New center aims to improve outcomes for patients with atrial fibrillation

A grant of $5 million was awarded to Stanford University School of Medicine to create a center focused on developing tools to help patients with atrial fibrillation, an irregular heartbeat, make what are often difficult decisions about their treatment plans.

Stanford was one of six universities awarded a total of $28 million by the American Heart Association to build collaborative research centers focused on improving outcomes for patients with this condition, which increases the risk of stroke.

An estimated 6.1 million or more Americans were living with atrial fibrillation as of 2010, making it the most common heart rhythm abnormality in the United States. That number is expected to rise to 12.1 million by 2030, according to the American Heart Association.

Patients must often decide whether to take physician-recommended anticoagulant drugs regularly to help prevent stroke. The decision is complicated by the different advantages and disadvantages of the many blood-clot-preventing drugs that are available. Excessive bleeding is a possible side effect of these medications.

“We recognize decision-making is a major problem for these patients,” said Paul Wang, MD, professor of cardiovascular medicine and director of the Stanford Cardiac Arrhythmia Service. “Anticoagulants don’t make you feel better. Patients make a choice between an increased risk of bleeding or preventing a stroke. We are trying to help patients make a choice they won’t regret.”

With funding from the award, the Stanford center will develop a smartphone app, along with other decision-making tools, to help patients better understand their choices. The center will also conduct comparative-effectiveness studies to determine the success and feasibility of these new tools.

The center will be led by Wang and Randall Stafford, MD, PhD, professor of medicine and director of the Stanford Program on Prevention Outcomes and Practices.

Stanford-Duke Cardiovascular Symposium

November 29-30, 2018

Leading US cardiovascular research centers, the Stanford Cardiovascular Institute and the Duke Cardiovascular Research Center, will once again join together to host the Stanford-Duke Cardiovascular Research Symposium.

Organized by Sean Wu MD, PhD, Joseph C. Wu, MD, PhD, and Howard A. Rockman, MD, the symposium will take place at Stanford University’s Li Ka Shing Center on November 29-30. Brian Kolbilka (2012 Nobel Prize in Chemistry) and Ivor Benjamin (AHA President) will give the keynote lectures. To register visit https://tinyurl.com/cviduke2018.

Recruitment for CVMed Chief

The Department of Medicine at Stanford University is recruiting a Chief for the Division Cardiovascular Medicine to lead the research, clinical, and educational activities of the Division. The Chief will be expected to lead the research, clinical, and educational activities of the Division and recruit additional faculty to support both laboratory and clinical research, and expand the clinical enterprise. The Chief will also be expected to strengthen the highly competitive fellowship program in Cardiovascular Medicine and increase its focus on the research opportunities prevalent at Stanford. For more information, please contact either Joseph C. Wu, MD, PhD or Y. Joseph Woo, MD (search committee chairs) or visit the website: https://tinyurl.com/yb83cu65
The Institute currently consists of over 241 faculty members representing physicians, surgeons, engineers, 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 of the Stanford Cardiovascular Institute at joewu@stanford.edu or Cathy Hutton, MBA, Senior Associate Director, Medical Center Development at cathy.hutton@stanford.edu.

For more information: http://med.stanford.edu/cvi/support-our-research.html and http://cvi.stanford.edu
Humans have unexpectedly high genetic variation in the receptor for a key pregnancy-maintaining hormone, according to research led by scientists at the Stanford University School of Medicine. The finding may help explain why some populations of pregnant women have an elevated risk of premature birth.

The researchers found that East Asian populations have one version of the progesterone receptor gene that appears to protect them against giving birth prematurely, whereas other populations with European or African ancestry have a higher prematurity risk and other versions of this gene. The discrepancies between the populations reflect relatively recent evolution.

The new study used data from the 1,000 Genomes Project, a publicly accessible database of complete human genomes from people of different ancestral backgrounds. The researchers compared genetic sequences for the progesterone receptor in three populations: Utah residents with European ancestry; Yoruba people in Nigeria; and Han Chinese in Beijing.

The variations in the progesterone receptor gene — consisting of single nucleotide polymorphisms, or one-letter changes in the genetic code—were found in regions of the gene that regulate when it is switched on and off.

Recent natural selection took the genetic code in different directions as different populations adapted to their local environments, the scientists found. The sequence in Han Chinese populations had an evolutionarily new variation, perhaps reflecting that premature birth would have been especially costly for the small group of ancestral humans who migrated from Africa to East Asia. In contrast, modern populations with European and African ancestry had a greater mixture reflecting new and ancestral versions in the gene.

The findings also predict that the genetic forms of the progesterone receptor seen in East Asians would not necessarily protect against premature birth in other populations. The researchers confirmed this prediction with data from 1,733 African-American women enrolled in a study called the Boston Birth Cohort; of these women, 461 had spontaneous preterm births and 237 had medically indicated preterm births, in which doctors deliver the baby early because of medical problems that have developed during pregnancy for the mother, fetus or both. African-American women who had genetic variants typically seen in East Asian populations had a higher risk of premature birth, the study found. The study’s underlying message is that genes that are helpful in one environment may not help in another, Shaw said. “Complex conditions such as prematurity are not likely caused completely environmentally or completely genetically; it’s the confluence of genes and environment that makes the difference in risk,” he said.

Michael Snyder, PhD, professor of genetics, is also a Stanford author of the paper. Shaw, Stevenson and Snyder are members of the Stanford Child Health Research Institute and of Stanford Bio-X. Stevenson is an affiliate of the Stanford Woods Institute for the Environment, and Snyder is a member of the Stanford’s Cardiovascular Institute, its Cancer Institute and its Neurosciences Institute.

Diseased heart muscle cells have abnormally shortened telomeres

Patients with cardiomyopathy have abnormally short telomeres in the cells responsible for heart contraction, Stanford researchers find. This disease hallmark opens new pathways for drug discovery.

People with a form of heart disease called cardiomyopathy have abnormally short telomeres in heart muscle cells responsible for contraction, according to a new study by researchers at the Stanford University School of Medicine. A telomere is a DNA sequence that serves as a protective cap on the ends of chromosomes.

The finding dovetails with a previous study showing that people with Duchenne muscular dystrophy, a genetic muscle-wasting disease, also have short telomeres in their heart muscle cells, or cardiomyocytes. These patients often die at an early age from heart failure.

Although it’s not yet known whether the stunted telomeres directly affect the function of the cardiomyocytes or arise as a result of heart failure, the finding opens the door to an intriguing line of research and drug discovery. It also may one day allow researchers and clinicians to identify people at risk for heart failure due to cardiomyopathy.

“The shortening of telomeres in cardiomyocytes appears to be a reliable hallmark of cardiac failures that arise due to genetic defects, and it’s very specific to cells that require the missing contractile proteins such as dystrophin, troponin T or myosin heavy chain, among others,” said Helen Blau, PhD, professor of microbiology and immunology and member of the Stanford Cardiovascular Institute.

Blau, the Donald E. and Delia B. Baxter Foundation Professor and director of the Baxter Laboratory for Stem Cell Biology, is the senior author of the study, which was published online Aug. 27 in Proceedings of the National Academy of Sciences. Alex Chang, PhD, an instructor of cardiovascular medicine and of microbiology and immunology, is the lead author.

In most cells, telomeres naturally shorten each time the cell divides. But cardiomyocytes divide infrequently, and their telomere lengths remain relatively stable throughout one’s life.

In humans, Duchenne muscular dystrophy, which is caused by a mutation in the dystrophin gene, is characterized by progressive muscle weakness and eventual death due to cardiac complications.

“Because we found in a previous study that cardiomyocytes from boys who had died of Duchenne muscular dystrophy had telomeres that were about 50 percent shorter than those from individuals without the disease,” Blau said, “we wondered whether people with other genetic heart conditions, such as cardiomyopathies, might also have cardiomyocytes with abnormally shortened telomeres.”

A cardiomyopathy is a condition in which the heart is unusually large, thickened or stiff. This affects its ability to pump blood effectively.

Chang compared the telomere length in cardiomyocytes from 11 patients with dilated or hypertrophic cardiomyopathy due to genetic mutations with nine people who had died from causes unrelated to heart disease. He found that telomeres from the cardiomyopathy patients were about 25-40 percent shorter than those of the control subjects. In contrast, the telomere length in nonbeating heart cells of the blood vessels did not vary significantly between the two groups.

Chang saw similar results in cardiomyocytes generated from induced pluripotent stem cells: Those generated from people with cardiomyopathies had significantly shorter telomeres than those generated from unaffected relatives.

“Within 20 days we could see the telomere shortening happening in the laboratory-grown cardiomyocytes from diseased patients, suggesting this is a cell-intrinsic property,” Blau said.

The ability to use iPSC cell technology to generate affected cardiomyocytes also means that it should be possible to quickly and easily test for compounds or drugs that interfere with the telomere shortening with a view to finding drugs to abrogate the disease in humans, the researchers believe.

“Now we can study this phenomenon in the lab in real time and start to ask questions about cause and effect,” Blau said.


Phillip Yang, MD, edits new WT1-Mapping book

Phillip Yang, MD, Associate Professor of Medicine (Cardiovascular Medicine), is the editor of a newly completed Springer textbook on WT1-Mapping in Myocardial Disease. This book details the advances in cardiac MRI that have enabled quantitative tissue characterization of the myocardium using myocardial and blood T1 measurements, which have enabled reliable detection of diffuse pathological processes in both the cardiomyocytes and the interstitial cells of the myocardium. The specific topics covered include principles of T1-mapping in cardiovascular disease and the role of T1-mapping in hypertensive heart disease and hypertrophic cardiomyopathy, cardiotoxicity, cardiac fibrosis, left ventricular hypertrophy in aortic stenosis, peri-infarct injury in ischemic cardiomyopathy, and stem cell therapy.
Researchers can forecast risk of deadly vascular condition from genome sequence

By Hanae Armitage, Office of Communication & Public Affairs

By combining genome-sequence information and health records, Stanford scientists have developed a new algorithm that can predict the risk of abdominal aortic aneurysm, and potentially could be used for any number of diseases.

A new approach that distills deluges of genetic data and patient health records has identified a set of telltale patterns that can predict a person’s risk for a common, and often fatal, cardiovascular disease, according to a new study from the Stanford University School of Medicine.

Although the method, which uses a form of artificial intelligence called machine learning, has so far only been used to predict the likelihood of this particular condition — called abdominal aortic aneurysm, or AAA — it’s proof that such an approach could decipher the molecular nuances that put people at risk for just about any complex genetic disease.

“Right now, genome sequencing is starting to make its mark,” said Michael Snyder, PhD, Professor and Chair of Genetics at Stanford. Typically, researchers and health care providers use genetic testing to look for DNA sequences that may correspond to an increased risk for a particular illness. Mutations in the BRCA1 and BRCA2 genes, for instance, may signal an increased risk of breast cancer. But the method that Snyder and his colleagues developed doesn’t work like that. It’s not looking for one standout gene or mutation; it’s looking for a slew of complex mutational patterns, and how those genetic errors play into a person’s health and risk for disease.

The method seeks to identify any likely disease-causing culprits in an “agnostic” manner, meaning that it combs through an onslaught of genetic information from patients with AAA, looking for commonalities. This, Snyder said, is the key to unraveling any number of genetic diseases.

The study was published Sept. 6 in Cell. Snyder and Philip Tsao, PhD, professor of medicine, share senior authorship. Instructor Jingjing Li, PhD; research manager Cuiping Pan, PhD; and postdoctoral scholar Sai Zhang, PhD, are the lead authors.

AAA afflicts upward of 3 million people every year and is the 10th-leading killer in the United States. Patients with AAA have an enlarged aorta, the main artery of the body, which slowly balloons over time until, in the worst of cases, it ruptures. AAA is pretty amenable to behavioral change.

Things like smoking and high blood pressure intensify the condition, while higher levels of HDL, or “good” cholesterol, help decrease the risk. So, if people know they are at risk early on, they can ideally adjust their lifestyle to avoid exacerbation or onset altogether.

“What’s important to note about AAA is that it’s irreversible, so once your aorta starts enlarging, it’s not like you can un-enlarge it. And typically, the disease is discovered when the aorta bursts, and by that time it’s 90 percent lethal,” said Snyder, the Stanford W. Ascherman, MD, FACS, Professor in Genetics. “So here’s this irreversible disease, no way to predict it. No one has ever set up a predictive test for it and, just from a genome sequence, we found that we could actually predict with about 70 percent accuracy who is at high risk for AAA.” When other details from electronic patient records were added, like whether a patient smoked and his or her cholesterol levels, accuracy increased to 80 percent, Snyder said.

The method Snyder and his team devised relies on an algorithm they call the Hierarchical Estimate From Agnostic Learning, or HEAL, which analyzed genomic data from 268 patients with AAA and scanned the mass of information for any genes that were found to be mutated across the population. The algorithm identified 60 genes that were hypermutated in the AAA patients. Some genes played roles in blood-vessel function and aneurysm development — a nod to HEAL’s accuracy — but others, more surprisingly, were associated with regulation of immune function, revealing that the mutational landscape of this disease is complex, involving niches of physiology that weren’t necessarily expected.

The team further confirmed their findings using HEAL in a control group, double-checking that the AAA-related mutational patterns were not seen among 133 healthy individuals. And indeed, there was no significant overlap.

Other Stanford authors of the study are Joshua Spin, MD, PhD, clinical assistant professor of cardiovascular medicine; life science research assistant Alicia Deng; professor of medicine Lawrence Leung, MD; and Ronald Dalman, MD, professor of vascular surgery.

Full story: https://tinyurl.com/y94flyl

Newly Appointed Vascular Faculty

We are excited to welcome Stanford Vascular Surgery graduates Dr. Elsie Gyang Ross and Dr. Michael Sgroi to the Stanford Division of Vascular Surgery Faculty. Dr. Ross is an Assistant Professor of Surgery and will be at Stanford Hospital and Palo Alto VA. Dr. Sgroi is a Clinical Assistant Professor of Surgery and will be at the Santa Clara Valley Medical Center.
Study solves mystery of genetic-test results for patient with suspected heart condition  by Tracie White

Although DNA testing is becoming increasingly quick, cheap and easy to perform, the results are sometimes ambiguous: Gene mutations called “variants of uncertain significance” can create uncertainty about a patient’s risk for a disease.

“This is a really big problem,” said Joseph C. Wu, MD, PhD, professor of cardiovascular medicine and of radiology at the Stanford University School of Medicine. “If someone tells me I have a genetic variant that could cause sudden cardiac death, I’m going to be very scared. The result could be a lifetime of unnecessary worry for a patient when, in fact, the variant may be completely benign.”

Now, Wu and a team of researchers have developed a technique that could shed light on the significance of such variants. In a new paper, they discuss how they used advanced genetic-editing tools and stem cell technology to determine whether a 39-year-old patient with one of these mysterious mutations was at increased risk for a heart-rhythm condition called long QT syndrome, which can cause erratic heartbeats, fainting and sudden cardiac death.

The paper was published June 26 in the Journal of the American College of Cardiology. Wu is the senior author, and Stanford postdoctoral scholar Priyanka Garg, PhD, is the lead author.

“An advantage of generating patient-specific iPS heart cells is that you don’t have to use any invasive procedures on the patient to get them,” Garg said. “You can generate a patient’s heart cells in a dish and study them just from a simple blood sample.”

Tests of the heart cells with the mutation showed the hallmark features of long QT syndrome, including electrical disturbances that delay heartbeats and a mild propensity for arrhythmias compared with the cells from a healthy patient, the study said. These results did not show up in tests on the cells in which the mutation was turned off or in unaltered cells from the healthy patient. The results confirmed that the patient did have a mild case of long QT syndrome, the study said.

The success of using these same methods to determine whether two different patients were at risk for two completely different diseases suggests that this platform is a promising risk-assessment tool for variants of uncertain significance in general, Wu said. “The results of these studies are particularly exciting to me because we used precision health methods to address an unmet need for a patient,” he said.

The study’s other Stanford authors are instructors Angelos Oikonomopouloos, PhD, and Yingxin Li, PhD; former postdoctoral scholar Haodong Chen, PhD; postdoctoral scholar Chi Keung Lam, PhD; Karim Sallam, MD, clinical assistant professor of cardiovascular medicine; and Marco Perez, MD, assistant professor of cardiovascular medicine.


Improving accuracy of predicting individuals' heart disease risk with gene technology

Recent research published in Circulation explores using human-induced pluripotent stem cells (iPSCs) and CRISPR/Cas9 to detect and determine that a variation of a gene may have pathogenic effect on a patient, sing gene-editing technology may help discern whether genetic variations with undetermined effects are harmless or dangerous.

The lead author is Ning Ma, PhD, a postdoctoral fellow at the Stanford Cardiovascular Institute; and the senior author is Joseph C. Wu, MD, PhD, Director of the Stanford Cardiovascular Institute.

The study demonstrates the unique potential of combining iPSC-based disease modeling and CRISPR/Cas9-mediated genome editing technology as a personalized risk-assessment platform for determining the disease-causing ability of a yet undescribed genetic variant with uncertain significance.

Researchers studied genetic variants associated with hypertrophic cardiomyopathy, a condition in which the heart muscle thickens. It is a common cause of sudden cardiac death in young people and young athletes.

They harvested DNA from 54 “healthy” or symptom-free individuals without heart disease, then sequenced their DNA using a custom DNA panel of 135 cardiomyopathy and congenital heart disease genes associated with sudden cardiac death. The sequence results uncovered 592 unique genetic variants, with 78 percent of genetic variants being classified as “benign,” “likely benign,” or a “variant of uncertain significance.” However, 17 genetic variants were annotated as “likely pathogenic” or disease-causing.

Other authors are Joe Zhang MD, PhD; Ilanit Itzhaki, PhD; Sophia Zhang, Haodong Chen, PhD; Francois Haddad, MD; Tomoya Kitani, MD, PhD; Kitchener D. Wilson, MD, PhD; Lei Tian, PhD; Rajani Shrestha; Haodi Wu, PhD; Chi Keung Lam PhD; and Nazish Sayed, MD, PhD.

The study, “Determining the Pathogenicity of a Genomic Variant of Uncertain Significance Using CRISPR/Cas9 and Human-Induced Pluripotent Stem Cells” can be found in the June 18th edition of Circulation or on Pubmed at https://www.ncbi.nlm.nih.gov/pubmed/29914921.

For more, visit the story by CNN: https://us.cnn.com/2018/06/18/health/crispr-stem-cells-heart-study/index.html.
Sanjiv Sam Gambhir, MD, PhD, receives Benedict Cassen Prize for Molecular Imaging Research

Sanjiv Sam Gambhir, MD, PhD, known for his pioneering work in multimodality molecular imaging, was awarded the Benedict Cassen Prize during the 2018 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) in Philadelphia, Pa. This honor is awarded every two years by the Education and Research Foundation for Nuclear Medicine and Molecular Imaging in recognition of outstanding achievement and work leading to a major advance in nuclear medicine science.

"The Cassen Prize Committee selected Sanjiv (Sam) Gambhir as the 2018 recipient in recognition of his advanced work into the study and development of in vivo multimodality molecular imaging. His pursuit of expanding molecular assays to study the biology of diseases, especially cancer, using multiple imaging modalities and in vitro assays has advanced not only the nuclear medicine field but health care in general." said ERF President Frances K. Keech, DHSc, RT(N), FSNMMI-TS.

Dr. Gambhir is currently the Virginia and D.K. Ludwig Professor of Cancer Research and Chair of the Department of Radiology at the Stanford University School of Medicine. He heads up the Canary Center at Stanford for Cancer Early Detection and directs the Molecular Imaging Program at Stanford (MIPS). He also heads up the new Precision Health and Integrated Diagnostics (PHIND) Center at Stanford. He received his MD and PhD from the University of California, Los Angeles (UCLA) Medical Scientist Training Program.

Faculty Awards

Dr. Nicholas Leeper receives AHA Transformational Project Award and Leducq Foundation award

Dr. Leeper’s AHA Transformational Project is in collaboration with Dr. Bryan Smith to develop macrophage-specific nanoparticles to target diseased blood vessels and promote the clearance of necrotic debris, a new method to treat atherosclerotic cardiovascular disease. Dr. Leeper’s 2018 Fondation Leducq award, part of a collaboration led by Drs. Gerald Pasterkamp and Gary Owens, will use advanced genomics approaches to investigate the contribution of matrix producing cells to atherosclerotic vascular disease. Additional details can be found at http://plaqomics.com/. Dr. Leeper is an Associate Professor of Vascular Surgery and Cardiovascular Medicine at the Stanford University Medical Center.

Dr. Elsie Ross receives Society of University Surgeon's Junior Faculty Award

Dr. Elsie Ross, who joined Stanford Medicine’s Division of Vascular Surgery as an Assistant Professor in July, was awarded the Society of University Surgeon’s Junior Faculty Award. The one-year $30,000 grant will fund her project: “A precision medicine approach for the early identification of PAD.”

Dr. Kevin Alexander receives American Heart Association-Harold Amos Medical Faculty Development Program award.

Dr. Kevin Alexander has won an American Heart Association-Harold Amos Medical Faculty Development Program award. His project is entitled “Novel molecular insights into V122I transthyretin cardiac amyloidosis.”

Drs. Mark Mercola and Ioannis Karakikes awarded Leducq Foundation award

Mark Mercola, PhD, Professor of Medicine-Cardiovascular, and Ioannis Karakikes, PhD, Assistant Professor, Cardithoracic Surgery, were awarded a grant from the Leducq foundation focusing on “Cure Phospholamban Induced Cardiomyopathy”. The grant will provide funding between Jan. 2019 and Dec. 2023. The Phospholamban (PLN) R14del mutation is associated with highly variable presentation of arrhythmogenic cardiomyopathy (ACM) and dilated cardiomyopathy (DCM). The overarching goal of this work is “to understand the PLN R14del pathophysiological pathways, which will enable us to develop novel therapeutic strategies for treating inherited ACM and DCM”, according to Dr. Mercola. They will direct a project to define the mechanisms underlying the disease phenotype using human cell-based in vitro models.
Stanford CVI-AHA Undergraduate Summer Research Program Completes First Year

The Stanford Cardiovascular Research Institute hosted seven undergraduate students from around the US for a paid 10-week research training program this summer. The inaugural cohort included:

- **Jose Acosta-Julbe** from the Universidad de Puerto Rico, Natural Sciences College, mentored by Dr. Vinicio de Jesus Perez
- **Lily Cheng** from the University of Michigan, Ann Arbor, mentored by Dr. Nazish Sayed
- **Cali Loblundo** from Villanova University, mentored by Dr. Joseph C. Wu
- **Ridhima Mishra** from Stanford University, mentored by Dr. David Paik
- **Tyler Muser** from Biola University, mentored by Dr. Mark Mercola
- **Kailey Totherow** from Stanford University, mentored by Dr. Joseph Woo
- **Joy Udoh** from Oberlin College, mentored by Dr. Daniel Bernstein

The program is designed to train students enrolled in a four-year undergraduate program majoring in a scientific discipline in cardiovascular research in the laboratories of CVI-affiliated faculty members. The program will be offered again next year.


Recruitment for T32 Fellowships

**Multi-Disciplinary Training Program in Cardiovascular Imaging T32 Training Grant.** The Multi-Disciplinary Training Program in Cardiovascular Imaging at Stanford is funded by the National Institute of Biomedical Imaging and Bioengineering of the National Institutes of Health. With the impact of cardiovascular disease on US and world health and the rapid advances in imaging technologies and cardiovascular biology, it is critical that fellows be provided a broad, multi-disciplinary, and collaborative training program to foster their ability to translate CV imaging research into clinical applications. The program is designed to train the next generation of CV imaging investigators by exposing them to three complementary areas—clinical, engineering, and molecular imaging. The directors of this grant are Joseph Wu, MD, PhD; John M. Pauly, PhD; and Koen Nieman, MD, PhD. [http://med.stanford.edu/cvi/education/cardiovascular-imaging-t32.html](http://med.stanford.edu/cvi/education/cardiovascular-imaging-t32.html)

**Mechanisms and Innovations in Cardiovascular Disease T32 Training Grant.** This program provides training in the following areas of vascular medicine and research: Vascular Reactivity and Thrombosis, Vascular Regeneration and Development, Metabolic or Lifestyle Influences on Vascular Outcomes, Proteomic Markers & Genetic Determinants of Vascular Disease, Gender and Ethnicity Differences in Vascular Disease, and Vascular Bioengineering. Twenty-nine faculty mentors from eighteen different departments within the School of Medicine and the University provide a variety of angles from which to address fundamental questions about vascular disease. The directors of this grant are Ronald Dalman, MD; Philip Tsao, PhD; and Nick Leeper, MD. [http://med.stanford.edu/cvi/education/mechanisms-and-innovations-t32.html](http://med.stanford.edu/cvi/education/mechanisms-and-innovations-t32.html)

**Research Training in Myocardial Biology T32 Training Grant.** The Multi-Disciplinary Research Training Program in Myocardial Biology is funded by the National Institutes of Health to bring together post-doctoral fellows and faculty from six complementary areas - genetics and genomics, cellular signaling, molecular imaging, physiology and phenotyping, cardiac development and regeneration and outcomes research and population science. Although many possible divisions exist in the spectrum of cardiovascular investigators, one of the most discrete is the division between those researchers interested in blood vessels and those primarily interested in the biology of the heart muscle itself. Myocardial biologists at Stanford are found in diverse departments and divisions within the wider Stanford community and this provides a natural vehicle for multidisciplinary training. The directors of this grant are Daniel Bernstein, MD; Euan Ashley, MD, PhD; and Thomas Quertermous, MD. [http://med.stanford.edu/cvmedicine/education/timbs.html](http://med.stanford.edu/cvmedicine/education/timbs.html)
Several junior members of the CVI were recently awarded postdoctoral fellowship and career development grants. Congratulations to the recipients!

**Alex Chia Yu Chang, PhD**  
07/1/2018–06/30/2021  
AHA Career Development Award  
**Targeting Mechanosensing Signaling in the Treatment of Systemic Sclerosis**

**Ewa Bielczyk-Macynska, PhD**  
7/1/2018–06/30/2020  
AHA Postdoctoral Fellowship  
**Cardioprotective Exosomal MicroRNA Cluster Restore the Injured Myocardium**

**Qing Liu, PhD**  
09/1/2018–08/30/2021  
AHA Career Development Award  
**Drug-induced Alterations in Metabolic Remodeling & Transcriptional Regulation During Cardiomyocyte Differentiation**

**Ji-Hye Jung, PhD**  
07/1/2018–06/30/2020  
AHA Postdoctoral Fellowship  
**Determining the Pathogenicity of HCM-Associated VUS Using CRISPR/Cas9 and iPSCs**

**Ning Ma, PhD**  
7/1/2018–6/30/2020  
AHA Postdoctoral Fellowship  
**The Role of CD47 in the Accumulation of Diseased Smooth Muscle Cells in Atherosclerosis**

**Robert Wirka, MD**  
7/1/2018–6/30/2021  
AHA Career Development Award  
**Mechanisms of TCF21 in Coronary Artery Disease**

**Huaxia Yang, PhD**  
7/1/2018–6/30/2020  
AHA Postdoctoral Fellowship  
**Interrogating the Cardiovascular Toxicity of Volatile Organic Compounds from E-Cigarettes in hiPSC-derived Vascularized Cardiac Organoids**

**Yang Wang, PhD**  
07/01/2018–06/30/2020  
AHA Postdoctoral Fellowship  
**The Role of CD47 in the Accumulation of Diseased Smooth Muscle Cells in Atherosclerosis**

**Soah Lee**  
6/1/2018–5/31/2021  
NHLBI: F32 Postdoctoral Fellowship  
**Elucidating Molecular Mechanism of Cardiac Gap Junction and Intercalated Disc Development**

**Albert J. (AJ) Rogers, MD, MBA**  
06/1/2018–05/30/2019  
Heart Rhythm Society  
**Clinical Research Award in Honor of Mark Josephson and Hein Wellens**  
**Novel Atrial Fibrillation Phenotypes Defined by Functional-Anatomical, Machine-Learned Classifications**
Video: History and Future of Heart Transplant at Stanford

In 1968, the very concept of transplanting a beating heart from one human to another seemed like science fiction. A visionary Stanford cardiothoracic surgeon named Dr. Norman E. Shumway set about to change that; and in the process created the standard by which nearly 2,000 life-saving surgeries are performed annually today. However Shumway’s legacy is cemented not only for those three hours of surgery in January 1968, but in his team’s decades-long commitment to further transforming transplant protocols and the translational science to lower patient rejection and increase survival rate.

Led by Dr. Joseph Woo, the current chair of Cardiothoracic Surgery at Stanford, this remarkable session featured insights from several pioneering leaders in the field who were trainees on Dr. Shumway’s team, including one of the first visionaries in cardiovascular medicine, the inventor of the first mechanical heart device, as well as Shumway’s partner in the first-ever heart-lung transplant. The panelists (Sharon Hunt, MD, Professor of Cardiovascular Medicine, Emerita; Phil Oyer, MD, PhD, Roy B. Cohn-Theodore A. Falasco Professor in Cardiothoracic Surgery; Bruce Reitz, MD, Norman E. Shumway Professor, Emeritus and Former Chair, Department of Cardiothoracic Surgery) explored the impact of this historic innovation at Stanford on human health and discussed the extraordinary new directions in cardiovascular medicine that Stanford is leading today. View video here: https://tinyurl.com/ycj9nvzr.

Faculty Funding Opportunities

**SEPTEMBER 2018**

**NIH Director's Pioneer Award (DP1 - Clinical Trial Optional) (RFA-RM-18-007)**
Amount of funding: $700K direct costs (plus indirects) per year x 5 years ($3.5M total direct costs plus indirects)

**NHLBI Program Project Applications (P01) PAR-18-405**
Amount of funding: $1,515,000 direct costs per year (5yr max)
Deadline: Sept. 25, 2018
PAR-18-405

**OCTOBER 2018**

**AHA Collaborative Sciences Award**
Required Letter of Intent Deadline: Tuesday, October 9, 2018
Deadline for Applicants Invited to Submit Full Application: Thursday, January 31, 2019
Total Award Amount: $750,000

**AHA Established Investigator Award**
Required Letter of Intent Deadline: Tuesday, October 23, 2018
Deadline for Applicants Invited to Submit Full Application: Tuesday, January 15, 2019
Total Award Amount: $400,000
AHA EIA

**AHA Innovative Project Award**
Required Letter of Intent Deadline: Tuesday, October 29, 2018
Deadline for Applicants Invited to Submit Full Application: Tuesday, January 17, 2019
Total Award Amount: $200,000

**Stanford RMG Funding Information Resource webpage:**
http://med.stanford.edu/rmg/funding/
Postdoctoral Funding Opportunities

OCTOBER 2018

NHLBI Mentored Career Development Award to Promote Faculty Diversity in Biomedical Research (K01)
Deadline: October 12, 2018
PA-18-369 Clinical Trial NOT allowed
PA-18-363 Clinical Trial Required

Mechanisms and Innovations in Vascular Disease T32 Training Grant
Stanford Cardiovascular Institute (CVI)
Deadline: Oct. 28, 2018 For Dec. 1 startdate
Visit: http://med.stanford.edu/cvi/education/postdoc-training-fellowships.html

NOVEMBER 2018

National Institutes of Health
K01 Mentored Research Scientist Development Awards
Deadline: November 12, 2018
PA-18-369 Clinical Trial NOT allowed
PA-18-363 Clinical Trial Required

Multi-Disciplinary Cardiovascular Imaging T32 Training Grant
Stanford Cardiovascular Institute (CVI)
Deadline: Rolling. Apply any time.
Visit: http://med.stanford.edu/cvi/education/postdoc-training-fellowships.html

DECEMBER 2018

Ruth L. Kirschstein National Research Service Awards (NRSA) for Individual Postdoctoral Fellows
Deadline: December 8, 2018
PA-18-670

National and Global Cardiovascular Conferences

OCTOBER 2018

Update in Clinical Cardiology Harvard Medical School
Oct 10-12, 2018
Boston, MA

Vascular Biology (NAVBO – North American Vascular Biology)
Oct 14-18, 2018
Newport, RI

Popular Pediatric Clinical Topics 2018
Oct 16-19, 2018
Fairmont Kea Lani, Wailea, HI (on the Island of Maui)

29th Annual Cardiovascular Interventions
October 23-26, 2018
La Jolla, CA

NOVEMBER 2018

Fourth Annual Dr. Lawrence H. and Mrs. Roberta Cohn Visiting Professor Lecture
Guest: Frederick Y. Chen, M.D., Ph.D.
Chief, Division of Cardiac Surgery
CardioVascular Center, Department of Surgery, Tufts Medical Center Professor of Surgery
8:30 - 9:30 a.m. Nov 5, 2018
James H. Clark Center Auditorium
Stanford, CA
Register: http://tinyurl.com/CohnLecture2018

World Congress of Cardiology & Cardiovascular Health 2018
December 5-8, 2018
Dubai, Saudi Arabia

2018 Colorado Heart Failure Summit
December 13-15, 2018
Colorado Springs, CO

DEVICE THERAPIES FOR HEART FAILURE 2018 (D-HF 2018)
December 14-15, 2018
Frankfurt, Germany

DECEMBER 2018

Inaugural Stanford Child Health Research Institute Symposium
November 16, 2018
Li Ka Shing Center
Stanford, CA

29th World Cardiology Conference
November 19-20, 2018
Edinburgh, Scotland

Stanford-Duke Cardiovascular Research Symposium
November 29-30, 2018
Stanford, California
Info/register: https://tinyurl.com/stanfordduke2018

AHA Scientific Sessions 2018
Cardiovascular Clinical Nursing Symposium: November 11
Nov 10-12, 2018
Chicago, IL

Controversies & Advances in the Treatment of Cardiovascular Disease
November 15-16, 2018
Carlsbad, CA
2018
RACE AGAINST PH
Sunday, November 4, 2018
Stanford Pac-12 Plaza

Fighting pulmonary hypertension
with every step!

Sign Up Today!
EARLY BIRD
discount ends
October 1st.

To register, fundraise or volunteer
visit raceagainstph.org

Stanford’s 5th Transcatheter Heart Valve
and Structural Heart Disease Summit

Saturday, October 20, 2018
Li Ka Shing Learning
and Knowledge Center
Stanford University
School of Medicine

Register online at https://tickets.stanford.edu/THVSummit

cvi.stanford.edu
Communication is at the heart of scientific advancement and innovation. This quarter, the Stanford Cardiovascular Institute members published over 350 original manuscripts and reviews, further contributing to our understanding of cardiovascular biology and disease. Here, we highlight selected manuscripts by our members.

**MAY**


JUNE


Right ventricular stroke work correlates with outcomes in pediatric pulmonary arterial hypertension. Yang W, Marsden AL, Ogawa MT, Sakarowitch C, Hall KK, Rabinovitch M, Feinstein JA. Pulm Circ. 2018 Jul-Sep;8(3).


AUGUST


Clinical Biomarker & Phenotyping Core Lab (BPCL)

BPCL provides 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: Francois Haddad, MD / fhaddad@stanford.edu

CVI Clinical Trials Core

The CVI Clinical Trials Core provides full spectrum of support to CVI members and their clinical trials. The coordinators has extensive clinical research experience in both industry and academia. The team provides services and support to principal investigators and sponsors, including:

- Consultation
- Study start-up management, including IRB applications, budget development
- Subject recruitment, site visits, and follow-ups (AE reporting and queries)
- Data management
- Regulatory compliance and documentation
- Closeout

Contact: Ed Finn, Clinical Trials Manager or Hoa Ly, Clinical Research Coordinator at (650) 498-6279

Stanford CVI Human iPSC Biobank Service

Normal and patient-derived reprogrammed cardiomyocytes are 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 peripheral blood mononuclear cell (PBMC) samples from selected patients can be sent to Stanford CVI for reprogramming free of cost.

SCVI biobank is supported in part by National Heart, Lung and Blood Institute (NHLBI) and the Stanford Cardiovascular Institute (CVI).

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

Contact: Joseph Wu, MD, PhD / joewu@stanford.edu
or Biobank manager, Yan Zhuge / yanzhuge@stanford.edu with any questions.

Cardiovascular Pharmacology (BioADD)

The Cardiovascular Pharmacology/Biomaterials and Advanced Drug Delivery (BioADD) Laboratory is a cutting edge research facility that specializes in the creation of biomaterials and drug delivery agents. The lab lends its expertise toward designing and analyzing biomaterials, developing drug delivery devices and formulations, pharmacokinetic and pharmacodynamic studies, and developing smart materials for biomedical applications. CVI Cardiovascular Pharmacology also offers trainings and lectures.

Contact: Jayakumar Rajadas, PhD jayraja@stanford.edu

3DQ Imaging Laboratory

Stanford’s 3DQ Imaging Laboratory develops new approaches to exploration, analysis and quantitative assessments of diagnostic images that result in new and/or more cost-effective diagnostic approaches, and new techniques for the design and monitoring of therapy. The lab processes over 1,200 clinical cases to deliver relevant visualization and analysis of medical imaging data at Stanford.

The lab is co-directed by Dominik Fleischmann, MD, Roland Bammer, PhD and Sandy Napel, PhD.

Contact: Dominik Fleischmann, MD d.fleischmann@stanford.edu
Leadership

Joseph C. Wu, MD, PhD
Director, Stanford Cardiovascular Institute
Simon H. Stertzer, MD, Professor of Medicine- 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
The Stanford Professor of Pulmonary and Critical Care Medicine, 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, Bioengineering and Medicine; and Professor, by courtesy, of Mechanical Engineering, Director, Byers Center for Biodesign

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