

CARDIOLOGY

Cardiovascular Genetics

In the near future, it may be routine for patients to undergo genetic testing as part of their treatment for heart problems. The addition of genetic testing has been discussed for years, but it's only been recently that Washington University cardiologists have used genetic testing in wider clinical applications.

"We've known for years that there is a hereditary basis for many forms of heart disease," says cardiology researcher **Nathan O. Stitzel, MD, PhD**. "Over the past 20 or so years, specific genes have been identified that cause heart disease. Now we can do precise genetic testing for those and then use the results to counsel both patients and their families."

Stitzel was instrumental in working with Washington University's Genomics and Pathology Services (GPS) to refine the CardioGene Set, a list of next-generation gene sequencing tests to pinpoint genetic abnormalities in several diseases related to arrhythmia and cardiomyopathy, including Long QT, Short QT, Brugada Syndrome, hypertrophic cardiomyopathy, and dilated cardiomyopathy, among others. With a background in both medicine and mathematics, Stitzel looks at cardiovascular genetics as a blossoming field that combines data analysis with science.

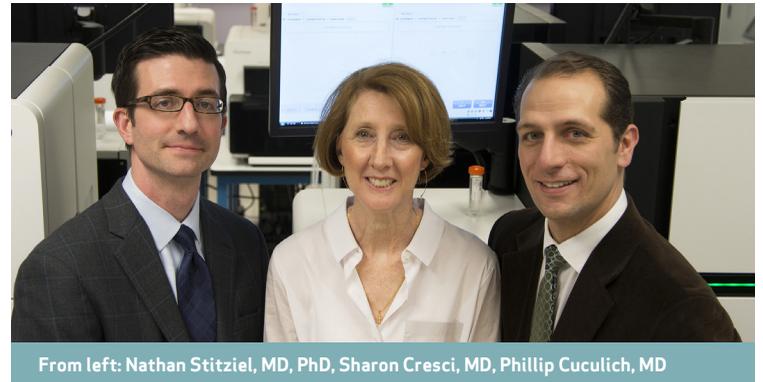
"The most appropriate use of gene testing is when you have a clear phenotype, the patient clearly has the disease, and you want to determine the best method of treatment," says electrophysiologist **Phillip S. Cuculich, MD**, who focuses on sudden cardiac death and arrhythmias and has used commercial gene testing on a handful of patients over the

past several years. "Genotyping can identify the various types of Long QT syndrome, for example. In one type, beta blockers are helpful to prevent life-threaten-

ing arrhythmias. In another, beta blockers are potentially harmful. By knowing the type we can tailor medical therapy and any recommendations for a defibrillator."

The larger benefit to genotyping is the ability to first confirm a hereditary component and then to test family members to see if they also carry a genetic mutation and should be monitored. Once a hereditary component is found, the next step is to figure out what triggers the gene(s) to turn on and off.

Sharon Cresci, MD, currently directs



From left: Nathan Stitzel, MD, PhD, Sharon Cresci, MD, Phillip Cuculich, MD

the Genomic Core Labs for the international Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes (BARI 2D) and multicenter Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status (TRIUMPH) studies. She specializes in pharmacogenomics research — identifying the genetic determinants that influence a positive or adverse drug effect. She studies patients with hypertrophic cardiomyopathy (HCM), looking for modifier genes. "HCM is an autosomal

Continued on page 2

Heart & Vascular Center



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.

Newest Fellowship Matches for Cardiovascular Division



Pedro Calderon, MD
Case Western



Matthew Chung, MD
Duke



Spencer Gaskin, MD
UTSW



Fartima Karaki, MD
BJH



Nathan Lo, MD
UTSW



Trevor Posenau, MD
Duke



David Raymer, MD
BJH



Nishtha Sodhi, MD
Cleveland Clinic



Sandeep Sodhi, MD
BJH



Tyson Turner, MD
UCSF

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888-210-8375

MESSAGE FROM THE CHIEF



Greetings! In this issue of our Winter alumni newsletter, we focus on a number of timely cardiovascular topics that have developed recently. Our lead story on cardiovascular genetics notes that the push to understand the underlying causes of cardiovascular disease is leading to more personalized and targeted treatments for patients. We know that genetic differences can dramatically alter the types of medications we prescribe to heart patients. Our new Center for Cardiovascular Genetics is an opportunity for patients with potentially life-threatening and inherited cardiovascular diseases to

benefit from this growing trend in translational medicine and genetic research.

I hope many of you had the opportunity to attend our annual AHA satellite symposium in Dallas, which focused on new developments in structural heart disease, and were able to attend our first Smith-Oliver Society alumni reception immediately following the symposium. The growing interest in structural heart disease was reflected in the number of participants, which was well over 100 people. To address this growing field of cardiovascular specialization within our own fellowship program, we are creating a new training pathway focused on structural heart disease that will be led by John Lasala, MD, Director of Structural Heart Disease.

We also had a successful symposium here in St. Louis — our second annual Cardiovascular Research Day — featuring cardiovascular research activities across Washington University. The highlight of the symposium was the first annual Sobel Lecture, presented by Eric N. Olson, PhD, Professor and Chairman of the Department of Molecular Biology at UT Southwestern Medical School in Dallas, Texas. I am proud to say that the Sobel Lectureship was made possible by the generous contributions of our faculty and alumni! We continue to support a significant number of research efforts, and we believe that our ongoing efforts will enhance the care we provide to patients and their families. I am also delighted to announce that we had another outstanding fellowship match, thanks to the efforts of our fellowship coordinator, Ava Ysaguirre, and Andy Kates.

I hope you will continue to keep us updated on your career paths. It's always a pleasure to hear from alumni who continue to excel in clinical care, practice, and research.

Douglas L. Mann, MD

Lewin Professor and
Chief, Cardiovascular Division

Cardiovascular Genetics

Continued from page 1

dominant disease that's inherited 50 percent of the time," Cresci says. "Through gene analysis, we are trying to predict which patient will get the disease and why."

The job is daunting because there are more than 1,000 causative mutations so far identified. Already, Cresci has found that there are both genetic variants and racial differences in the way that patients respond to a class of drugs that are the most common first-line medical therapy for HCM known as beta blockers. She has an NIH R01 grant that funds a pilot study known as PRISM GENOMICS that will ultimately lead to the implementation of a comprehensive cardiac analysis tool that combines genetic testing and analysis of other patient characteristics to

individualize treatment of cardiovascular disease. "Personalized medicine may have genetic, racial, even environmental influences and we have to take that into account when we treat patients," she says.

Last year, the Division debuted the Center for Cardiovascular Genetics. Headed by Stitzel, the Center coordinates genetic testing and offers counseling to patients as well as their families. It is the only center of its kind in the region.

"Because we focus solely on addressing the genetic questions related to cardiovascular disease, we have the ability to really hone in on the nuances of genetic test results, Stitzel says. "And with both research and a subspecialty clinical practice, we hope to become a regional resource not only for families but also other cardiologists who may suspect a genetic etiology in a patient's heart problems."



From Left: Jose Madrazo, MD, Kathryn Lindley, MD, Justin Sadhu, MD, Andrew Kates, MD

by Andy Kates, MD

Fellowship Program Director

Our cardiovascular fellowship program is known both as an environment rich in experience and practice and as one that offers a wide range of career path options. The flexibility of our third year, in which we offer 10 cardiology career training paths, is the hallmark of our program.

For those desiring a career in general cardiology, we now have a new aspect of our program that gives fellows the real-life experience of working in a fully staffed cardiology clinic. The Cardiovascular Fellows Clinic — launched in September — provides select senior fellows with greater autonomy commensurate with their level of training. The clinic provide fellows with nursing and resident support as well as office support. Fellows order and follow up on lab tests.

In this setting, patients identify with these fellows as their primary cardiologists. They are, of course, under the supervision of several attendings, but the goal is to help launch their independent mindset and their management skills so that they are truly ready to step into a busy cardiology practice.

The first two senior fellows already are working in the clinic. These general cardiologists are able to experience the in-depth nature of their specialty much like those who follow prescribed subspecialty paths in electrophysiology, imaging, or heart failure. The overwhelming majority of our fellows will pursue a general cardiology career; it makes sense to develop the training program so that our fellows leave fully prepared to run their own successful practice.

Alumni Update

Michael Sack, MD, PhD

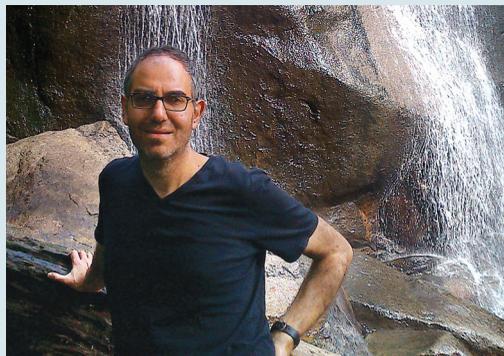
(Clinical Cardiology Fellow 1994 – 1997)

Currently: Acting Chief, Cardiovascular and Pulmonary Branch of the National Heart, Lung, and Blood Institute in Bethesda, Maryland

Dr. Sack joined the NHLBI in 2003. In 2012, he received the NHLBI's Star Award for Excellence in Clinical Care. Now as acting chief of the Cardiovascular and Pulmonary Branch, Dr. Sack is moving to re-invigorate the program through both research and in contributions toward the training and advancement of the next generation of physician scientists. In research, he hopes to focus the NHLBI's work on understanding the genetic, environmental, and social factors that impact and interact the development and progression of cardiometabolic and pulmonary diseases. He also wants to hone in on the mechanisms underpinning those diseases in order to develop novel therapeutic targets.

Favorite Leisure Activities: Hiking! I've climbed Mount Kilimanjaro, hiked to the basin of the Grand Canyon, and spent last summer with my family exploring the Blue Ridge Mountains. I also enjoy U.S. and world history and belong to an active book club.

Favorite Fellowship Memories: The diversity of scientific pursuit at Washington University inspired me to pursue biomedical research as a career. I learned to be a molecular biologist in the laboratory of Dan Kelly. Phil Barger was a great mentor in exposing me to the thrills of fundamental discovery. Clinically, I found that the long hours spent in the dark echo lab, under the supervision of Julio Perez, have been of exceptional benefit in my patient care responsibilities.



Michael Sack, MD, PhD, at Mount Pisgah National Park, NC

2013 Fellows

Welcome to our 2013 first year fellows:



Luigi Adamo, MD



Mirnela Byku, MD



Rafael Garcia-Cortes, MD



Tracy Hagerty, MD



Gmerice Hammond, MD



Paul Lavigne, MD



Deana Mikhalkova, MD



Michael Nassif, MD



Praveen Rao, MD

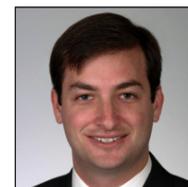


Casey Wong, MD

2013 Subspecialty Fellows:



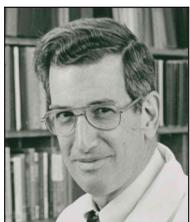
Alejandro Aquino, MD
Interventional



Robert Shapiro, MD
Interventional



Justin Vader, MD
Heart Failure



Burton E. Sobel, MD



Eric N. Olson, PhD

Burton E. Sobel Lecture

2013 Keynote Speaker — Eric N. Olson, PhD

Eric N. Olson, PhD, Professor and Chairman of the Department of Molecular Biology at the University of Texas Southwestern Medical Center in Dallas, was the keynote speaker for the Division's inaugural Burton E. Sobel Lecture. The lecture was held during Cardiovascular Research Day, an annual event sponsored by the Division and the Center for Cardiovascular Research.

Olson, who holds the Robert A. Welch Distinguished Chair, the Pogue Distinguished

Chair in Research on Cardiac Birth Defects, and the Annie and Willie Nelson Professorship in Stem Cell Research, spoke about “Deciphering the Mechanisms of Heart Development, Disease, and Regeneration.”

“Dr. Olson is an outstanding investigator who has made many seminal contributions to our present understanding of cardiovascular development, physiology, and pathophysiology,” says Jeanne M. Nerbonne, PhD, Director of the Center for Cardiovascular Research. “Working at the interface between developmental biology and medicine, Dr. Olson and his colleagues have provided novel insights into the fundamental mechanisms that control heart formation. They also have identified new pathways and concepts that hold great promise for novel cardiovascular therapeutics.”

Olson earned his doctorate in biochemistry from Wake Forest University. After postdoctoral training at Washington University School of Medicine with Luis Glaser,

PhD, he joined the Department of Biochemistry and Molecular Biology at MD Anderson Cancer Center in 1984 and became Professor and Chairman in 1991. In 1995, he founded the Department of Molecular Biology at The University of Texas Southwestern Medical Center.

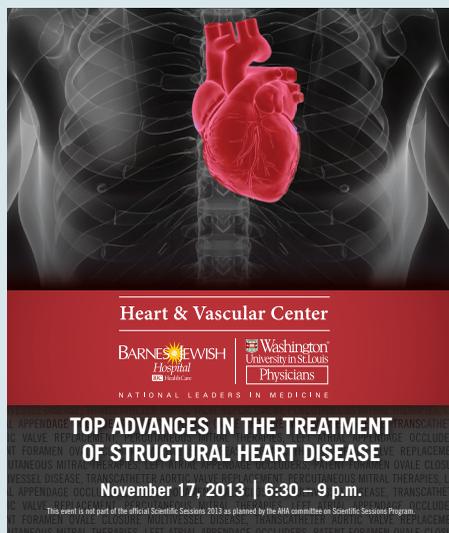
In addition to his academic accomplishments, Olson has co-founded multiple biotechnology companies to design new therapies for heart muscle disease based on his research. His work has been honored by multiple organizations, including the American Heart Association. In 2009, the French Academy of Science awarded Dr. Olson the Fondation Lefoulon-Delalande Grand Prize for Science.

The Sobel lectureship is named in memory of Burton E. Sobel, MD, the former head of the Cardiovascular Division at Washington University School of Medicine. Sobel, who served as chief of cardiology from 1974 to 1994, passed away in 2013.

2013 AHA Satellite Symposium: Top Advances in Structural Heart Disease Treatments

The 4th Annual AHA Satellite Symposium hosted by the Cardiovascular Division was held in Dallas in mid-November. More than 100 people attended the symposium, which focused on structural heart diseases.

“It’s a burgeoning field that includes congenital diseases such as atrial or ventricular septal defects and patent foramen ovale (PFO) as well as abnormalities of the valves and other structures of the heart that may develop later in life,” says John M. Lasala, MD, PhD, Director of Structural Heart Disease and lead coordinator of the AHA satellite symposium. “We have been on the frontlines for most



of the seminal trials related to treatments for structural heart diseases and had excellent presentations and discussions about the latest advancements.”

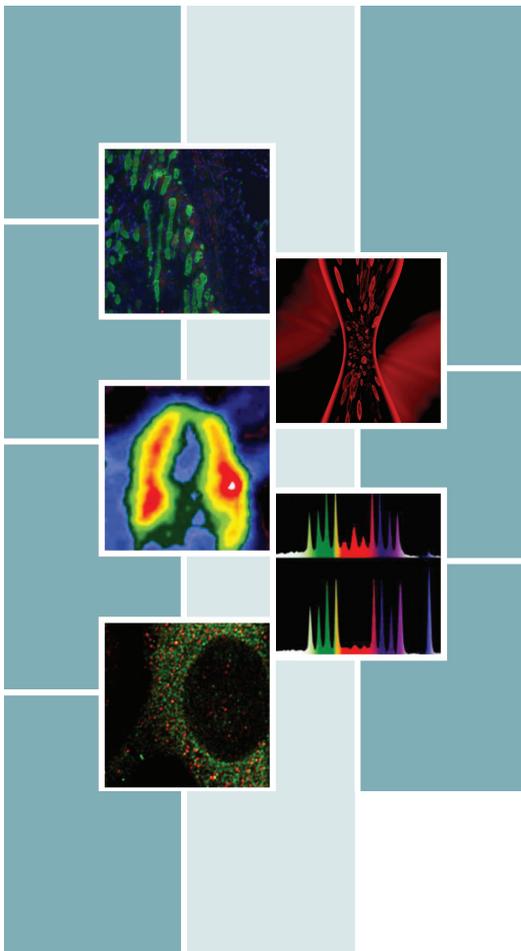
Among the topics was the use of the MitraClip®, a device just approved by the FDA in October 2013 for patients with symptomatic degenerative mitral regur-

gitation (MR). The Division was among the first sites that evaluated the clip’s effectiveness in high-risk patients deemed ineligible for surgical intervention. “We’ve seen success in 75% of cases,” says Lasala.

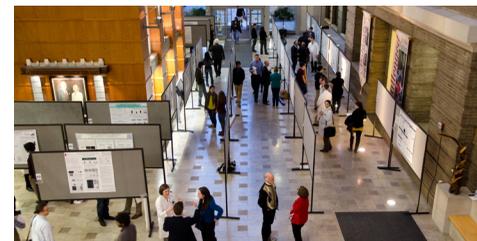
Other topics updated included the latest approaches to transcatheter aortic valve replacements (TAVR). Along with Lasala, Washington University cardiothoracic surgeons Hersh Maniar, MD, and Ralph J. Damiano Jr., MD, and interventional cardiologists Alan Zajarias, MD, have been at the forefront of developing the less-invasive TAVR procedure for patients diagnosed with severe aortic stenosis. Another lecture focused on the differing opinions related to the use of blood thinners or the Amplatzer PFO Occluder to prevent recurrent clots or strokes in young patients with PFOs.

Says Lasala, “All in all, it was an informative seminar on a number of contemporary cardiology topics.”

DIVISION RESEARCH HIGHLIGHTS



First year fellow, Ed Coverstone, MD, (left) discusses his research findings on the CHRNA5-ADAMTS7 haplotype and clinical outcomes following acute myocardial infarction.



The Second Annual Research Day Symposium featured 64 different posters presented by graduate students, post-doctoral research fellows, medical residents and cardiology fellows.

Second Annual Cardiovascular Research Day

The long-standing tradition of excellence in cardiovascular research at Washington University was highlighted on Cardiovascular Research Day, sponsored by the Cardiovascular Division and the Center for Cardiovascular Research. The event, held in early December, drew more than 150 participants and focused on a wide variety of basic, clinical and translational cardiovascular research efforts.

“The event celebrates cardiovascular research across multiple departments, divisions and research centers at the medical center campus as well as at the main Danforth campus of Washington University,” says Jeanne M. Nerbonne, PhD, Director of the Center for Cardiovascular Research. “It is a time when we can highlight the research efforts and accomplishments of our graduate students, postdoctoral fellows, residents and clinical fellows in poster presentations, as well as hear about the developing independent research programs of some of our junior cardiovascular faculty in platform sessions.”

The junior faculty making research presentations at Cardiovascular Research Day 2013 were:

Phillip S. Cuculich, MD
*Assistant Professor,
Cardiovascular Division
Department of Medicine*

Jennifer G. Duncan, MD
*Assistant Professor,
Critical Care Medicine
Department of Pediatrics*

Carlos Bernal-Mizrachi, MD
*Assistant Professor,
Endocrinology, Metabolism
& Lipid Research
Department of Medicine*

Joel D. Schilling, MD, PhD
*Assistant Professor,
Cardiovascular Division
Department of Medicine.*

Another highlight of the Cardiovascular Research Day 2013 was the inaugural Burton E. Sobel Lecture. The first lecturer was the distinguished cardiovascular researcher Eric N. Olson, PhD, Professor and Chairman of the Department of Molecular Biology at the University of Texas Southwestern Medical Center in Dallas.



(Top) Drs. Mann, Nerbonne, Olson, and Corr. Peter Corr, PhD, spoke about Dr. Sobel's legacy during his introductory remarks at the first annual Burton E. Sobel lecture.

(Bottom) Over 100 people attended the research presentations by junior faculty and the first Burton E. Sobel lecture given by Eric Olson, PhD.

International photographer creates image for Heart and Vascular Center

For more than 40 years, internationally renowned photographic artist Michael Eastman has pointed his lens at urban and European architecture, animals, and sublime landscapes. His work is in private and public collections worldwide, including at The Metropolitan Museum of Art and the Saint Louis Art Museum. But it was after a 2001 heart attack that Eastman became interested in the visual aspects of the human body's internal pump.

"My heart attack was very sudden and happened when I was 55 years old," he recalls. "I was doing push-ups in a gym and couldn't catch my breath. I was always a healthy person, but my father also had a heart attack and he died at age 59."

Eastman turned to Alan Braverman, MD, professor of cardiovascular diseases at Washington University School of Medicine, to get him back on the road to health. "Dr. Braverman is a remarkable person who really cares about his patients," says Eastman. "When I was asked if I would like to create an artwork for the Heart and Vascular Center, I was happy to do so."

Eastman researched a multitude of heart images for the project. Along the way, he created a new type of photographic medium that he calls "plexigraph." "It's a transparent, multi-layered print that creates the



Michael Eastman



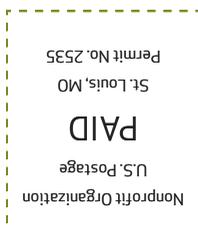
illusion of depth between layers of imagery," he explains. "In this case, I wanted people to feel like they were looking into a pool of water so that it would create an inner sense of peace in the midst of a sterile hospital environment."

Eastman was deliberate in his choice of colors, moving away from the traditional red often used for heart images and, instead, using cool blues and greens. The result is a five-panel illuminated artwork that combines the serene colors with cardiac images such as blood vessels and echocardiograms. Hanging directly behind the reception desk, it draws the eyes of everyone coming into the Heart and Vascular Center.

Eastman, who received high acclaim for a recent series of architectural photographic artworks called Urban Luminosity and now hopes to refine his luminous imagery in plexigraphs, says the recovery from his heart attack gives him new appreciation toward physicians and to life.

"This whole process has enlightened me as to how fragile life is," he says. "I smell the roses more often now."

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