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, contact either Joseph C. Wu, MD, PhD or Y. Joseph Woo, MD (search chairs) or visit the website: https://tinyurl.com/yb83cu65.
**PARTICIPANTS INCLUDE:**

- **Anthony Adamis, MD:** Senior Vice President of Development and Innovation, Genetech
- **Jeffery Bluestone, PhD:** CEO and President, Parker Institute for Cancer Immunotherapy
- **Jim Doroshow, MD:** Deputy Director for Clinical and Translational Research, NCI
- **Brian Druker, MD:** Director, Knight Cancer Institute, OHSU
- **Victor Dzau, MD:** President, National Academy of Medicine
- **Peter Fitzgerald, MD, PhD:** Professor Emeritus, Medicine & Engineering; Director, Center for CV Innovation, Stanford; Co-Founder, Triventures
- **Sandra Horning, MD:** Executive Vice President, Global Development and Chief Medical Officer, Genentech
- **Allan Jones, PhD:** President and CEO, Allen Institute
- **Crystal Mackall, MD:** Prof., Pediatrics, Medicine, Stanford; Founding Dir., Stanford Ctr. for Cancer Cell Therapy; Dir., Parker Inst. for Cancer Immunotherapy
- **Mathai Mammen, MD, PhD:** Global Head of R&D, Janssen Pharmaceutical Company of J&J
- **John C. Martin:** Chairman, Board of Directors; Former CEO, Gilead
- **Peter Marks, MD, PhD:** Director, Center for Biologics Evaluation & Res, US FDA
- **Maria Millan, MD:** President and CEO, CIRM
- **Lloyd Minor, MD:** Dean, Stanford School of Medicine
- **Beverly Mitchell, MD:** Director Emeritus and Senior Advisor, Stanford Cancer Institute
- **Andrew Plump, MD, PhD:** CSO and CMO, Takeda
- **John Reed, MD, PhD:** Executive Vice President, Global Head of R&D, Sanofi
- **Alan Sachs, MD, PhD:** CSO, Thermo Fisher
- **Camille Samuels, MBA:** Partner, Venrock
- **Randy Schekman, PhD:** HHMI Investigator and Professor, UC Berkley; Nobel Prize 2013
- **Carla Shatz, PhD:** Professor of Biology & Neurobiology; David Starr Jordan Director, Stanford Bio-X
- **Ram Shriram:** Founder, Sherpalo Ventures
- **Orla Smith, PhD:** Managing Editor, Science Translational Medicine, Science (AAAS)
- **Young Sohn:** President and co-CSO, Samsung Electronics
- **Marc Tessier-Lavigne, PhD:** President and Bing Presidential Professor, Stanford University
- **Sandy Weill:** Chairman Emeritus and former CEO, Citigroup
- **George Yancopoulos, MD, PhD:** President & CSO, Regeneron Pharmaceuticals, Inc
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• Start date is moderately flexible

ELEGIBILITY
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• Must be enrolled in a US College or University
• No previous research experience required
• Must be majoring in a STEM discipline

Individuals from groups underrepresented in academia (including but not limited to: racial/ethnic minorities, gender/sexual minority, first gen college students, disabled, from a rural area, low income) are particularly encouraged to apply!

For more info and to apply go to https://tinyurl.com/cviundergradinfo or contact Megan.Mayerle@Stanford.edu
Recruitment for Assistant, Associate, or Full Professor, Stanford BASE Initiative

The Stanford Children’s Health Betty Irene Moore Children’s Heart Center is inaugurating a major initiative in Basic Science and Engineering (BASE). Scientists will be appointed to the Children’s Heart Center and as tenure track Assistant, Associate or Full Professors in the Basic Science or Engineering Departments of Stanford University. Our goal is to leverage cutting edge research to address the challenges we face in children with heart disease.

For information on the program and how to apply, please visit http://www.med.stanford.edu/base. Applications will be received starting September 15, 2018 and review will begin December 15, 2018. Inquiries to: Marlene Rabinovitch, MD c/o Michelle Fox, Research Administrator mfox1@stanford.edu.

Surgical adhesions can be treated, prevented in mice

A cellular culprit — as well as a possible treatment — for a common, sometimes life-threatening post-surgical complication has been identified by researchers at the Stanford University School of Medicine.

The condition arises when abnormal fibrous connections called adhesions form after abdominal surgery, tethering our normally slippery organs together or anchoring them to the abdominal wall. Symptoms can include chronic pain, female infertility, bowel obstruction and, occasionally, death. According to the National Institutes of Health, the annual cost of treating post-surgical adhesions in the United States surpasses $1 billion.

“This is a very common surgical complication, but it’s not well-studied,” said Jonathan Tsai, MD, PhD. “We’ve come up with a way to isolate the injured tissue before they form the adhesions, and identify the molecular pathways involved.”

In a study published in Science Translational Medicine, the researchers developed and studied a mouse model of adhesion formation to identify the cell responsible for the initial steps. They also showed that an antibody-based therapy could break down those that had already formed.

The researchers found that a combination of two antibodies — one that targets the cells responsible for adhesion formation and another that silences a “don’t eat me” signal that cancer cells use to evade the immune system — could significantly reduce the severity of established adhesions.

“Although we used a mouse model to study adhesion formation,” Irving Weissman said, “we found similar characteristics in adhesions from patients, which makes us think this approach could be translated into the clinic.”


Compound identified that may help treat heart failure

Heart attack survivors may think the worst is behind them. But many later develop heart failure, a progressive disease marked by shortness of breath and swelling in the legs. Symptoms can prevent patients from working, exercising — even picking up grandchildren.

Heart failure occurs after a heart attack when enough of the heart muscle dies, causing the rest of the heart to overwork, which leads to more damage. To protect an overworked, failure-prone heart, cardiologists typically prescribe medications that encourage the heart to take it easy, said Daria Mochly-Rosen, PhD, professor of chemical and systems biology and the George D. Smith Professor in Translational Medicine.

One contributor to heart failure following a heart attack is the accumulation of broken or dysfunctional mitochondria, the small organelles in cells that produce energy. The researchers identified a pair of proteins that, when bonded, gum up the normal activity of mitochondria and contribute to heart failure. One, protein kinase C beta 2, is found in higher levels in failing human and rodent hearts.

The researchers tapped their chemistry know-how to develop a compound called SAMßA (pronounced “samba”), which can prevent these proteins from bonding, thereby improving mitochondrial function and providing more energy for the heart.

“We greatly improved their hearts,” Mochly-Rosen said. “If humans are going to be like rats, perhaps we can treat them with a drug that prevents this deterioration. I’m hopeful SAMßA will be accepted by the industry for drug development because it appears very promising,” Mochly-Rosen said. Published in Nature Communications.

Nicholas Leeper, MD won an NIH NHLBI R35 Emerging Investigator Award, which promotes high-risk, high-reward research. This project focuses on the process of atherosclerosis, and the development of novel translational therapies for heart attack and stroke.

Dr. Leeper will also join the American Heart Association’s (AHA) Science Advisory and Coordinating Committee (SACC), which is the organization’s highest scientific body, and is responsible for mapping its scientific agenda.

Koen Nieman, MD, PhD was awarded an R01 grant "Comprehensive CT Guided Coronary Artery Bypass Graft Surgery". Co-investigators include Alison Marsden, James Zou, Jack Boyd, Tricia Nguyen, and Andy Kahn (UCSD).

June-Wha Rhee, MD was awarded a US Department of Defense Peer Reviewed Medical Research Program Discovery Award focusing on studying Statin Myopathy.

Mahmood Alhusseini, MS was a European Heart Rhythm Association Young Investigator Award Finalist.

Miguel Rodrigo Bort, PhD was awarded the Heart Rhythm Society Eric N. Prystowsky Fellowship Award.

Hongchao Guo, PhD received a 2019 New Investigator award for Best Abstract at the Society for Research on Nicotine and Tobacco.

Gentaro Ikeda, MD was awarded a Stanford Dean’s Fellowship Grant.

Edward Lau, PhD was awarded an NIH K99/R00 fellowship.

George Leef, MD received an Asia-Pacific Heart Rhythm Society Young Investigator 1st Place (Fellow) Award.

Francesca Tongco joins 2019 CVI Team team

Francesca has a BS in Health Care Administration from Sacramento State and has been with Stanford since Nov. 2015. Before Stanford, she worked at the Department of Justice and UC Davis Cancer Center. Welcome Francesca!

Dilip Thomas, PhD was awarded a TDRP postdoctoral fellowship.

Donate to the Stanford Cardiovascular Institute

The Institute currently consists of over 240 faculty members representing physicians, surgeons, engineers, basic and clinical researchers. The Institute's mission 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, CVI Director at joewu@stanford.edu or Cathy Hutton, 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
Scientists identify reversible molecular defect underlying rheumatoid arthritis

Rheumatoid arthritis is one of the most common autoimmune diseases, affecting about 1 percent of the population. It involves destruction of synovia, soft tissue that lubricates joints to prevent bones from scraping together. Whereas osteoarthritis is attributable to age-related wear and tear, rheumatoid arthritis results from a chronic attack on the synovia by cells of the body’s immune system. The inflammatory character of rheumatoid arthritis also causes systemic problems.

Existing rheumatoid-arthritis medications relieve symptoms but don’t actually eradicate the disease by rectifying the behavior of the immune cells causing it, Weyand said. Why those cells go on the attack to begin with has been mysterious. The errant cells are helper T cells. After infiltrating synovial tissue, they send out signals that call in other super-aggressive immune cells and cause ordinary synovial cells to become inflamed and destructive.

In prior work, Weyand’s group noticed telling differences between the helper T cells of patients with rheumatoid arthritis and those of healthy people. The former, for instance, have low reserves of a molecule called ATP, which serves as cell’s internal energy currency, accepted by all of a cell’s myriad metabolic enterprises. Yet instead of directing their primary energy source, glucose, toward ATP production, these cells divert their glucose supplies toward fashioning various materials — proteins, nucleic acids, membranes and the like — used to build new T cells that will contribute to further damage.

That shouldn’t happen. Like all cells, T cells contain AMPK, a regulatory molecule that senses ratios of ATP and its two main breakdown products. If it finds ATP too outnumbered by these breakdown products, AMPK clamps down on the T cell’s cell-building program and, instead, sends glucose off to the cell’s ATP-generating apparatus. The new study provides an answer to the question of why AMPK fails to perform its energy-monitoring function in the faulty helper T cells of patients with rheumatoid arthritis.

Weyand’s team obtained blood samples from 155 rheumatoid arthritis patients, an equivalent number of healthy subjects and a smaller number of patients with other autoimmune disorders. Rheumatoid arthritis patients’ T cells had just as much AMPK as cells from healthy subjects or patients with other autoimmune diseases did. But their AMPK molecules weren’t getting activated. Nor were they as likely to turn up on lysosomal surfaces. AMPK molecules in these cells were also much less likely to feature molecules of a substance called myristic acid affixed to their back ends.

An exploratory compound, A769662, that causes AMPK to become activated even when it’s just floating around in a cell’s cytoplasm rather than anchored to a lysosome reversed rheumatoid-arthritis helper T cells’ inflammatory output and their propensity to infiltrate and damage human synovial tissue in the mice, the study found. Weyand said she expects to test the efficacy of the compound, or a derivative, among rheumatoid arthritis patients in a clinical trial, hopefully in the near future. Published in Nature Immunology.

No evidence to support the 'Hispanic Paradox' of cardiovascular disease

Hispanic individuals are the fastest growing ethnic group in the United States and face lower socioeconomic status compared with non-Hispanic white individuals. However, Hispanic individuals tend to experience better health outcomes than expected, a phenomenon known as the Hispanic paradox. Little is known about how higher socioeconomic status is associated with Hispanic cardiovascular risk factor burden and outcomes.

A new study published in JAMA Cardiology led by Stanford Assistant Professor Fatima Rodriguez, MD set out to determine cardiovascular risk and outcomes among highly educated Hispanic versus Non-Hispanic white individuals in a preventive medicine clinic.

This longitudinal cohort study that included 1351 Hispanic and 43,736 Non-Hispanic white participants with high educational attainment found that Hispanic individuals had greater prevalence of cardiometabolic risk factors but no difference in predicted cardiovascular risk. No significant ethnic differences in subclinical atherosclerosis or mortality were found. This means that, in a highly educated Hispanic population, there is no evidence for the Hispanic paradox in cardiovascular risk, subclinical coronary atherosclerosis, or mortality.

Source: https://jamanetwork.com/journals/jamacardiology/article-abstract/2718500
Protein promotes small artery growth to damaged heart tissue in mice

By CHRISTOPHER VAUGHAN

A collaboration between basic and clinical scientists at Stanford University recently published in Cell has revealed a protein that promotes the growth of small arteries leading into oxygen-starved heart tissues in mice.

Kristy Red-Horse, PhD, associate professor of biology, and Joseph Woo, MD, professor of cardiothoracic surgery, think the growth of these new arteries may help heal damage caused by heart disease or heart attack, or even help prevent that damage.

In clinical practice, Woo has observed that patients with blockages in major arteries feeding the heart often have different outcomes. “Some patients have a blockage in one coronary artery and die; others have blockages in multiple areas but can run marathons”.

The difference, Woo said, may be that this second group of patients has collateral arteries, tiny arteries that bypass blockages in hearts’ major arteries and feed areas of the heart starved of oxygen. “They are like the side streets that let you get around a traffic jam on the freeway,” Woo said. Such collateral arteries could help people with atherosclerosis or people recovering from a heart attack, except that collateral arteries are only seen in a minority of patients.

Now Woo, Red-Horse and their colleagues have discovered how these collateral arteries are formed and a signaling molecule that promotes their growth in adult mice, offering hope that collateral arteries may be coaxed to grow in human patients.

“Neonatal mice have a robust ability to heal injured heart tissue, but they no longer have that ability in adulthood,” Red-Horse said.

Red-Horse and Woo knew that the molecule CXCL12 is an important signal during embryonic development of arterial cells, and has been shown to improve cardiac recovery and function after heart attacks. They investigated whether CXCL12 could help adult heart tissue grow collateral arteries.

After inducing heart attacks in adult mice, they injected CXCL12 into the injured areas. Sure enough, 15 days after the injuries, there were numerous new collateral arteries formed by the detaching and migrating artery cells.

Red-Horse and Woo think the complete story is not this simple. “We speculate that there is a whole suite of proteins that support cell migration out of arteries and promotes cell proliferation among the injured cells,” Red-Horse said.

“The question now is whether this mechanism we have discovered can be manipulated therapeutically to generate collateral arteries in human patients,” Woo said.


Showing support for women’s cardiovascular health

Friday, Feb. 1, was National Wear Red Day, an event organized by the American Heart Association and the National Heart, Lung and Blood Institute. Staff, faculty, and residents joined the movement, sporting all things red to raise awareness of women’s cardiovascular health. Stanford’s Twitter highlights:

A novel immunotherapy appears safe for use in patients with a type of blood cancer called non-Hodgkin’s lymphoma, according to a phase-1 multicenter clinical trial led by a researcher at the Stanford University School of Medicine.

The therapy combines an experimental antibody developed by researchers at Stanford and a commercially available anti-cancer antibody called rituximab. The experimental antibody, known as Hu5F9-G4, blocks the protein CD47, a “don’t eat me” signal that inhibits immune attacks on cancer cells. The antibody combination was used to treat people with two types of non-Hodgkin’s lymphoma: diffuse large B-cell lymphoma and follicular lymphoma.

Half of the 22 people enrolled in phase 1 of the trial had a positive response to the therapy, and about one-third went into complete remission from their cancer.

“It was very gratifying to see how the treatment was well-tolerated and showed a clinically meaningful response,” said Ranjana Advani, MD, professor of medicine at Stanford.

A paper describing the results of the phase-1 trial was published in *The New England Journal of Medicine*.

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**Anti-CD47 cancer therapy safe, shows promise in small clinical trial**

By CHRISTOPHER VAUGHAN and KRISTA CONGER

A novel immunotherapy appears safe for use in patients with a type of blood cancer called non-Hodgkin’s lymphoma, according to a phase-1 multicenter clinical trial led by a researcher at the Stanford University School of Medicine.

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**Novel mechanism identified for widely used diabetes drug**

By AMANDA CHASE

Metformin is the fourth most prescribed drug worldwide, yet its mechanism of action is not fully understood. Based on their research, Stanford investigators have published a novel unifying framework for how metformin works.

Metformin was introduced over 60 years ago and remains standard of care in the initial treatment of type 2 diabetes. The American Diabetes Association and the American College of Physicians recommend prescribing metformin for all newly diagnosed patients with type 2 diabetes before trying any other drug based on its effectiveness, low cost, minimal side effects, and long-term safety profile.

Beyond its well-established beneficial effects on glucose metabolism in diabetes, there is evidence that metformin may have a protective effect against particular cancers, cardiovascular disease, and certain degenerative processes associated with aging. Despite its long history of use and extensive research, there has been no unified understanding of its mechanism of action until now.

Recent work published in *G3: Genes, Genomes, Genetics* by Dr. Xiyan Li, Dr. Xin Wang, and senior author Dr. Michael Snyder, Professor and Chair of the Department of Genetics at Stanford University, supports a unifying framework for metformin effects based on direct interaction with heme-containing and other porphyrin-containing groups.

The researchers first used yeast to begin to elucidate the mechanism of metformin. Then in an elegant series of experiments, they extended their findings by studying the effects of metformin in primary human red blood cells, liver cells, a proliferative myelogenous cell line, and a simple cell-free system.

The researchers found that metformin reduced heme levels in proliferating cells that were capable of heme synthesis and helped preserve heme in cells that were unable to produce heme. Furthermore, they found that metformin reduced loss of ferrous heme in red blood cells due to spontaneous oxidation.

The authors speculated that given the high metformin dose required for clinical effect and high abundance of hemoproteins, metformin effects might be mediated through direct interaction with heme.

In a cell-free system, they demonstrated that metformin suppresses heme oxidation and enzyme activity in three protein scaffolds: cytochrome c, myoglobin and hemoglobin at concentrations suggestive of a direct effect. Finally they showed that metformin also inhibited NADPH cytochrome c reductase and decreased cytochrome c reduction at levels suggesting a direct effect on heme reduction.

This study is the first to describe a unified mechanistic framework for metformin based on direct effects on the redox equilibrium of heme and heme-like molecules. This framework suggests new avenues for investigation and may help guide clinical applications in the treatment of diabetes and other diseases.

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**Source:** https://www.ncbi.nlm.nih.gov/pubmed/30554148
Ronald Dalman named Associate Dean for Market Development

Ronald Dalman, MD, the Walter Clifford Chidester and Elsa Rooney Chidester Professor of Surgery and chief of vascular surgery, has been appointed associate dean for market development at the School of Medicine. In this new role, Dalman will serve as faculty partner for Stanford Health Care market and business development leadership. He will also work closely with clinical chairs, chiefs and staff to identify and optimize network and affiliation agreements across the region to achieve established goals of the integrated strategic plan.

Dalman’s research laboratory studies the pathophysiology of abdominal aortic aneurysm disease and is actively engaged in identifying and validating new treatment measures for AAA. He has received 19 years of continuous National Institutes of Health funding as principal investigator or co-principal investigator on AAA-related clinical and translational research studies.

Dalman is the current vice president of the Society for Vascular Surgery, the world’s largest and oldest professional organization dedicated exclusively to improving vascular health. He will become president-elect of the society in 2019.


Paul Yock wins National Academy of Engineering’s Russ prize

By STACEY PARIS MCCUTCHEON

Paul Yock, MD, professor of medicine and of bioengineering at Stanford University and the founder and director of the Stanford Byers Center for Biodesign, is one of five innovators chosen to receive the National Academy of Engineering’s 2019 Fritz J. and Dolores H. Russ Prize. Yock, who was the founding co-chair of Stanford’s Department of Bioengineering, is known internationally for his work inventing and testing new medical devices in the field of interventional cardiology. The Russ Prize honors two of his inventions: the Rapid Exchange stenting and balloon angioplasty system, which is now the primary system in use worldwide; and intravascular ultrasound (IVUS), a medical imaging technology.

The Rapid Exchange system simplified interventional cardiology procedures by replacing the “over-the-wire” approach that required two operators to manage an extremely long guidewire that stretched from the groin (the point of access) into the heart, and extended outside the body sufficiently to accommodate the catheter that would be threaded along its length. “I saw an opportunity to redesign the catheter so that a single operator could do the procedure with a guidewire that was roughly half as long, making it faster and safer to move the catheter in and out of the body,” recalled Yock. Yock also invented the fundamental approach to IVUS, a high-resolution imaging technology that allows doctors to see inside arteries.

Yock is sharing the 2019 Russ Prize with Julio Palmaz, Leonard Pinchuk, Richard Schatz and John B. Simpson. The Russ Prize, the Gordon Prize and the Draper Prize, all awarded by the NAE, are considered to be the “Nobel Prizes of Engineering.” Yock was honored with the Gordon Prize in 2018.


Doctors Sanjiv Gambhir and Joseph Wu recognized as Highly Cited Researchers of 2018

Drs. Sanjiv Sam Gambhir and Joseph Wu have both been recognized as Highly Cited Researchers of 2018 (top 1% by citations for field and year in Web of Science). Researchers were selected for their exceptional performance in one or more of 21 fields (those used in Essential Science Indicators (ESI)) or across several fields. This year, for the first time, Highly Cited Researchers introduced a new “Cross-Field” category to identify researchers with substantial influence across several fields during 2006-2016.

Congratulations, Dr. Gambhir and Dr. Wu!

Consortium fosters innovation in pediatric medical devices

By ERIN DIGITALE

Each year, far fewer medical devices are approved by the Food and Drug Administration for children than adults. This means pediatricians don’t always have top-notch tools available to address medical challenges in babies and kids.

Now, a team of scientists and physicians at two of the Bay Area’s leading research institutions are collaborating to address the problem. Researchers at Stanford University and the University of California-San Francisco are nurturing the development of new medical devices through the UCSF-Stanford Pediatric Device Consortium, established last year with an award of $6.7 million from the FDA.

“This is the right time for a big push in pediatric technologies,” said Paul Yock, MD, director of the Stanford Byers Center for Biodesign and an adviser to the consortium. Not only could pediatric devices fill gaps in hospital care, they could also help monitor children’s health and keep them out of the hospital in the first place, said Yock, who is also a professor of bioengineering and of medicine.

The consortium has built a three-phase process for spurring pediatric innovation, drawing on the strengths of UCSF’s history as a hub of pediatric device design and Stanford’s successful biodesign center. (James Wall, MD helps direct the Stanford Biodesign Innovation Fellowship.)

The consortium draws on strengths of both universities, Wall said. “UCSF has experts who have figured out the local infrastructure for developing pediatric devices, and has great clinical strengths,” he said. “We bring the strength of our biodesign process — of infusing discipline early into the innovation process to understand the downstream barriers to product development, such as regulatory hurdles, clinical trial requirements to drive adoption and insurance reimbursement challenges.”

Because most children are healthy, the market for many possible pediatric medical devices is small, he added. “There’s not as much room for error,” Wall said. “You have to be very strategic in how much money you spend to deliver a product to a relatively small number of patients. But Stanford is well-known for developing health technologies, and now we have a mechanism to highlight pediatrics as an opportunity. We want innovators to know that it can be done — it should be done — and our team can help.”


Why do some hearts get too thick?

By MEGAN MAYERLE

Worldwide, more people die of cardiovascular disease than any other cause. Hypertrophic cardiomyopathy (HCM) is the most common form of inherited heart disease, affecting one out of every 500 people, and can lead to progressive heart failure and sudden cardiac death.

The left ventricular walls of HCM patients’ hearts are unusually thick and have trouble pumping blood. Specific variations of two genes, myosin heavy chain 7 and myosin-binding protein C3 (MYBPC3), have been linked to HCM. Most disease-associated variants of MYBPC3 encode directions to make proteins that are too short, which are broken down by specific cellular quality control mechanisms used by cells to avoid wasting resources on making nonfunctional proteins. Diseases like HCM are thought to arise because cells are unable to make enough normal, functional proteins to work correctly.

In a study recently published in Circulation, lead author Timon Seeger, MD and colleagues generated heart muscle cells from stem cells isolated from HCM patients carrying disease-associated, truncated variants of MYBPC3. Using latest tools to edit the genome of these stem cells (CRISPR), the scientists corrected the underlying mutations generating perfect controls.

From comparative analyses, the team learned that although the heart muscle cells generated from HCM patients appear similar to their corrected, healthy control heart muscle cells, they have trouble properly handling calcium, which can lead to difficulties in heart muscle cell contraction.

“These findings indicate very early, even pre-disease molecular mechanisms in the onset of HCM, that can be investigated using iPSC technology aiming at developing specific therapeutic approaches, still absent in HCM to date,” lead author Timon Seeger explains.

This study is the first to describe a unified mechanistic framework for metformin based on direct effects on the redox equilibrium of heme and heme-like molecules. This framework suggests new avenues for investigation and may help guide clinical applications in the treatment of diabetes and other diseases.

Why are so few interventional cardiologists women? A new study offers a few clues

By MANDY ERICKSON

As a fellow-in-training, Celina Yong, MD, found her passion in interventional cardiology. Threading catheters through arteries to open blockages in heart attack patients, she said, “was very rewarding, and it was fun.” It wasn’t until Yong, now an assistant professor in cardiovascular medicine, attended a national conference that she realized what an anomaly she was.

While women make up a little more than half of medical school students and are reaching parity in many medical specialties, they constitute less than 13% of cardiologists, and a mere 4.5% of practicing interventional cardiologists—physicians who primarily use catheters to treat a variety of heart conditions. Yet half of their patients are women, Yong pointed out, creating a drastic imbalance.

Knowing that a gender-lopsided field can affect patient care, Yong decided to study why so few female trainees choose the subspecialty. From a survey of 574 cardiology fellows in training, she found that women are put off by the unpredictable hours, the radiation used during procedures and the male-dominated culture. In the survey, more women than men said they were concerned about the conflict between family life and the job demands.

The X-ray machines the interventional cardiologists use to guide their catheters also scared off some women taking the survey, Yong found. Some respondents said they were afraid of their effect on fertility and pregnancy, although data suggests that the work can be safe with appropriate precautions, according to the research paper. In addition, more female than male trainees who took the survey worried about the weight of the heavy lead aprons worn to protect against radiation. Yong said that some interventional cardiologists experience back problems after years of donning the aprons. The lack of female mentors, an “old boys’ club” culture, and discrimination also deterred some women. “Overcoming the culture is going to take a concerted effort.”

But it would be worth it and benefit patients, Yong is convinced. “Women approach patients’ problems differently,” she said, which can expand possibilities for effective treatment. Also, women can bring a different perspective when it comes to research: “When both men and women design studies and analyze data together, we do a better job, especially when it comes to treatment of female patients.” The study was published in *JACC: Cardiovascular Interventions*.

Source: https://scopeblog.stanford.edu/2019/02/04/why-are-so-few-interventional-cardiologists-women-a-new-study-offers-a-few-clues/

5 Questions: Gardner on the intersection of meat, protein and the environment

By HANAE ARMITAGE

Vegetarians may be on to something: It’s entirely possible to get the National Academy of Medicine’s recommended amount of protein without eating meat.

Americans consume the most protein in the world, and they eat the most meat, according to an article published Feb. 6 in *Nutrition Reviews*. The article, a literature review, analyzes recent protein consumption nationwide. Yet gorging oneself on protein doesn’t yield health benefits. In fact, excess calories—in the form of protein or anything else—end up stored as carbohydrate or fat and can lead to weight gain. What’s more, studies have shown that raising enough livestock to satiate current American meat consumption contributes substantially to carbon emissions and requires trillions of gallons of water.

In the article, nutrition scientist Christopher Gardner, PhD, professor of medicine at Stanford and the Rehnborg Farquhar Professor, and his co-authors recommend steps that individuals can take to curb carbon emissions and reduce the resources required to raise livestock, as well as improve their health.

In a conversation with science writer Hanae Armitage, Gardner discussed the problems with current protein consumption and how much individuals should be eating, as well as how he thinks the two can be reconciled in a way that will benefit the environment.

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.

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.

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.
Funding Opportunities

March 2019

NHLBI Outstanding Investigator Award (R35 Clinical Trial Optional). Up $600,000 direct costs per year for up to 7 years. Eligibility: Are currently PD/PI on at least two NHLBI R01-equivalent awards. Deadline: March 14, 2019. RFA-HL-20-011.

NHLBI Emerging Investigator Award (R35 Clinical Trial Optional). Up $600,000 direct costs per year for up to 7 years. Eligibility: Are currently PD/PI on at least two NHLBI R01-equivalent awards. One of the awards must be an NHLBI-funded NIH Early Stage Investigator (ESI) R01. Deadline: March 14, 2019. RFA-HL-20-012.

April 2019

The Breakthrough Prizes in Life Sciences. These prizes are awarded to individuals who have made transformative advances in understanding living systems and extending human life. Amount of the prize-Breakthrough Prizes in Life Sciences: $3 million each (up to 4 to be awarded). One of the four awards will specifically recognize advances in Parkinson’s Disease or other neurological disorders. Deadline: April 1, 2019. https://breakthroughprize.org.


May 2019

Children’s Heart Foundation - Medical Research Grant. Up to $100K/yr for 2 years. Supports clinical and basic science research in congenital heart disease—including but not limited to these areas: molecular genetics, biochemistry, pharmacology devices, and procedural research (cardiac catheterization and surgery) and long-term care of adults with congenital birth defects.. Eligibility: faculty with PI eligibility and CE faculty (with an approved CE faculty PI waiver). Deadline: June 7, 2019. https://www.childrensheartfoundation.org/for-researchers/.

June 2019

NIH R01 Research Project Grant. Improving Patient Adherence to Treatment and Prevention Regimens to Promote Health (R01 Clinical Trial Optional). Deadline: June 5, 2019. PA-18-722.

NIH R01 Research Project Grant. Implementation of shared decision making for HLBS diseases and conditions (R01 Clinical Trial Optional). Deadline: June 5, 2019. PA-19-166.

NIH Research Project Grant (Parent R01-Clinical Trial Not Allowed). Eligibility: faculty with PI eligibility and CE faculty (with an approved CE faculty PI waiver). Deadline: June 5, 2019 (Standard R01 deadlines). PA-19-056.

NIH Research Project Grant (Parent R01 Clinical Trial Required). Note that NHLBI only accepts mechanistic studies. Eligibility: faculty with PI eligibility and CE faculty with an approved CE faculty PI waiver. Deadline: June 5, 2019 (Standard R01 deadlines). PA-19-055.

NIH Mentored Clinical Scientist Research Career Development Award (Parent K08 Independent Clinical Trial Not Allowed). Deadline: June 12, 2019 (Standard K deadlines.) PA-19-117.

NIH Mentored Clinical Scientist Research Career Development Award (Parent K08 Independent Clinical Trial Required). Deadline: June 12, 2019 (Standard K deadlines). PA-19-116.

NIH Mentored Patient-Oriented Research Career Development Award (Parent K23 Independent Clinical Trial Required). Deadline: June 12, 2019 (Standard K deadlines). PA-19-118.


July 2019


Mini Proposal Bootcamp
Saturday, March 16, 2019, 10:00am – 4:00pm

This 1-day bootcamp is based on the Grant Writing Academy’s award-winning 8-week Proposal Bootcamp. It provides a time and place to write plus lunch, coffee, and snacks. Join *optional* short lightning talks about writing grants, and receive feedback and one-on-one coaching from the Grant Writing Academy’s Grant Coaches. Questions? Email Crystal Botham, PhD. https://grantwriting.stanford.edu/mini-proposal-bootcamp/
MARCH 2019

Workshop on 2-D & Doppler Echocardiography at Vail. March 3 - 7, 2019. Vail Marriott, Vail, CO.


Heart Failure Management for Nurse Practitioners, Physician Assistants, and Primary Care Providers. March 21-23, 2019. Disney’s Boardwalk Inn, Lake Buena Vista, FL.


APRIL 2019

QCOR 2019 Scientific Sessions. Quality of Care and Outcomes Research. April 5 - 6, 2019. The Ritz-Carlton Pentagon City, Arlington, VA.


MAY 2019


12th Annual Cardiology for the Primary Care Practitioner. May 11, 2019. Li Ka Shing Center, Stanford, CA.

Big Data in Biomedicine Conference. May 22 - 23, 2019. Li Ka Shing Center, Stanford, CA.


JUNE 2019


23rd Annual Hypertension, Diabetes and Dyslipidemia Conference. June 21 - 23, 2019. Hyatt Place + Hyatt House Historic District, Charleston, SC.

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, PhD / yanzhuge@stanford.edu with any questions.

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

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. The 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. Stertz, 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