Discoveries & Growth in Center for Cardiovascular Research

A multi-year planned progression and expansion of cardiovascular research within the Cardiovascular Division is paying multiple dividends in terms of nationally recognized discoveries in a broad swath of research areas.

“The Center for Cardiovascular Research has been at Washington University for 25 years,” says CCR director Jeanne Nerbonne, PhD. “But over the past decade, there has been a concerted effort to expand not only the number of physician scientists within the Center but also the depth and breadth of research activities.”

Nerbonne took the helm of the CCR in 2012. At the time, the center housed six laboratories, primarily focused on the metabolic origins of cardiovascular disease. Today the CCR is home to 13 independent research labs focused on diverse areas such as genomics, heart failure, inflammation, myocardial biology, arrhythmias, vascular biology and atherosclerosis. Key to the center’s growing success in basic and translational research has been a concerted effort to create a cross-disciplinary research environment that today spans 13 departments, five divisions, five centers, and three institutes across all of Washington University and the School of Medicine. The center also is home to the nation’s leading mouse cardiovascular phenotyping core and a human tissue bank and repository to facilitate genomic studies and other investigations.

The push to increase the number of physician-scientists in the division began in 2009, when Douglas Mann, MD, was named chief of the Division. “There was a critical unmet need in all of academic medicine for physician-scientists, including here,” he says frankly. “A few research programs had ended, and half of our labs were empty when I arrived. To really change the practice of medicine, we needed a robust and sustainable basic, translational and clinical research program.”

Mann and then Nerbonne made it a priority to recruit promising young investigators. In addition to looking across the country, they identified a critical pipeline — WU’s Medical Scientist Training Program (MSTP) and, more recently, the Department of Medicine’s own rigorous Physician Scientist Training Program (PSTP). The two also established critical benchmarks for success. One was to utilize the Division’s T32 training grant, one of the nation’s longest running, NIH-funded training programs in the country, to provide early financial support. Strong mentors were then recruited to help guide young investigators, with an eye toward having all research trainees successful at obtaining early career investigator awards.

“We have a 100 percent success rate in our young researchers obtaining K08...”

Continued on page 2

Heart & Vascular Center

The mission of the Washington University and Barnes-Jewish Heart & Vascular Center is to achieve excellence in patient care, research and education through seamless integration of heart and vascular care. The Heart and Vascular Center is committed to promoting heart and vascular health through education, prevention and treatment of heart and vascular disease.
Last summer in this newsletter, we focused on our extensive efforts within the division to deal with the COVID-19 pandemic and its impact on cardiovascular care. Here it is, six months later, and we still need to be flexible and nimble even as the first vaccines are being delivered across the country. We moved the cardiovascular intensive care unit at Barnes-Jewish Hospital multiple times over the past year and we don’t think it will be any time soon that the team returns to the original 8200 location due to the influx of coronavirus patients.

Cardiovascular research has been ongoing in the division despite the pandemic. Last spring, we forced a short but temporary shutdown of lab activity until protocols were established for social distancing and daily COVID screenings of researchers and staff. We also developed work-from-home guidelines. Clinical trials met additional challenges. Stringent protocols for screening and recruiting participants were added, along with tele-health components.

All of this helped maintain our momentum in a wide range of cardiovascular research efforts, which as you can see in our lead story, is a top priority within the division. We oversee one of the largest and most comprehensive centers for cardiovascular research in the nation and our researchers are prolific in the publication of novel studies that point to promising therapeutics or better understanding of cardiovascular disease. Of particular note is our proud history of award winners from the Northwestern Cardiovascular Young Investigators’ Forum; this year is no exception and I credit that to a university-wide commitment to mentor promising young researchers.

Moving forward, we recognize that education, research and patient care have changed as a result of the pandemic. It’s been hard work, but in all areas, we have identified avenues to continue our commitment to excellence.

Gregory A. Ewald, MD, FACC
Interim Chief, Cardiovascular Division

The following physicians have made donations in the past year to the Cardiovascular Division. Your support helps us to advance the field of cardiology by enhancing our fellowship training programs and supporting distinguished lectureships and other activities. Thank you for your support!

- Dr. Michael Cain
- Dr. Mohit Chawla
- Dr. Ali Ehsani
- Dr. Paul Eisenberg
- Dr. Jerome Fleg
- Dr. Lisa de las Fuentes

If you are interested in making a donation to the Cardiovascular Division, please contact Rachel A. Hartmann in the Washington University Medical Alumni and Development office at 314-935-9715 or rachel_hartmann@wustl.edu.

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Gregory A. Ewald, MD, FACC
Interim Chief, Cardiovascular Division
COVID-19 forced training programs across the country to cancel onsite recruitment activities this past year and move to a completely virtual format. The change gave us the opportunity to expand our presence online and broadened how we interacted with prospective fellows.

If you visit our website, you’ll notice that we created new videos and showcased interviews with senior fellows and former fellows who highlighted the unique benefits of our program as well as our commitment to diversity and physician well-being. Instead of a day-long onsite visit where prospective fellows could meet with multiple faculty and fellows, we transitioned to half-day virtual interviews and connected prospective applicants to specific faculty for follow-up conversations. Virtual visits meant that those who were interested in our program no longer had to contend with the expense of travel. As a result, programs nationwide saw increases in the number of applicants. We had more than 700 applicants, a 35 percent increase over 2019.

A diverse selection committee of 18 faculty and our chief fellow reviewed all applications. We took a holistic approach to identifying prospective trainees, looking beyond board scores and where they trained to also include life experiences, research interests, and other accomplishments. Two new Associate Program Directors joined us in these efforts: Katie Zhang as APD for Recruitment, and Karen Joynt-Maddox as APD for Diversity, Equity and Inclusion. We had a special focus on recruiting women, expanding underrepresented minorities, and recruiting physician scientists to our Division, which, in particular, will serve to enhance the depth and breadth of the Cardiovascular Research Center.

As we discuss nationally whether to resume onsite visits, continue with a virtual recruitment or offer a hybrid of the two this coming year, we are proud to introduce you to the newest fellows entering our program in July 2021.

**Fellowship Program Update**

**Andrew Kates, MD**

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**Alumni Update**

**George S. Chrysant, MD, FACC, FSCAI, FSCCT**

Cardiology Fellow, 2000-2003
Interventional Cardiology Fellow, 2003-2004

Currently: Chief Medical Officer, INTEGRIS Cardiovascular Physicians, INTEGRIS Heart Hospital, Oklahoma City, OK

Chrysant moved to the CMO leadership position after serving as director of advanced cardiac imaging and then chairman of the Department of Cardiology at INTEGRIS Baptist Medical Center in Oklahoma City. He also serves on the faculty of the University of Oklahoma Health Sciences Center, a position he’s held since 2006. The move to Oklahoma was a homecoming of sorts, as Chrysant previously earned his medical degree from the University of Oklahoma. He is board-certified in cardiology, cardiac CT and interventional cardiology with advanced training in cardiac MRI and has particular interest in carotid and peripheral intervention, structural heart disease and cardiac imaging. In his role as chief medical officer, Chrysant is responsible for overall research and quality efforts and leads the identification and implementation of best cardiovascular care practices. In this role, he says, “I enjoy staying on top of technology and science; it forces me to be up to date and I am always on the lookout to review the latest clinical trials and research efforts to effect changes in our practice and in the care of patients.”

Favorite Fellowship Memories: I truly believe I was lucky to train at Washington University. I still keep in regular contact with several faculty, Jasvinder Singh is like my older brother! Along with the great mentoring and both clinical and research opportunities, I think one of the fun highlights from my fellowship was when our soccer team, Med United, won the CYC championship in 2002. We played weekly games in Forest Park.

Favorite Leisure Activities: I still play competitive indoor soccer here in Oklahoma. My kids also play soccer and I enjoy seeing them get better and better. We love to travel and we typically go to Greece annually to see family for vacation. We love outdoor activities such as biking, hiking and skiing and our favorite place to get away is probably Jackson Hole, WY.

**2021 First Year Cardiology Fellows**

- Nicholas Arnold, MD
  University of Iowa
- Elin Beck, MD
  University of Iowa
- Douglas Hall, MD
  Washington University School of Medicine
- Stephen Philip, MD
  UT Southwestern
- Cliff Pruett, MD
  Washington University School of Medicine
- Walter Schiffer, MD
  Washington University School of Medicine
- Kristin Wong, MD
  UT Southwestern
- Raja Zaghool, MD
  Georgetown University
- Shiyang (Steven) Zhang, MD
  Washington University School of Medicine
High Protein Diets and Link to Cardiovascular Disease

A study led by Babak Razani, MD, PhD, has found that high protein diets can lead to the development of unstable plaque, which can increase the risk of heart attack. Specifically, researchers found that excess amino acids from a high protein diet activated mTOR, a protein in macrophages. Once triggered, mTOR blocked the cell’s ability to clean up plaque and other toxic waste. In laboratory studies, researchers found that mice fed a high-fat, high-protein diet developed 30 percent more plaque in their arteries as compared to those on a high-fat, low-protein diet. The mice developed the excess plaque despite not gaining weight.

Says Razani, “Not only did we identify a causal link between high protein diets and cardiovascular disease, we also identified a pathway where we have been successful in blocking the damaging effects of the mTOR protein, which could lead to the development of translational therapeutics to treat arterial disease and, in turn, heart attacks.”

The research was published in the January 23, 2020 edition of Nature Metabolism. Since then, researchers have started an IRB-approved clinical trial to evaluate the effect of high dietary protein intake on the immune cells of healthy volunteers to see if the same signaling pathways that were activated in mouse models also are activated in humans. “Completion of this trial would provide the first mechanistic glimpse of these important pathways in humans and set the stage for larger and more insightful clinical studies,” says Razani.

SVEP1 Promotes Atherosclerosis

Using Mendelian Randomization in humans and targeted gene deletions in mice, scientists in the Center for Cardiovascular Research have found that the extracellular matrix protein SVEP1 is causally related to the development of coronary artery disease. The research, led by cardiologist and human geneticist Nathan Stitziel, MD, PhD, builds upon ten years of research focused on the identification of novel genes and pathways that underlie the inheritance of coronary artery disease. Previously, a large-scale genetic study led by Stitziel identified a DNA sequence variant in SVEP1 that was associated with increased coronary disease in humans. A recent study from the Stitziel Lab, led by Postdoctoral Research Fellow In-Hyuk Jung, PhD and MSTP student Jared Elenbaas, MS, now finds that humans and mice with SVEP1 deficiency have a significant reduction in the development of atherosclerosis without a change in plasma lipid levels. Their research, in preprint with revisions under re-review, suggests that SVEP1 may represent a novel non-lipid therapeutic target for coronary artery disease.

Stitziel, an internationally recognized human geneticist investigating the mechanisms behind the development of cardiovascular disease, also oversees a large whole genome sequencing (WGS) program in Washington University’s McDonnell Genome Institute. Erica Young, MD, a cardiology fellow in Stitziel’s lab, is leading the analysis of WGS data from more than 50,000 multi-ethnic participants to identify novel genes underlying coronary artery disease. Early work from the program leveraged WGS data to study structural variation in the genomes of the first 17,000 participants. Says Stitziel, “Structural variants are difficult to identify using other techniques. As a result, little was previously known about the general characteristics and impact of this class of DNA variation in human populations.” The study was published in the July 2020 edition of Nature.

Increased Notch Pathway Activity Predisposes to AF

In research published in the September 17, 2020 edition of JCI Insight, cardiovascular researchers have found that Notch activation within left atrial cardiomyocytes generated a transcriptomic “fingerprint” resembling atrial fibrillation (AF) and could lead to better understanding and treatment of AF.

Up to 50 percent of patients with severe heart failure also have AF. The research, in the lab of Stacey Rentschler, MD, PhD, identified specific gene expression changes in tissue from patients with both AF and heart failure that were not present in those with just heart failure. Using a novel multidisciplinary cardiac reprogramming approach, researchers found that there were distinct cellular electrophysiologic responses in left atrial cardiomyocytes that were not generated in right atrial cardiomyocytes.

“In both animal models and in human tissue studies, there are distinct transcriptional networks within the left and right atria,” says Rentschler. “Our ongoing studies show that more genes are differentially regulated than similarly regulated between human atria in the setting of atrial fibrillation and although atrial fibrillation is considered to be more of a left atrial disease, pathways in the right atrium may also impact the development of AF through different mechanisms.”

This research is part of a large UH3 grant from the National Center for the Advancement of Translational Science/National Heart Lung and Blood Institute which spans from the patient’s bedside (EP lab) to transcriptomic studies to in vitro models of human atria (explanted human hearts and stem cell models).
School of Medicine Launches New Medical School Curriculum

Earlier clinical immersions, including cardiology

The matriculating class of students entering Washington University School of Medicine in fall 2020 arrived to experience its first major curriculum change in 20 years. The new educational program, called the Gateway Curriculum represents an overhaul from the prior curricular model. Under the new curriculum, students learn about health, disease, and illness in an integrated manner that aims to tie together the basic, clinical, and social sciences.

The curriculum also provides early clinical experiences for students to see firsthand how healthcare is delivered and how various healthcare professionals work in an interdisciplinary and collaborative way to provide care. These clinical “immersion” experiences are spaced throughout the first phase of their training.

“Cardiology is one of the first clinical immersion specialties students may experience during their first year,” says cardiologist Justin S. Sadhu, MD, MPH, FACC. “We are excited to design a rotation that exposes them to the broad range of careers available in cardiology, including in interventional cardiology, advanced imaging, electrophysiology, and heart failure. Major emphases of the Immersions include understanding the patient experience and reflecting on professional identity formation—the process of becoming a physician.

Sadhu serves as a team leader for the Circulation and Breathing module in Phase 1 of the curriculum. He previously served as course director for the cardiovascular pathophysiology course in the former curriculum model. He says the education re-design not only emphasizes a firm foundation of scientific and biologic knowledge, it also highlights how environmental, social, and structural factors influence the provision and outcome of care. Healthcare equity, diversity, and wellness also are prominent focal points within the curriculum.

Sadhu is among the first members of the School’s new Academy of Educators and was in the inaugural class of the University’s Teaching Scholars Program, which is designed to mentor and develop future leaders in healthcare education. “I have enjoyed pursuing my passion for medical education,” he says. “It’s been very rewarding to work alongside faculty in cardiology and from other diverse disciplines at the medical school to develop the Gateway curriculum. Washington University has a long and cherished history of developing leaders in medicine, and we are excited as the Cardiovascular Division to have a major role in training the next generation of physicians.”

National Research Awards

Two physician-scientists within the Division received awards during the 2020 Northwest Cardiovascular Young Investigator’s Forum, held virtually in September. Assistant Professor of Medicine Ali Javaheri, MD, PhD, received a First Place Award in the Junior Faculty Basic Science Category and cardiovascular research fellow Chien-Jung Lin, MD, PhD, received a Third Place Award in the Fellows Basic Science category.

Javaheri is a three-time winner at the NW Forum and himself a past NW Forum award winner. He is thrilled to design a rotation that exposes students to the broad range of careers available in cardiology, including in interventional cardiology, advanced imaging, electrophysiology, and heart failure. Javaheri states, “Ali and Chien continue in the long tradition of physician-scientists from the Division who have won awards at this forum and other national competitions.”

Diwan serves as Javaheri’s mentor on an NIH K08 Career Development Award. Lin is mentored by Robert Mechem, PhD, in the Department of Cell Biology & Physiology and co-mentored by Nathan Stitziel, MD, PhD, an investigator in the CCR with dual appointments in the Cardiovascular Division and Department of Genetics.

Diwan discusses the success of the Division’s T32 training program at https://cardiology.wustl.edu/training-programs/hear-from-our-fellows/
He once stood in the same place as our current fellows — a clinical cardiology fellow and then a cardiology research fellow at Washington University School of Medicine before joining the faculty in 1985. For Joseph Kenzora, MD, clinical cardiology was a joy after fellowship, but educating the next generation of cardiologists was his passion. Over his 35 year tenure in the Cardiovascular Division, Kenzora taught the intricacies of cardiac catheterization techniques.

"I trained five fellows annually for a total of 175 fellows over my time here," he says. "You try to show them how to do it and then allow them to learn it themselves. The biggest thing is that, as educators, we have to be patient and serve as a guide and a mentor to those we train."

Kenzora, who retired in October 2020, says when he first joined the faculty, most of the procedures he performed were routine cardiac catheterizations and diagnostic procedures. Almost all were done through a femoral approach. "In some cases, we'd enter through the arm, but femoral procedures were the standard back then," he recalls. "Catheterization procedures have now evolved to include subspecialties such as percutaneous interventions and the use of stents and percutaneous valves."

Among those who influenced Kenzora’s teaching style and dedication were Philip Ludbrook, MD, and Alan Tiefenbrunn, MD. Ludbrook established the first cardiac catheterization laboratory at Barnes Hospital/Washington University School of Medicine. "A lot of the people I’ve trained have gone on to run their own cardiac cath labs," Kenzora says. "You always hope you do a good job to pass along knowledge to the next generation by guiding and showing shortcuts or novel ways to do procedures. Every year, I tried to do a better job than the year before."

Kenzora says he hopes to stay in touch with faculty and former fellows even in retirement. He’ll miss the day-to-day interactions with colleagues, but he says he and his wife now want to travel. Hoping for the COVID pandemic to end, their dream is to head to Italy. At age 72, Kenzora notes with trademark humbleness, "It was a great enjoyment for me to work with fellows and staff here and I spent my career here."

He adds with a smile, "As it turns out, I think that worked out just fine."