

#### QUARTERLY | SUMMER 2015

## Stanford MEDICINE 下 🖌 🔰 🖬

## Kobilka, Snyder Elected to AAAS Membership By Office of Communication & Public Affairs

Brian Kobilka, MD, and Michael Snyder, PhD, will be inducted into the American Academy of Arts and Sciences this fall. The two School of Medicine faculty members were among the

of Arts and Sciences in 2015.





Brian Kobilka, MD

Michael Snyder, PhD

The new class will be inducted at a ceremony on October 10 in Cambridge, Mass. The academy, one of the country's most prestigious honorary societies, is a leading center for

197 "thinkers and doers" elected to the American Academy

independent policy research. Members contribute to academy-led studies of science and technology policy, global secu-

rity, social policy and American institutions, the humanities and education.

### 2015 SEED GRANTS



http://tinyurl.com/cviseedgrant2015 APPLY HERE!

## Whole-Heart CT Scanner

Stanford is now home to the third-generation dual-source CT (DSCT) scanner. A system equipped with whole-heart CT perfusion capabilities and for the first time, CT scans with a full field of view of 50 cm at scan speeds within a heartbeat.

In the spirit of innovation and advancing patient-health, a reception is planned for July.

With this new imaging capability comes the opportunity to build analytic tools for preventing, diagnosing and tracking disease based on a patient's own physiological blueprints. Three-dimensional modeling (3D printing) of a patient's heart and vasculature provides unique clinical applications like planning complicated surgical procedures, testing devices, and monitoring response after treatment. For more see '3DQ Imaging Laboratory' on p. 14



## Sager Chair of FDA Committee



Philip Sager, MD, CVI Consulting Professor, is now the Chair of the FDA Cardio-Renal Advisory Committee as of July 1. He is actively involved in developing collaborations among regulators, industry, and academia on new approaches to innovate drug development as well as CV safety assessment of pharmaceuticals and devices. He is also the Chair of the Scientific Programs Committee of the FDA-sponsored Cardiac Safety Research Consor-

Philip Sager, MD tium.

### FEATURED EVENTS

2015 Cardiovascular Research & Medicine at Stanford October 27th, 2015 Register here: http://tinyurl.com/cvi2015

Lawrence H. and Roberta Cohn Lecture November 2, 2015

## Bioengineering Scaffolds





Ngan Huang, PhD

Karina H. Nakayama, PhD

Nanopatterned scaffolds serve as substrates that elicit morphological and biochemical cellular changes. Published in the journal, *ACS Nano,* Ngan Huang's group recently showed that ischemia can be significantly resolved by implantation

of human endothelial cells seeded on parallel-aligned nanofibrillar scaffolds, in contrast to cell-seeded non-patterned scaffolds. Aligned nanofibrillar scaffolds have been shown to reorganize the cytoskeleton and increase cell survival of endothelial cells. In the publication entitled, 'Aligned-Braided Nanofibrillar Scaffold with Endothelial Cells Enhances Arteriogenesis,' the authors show that integrin alpha 1 gene expression is fine tuned by the particular organization of the scaffold, and use for the first time NIR II fluorescence imaging to visualize induction of arteriogenesis.

Karina H. Nakayama, PhD, is the lead author and was a CVI T32 fellow on the Mechanism & Innovations in Vascular Disease training grant.

For the article in ACS Nano visit: http://www.ncbi.nlm.nih.gov/ pubmed/26061869



## A Novel Strategy for Ablating Cardiac Progenitor Cells





Sean Wu, MD, PhD Antl

Anthony Sturzu, MD



A wealth of studies support the importance of developmental signaling molecules in promoting proper heart formation. Disruption in these formative events during embryonic development has a profound impact on human life, as congenital heart disease remains a common cause of birth defects worldwide. However, whether there is a requirement for a specific number of progenitor cells to fashion a normal mammalian heart and the potential mechanisms that exist to compensate for unexpected cell loss during embryonic development have not been explored. To investigate whether a mechanism is present in the developing heart to compensate for the loss of cardiac cells during the early stages of heart formation, we used a novel cell ablation strategy that could temporally ablate cardiac progenitor cells or immature cardiomyocytes in quantifiable fractions. The fundamental discovery described in the article is that during multiple stages of its early formation, a mammal's heart can tolerate the loss of over half of its cells and yet still sustain normal embryonic development. This occurs in part because the embryo is able to rapidly modulate the proliferative rate of the remaining cardiac cells. That such a robust injury-feedback mechanism exists in the embryo to precisely regulate cardiac cell number and therefore maintain normal homeostasis is an intriguing finding opening up many new avenues of study.

The Fetal Mammalian Heart Generates a Robust Compensatory Response to Cell Loss. **Sturzu AC**, Rajarajan K, Passer D, Plonowska K, Riley A, Tan TC, Sharma A, Xu AF, Engels MC, Feistritzer R, Li G, Selig MK, Geissler R, Robertson KD, Scherrer-Crosbie M, Domian IJ, **Wu SM**. *Circulation*. 2015 May 20.

For the article in Circulation visit: http://www.ncbi.nlm.nih.gov/pubmed/25995316

Sean Wu, MD PhD, Assistant Professor - Cardiovascular Medicine and, by courtsey, of Pediatrics was the senior author. He is also a Consulting Editor at *Circulation Research*.

## Cell Type Responsible for Scarring, Skin-Cancer Growth Identified By Krista Conger | Medical School's Office of Communication & Public Affairs





Longaker, MD





Yuval Graham Rinkevich, PhD Walmsley A single cell type in the skin of mice is a major contributor to scarring after wound healing or radiation damage, and facilitates the growth of melanoma. Blocking the cell's activity in humans may be possible with currently approved drugs.

"The biomedical burden of scarring is enormous," said Michael Longaker, MD, co-director of Stanford's Institute for Stem Cell Biology and Regenerative Medicine. "About 80 million incisions a year in this country heal with a scar, and that's just on the skin alone. Internal scarring is responsible for many medical conditions, including liver cirrhosis, pulmonary fibrosis, intestinal adhesions and even the damage left behind after a heart attack."

A paper describing the researchers' findings was published in *Science*. Michael Longaker, MD, a Professor of Surgery, and SCBR Institute Director Irving Weissman, MD, a Professor of Pathology and of Developmental Biology, are the senior authors. Postdoctoral scholar Yuval Rinkevich, PhD, and graduate student Graham Walmsley share lead authorship.

Full story at https://med.stanford.edu/news/all-news/2015/04/cell-type-responsible-for-scarring-skin-cancer-growth-identified.html

## Precision Health: Predicting and Preventing Disease — Not Just Treating It By Ruthann Richter | Medical School's Office of Communication & Public Affairs

Precision health takes a big-data approach to disease prevention and detection, focusing on the various factors that help maintain health throughout life.



Imagine a system where doctors can quickly comb through millions of anonymized patient records to find people with conditions and medical experiences just like yours. Through this massive, searchable database, doctors could determine how best to treat you, based on what has worked effectively for others with similar symptoms and characteristics.

Stanford Medicine is laying the groundwork for such a system, which will be able to quickly analyze information from large patient databases, medical literature, mobile monitoring and patients' real-life experiences with drugs, among other sources, to provide an evidence-based approach to medicine that's not been possible before.

The planned system is an example of how clinicians at Stanford Medicine are tapping health data to provide targeted, predictive and personalized

care, an approach known as "precision health." What makes precision health unique is that it goes beyond treating existing diseases and conditions to predicting and preventing diseases before they manifest, said Lloyd Minor, MD, dean of the School of Medicine. It stands at the intersection of medicine, technology and big data, offering new ways to keep people healthy.

"Precision health is a way of translating data into information that can lead us to take care of our health in a way that we might not have done before," Minor said. "We are poised to have a whole new level of precision in maintaining health."

## CRISPR Marches Forward By Krista Conger | Medical School's Office of Communication & Public Affairs

CRISPR is a breakthrough way of editing the genome of many organisms, including humans — a kind of biological cut-and-paste



function that is already transforming scientific and clinical research. However, there are still some significant scientific hurdles that exist when attempting to use the technique in cells directly isolated from human patients (these are called primary cells) rather than human cell lines grown for long periods of time in the laboratory setting.

Matthew Porteus, MD, PhD



Now pediatric stem cell biologist Matthew Porteus, MD, PhD, and postdoctoral scholars Ayal Hendel, PhD, and Rasmus Bak, PhD, have collaborated with researchers at Santa Clara-based Agilent Research Laboratories to show that chemically modifying the

Ayal Hendel, PhD



guide RNAs tasked with directing the site of genome snipping significantly enhances the efficiency of editing in human primary blood cells — an advance that brings therapies for human patients closer. The research was published recently in *Nature Biotechnology*.

Rasmus Bak, PhD

As Porteus, who hopes to one day use the technique to help children with genetic blood diseases like sickle cell ane-



Crisper/Cas9 illustration courtesy of Ayal Hendel

mia, explained, "We have now achieved the highest rates of editing in primary human blood cells. These frequencies are now high enough to compete with the other genome editing platforms for therapeutic editing in these cell types."

Pubmed: http://www.ncbi.nlm.nih.gov/pubmed/26121415

For more visit: http://scopeblog.stanford.edu/2015/06/29/crispr-marches-forward-stanford-scientists-optimize-use-in-human-blood-cells/

## Pulmonary Artery Pulsatility Index

Right ventricular failure (RVF) is a major cause of morbidity and



mortality following left ventricular assist device (LVAD) implantation. The pulmonary artery pulsatility index (PAPi) is a novel hemodynamic index that predicts RVF in the setting of myocardial infarction, though it has not been shown to predict RVF after LVAD implantation. A recent study published in *The Journal of Heart and Lung Transplantation* performed a retrospective, single center

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Dipanjan Banerjee, MD, MS

analysis to examine the utility of the PAPi as a predictive tool in



For more visit: *http://www.jhltonline.org/article/ \$1053-2498%2814%2900280-0/abstract* 

## About the Stanford Cardiovascular Institute



Cathy Hutton

Ingrid Ibarra, PhD

The Institute, currently consists of 124 faculty members representing, engineers, physicians, surgeons, basic and clinical researchers. The mission 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 please contact Joseph C. Wu, MD, PhD, Director CVI (joewu@stanford.edu), or Ingrid Ibarra, Assistant Director of CVI (iibarra@stanford.edu) or Cathy Hutton, Senior Associate Director, Medical Center Development (cathy.hutton@stanford.edu).

For ways to give: http://cvi.stanford.edu/support-our-research.html and http://cvi.stanford.edu

## Reversing Pulmonary Hypertension

Recently researchers at Stanford led by **Marlene Rabinovitch**, **MD**, Professor in Pediatric Cardiology, identified a molecular path that links mitochondrial function to pulmonary aterial endothelial cell survival and bone morphogenetic protein receptor 2 (BMPR2). This work provides clues into PAH therapies and other lung conditions with disrupted endothelial cell function.

In Pulmonary arterial hypertension (PAH), sevearl features are notable: the arterial endothelial cells undergo death, there is a decrease in microvessels, and occlusive vascular remodeling. In addition, mitochondrial dysfunction, inflammation, and mutations in BMPR2 are also associated with this yet incurable disease. These features can be recapitulated in mice and in doing so the authors show signaling that emerges with BMPR2 and culminates in the mitochondria. The article was published in *Cell Metabolism* and entitled, 'BMPR2 preserves mitochondrial function and DNA during reoxygenation to promote endothelial cell survival and reverse pulmonary hypertension.'

#### Authors include postdoctoral fellows Isabel Diebold, MD, Jan K. Hennigs, MD, and Kazuya Miyagawa, MD, PhD.





Marlene Rabinovitch, MD Isabel Diebold, MD



Jan K. Henniqs, MD



Kazuya Miyagawa, MD, PhD

To see the article in Cell Metabolism visit: http://www.ncbi.nlm.nih.gov/pubmed/25863249

## Molecular Cause of Heart Condition Identified by Researchers By Krista Conger | Medical School's Office of Communication & Public Affairs

The beta adrenergic pathway is dysfunctional in dilated cardiomyopathy. Now, researchers have learned how a mutation that causes the disease affects the pathway, and how to mitigate its effects. In 2012, researchers at the Stanford University School of Medicine showed that heart muscle cells made from the skin of people with a cardiac condition called dilated cardiomyopathy beat with less force than those made from the skin of healthy people. These cells also responded less readily to the waves of calcium that control the timing and strength of each contraction. Now, the same research team has teased apart the molecular basis for these differences and identified a drug treatment that at least partially restores



cvi.stanford.edu

Jared Churko, PhD

function to diseased cells grown in a laboratory dish. They also observed how a key cardiac signaling cascade, called the beta-adrenergic pathway, develops as heart muscle cells mature, and identified key aspects about how it functions in both normal and diseased cells.

The researchers hope that the findings will help clinicians better hone treatments for a variety of cardiac conditions, which are now often treated with a one-size-fits-all approach.

"Right now, nearly all patients with cardiomyopathy are given drugs to modulate the beta-adrenergic pathway in the heart, which is known to be dysfunctional," said **Joseph Wu, MD, PhD,** Director of Stanford's Cardio-



Elena Matsa, PhD



Arun Sharma

vascular Institute. "But until now, we've not known what exactly is going wrong with this pathway at a molecular level."

A paper describing the research was published online June 18 in *Cell Stem Cell*. Wu, a professor of medicine and of radiology, is the senior author of the paper, and postdoctoral scholar **Haodi Wu, PhD,** is the lead author. (Note: Joseph Wu and Haodi Wu are not related.)

Stanford co-authors are postdoctoral scholars Mingxia Gu, PhD, Feng Lan, PhD, and Jared Churko, PhD; cardiovascular medical fellow Karim Sallam, MD; Instructor Elena Matsa, PhD; graduate student Arun Sharma; and senior research scientist Joseph Gold, PhD. The work was funded by the American Heart Association and the National Institutes of Health.

For more visit: http://med.stanford.edu/news/ all-news/2015/06/molecular-cause-of-heart-condition-identified-by-researchers.html; Cell Podcast: http://www.cell.com/pb-assets/journals/research/ cell/PaperClips/AUDIO/podcasts/0618cell2015.mp3; and Stanford Daily: http://www.stanforddaily. com/2015/07/08/researchers-develop-patient-specific-heart-cells-from-stem-cells/

## Tissue Engineering: Repairing the Heart

The Stanford Cardiovascular Institute, with support from the National Heart, Lung and Blood Institute (NHLBI) and the California Institute of Regenerative Medicine (CIRM) hosted, its second annual Cardiovascular Regenerative Medicine Conference on May 22nd. It was a full house. Over 200 registered students, fellows, and faculty in attendance. Speakers represented 14 universities from around the U.S. and Europe. Gordana Vunjak-Novakovic, PhD, Mikati Foundation Professor of Biomedical Engineering and Director of Laboratory for Stem Cells and Tissue Engineering at Columbia University, gave the keynote address. The meeting concluded with Laura Niklason, MD PhD, Professor at Yale School of Engineering and Applied Science presenting pioneering work on engineering arteries. The awardees of the conference's research posters are below.



### WINNING ABSTRACTS:



*Epigenetic Modifications of Phosphodiesterase Contribute to Compromised-Adrenergic Signaling during the Pathogenesis of DCM-specific iPSC-derived Cardiomyocyte* by **Haodi Wu**, Jaecheol Lee, Mingxia Gu, Feng Lan, Jared Churko, Karim Sallam, Elena Matsa, Arun Sharma, Joseph D. Gold, Donald M. Bers, Joseph C. Wu.

Single-Cell Stethoscopes for Functional Analysis of Stem Cell-Derived Cardiomyocytes by Sally A. Kim, Catherine Jan, John Huguenard, Olav Solgaard, Nicholas Melosh. Neurology & Neurological Sciences and Electrical Engineering, at Stanford University

*Effect of Donor Cell Source on Human iPSC-based Cell Therapy* by **Ming-Tao Zhao**, Shijun Hu, Rajini Srinivasan, Fereshteh Jahaniani, Ning-Yi Shao, David Knowles, Won Hee Lee, Tomek Swigut, Joanna Wysocka, Michael P. Snyder, Joseph C. Wu.





Malte Tiburcy, MD (left) Oscar Abilez, MD, PhD (right)



Brenda Olge, PhD, and Sean Palecek, PhD





Gordana Vunjak-Novakovic, PhD, and Ibrahim Domian, MD, PhD

### Travel & Exchange Ideas Award

For more visit: http://cvi.stanford.edu/research/travel\_grant\_awards/2015\_mar\_travel\_grant\_awards.html



**Daniel Kaiser, MD** Mintu Turakhia, MD Heart Rhythm 2015 Scientific Session

'Paradoxical Sex Differences in Clinical Outcomes after Catheter Ablation of Atrial Fibrillation'



**Vivek Nanda, PhD** Nicholas J. Leeper, MD Society for Vascular Medicine 2015

'Cyclin-Dependent Kinase Inhibitor 2B Regulates Transforming Growth Factor Beta 1 Mediated Smooth Muscle Cell Recruitment to Ischemic Blood Vessels'. | Nanda was also awarded the Jay D. Coffman Award from the Society for Vascular Medicine



Yukari Kobayashi, MD Ingela Schnittger, MD ACC Scientific Sessions 2015

'Impact of Myocardial Deformation Imaging on the Diagnosis of Myocardial Bridge'



**Tejaswini Mishra, PhD** Michael Snyder, PhD The Biology of Genomes

<sup>•</sup>Understanding Obesity Mediated Insulin Resistance Through Integrative Personal Omics Profiling (iPOP) During Weight Gain and Loss<sup>•</sup>



Kozo Okada, MD William F. Fearon, MD ACC Scientific Session 2015

'Paradoxical Arterial Remodeling of the Proximal Segment of the Left Anterior Descending Artery Predicts Long-Term Mortality after Heart Transplantation'



Fatima Rodriguez, MD Paul Heidenreich, MD ACC Scientific Sessions 2015

'Use of high potency statins for patients with established atherosclerotic cardiovascular disease: practice impact of the new cholesterol guidelines'



Kathia Zaleta, PhD Euan Ashley, MD 2015 CSHL Meeting on RNA and Oligonucleotide Therapeutics

'Oligonucleotide therapeutic approaches for allele silencing of hRLC-47K and hMHC-403Q mutations in Hypertrophic Cardiomyopathy'



**Junaid Zaman, MD** Sanjiv Narayan, MD European Cardiac Arrhythmia Society Annual Congress 2015

'Electrograms: More than the Sum of Their Parts-A New Rat Model of Atrial Arrhythmias'. | Dr. Zaman was also awarded a UK-US Fulbright BHF award

### Postdoctoral Fellowship Research Award: \$10,000 salary support Deadline <u>August 15, 2015</u>. Apply: <u>http://tinyurl.com/cvi2015research1</u> Fellows should submit: Score of prior grant application (NIH, AHA, CIRM, NSF etc.), NIH biosketch, One-page research proposal



Deadline

Aug. 15, 2015

http://cvi.stanford.edu/education/ cvi\_fellowship\_training\_program. html

### Fellows



**Paul W. Burridge, PhD,** is embarking on a new venture as a founding faculty of the Center for Pharmocogenomics at Northwestern University. Professor Burridge received his PhD from the University of Nottingham, UK, studying stem cell biology and completed his postdoc-

toral fellowship at Stanford University in Joseph C. Wu's laboratory. His new lab will focus on the genomics of drug response. "Currently we are concentrating on modeling chemotherapy-induced cardiomyopathy using human induced pluripotent stem cell-derived cardiomyocytes, endothelial cells, and fibroblasts. This allows us to recapitulate a patient's off-target cardiotoxic response to drugs such as anthracylines and tyrosine kinase inhibitors," said Burridge.



**Raiyan Zaman, PhD**, was recently awarded a Pathway to Independence (K99/R00) funding by the National Institutes of Health for 'A Novel Intravascular CRI-PAT Imaging System to Characterize Vulnerable Plaque'. She completed her biomedical engineering degree at the Universi-

ty of Texas at Austin (2011). As an American Heart Association postdoctoral fellow, Zaman developed a novel catheter-based imaging system to detect vulnerable plaques. Her mentors include Michael V. McConnell, MD, Professor of Professor of Medicine (Cardiovascular), and Lei Xing PhD, Professor of Radiation Oncology and by courtesy, Electrical Engineering.



**Jared Churko**, **PhD**, was recently awarded a Pathway to Independence (K99/ROO) funding by the NIH for "Notch signaling in cardiomyocyte transcriptome signatures". In Joseph C. Wu's lab, he will study how perturbations in notch signaling impacts cardiomyocyte function and disease.

By using CRISPR-Cas9 technology, he will knock out genes associated with the notch signaling pathway within induced pluripotent stem cells. These cells will be differentiated into cardiomyocytes and RNA-seq will be performed on these cells to map notch transcriptome interaction networks. Ultimately, this proposal will further our understanding of heart diseases associated with notch signaling.

### Medical Students



**Chiaka Aribeana** was awarded a highly competitive summer internship scholarship in cardiothoracic surgery from the American Association for Thoracic Surgery. She works in the laboratory of Joseph Woo, MD, Professor and Chair of Cardiothoracic Surgery, and con-

ducts basic science and translational research focused on cardiac tissue engineering and myocardial regeneration to treat heart failure.



**Christopher Jensen** will join Joseph Woo's team and work on post-infarction cardiac remodeling. Chris was one of five Stanford medical students named Howard Hughes Medical Institute Research Fellow. The students receive one year of mentored research training and financial support.

#### Faculty



**William Fearon, MD,** was promoted to Professor of Medicine, effective April 1. His research focuses on the invasive assessment of coronary physiology using a wire-based technique. He has been instrumental in the development of a robust

transcatheter aortic valve replacement program, which has treated more than 500 patients over the past seven years.



Jason T. Lee, MD, was promoted to Professor of Surgery in the Division of Vascular Surgery, effective April 1. He serves as Director of Endovascular Surgery at Stanford. Since 2011, Dr. Lee has been Program Director of the Integrated and Independent Vascular Training Residency Programs.



**Edda Spiekerkoetter, MD**, Assistant Professor of Medicine, has received the American Society of Clinical Investigator's Young Physician-Scientist Award. Her research focuses on pulmonary hypertension and methods to improve heart function. In particular, she studies the BMPR2 signaling pathway.





Joshua Knowles, MD, PhD, Assistant Professor of Cardiovascular Medicine, and Atsushi Tachibana, MSc, received the American College of Cardiology Herman K. Gold Young Investigators Awards in Molecular and Cellular Cardiology. Knowles, Assistant Professor of Medicine, received the second-place award in recognition of his work using large-scale genomic studies to identify the genes associated with insulin resistance. Tachibana, a graduate student, received the third-place award. He is a research fellow in

the laboratory of Phillip Yang, MD, Associate Professor of Medicine, where he focuses on the in vivo imaging of cardiovascular stem cells and myocardial regeneration.



## Vascular Surgery News



**Eri Fukaya, MD**, will be joining Nicolas Leeper MD, in the Vascular Medicine practice at Stanford, beginning in August. Fukaya's principal research interest includes interventions to increase physical activity and utilizing mobile health with information technology to diagnose, treat and prevent disease.



Venita Chandra, MD, successfully initiated Stanford as a participating site in the NHLBI-sponsored multi center trial BEST-CLI, comparing primary approaches to lower extremity limb salvage starting with either endovascular or open surgical revascularization. This is a \$25M trial being led by both vas-

cular surgery and cardiology principle investigators.



The Division of Vascular Surgery is pleased to announce the recruitment of Dr. Tina Desai as Clinical Associate Professor effective July 1st, 2015. **Dr. Tina Desai** earned her MD (1991) from the Brown University Medical Education Program in Providence, Rhode Island. She then completed a surgical

residency in General Surgery at the University of Chicago Hospitals and Clinics, including a 2-year research fellowship. She completed her Vascular Surgery Fellowship training at the University of Chicago Hospitals (1999).



Yoko Kojima, MD, PhD, was awarded the 2015 inaugural Employee of the Year in the Division of Vascular Surgery. This is an testament to her unwavering commitment to outstanding research and unparalleled contributions to Nicholas Leeper, MD's team's discovery efforts.



**Ronald Dalman, MD,** Professor of Vascular Surgery will oversee the Vascular Annual Meeting of the Society for Vascular Surgery. The VAM is the largest single meeting devoted to the care of the vascular patient worldwide, and has been held annually since 1947. For this year and the subsequent two years Dalman

served as Program Chairman for the VAM/SVS. Approximately 1,500 professional members attend the VAM annually. The Society for Vascular Surgery has approximately 4,000 members in North American and chapters around the world. For more visit: *www.vascularweb.org.* 







Vascular Surgery added an additional fellow to their training program this year to include the practice at Santa Clara Valley Medical Center in San Jose. **Kathleen "Katy" Balazy** (*left*), from Harvard Medical School will be the eighth resident to join the integrated vascular surgery training program since its inception in 2008. She received her Bachelor's Degree from John Hopkins University in 2007, her M.D. from Harvard Medical School in 2014 and is expected to receive her M.P.H. from the University of California, Berkeley in June. **Andy Lee** (*middle*) received his MD from the University of Illinois College of Medicine and completed his Residency at Beth Israel Deaconess Medical Center, in Boston. **Tiffany Wu** (*right*), received her MD from Keck School of Medicine of the University of Southern California, and finished her residency at Huntington Hospital, Pasadena, CA.

## Join Our Team: CVI/CT-Surgery Faculty Search

The Stanford Cardiovascular Institute (CVI) and the Stanford Department of Cardiothoracic Surgery (CTS) is seeking an academic cardiovascular investigator at the Assistant Professor (Non-Tenure Research Line) level to develop and maintain a productive research program, participate in education and scholarly collaborative activities of the CVI, and provide mentorship for trainees.

We seek outstanding candidates with a PhD, MD, or MD/PhD degree and appropriate postdoctoral experience who have demonstrated the ability to develop a high-quality independent research program distinguished by exceptional originality and productivity. We are particularly interested in an outstanding investigator with expertise in the fields of, but are not limited to, gene therapy, stem cell biology, regenerative medicine, non-coding RNAs, cardiac lineage differentiation and cell fate, and/or in vitro and in vivo model systems of cardiovascular disease.

For a full job description, application requirements, and any other questions please contact Ms. Corrine Sanchez (corrine.sanchez@stanford.edu); or visit: http://cvi.stanford.edu/content/dam/sm/cvi/documents/news\_documents/cvi-cv-investigator-position.docx.

Mail your applicaitons to: Joseph Woo, MD, Search Committee Chair, c/o Corrine Sanchez, CVRB, Falk Bldg., Mail Code 5407, 300 Pasteur Drive, Stanford, CA, 94305-5407.

## Doctor, Nurses Honored for Advances Made in Early Days of Cardiac Care By Sara Wykes, Stanford Hospital & Clinics communications office



Photos: Steve Fisch

Patricia Ballard (top left) a longtime secretary in the coronary care unit; Joan Mersch (top middle), a former nurse coordinator; and Joy Oeth Paris (top right), a former nurse, attend a celebration marking the official announcement of a gift to the unit. Alfred Spivack (lower center) taught nurses to do a number of jobs generally restricted to doctors in the early days of Stanford's coronary care unit. In 1966, Stanford Hospital joined the handful of hospitals worldwide with a dedicated nursing unit for coronary care. That specialized unit, with only four patient beds, was advanced for its time — and so, too, was what followed for the nurses who worked there.

"Nurses then couldn't start IVs," said Joan Fair, PhD, RN, MSN, NP, one of the unit's original nurses and now a cardiovascular researcher and fellow of the American Heart Association. "And I was trained to stand up when a doctor entered the room." Alfred Spivack, MD, the unit's founding director, wasn't a fan of that kind of thinking.

He taught its first head nurse, Bonnie Goddard Burnham, and the nurses in the unit to do a number of jobs generally restricted to doctors in those days, such as reading electrocardiograms. He also taught them a technique he pioneered to monitor heart failure: It required threading a catheter from the arm to the major vein leading into the heart to measure oxygen and blood pressure — another type of procedure considered outside the bounds of a nurse's duties then.

The coronary care unit is now approaching its 50th anniversary. In April, Spivack, now a Professor Emeritus of Medicine at Stanford, and many of the nurses who worked in the unit over the decades were honored at a special dinner. The occasion was the official announcement of a major gift from Spivack to honor the nurses who pioneered the unit's specialized critical care for cardiac patients. The gift will fund the nursing station when the unit is relocated to the new adult hospital, where it will be called the heart acute care unit. The new hospital is slated to open in 2018.

http://med.stanford.edu/news/all-news/2015/05/doctor-nurses-honored-for-early-advanc-es-in-cardiac-care.html

## Consulting Professor Joins Stanford CVI

Stefan Jovinge MD, PhD, is best known for his work in the area of cardiac regeneration. He leads a team of researchers and clinicians at



the Spectrum Health Frederik Meijer Heart & Vascular Institute and Van Andel Research Institute in Grand Rapids. His background as a physician scientist in cardiac regenerative biology and medicine will be a tremendous asset for Cardiovascular Institute members in forming productive collaborations. Jovinge has pub-

Stefan Jovinge, MD, PhD

lished more than 50 original studies with a number of them in the high impact journals such as *New England* 

*Journal of Medicine*, *Science*, *Nature Medicine*, *Nature Cell Biology*, and others.



### Celebrated Anniversaries at Stanford Medical School

Each year, the School of Medicine honors employees who have reached their 5, 10, 15, 20, 25, 30, 35, 40 and 45 years of service at the University.



The Stanford Cardiovascular Institute acknowledges Postdoctoral Affairs Administrator, **Jenifer Soboleski** (*15 years*); Clinical Research Coordinator, **Ed Finn** (*5 years*), center; and Program Manager ,**David** L. M. **Preston** (*5 years*), right, for their outstanding dedication.

## Sex as a Biological Variable in NIH-funded Research

The National Institutes of Health have recognized major gaps in our understanding of the differences between men and women in disease progression and therapeutic outcomes. In June the NIH released a statement: "NIH expects that sex as biological variable will be factored into research designs, analyses and reporting in vertebrate animal and human studies."

Gender differences in cardiovascular health and disease are areas of active research at Stanford. In fact, the Center for Women & Sex Differences in Medicine and the Stanford Women's Heart Health Clinic both provide annual seed funding for research projects aimed at advancing women's health and sex differences research.

In April, Stanford held a reception, "Why Sex Matters: Women, Men and Medicine," featuring a special panel of experts to discuss the next steps in making an impact in clinical trial design, stem cell research and population science that factor sex as a variable. The discussion focused on insights into how sex difference impact the scientific investigations of individual researchers, informs researching funding policies at the national level, and ultimately affect medical care for patients.

As we learned, the "one size fits all" approache does not benefit every patient. This is especially true for women in the area of pharmaceutical standards. There is a pressing need to explore the importance of sex differences in medicine, and Stanford is poised to make significant advances in this area.

The panel included Janine Clayton, Associate Director, National Institutes of Health (NIH) Research on Women's Health; Director, NIH Office of Research on Women's Health, Vera Regitz-Zagrosek, MD,



Director, Institute of Gender in Medicine, Center for Cardiovascular Research, Charité University, Berlin and Art Arnold, Editor-in-Chief, Biology of Sex Differences; Chair, Department of Physiological Science, University of California, Los Angeles.

The Stanford panel included: **Jennifer Tremmel, MD,** Assistant Professor of Medicine (Cardiovascular), Clinical Director Women's Heart Health at Stanford and Director Secondary Prevention Program; **Sean M. Wu, MD, PhD,** Assistant Professor of Medicine (Cardiovascular), and, by courtesy, of Pediatrics; **Marcia Stefanick, PhD,** Professor of Medicine and of Obstetrics and Gynecology, Co-Founder and Co-Director Stanford Center for Health Research on Women and Sex Differences (WSDM); and **Kenneth Mahaffey, MD,** Professor of Medicine (Cardiovascular), Vice Chair, Clinical Research, Department of Medicine, and Director, Stanford Center for Clinical Research.

http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-102.html

## Sports Medicine



Victor Froelicher, MD



Francois Haddad, MD

Marco Perez, MD

Jonathan Myers, PhD

**Victor Froelicher, MD,** Emeritus Professor of Medicine (Cardiovascular) served as guest editor in the Journals of Electrocardiology and Current Sports Medicine Reviews, this past May. "We are grateful to our authors who have been major contributors to the field of sports medicine and specifically regarding electrocardiology.' In an editorial, Froelicher stated that 'we are at a point where there is considerable interest in turning the debate upside down with the realization that the ECG could have greater screening value than the long recommended physical exam and patient history.'

In Current Sports Medicine Reports (CSMR), he combined a sports medicine physician with a specialist to make recommendations for each of the elements of the AHA CV risk assessment of young athletes. Both symposia included experts from the Stanford Cardiovascular Institute as authors including **Marco Perez**, **MD**, Assistant Professor of Medicine (Cardiovascular Medicine), **David Liang, MD PhD**, Associate Professor of Medicine (Cardiovascular) and, by courtesy, of Electrical Engineering, **Francois Haddad**, **MD**, Clinical Assistant Professor, Medicine and **Euan Ashley**, **MD**, Associate Professor of Medicine (Cardiovascular), of Genetics, and **Jonathan Myers**, **PhD**, Clinical Professor (Affiliated).

## Center for Clinical Trials Achieves Milestones

The Stanford Center for Clinical Research (SCCR) has achieved a number of key milestones and tremendous growth. SCCR continues to grow and refine services to support research of the faculty and



Kenneth Mahaffey, MD

staff in the Department of Medicine and other areas.

SCCR's Director, **Kenneth Mahaffey, MD,** Vice Chair of Clinical Research in Medicine, stated, "We have partnered with many investigators across the Department of Medicine and School of Medicine to develop research programs in important therapeutic areas and are also working to launch

programs that will transform the operational conduct of clinical research at Stanford," said Mahaffey.

The center involves three core enterprises; site-based research, led by Rebecca McCue, a coordinating center, led by Amol Rajmane, MD, and education training. SCCR's mission is to facilitate clinical research initiatives by providing operations support to aid faculty and staff to perform efficient, high-quality and impactful clinical research at Stanford.

The Coordinating Center enterprise within SCCR to date has a leadership role in 8 awards with another 11 submitted or in preparation for submission in conjunction with 10 faculty members across the SOM Funding sources include both Industry and government (NIH and DoD) awards. One pivotal project in particular, the AMP study under Principal Investigator **P.J. Utz, MD,** is a big success for SCCR. The Coordinating Center is working with a number of investigators across the University providing project leadership, protocol development, clinical event adjudication (CEC), data safety monitoring boards (DSMB), and biostatistics and data management in partnership with Manisha Desai's Quantitative Sciences Unit (QSU). This includes **Matthew**  **Mell, MD**,'s Vorapaxar AV Fistula trial funded by Merck, and **Jamshid Ghajar, MD, PhD**'s BTEC consortium funded through Department of Defense (DoD).

Within SCCR's Site-Based Research arm, Associate Director Rebecca McCue has been focusing on the Baseline study in partnership with Duke University and Google[x], which includes a focus on Cardiology and Oncology. The study is a great example of SCCR's collaborative partnerships – spanning multiple Divisions and Departments across the School of Medicine – with leadership including **David Maron, MD** (Cardiology), **George Sledge, Jr., MD**, (Oncology), **Michael Snyder, PhD**, (Genetics), and Dr. Mahaffey (Cardiology and SCCR), led by Stanford Principal Investigator **Sam Gambhir, MD**, **PhD** (Radiology); and operational support in Radiology and SCCR.

SCCR is also excited to be partnering with Stanford's CTSA-funded Spectrum to launch a Clinical Trials Management System (CTMS), OnCore, later this year (http://med.stanford.edu/news/allnews/2015/06/software-will-help-researchers-manage-track-clinical-trials.html). This tool will fundamentally change how studies and resources are tracked and will give researchers and leadership access to key metrics to enable strategic planning for clinical research.

To support the CTMS deployment, SCCR is also partnering with the Cardiovascular Institute, the Division of Cardiovascular Medicine, and the Division of Gastreoenterology and Hepatology to roll-out a Research Manager structure. Providing hands-on support and streamlined process recommendations for Faculty and Staff, this model aims to improve study startup and enhance project success. Tine Bjornlund joined SCCR in May, 2015, to assume this new Research Manager role and is piloting a shared Coordinator pool, Coordinator cross-coverage, new budgeting tools, and overall project management.

## Clinical Biomarker Discovery Lecture Series



The Stanford Cardiovascular Institute has been supporting a new lecture series focused on Modern Technologies and Applications in Biomarker Discovery, geared for for post-doctoral researchers, faculty, and clinicians.

Jayakumar Rajadas, PhD

The lectures are held from 4:30 - 6 p.m. the first Monday of every month in the Lorry Lokey (SIM1) Stem Cell Building on the Stanford Campus. The series is managed

by **Jayakumar Rajadas, PhD,** *Founding Director, Biomaterials and Advanced Drug Delivery Laboratory LC-MS-Based Method for Quantification of Biomarkers from Bio Fluids.* 



For more visit: http://cvi.stanford.edu

cvi.stanford.edu



Marlene Rabinovitch, MD NIH | 'Pulmonary Hypertension In Genetically Modified Mice'



Nicholas J. Leeper, MD NIH | 'The Role of CDKN2B in Efferocytosis and Atherosclerosis'



Calvin J. Kuo, MD, PhD

NIH | Stanford Cooperative Research Center for Novel, Alternative Model Systems for Enteric Diseases



Joseph C. Wu, MD, PhD

NIH | 'Genome Editing of Human iPSCs to Study Inherited Hypertrophic Cardiomyopathy'



Fan Yang, PhD NIH | 'Microribbon-based Scaffolds for Bone Repair'



Eric Gross, MD PhD

NIH | Diversity Supplement for: Role of the TRPV1 Channel in Myocardial Salvage from Ischemia-Reperfusion Injury



Joshua W. Knowles, MD, PhD

AHA | 'Use of Electronic Phenotyping and Machine Learning to Identify Familial Hypercholesterolemia in EHRs'



Daniel Bernstein, MD



Michael Snyder, PhD

Pediatric Cardiac Genomics Consortium (PCGC) Funding | 'Genetics of Hypoplastic Left Heart Syndrome'. This study is a joint venture between the Gladstone, UCSF and Stanford. The leading investigators at Stanford are Daniel Bernstein, MD, Professor in the Department of Pediatrics at Stanford and Michael Snyder, PhD, Professor and Chair in the Department of Genetics will serve as co-investigator.

### New Clinical Trials



**Euan Ashley, MD** | Safety, Tolerability, Preliminary Pharmacokinetics and Pharmacodynamics of Single Ascending Oral Doses of MYK-461 in Patient Volunteers with Hypertrophic Cardiomyopathy: A First in Human Study



Jeffrey A. Feinstein, MD | A Multicenter, Open-Label, 24-Week, Uncontrolled Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of Oral Treprostinil Extended Release Tablets Following Transition from Remodulin or Inhaled Prostacyclin Therapy or as Add-on to Current PAH Therapy in De Novo Prostacyclin Pediat-

ric Subjects Aged 7 to 17 Years with Pulmonary Arterial Hypertension.



Matthew Mell, MD | was recently awarded a large research award in collaboration with Kenneth Mahaffey, MD. The clinical trial is focused on the drug," Vorapaxar (Zontivity)" which is geared to Improve Maturation of Arteriovenous Fistulae in Hemodialysis.



Alan Yeung, MD | REPRISE III: Repositionable Percutaneous Replacement of Stenotic Aortic Valve through Implantation of Lotus™ Valve System - Randomized Clinical Evaluation



**Roham T. Zamanian, MD** | Leukotriene B4-mediated Pulmonary Arterial Hypertension and A Dose-Ranging Study of the Efficacy and Safety of Bardoxolone Methyl in Patients with Pulmonary Arterial Hypertension.

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### Biobank



### Stanford CVI Human iPSC Biobank Service

Normal and patient-derived reprogrammed cardiomyocytes is a tremendous resource for researchers and physicians here at Stanford and around the country. 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.

To facilitate research in a dish that allows screening of new compounds or characterization of human disease phenotypes using cardiomyocytes, the Institute created a service by which de-identified PBMC samples can be sent to Stanford CVI for reprogramming free of cost. Please contact Joseph Wu, MD, PhD (joewu@stanford.edu) or Biobank manager, Justin Vincent (justin81@stanford.edu).

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). Stanford iPSC Biobank was recently mentioned in Nature Methods news: http://www.nature.com/nmeth/journal/v12/n2/full/nmeth.3263.html.

### Lab Resources

## Clinical <u>B</u>iomarker & <u>P</u>henotyping <u>C</u>ore <u>L</u>ab (BPCL)

## **Our Mission**

We provide quantitative assessment of clinical cardiovascular phenotypes for translational research and clinical trials. These cardiovascular phenotypes include evaluating cardiac structure and function, measuring carotid intimal thickness and arterial stiffness, and testing endothelial function and cardiopulmonary exercise testing.

In collaboration with the Human Immune Monitoring Center at Stanford and members of the Cardiovascular Institute, we also offer central blood processing and banking capabilities. In addition, we develop new biomarker platforms and imaging modalities.

### **Contact Us**

Francois Haddad, MD, (fhaddad@ stanford.edu) or Ingrid Ibarra, PhD, (iibarra@stanford.edu) at the CVI.



#### Perfusion Imaging

#### **Key Initiatives**

1. **Stanford Athletic Screening Program.** The BPCL is the core laboratory responsible for the echocardiographic studies of Stanford Athletic Screening Program and has imaged more than 500 athletes.

#### 2. Stanford Immune Aging Longitudinal

**Study.** The BPCL is the core providing clinical cardiovascular phenotypes for collaboration through the NIH funded projects of the Immunity Transplantation and Infection Institute led by Mark Davis, MD.

3. The Pulmonary Hypertension Wall Center Outcome and Physiology Studies. The BPCL works closely with the Vera Moulton Wall Center for Pulmonary Vascular Disease to provide quantitative echocardiographic assessment of the right heart.

#### 4. The CCML-Stanford Collaborative Effort.

Through a close collaboration with the University of Paris and the Marie-Lannelongue surgical center (CCML), the BPCL is providing quantitative analysis of experimental and clinical studies focused on right heart physiology. The CCML is a recognized worldwide center of expertise in pulmonary hypertension (Elie Fadel MD PhD and Olaf Mercier MD PhD).

## 3DQ Imaging Laboratory

Stanford's 3DQ Imaging Laboratory was established in 1996 at Stanford by Geoffrey Rubin, MD, and Sandy Napel, PhD, Professor of Radiology (General Radiology) and, by courtesy, Electrical Engineering. Today the center is co-directed by **Dominik Fleischmann, MD,** Professor of Radiology (General Radiology) and Roland Bammer, PhD, Associate Professor (Research) of Radiology.

Currently the lab processes over 1,200 clinical cases per month. Linda Horst, Marc Sofilos, and Shannon Walters are an integral part of the 3DQ Lab management team.

For more visit: http://3dqlab.stanford. edu/



### **FACULTY**

#### JULY

#### AMERICAN HEART ASSOCIATION

Innovative Research Grant Amount of funding: \$75,000 over 2 years Deadline: July 21, 2015

**Established Investigator Award** Amount of funding: \$400,000 over 5 years Deadline: July 21, 2015

**Beginning Grant-in-Aid** Amount of funding: \$140,000 over 2 years Deadline: July 24, 2015

**Grant-in-Aid** Amount of funding: \$140,000 over 2 years Deadline: July 24, 2015

### **Cardiovascular Institute Seed Grant**

\$15K-40,000 for 1 year Deadline: August 15, 2015



#### SEPTEMBER

#### STANFORD UNIVERSITY

**Spectrum Pilot Grants** Amount of funding: \$15-50K for 1 year Deadline: Sept. 2015

#### OCTOBER

#### NATIONAL INSTITUTE OF HEALTH

Research Project Grant (Parent R01) Deadline: Oct. 5, 2015

NIH Director's Pioneer Award (DP1) Deadline: October 9, 2015

NIH Director's Pioneer Award (DP2) Deadline: October 16, 2015

### POSTDOCTORAL FELLOWS

#### JULY

National Scientist Development Grant \$308,000 over 4 years Deadline: July 21, 2015

#### AMERICAN HEART ASSOCIATION

AHA Mentored Clinical and Population Research \$140,000 - \$154,000 over 2 years Deadline: July 24, 2015 (Western); July 21, 2015 (National) **AHA Postdoctoral Fellowship** 

\$100,000 over 2 years Deadline: July 24, 2015

#### JUVENILE DIABETES RESEARCH FOUNDATION

**Postdoctoral Fellowships Advanced Postdoctoral Scholar Fellowship** Deadline: July 30, 2015

#### STANFORD UNIVERSITY

Katherine McCormick Committee to Support Women in Academic Medicine Advanced Postdoctoral Scholar Fellowship \$35,000 for 1 year Deadline: July 2015

Walter V. and Idun Berry Postdoctoral Fellowship Program Amount of funding: \$55,000 for 1 year Deadline: July 2015

**Translational Research Applied Medicine (TRAM) Pilot Grant** Amount of funding: \$5K-30,000 for 1 year Deadline: July 15, 2015

#### AUGUST

#### BURROUGHS WELLCOME FUND

**Career Awards for Medical Scientists (CAMS)** \$700,000 transition award for physician scientistspostdoctoral and clinical fellows and Instructors Pre-proposals (required) deadline: Aug. 5, 2015

#### NATIONAL INSTITUTE OF HEALTH

Ruth L. Kirschstein National Research Service Awards (NRSA) for Individual Postdoctoral Fellows Deadline: August 8, 2015

#### OCTOBER

K01 Mentored Research Scientist Development Awards Deadline: Oct. 12, 2015

K08 Mentored Clinical Research Career Development Award Deadline: Oct. 12, 2015

K23 Mentored Patient-Oriented Research Career Development Award Deadline: Oct. 12, 2015

### MEDICAL STUDENTS

iHeart Research Award Award for Stanford Medical Students Up to \$10,000 Deadline: Oct. 1, 2015 Apply: http://tinyurl.com/cviheart2015

### Cardiovascular Global Conferences

### Stanford Conferences

#### JULY

**American Heart Association** (AHA) Basic Cardiovascular **Sciences Scientific Sessions** July 13-16, 2015 New Orleans, LA BCVS 2015

#### AUGUST

**European Society of** Cardiology - Congress 2015 August 29–September 2, 2015 London, United Kingdom ESC Congress 2015

#### **SEPTEMBER**

EMBO: Cell therapy today: September 9-12, 2015 Manchester, UK

**NHLBI Symposium of Cardiovascular Regenerative** Medicine September 29–30, 2015 Bethesda, Maryland

**Heart Failure Society** of America Annual Scientific Meeting September 26-29, 2015 Washington, DC hfsa meeting

**Hypertension 2015** September 16-19, 2015 Washington, DC **HBPR 2015** 

Karolinska Cardiovascular **Institute Meeting** September 24-25

Western Vascular Society September 19-22, 2015 Maui, HI Western Vascular Society

#### **OCTOBER**

Vascular Biology (NAVBO - North American Vascular Biology) October 18-22, 2015 Hyannis, MA NAVBO

### Stanford Coronary Physiology **Conference 2015**

October 9-10, 2015 LKSC, Stanford, CA cme.stanford.edu/cardio

#### EP in the West 2015

October 23 - 24, 2015 Hyatt Regency, Monterey, CA cme.stanford.edu/cardio

### Cardiovascular Research and Medicine at Stanford

October 27, 2015 Paul Berg Hall, Li Ka Shing Center, Stanford, CA Register here: http://tinyurl.com/cvi2015

### **KEYNOTE SPEAKERS:**

**Garrett Fitzgerald, MD** Director, Translational Research Center University of Pennsylvania

Clyde W. Yancy, MD Chief, Division of Medicine-Cardiology Northwestern University

The Stanford Women and Sex Differences in Medicine and the **Cardiovascular Instititute** will be hosting a half-day symposium focused on sex differences research at Stanford

February 24, 2016 Li Ka Shing Center for Knowledge and Learning



### Speakers Include:



Marcia Euan Stefanick, PhD Ashley, MD



Jennifer Tremmel, MD



William Fearon, MD

Patricia

Nguyen, MD



Yang, MD



Mintu Turakhia, MD



# Frontiers in Cardiovascular Science

Lunch with Leaders in Cardiovascular Research and Medicine: Tuesdays | 12 - 1 p.m.



The Frontiers in Cardiovascular Science seminar series features leaders in the cardiovascular field around the country and Stanford.

LEFT: Frontiers speaker Eric N. Olson, PhD, Professor and Chairman of the Department of Molecular Biology at UT Southwestern Medical Center at Dallas, spoke to a crowd of 170 faculty, postdocs and students, about "Understanding Muscle Development Disease and Regeneration."

#### **SEPTEMBER 15, 2015**

Michael S. Parmacek, MD Chair, Department of Medicine Univ of Pennsylvania, Perelman School of Medicine

#### SEPTEMBER 22, 2015

**Elizabeth M. McNally, MD, PhD** Director, Center for Genetic Medicine Northwestern University Feinberg School of Medicine

#### OCTOBER 6, 2015

#### Dean Y. Li, MD, PhD

HA and Edna Bennign Professor of Medicine, Associate Vice President for Research and Chief Scientific Officer, Health Sciences; Vice Dean for Research, School of Medicine

#### OCTOBER 20, 2015

Michael R. Bristow, MD, PhD Professor of Medicine, Cardiology CU Cardiovascular Institute (CU CVI)

### DECEMBER 01, 2015

**Donald M. Bers, PhD** Professor and Chair, Department of Pharmacology University of California, Davis

#### DECEMBER 08, 2015

Anthony Rosenzweig, MD Professor and Chief, Cardiovascular Medicine Harvard, Massachusetts General Hospital

#### DECEMBER 15, 2015

Gordon F. Tomaselli, MD, Professor and Chief, Cardiovascular Medicine Johns Hopkins University

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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, MB, ChB, D.Phil; Joseph Hill, MD, PhD; and Joseph Wu, MD, PhD.

For additional information on the Frontiers in Cardiovascular Science seminar series, and on how to attend, contact CVI Program Manager David L. M. Preston at preston@ stanford.edu.



## MONTHLY CVI FACULTY CLUB

Discuss your latest research or just unwind with your peers with wine & cheese Monthly, 4:30 p.m. in Lorry Lokey G1161 This informal meetup is meant for faculty, junior faculty and instructors to discuss collaborations or data to be submitted and receive input of aims for grant submissions. Contact **Crystal Botham, PhD** (cbotham@stanford.edu) to participate in the CVI Faculty Club.

September 09, 2015 Susan Fernandes, LPD, PA, MHP 2014 Seed Award recipient

October 07, 2015 Matthew Porteus, MD 2014 Seed Award recipient Associate Professor of Pediatrics (Cancer Biology) Pediatrics - Stem Cell Transplantation

#### November 04, 2015

"Bioengineering control of human stem cell biology" Oscar Abilez, MD, PhD Instructor, Medicine -Cardiovascular Medicine

December 02, 2015 Clint Miller, PhD Instructor, Medicine-Cardiovascular Medicine

### 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.

### April 2015: Selected Publications

Correction of human phospholamban R14del mutation associated with cardiomyopathy using targeted nucleases and combination therapy. **Karakikes I**, Stillitano F, Nonnenmacher M, Tzimas C, Sanoudou D, Termglinchan V, Kong CW, Rushing S, Hansen J, Ceholski D, Kolokathis F, Kremastinos D, Katoulis A, Ren L, Cohen N, Gho JM, Tsiapras D, Vink A, **Wu** JC, Asselbergs FW, Li RA, Hulot JS, Kranias EG, Hajjar RJ. *Nat Commun.* 2015 Apr 29;6:6955.

The genetic basis of peripheral arterial disease: current knowledge, challenges, and future directions. Kullo IJ, Leeper NJ. *Circ Res.* 2015 Apr 24;116(9):1551-60.

Induced pluripotent stem cells. Wilson KD, **Wu JC**. JAMA. 2015 Apr 28;313(16):1613-4.

Heterogeneous growth-induced prestrain in the heart. Genet M, Rausch MK, Lee LC, Choy S, Zhao X, Kassab GS, Kozerke S, Guccione JM, **Kuhl E**. *J Biomech.* 2015 Apr 3.

64Cu-Labeled Divalent Cystine Knot Peptide for Imaging Carotid Atherosclerotic Plaques. Jiang L, Tu Y, Kimura R, Habte F, Chen H, Cheng K, Shi H, **Gambhir SS**, Cheng Z. *J Nucl Med.* 2015 Apr 23.

Risk of Cardiovascular Events Associated with Current Exposure to HIV Antiretroviral Therapies in a US Veteran Population. Desai M, Joyce V, Bendavid E, **Olshen RA**, **Hlatky M**, Chow A, Holodniy M, Barnett P, Owens DK. *Clin Infect Dis*. 2015 Apr 22.

Segmental Aortic Stiffening Contributes to Experimental Abdominal Aortic Aneurysm Development. **Raaz U**, Zöllner AM, Schellinger IN, Toh R, Nakagami F, **Brandt M**, Emrich FC, Kayama Y, Eken S, **Adam M**, Maegdefessel L, Hertel T, Deng A, Jagger A, Buerke M, **Dalman RL**, **Spin JM**, **Kuhl E**, **Tsao PS**. *Circulation*. 2015 Apr 22.

Opinion: Sex inclusion in basic research drives discovery. Klein SL, Schiebinger L, **Stefanick ML**, Cahill L, Danska J, de Vries GJ, Kibbe MR, Mc-Carthy MM, Mogil JS, Woodruff TK, Zucker I. *Proc Natl Acad Sci U S A*. 2015 Apr 28;112(17):5257-8.

MicroRNA-mediated regulation of differentiation and trans-differentiation in stem cells. **Ong SG**, Lee WH, Kodo K, **Wu JC**. *Adv Drug Deliv Rev.* 2015 Apr 14.

Percutaneous tricuspid valve implantation: two-center experience with midterm results. Eicken A, Schubert S, Hager A, Hörer J, **McElhinney DB**, Hess J, Ewert P, Berger F. *Circ Cardiovasc Interv.* 2015 Apr;8(4).

Feasibility of Extended Ambulatory Electrocardiogram Monitoring to Identify Silent Atrial Fibrillation in High-risk Patients: The Screening Study for Undiagnosed Atrial Fibrillation (STUDY-AF). **Turakhia MP**, Ullal AJ, Hoang DD, Than CT, Miller JD, Friday KJ, **Perez MV**, Freeman JV, **Wang PJ**, **Heidenreich PA**. *Clin Cardiol*. 2015 Apr 14. Site-level variation in and practices associated with dabigatran adherence. Shore S, Ho PM, Lambert-Kerzner A, Glorioso TJ, Carey EP, Cunningham F, Longo L, Jackevicius C, Rose A, **Turakhia MP**. *JAMA*. 2015 Apr 14;313(14):1443-50.

Intermediate Outcomes in the Prospective, Multicenter Coarctation of the Aorta Stent Trial (COAST). Meadows J, Minahan M, **McElhinney DB**, McEnaney K, Ringel R; COAST Investigators. *Circulation*. 2015 Apr 13.

A "Repair-All" Strategy for Degenerative Mitral Valve Disease Safely Minimizes Unnecessary Replacement. Goldstone AB, Cohen JE, Howard JL, Edwards BB, Acker AL, Hiesinger W, MacArthur JW Jr, Atluri P, **Woo YJ**. Ann Thorac Surg. 2015 Apr 9.

Scintillating-Balloon-Enabled Fiber-Optic System for Radionuclide Imaging of Atherosclerotic Plaques. **Zaman RT**, Kosuge H, Carpenter C, Sun C, **Mc-Connell MV**, Xing L. *J Nucl Med*. 2015 Apr 9.

Association of spontaneous bleeding and myocardial infarction with longterm mortality after percutaneous coronary intervention. Kazi DS, Leong TK, **Chang TI**, Solomon MD, **Hlatky MA**, Go AS. *J Am Coll Cardiol*. 2015 Apr 14;65(14):1411-20.

Elafin Reverses Pulmonary Hypertension via Caveolin-1 Dependent Bone Morphogenetic Protein Signaling. Nickel NP, **Spiekerkoetter E**, Gu M, Li CG, Li H, Kaschwich M, Diebold I, **Hennigs JK**, Kim KY, Miyagawa K, **Wang** L, Cao A, Sa S, Jiang X, Stockstill RW, **Nicolls MR**, **Zamanian RT**, **Bland RD**, **Rabinovitch M**. *Am J Respir Crit Care Med*. 2015 Apr 8.

Propensity-Matched Comparisons of Clinical Outcomes after Transapical or Transfemoral TAVR: A PARTNER-I Trial Substudy. Blackstone EH, Suri RM, Rajeswaran J, Babaliaros V, Douglas PS, **Fearon WF**, **Miller DC**, Hahn RT, Kapadia SR, Kirtane AJ, Kodali SK, Mack M, Szeto WY, Thourani VH, Tuzcu EM, Williams MR, Akin JJ, Leon MB, Svensson LG. *Circulation*. 2015 Apr 1.

Geometric perturbations in multiheaded papillary tip positions associated with acute ovine ischemic mitral regurgitation. Timek TA, Lai DT, Bothe W, Liang D, Daughters GT, **Ingels NB, Miller DC**. *J Thorac Cardiovasc Surg.* 2015 Apr 25.

Small studies are more heterogeneous than large ones: a meta-meta-analysis. IntHout J, **Ioannidis JP**, Borm GF, Goeman JJ. *J Clin Epidemiol*. 2015 Apr 2.

Greater asymmetric wall shear stress in Sievers' type 1/L-R compared with 0/LAT bicuspid aortic valves after valve-sparing aortic root replacement. Stephens EH, Hope TA, Kari FA, Kvitting JP, **Liang DH**, **Herfkens RJ**, **Miller DC**. *J Thorac Cardiovasc Surg*. 2015 Apr 10.

#### May 2015: Selected Publications

COCATS 4 Task Force 15: Training in Cardiovascular Research and Scholarly Activity. **Harrington RA**, Barac A, Brush JE Jr, Hill JA, Krumholz HM, Lauer MS, Sivaram CA, Taubman MB, Williams JL. *J Am Coll Cardiol.* 2015 May 5;65(17):1899-906.

#### May 2015: Selected Publications, cont

Naive T Cell Maintenance and Function in Human Aging. Goronzy JJ, Fang F, Cavanagh MM, Qi Q, **Weyand CM**. *J Immunol*. 2015 May 1;194(9):4073-4080. Review.

Glycoprotein IIb/IIIa Receptor Inhibitors in Combination With Vorapaxar, a Platelet Thrombin Receptor Antagonist, Among Patients With Non-ST-Segment Elevation Acute Coronary Syndromes (from the TRACER Trial). Cornel JH, Tricoci P, Lokhnygina Y, Moliterno DJ, Wallentin L, Armstrong PW, Aylward PE, Clare RM, Chen E, Leonardi S, Van de Werf F, White HD, Held C, Strony J, **Mahaffey KW, Harrington RA**. *Am J Cardiol.* 2015 May 15;115(10):1325-32.

Cell adhesion. Mechanical strain induces E-cadherin-dependent Yap1 and  $\beta$ -catenin activation to drive cell cycle entry. Benham-Pyle BW, **Pruitt BL**, Nelson WJ. *Science*. 2015 May 29;348(6238):1024-7.

Interspecific in vitro assay for the chimera-forming ability of human pluripotent stem cells. Masaki H, Kato-Itoh M, Umino A, Sato H, Hamanaka S, Kobayashi T, Yamaguchi T, Nishimura K, Ohtaka M, Nakanishi M, **Nakauchi H**. *Development*. 2015 May 28.

Coronary Artery Disease Associated Transcription Factor TCF21 Regulates Smooth Muscle Precursor Cells That Contribute to the Fibrous Cap.

Nurnberg ST, Cheng K, Raiesdana A, Kundu R, **Miller CL**, Kim JB, Arora K, Carcamo-Oribe I, Xiong Y, Tellakula N, Nanda V, Murthy N, Boisvert WA, Hedin U, Perisic L, Aldi S, Maegdefessel L, Pjanic M, Owens GK, Tallquist MD, **Quertermous T**. *PLoS Genet*. 2015 May 28;11(5):e1005155.

Mitochondrial Reactive Oxygen Species at the Heart of the Matter: New Therapeutic Approaches for Cardiovascular Diseases. Kornfeld OS, Hwang S, Disatnik MH, Chen CH, Qvit N, **Mochly-Rosen D**. *Circ Res*. 2015 May 22;116(11):1783-1799. Review.

Are the QRS duration and ST depression cut-points from the Seattle criteria too conservative? Dunn T, Abdelfattah R, Aggarwal S, Pickham D, Hadley D, **Froelicher V.** *J Electrocardiol*. 2015 May-Jun;48(3):395-8.

Race and ethnicity, obesity, metabolic health, and risk of cardiovascular disease in postmenopausal women. Schmiegelow MD, Hedlin H, Mackey RH, Martin LW, Vitolins MZ, **Stefanick ML**, **Perez MV**, Allison M, **Hlatky MA**. *J Am Heart Assoc*. 2015 May 20;4(5).

Adaptable Hydrogel Networks with Reversible Linkages for Tissue Engineering. Wang H, **Heilshorn SC**. *Adv Mater.* 2015 May 19.

Comparable calcium handling of human iPSC-derived cardiomyocytes generated by multiple laboratories. Hwang HS, Kryshtal DO, Feaster TK, Sánchez-Freire V, Zhang J, Kamp TJ, Hong CC, **Wu JC**, Knollmann BC. *J Mol Cell Cardiol*. 2015 May 14;85:79-88.

Right Heart Score for Predicting Outcome in Idiopathic, Familial, or Drugand Toxin-Associated Pulmonary Arterial Hypertension. **Haddad F**, Spruijt OA, Denault AY, Mercier O, Brunner N, Furman D, Fadel E, Bogaard HJ, **Schnittger I**, Vrtovec B, **Wu JC**, **de Jesus Perez V**, Vonk-Noordegraaf A, **Zamanian RT**. *JACC Cardiovasc Imaging*. 2015 May 6. Editing the genome to introduce a beneficial naturally occurring mutation associated with increased fetal globin. Wienert B, Funnell AP, Norton LJ, Pearson RC, Wilkinson-White LE, Lester K, Vadolas J, **Porteus MH**, Matthews JM, Quinlan KG, Crossley M. *Nat Commun.* 2015 May 14;6:7085.

Insulin Resistance and Risk of Cardiovascular Disease in Postmenopausal Women: A Cohort Study From the Women's Health Initiative. Schmiegelow MD, Hedlin H, **Stefanick ML**, Mackey RH, Allison M, Martin LW, Robinson JG, **Hlatky MA**. *Circ Cardiovasc Qual Outcomes*. 2015 May;8(3):309-16.

Fasting plasma triglyceride concentration: A possible approach to identify increased risk of statin-induced type 2 diabetes. Sung KC, **Reaven G**. *Diab Vasc Dis Res.* 2015 May 11.

COCATS 4 Task Force 4: Training in Multimodality Imaging. Narula J, Chandrashekhar YS, Dilsizian V, Garcia MJ, Kramer CM, Malik S, Ryan T, Sen S, **Wu JC**. *J Am Coll Cardiol.* 2015 May 5;65(17):1778-85.

COCATS 4 Task Force 2: Training in Preventive Cardiovascular Medicine. Smith SC Jr, Bittner V, Gaziano JM, **Giacomini JC,** Pack QR, Polk DM, Stone NJ, Wang S. *J Am Coll Cardiol.* 2015 May 5;65(17):1754-62.

#### June 2015: Selected Publications

The Missing Link: Studying the Alternative TGF-β Pathway Provides a Unifying Theory for Different Components of Diabetic Nephropathy. **Zheng X**, **Bhalla V**. *Diabetes*. 2015 Jun;64(6):1898-900.

Clinical and Hemodynamic Outcomes up to 7 Years After Transcatheter Pulmonary Valve Replacement in the US Melody Valve Investigational Device Exemption Trial. Cheatham JP, Hellenbrand WE, Zahn EM, Jones TK, Berman DP, Vincent JA, **McElhinney DB**. *Circulation*. 2015 Jun 2;131(22):1960-70.

The precision medicine initiative: a new national effort. **Ashley EA**. *JAMA*. 2015 Jun 2;313(21):2119-20.

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