Over 500 people attended the fourth annual Stanford Drug Discovery Symposium. The attendees were a mix of industry and academia. The meeting was a highly successful two days of thought-provoking presentations. It was an opportunity to interact with federal and foundation policy makers, leaders from major pharmaceutical companies, and pioneers in drug discovery research. Dr. John Martin was awarded the Lifetime Achievement Award. More on page 2.

CVI Welcomes 2019 Summer Undergraduate Interns

A diverse group of undergrads from across the country join us to learn about cardiovascular research.

Natasha Auer
UC Santa Barbara
Mentor: Dr. de Jesus Perez

Lauren D’Amico
Univ. of Washington
Mentor: Dr. Bernstein

Kelly Lancaster
UC Berkeley
Mentor: Dr. Liao

Taylor Montiel
San Jose City College
Mentor: Dr. Woo

Julianne Ballon
University of Guam
Mentor: Dr. Fishbein

Nashielli Diaz
Tufts University
Mentor: Dr. Karakikes

Rachel Lippman
Cornell University
Mentor: Dr. Mercola

Raquel Racelis
San Francisco State
Mentor: Dr. Red-Horse

Christian Beke Onana
Univ. of Houston Dtn
Mentor: Dr. Hiesinger

Gabriela Escobar
Stanford University
Mentor: Dr. Sean Wu

Joseph Lohmann
Univ. of Pennsylvania
Mentor: Dr. Priest

Samantha Roach
Spelman College
Mentor: Dr. Shudo

Lily Cheng
Univ. Mich. Ann Arbor
Mentor: Dr. Sayed

Breana Franklin
Clemson University
Mentor: Dr. Sayed

Sarah Madira
Cal State Los Angeles
Mentor: Dr. Anson Lee

Caydin Sablan
Univ. of San Francisco
Mentor: Dr. Liao

Beatrice Choi
Stanford University
Mentor: Dr. Rhee

Roberto Guzman
Univ. of Puerto Rico
Mentor: Dr. Yuan

Rachael Mezynski
North Carolina State
Mentor: Dr. Joe Wu
SDDS 2019 Highlights

On April 22-23, 2019, the fourth annual Stanford Drug Discovery Symposium was held at the Li Ka Shing Center. The meeting featured presentations and panel discussions from federal and foundation policy makers, leaders from major pharmaceutical companies, and pioneers in drug discovery research. There was a Showcase panel event with venture capitalists and leaders from Caribou Biosciences, Immune-Onc Therapeutics, and Appollomics.

2019 Featured Speakers: Anthony Adamis, Genetech; Jeffery Bluestone, Parker Institute; Jim Doroshow, NCI; Brian Druker, Knight Cancer Institute; Victor Dzau, National Acad of Medicine; Peter Fitzgerald, Triventures; Sandra Horning, Genentech; Allan Jones, Allen Institute; Crystal Mackall, Stanford, Parker Institute; Mathai Mammen, Janssen Pharmaceuticals; John C. Martin, Gilead; Peter Marks, FDA; Maria Millan, CiRM; Lloyd Minor, Dean, Stanford Medicine; Andrew Plump, Takeda; John Reed, Sanofi; Alan Sachs, Thermo Fisher; Camille Samuels, Venrock; Randy Schekman, HHMI, UC Berkley, Nobel Prize; Orla Smith, Science Translational Medicine; Young Sohn, Samsung Electronics; Marc Tessier-Lavigne, Stanford President; Sandy Weill, Citigroup; George Yancopoulos, Regeneron Pharmaceuticals

Meeting organizers Sanjay Malhotra, Mark Mercola, Kuldev Singh, Joseph C. Wu, Amanda Chase, and David Preston hope you will join us next year, April 20-21 2020, for SDDS 2020.
E-Cigarette use, flavorings, may increase heart disease risk, study finds

By Krista Conger

The flavoring liquid for electronic cigarettes, or e-cigarettes, may increase the risk of cardiovascular disease when inhaled, according to a study led by researchers at the School of Medicine. The scientists investigated the effect of the e-liquids on cells called endothelial cells that line the interior of blood vessels. They found that, when grown in a laboratory, endothelial cells exposed to the e-liquids — or to blood collected from e-cigarette users shortly after vaping — are less viable and exhibit significantly increased levels of molecules implicated in DNA damage and cell death. The cells are also less able to form new vascular tubes and to migrate and participate in wound healing. The severity of the damage, aspects of which occur even in the absence of nicotine, varies among popular flavors, the researchers said. Cinnamon and menthol were found to be particularly harmful. “Until now, we had no data about how these e-liquids affect human endothelial cells,” said Joseph Wu, MD, PhD, director of the Stanford Cardiovascular Institute and professor of cardiovascular medicine and of radiology. “This study clearly shows that e-cigarettes are not a safe alternative to traditional cigarettes. When we exposed the cells to six different flavors of e-liquid with varying levels of nicotine, we saw significant damage. The cells were less viable in culture, and they began to exhibit multiple symptoms of dysfunction.”

The researchers studied human endothelial cells generated in the laboratory from what are called induced pluripotent stem cells, or iPS cells. Human iPS cells can become many different cell types, and they provide an ideal way for researchers to closely study cells that would be difficult to isolate directly from a patient.

This study was the first to use endothelial cells derived from iPS cells to directly investigate the effect of e-liquids with and without nicotine on their viability and function.

A paper describing the findings was published online May 27 in the *Journal of the American College of Cardiology*. Wu is the senior author. Former postdoctoral scholars Won Hee Lee, PhD, now an assistant professor at the University of Arizona, and Sang-Ging Ong, PhD, now an assistant professor at University of Illinois-Chicago, are the lead authors.

“One in five high school students have tried e-cigarettes, perhaps because they feel they are relatively safe,” Lee said. “But we found the e-liquids caused changes in the endothelial cells that are closely related to those seen during the development of cardiovascular disease.”

The researchers compared the levels of nicotine in the blood serum of people after they had vaped e-cigarettes with the levels in people who smoked traditional cigarettes. They found that the amounts of nicotine in the blood were similar between the two groups after 10 minutes of smoking at a constant rate.

“When you’re smoking a traditional cigarette, you have a sense of how many cigarettes you’re smoking,” Wu said. “But e-cigarettes can be deceptive. It’s much easier to expose yourself to a much higher level of nicotine over a shorter time period. And now we know that e-cigarettes are likely to have other significantly toxic effects on vascular function as well. It’s important for e-cigarette users to realize that these chemicals are circulating within their bodies and affecting their vascular health.”

This work was also covered by The New York Times, Business Insider, CNN, CBS, AP, Fox, and Yahoo.


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Stanford-UPenn Cardiovascular Research Conference

November 4 - 5, 2019, Li Ka Shing Center, Stanford

Keynotes: Paul Yock, Dan Rader


tinyurl.com/StanfordPennCV
Women leaders in cardiac transplantation

by Megan Mayerle, PhD

The first successful heart transplant in the United States was performed at Stanford in 1968. Chief Surgeon Norman Shumway replaced the diseased heart of Mike Kasperak, a retired steelworker. He survived for only 15 days. However, due to innovations in post-transplant patient care, today heart transplantation has become commonplace, and the surgery ensures patients a relatively high quality of life for years and often decades after surgery.

Sharon Hunt, MD, was a medical student at Stanford in 1968. By the time she finished her cardiology fellowship at Stanford, patient survival rates had begun to improve, and Hunt was one of four cardiologists asked to provide long term care for transplant recipients. Now a Professor Emerita of Cardiovascular Medicine at Stanford, Hunt is well known for her innovations in the care of patients after heart transplantation.

In an article published in February 2019 in Circulation, Hunt discusses the impact of women leaders in Cardiac Transplantation.

Currently 26% of board-certified transplantation care specialists in the US are women, a ratio that, though not equal, is far better than many other cardiac subspecialties. Hunt is quick to point out that the often-credited work-life balance and flexible hours are not the reason for the relatively high number of women in this subspecialty. She instead points to the fact that “Women have been in the field from the beginning, continue to be successful as specialists, hold leadership positions and have many relatable role models.”

Grants and Awards

Nicholas Leeper, MD, received the AHA Established Investigator Award.

Edda Spiekerkoetter, MD, received a Department of Defense grant to address hereditary hemorrhagic telangiectasia.

Helen Blau, PhD, was elected to the American Institute for Medical and Biological Engineering (AIMBE).

Tim Assimes, PhD, 2019 recipient of the AHA Genomic and Precision Medicine and Epidemiology Mid-Career Research Award and Lecturer.

Robert Wirka, MD, was awarded the Irvine H. Page Young Investigator Award at 2019 ATVB.

Jason Lee, MD, elected to the Vascular Surgery Board of the American Board of Surgery.

Fatima Rodriguez, MD, MPH, FACC, was awarded an NIH K01 on "SURPASS (Statin Use and Risk Prediction of Atherosclerotic Cardiovascular Disease in minority Subgroups)".

Ngan Huang, PhD, was awarded a Department of Veteran Affairs grant on "Engineering Vascularized Skeletal Muscle for Treatment of Volumetric Muscle Loss", and an Alliance for Regenerative Rehabilitation and Research Training grant on "Stretchable Tissue Chips for Customizable Rehabilitative Microenvironments".

Linda Ottoboni, PhD, FHRS, CCDS, was appointed to the Heart Rhythm Society National Governing Committee.

Kuninobu Kashiyama, MD, received ACC Best Poster Award at the 2019 Annual Scientific Session.

Kevin Cyr was awarded Grand Prize at Stanford Medical School Research Symposium.

Sharon Paige, MD, joined the Department of Pediatrics Instructor Pipeline Program.

Maedeh Zamani, PhD, was awarded an AHA postdoctoral fellowship.

Ji Hye Jung, PhD, was awarded an AHA postdoctoral fellowship.

Mark Nicolls, MD, and Amy Tian, PhD, were awarded an NIH R01 grant to evaluate the role of inflammation in lymphedema.

Sangkyun Cho, PhD, was appointed as a new Cardiovascular Imaging T32 trainee.

Joseph Shrager, MD, received an R01 grant on "A Mechanistic Clinical Trial of JAK Inhibition to Prevent Ventilator-induced Diaphragm Dysfunction".

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
2018 Manuscript Award Winners

**Jingjing Li, PhD**
Lab: Michael Snyder, PhD; Phil Tsao, PhD

**Takeshi Nishi, MD**
Lab: William Fearon, MD; Peter Fitzgerald, MD, PhD

**Darshan Trivedi, PhD**
Lab: James Spudich, PhD

**Ning Ma, PhD**
Lab: Joseph Wu, MD, PhD

**David Paik, PhD**
Lab: Joseph Wu, MD, PhD

**Ke Yuan, PhD**
Lab: Vinicio de Jesus Perez, MD

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AI identifies risk of cholesterol-raising genetic disease

A new algorithm can determine whether a patient is likely to have a cholesterol-raising genetic disease that can cause early, and sometimes fatal, heart problems, reports a new study conducted by researchers at the Stanford University School of Medicine and their collaborators. The disease, known as familial hypercholesterolemia (FH), is often misdiagnosed as garden-variety high cholesterol. “We think that less than 10 percent of individuals with FH in the United States actually know that they have it,” said Joshua Knowles, MD, PhD, assistant professor of cardiovascular medicine at Stanford. “It’s a serious oversight, because an FH patient with high cholesterol is three times more likely to develop early heart disease than someone who has high cholesterol but not FH. A person with FH faces 10 times the risk of heart disease as someone with normal cholesterol.”

Knowles and Nigam Shah, MBBS, PhD, associate professor of medicine and of biomedical data science, have come up with a solution to help catch more cases of FH: a computer algorithm that flags patients who are likely to have the disease. In test runs of the algorithm, it correctly identified 88 percent of the cases it screened. Theoretically, if the algorithm were used in a clinic, any patient it flagged as having FH could undergo further genetic testing to verify the algorithm’s calculation.

A paper describing the research was published in _npj Digital Medicine_. Shah and Knowles, who is the director of the FH clinic at Stanford Health Care’s Center for Inherited Cardiovascular Disease, share senior authorship. Juan Banda, PhD, a former research scientist at Stanford, is the lead author. The project is part of a larger initiative called Flag, Identify, Network, Deliver FH, or FIND FH, a collaborative effort involving Stanford Medicine and established by the nonprofit Familial Hypercholesterolemia Foundation that aims to identify and engage individuals and families affected by the disease by leveraging machine learning and big data.

Now, Knowles and Shah are working on ways to implement the algorithm in doctors’ offices. The work is an example of Stanford Medicine’s focus on precision health, the goal of which is to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill.

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.

Inquiries to: Marlene Rabinovitch, MD c/o Michelle Fox, RA mfox1@stanford.edu. http://www.med.stanford.edu/base

### Modeling patient-specific responses to common calcium channel blocker using iPS Cells

by Megan Mayerle

Human induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) have been shown to be a great tool for modeling CVD and drug screening, and are also being used for transplantation into injured heart muscle as a potential therapy. A limitation to the use of these iPSC-CMs is that they are considered to be immature, similar to early human embryonic cardiomyocytes. To fully realize the potential of iPSC-CMs, they need to be more mature. It has been shown that iPSC-CMs show maturation over a longer period of time in culture, but no work has been done to characterize events that control transitions of cardiac cells during developmental progression. In a paper recently published in *Circulation Research*, Stanford Cardiovascular Institute researchers led by instructor Chi Keung Lam used cardiomyocytes made from induced pluripotent stem cells (iPSC-CMs) isolated from three individuals to understand how four commonly prescribed CCBs (nifedipine, amlodipine, diltiazem, and verapamil) affected cardiomyocyte function in different people.

“iPSC technology allows us the opportunity to study how individual drugs will affect each patient, so we can decide on optimized, individualized treatment strategies”, Lam says.

Because they used multiple iPSC-CM cell lines isolated from different patients, Lam and colleagues were able to identify patient specific responses to each of the four CCBs tested. They were also able to determine a drug-specific gene expression signature for each CCB. Combining these findings, Lam and colleagues were able to pinpoint specific genes that could be used to predict how well individual hypertrophic cardiomyopathy patients would respond to verapamil, a specific CCB.


### Understanding metabolism and maturation of iPSC cardiomyocytes

by Amanda Chase, PhD

Advances in treatment strategies and therapeutics allow individuals with chronic conditions a high quality of life. The symptoms of a wide variety of diseases can be mitigated simply by taking a pill. Many patients with hypertension are prescribed calcium channel blockers (CCBs) to control their blood pressure, which they take for the rest of their life. Although the acute effects of CCBs are well understood, very little is known about how these drugs impact cardiomyocyte physiology and gene expression patterns. Calcium is very important to heart cell function, and it is possible that CCBs could alter various cardiac cellular processes.

In a paper recently published in *Circulation Research*, Stanford Cardiovascular Institute researchers sought to understand functional and metabolic transitions of cardiac cells during development, which could provide insight into maturing iPSC-CMs.

These efforts were led by Antje Ebert, Ph.D., who is now a group leader at the University of Goettingen, Medical Center in Germany. They used iPSC-CMs that were kept in culture for different lengths of time (early, medium, and late), and then looked at network pathways at each time point and comparing between them. They were able to describe a novel mechanism governing metabolic output during long-term culture. Dr. Ebert explains that “this study shows that iPSC-CMs can serve as a model for studying human cardiomyocyte development progression during maturation. We also show that modulation of cardiomyocyte metabolism during development affects contractility of cardiomyocytes.” That is an important distinction for mature CMs. “Our study provides options for maturing iPSC-CMs, which is extremely useful for disease modeling, drug testing, and future regenerative approaches,” explains senior author Joseph C. Wu, M.D., Ph.D., Director of Stanford Cardiovascular Institute.

3D nanostructures improve skeletal muscle regeneration

by Megan Mayerle, PhD

Our muscles get stronger through repeated cycles of injury and repair. Exercise damages muscle, but at the same time activates muscle stem cells that differentiate into new skeletal muscle fibers, repairing and strengthening the tissue. However, sometimes the amount of damage done to muscle is too much, and, unable to properly heal, chronically inflamed scar tissue forms. In order to heal from this type of injury, the body must not only produce new skeletal muscle cells, it must also make sure that these cells orient properly to contract.

In a study recently published in Communications Biology, Stanford Cardiovascular Institute researchers Karina Nakayama, PhD, Ngan Huang, PhD, and colleagues describe a method to fabricate skeletal muscle using spatially patterned bioengineered scaffolds. These scaffolds help newly formed skeletal cell muscles align, and when implanted into a damaged area, help mice recover from injury.

The researchers created aligned nanofibrillar scaffolds and then seeded them with myoblasts and endothelial cells, the cell types that make up skeletal muscle tissue. The nanofibrillar scaffolds organized the cells, producing long skeletal muscle myotubules capable of contracting strongly and consistently. Alignment also affected cellular gene expression, inducing differential transcriptional pathways that may regulate how engineered muscle behaves.

To test this engineered muscle, the scientists transplanted their aligned engineered skeletal muscle to a site of injury in the mice. The aligned tissue integrated into the site of injury without significant scarring. It also aided in tissue revascularization, which is critical for recovery from injury.

This method shows translational promise, as the researchers were also able to show that human cells aligned on bioengineered scaffolds functioned similarly to the mouse cells and highlights the importance of how cells are positioned in 3D in regenerative medicine approaches.


Ngan Huang, PhD
Apple Heart Study demonstrates ability of wearable technology to detect atrial fibrillation

Researchers from the Stanford University School of Medicine today presented preliminary results of the Apple Heart Study, an unprecedented virtual study with over 400,000 enrolled participants. The researchers reported that wearable technology can safely identify heart rate irregularities that subsequent testing confirmed to be atrial fibrillation, a leading cause of stroke and hospitalization in the United States.

The study was launched with sponsorship by Apple Inc. in November 2017 to determine whether a mobile app that uses data from a heart-rate pulse sensor on the Apple Watch can identify atrial fibrillation. The condition often remains hidden because many people don’t experience symptoms. “The results of the Apple Heart Study highlight the potential role that innovative digital technology can play in creating more predictive and preventive health care,” said Lloyd Minor, MD, dean of the Stanford School of Medicine. “Atrial fibrillation is just the beginning, as this study opens the door to further research into wearable technologies and how they might be used to prevent disease before it strikes — a key goal of precision health.”

The Stanford principal investigators were Mintu Turakhia, MD, associate professor of cardiovascular medicine, and Marco Perez, MD, associate professor of cardiovascular medicine, and the study chair was Kenneth Mahaffey, MD, professor of cardiovascular medicine.

Drug reduces risk of kidney failure in people with diabetes

A new landmark clinical trial shows that a drug lowers the risk of kidney failure by a third in people with Type 2 diabetes and kidney disease. “For the first time in 18 years, we have a therapy for patients with Type 2 diabetes and chronic kidney disease that decreases kidney failure,” said Kenneth Mahaffey, MD, professor of medicine at the School of Medicine and co-principal investigator of the trial. “Now, patients with diabetes have a promising option to guard against one of the most severe risks of their condition.” The trial involved 4,401 participants in 34 countries.

The drug, canagliflozin, improves on a nearly two-decades-old therapy that is currently the only treatment approved to protect kidney function in people with Type 2 diabetes. In the trial, canagliflozin also was found to reduce the risk of major cardiovascular events. It has already been approved to lower blood glucose in patients with Type 2 diabetes and to reduce the risk of major adverse cardiovascular events in patients with Type 2 diabetes and existing heart disease.

A paper describing the findings of the CREDEENCE trial was published April 14 in *The New England Journal of Medicine* and presented at the International Society of Nephrology’s World Congress of Nephrology in Melbourne, Australia. Mahaffey, who is director of the Stanford Center for Clinical Research, is the study’s senior author. The lead author is Vlado Perkovic, MBBS, PhD, executive director of The George Institute for Global Health Australia, and a professor of medicine at the University of New South Wales in Sydney. Other Stanford researchers assisting in the trial were Glenn Chertow, MD, professor of medicine, and Tara Chang, MD, assistant professor of medicine, who were national co-leads; and Sun Kim, MD, associate professor of medicine, who was a site investigator.


Patient-specific hemodynamics for the treatment of Kawasaki Disease

Kawasaki disease (KD) causes inflammation in arterial walls throughout the body and is most prevalent in children under 5 years of age. While most children recover, Kawasaki disease can cause coronary artery aneurisms, which can lead to thrombosis. To prevent this, many patients are prescribed anticoagulants. However, guidelines of anticoagulant use rely on anatomical measurements alone, without considering the impact of flow patterns.

Stanford researchers Noelia Grande Gutierrez, Alison L. Marsden, and colleagues have come up with an innovative solution to this problem. They developed a computational fluid dynamics simulation that uses information derived from non-invasive vascular imaging data to provide patient-specific hemodynamic measurements. The hemodynamic variables identified by Gutierrez et al. are superior to traditionally used anatomical measurements for KD aneurysms assessment and can be used to identify aneurysmal regions at higher risk of thrombosis. In the future, personalized hemodynamics could help doctors determine how and when to use anticoagulants for Kawasaki disease patients.

The study was published in the April 15 issue of the *International Journal of Cardiology*.


Stem cell-derived cardiomyocyte tool could improve drug safety

Patient-derived cardiomyocytes (iPSC-CMS) provide a platform for better drug screening and disease modeling, as well as and the first step toward realizing the beginnings of a more personalized approach to studying and treating heart disease. Furthermore, they can be used to generate engineered heart tissue (EHT) to better mimic the complex environment of a living human heart. Having a highly homogeneous pool of ventricular or atrial CMs would be beneficial for applications such as: determining drug safety, cardiac evaluation, and cell therapy for heart attacks by allowing personalized cardiac repair.

A team of researchers primarily affiliated with the Stanford Cardiovascular Institute sought to find a way to make the heterogenous iPSC-CMs into more homogenous population of cells. Led by first author Joe Z. Zhang, PhD., and senior author Joseph C. Wu, M.D., PhD., Director of Stanford Cardiovascular Institute, they developed an innovative tool to help isolate specific cardiovascular subpopulations to generate a purer population of cells. The work was published in *Cell Stem Cell*. The tool developed by these researchers allows, for the first time, isolation of lineage-specific cardiovascular cells.

A new role for PPARγ in pulmonary arterial hypertension

by Megan Mayerle, PhD

Pulmonary arterial hypertension (PAH) is a form of pulmonary hypertension that results from the loss and narrowing of the lumen of small arteries of the lungs which causes an increase in blood pressure. Over time, this increased blood pressure can damage the heart. PAH generally affects young and otherwise healthy individuals and strikes women twice as often as men. Estimates indicate that there are between 10,000 and 20,000 PAH patients in the US.

While PAH is not yet understood at the molecular level, dysfunctional peroxisome proliferator activated receptor γ (PPARγ), a nuclear receptor that acts as a part of a transcription factor complex in vascular and other cell types, has been linked to many vascular diseases including PAH. Furthermore, in PAH, dysfunction of endothelial cells, the cells that line the interior of blood vessels, has been linked to the loss and narrowing of blood vessels. This leads to increased resistance to pulmonary blood flow and can culminate in heart failure and the need for a lung transplant.

In a study recently published in Cell Reports, lead author Dr. Caiyun Grace Li, corresponding author Dr. Marlene Rabinovitch, and colleagues reveal a new role for PPARγ, linking it to the cellular DNA damage response and to DNA repair. In addition to providing a clearer understanding of the role that PPARγ plays in PAH pathogenesis, these novel findings lay the groundwork for potential new PAH therapeutics and treatment strategies.


Study shows how big data can be used for personal health

by Hanae Armitage

Scientists at Stanford and their collaborators followed a cohort of more than 100 people over several years, tracking the biology of what makes them them. Now, after collecting extensive data on the group’s genetic and molecular makeup, the researchers are piecing together a new understanding of what it means to be healthy and how deviations from an individual’s norm can flag early signs of disease. The results point to a need for a paradigm shift, said Michael Snyder, PhD, professor and chair of genetics. “I would argue that the way medicine is practiced is deeply flawed and could be significantly improved through longitudinal monitoring of one’s personal health baseline,” said Snyder, who holds the Stanford W. Ascherman, MD, FACS, Professorship in Genetics. “We generally study people when they’re sick, rarely when they’re healthy, and it means we don’t really know what ‘healthy’ looks like at an individual biochemical level.”

The researchers uncovered more than 67 clinically actionable health discoveries that ranged from high blood pressure, arrhythmias, cardiomyopathy and early stage cancer detection, among others. The study intertwined data from wearable technologies, genome sequencing and microbial and molecular profiling to establish a baseline of sorts for each participant. Every person’s broad swath of data painted a picture of their biological baseline, and as scientists tracked how that picture changed, they also kept tabs on any abnormalities that could signal the development of disease.

A paper describing the research findings were published May 8 in Nature Medicine. Snyder and Francois Haddad, MD, clinical associate professor of medicine, are co-senior authors. Sophia Miryam Rose, MD, PhD, instructor of neurosurgery, and Kévin Contrepois, PhD, scientific director at Stanford Metabolic Health Center, share lead authorship.

Outside of participant health, the researchers think they may have even discovered new biomarkers for certain diseases and possibly new molecular markers for cardiovascular disease risk, among other things. For now, these are preliminary findings; the researchers will have to conduct follow-up studies to confirm their suspicions.

“I can’t tell you exactly what we’re going to find if we follow a group of 100 people over time with advanced technologies, but I can tell you we will often find things that are important for their health,” Snyder said. “Right now, we’re pretty much in the dark until we profile people, but this approach could provide us a much better view of people’s norms, what it means to be healthy and what it means when people deviate from that. Ultimately, we want to shift the practice of medicine from treating people when they are ill to a focus on keeping them healthy by predicting disease risk and catching disease before it is symptomatic.”

Source: https://med.stanford.edu/news/all-news/2019/05/study-shows-how-big-data-can-be-used-for-personal-health.html
Lab-grown heart cells reveal secrets of "kissing bug" disease

by Krista Conger

People infected with the parasite Trypanosoma cruzi develop (among other symptoms) fever, aches, fatigue, diarrhea and vomiting. About 30 percent of those infected go on to develop chronic Chagas disease, which can cause long-term health complications including heart failure and digestive problems. Varieties of the bug are found in 28 states, mostly in the southern parts of the country. It is widespread in South America, and Chagas disease is estimated to contribute to more than 10,000 deaths each year.

Now cardiologist and stem cell researcher Joseph Wu, MD, PhD, together with visiting scholar Adriana Bozzi, PhD, have used lab-grown heart muscle cells called cardiomyocytes to investigate at a cellular level how the infection spread by the bugs affects cardiac function. They published their findings recently in Stem Cell Reports.

Source: https://scopeblog.stanford.edu/2019/05/21/lab-grown-heart-cells-reveal-secrets-of-kissing-bug-disease/

Failure to take statins leads to higher mortality

by Mandy Erickson

More than a third of patients with cardiovascular disease who have been prescribed statins to reduce cholesterol failed to take them daily. Women and non-whites were least likely to take their prescriptions, as were the oldest and youngest patients.

“The take-away for clinicians is not to become complacent about stable patients with cardiovascular disease,” said Stanford cardiologist Fatima Rodriguez, MD, the lead author of a study published in JAMA Cardiology. Rodriguez and colleagues examined the health records of 347,104 patients with atherosclerotic cardiovascular disease — caused by fatty deposits in their arteries — who had been prescribed statins. Even those who were pretty good — but not perfect — at picking up their prescriptions showed some increased mortality, Rodriguez said. Stanford cardiologist Paul Heidenreich, MD, the senior author of the study, said that physicians can often do more to encourage their patients to take their medications daily.

Source: https://scopeblog.stanford.edu/2019/02/14/failure-to-take-statins-leads-to-higher-mortality/

Recruitment for T32 Fellowships

Multi-Disciplinary Training Program in Cardiovascular Imaging T32 Training Grant - 2 Openings

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 U.S. 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.

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 Regulation 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.

http://med.stanford.edu/cvi/education/mechanisms-and-innovations-t32.html

Research Training in Myocardial Biology T32 Training Grant - 2 Openings

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.

http://med.stanford.edu/cvmedicine/education/timbs.html
Funding Opportunities

June 2019

2020 Sanofi Innovation Awards (iAwards). Eligibility: faculty with PI eligibility and CE faculty (with an approved CE faculty PI waiver) involved in multi-therapeutic areas including: immune-oncology, molecular oncology, immunology and inflammation, rare diseases, neurosciences, diabetes, and cardiovascular diseases. Deadline: June 29, 2019 to Lisa Chen at lisc@stanford.edu.

July 2019

AHA Merit Award. $200,000 per year for 5 years. Eligibility: Stanford tenured or tenure-track Associate Professors or higher, PhD and/or MD, PI on multiple active, national, peer-reviewed awards. Must devote 75% effort. Deadline: July 11, 2019 Letter of Intent; September 24, 2019 full proposal.

NIH Pathway to Independence Award. (Parent K99/R00 Independent Clinical Trial Required). Deadline: July 12, 2019. PA-19-129.


NIH/NHLBI Notice of Special Interest (NOSI): Bold New Bioengineering Research for Heart, Lung, Blood and Sleep Disorders and Diseases. Area of special interest in exploring bold, new bioengineering approaches or concepts that are important to a substantive heart, lung, blood or sleep area. Applications in response to this Notice must be submitted through NIH Parent Announcement: NIH Exploratory/Developmental Research Grant Program (Parent R21 Clinical Trial Not Allowed). Deadline: July 16, 2019. PA-19-053

AHA Institute for Precision Cardiovascular Medicine. AHA Grand Challenge: Precision Health and Precision Medicine. $250,000 per year for 4 years. Eligibility: Stanford faculty with PI eligibility and CE faculty (with an approved CE faculty PI waiver). Deadline: July 31, 2019.

August 2019


American Heart Association Postdoctoral Fellowship. Amount: $51,484 - $125,120. See guidelines for budget information. Deadline: August 15, 2019


NIH Director’s New Innovator Award Program (DP2 Clinical Trial Optional). Supports early stage investigators of exceptional creativity who propose highly innovative research projects with the potential to produce a major impact on broad, important problems relevant to the mission of NIH. Deadline: August 26, 2019. RFA-RM-19-006.

September 2019

NIH Director’s Pioneer Award (DP1 Clinical Trial Optional). Amount: $700,000. Deadline: September 6, 2019. RFA-RM-19-005.


Nina Starr Braunwald Research Award. Amount: up to $40,000 per year for 2 years. Eligibility: faculty with PI eligibility and CE faculty (with an approved CE faculty PI waiver); early-career women cardiac surgeon. Deadline: Sept. 15, 2019.

Nina Starr Braunwald Research Fellowship Award. Amount: up to $30,000 per year for 2 years. Eligibility: woman resident working in a cardiac surgical clinic or laboratory research program who has not yet completed cardiothoracic surgical training. Deadline: Sept. 15, 2019.


NIH Director’s Transformative Research Awards (R01 Clinical Trial Optional) (no budget limit). Deadline: Sept. 20, 2019. RFA-RM-007.
JUNE 2019


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


JULY 2019


American Heart Association Basic Cardiovascular Sciences Scientific Sessions. July 29-August 1, 2019. Westin Boston Waterfront, Boston, MA.

AUGUST 2019


American College of Cardiology ACC/SCAI Premier Interventional Cardiology Overview and Board Preparatory Course. August 8-11, 2019.


SEPTEMBER 2019


Interventional Cardiology Review Course for Boards and Recertification. September 6-8, 2019. Hilton Rochester Mayo Clinic, Rochester, MN.


American College of Cardiology 2019 Cardiovascular Service Lines 101 Webinar. 12-1 pm September 12, 2019.

Challenges in Clinical Cardiology: A Case-Based Update. September 27-29, 2019. Swissotel Chicago, Chicago, IL.

OCTOBER 2019

Echo in Congenital Heart Disease: Special Emphasis on Adult Congenital Heart Disease: Including Uses of Multimodality Imaging. October 2-5, 2019. Hyatt Regency Coconut Point, Bonita Springs, FL.

American College of Cardiology Core Curriculum for the Cardiovascular Clinician. October 2- 5, 2019. Washington, DC.

American College of Cardiology Heart Valve Summit: Medical, Surgical and Interventional Decision Making. October 3- 5, 2019. Chicago, IL.


Cases in Echocardiography, Cardiac CT, and MRI. October 23-26, 2019. The Meritage Resort, Napa, CA.

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

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.

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
- Closeout

Contact: Ed Finn, Clinical Trials Manager at efin@stanford.edu

CVI Cores

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.

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Contact: Joseph Wu, MD, PhD / joewu@stanford.edu
or Biobank manager, Yan Zhuge, PhD / 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. 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, at d.fleischmann@stanford.edu


April


May


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