is related specifically to these risk factors or because the patients with these risk factors tend to be older and have other associated comorbidities.

**Q It's also been suggested that COVID-19 can cause cardiac injury in otherwise healthy patients. How does the coronavirus affect the heart?**

**A** Coronavirus affects the heart indirectly, and less commonly via its direct infection of the heart. Elevation of a specific cardiac biomarker called troponin, which can be detected when there is myocardial injury, has been associated with increased mortality in patients infected with COVID-19. Myocardial injury likely occurs as a result of patients having underlying coronary disease who are now under significant stress from their infection. Less commonly, it results from a direct effect on the heart due to the inflammatory reaction that is seen in patients with severe COVID-19.

There have been a number of reports of patients who present with ECG abnormalities that are consistent with an acute heart attack who, when they undergo coronary angiography, do not have significant heart blockages. This indicates that the ECG abnormalities are likely the result of an inflammation of the heart rather than a true heart attack.

**Q What findings are cardiologists observing in COVID-19 patients who receive echocardiograms relative to those without COVID-19?**

**A** There is limited data on patients who have had an assessment of heart function who have COVID-19. In general, they have shown relatively normal function early in the course of the disease, with some patients with severe infection developing heart dysfunction. In this small group, patients who recover from the infection have recovery of heart function, although data is currently limited.

**Q Are there any treatments for COVID-19?**

**A** There are a number of potential treatments for COVID-19 that have been in the news that are currently undergoing investigation. One that has been frequently commented upon is hydroxychloroquine, which is a commonly used for the treatment of lupus, and chloroquine, which has been used to treat malaria. Although initial small studies suggested a possible benefit, more recent larger trials have cast doubt, with some even indicating a harm with treatment. Larger, randomized studies are clearly needed as both drugs can have significant side effects. Other drugs that are undergoing investigation include antiviral drugs such as remdesivir (with VCU being one of the first institutions to be included in these trials) and anti-inflammatory drugs.

**Q What questions do your patients ask about COVID-19, and what are you telling them?**

**A** Patients often ask what symptoms to look for. Fevers, fatigue, cough and shortness of breath are common symptoms; however, gastrointestinal symptoms have also been noted. Treatment in general is symptomatic, with approximately 85% of patients infected having self-limited infection and not requiring hospitalization. Approximately 15% of patients will develop more severe symptoms that require hospitalization. Patients also ask what they can do to decrease risk. Social distancing and frequent hand washing are key.

**Q During this pandemic, what measures are you taking to ensure heart patients stay safe but also receive any necessary clinical care? For instance, have you adopted/increased the use of telemedicine?**

**A** Because of recommendations on social distancing, VCU Health has implemented the use of telemedicine to provide cardiac care to outpatients while at the same time ensuring the safety of all patients and clinic staff. For those who do require further evaluation, the option of seeing a provider in the office is still available. Patients with severe symptoms should not avoid seeking care, as delay may lead to worse outcomes.

**Q Do you have anything else that you would like to add?**

**A** There has been some controversy over whether patients taking medications called angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARBs), two common blood pressure and heart failure medications, have worse outcomes if they get COVID-19. Currently, there is no data indicating that these medications are harmful, and discontinuing them without physician consultation is not recommended. This is consistent with guidelines from multiple organizations, including the American College of Cardiology and the American Heart Association.

Visit [vcuhealth.org/covid-19](https://vcuhealth.org/covid-19) to learn more about this virus.

## More to the story

News about the COVID-19 crisis changes every day. To read the latest about how our Pauley team has responded to the pandemic, see the fall 2020 issue of The Beat.

# Congratulations to Dr. Thomas Porter, a 2019 VCU Alumni Star honoree.



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**Dr. Thomas Porter**

The university-level award, given biennially by the VCU Office of Alumni Relations, recognizes outstanding alumni for their career and humanitarian achievements. Sixteen honorees were selected through faculty recommendations and alumni committees from across the university.

Porter, a former resident and cardiology fellow at the Medical College of Virginia, is the Theodore F. Hubbard Distinguished Chair of Cardiology at the University of Nebraska Medical Center. He has spent many years studying the efficacy of microscopic bubbles, known as microbubbles, combined with ultrasound imaging to break up blood clots. Interest in this work began in 1990 at VCU. At that time, he explored using tiny bubbles as an ultrasound-enhancing agent for imaging, work that he continued when he joined the faculty of UNMC in 1992.

Porter was in good company, sharing the spotlight with honorees Rodney F. Ganey, Ph.D., founder of Press Ganey Associates, and Dr. Ali Khan, VCU School of Medicine graduate and member of Doctors for America, American College of Physicians and Physicians for Human Rights, along with thirteen others.

Alumni Star recipients were honored Nov. 7, 2019, at the Science Museum of Virginia.

Read more about Porter in the Autumn 2019 issue of *The Beat*. For more information about the 2019 Alumni Stars, visit [vcualumni.org](http://vcualumni.org). ❤️

## Discovery Series comes to Richmond

### Panel discussion focuses on innovation and patient care



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**From left: Panelists Dr. Kandace McGuire, Dr. Kenneth Ellenbogen and Dr. Kelly Gwathmey**

**Each year, the MCV Foundation sponsors a Discovery Series in Williamsburg, Va., providing guests with immediate access to the latest exciting work of VCU Health scholars, researchers and clinicians. Last October's event, the sixth in the series and the first in Richmond, highlighted innovative treatments and patient care.**

More than 100 invited guests attended the inaugural Discovery Series RVA, an intimate occasion held at the Country Club of Virginia that included a welcome reception, program and discussion, strolling supper, and question-and-answer session.

Dr. Peter Buckley, dean of the VCU School of Medicine and interim senior vice president for VCU Health Sciences and interim CEO of VCU Health System, moderated the discussion, "The Doctor Is In: A Panel of Experts from VCU Health Discuss Innovative Treatments and Patient Care." The multidisciplinary panel included VCU faculty Dr. Kenneth Ellenbogen, professor, Department of Internal Medicine, and chair, Division of Cardiology; Dr. Kelly Gwathmey, assistant professor, Department of Neurology; Dr. Jordana Kron, associate professor, Department of Internal Medicine, Division of Cardiology; Dr. Kandace McGuire, associate professor, Department of Surgery, Division of Surgical Oncology; Dr. Saïd Sebti, professor, Department of Pharmacology and Toxicology, associate director for basic research, Massey Cancer Center; and Dr. Gordon Smith, chair and professor, Department of Neurology.

The theme of the night was interdisciplinary collaboration, which Kron described as critical "both for scientific advancement and for patient-focused, family-focused clinical care." Kron works with an interdisciplinary team of physicians in VCU Health's sarcoidosis clinic. "The future of medicine," she noted, "is teamwork to find new therapies for diseases and then bring those treatments to patients and their caregivers in a compassionate way."

A highlight of the event, Kron and Ellenbogen each discussed innovations in the treatment of heart disease. Kron, a recent recipient of the American Heart Association's Collaborative Sciences Award and a Pauley Pilot Research Grant, discussed what VCU Health is doing to address sarcoidosis, a debilitating systemic condition that can affect the heart and nervous system. Ellenbogen, a highly sought-after clinician, researcher and educator, described how VCU Health has developed a national reputation in the diagnosis and treatment of atrial fibrillation. "It was a great opportunity to share the knowledge and drive of the Pauley Heart Center faculty with the public," Ellenbogen said of his participation.

"Bringing the Discovery Series home to Richmond was very exciting, and significant," Kron added. "VCU plays such an important role both in downtown Richmond and in the surrounding communities, but sometimes people that live locally may not know all of the cutting-edge research and amazing patient care that is going on right here." ❤️



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**From left: Judy Brown, Dr. Kenneth Ellenbogen and Carrie Mills**





From left: Dr. Greg Hundley, Rick Burton, Kathy Pauley Hickok, Dr. Kenneth Ellenbogen, Mitch Haddon, Nancy Belleman, Roger Boevé, Dr. George Vetrovec, Charles Reed, Dr. Vigneshwar Kasirajan, Ken Blaisdell, Marshall Orr.

## Inaugural advisory board kicks off year of service

### Goals include fundraising, “friend-raising” and advocacy

**Fulfilling the vision of director Greg Hundley, M.D., the inaugural Pauley Heart Center Advisory Board held its kickoff dinner in November 2019.**

“In addition to increasing engagement in our community in the mission of Pauley, I am excited to have a close network of professionals I can call on for advice,” Hundley said of the philanthropists, community leaders and business leaders who comprise the board. “I admire the unique and extremely valuable experience they bring to the table.”

Each of the board’s 12 members is eligible to serve two three-year terms to help Pauley implement objectives in the areas of education, research and clinical care. The board members’ formal duties include making the center a priority in their philanthropic giving, engaging their personal networks for fundraising or educational events, and advocating on behalf of the center to all constituents.

The well-rounded board includes individuals with deep ties to Richmond and who represent a variety of industries.

Roger Boevé, retired executive vice president of Richmond-based Performance Food Group, is the Pauley Heart Center advisory board chair. “I currently serve on several advisory boards and understand the power an advisory board can generate to support a cause,” said Boevé, a member of the Massey Cancer Center advisory board and the MCV Foundation Leadership Council.

Pauley Heart Center’s mission, he said, is critical and compelling.

“Heart failure affects millions and can affect anyone at any time,” Boevé said. “We are fortunate to have available in our area a world-class cardiovascular care center, equal to none. Each year, thousands of patients are treated here, ranging from noninvasive cardiology procedures to heart transplantation. The center has become known worldwide for its groundbreaking work.”

The advisory board will capitalize on Pauley Heart Center’s reputation for excellence through advocacy, “friend-raising” and fundraising.

A deep, personal connection to Pauley’s mission motivated Rick Burton to join the advisory board. His spouse, Mike, was successfully treated at Pauley for a persistent cardiac arrhythmia that confounded physicians in other practices. “A doctor friend sent us to Dr. Ken Ellenbogen at Pauley, who performed an ablation,” he said. “It returned Mike to a normal life in every way. Indeed, it’s certainly fair to say that it gave us his life back.”

Burton, a retired attorney, sees his role on the board as an ambassador for Pauley — both to make the community aware of the extraordinary work and research being done there and to encourage individuals and businesses to financially support Pauley’s mission.

For advisory board member Nancy Rosenthal Belleman, the opportunity to promote and connect Pauley’s services to the community proved irresistible. “As a former board member of the Jenkins Foundation [a grant-making foundation devoted to improving the health of greater Richmond], I’m attuned to underserved and uninsured populations in the city of Richmond,” she said. “The research arm of the Pauley Heart Center will directly impact those most in need.”

With 2020 underway, the advisory board is ready to get to work.

“This is an exciting time at Pauley,” Boevé said. ❤️

#### 2019-22 Pauley Heart Center Advisory Board members

Nancy Rosenthal Belleman	Kathy Pauley Hickok
Henry Berling	Bill McAllister
Ken Blaisdell, Ph.D.	Marshall Orr
Roger Boevé, chair	Charles Reed
Rick Burton	George Vetrovec, M.D.
John Congdon	Stanley F. Pauley <i>(honorary member)</i>
Mitch Haddon, vice chair	

# Alumnus spotlight: Jennifer S. Lawton, M.D.

**In recent decades, cardiac medicine has made great strides. With the percentage of patients surviving heart attacks and thriving in the wake of heart disease, there's no question how far the field has come.**

Over the course of those advancements, however, are studies showing more women dying of heart disease than all cancers combined, and females making up just 5% of the field of cardiology. VCU School of Medicine alumna Dr. Jennifer S. Lawton, the Richard Bennett Darnall Professor of Surgery at Johns Hopkins, has taken up the cause for bringing equality to cardiac medicine.

It's a story that proves the importance of female perspectives and leadership. As the first woman to serve as chief of Johns Hopkins' Division of Cardiac Surgery and an avid researcher whose expertise spans more than two dozen areas of cardiology, Lawton balances a desire to save and improve lives with the need for advancing female-centric cardiac medicine.

## Lawton balances a desire to save and improve lives with the need for advancing female-centric cardiac medicine.

Though she had an early affinity for math and science, it was tragedy that sparked her initial interest. After losing a grandparent to bypass surgery, Lawton immediately began studying heart disease, a mission that drove her to Allegheny College and eventually to Drexel University College of Medicine, where she earned her medical degree.

Initially, she wanted to be a pediatrician. "But once I took anatomy," she said, "that completely changed." Instead, she keyed in on surgery, a passion that brought her to VCU, where she says she was drawn to the leadership of then-chair of surgery Andrew Wechsler, M.D. During her residency, Lawton was invited by VCU's cardiac surgeons to sit in "as often as I liked." Add to that two years' worth of laboratory-based research and, she said, "I knew this was where I wanted to be." She'd found her home in academic medicine.

In the years that followed, Lawton became a prolific researcher and an avid leader. As professor of surgery and chief of the cardiac surgery division, as well as director of the Cardiac Surgery Research Laboratory and program director for the cardiothoracic fellowship training program,

she has 81 peer-reviewed publications, seven book chapters and 18 abstracts. She's delivered more than 50 invited lectures while serving as a member of more than a dozen associations and societies. Her honors include a fellowship with the American Heart Association and serving as an invited attendee for the American Association for Thoracic Surgery Leadership Academy for Division Chiefs/Potential Chiefs. In May 2018, she returned to VCU as the Brooks-Lower Visiting Professor.

As a surgeon, Lawton remains patient-centered, connecting not only with the medical needs of each patient, but also with

the lives of each patient. As a researcher, her work examines myocyte volume regulation, ATP-sensitive potassium channels and myocardial protection.

Over the course of her career, however, she has also taken aim at macro-level issues, including an imbalance between male- and female-centric practices. After becoming a cardiac surgeon, Lawton says it became apparent to her that, while women's health has made great strides across countless areas of medicine, her field had so far overlooked the implications of heart disease for women. As a result, it was ignoring or mistreating the needs of female patients. As late as the 1970s, "People thought that cardiovascular disease was a disease only in men," she said. As a result, between the years of 1984 and 2013, more women than men died of cardiovascular diseases.

"You see at NFL football games the players wearing pink to support breast cancer. And I totally love that," Lawton said. "But most people don't realize that more women die of cardiovascular disease than all cancers combined, so we should also be wearing red."



Dr. Jennifer S. Lawton

Retrospective studies show longer times to hospital admission and testing, she says. Women also tend to be referred for surgery less often.

"Is that bias?" she asked. "Is it referral bias? Is it a lack of knowledge about the disease? We need to figure this out."

As a result, her research cues in on female heart disease and gender differences, as she's spent much of her career raising awareness of heart disease as the leading cause of death for adult women in the U.S. But there are other gender-related issues that she aims to correct. For instance, the number of women working in the field of cardiology, she said, is around 20%. In the field of cardiac surgery, that number is more like 5%.

"There is a quote that says, 'If you don't see it, you can't be it,'" she said. "And 50% of the people getting Ph.D.'s and M.D.'s these days are women, so we're missing half of that talent if we aren't recruiting them into cardiac surgery. If they don't see women leaders in the field, they cannot perceive that it's a viable goal."

To upend that dilemma, Lawton's exemplary leadership has spanned numerous roles. She has served as chair of the surgery study section of the American Heart Association, vice chair of the Accreditation Council for Graduate Medical Education residency review committee and president of Women in Thoracic Surgery.

In the meantime, she hasn't lost sight of the moral impetus that brought her to surgery.

"I like cardiac surgery because you can perform an operation and cure someone of a disease, giving them a longer life," she said. "That's a pretty amazing thing to give a person." ❤️



# Welcome, Dr. Medalion!



**Dr. Benjamin Medalion has joined the Department of Surgery as professor and chair for the Division of Cardiothoracic Surgery.**

Medalion received his medical degree from Technion School of Medicine in Haifa, Israel, and completed his cardiothoracic residency at Carmel, Shaarei Zedek and Hadassah

medical centers. He then joined the Cleveland Clinic Foundation, where he completed his cardiothoracic fellowship.

Medalion held a variety of positions at prestigious institutions, including the Edith Wolfson Medical Center in Holon, Israel, and Case Western Reserve University. Prior to joining VCU Health, Medalion served as the director for cardiac surgery at the Ahuja Medical Center and the director

of mechanical support and transplant surgery at the Harrington Heart and Vascular Institute at University Hospitals of Cleveland. Additionally, Medalion completed a surgical leadership certificate from Harvard Medical School in 2019.

Medalion's expertise in adult cardiac surgery, including heart and lung transplantation, will continue to enhance the capabilities at VCU Health. ❤️

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## Drug trials highlight novel therapies for age-related cardiomyopathy

### VCU leads recruitment efforts

**VCU Medical Center is leading an international effort to screen patients with transthyretin amyloid cardiomyopathy (ATTR-CM) and enroll them into a clinical trial testing a novel therapy called AG10. Among 51 recruitment centers in the U.S. and abroad, VCU ranks among the top 5 in recruiting patients into the trial.**

"Enrollment has been fantastic," said Dr. Keyur Shah, chief of the section of heart failure at Pauley and medical director of VCU's Mechanical Circulatory Support Program. "It's given our patients access to treatment they wouldn't have had, because the only drug that's available, Tafamidis, is unaffordable to many."

"These achievements in enrollment not only increase Pauley's visibility, they highlight VCU Health's access to novel therapies for patients across Virginia," added Laura Cei, clinical research nurse coordinator in the Department of Internal Medicine.

Years ago, VCU Health made a commitment to the research, diagnosis and treatment of amyloidosis. Shah leads a renowned, multidisciplinary team of top physicians and surgeons in a center of expertise for patients in need of amyloidosis treatment and resources.

"We're one of the leading enrollment centers in all of the U.S. because of a high population of referrals for TTR amyloidosis," he said. "Part of that has to do with improved recognition of the disease here in the community through outreach and education."

Transthyretin amyloid cardiomyopathy is a rare, life-threatening heart condition affecting more than 400,000 people worldwide. The accumulation of an abnormal protein called transthyretin amyloid results in thickening and stiffening of the heart, which often leads to heart failure or even death.

Running through May 2023, a placebo-controlled clinical trial called ATTRIBUTE is testing the efficacy and safety of AG10 in 510 adults with symptomatic ATTR-CM. An alternative to Tafamidis, the first FDA-approved drug to slow the progression of amyloid heart disease, AG10 was developed to bind the four arms of TTR protein and prevent it from turning into amyloid. The impact of AG10 versus the placebo is being evaluated in patients after 12 months and 30



**Dr. Keyur Shah with a patient**

months of treatment. At the end of 30 months, study participants may be eligible to receive AG10 with no placebo.

In addition to ATTRIBUTE, two clinical trials recently underway and running through 2024 are testing ATTR-CM novel drugs called AKCEA-TTR-LRx and Vutrisiran.

Participation in ATTRIBUTE, and future trials, is a win-win for both patients and Pauley.

"By conducting these clinical trials at VCU, we are able to spread awareness of ATTR-CM," Cei said. "We can also provide patients with a hub in which they can obtain ongoing support and continuing education about this disease."

*To learn more about amyloidosis and the VCU Health multidisciplinary team, visit [vcuhealth.org/pauley-heart-center/our-expertise](https://vcuhealth.org/pauley-heart-center/our-expertise). ❤️*

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### Huizar continued from Page 3

PVCs are eliminated. “It seems to me that there is some patient susceptibility that we don’t understand yet,” Huizar said, describing the study’s impetus.

He continued, “If you look at the patients that have PVCs versus those who don’t, they tend to have more heart failure in the long term. In general, sudden cardiac death is not that increased. But, if you look at the patients who have had sudden cardiac death versus no sudden cardiac death, those who have had sudden cardiac death have had more PVCs than the ones that haven’t. It indicates some risk.

“We think that there is some susceptibility, maybe genetic or in phenotype,” he added. “So, we’re trying not only to understand the weakening of the heart, but also mechanistically what PVCs have to do with the risk for arrhythmias and sudden death. Obviously, it gets very complicated when you go into a cellular level, and that’s why you need collaboration at a lot of different levels.”

### A place for research

Under the direction of Ellenbogen, Pauley Heart Center has gained international recognition in the management of heart

## Huizar, with his unique expertise and interest, has helped make Pauley one of the select centers in the U.S. for PVCs research.

disease related to harmful heart rhythms. At Pauley’s electrophysiology clinic, patients with arrhythmias, including PVCs, are evaluated and treated by one of the most highly respected cardiac electrophysiology teams in the country. The team’s experience and expertise place the clinic among the top referral centers for evaluation and treatment of complex arrhythmias.

Pauley cardiologists are also leaders in research and part of an active cardiovascular disease research program that furthers knowledge of heart disease, its treatments and its cures. Huizar, with his unique expertise and interest, has helped make Pauley one of the select centers in the U.S. for PVCs research.

“Dr. Huizar is an important member of our cardiac electrophysiology team and an important contributing member to Pauley Heart Center,” Ellenbogen said. “He is

focused, thoughtful, creative and persistent. That is what it takes to be successful at research and innovation. Equally important, he is surrounded by a team of collaborators that all work together.” Collaborators like cardiac electrophysiologists Tan and Kaszala, frequent co-investigators who add another layer of research to the knowledge and understanding of PVCs through their own work on the subject.

“VCU really nurtures people that want to do research. They support you here,” Huizar said. He cites colleagues Ellenbogen, Hundley, Dr. Clive Baumgarten and the late Dr. Mark Wood as mentors. “One of the reasons I’m at VCU is for research. I knew that there was no better place for me. There’s never a ‘no’ for an answer.”

Saying yes to research opens the door for bench-to-bedside innovations that benefit patients.

“We’re about the discovery of new ways to reduce heart disease,” Hundley reminded. “Dr. Huizar is researching a frequently encountered problem of palpitations, which his research shows reduce heart performance. Solving this will improve our patients’ well-being.” ❤️

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### COVID-19 continued from Page 8

(Antonio Abbate, M.D., Ph.D., and Benjamin Van Tassell, Pharm.D.) and VCU research and ethics staff.

“This has been really an exceptional team,” Sanyal said. “We were able to get the trial off the ground, meeting all of the complex regulatory requirements along the way, within a 72-hour time frame primarily because of the alignment of mission and vision and an extraordinary team effort from everybody involved.”

It is not one person’s trial, he added. The physicians, nursing staff, pharmacists and administrative staff came together to integrate the trial conduct with routine clinical care for eligible patients.

At VCU and VCU Health, the research represents just one response to a pandemic that has killed more than 350,000 people worldwide, including 100,000 in the United States. With no approved medications to treat the virus currently, there is an urgent need for effective treatments.

“These clinical trials and the ongoing research of nationally prominent universities like VCU will quickly advance how health care teams treat COVID-19 around the world,” said VCU President Michael Rao, Ph.D. “We

## “These clinical trials and the ongoing research of nationally prominent universities like VCU will quickly advance how health care teams treat COVID-19 around the world.”

are proud of our research and health care teams that are working hard to save lives and find solutions for patients with COVID-19.”

VCU Health is prepared for and is responding to the threat of the virus, and doctors are taking precautions to ensure the safety of all visitors, team members and patients, including those with suspected or confirmed cases of COVID-19 at the hospital. Those in the trials are isolated.

“Our team members at VCU and VCU Health have been actively searching for ways to combat COVID-19, a virus that has disrupted our lives and the lives of those we serve,” said Dr. Peter Buckley, dean of the VCU School of Medicine and interim senior vice president for VCU Health Sciences and

interim CEO of VCU Health System. “Our teams are working seamlessly to make this investigational drug therapy available to those who are most affected by this virus.”

Sanyal, the principal investigator for the remdesivir trials, is a researcher at VCU Massey Cancer Center and the associate director of the KL2 program for training faculty in research at VCU’s C. Kenneth and Dianne Wright Center for Clinical and Translational Research, which oversees clinical trials at the university with the help of a \$21.5 million National Institutes of Health grant.

The Wright Center, in collaboration with Sanyal’s team, developed a patient referral portal that allows doctors at other institutions to communicate with the trial team at VCU about possible participation for patients who meet the criteria — positive for COVID-19, hospitalized with a documented fever. If a patient from another health care provider qualifies, the patient could be eligible to transfer to VCU Medical Center to participate in the trial.

Learn more about Pauley Heart Center’s response to the COVID-19 pandemic in the fall 2020 edition of The Beat. ❤️



# Is food the best medicine for heart failure?

## Researchers definitively link diet and heart health

**Despite our satisfaction from polishing off a hearty breakfast or fast-food lunch, our hearts may beg to differ, statistically speaking. Preclinical and clinical studies at Pauley confirm what we've known for years: A diet high in refined sugars and saturated fats will likely catch up with our heart health.**

Researchers looked at the effects of a diet rich in sugars and saturated fats, known as a Western diet, starting with a study published in 2015. "We were most interested in cardiac function — to see how the heart is affected by eating an unhealthy diet," said principal investigator Dr. Salvatore Carbone, assistant professor in the Department of Kinesiology and Health Sciences, College of Humanities and Sciences at VCU. Carbone, a native of Italy, sought to determine if a diet rich in foods containing healthy fats, such as extra-virgin olive oil and tree nuts, that resembled the Mediterranean dietary pattern, could improve body composition, cardiac function and, ultimately, exercise capacity in people who were obese and had a specific form of heart failure called heart failure with preserved ejection fraction.

Also known as HFpEF, heart failure with preserved ejection fraction occurs when the heart pumps blood and contracts relatively normally, but is too stiff to fill and relax properly. About 6.5 million adults in the U.S. have heart failure, according to the Centers for Disease Control and Prevention, and about half of those people present with HFpEF. In the U.S., more than 80% of people who have HFpEF are overweight or obese. Importantly, to date, there are no drugs approved by the Food and Drug Administration to improve clinical outcomes in HFpEF, clearly highlighting the need to develop novel efficacious therapies.

Carbone launched a preclinical study in 2014. In a laboratory, he fed mice a high-sugar and high-saturated fat diet. Within eight weeks, the mice developed cardiac dysfunction and became obese. Importantly, when the mice were switched to a healthy diet with lower calories, the cardiac function returned to the baseline values, showing that the cardiac dysfunction induced by unhealthy diet is reversible, "suggesting there is hope — if you change your diet and your lifestyle."

Carbone and his colleagues also wanted to know whether, independent of caloric intake, improving the quality of the diet



could prevent the cardiac dysfunction. In a follow-up study, the Western diet was modified. Unsaturated (read: "healthy") fats were substituted for the saturated fats typically found in the Western diet. After being on the "high-healthy fat" diet for eight weeks, which is equal to several years in humans, Carbone said, cardiac function was preserved and mice did not become obese, despite consuming the same amount of calories."

After conducting the second round of preclinical research and observational study (i.e., without interventions) in patients with obesity and HFpEF, Carbone felt ready to launch a feasibility study to ensure that people would comply with a prescribed diet of increased unsaturated fatty acids. With pilot funding from Pauley and the VCU School of Medicine Department of Internal Medicine, he and his research team enrolled nine VCU Health patients in a 12-week dietary

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**Pauley researchers have determined a diet rich in healthy fats improves body composition and cardiac function.**

intervention aimed at having participants consume a recommended daily amount of foods rich in unsaturated fatty acids.

The results of the study, published last fall, demonstrated for the first time in scientific history that a dietary intervention aimed at increasing unsaturated fatty acid consumption was feasible and had the potential to improve cardiorespiratory fitness in people with severe obesity and HFpEF.

"Larger randomized controlled trials to test the efficacy of unsaturated fatty acids supplementation on cardiorespiratory fitness (i.e., exercise capacity) and clinical outcomes, as well as understanding the mechanisms through which unsaturated fatty acids may exert these beneficial effects are clearly warranted," Carbone said in the journal article. ❤️

### Next step: a larger study

Based on the data obtained through the feasibility study, Carbone was able to secure a three-year, \$231,000 grant from the American Heart Association to continue his research. He hopes the data he gathers from his work at the Clinical Research Unit will inform a larger, multicenter clinical trial that will examine the effects of a diet rich in healthy fats on clinical outcomes such as reduced mortality and reduced risk of hospitalization for HFpEF.

"If this study goes well, we will be able to do a larger study where we don't just look at exercise capacity and biomarkers," he said, adding that he plans to apply for funding from the National Heart, Lung, and Blood Institute at the conclusion of the current clinical research study. "A dietary intervention aimed at improving the quality of the diet, independent of changes in daily caloric intake, has the potential to change the way we treat patients with obesity and HFpEF."



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### Letter from the director

**While we were producing this issue of The Beat, the coronavirus pandemic hit the United States and changed the way we live and work. During this difficult time, each person in our VCU Health community has played an important role in combating COVID-19. I am grateful for everyone's efforts to fight a global risk that threatens the health of millions.**

As it came to light that COVID-19 can cause or exacerbate cardiovascular conditions, our Pauley team jumped into action to disseminate expert information and explore a possible vaccine. In the pages that follow, Drs. Michael Kontos and Hem Bhardwaj address some of the most pressing questions about this novel coronavirus and its relationship to heart health. You'll also learn about the multidisciplinary efforts behind a VCU Health clinical trial of remdesivir, a potential drug to treat COVID-19. Dr. Antonio Abbate's knowledge of inflammation and cytokines was invaluable as this drug therapy was being tested. In the months ahead, we'll no doubt have more stories to tell as the crisis, and our response to it, evolves. Look for that coverage in the fall.

A crisis like the COVID-19 pandemic certainly brings out the best in people, but on any given day, in any week, in any year, the work at Pauley Heart Center makes me proud.

Our cover story highlights Dr. Jose Huizar's innovative response to a significant health problem called PVC-induced cardiomyopathy. Recognizing the importance of his work, which spans more than a decade, the National Institutes of Health is currently funding two of his studies. We describe those in detail here.

We're also excited to spotlight the Pauley Family Foundation's latest \$5 million gift to expand imaging into the field of electrophysiology, and the inaugural Discovery Richmond series that brought together Pauley donors, researchers and clinicians to discuss and share their work. The event was a career highlight for Dr. Jordana Kron, whose nationally recognized research into sarcoidosis, a debilitating systemic condition, we feature.

Rounding out this issue are additional Pauley team member accomplishments that give us a bit of cheer during these turbulent times. Every day, they're practicing our mission of taking each patient's heart health personally. I hope you'll enjoy learning about these exceptional individuals.

Sincerely yours,  
Dr. Greg Hundley



A publication of  
VCU Health Pauley Heart Center

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Gifts to VCU Health Pauley Heart Center allow us to invest resources in transforming patient care, education and research. For more information on how to honor a loved one or a caregiver, please contact Carrie Mills at (804) 828-0453 or [carrie.r.mills@vcuhealth.org](mailto:carrie.r.mills@vcuhealth.org).



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