

Cardiology

Physician Scientists – Not an Endangered Species at WU

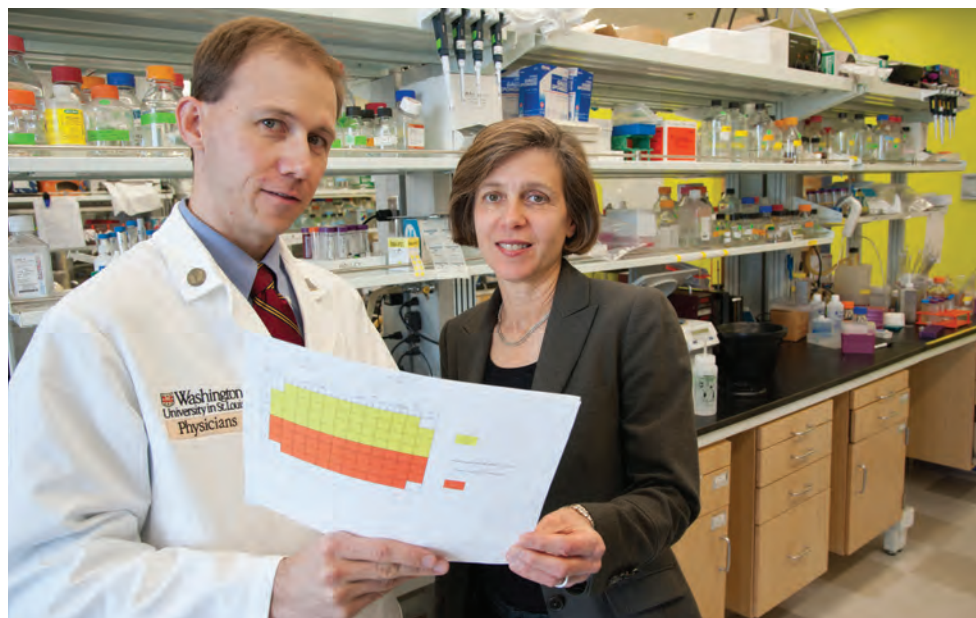
In the past two years, Washington University's Cardiovascular Division has lured eight physician scientists to join its faculty. The group is researching everything from the connection between diabetes and cardiovascular disease to the role immune cells play in helping cardiac tissue heal after injury. Complex studies on the development of cardiac fibrosis and heart failure as well as ways to engineer cardiac conduction tissues also are under way.

The robust research activities in the division contradict a national trend highlighted in a 2008 book, *The Vanishing Physician*, edited by Andrew Schaefer, MD, who noted that the number of physician scientists — MDs who dedicate a significant portion of their time to medical research — appears to be dwindling at medical institutions across the country.

"Physician scientists should be considered an endangered species," says **Joel Schilling, MD, PhD**, one of the newer faculty members. "The combination of increased clinical demands and tight research funding has led many to choose one path or the other. However, this occurs in a research climate that emphasizes translational medicine and which requires successful physician scientists to lead the charge."

The development of physician scientists is a key priority in the Cardiovascular Division, which offers protected research time and a collegial atmosphere for career mentoring of younger faculty members.

"I have mentors in cardiology and developmental biology," says **Stacey Rentschler, MD, PhD**. "Two have shared their laboratories, enabling me to get experiments going even before I have all the needed equipment



Christopher Holley, MD, PhD with research mentor Jean Schaffer, MD

in my own lab, "Others keep tabs on me to make sure I have the resources I need to be successful. I am very grateful."

Also key is start-up funding. "Clinical departments are becoming strapped for dol-

continued on page 2

Heart & Vascular Center

BARNES JEWISH
Hospital
BJC HealthCare

Washington
University in St. Louis
Physicians

NATIONAL LEADERS IN MEDICINE

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.

New CCR Director Named

Jeanne Nerbonne, PhD, the Alumni Endowed Professor of Molecular Biology and Pharmacology in the Department of Developmental Biology at Washington University School of Medicine, has been named the new Director of the Center for Cardiovascular Research (CCR), effective July 1, 2013.

The CCR supports basic research laboratories that focus on understanding the biologic processes that are responsible for cardiovascular disease. The CCR brings together cardiovascular researchers from wide ranging disciplines, including molecular and cellular biology, physiology, biophysics and bioorganic chemistry.

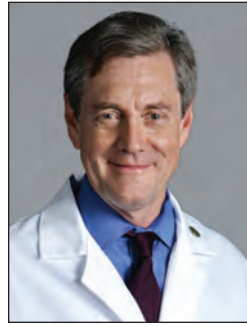
Nerbonne, who has been honored with a Distinguished Investigator Award from the School of Medicine, has been the recipient of numerous NIH grants focused on cardiovascular and neurobiology research and training. Nerbonne has been a leader in the field of ion channel physiology, with a focus on delineating the mechanisms involved in the regulation and modulation of voltage-gated ion channels in cardiac myocytes and cortical neurons.

In recruiting Nerbonne to the position, Douglas Mann, Lewin Professor and Chief of the Cardiovascular Division notes, "Jeanne is a terrific scientist and a wonderful mentor for many of our fellows and young physician scientists. I am confident she will establish the CCR as one of the premier cardiovascular research programs in the Country."

For more information about the Center for Cardiovascular Research, visit cardiology.wustl.edu/ccr-home.html.

To read more about Nerbonne's research interests, visit devbio.wustl.edu/nerbonne.htm

MESSAGE FROM THE CHIEF



As we were finalizing the June edition of the Alumni Newsletter we were saddened by the news of Dr. Burton E. Sobel's death on May 3rd (see back page). Burt's contributions to cardiology and the treatment of acute coronary syndromes were enormous and continue to be felt throughout the world. His contributions to the Cardiovascular Division were equally "huge." I have the privilege of seeing them every day through my interactions with the faculty and fellows that he trained. Many of you have contacted me about donations and ways to honor his memory, and I promise you that we will find a fitting way to do that.

The theme for this edition of the newsletter was the Cardiovascular Division's focus on developing the next generation of physician scientists, which was something that Burt told me that he was incredibly proud of and supportive. As our lead story highlights, physician scientists in the Cardiovascular Division are not "vanishing." Indeed, they are thriving. With the addition of Jeanne Nerbonne, PhD, a superb scientist who will head our Center for Cardiovascular Research (CCR), we are positioning the Division to remain as a leading center for basic and translational research. Our incoming fellows will benefit from the richness of the environment that has been created through recruitment of outstanding faculty and investment in our research programs. We'll continue to keep you posted on our continued efforts to enhance our tripartite missions of patient care, research and education. As always, I invite you to keep in touch as your career takes you beyond your initial training at Washington University. I hope to see you at national meetings in the future.



Douglas L. Mann, MD

Lewin Professor and
Chief, Cardiovascular Division

Physician Scientists

continued from page 1

lars, impacting their ability to support young investigators," says **Slava Epelman, MD, PhD**. "Fortunately, Washington University, and, in particular, the Cardiovascular Division, continues to value physician scientists by providing support, especially during the early stages of an investigator's career."

Christopher Holley, MD, PhD, an instructor in the Division's heart failure section, sees some national trends impacting potential physician scientists. "The increasing complexity of clinical medicine coupled with a difficult economic environment in healthcare today has led to rising numbers of clinical-only faculty in many university settings," he says. "While they can focus 100% on maintaining the highest level of clinical skills, it

also means that they are not engaged in any research. This is one of the few top-10 institutions in the country that has been actively recruiting physician scientists to cardiology in the past couple of years."

Adds **Nathan Stitzel, MD, PhD**, "The ability to frame scientific investigation through the prism of clinical patient care is the fundamental power of the physician scientist. This unique amalgam of clinical practice and investigation has a tradition of producing meaningful advances in the basic understanding of disease mechanisms along with the development of novel diagnostic and therapeutic strategies. The division has had a long and rich history of scientific investigation. Its commitment to research and support for physician scientists reflects both this strong history and its vision for the future."

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ALUMNI

News & Awards



Fellowship Program Update

by Andy Kates, MD
Fellowship Program Director

I am thrilled to see the caliber and inquisitive nature of our incoming class. We have successfully recruited a group of fellows that is quite diverse, both in backgrounds and career plans. Several have advanced degrees, including two PhDs and one MPH; one has served in the National Health Corps; several were chief residents; one wants to develop a transplant program back in his home state

of Hawaii; another wants to focus on heart disease prevention in urban settings; and a third hopes to return and establish a research program and practice in Italy. All come here to a program rich in both its diversity of fellows and faculty as well as wide-ranging career options. To better instill the knowledge and critical thinking skills they need to succeed and advance the field of cardiology, we re-designed our educational curriculum over the last few years to make it more case-based and interactive between faculty and fellows. Conferences now include three targeted conferences on congenital heart disease, heart failure, and electrophysiology. For former fellows, our Wednesdays have a whole new look. Our divisional Grand Rounds, held bimonthly, regularly feature guest faculty

from around the country with outstanding national and international reputations. An informal lunch follows with our fellows to continue the discussion. Grand Rounds alternate with the Patient Management Conference, which highlights the clinical approach to patient care and features interactive discussions from faculty within the division and around the medical school; and the Morbidity and Mortality Conference which is now division wide and provides a forum for fellows and faculty to discuss adverse patient outcomes and identify system process improvements. I'm confident the changes we've made will have a long-term impact on how our fellows approach patient care and research, no matter where their careers take them.

Alumni Update

Howard J. Eisen, MD, FACC, FAHA, FACP

(Clinical Cardiology Fellow '84-86, Research Cardiology Fellow/Instructor '86-87)

Currently: Thomas J. Vischer Professor of Medicine and Chief, Division of Cardiology, Drexel University College of Medicine and Hahnemann University Hospital

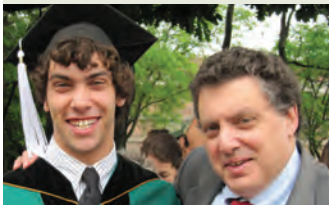
My goal was to rebuild and expand full-time cardiology faculty from five members in 2005 to 15 currently. We also expanded

clinical programs and broadened outreach by establishing cardiac care services at other nearby hospitals and outpatient facilities. At Hahnemann, I established a Cardiology Inpatient Hospitalist Service. We have scientific collaborations with Drexel's School of Biomedical Engineering and other academic departments such as physiology, biochemistry, and pharmacology. We also have a growing reciprocal relationship with Sejong General Hospital in South Korea

Favorite Leisure Activities: Travelling with my family here and abroad. I also spent time in St. Louis while my son, Jonathan, was at WU. He is now a medical student at Mt. Sinai. Our daughter, Miriam, is at Cornell.

Favorite Fellowship Memories: The mid-1980s were incredibly exciting with numerous advances ranging from thrombolysis to cardiac transplantation. I was part of the team

that established Barnes' cardiac transplant program. The fact that you could treat what had been incurable, advanced heart failure was staggering and the nuances of managing immunosuppression were sobering. I conducted immunology research in the lab of Steve Bergmann, who was a great mentor. The Division had a large NIH SCOR grant and weekly SCOR seminar. I have never prepared so hard for a talk before or after as I did for my SCOR seminar. On the clinical side, I enjoyed the echo lab with Julio Perez and Ben Barzilai. I also enjoyed the EP rotations with Mike Cain and Bruce Lindsay, although the reams of paper generated and lengthy studies convinced me that I should focus on other aspects of cardiology! My foundations as a clinician and clinical investigator were established during my fellowship at WU and I don't think I could have gotten better training anywhere.



Howard Eisen (right) with son Jonathan at 2010 WU graduation.

Career Paths - Departing Fellows

Elisa Bradley: Adult Congenital Cardiology Subspecialty Fellow at Ohio State University and Nationwide Children's Hospital

Jeremiah Depta: Interventional Cardiology Fellow at Brigham and Womens' Hospital

Ajit Janardhan: Electrophysiologist, Prairie Cardiovascular Associates, Belleville, IL

Shane LaRue: Instructor in Medicine, Washington University School of Medicine

Ashwin Ravichandran: Heart Failure and Transplant Cardiologist at St. Vincent's Medical Group, Indianapolis, IN

Shimoli Shah: Assistant Professor of Medicine at the Knight Cardiovascular Institute, Oregon Health & Science University, Portland, OR

Shivak Sharma: Staff Cardiologist, Southern California Kaiser Permanente Medical Group, San Diego, CA

Veli Topkara: Advanced Heart Failure & Transplant Cardiology Fellow at Columbia Presbyterian Hospital, NY

FACULTY

News & Awards

Perez Honored as Gifted Educator

Julio E. Perez, MD, FACC, Professor of Medicine and Director of Echocardiography, is the distinguished recipient of four honors highlighting his passion and skill at educating the next generation of cardiologists. Perez received the ACC's Gifted Educator Award as well as the American Society of Echocardiography's Richard Popp Excellence in Teaching Award. He also received WU School of Medicine's 2013 Distinguished Educator-Clinical Fellow Mentoring Award and the Medical Center Alumni Association's Faculty Achievement Award. "He has made it his life's mission to teach cardiac physiology and pathophysiology through echocardiography, says Linda Peterson,



Perez with ACC President William Zoghbi, MD

MD, Associate Professor of Medicine and Radiology, who nominated Perez for an award. "Julio has taught over 300 cardiology fellows at Barnes-Jewish Hospital. Anyone who has heard Julio lecture, watched him perform, or watched him read an echo is a better physician because of it." Adds Jose Banchs, MD, Director of Echocardiography at MD Anderson who trained under Dr. Perez, "For over 30 years, he has been a standard in the field of cardiovascular ultrasound and in education. His teaching accomplishments, his outstanding level of

professionalism, gentleness, and caring sets him apart from all others and will make for my own lifelong quest to emulate."

Mann Receives AHA Award

Douglas Mann, MD, Lewin Professor and Chief of the Cardiovascular Division, is the recipient of the 2013 Hugh D. McCulloch Award given by the Greater St. Louis Division of the American Heart Association. The award recognizes physicians who help further the mission of the AHA in "building healthier lives free of cardiovascular diseases and stroke." In nominating Dr. Mann for the award, his colleague Michael Lim, MD, a St. Louis board member for the AHA and a member of the faculty at Saint Louis University School of Medicine, noted that "Doug has never missed an opportunity for promotion of any endeavor that may lead to increased awareness or improved cardiovascular health within the St. Louis community." Dr. Mann has been head of the cardiology division at Washington University School of Medicine for the past four years. He also serves as editor of *Heart Failure, A Companion to Braunwald's Heart Disease*, 2nd edition, and a co-editor of *Braunwald's Heart Disease*, 9th edition, the leading textbook in cardiovascular medicine. In addition to serving as chief of cardiology, Dr. Mann is the medical director of the Washington University/Barnes-Jewish Hospital Heart & Vascular Center. In 2012, he received the hospital's President's Achievement Award for Excellence in Patient Care. "My patients are



the most important part of the work I do," Mann says.

Douglas Mann, MD (center) with AHA Board President George Kichura, MD (left), and AHA board member Doug Knowling.

Electrophysiology Pioneer Speaks at Annual Boineau Lecture



Melvin Scheinman

Renowned cardiologist Melvin Scheinman, MD, Professor of Medicine, Walter H. Shorenstein Endowed Chair in Cardiology at the University of California-San Francisco, was the guest lecturer at the 2nd Annual John P. Boineau Memorial Lecture held in March. Scheinman, who discussed the history of Wolff-Parkinson-White Syndrome, is one of the founding

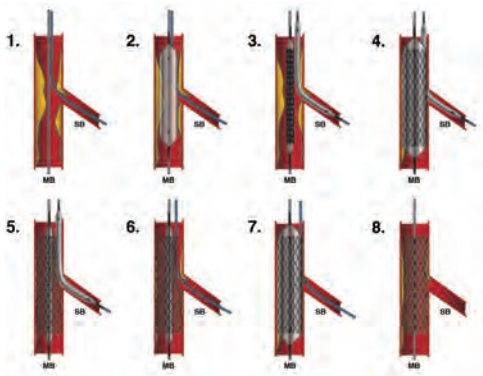
fathers of the field of cardiac electrophysiology. He is best known as the first person to have performed catheter ablation in humans. He also is well-known for his work defining the role of electrophysiologic studies in determining the need for pacemakers in patients with AV conduction disturbances. He was the first to initiate combined pacemaker and beta-blocker therapy for patients with long QT syndrome. His current interests revolve around the use of new anti-arrhythmic agents and in defining the basic mechanisms of unusual forms of atrial flutter. The Boineau Memorial Lecture, co-sponsored by the Cardiovascular Division and Division of Cardiothoracic Surgery, was started in 2012 to commemorate the spirit and memory of John P. Boineau, MD, who passed away in 2011. He was a pioneer in the surgical treatment of Wolff-Parkinson-White Syndrome and was instrumental in helping to develop the Maze procedure for the treatment of atrial fibrillation.

DIVISION RESEARCH HIGHLIGHTS

Retrospective Study Shows Value of Provisional “Jailed-Balloon”

Stenting Technique

A retrospective study of 100 WU cardiology patients has found that the use of a modified provisional stenting technique with a “jailed balloon” during percutaneous coronary intervention (PCI) is highly effective to maintain or restore side branch arterial flow during treatment for complex bifurcation lesions. PCI is challenging in bifurcation lesions because stenting of the main branch artery can negatively impact the side branch, requiring it also to be stented in up to 51 % of cases. The modified stenting technique, developed by interventional cardiologist **Jasvinder Singh, MD**, involves accessing both the main and side branch arteries with coronary guidewires. Once an uninflated balloon is placed into the side branch, a coronary stent is deployed in the main branch over the lesion. If the side branch is not compromised, the uninflated balloon is removed. Routine angioplasty is performed if the side branch becomes occluded and needs to be re-opened. Singh says provisional stenting is associated “with a high



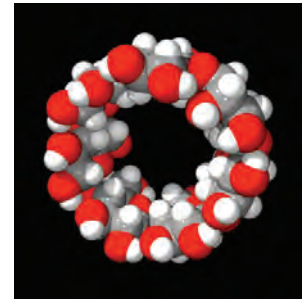
success rate, improved side branch patency and a low rate of adverse cardiac events.” The study appeared in the June 2012 edition of the *Journal of Interventional Cardiology*.

New Low-Energy Atrial Defibrillator Therapy Developed

A cardiac electrophysiology fellow and a professor of biomedical engineering at Washington University have developed a low-energy defibrillation therapy that significantly reduces the energy needed to re-establish a normal heart rhythm in patients with a sudden, life-threatening abnormal heartbeat called ventricular tachycardia. The new electrotherapy, published with a complementary editorial in an online edition of the *Journal of American College of Cardiology*, is aimed at reducing the pain and damage to the heart caused by shocks delivered from existing implantable defibrillators. “These devices save lives, but also damage the heart,” says **Ajit H. Janardhan, MD, PhD**, cardiac electrophysiology fellow. “Some patients are so stressed by the pain and trauma from a sudden shock that they ask their physician to remove the defibrillator.” Instead of a single high-voltage shock, Janardhan and Igor Efimov, PhD, endowed professor of biomedical engineering, showed that a sequence of multiple, closely-timed, low-voltage shocks were not only more effective at restoring heart rhythm, but also enabled them to reduce the peak shock amplitude from in excess of 200 volts to under 10 volts, and to reduce the total shock energy by nearly 100 fold. The two have received an NIH grant to develop a low-energy atrial defibrillator and will begin clinical trials in the near future.

WU-NIH Partnership to Study Rare Disorder

Washington University researchers are helping to test a new application of a cyclic sugar compound called cyclodextrin in hopes that it will reduce excess cholesterol that can accumulate in the brain, liver, and spleen. Specifically, researchers are trying to find effective treatments for a rare disorder called Niemann-Pick Type C. The disease affects an estimated 500 children worldwide and



causes cholesterol to build up inside lysosomes, eventually leading to neurodegeneration and death.

In laboratory

tests, high doses of cyclodextrin have been found to be effective at breaking up the excess cholesterol. “It’s superior to all other compounds we have tested,” says **Daniel S. Ory, MD**. In studies, cyclodextrin delivered directly to the brain acted as a key that unlocked trapped cholesterol, allowing it to be properly metabolized and removed. Phase I efficacy trials are under way in collaboration with the NIH Clinical Center. Ory and his colleagues also identified new ways to diagnose Niemann-Pick Type C and now hope to adapt those techniques for newborn screenings. “If we can diagnose at birth and have treatments like the one we are testing, we could intervene before the onset of neurological symptoms.”

Research Awards

The following new research awards were made to cardiology faculty during January – May 2013.

Shelton Caruthers: ICTS: Improved Diagnosis of Transplant Coronary Artery Disease by Contrast-Enhanced MRI

Peter Crawford: Children’s Discovery Institute: Integration of the Ketogenic-Ketolytic Axis with Metabolic

Gregory M. Lanza/Y. Andrew Wang: NIH R42: Targeted Nanoparticles of Bismuth Organo Complexes for Spectral CT Imaging of Coronary Ruptured Plaque

Dan Ory/Jean Schaffer: NIH RO1: Oxysterol Biomarkers for Niemann-Pick C Disease

Linda Peterson: ICTS: Dietary Nitrates for Heart Failure

Jean Schaffer: NIH P20: Pilot and Feasibility Project

Sam Wickline/Joshua Hood: The Campbell Foundation: Topical Fusogenic Nanosnares for HIV Prophylaxis

Burton Sobel — The Passing of a Cardiovascular Pioneer



Burton E. Sobel, MD, internationally known leader in cardiovascular medicine, prolific scientist and former longtime director of the Cardiovascular Division at Washington University School of Medicine, died this past May at his home in Vermont. He was 75. Sobel served as chief of cardiology at Washington

University and Barnes Hospital from 1974 until 1994. He came to Washington University in 1973 as an associate professor of medicine and director of the Cardiovascular Division at the School of Medicine and at Barnes and Wohl Hospitals. He was named the Tobias and Hortense Lewin Distinguished Professor in Cardiovascular Disease in 1985. After his tenure in St. Louis, Sobel joined the faculty of the University of Vermont as chair of the Department of Medicine in 1994. He served as a University Distinguished Professor of Medicine and a professor of biochemistry as well as founder and first director of the University of Vermont's Cardiovascular Research Institute.

Sobel's research was far reaching and included major contributions to the treatment of heart attack, including best methods for dissolving blood clots, and the understanding of cardiovascular disease in the context of type 2-diabetes and insulin resistance. He pioneered the development of tissue plasminogen activators (tPA), among the most commonly used clot-busting drugs. Sobel's early work in this area laid the founda-

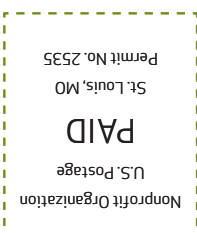
tion for his leadership roles in multicenter clinical trials that showed the effectiveness of drugs, including tPA, heparin and aspirin, in dissolving clots and reducing deaths due to heart attacks and coronary artery disease. More recently, Sobel was a leader in the evolving understanding of the relationship between diabetes and heart disease.

A prolific academic, Sobel published more than 900 peer-reviewed articles, invited reviews, editorials and book chapters. He also held positions on the editorial boards of many high-profile medical journals focused on cardiology, including editor of *Circulation*, associate editor of *The Journal of Clinical Investigation*, and board member of *Annals of Internal Medicine* and *The American Journal of Cardiology*. As editor of *Circulation*, he is credited with innovations that raised the journal's profile and shaped the field of cardiology and its current directions.

"Dr. Sobel was the consummate physician scientist who translated basic science concepts regarding clot-dissolving agents into clinical trials that have saved the lives of countless patients," said Douglas L. Mann, MD, the Tobias and Hortense Lewin Professor of Medicine and current chief of Washington University School of Medicine's Cardiovascular Division. "He also was responsible for putting our Division on the map. His academic legacy lives on here through the innumerable residents, fellows and faculty that he trained and supported."

Sobel is survived by his wife of 55 years, Susan; his children, Jonathan and Elizabeth; and a granddaughter.

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