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 $10,000 stipends 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

Institute:

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

Biomarker Technology Lecture Series

‘Omics analyses of Complex Diseases’

January 5th, 2015. 5-6:30pm Lorry Lokey (SIM1) G1161
Register: http://goo.gl/J0G4UZ

This series is organized by Jayakumar Rajadas, PhD and held the first Monday of every month.

Institute:

CLINICAL HIGHLIGHT

Department of Medicine launches the Stanford Center for Clinical Research

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 | Full story: see Page 8

NEW 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. Dr. Palaniappan’s currently studies the clinical effectiveness of structured physical activity programs for diabetes management and best exercise regimens for normal-weight diabetics. She recently published a study that examines mortality and socioeconomic differences between diverse Asian subgroups in the U.S. Article at: http://content.onlinejacc.org/article.aspx?articleID=2022248

Kenneth Mahaffey, MD

Latha Palaniappan, MD

Latha Palaniappan, MD

Michael Snyder, PhD
Chair, Department of Genetics

Latha Palaniappan, MD

Article at: http://content.onlinejacc.org/article.aspx?articleID=2022248

cvi.stanford.edu
Given in awards to 70 projects since 2006 // The Stanford Cardiovascular Institute has supported early stage clinical and basic research since the establishment of seed grant awards in 2006. More than 2 million dollars have been awarded. 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.

**Explores 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.

**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.

**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).

**About the Stanford Cardiovascular Institute**

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
‘The Role of Telomere Dysfunction in the Pathogenesis of Familial Dilated Cardiomyopathy’

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.

‘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 Positron Emission Tomography / Magnetic Resonance Imaging (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.

‘Isogenic iPS Derived Cardiomyocytes Corrected for the Myotonic Dystrophy Expanded Triplet Repeat’

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. Matthew Porteus, MD, Ayal Hendel, PhD.

‘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. Vivek Bhalla, MD.
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.

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.”


cvi.stanford.edu
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 a difference 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 Speikerkoeytter, 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), focuses on the contribution of inflammation to the development of PH.

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, 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

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

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 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.


cvi.stanford.edu

Joshua W. Knowles, MD, PhD

William F. Fearon, MD

Jonathan Schwartz, MD

WINTER 2014 | 6
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.

“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

State of the Art: Cardiac Transplantation

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


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 Vincent 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 and Feng Lan 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 diner on Monday, Nov. 17 at the Volare Restaurant.
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

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.
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, 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. 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.


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.

Joseph Wu, Director of the Institute, has initiated the Stanford Cardiovascular Institute (SCVI) Biobank to generate iPSC cells 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 funded by NHLBI/NIH R24 HL117756, a shared resource grant. 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 Karakies, PhD (ioannis1@stanford.edu).

Patients with Peripheral Artery Disease

**PACE Trial (Patients with Intermittent Claudication Injected with ALDH Cells)**

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).

Full details: [http://cvi.stanford.edu/research/trials/#studyId=NCT01774097](http://cvi.stanford.edu/research/trials/#studyId=NCT01774097)

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/](http://cvi.stanford.edu/research/trials/).
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, PhD**: was recently awarded 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 support to investigate, ‘High Dose Efficiency CT System’

- **Ioannis Karakikes**: received an AHA Beginning Grant in Aid on ‘Genetic Correction of Phospholambin Mutations in an iPSC-based Disease Model of Familial Dilated Cardiomyopathy’

- **Kiran Kaur Khush, MD**: was recently awarded an 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**: 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.


NHLBI Talk: Funding for 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.

## 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 year  
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  

**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

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

Lunch provided

<table>
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<tr>
<th>Date</th>
<th>Speaker, Title, Affiliation</th>
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<tbody>
<tr>
<td>1/13/2015</td>
<td>Beth Pruitt, PhD, Stanford, Associate Professor of Mechanical Engineering</td>
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<td>1/20/2015</td>
<td>Eric Olson, PhD, Professor and Chair, UT Southwestern</td>
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<td>1/27/2015</td>
<td>Richard Lawn, PhD, Stanford, CVI Consulting Professor</td>
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<td>2/03/2015</td>
<td>Roberto Bolli, MD, Professor and Chief Division of Cardiology, U. Louisville</td>
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<td>2/10/2015</td>
<td>Kristine Red-Horse, PhD, Stanford, Assistant Professor, Dept. of Biology</td>
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<td>2/17/2015</td>
<td>Laura C. Lazzeroni, PhD, Associate Professor (Research) Psychiatry and Behavioral Sciences</td>
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<td>2/24/2015</td>
<td>Jeffery D. Molkentin, PhD, Professor, Children’s Hospital Medical Center, HHMI Investigator</td>
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<td>3/03/2015</td>
<td>Andrew Plump, MD, PhD, Deputy Head Research and Translational Medicine at Sanofi-Aventis</td>
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<td>3/10/2015</td>
<td>James T. Willerson, MD, President and Medical Director, Texas Heart Institute</td>
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<td>3/17/2015</td>
<td>Joseph Loscalzo, MD, PhD, Chair, Dept. of Medicine, Brigham and Women’s Hospital</td>
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<td>3/31/2015</td>
<td>Mark Fishmen, MD, President of the Novartis institutes for BioMedical Research</td>
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<td>4/07/2015</td>
<td>Irv Weissman, MD, Director Stanford Institute for Stem Cell Biology &amp; Regenerative Medicine</td>
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<td>4/14/2015</td>
<td>William Slikker, Jr., PhD, Director, FDA National Center for Toxicological Research</td>
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<td>4/21/2015</td>
<td>Leslie Leinwand, PhD, Prof., Molecular, Cellular &amp; Developmental Biology, U. Colorado-Boulder</td>
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<td>4/28/2015</td>
<td>Junichi Sadoshima, MD, PhD, Professor, Cell Biology &amp; Molecular Medicine, Rutgers U.</td>
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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, JMB; and Joseph Hill, MD, PhD.

Six Young Investigators Awarded the Winter 2014 Cardiovascular Institute Travel and Exchange 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
**Jan 2015**

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

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

**Feb 2015**

**International Stroke Conference**
- Feb 11-13, 2015
- Nashville, TN
  
  www.nashvillestrokeconference.org

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

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

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

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

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

**Cardiovascular Research Foundation - Coronary Physiology and Intravascular Imaging Symposium**
- Mar 27-28, 2014
- Washington, DC
  
  www.crf.org

**Society for Clinical Vascular Surgery Annual Symposium**
- Mar 29 – Apr 2, 2015
- Miami, Florida
  
  scvs.org

**Mar 2015**

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

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

**APRIL**

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

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

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

**International Stroke Conference**
- Apr 28 – May 1, 2015
- Seoul, Korea
  
  Cardiovascular Summit

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

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

**May 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/

**June 2015**

**PCNA 21st Annual Symposium and Pharmacology Preconference**
- Apr 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
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


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**Geroscience: linking aging to chronic disease.** Kennedy BK, Berger SL, Brunet A, Campisi J, Cuervo AM, Eibl ES, Franceschi C, Lithgow GJ, Morimoto RI, Pessin JE, Brunet A, Campisi J, Cuervo AM, Epel ES, Franceschi C, Lithgow GJ, Geroscience: linking aging to chronic disease.


Leadership

Joseph C. Wu, MD, PhD
Director, Stanford Cardiovascular Institute
Professor, Dept. of Medicine (Cardiovascular) and Radiology

Robert A. Harrington, MD
Arthur L. Bloomfield Professor of Medicine
Chair, Dept. of Medicine

Ronald L. Dalman, MD
Walter C. and Elsa R. Chidester Professor of Surgery
Chief, Division of Vascular Surgery

Stephen J. Roth MD, MPH
Professor and Chief, Pediatric Cardiology
Director, Children’s Heart Center

Dominik Fleischmann, MD
Professor, Dept. of Radiology
Chief, Cardiovascular Imaging

Michael Snyder, PhD
Professor and Chair, Dept. of Genetics
Director, Stanford Center for Genomics and Personalized Medicine

Kenneth Mahaffey, MD
Professor, Dept. of Medicine
Vice Chair of Medicine for Clinical Research

Y. Joseph Woo, MD
Norman E. Shumway Professor in Cardiothoracic Surgery
Chair Dept. of Cardiothoracic Surgery

Mark Nicolls, MD
Associate Professor, Dept. of Medicine
Chief, Pulmonary and Critical Care Medicine

Alan Yeung, MD
Li Ka Shing Professor of Medicine
Co-Chief (Clinical), Division of Cardiovascular Medicine

Tom Quertermous, MD
William G. Irwin Professor of Medicine
Co-Chief (Research), Division of Cardiovascular Medicine

Paul Yock, MD
Martha Meier Weiland Professor of Bioengineering and Medicine;
and Professor, by courtesy, of Mechanical Engineering
Director of Biodesign

Marlene Rabinovitch, MD
Dwight and Vera Dunlevie Professor in Pediatric Cardiology