Stanford Cardiovascular Institute

Stanford MEDICINE

CONVERGING DISCIPLINES IN CARDIOVASCULAR RESEARCH

QUARTERLY | WINTER 2014

# The Future Minds of Cardiovascular Medicine

Through a generous $2.2 million gift from the Dorothy Dee and Marjorie Helene Boring family, the Stanford Cardiovascular Institute is establishing its first research award for medical students. Starting in 2015, the award will support three to four talented medical students that have demonstrated excellence and dedication to cardiovascular medicine at Stanford.

*"We are very grateful for this generous endowment by the Boring Family Trust. Philanthropy enhances our educational mission and helps support the best and brightest young trainees within the Cardiovascular Institute."*

*— Joseph C. Wu, MD, PhD, Stanford CVI Director*

Award perks include access to mentors from diverse clinical and research disciplines and up to a $10,000 stipend that includes travel to conferences. Students will enroll in MED223, a class designed to fine-tune critical thinking skills paramount to a future in science and medicine.

*Institute disciplines: http://cvi.stanford.edu/research/research_disciplines.html*

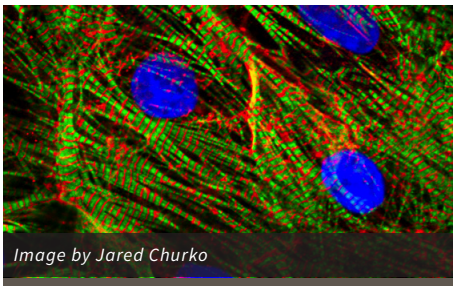


*Image by Jared Churko*

## Cardiovascular Tissue Engineering Symposium

Significant advances in our understanding of how to coax stem cells towards a cardiovascular cell fate has made it possible to now consider whether these cells are ready for human tissue repair. The Stanford Cardiovascular Institute is hosting its 2nd Annual Cardiac Regenerative Medicine Meeting on May 22, 2015. For event details visit: http://cvi.stanford.edu/about/cardiac-engineering-symposium.html

## CLINICAL HIGHLIGHT

### Department of Medicine Launches the Stanford Center for Clinical Research

*Kenneth Mahaffey, MD*

The infrastructure necessary to run clinical research has come into new focus at Stanford. In September, the Center for Clinical Research was launched by Kenneth Mahaffey, MD, Vice Chair of Clinical Research in Medicine. SCCR's mission is to facilitate investigator research initiatives by providing operations to aid faculty and staff to perform efficient, high-quality and impactful clinical research at Stanford. *Watch at http://tinyurl.com/cvifrontiers* | *For Details: see Page 8*

## NEW GENERAL MEDICINE FACULTY

Latha P. Palaniappan, MD, MS, joined the Stanford Division of General Medical Disciplines as Clinical Professor on Sept. 1, 2014. She was formerly Medical Director of Clinical Research at the Palo Alto Medical Foundation Research Institute, where her studies focused on the study of different racial/ethnic populations in the areas of obesity, insulin resistance, and cardiovascular risk, particularly in Asian subgroups and other understudied racial/ethnic minorities.

*Latha Palaniappan, MD*

Dr. Palaniappan's current studies include examining the clinical effectiveness of structured physical activity programs for diabetes management (Initiate and Maintain Physical Activity in Clinics – IMPACT study - R18), as well as best exercise regimens for normal-weight diabetics (Strength Training Regimen for Normal Weight Diabetics - STRONG-D - R01).

She is site-PI for an international study of aspirin in the elderly, ASPREE (5U01). She is also co-principal investigator on the CAUSES (R01 MD 007012) study, which examines mortality and socioeconomic differences between diverse Asian subgroups in the U.S. Findings from this study were recently published in the December issue of the *Journal of the American College of Cardiology*. Article at: http://content.onlinejacc.org/article.aspx?articleID=2022248

Stanford Children's Health

# Awarding New Ideas

## 2014 Seed Grant Recipients

# $2,125,000

**Given in awards to 70 projects since 2006 //** The Stanford Cardiovascular Institute has supported early stage clinical and basic research since the establishment of its seed grants: awarding more than $2 million since its inception. Seed grants are geared to ignite new approaches that ultimately impact cardiovascular health in children, women and men. The next two pages highlight the proposed research of the 2014 seed grant awards.

'Parental Acquisition of Echocardiographic Images in Heart Transplant Recipients Using ' Pocket' Ultrasound: A Tele-health Feasibility Study'

*Seda Tierney, MD*

*David Rosenthal, MD*

## 'Exploring the Role of Maternal Insulin Resistance in Congenital Heart Defects'

Clinicians have long observed the association between maternal diabetes and congenital heart defects (CHD), the assumption has been that glucose itself is the teratogen. We aim to investigate the specific relationship between maternal insulin resistance and risk of offspring with CHD by looking at biomarkers (glucose and insulin levels) during pregnancies that resulted in infants with CHD and matched controls.

*Joshua W. Knowles MD, PhD*

*James Priest, MD*

*Gary Shaw, PhD*

### 'A Novel Signal Analysis Tool for Ablation of Wolff-Parkinson-White Syndrome in Children'

Wolff-Parkinson-White syndrome affects 0.1 to 0.3% of all individuals. Children with WPW are prone to arrhythmias (supraventricular tachycardia and sudden cardiac death). To improve the success rates for ablation of WPW, an electronic, fully automated, objective signal analysis tool will help confirm whether an electrocardiographic signal will prove to be a successful location for the ablation of an accessory pathway in WPW.

*Scott Ceresnak, MD*

### 'Predicting 10-Year Mortality in Adults with Congenital Heart Disease'

Today the first set of survivors of complex Congenital Heart Disease (CHD) are reaching their 5th, 6th and 7th decade of life. The focus of this study is to characterize the 10-year mortality rate in adults with CHD using an index tool of 12 independent predictors (age, gender, diabetes, cancer, lung disease, heart failure, tobacco use, body mass index) and four variables assessing functional capacity (bathing, walking, managing money, pushing large objects).

*Susan M. Fernandes*

## About the Stanford Cardiovascular Institute

*Ingrid Ibarra, PhD Assistant Director*

The Institute, currently consists of 110 faculty members representing, engineers, physicians, surgeons, basic and clinical researchers. The core of the Institute is integrating fundamental research across disciplines and applying technology to prevent and treat cardiovascular disease. To support cardiovascular research and education at CVI contact Cathy Hutton, Senior Associate Director, Medical Center Development (cathy.hutton@stanford.edu); Joseph C. Wu, MD, PhD, CVI Director (joewu@stanford.edu); or Ingrid Ibarra (iibarra@stanford.edu). For more information: http://cvi.stanford.edu/waystogive.html

Campaign for Stanford Medicine

## 'The Role of Telomere Dysfunction in the Pathogenesis of Familial Dilated Cardiomyopathy'

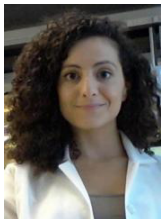
*Ioannis Karakikes, PhD*

*Helen Blau, PhD*

Human iPSCs present an exciting opportunity for disease modeling ex-vivo to better understand the pathogenesis of dilated cardiomyopathy (DCM). Combining iPSC-based disease modeling and gene editing technologies will allow us to investigate the importance of telomere shortening in the etiology of DCM. Ioannis Karakikes, PhD, Helen Blau, PhD, Alex Chia-Yu Chang, PhD.

## 'Therapeutic siRNA delivery into human engineered heart muscle'

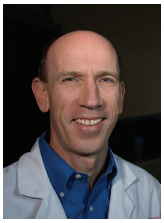
*Jayakumar Rajadas, PhD*



*Elena Matsa, PhD*

## 'PET/MRI of Coronary Biology'

One of the most important unmet needs in healthcare is the detection and characterization of coronary atherosclerosis, both to predict these clinical events and to determine the effectiveness of preventive therapy. Clinical imaging of biologically active plaques has been challenging as the main site of lethal disease is within small, highly mobile coronary arteries. The new Stanford **P**ositron **E**mission **T**omography / **M**agnetic **R**esonance **I**maging (PET/MRI) scanner is the world's first time-of-flight (ToF) PET system integrated with a 3T MRI system. The goal is to perform the first-in-human cardiovascular studies of an alternative PET agent developed at Stanford. Michael V. McConnell, MD, Craig S. Levin, PhD, Andrei Lagaru, MD, John M. Pauly, PhD, Dwight G. Nishimura, PhD.



*Michael V. McConnell, MD*

*Craig S. Levin, PhD*

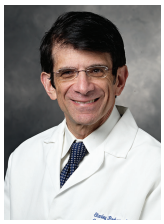
## 'Isogenic iPSC Derived Cardiomyocytes Corrected for the Myotonic Dystrophy Expanded Triplet Repeat'

*Matthew Porteus, MD*

*Ayal Hendel, PhD*

Myotonic dystrophy type I (DM1) is one of a class of devastating neurologic, cardiac, and neuromuscular diseases caused by expanded CAG/CTG triplet repeats. Clinically, patients with DM1 present with generalized muscle weakness, cardiac conduction abnormalities causing arrhythmias and cardiomyopathies. Genome editing of patient-derived DM1 iPS cells will create an isogenic iPS cell line that lacks the contracted repeat.

## 'Biomarker Detection of Latent Lymphedema Risk'



*Stanley Rockson, MD*

*Vivek Bhalla, MD*

## 'Validation of Novel Antibody Biomarkers for Human Diabetic Kidney Disease'

Diabetic kidney disease (DKD) is the most common cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) in the United States and the world. Current diagnostic strategies fail to predict which individuals with diabetes will develop CKD. While family history, poor glycemic control and hypertension are associated with the development of nephropathy, the array of demographic, clinical and laboratory cannot reliably predict who will develop overt DKD. Biomarkers are needed to predict DKD because of the associated cardiovascular co-morbidities at this "late stage" of diagnosis.

# HEART ACROSS AMERICA

Every 40 seconds someone in the U.S. has a stroke and every 4 minutes someone dies from a stroke. Each year, about 795,000 Americans suffer a new or recurrent stroke. There are 6.8 million Americans 20 and older that have had a stroke and this number will increase by 30% by 2030. Sean Maloney, chairman of the Silicon Valley American Heart Association Board of Directors, will set off on his bike and ride 5,000 miles from San Francisco to New York City. He will stop in 15 large cities for events, speeches, and to provide ultrasound check-ups along the way. Sean is challenging executives, entire corporations, stroke survivors, cycling enthusiasts, and everything in between to bike a part of the way with him and to do their part in sharing the valuable information that could prevent a stroke and heart disease.

***Nicholas Leeper, MD is leading the Stanford effort for the ride.*** *Join the ride and visit http://www.heartacrossamerica.org/ for details on how to contribute.*

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## Stanford team designs process for reducing stroke disability, costs

*By Kris Newby is the communications manager for Spectrum, the Stanford Center for Clinical and Translational Research and Education.*

New stroke care strategies for prevention, acute treatment and post-stroke care could lower U.S. health-care costs by as much as $1.6 billion per year.

A new stroke care delivery model, developed by researchers at the Stanford Clinical Excellence Research Center, offers evidence-based strategies that enable clinics and hospitals to improve stroke patient outcomes while at the same time lowering costs related to their care.

The main components of the new stroke care delivery model include the following:

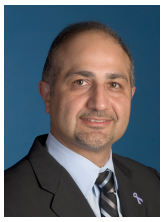
- Better stroke prevention by coaching at-risk patients to take preventive medications and to make lifestyle changes.
- Reduction of unnecessary hospital admissions of low-risk, transient ischemic attack patients by setting up TIA outpatient clinics for urgent evaluation.
- Reduction of prolonged hospital stays for mild ischemic stroke patients through a more efficient, 24-hour protocol for in-hospital stroke care.
- Redesign of emergency care to more rapidly administer the clot-busting tissue-plasminogen activator, or tPA, to all eligible ischemic stroke patients.
- Reduction of hospital readmissions by improving the transition of stroke patients to post-hospital care in the community.

The research team estimates that implementing all its recommendations would significantly improve patient care and reduce U.S. health-care costs. The care model and its potential cost savings were described in the Oct. 22 issue of Stroke.

“Our nation needs to find ways to safely treat more patients for less money,” said Arnold Milstein, MD, the center’s director, who helps shape national health policies. “Our center’s innovative care models provide clinicians and administrators with a road map to improving patient outcomes while simultaneously responding to this national imperative.”

*Full story: http://med.stanford.edu/news/all-news/2014/12/stanford-team-designs-process-for-reducing-stroke-disability.html*

# PULMONARY HYPERTENSION



*Roham Zamanian, MD*

*Marlene Rabinovitch, MD*

*Mark Nicolls, MD*

*Vinicio de Jesus Perez, MD*

*Edda Speikerkoetter, MD*

*Kristina Kudelko, MD*

### DISEASE PROFILE

- Characterized by high blood pressure in the lungs and right side of the heart
- Untreated results in fewer than 50% survival, 3 years after diagnosis
- Even with treatment, only three out of five patients live for 5 years
- Age 40-50
- 15-20 cases per million people

### NATURE OF PRESENTING SYMPTOMS

- Shortness of breath
- Dizziness
- Edema / Cough
- Confused with asthma

In November, Stanford's Adult Pulmonary Hypertension (PH) program was accredited as an official Center of Comprehensive Care, currently one of only six programs in the nation. Accreditation recognizes three main terms: (1) Commitment to PH patients; (2) Breadth of health care professionals involved; and (3) Scope of provided services.

Fourteen years ago, with a generous donation from an anonymous family, The Vera Moulton Wall Center for Pulmonary Vascular Disease was established. The initial growth period build an infrastructure that included a formal outpatient clinic, in-patient admitting and rounding team, the development of a clinical database and a staff of two physicians, a nurse practitioner, a coordinator, a social worker, and one research nurse. Under the leadership of Roham Zamanian, MD, Associate Professor of Medicine (Pulmonary and Critical Care Medicine) and Director of the adult pulmonary-hypertension service the PH program is now a team of seven physicians with double the staff.

The long-term success of the PH program is rooted in the development of a formal pulmonary vascular clinical training fellowship, which has now graduated 13 physicians. Being able to quickly diagnosis PAH is critical and training physicians to recognize PH is one-way Stanford is making a difference.

Research is paramount to making an impact in the clinical treatment of PH. For this Marlene Rabinovitch, MD Professor in Pediatric Cardiology, is leading three NIH funded clinical programs, including the Proteomic center for NIH pulmonary vascular disease, Elafin in microcirculatory disorder and a U01 stem cell/genomics projects. Edda Spiekerkoetter, Assistant Professor of Medicine (Pulmonary and Critical Care Medicine), is targeting bone morphogenetic protein receptor 2 (BMPR2) as a therapeutic in pulmonary-vascular and cardiac disease. Vinicio de Jesus Perez, MD, Assistant Professor of Medicine (Pulmonary and Critical Care Medicine) is defining the biology of endothelial and smooth muscle cells that reside in the pulmonary tissue. Cardiovascular Institute member, Mark Nicolls, MD, Associate Professor of Medicine (Pulmonary and Critical Care), and Chief, Pulmonary and Clinical Care, focuses on the contribution of inflammation to the development of PH.

Dr. Nicolls, notedly, has also been recently awarded a few grants, including: An R56 grant on 'Autoimmunity in PAH' (focusing on regulatory T-cells), which started last October; and a new R01, starting this December, on Leukotriene B4 in PAH.

Years from now with these tremendous efforts we will recall a time when a silent disease often confused with asthma is loud and clear pulmonary hypertension.

# FAMILIAL HYPERCHOLESTEROLEMIA

Familial Hypercholesterolemia (FH) is a genetic condition characterized by very elevated levels of low-density lipoprotein cholesterol (LDL-C) caused by mutations in genes that alter the ability of the liver to clear LDL-C from the blood. If untreated, FH causes a 20-fold increased risk of heart disease. The Netherlands pointed the way over twenty-years ago, by establishing the first national screening program incorporating genetic testing to enhance the identification of families with FH. Since the inception of the program in the Netherlands, over 25,000 people with FH have been identified and offered potentially life saving therapy.

*Joshua W. Knowles MD, PhD*

Joshua W. Knowles, MD, PhD, attending physician at the Stanford Center for Inherited Cardiovascular Disease is the Chief Medical Officer of the FH Foundation (www.thefhfoundation.org) emphasizes that "FH is a 'winnable battle' because once identified, it can usually be treated quite effectively." One of the major goals of the FH Clinic at Stanford is to screen the families of FH patients to find these individuals early in life and prevent the serious consequences due to a lifetime of elevated cholesterol levels.

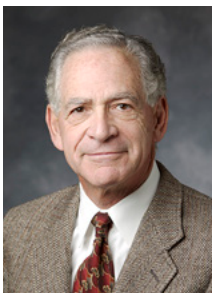
## Take Away Notes:

- FH is under diagnosed and undertreated
- An LDL cholesterol level > 190 mg/dl is a red flag
- If untreated FH causes a 20 fold increased lifetime risk of heart disease
- If treated with cholesterol lowering medications, the risk of heart disease can be reduced by 80%
- Mutations in either of 3 genes (LDLR, APOB, PCSK9) cause FH

## Transplant Turnabout: Weaning Patients Off Drugs

*By Becky Bach Office of Communication & Public Affairs at the School of Medicine*

The last 12 years of kidney transplant patient Lupe Alcaraz's life were awful. She was often sick, her immune system crippled from decades of taking immunosuppressive drugs. She needed steroids too, which weakened her bones.



*Samuel Strober, MD*

"It was just really ugly," recalls her daughter, Cynthia Alcaraz-Jew.

When Alcaraz died in 2010, Alcaraz-Jew's own kidneys were failing — her family suffers from a genetic condition called Alport syndrome, which causes kidney, eye and ear problems. Months later, as Alcaraz-Jew, now 47, slogged through yet another year of dialysis, she got some wonderful news: Her younger brother, Xavier, could donate his perfectly matched kidney, and she qualified for a Stanford study that attempts to wean transplant patients off the immunosuppressive drugs.

"I couldn't have been happier," she says.

Now, less than two years after her transplant, Alcaraz-Jew is drug free, living proof that an experimental treatment developed by Stanford immunologist Samuel Strober, MD, and his colleagues has the potential to improve the health of hundreds, perhaps thousands, of transplant patients. Stanford is one of just a few research institutes working to wean these patients off immunosuppressants.

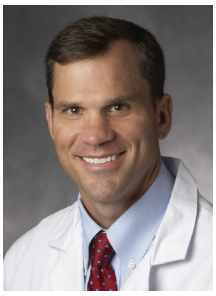
Strober studied the immune system for decades before formulating the treatment, which thwarts the battle between a patient's immune system and a donated organ. The medications dampen the response, but they can also cause heart disease, infections and even kidney failure — a bitter irony for someone who just received a new kidney, says Strober, a professor of immunology and rheumatology.

The treatment starts the day after the transplant. For 10 days, the team irradiates the primary immune organs, including the lymph nodes, thymus and spleen, then injects a serum that contains antibodies allowing it to recognize and kill a type of immune cell called a T cell.

Several weeks later, Strober's team injects the patient with cells from the donor: a combination of mature and immature immune cells. Once injected, the immature cells, known as stem cells, must mature and mix with the patient's cells to prevent an immune attack.

*Full story: http://stanmed.stanford.edu/2014fall/tolerance.html*

# Re-Thinking Therapeutic Decision-Making for Multi-Vessel Coronary Artery Disease



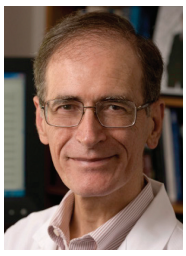
*William F. Fearon, MD*

Historically, the gold standard diagnostic test for coronary artery disease (CAD) is based on visual assessment via angiography. This approach utilizes contrast to characterize coronary artery stenosis (narrowing of blood vessel). A recent review article, published in *Coronary Artery Disease*, by Jonathan Schwartz, MD, Clinical Fellow and William F. Fearon, MD, Associate Professor of Medicine (Cardiovascular Medicine), highlights the benefits of incorporating Fractional Flow Reserve (FFR) measurements into the diagnostic and decision-making process in the setting of multi-vessel CAD. FFR is a technique measuring the maximal flow down a vessel to assess the hemodynamic significance of a stenotic lesion.

Interestingly, ischemic lesions with similar angiographic appearance can differ when FFR is measured, which leads to different treatment strategies. Lesions identified as significant by FFR tend to cause more adverse events when compared to nonischemic FFR lesions. Incorporating FFR into the diagnostic testing of patients with multiple vessel CAD guides revascularization resulting in fewer adverse outcomes, including persistent angina, myocardial infarction, and mortality. The mechanism explaining this phenomena remains unclear, though, the authors postulate an impact of mechanical forces, increasing inflammatory mediators, and amount of distal myocardial tissue at risk as potential explanations. The take home message is that overlaying both anatomic and functional assessment of coronary lesions in CAD patients ought to be considered.

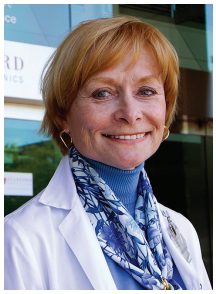
For article: *http://www.ncbi.nlm.nih.gov/pubmed/25072658*

Above: Ke Yuan, PhD, left postdoctoral scholar, speaks to her mentor Vinicio de Jesus Perez at the AHA in Chicago. Yuan received the AHA Cournand and Comroe Award. Below: Over 30 CVI members attended the annual CVI AHA dinner, held at Volare Restaurant.



Above: Mark Hlatky, MD, received the AHA's 'Distinguished Scientist Award'.

# State of the Art: Cardiac Transplantation



*Sharon A. Hunt, MD*

Many will agree that organ transplantation remains a heroic act. The team of physicians performing the surgery, the team ensuring patient-care and the patient and families who must endure the procedure challenges ahead.

In a recent article, published in *Trends Cardiovascular Medicine*, Margot K. Davis and Sharon A. Hunt, MD, Professor of Medicine (Cardiovascular Medicine) reviewed the current state of heart transplantation. The article discusses the current understanding of best practices for the management of heart transplant recipients and describe recent advances and active areas of research. Sharon is a pioneering figure in the field of cardiology.

"The holy grail of immune tolerance remains beyond our reach at this time, but has the potential to completely alter the heart transplant landscape and should continue to be a target of active research." — *Sharon Hunt, MD*

For article: *http://www.ncbi.nlm.nih.gov/pubmed/25258115*

# American Heart Association Meeting

The American Heart Association Scientific Sessions conference, uniting cardiologists from around the world, was held in Chicago, IL, from Nov. 15 to 19, 2014. Robert Harrington, MD, Professor of Medicine, was Chair of the Committee on Scientific Sessions Program. This years programming focused on seven multidisciplinary cardiovascular core science areas: Cardiovascular Imaging, Epidemiology and Prevention of CV Disease: Physiology, Pharmacology and Lifestyle, Genetics, Genomics and Congenital CV Disorders Heart Rhythm Disorders and Resuscitation Science Myocardium: Function and Failure Catheter-Based and Surgical Intervention Vascular Disease: Biology and Clinical Science.

Mark Hlatky, MD, Stanford Professor of Health Research and Policy (Health Services Research) received the 'Distinguished Scientist Award' at the opening session. Ke Yuan, postdoctoral scholar in Vinicio de Jesus Perez's Laboratory, received the AHA Cournand and Comroe Award, the top award for a young investigator offered by the AHA 3CPR Council for her work on pulmonary hypertension. Andrew Lee, Feng Lan, Ping Liang received the Best Basic Science Manuscript Award in *Circulation*. Also, several Cardiovascular Institute members presented their work and moderated sessions.

Finally, CVI members held their annual AHA dinner on Monday, Nov. 17 at the Volare Restaurant.

## Research Updates

# Engineering New Materials for Cell-therapy

*Ngan Huang, PhD*

*Sarah Heilshorn, PhD*

Two of the most challenging bottlenecks in regenerative medicine using cell-based therapy are the ability to deliver cells into their site of action and maintaining their viability. Cardiovascular Institute members, Ngan Huang, Assistant Professor Cardiothoracic Surgery and Sarah Heilshorn, Associate Professor Materials Science & Engineering have teamed up to synthesize proteins that self-assemble into hydrogels upon simple mixing. The team secured funding for a total of $125,000 from Stanford ChEM-H to address the need to develop new materials for applications in biology and medicine. The project entitled 'Protein-Engineered Hydrogels for Improved Efficacy of Stem Cell-Based Injection Therapy in a Murine Model for Peripheral Arterial Disease', will use Mixing-Induced Two-Component Hydrogels (MITCH), a shear-thinning and self-healing material system comprising two complementary engineered proteins that self-assemble into hydrogels upon mixing.

"We will apply MITCH towards injection of human induced pluripotent stem cell-derived endothelial cells (iPSC-ECs) for treatment of peripheral arterial disease (PAD). PAD patients have obstructed blood flow to the lower extremities, so enhancing angiogenesis using iPSC-ECs may be a promising treatment, and maintaining the viability of these cells is critical to their efficacy". — *Ngan Huang, PhD*

*Continued from page 1*

The center involves three core enterprises: Site-based research, led by Rebecca McCue; a coordinating center, led by Amol Rajmane, MD; and education and training.

*Rebecca McCue*

*Amol Rajmane, MD*

# Stem Cell Study Explains How Mutation Common in Asians Affects Heart Health

*By Krista Conger Office of Communication & Public Affairs at the School of Medicine*

*Antje D. Ebert, PhD*

Many Asians carry a mutation that causes their faces to flush when they drink alcohol. The affected gene is called ALDH2, and it also plays a role in cardiovascular health. Carriers are more susceptible to coronary artery disease and tend to recover more poorly than non-carriers from the damage caused by a heart attack. Now Stanford cardiologist Joseph Wu, MD, PhD; Professor, Chemical and Systems Biology Daria Mochley-Rosen, PhD; and postdoctoral scholar Antje Ebert, PhD, have learned why. The research was published in *Science Translational Medicine*, 2014 Sep 24;6(255):255ra130.

The study showed that the ALDH2 mutation affects heart health by controlling the survival decisions cells make during times of stress. It is the first time ALDH2, which is involved in many common metabolic processes in cells of all types, has been shown to play a role in cell survival of iPSC-derived heart cells. In particular, ALDH2 activity, or the lack of it, influences whether a cell enters a state of programmed cell death called apoptosis in response to stressful growing conditions.

Full story: *http://med.stanford.edu/news/all-news/2014/09/scientists-use-stem-cells-to-learn-how-common-mutation-in-asians.html*

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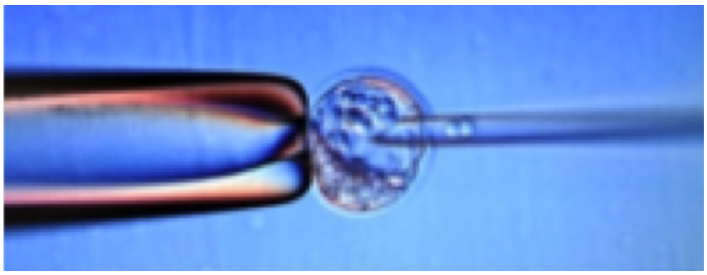
# Pluripotent Cells Created by Nuclear Transfer Can Prompt Immune Reaction

*by Christopher Vaughan, communications manager, Stanford Institute for Stem Cell Biology and Regenerative Medicine*



Stanford researchers find that genetic differences in mitochondria contained in egg cells used in a process known as nuclear transfer can prompt rejection by the immune system in mice.

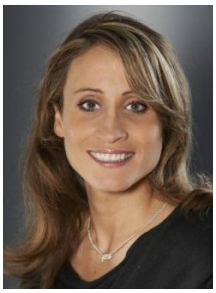
Mouse cells and tissues created through nuclear transfer can be rejected by the body because of a previously unknown immune response to the cell's mitochondria, according to a study in mice by researchers at the Stanford University School of Medicine and colleagues in Germany, England and at MIT.

The findings reveal a likely, but surmountable, hurdle if such therapies are ever used in humans, the researchers said.

Stem cell therapies hold vast potential for repairing organs and treating disease. One significant hope rests on the potential of pluripotent stem cells, which can become nearly any kind of cell in the body. One method of creating pluripotent stem cells is called somatic cell nuclear transfer (SCNT), and involves taking the nucleus of an adult cell and injecting it into an egg cell from which the nucleus has been removed.

The promise of the SCNT method is that the nucleus of a patient's skin cell, for example, could be used to create pluripotent cells that might be able to repair a part of that patient's body. "One attraction of SCNT has always been that the genetic identity of the new pluripotent cell would be the same as the patient's, since the transplanted nucleus carries the patient's DNA," said cardiothoracic surgeon Sonja Schrepfer, MD, PhD, a co-senior author of the study, published online Nov. 20 in Cell Stem Cell.

"The hope has been that this would eliminate the problem of the patient's immune system attacking the pluripotent cells as foreign tissue, which is a problem with most organs and tissues when they are transplanted from one patient to another," added Schrepfer, who is a visiting scholar at Stanford's Cardiovascular Institute. She is also a Heisenberg Professor of the German Research Foundation at the University Heart Center in Hamburg, and at the German Center for Cardiovascular Research.

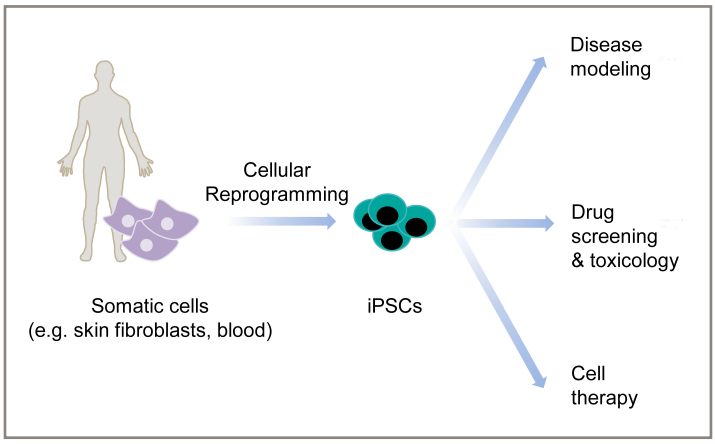


*Sonja Schrepfer, MD, PhD*

*Full story: http://med.stanford.edu/news/all-news/2014/11/pluripotent-cells-created-by-nuclear-transfer-can-prompt-immune-.html*

Institute Resources

# Cardiac iPSC Biobank: 'Clinical Trials in a Dish'




From Matsa E, Circ Res 2014

Joseph Wu, Director of the Institute, has initiated the Stanford Cardiovascular Institute (SCVI) Biobank to generate induced pluripotent stem cells (iPSC) from about 1,000 people of many different ethnic backgrounds and health histories.

"This is one of our main priorities," Wu said. "In California, we boast one of the most diverse populations on Earth. We'd like to include male and female patients of major representative ethnicities, age ranges and cardiovascular histories. This will allow us to conduct 'clinical trials in a dish' on these cells, a very powerful new approach, to learn which therapies work best for each group."

Normal and patient-derived reprogrammed cardiomyocytes is a tremendous resource for researchers and physicians. Understanding the disease process directly at the population level and observing these cells as surrogates under a myriad conditions has the potential to be a game-changer for cardiovascular medical research.

SCVI biobank is supported in part by National Heart, Lung and Blood Institute (NHLBI), the California Institute for Regenerative Medicine (CIRM), and the Stanford Cardiovascular Institute (CVI). The SCVI Biobank is currently recruiting patients from institutions around the world. To learn more about the lines currently available or to find out how to include patients from your institution contact Biobank manager, Justin Vincent (justin81@stanford.edu) or Ioannis Karakikes, PhD (ioannis1@stanford.edu).

# Patients with Peripheral Artery Disease

## **PACE** Trial (**P**atients with Intermittent Claudication Injected with **A**LDH **Ce**lls)

Atherosclerotic lower extremity peripheral artery disease (PAD) is one of the most common, morbid and mortal cardiovascular diseases, affecting between 7-12 million Americans. A Phase 2 Clinical Trial called PACE was designed to test the efficacy of purified aldehyde dehydrogenase expressing bone marrow cells in patients with atherosclerotic peripheral artery disease with classic claudication. Purified cells are injected intramuscularly into affected calf and lower thigh muscles and improvements in blood flow and/or peak walking time measured. This clinical trial is sponsored in part by National Heart, Lung and Blood Institute (NHLBI).

For more information or to sign-up to participate please contact Phillip Yang, MD, (phillip@stanford.edu) or Nicholas Leeper, MD, (nleeper@stanford.edu). You may also call Fouzia Khan at 650-736-1410.

Full details: *http://cvi.stanford.edu/research/trials/#studyId=NCT01774097*

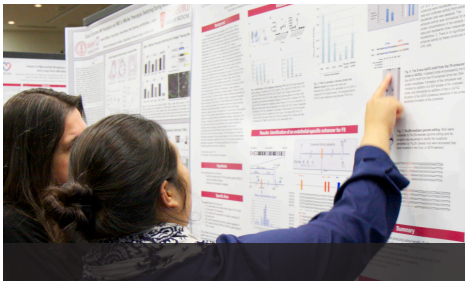
## Cardiovascular Institute Clinical Trial Coordinators

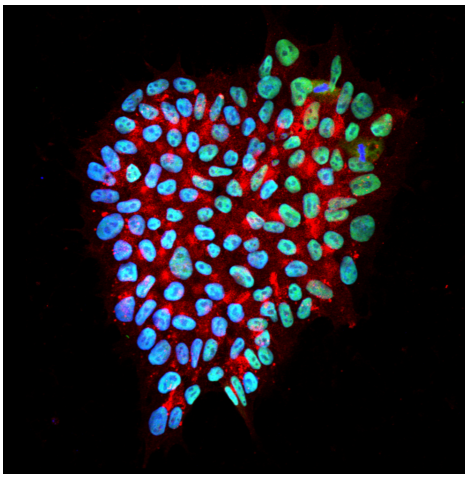
*Ashima Goel*

*Ed Finn*

For coordinating Cardiovascular-related trials, contact Ashima Goel, Clinical Research Manager, (ashima.goel@stanford.edu) and Ed Finn (efinn@stanford.edu).

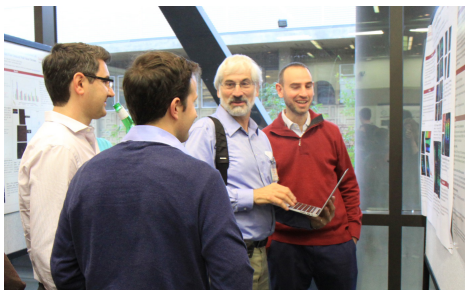
For Clinical Cardiovascular Trials at Stanford, visit: http://cvi.stanford.edu/research/trials/.





220 attendees at this year's annual retreat

Doug Mann, MD, keynote speaker, discusses the 'Role of Innate Immunity in Cardiac Injury and Repair'



Clinical and Basic research judges evaluate 58 posters during reception

# 2014 CVI Retreat: Leading the Way in Innovation

The Cardiovascular Institute held its annual Retreat, "The Future of Cardiovascular Medicine and Research" in Paul Berg Hall in the Li Ka Shing Center. The meeting featured keynote guest speaker Douglas L. Mann, MD, Chief of the Cardiovascular Division at Washington University and a welcome message from CVI Director, Joseph Wu, MD, PhD and Dean Lloyd Minor, MD.

Fifteen leading Stanford faculty presented their work on cutting-edge basic, translational and clinical research from their departments: Y. Joseph Woo, MD; Ronald L. Dalman, MD; Stephen J. Roth, MD, MPH; Alan C. Yeung, MD; Victor Froelicher, MD; Mark R. Nicolls, MD; Hiro Nakauchi, PhD; Michael Snyder, PhD; Marcia Stefanick, PhD; Sandra Tsai, MD, MPH; Ada Poon, PhD; and fellow Alexandre Ribeiro, PhD, from the lab of Beth Pruitt, PhD. With this team, Stanford is poised to lead the way in medicine and research.

## Clinical and Basic Research Awards

**Daniel DiRenzo**
*Nicholas Leeper Lab*
'Cdkn2b regulates Mϕ polarization and SMC to 'Mϕ-like' phenotypic switching during atherosclerosis'

**Eric Gross**
*Assistant Professor of Anesthesiology*
'Cost Variation and Associated Outcomes of Catheter Ablation for Atrial Fibrillation'

**Ryoko Hamaguchi**
*Sean Wu Lab*
'An In Vitro Human Induced Pluripotent Stem Cell-Derived Cardiomyocyte Model Reveals Alternations in Iron Metabolism in Doxorubicin-Induced Cardiotoxicity'

**Patricia Nguyen**
*Assistant Professor of Medicine (Cardiovascular Medicine)*
'Assessment of the Radiation Effects of Cardiac Computed Tomographic Angiography Using Protein and Genetic Biomarkers'

**Brian Piening**
*Michael Snyder Lab*
'Comprehensive Longitudinal Multi-Omic Profiling During Periods of Weight Gain and Loss'

**Alexander Perino**
*Mintu Turakhia Lab*
'Inhibition of the Calcineurin Interaction Site on TRPV1 Reduces Myocardial Infarct Size in Rats'

ABSTRACT JUDGES | **Basic Research**: Dan Bernstein, MD, Nicholas Leeper, MD, Phil Tsao, PhD
**Clinical Research:** Robert Harrington, MD, Kenneth Mahaffey, MD, David J. Maron, MD

## Recently Awarded Projects

**Nicholas J. Leeper, MD**, *was recently awarded an NIH RO1 grant to study 'the paradoxical role of CDKN2B in blood vessel sprouting and maturation'*

**Sean M. Wu, MD PhD** *is a recipient of the NIH Director's Pioneer Award. The award for 'Enabling Technologies for Human-Machine Hybrid Tissues'*

**Norbert J Pelc, Sc.D** *received an NIH award to investigate, 'High Dose Efficiency CT System'*

**Ioannis Karakikes** *received an AHA Beginning Grant in Aid on 'Genetic Correction of Phosp holambin Mutations in an iPSC-based Disease Model of Familial Dilated Cardiomyopathy'*

**Kiran Kaur Khush, MD** *was recently awarded an NIH RO1 grant entitled 'Evidence Based Evaluation and Acceptance of Donor Hearts for Transplantation.*

**Manish J. Butte, MD, PhD** *Assistant Professor of Pediatrics (Immunology) was awarded an NIH grant to investigate 'Influences of nanomechanical forces on T cells'*

**Katrin Andreasson, PhD** *Professor of Neurology at the Stanford University Medical Center, was awarded an NIH grant for 'Microglial and macrophage PGE2 signaling in post-stroke inflammation'*

**Ronald Dalman, MD**

**Phil Tsao, PhD**

**The NIH/NHBLI 'T32 Mechanisms and Innovation in Vascular Disease' Training Grant**
*has been awarded to the Cardiovascular Institute and will support up to six postdoctoral fellows per year for the next 5 years. Ronald Dalman, MD and Phil Tsao, PhD, are directors of the program.*

## Three Cardiovascular Institute Member Professors Elected Fellows of AAAS

Russ Altman, Sanjiv Gambhir and Michael Snyder have been elected fellows of the American Association for the Advancement of Science.

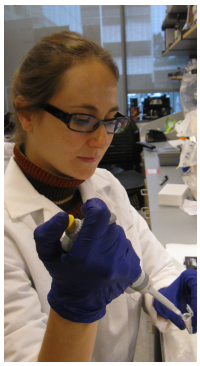
**Sam Gambhir, MD, PhD** *professor and chair of radiology and director of the Canary Center for Cancer Early Detection at Stanford, was elected for his work in multimodal molecular imaging of living subjects.*

**Michael Snyder, PhD**, *professor and chair of genetics, was elected for contributions to the field of genomics, particularly for inventing or pioneering chromatin-immunoprecipitation sequencing, RNA sequencing, tiling array, protein microarray and personalized medicine technology.*

**Russ Altman, MD, PhD** *professor of bioengineering, of genetics and of biomedical informatics research, was elected for contributions in the field of bioinformatics, particularly for analysis of targets for drug action and of the impact of human variation on drug responses.*

For more: *https://med.stanford.edu/news/all-news/2014/12/four-medical-school-professors-elected-fellows-of-aaas.html*

## NHLBI Seminar: Lab to Market



Learn about NIH/NHBLI initiatives for start-ups and researchers to support innovative heart, lung, blood, and sleep technologies and tips gain on how to write a competitive application for these exciting funding opportunities.

*Information session:*
Thursday, January 15, 12:00–1:00 p.m.
*1-on-1 meetings:* 1:30 p.m.–3:30 p.m.

Lorry Lokey (SIM1): Room G1002

This event is sponsored by the NHLBI.

Register at: *http://bit.ly/CVI-NHLBI-2015*

# Funding Opportunities

## JANUARY

THE INTERNATIONAL SOCIETY FOR HEART & LUNG TRANSPLANTATION

**Norman E. Shumway Career Development Award**
Amount of funding: $160,000 over 2 years
Deadline: Jan 15, 2015
Shumway Career Development Award

**Research Fellowship Award**
Amount of funding: $40,000 over 1 years
Deadline: Jan 15, 2015
Research Fellowship

AMERICAN HEART ASSOCIATION

**Mentored Clinical and Population Research**
Amount of funding: $140,000 over 2 years
Deadline: Jan. 15 or 22, 2015

**Beginning Grant-in-Aid**
Amount of funding: $140,000 over 2 years
Deadline: Jan. 15, 2015

**Grant-in-Aid**
Amount of funding: $140,000 over 2 years
Deadline: Jan. 15, 2015

**Postdoctoral Fellowship**
Amount of funding: ~$100,000 over 2 years
Deadline: Jan. 15, 2015

**National Fellow-to-Faculty Transition Award**
Amount of funding: $197,000 over 5 years
Deadline: Jan. 22, 2015

**National Scientist Development Grant**
Amount of funding: $308,000 over 4 years
Deadline: Jan. 22, 2015

STANFORD COULTER TRANSLATIONAL RESEARCH GRANT PROGRAM

**Stanford Coulter Translational Research Grant**
Deadline: Jan. 26, 2015

NATIONAL INSTITUTE OF HEALTH

**Director's Early Independence Award (DP5)**
Deadline: Jan. 30, 2015
RFA-RM-14-004

## FEBRUARY

STANFORD CHILD HEALTH RESEARCH INSTITUTE (CHRI)

**Clinical Trainee Support**
Amount of funding: $100,000
Deadline: Feb. 2, 2015

NATIONAL INSTITUTE OF HEALTH

**K99/R00 NIH Pathway to Independence Award**
Deadline: Feb. 12, 2015

**K08 Mentored Clinical Research Career Development Award**
Deadline: Feb. 12, 2015
PA-14-046

**K23 Mentored Patient-Oriented Research Career Development Award**
Deadline: Feb. 12, 2015
PA-14-049

## MARCH

THRASHER RESEARCH FUND

**Early Career Awards**
Amount of funding: $25K over 2 years
Deadline: March 6, 2015

## APRIL

NATIONAL INSTITUTE OF HEALTH

**K01 Biomedical Big Data Science Award**
Deadline: April 1, 2015
RFA-HG-14-007

**Ruth L. Kirschstein National Research Service Awards (NRSA) for Individual Postdoctoral Fellows**
Deadline: April 8, 2015
PA-14-149

# 2015 Frontiers in Cardiovascular Science Seminars

**Every Tuesday, 12 noon – 1 p.m. Li Ka Shing Center** *Lunch provided*

*http://cvi.stanford.edu/about/seminars.html*

Beth Pruitt, PhD 1/13/2015
Stanford, Associate Professor of Mechanical Engineering

Eric Olson, PhD 1/20/2015
Professor and Chair, UT Southwestern

Richard Lawn, PhD 1/27/2015
Stanford, CVI Consulting Professor

Roberto Bolli, MD 2/03/2015
Professor and Chief Division of Cardiology, U. Louisville

Kristine Red-Horse, PhD 2/10/2015
Stanford, Assistant Professor, Dept. of Biology

Laura C. Lazzeroni, PhD 2/17/2015
Associate Professor (Research) Psychiatry and Behavioral Sciences

Jeffery D. Molkentin, PhD 2/24/2015
Professor, Children's Hospital Medical Center, HHMI Investigator

Andrew Plump, MD, PhD 3/03/2015
Deputy Head Research and Translational Medicine at Sanofi-Aventis

James T. Willerson, MD 3/10/2015
President and Medical Director, Texas Heart Institute

Joseph Loscalzo, MD, PhD 3/17/2015
Chair, Dept. of Medicine, Brigham and Women's Hospital

Mark Fishmen, MD 3/31/2015
President of the Novartis institutes for BioMedical Research

Irv Weissman, MD 4/07/2015
Director Stanford Institute for Stem Cell Biology & Regenerative Medicine

William Slikker, Jr., PhD 4/14/2015
Director, FDA National Center for Toxicological Research

Leslie Leinwand, PhD 4/21/2015
Prof., Molecular, Cellular & Developmental Biology, U. Colorado-Boulder

Junichi Sadoshima, MD, PhD 4/28/2015
Professor, Cell Biology & Molecular Medicine, Rutgers U.

Visit the CVI YouTube Channel for selected past talks: *http://tinyurl.com/cvifrontiers*

Available videos feature talks by: Roy P. Vagelos, MD; Jonathan Lindner, MD; Bernard Gersh, MB, ChB, D.Phil; Joseph Hill, MD, PhD; and Joseph Wu, MD, PhD.

# Six Young Investigators Awarded the Winter 2014 Cardiovascular Institute Travel and Exchange Ideas Award:

**Yuhei Kobayashi:** *Jennifer Tremmel Lab* **//** Impact of Sex Differences on Invasive Measures of Coronary Microvascular Dysfunction in Patients With Angina in the Absence of Obstructive Coronary Artery Disease

**Kozo Okada:** *William F. Fearon Lab* **//** Coronary Artery Negative Remodeling and Intimal Thickening Predict Long-Term Clinical Outcomes after Heart Transplantation

**Karina Nakayama:** *Ngan F. Huang Lab* **//** 3D Tri-culture Model Promotes Enhanced Mechanical Forces and Sustained Long-Term Contractility of Human Pluripotent Stem Cell-Derived Cardiomyocytes

**Guang Li:** *Sean Wu Lab* // Identification of Cardiovascular Lineage Descendants At Single Cell Resolution

**Caiyun G Li:** *Marlene Rabinovitch Lab* **//** PPARγ Plays a Novel, Pivotal Role in DNA Damage Sensing and Repair, That is Perturbed in Pulmonary Arterial Hypertension

**Antje Ebert:** *Joseph C. Wu Lab* // Direct Comparison of Disease-Specific versus TALEN-Corrected iPSC-Derived Cardiomyocytes from Dilated Cardiomyopathy Patients

**This award is available to nurses, students and fellows. 2015 Deadline: March 10, 2015**
Visit: http://cvi.stanford.edu/research/travel_grant_awards.html

# Cardiovascular Conferences

## JANUARY

**Keystone Symposia - Mitochondria, metabolism and Heart Failure (J5)**
January 27 – February 1, 2015
Santa Fe, New Mexico
*www.keystonesymposia.org*

**Vascular and Endovascular Surgery Society – Annual Winter Meeting**
January 29 – February 1, 2015
Vail, CO
*www.pvss.org*

## FEBRUARY

**International Stroke Conference**
February 11-13, 2015
Nashville, TN
Stroke Conference

## MARCH

**Keystone Symposia – Heart Disease and Regeneration: Insights from Development (X1)**
March 1 - 6, 2015
Copper Mountain, Colorado
*www.keystonesymposia.org*

**Keystone Symposia – Cell Biology of the Heart: Beyond the Myocyte-Centric View (X2)**
March 1 - 6, 2015
Copper Mountain, Colorado
*www.keystonesymposia.org*

**Epidemiology and Prevention; Lifestyle and Cardiometabolic Health**
March 3 – 6, 2015
Baltimore, MD
EPI LIFESTYLE 2015

**American College of Cardiology Scientific Session**
March 14 – 16, 2015
San Diego, CA
*accscientificsession.cardiosource.org/ACC.aspx*

**International Congress of Update in Cardiology and Cardiovascular Surgery**
March 26 – 29, 2015
Istanbul, Turkey
UCCVS 2015

**Society for Clinical Vascular Surgery Annual Symposium**
March 29 – April 2, 2015
Miami, Florida
*scvs.org*

## APRIL

**Innovations in Valve and Structural Heart Disease**
April 2 – 4, 2015
Paradise Island, Bahamas
Innovations

**The European Stroke Organisation Conference 2015**
April 17 – 19, 2015
Glasgow, United Kingdom
ESO 2015

**International Conference on Clinical & Experimental Cardiology**
April 27 – 29, 2015
Philadelphia, PA
*cardiology2014.conferenceseries.net/index.php*

**Cardiovascular Summit TCTAP 2015**
April 28 – May 1, 2015
Seoul, Korea
Cardiovascular Summit

**Asian Pacific Society of Cardiology Congress**
April 29 – May 2, 2015
Abu Dhabi, United Arab Emirates
APSC 2015

**Quality of Care and Outcomes Research 2015**
April 29 – May 1, 2015
Baltimore, MD
QCOR 2015

The 2015 Organization for the Study of Sex Differences (OSSD) meeting will be held on the campus of Stanford University, on April 21-23, 2015. The local hosts of the meeting are Marcia Stefanick, PhD and Jennifer Tremmel, MD.

*http://www.ossd.wildapricot.org/*

Stanford WSDM Center

Women's HeartHealth at Stanford

PCNA 21st Annual Symposium and Pharmacology Preconference
April 8-11, 2015 | Anaheim Marriott | Anaheim, CA

Join us for an exciting and informative event, featuring world-renowned speakers, cutting-edge information, networking, exhibits, awards and moderated poster sessions.

*http://pcna.net/meetings/annual-symposium*

PCNA
PREVENTIVE CARDIOVASCULAR NURSES ASSOCIATION

# Member Publications

Communication is at the heart of scientific advancement and innovation. This quarter the Stanford Cardiovascular Institute members published over 240 original manuscripts and reviews further contributing to our understanding of cardiovascular biology and disease. In the following pages we highlight selected manuscripts by our members.

## SEPTEMBER 85 Publications

Characterization of the molecular mechanisms underlying increased ischemic damage in the aldehyde dehydrogenase 2 genetic polymorphism using a human induced pluripotent stem cell model system. Ebert AD, Kodo K, Liang P, Wu H, Huber BC, Riegler J, Churko J, **Lee J**, de Almeida P, Lan F, **Diecke S**, **Burridge PW**, Gold JD, **Mochly-Rosen D**, **Wu JC**. *Sci Transl Med.* 2014 Sep 24;6(255):255ra130.

Vorapaxar in patients with peripheral artery disease and acute coronary syndrome: insights from Thrombin Receptor Antagonist for Clinical Event Reduction in Acute Coronary Syndrome (TRACER). Jones WS, Tricoci P, Huang Z, Moliterno DJ, **Harrington RA**, Sinnaeve PR, Strony J, Van de Werf F, White HD, Held C, Armstrong PW, Aylward PE, Chen E, Patel MR, **Mahaffey KW**. *Am Heart J.* 2014 Oct;168(4):588-96.

A Balanced Look at the Implications of Genomic (and Other "Omics") Testing for Disease Diagnosis and Clinical Care. Boyd SD, Galli SJ, Schrijver I, **Zehnder JL**, **Ashley EA**, Merker JD. *Genes (Basel)*. 2014 Sep 1;5(3):748-66.

Natural history of coexistent tricuspid regurgitation in patients with degenerative mitral valve disease: Implications for future guidelines. Goldstone AB, Howard JL, Cohen JE, MacArthur JW Jr, Atluri P, Kirkpatrick JN, **Woo YJ**. *J Thorac Cardiovasc Surg.* 2014 Dec;148(6):2802-10.

Association between success rate and citation count of studies of radiofrequency catheter ablation for atrial fibrillation: possible evidence of citation bias. Perino AC, Hoang DD, Holmes TH, Santangeli P, **Heidenreich PA**, **Perez MV**, **Wang PJ**, **Turakhia MP**. *Circ Cardiovasc Qual Outcomes.* 2014 Sep;7(5):687-92.

Cardiac tissue slice transplantation as a model to assess tissue-engineered graft thickness, survival, and function. **Riegler J**, Gillich A, Shen Q, **Gold JD**, **Wu JC**. *Circulation*. 2014 Sep 9;130(11 Suppl 1):S77-86.

Cross talk of combined gene and cell therapy in ischemic heart disease: role of exosomal microRNA transfer. **Ong SG**, Lee WH, Huang M, Dey D, Kodo K, Sanchez-Freire V, Gold JD, **Wu JC**. *Circulation*. 2014 Sep 9;130(11 Suppl 1):S60-9.

Engineering a vascularized collagen-β-tricalcium phosphate graft using an electrochemical approach. Kang Y, Mochizuki N, Khademhosseini A, Fukuda J, **Yang Y**. *Acta Biomater.* 2015 Jan 1;11:449-58.

Reasons for warfarin discontinuation in the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). O'Brien EC, Simon DN, Allen LA, Singer DE, Fonarow GC, Kowey PR, Thomas LE, Ezekowitz MD, **Mahaffey KW**, Chang P, Piccini JP, Peterson ED. *Am Heart J.* 2014 Oct;168(4):487-94.

State of the art: Cardiac transplantation. Davis MK, **Hunt SA**. *Trends Cardiovasc Med.* 2014 Nov;24(8):341-349.

Predictors of mortality in pediatric patients on venoarterial extracorporeal membrane oxygenation*. Punn R, Axelrod DM, Sherman-Levine S, **Roth SJ**, **Tacy TA**. *Pediatr Crit Care Med.* 2014 Nov;15(9):870-7.

Incidence and sequelae of prosthesis-patient mismatch in transcatheter versus surgical valve replacement in high-risk patients with severe aortic stenosis: a PARTNER trial cohort--a analysis. Pibarot P, Weissman NJ, Stewart WJ, Hahn RT, Lindman BR, McAndrew T, Kodali SK, Mack MJ, Thourani VH, **Miller DC,** Svensson LG, Herrmann HC, Smith CR, Rodés-Cabau J, Webb J, Lim S, Xu K, Hueter I, Douglas PS, Leon MB. *J Am Coll Cardiol.* 2014 Sep 30;64(13):1323-34.

An engineered Axl 'decoy receptor' effectively silences the Gas6-Axl signaling axis. Kariolis MS, Miao YR, Jones DS 2nd, Kapur S, Mathews II, Giaccia AJ, **Cochran JR**. *Nat Chem Biol.* 2014 Nov;10(11):977-83.

High-risk plaque in the superficial femoral artery of people with peripheral artery disease: Prevalence and associated clinical characteristics. Polonsky TS, Liu K, Tian L, Carr J, Carroll TJ, Berry J, Criqui MH, Ferrucci L, Guralnik JM, Kibbe MR, Kramer CM, Li F, **Xu D**, Zhao X, Yuan C, McDermott MM. *Atherosclerosis*. 2014 Nov;237(1):169-76.

Inflammatory cytokines and the lymphatic endothelium. **Rockson SG**. *Lymphat Res Biol.* 2014 Sep;12(3):123.

Genome-wide map of regulatory interactions in the human genome. Heidari N, Phanstiel DH, He C, Grubert F, Jahanbani F, Kasowski M, Zhang MQ, **Snyder MP**. *Genome Res.* 2014 Dec;24(12):1905-17.

Cellulose Nanoparticles are a Biodegradable Photoacoustic Contrast Agent for Use in Living Mice. Jokerst JV, Van de Sompel D, Bohndiek SE, **Gambhir SS**. *Photoacoustics.* 2014 Sep 1;2(3):119-127.

Predictors of contemporary coronary artery bypass grafting outcomes. Weisel RD, Nussmeier N, Newman MF, **Pearl RG**, Wechsler AS, Ambrosio G, Pitt B, Clare RM, Pieper KS, Mongero L, Reece TL, Yau TM, Fremes S, Menasché P, Lira A, **Harrington RA**, Ferguson TB; RED-CABG Executive and Steering Committees. *J Thorac Cardiovasc Surg.* 2014 Dec;148(6):2720-2726.e2.

Human Atrial Fibrillation Initiates via Organized Rather Than Disorganized Mechanisms. Schricker AA, Lalani GG, Krummen DE, Rappel WJ, **Narayan SM**. *Circ Arrhythm Electrophysiol.* 2014 Oct;7(5):816-24.

On-line visualization of ischemic burden during repetitive ischemia/reperfusion. Pavo N, Emmert MY, Giricz Z, Varga ZV, Ankersmit HJ, Maurer G, Hoerstrup SP, Ferdinandy P, **Wu JC**, Gyöngyösi M. *JACC Cardiovasc Imaging.* 2014 Sep;7(9):956-8.

Higher risk of death and stroke in patients with persistent vs. paroxysmal atrial fibrillation: results from the ROCKET-AF Trial. Steinberg BA, Hellkamp AS, Lokhnygina Y, Patel MR, Breithardt G, Hankey GJ, Becker RC, Singer DE, Halperin JL, Hacke W, Nessel CC, Berkowitz SD, **Mahaffey KW**, Fox KA, Califf RM, Piccini JP; on behalf of the ROCKET-AF Steering Committee and Investigators. *Eur Heart J.* 2014 Sep 10.

Impact of the lung allocation score on survival beyond 1 year. Maxwell BG, Levitt JE, Goldstein BA, Mooney JJ, **Nicolls MR**, Zamora M, Valentine V, **Weill D**, **Dhillon GS**. *Am J Transplant.* 2014 Oct;14(10):2288-94.

Long-term outcomes of inoperable patients with aortic stenosis randomly assigned to transcatheter aortic valve replacement or standard therapy. Kapadia SR, Tuzcu EM, Makkar RR, Svensson LG, Agarwal S, Kodali S, Fontana GP, Webb JG, Mack M, Thourani VH, Babaliaros VC, Herrmann HC, Szeto W, Pichard AD, Williams MR, Anderson WN, Akin JJ, **Miller DC**, Smith CR, Leon MB. *Circulation*. 2014 Oct 21;130(17):1483-92.

Design and utilization of macrophage and vascular smooth muscle cell co-culture systems in atherosclerotic cardiovascular disease investigation. Zuniga MC, White SL, **Zhou W**. *Vasc Med.* 2014 Oct;19(5):394-406.

Non-contrast-enhanced peripheral angiography using a sliding interleaved cylinder acquisition. Kwon KT, Kerr AB, Wu HH, Hu BS, Brittain JH, **Nishimura DG**. *Magn Reson Med.* 2014 Sep 9.

Reanalyses of randomized clinical trial data. Ebrahim S, Sohani ZN, Montoya L, Agarwal A, Thorlund K, Mills EJ, **Ioannidis JP**. *JAMA*. 2014 Sep 10;312(10):1024-32.

A Prospective Evaluation of Using IVUS during Percutaneous Superficial Femoral Artery Interventions. Hitchner E, Zayed M, Varu V, Lee G, **Aalami O**, **Zhou W**. *Ann Vasc Surg.* 2014 Sep 3.

Anatomic Suitability of Aortoiliac Aneurysms for Next Generation Branched Systems. Pearce BJ, Varu VN, Glocker R, Novak Z, Jordan WD, **Lee JT**. *Ann Vasc Surg.* 2014 Sep 3.

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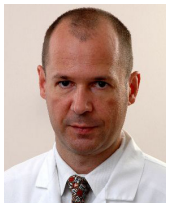

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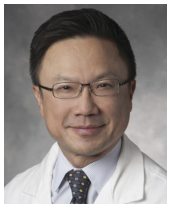

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