

Sanjiv Sam Gambhir, Pioneer in Molecular Imaging, Leaves Behind a Legacy Article By Hanae Armitage

Sanjiv Sam Gambhir, MD, PhD, professor and chair of radiology at the Stanford School of Medicine and an internationally recognized pioneer in molecular imaging, died July 18 of cancer. He was 57. The Virginia and D.K. Ludwig Professor of Cancer Research, Gambhir dedicated his career to developing methods of early disease detection, ushering in a new era of molecular imaging to flag signals of disease in its nascent stages.

“Sam was a true visionary and a scientist of the highest caliber. His research and innovations have, with no uncertainty, founded modern medicine’s approach to early disease diagnostics and will continue to guide the future of precision health,” said Lloyd Minor, MD, dean of the School of Medicine. “Sam’s contributions to Stanford, to human health, to the science of diagnostics and to the many lives he has touched and impacted throughout his career have been immeasurable.”

Within the field of radiology, Gambhir was known for the development of positron emission tomography reporter genes, which can flag molecular activity that signals something’s gone awry in the body. To colleagues far and wide, he was known as a leader and scientist with sprawling expertise and a work ethic to aspire to. More than that, colleagues said he was a kind and generous friend, a nurturing mentor and a catalyst for collaboration. Thoughts and stories about Gambhir may be shared on this memorial page: <https://web.stanford.edu/group/radweb/cgi-bin/ssg/>.

<https://med.stanford.edu/news/all-news/2020/07/sanjiv-sam-gambhir-pioneer-in-molecular-imaging-dies.html>



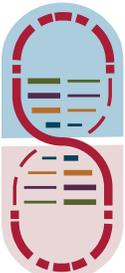
Sanjiv Sam Gambhir was a global leader in advancing techniques for molecular imaging and early cancer detection.

Stanford Cardiology & Heart Surgery Ranked 9th Nationwide by US News & World Report Article By Becky Bach

Recognizing Stanford Health Care’s commitment to safety and quality, U.S. News & World Report has included Stanford Hospital on the 2020-21 Best Hospitals Honor Roll. The honor roll ranks the leading 20 hospitals nationwide. “Providing high-quality, equitable care to patients in the Bay Area and beyond is core to Stanford Medicine’s mission,” said Lloyd Minor, MD, dean of the Stanford School of Medicine. “Earning a place on the U.S. News & World Report honor roll affirms our talented faculty and staff’s commitment to delivering the best possible outcomes for patients through a high-tech, high-touch approach to medicine.”

Stanford Health Care’s ranking for cardiology and heart surgery programs is on an upward trajectory, reaching ninth this year. The positive trend can be traced, in part, to increasing clinical volume, enhanced outcomes and a focus on complex operations performed at Stanford Hospital, including complicated valve repairs, minimally invasive surgeries, multi-organ transplantation, artificial heart device implantation and the use of innovative catheter-based technology, said Joseph Woo, MD, professor and chair of cardiothoracic surgery. “The rankings are a source of pride,” Woo said. Stanford Health Care’s success is also fueled by its location at Stanford University, Woo added. “We’re extraordinarily privileged to have the ability to integrate with scientists and engineers at a world-class institution. We’re delivering innovations directly to the operating room.”

<https://med.stanford.edu/news/all-news/2020/07/stanford-hospital-ranked-among-top-20-hospitals-nationwide.html>



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John Schiller, PhD: Deputy Chief, Laboratory of Cellular Oncology, National Cancer Institute

Doug Lowy, MD: Acting Director National Cancer Institute

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John Schiller, PhD
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National Cancer Institute



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Highlighted Speakers



Hal Barron, MD
CSO and President of R&D
GlaxoSmithKline



Roger Kornberg, PhD
Mrs. George A. Winzer Professor in Medicine
Stanford University
Nobel Prize in 2006



Wendy Young, PhD
Senior Vice President, Small Molecule Drug Discovery
Genentech



Robert Califf, MD
Head of Strategy and Policy
Verily Life Sciences and Google Health Divisions of Alphabet



Dean Li, MD, PhD
Senior Vice President, Discovery Sciences and Translational Medicine
Merck Research Laboratories



Elias Zerhouni, MD
Former President for Global R&D, Sanofi;
Former Director, NIH;
Former US Presidential Science Envoy



Jürgen Eckhardt, MD
SVP and Head of Leaps by Bayer
Bayer



Mathai Mammen, MD, PhD
Global Head of Research and Development
Janssen



Anthony Fauci, MD
Director, National Institute of Allergy and Infectious Diseases (NIAID)



Joan Mannick, MD
Co-Founder and Chief Medical Officer
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Levi Garraway, MD, PhD
Executive VP, Head of Product Development, CMO
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Mark Smith, MD, MBA
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Brian Kobilka, MD
Helene Irwin Fagan Chair in Cardiology
Stanford University
Nobel Prize in 2012



Janet Woodcock, PhD
Director of the Center for Drug Evaluation and Research (CDER)
FDA

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For more: <http://med.stanford.edu/cvi/support-our-research.html> and <http://cvi.stanford.edu>



*Joseph C. Wu,
MD, PhD*



*Cathy Hutton,
MBA*

Frontiers in Cardiovascular Sciences Seminar Series

Join us from 1:00- 2:00 pm Tuesday afternoons to hear the latest in cardiovascular and pulmonary research.

Zoom links and additional details available at <https://med.stanford.edu/cvi/mission/frontiers-in-cv-science.html>



September 15, 2020

DIANNA M. MILEWICZ, MD, PHD

President George H.W. Bush Chair of Cardiovascular Medicine, Vice Chair of the Department of Internal Medicine, Director of the Division of Medical Genetics, Director of the Medical Scientist Training Program and Director of the John Ritter Research Program, University of Texas Health Science Center at Houston, McGovern Medical School



November 3, 2020

ROBIN M. SHAW, MD, PHD

Director of the Nora Eccles Harrison Cardiovascular Research and Training Institute, Nora Eccles Harrison Presidential Endowed Chair and Professor of Medicine, University of Utah



September 22, 2020

ROBERT K. JACKLER, MD

Sewall Professor and Chair, Department of Otolaryngology-Head & Neck Surgery, Stanford University



November 10, 2020

YIBING QYANG, PHD

Associate Professor of Medicine (Cardiology) and of Pathology and Director of Yale Stem Cell Research Forum, Yale Stem Cell Center, Yale University School of Medicine



MASATAKA NISHIGA, MD, PHD

Postdoctoral Research Fellow, Joseph Wu Lab, Cardiovascular Institute, Stanford University



November 17, 2020

RHIAN M. TOUYZ, MBBCH, PHD

Professor, British Heart Foundation Chair in Cardiovascular Medicine and Director of the Institute of Cardiovascular & Medical Sciences, BHF Glasgow Cardiovascular Research Centre, University

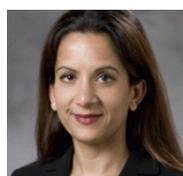
of Glasgow



September 29, 2020

SUMET S. CHUGH, MD

Price Professor and Associate Director of the Smidt Heart Institute, Medical Director of the Heart Rhythm Center, Director of the Center for Cardiac Arrest Prevention and Director of the Division of Artificial Intelligence in Medicine, Department of Medicine, Cedars Sinai



November 24, 2020

SVATI SHAH, MD, MHS

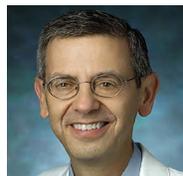
Professor of Medicine, Associate Dean of Genomics and Director of Precision Genomics Collaboratory, Director of Duke Adult Cardiovascular Genetics Clinic, Co-Director of Translational Research Duke Molecular Physiology Institute, and Vice-Chief of Translational Research, Division of Cardiology, Duke University School of Medicine



October 6, 2020

YING GE, PHD

Professor, Department of Cell and Regenerative Biology, Department of Chemistry and Director of Human Proteomics Programs, University of Wisconsin-Madison



December 1, 2020

CHARLES LOWENSTEIN, MD

Professor and Chief of Cardiology, Co-Director of John Hopkins Heart and Vascular Institute and Professor of Medicine, John Hopkins



October 13, 2020

YOUNG-SUP YOON, MD, PHD

Director of Stem Cell Biology, Bruce R. Logue Chair of the Division of Cardiology and Professor of Medicine and Biomedical Engineering, Emory University School of Medicine



December 8, 2020

PILAR ALCAIDE, PHD

Kenneth and JoAnn G. Wellner Professor and Associate Professor of Immunology, Tufts University School of Medicine



October 20, 2020

KALYANAM SHIVKUMAR, MD, PHD

Professor of Medicine (Cardiology) & Radiology, Bioengineering, Director of the UCLA Cardiac Arrhythmia Center & EP Programs, Director & Chief of the UCLA Interventional CV Programs & Cardiac Catheterization Laboratories, David Geffen School of Medicine & UCLA Health System and Editor-in-Chief, JACC: Clinical Electrophysiology



December 15, 2020

KATHERINE YUTZEY, PHD

Professor Molecular Cardiovascular Biology The Heart Institute, Cincinnati Children's Medical Center



October 27, 2020

LI QIAN, PHD

Associate Professor of Pathology and Laboratory Medicine, Associate Director of McAllister Heart Institute, and Faculty Director of UNC Human Pluripotent Stem Cell Core, UNC School of Medicine

Host: Joseph C. Wu, MD, PhD

Email: joewu@stanford.edu

<https://med.stanford.edu/cvi/mission/frontiers-in-cv-science.html>

From the Heart: Stanford Cardiology Chief Reflects on His Experience as a Black Physician

By Lindsey Baker

Eldrin Lewis, MD, MPH, is chief of cardiovascular medicine at Stanford. But during his career as a Black physician, assumptions made about him and his role in medicine have made it clear that many people, including colleagues, patients and police, see all Black men in the same way.

"What it made me realize," Lewis writes in a Medscape commentary, "is that I could have easily been George Floyd. Because if I get pulled over, they will treat me just like every other Black man. I always drive with my hospital ID in the car. I always keep my hands in plain sight. I have that level of anxiety every time I get behind the wheel of my car."

Growing up in the Mississippi Delta, Lewis's upbringing was shaped by race and racism. His history book featured a Confederate flag on the cover. His high school did not hold a desegregated prom until 1987. "Even though I was valedictorian of my high school," he reflects, "not a single counselor told me I should apply to Harvard or Yale or Princeton or Cornell. They didn't give me any advice. I had no clue."

Lewis eventually left Mississippi. He earned degrees from Penn State University, the University of Pennsylvania and Harvard University, and he trained at Brigham and Women's Hospital, where he also worked and taught. But Lewis did not escape racism when he moved north. He writes: "When I went away to school, what I thought was, 'I'm leaving Mississippi. I know there's racism here. But in Pennsylvania, that's the north and it'll be fine.' But you see the same racism — maybe not the same degree, but you see it."

In the essay, Lewis describes some of the indignities he's faced throughout his career, such as hearing racial epithets or being repeatedly asked where he went to medical school. He writes about being mistaken for a patient transporter, even though he was dressed in his white coat and carrying a stethoscope. "Every part of the hospital, every job is truly important, and we all work together," he writes, "but it's frustrating when you work so hard for so long — four years of college, four years of medical school, and seven years of training — and you get confused for transport."

Black patients also face racial prejudice, and the health consequences can be severe, Lewis writes. "One thing that's hard for me, for many reasons, are the poor outcomes we see in so many Black cardiology patients. I lost a family member at an early age from a heart attack," he writes. "He lived in a small town in Mississippi. He had a heart attack at the typical time you have a heart attack, 1:00 in the morning." He continues: "Why are there more complications in Black patients? Are our arteries different, or is the quality received from the doctor different? ... There are a lot of times we have to look in the mirror as physicians and say, 'Do we care enough?'"

Lewis joined Stanford as the chief of cardiovascular medicine in March. He sees the role as an opportunity to make lasting contributions that will benefit his Black patients, trainees and colleagues. "If you look at the top cardiology programs, there are only three Black chiefs of cardiovascular medicine," he writes. Just by being here, Lewis hopes he will help clear the path for others: "I'm excited to be the new chief of cardiovascular medicine at Stanford. I'm hoping by being here and doing a good job, others will say, 'I can do that, too.'"

<https://scopeblog.stanford.edu/2020/08/04/from-the-heart-stanford-cardiology-chief-reflects-on-his-experience-as-a-black-physician/>



Eldrin Lewis, MD, MPH, chief of cardiovascular medicine at Stanford Medicine, says in a commentary, "We have to look in the mirror as physicians and say, 'Do we care enough?'"



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Precision Drug Design: Using Patient Cells to Improve Treatments *By Amanda Chase, PhD*



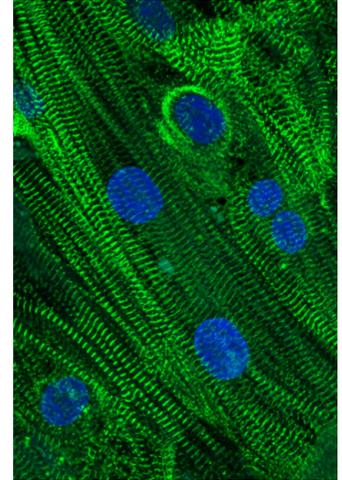
14 years ago, it was found that skin or blood cells could be turned back into an embryonic-like type of cells that can then be turned into any other cell type. These cells, called induced pluripotent stem cells (iPSCs), can be directed to become specific types of adult cells, such as heart cells (cardiomyocytes; CMs). Importantly, differentiated cells derived from iPSCs recapitulated disease features of the patients not seen in cells from healthy patients. The reproduction of human disease in the cell culture dish makes it possible to directly evaluate the effects of new drugs that are under development, without the risk of treating the patients themselves.



Wesley McKeithan, PhD

Mark Mercola, PhD

Despite the promise iPSCs hold for the drug discovery, only a few large-scale drug development efforts have used iPSCs. A group of researchers, led by first author Wesley McKeithan, PhD, and senior-author Mark Mercola, PhD describe, for the first time, the use of iPSCs in large-scale drug development in the journal *Cell Stem Cell*. Their study, conducted in collaboration with John Cashman, PhD, used heart cells from patients with a heart rhythm disorder to chemically refine a drug used to treat the disease, showing the potential for precision drug design.



Human cardiomyocytes derived in vitro from induced pluripotent stem cells (iPSCs). Membranes are stained with a fluorescent probe.

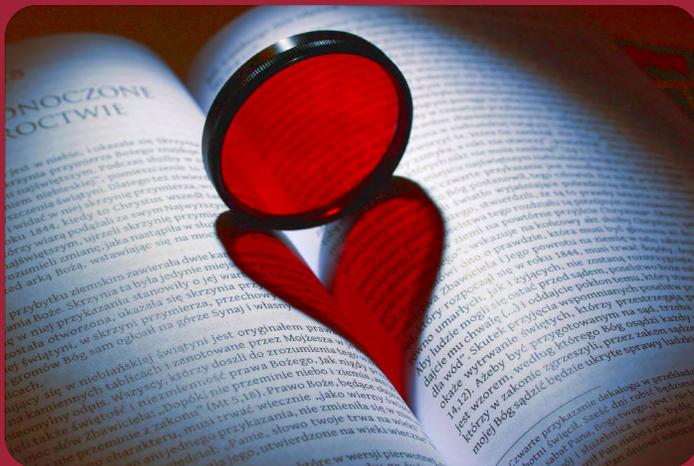
Long QT syndrome (LQTS) is a heart rhythm disorder that represents a leading cause of sudden death in younger patients. Mexiletine is a drug that stabilizes heart rhythm, and is considered to be an especially good therapy for certain forms of LQTS, however it has side effects. iPSCs turned into cardiomyocytes (iPSC-CMs) from patients with LQTS provide the opportunity to identify improved treatments. Using cells from a patient with LQTS, the research team was able to determine how well the drugs could stabilize the heartbeat, and if any were more efficacious than mexiletine. The researchers also used iPSCs from healthy individuals to test for unwanted side effects. “We used this information to iteratively test many structural analogues of mexiletine, to discover the reasons for good and bad effects, and to ultimately design a better version,” says Dr. Cashman.

Ultimately, the team identified several refined versions of mexiletine. Perhaps more importantly, they showed, for the first time, that iPSC-CMs from patients with a specific disease can guide drug optimization in a large-scale manner. “Our approach demonstrates the feasibility of introducing human disease models earlier in the drug development pipeline and opens the door for precision drug design to improve therapies for patients,” says Dr. McKeithan.

http://med.stanford.edu/cvi/mission/news_center/articles_announcements/precision-drug-design-using-patient-cells-to-improve-treatments.html

CVI Seed Grant Awards

Due October 1, 2020



Our goal is to ignite and support new ideas that will change how we diagnose and treat cardiovascular disease. To achieve this mission, the CVI is offering two calls for Seed Grant Proposals. We highly encourage proposals that establish new interdisciplinary collaborations. Focus on topics relevant to COVID-19 are welcome.

2020 Stanford CVI Seed Grant Competition:

Maternal and Child Health

Sudden Cardiac Death

Eligibility: Stanford faculty or instructor CVI members

Application and more information: <https://med.stanford.edu/cvi/funding-opportunities/current-seed-grants.html>

Clinical Trial in a Dish: A Novel Strategy for Drug Development in Heart Disease

By Amanda Chase, PhD



Dilated cardiomyopathy (DCM) is a disease of the heart muscle that decreases the heart's ability to pump blood, which can lead to irregular heartbeats (arrhythmias), blood clots, heart failure, or sudden cardiac death. While there are several contributing factors to the development of DCM, it is known that up to one-third inherit it from their parents: familial DCM. Familial DCM is known to be caused by changes in different genes, the most common being variants (mutations) in the gene that encodes what is known as lamin A and C (LMNA). Although LMNA-associated DCM accounts for 6% of all familial cases, there are no targeted drug to prevent onset or progression of the disease, and the mechanisms that result in the disease are not known.

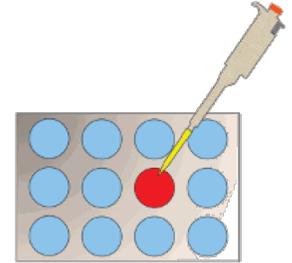


Nazish Sayed, MD, PhD



Chun Liu, PhD

Stanford CVI scientists, Nazish Sayed, MD, PhD, and Joseph Wu, MD, PhD, addressed both important needs in a paper recently published in *Science Translational Medicine*. They studied a large family cohort spanning four generations that had LMNA-associated DCM. Induced pluripotent stem cells (iPSCs), adult blood cells that were reprogrammed into stem cells, made from this family (members with DCM and healthy controls) allowed researchers to directly address questions of mechanism, especially in the tissue lining blood vessels and heart (endothelium). As iPSCs can be turned into any other kind of cells, the team generated iPSC-derived endothelial cells (iPSC-ECs) and were able to confirm a direct link between the mutation in LMNA and the narrowing of large blood vessels.



Clinical trials in-a dish: A revolutionary strategy for drug development and precision medicine.

Using next-generation sequencing, Stanford CVI researchers were able to identify a protein that plays a crucial role in mediating EC dysfunction in these cardiomyopathy family members. With the target identified, the team leveraged the iPSC platform to conduct a "clinical trial in-a dish" to identify drugs that could alleviate their observed clinical EC dysfunction. Importantly, they found that lovastatin can help restore endothelial cell function. "This was a significant discovery as it allowed us to repurpose lovastatin, an already FDA-approved drug for cardiomyopathy and allowed us to move from cells to patients", said Dr. Wu.

This study has important findings for understanding and treating a common form of DCM, and provides a potential therapeutic for delaying progression. Equally important, it demonstrates a workflow for identifying and validating potential drug treatments for patients that includes iPSCs (clinical trial in-a-dish).

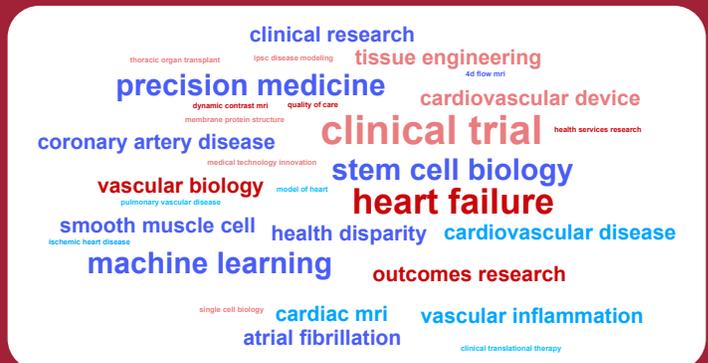
https://med.stanford.edu/cvi/mission/news_center/articles_announcements/clinical-trial-in-a-dish--a-novel-strategy-for-drug-development.html

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A Subset of Cells That Can Break Your Heart By Adrienne Mueller, PhD

Every year, approximately 1 out of every 3850 babies in the US is born with a heart defect called hypoplastic left heart syndrome (HLHS). This disorder is characterized by the underdevelopment of heart valves as well as the left ventricle, the main pumping chamber of the heart (Figure). However, the cause for why these hearts develop abnormally is not well understood. Scientists have long sought the mechanism responsible for the developmental abnormalities in the heart muscle of HLHS patients, however, the cells that exhibit deficits that could help explain the malformation seen in HLHS hearts remain elusive. Recently, a group of Stanford Cardiovascular Institute and affiliated researchers report the identification of endocardial cells as a key cell type in heart of HLHS patients responsible for the onset of this disease.

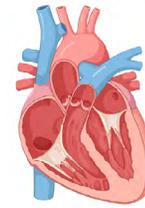
Endocardial cells are specialized cells that form the innermost layer of the heart wall, also known as the endocardium. The endocardium is very important for heart development. Interactions between endocardial cells and heart muscle cells are also important for maturation of the heart chambers. Since HLHS is characterized by structural abnormalities in the valves and underdevelopment of the left ventricle, it has been speculated that a defect in the endocardium may be the mechanism underlying HLHS.

To test this hypothesis, a group of scientists, led by co-first authors Yifei Miao, PhD and Lei Tian, PhD and senior author Mingxia Gu, MD, PhD, compared the endocardial cells derived from human induced pluripotent stem cell (hiPSCs) from healthy individuals and individuals with HLHS. In collaboration from members of Sean M. Wu, MD, PhD lab, the investigative team sought to identify differences in the genes expressed between these two groups. The investigators employed single-cell RNA-sequencing to profile genes expressed in endocardial cells derived from HLHS patients and normally-developing endocardial cells. By carefully profiling the expression of the different cells they collected, the investigators identified a subpopulation of endocardial cells that were developmentally impaired in HLHS hiPSC-derived endocardial cells. These investigators then went on to demonstrate that the HLHS hiPSC-derived endocardial cells were functionally impaired in several ways. Several key signaling pathways important for valve development were suppressed. The interface between the endocardium and the heart muscle was abnormal. And, the ability to develop new vessels was impaired. This study, recently reported in *Cell Stem Cell*, has uncovered a mechanism that helps to explain the congenital heart defects seen in HLHS patients. Not only does this work help explain the cause of HLHS, but it suggests that approaches that focus on endocardial function could be a fruitful avenue for treating other heart diseases.

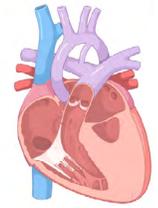
https://med.stanford.edu/cvi/mission/news_center/articles_announcements/a-subset-of-cells-that-can-break-your-heart.html



Normal Heart



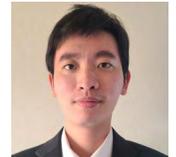
HLHS Heart



Hypoplastic left heart syndrome (HLHS) is characterized by the underdevelopment of heart valves as well as the left ventricle, the main pumping chamber of the heart.



Yifei Miao, PhD



Lei Tian, PhD



Mingxia Gu, MD, PhD

CVI Undergraduate Summer Research Program



This summer 21 phenomenal undergraduate students participated in Stanford CVI's 10-week long virtual research program. In addition to attending over fifty scientific, professional development and social events hosted by Stanford CVI members and affiliates, the students also partook in career development and scientific events hosted by AHA-SURE partner institutions: Boston, Northwestern and Vanderbilt Universities. However, the majority of our students' remote training was accomplished in the labs of their fantastic Mentors:

Daniel Bernstein	Alison Marsden	Yasuhiro Shudo
Vivek Bhalla	Patricia Nguyen	Edda Spiekerkoetter
Vinicio de Jesus Perez	Marlene Rabinovitch	Katrin Svensson
Michael Fischbein	Kristy Red-Horse	Joseph C. Wu
Rongliu Liao	Fatima Rodriguez	Sean Wu
Michael Ma	Elsie Ross	Phillip Yang

For more information and to view the CVI Undergraduate Summer Research Program Symposium visit:

<https://med.stanford.edu/cvi/education/aha-cvi-undergraduate-summer-research-program.html>

Applications for Summer 2021 open October 15th!

This program is supported by an AHA institutional undergraduate award, the AHA SURE pilot program dedicated to increasing the pipeline of individuals from underrepresented racial and ethnic groups in science, and an NIH NHLBI R25 award dedicated to increasing diversity in health-related research.

When Angelina Cossey Dellacqua finally got the liver transplant her mother had been praying for, she was already so sick and weak that it remained a daily struggle to survive. “Angelina required maximal support and close care throughout the day and night,” said June-Wha Rhee, MD, who was a cardiology fellow at Stanford Medicine at the time. “She used to be a healthy, active young mother. She was a fighter, so motivated to get better for her 3-year-old daughter.”

But on Oct. 19, 2015, Dellacqua died of acute heart failure due to a complication of an underlying disorder called hemochromatosis, which causes a toxic buildup of iron in various organs of the body. She was 29.

The memory of Angelina Dellacqua, and other patients like her, has been the motivation behind Rhee’s subsequent years of research to find a treatment option that could have saved the young mother’s life. In a recently published study in *Cell Reports*, Rhee and her colleagues determined that a drug called ebselen may be able to prevent heart failure in patients with iron-overload disease.

“We were able to use technology developed in our lab to come up with a model to show the mechanisms of iron overload in the heart,” said Joseph Wu, MD, PhD, director of the Stanford Cardiovascular Institute and senior author of the study. “We previously developed this technique using stem cells so that it can be used to screen medications for various forms of heart toxicity, such as this one.”

Hemochromatosis is a common condition in which excess iron can lead to multiorgan dysfunction and damage. Excess iron deposits in the heart can cause heart failure, which is what happened in Dellacqua’s case.

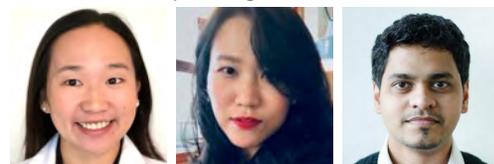
To investigate the effects of iron overload in the heart, the researchers developed cardiomyocytes, or heart cells, in the lab from induced pluripotent stem cells, which can be coaxed into many tissue types. The cardiomyocytes were further developed into uniformly sized, three-dimensional spheroids of thousands of cells. Each spheroid was about the size of a grain of sand. “These ball-shaped cell clusters are spontaneously beating in synchrony,” said Dilip Thomas, PhD, a postdoctoral scholar in Wu’s lab. Thomas created the spheroids to mimic the mature cell function of a human heart. To mirror iron-overload disease in the lab, the researchers exposed the balls of heart cells to increasing concentrations of iron. As expected, they saw a similar darkening of the heart tissue in MRI images of the miniature heart spheroids, indicating toxic buildup of iron. Further investigations led to a better understanding of the molecular mechanisms of the disease, and researchers were able to identify the channels used by the iron to enter the heart cells.

“I’m so sorry I had to lose my girl, but I’m so glad that they are doing research so that someone else can be alive today,” Vickie Dellacqua said. “I call it Angelina’s research. I never want anybody to forget her.”

<https://med.stanford.edu/news/all-news/2020/09/researchers-find-potential-cure-for-deadly-iron-overload-disease.html>



Angelina Cossey Dellacqua, who died of iron overload, with her daughter. Picture courtesy of Vickie Dellacqua, Angelina’s mother.



June-Wha Rhee, MD Hyoju Yi, PhD Dilip Thomas, PhD



CVI Grant Writing Workshops

CVI K Club

Wednesday, September 23, 2020
from 9-11 am

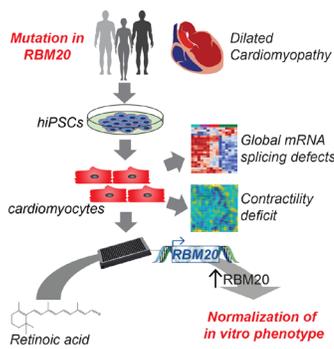
A 2-hour session that will provide support and peer-review feedback on your Specific Aims to enable you to write your strongest proposal.

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A family with inherited dilated cardiomyopathy (DCM) was found to have a specific change in RBM20. The induced pluripotent stem cell (iPSC) platform was used to make heart cells (cardiomyocytes) to understand how the mutation leads to DCM. The platform also shows that retinoic acid could be a therapy to increase levels of RBM20 to treat DCM.



Francesca Briganti, PhD



Han Sun, PhD



Mark Mercola, PhD



Lars Steinmetz, PhD

Using Genetics and Personalized Medicine to Treat Cardiovascular Disease

By Amanda Chase, PhD



Dilated cardiomyopathy (DCM) is a leading cause of heart failure, affecting 1 in 250 people. DCM is characterized by an increase in the left ventricle of the heart, the main pumping chamber. DCM is also the most common reason for heart transplant. Despite years of work to improve patient survival after transplantation, there is still only a 10-year survival rate of 50%. DCM patient health, therefore, would be significantly improved with better treatment options prior to the need for a heart transplant.

Many instances of DCM are caused by inherited changes (mutations) in a person's DNA. Yet, despite detailed knowledge of the mutations, there are no mutation specific therapies. The relatively recent ability to make cardiomyocytes from induced pluripotent stem cells (iPSC-CMs) has made it possible to model and understand genetic heart disease as well as search for treatments. A group of researchers, led by first-authors Francesca Briganti, PhD, and Han Sun, PhD, and senior authors Mark Mercola, PhD, and Lars Steinmetz, PhD, in collaboration with Ioannis Karakikes, PhD, used a combination of iPSC-CMs and genome editing to identify a new mutation causing DCM and in doing so discovered a potential treatment option.

In their paper, recently published in *Cell Reports*, the researchers had the unique opportunity to study a single family with inherited DCM to understand the cause of their disease. As an inherited disease, information on the genome, or complete set of DNA and genes, can provide important information on the mutation causing the disease. Each gene contains instructions for making a specific protein needed by the cell, including changes in the protein that result in diseases such as inherited DCM. In this case, the team compared the genomic pieces that make up the proteins (the exome). By studying a family, they were able to look for differences in the exomes of someone who had passed away with a diagnosis of DCM, had been diagnosed with DCM, or was unaffected by DCM. This comparison allowed them to find a single mutation (P633L) in a protein, RBM20, that was disease causing.

The iPSC-CM platform is a powerful tool for studying specific cardiovascular diseases such as inherited DCM. Importantly, the iPSC-CM platform also allowed the researchers to test the use of a potential treatment of DCM. The researchers were able to show that using drugs to increase the levels of RBM20 in the heart cells is a promising treatment option for inherited DCM patients, and potentially as a general approach for patients with other diseases.

https://med.stanford.edu/cvi/mission/news_center/articles_announcements/using-genetics-and-personalized-medicine-to-treat-cardiovascular.html

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An Improved Stem Cell-Based Treatment for Peripheral Arterial Disease By Adrienne Mueller, PhD



Peripheral arterial disease (PAD) is a significant disorder that affects over 10 million people in the United States. PAD is caused by a narrowing of the blood vessels in the arms and legs. Currently, we treat PAD with surgical interventions, such as grafting vessels into the affected limb to try to restore blood flow. Unfortunately, many patients, especially those with severe forms of the disease, lack suitable vessels for this surgery. There is therefore a pressing need for alternative treatments. Delivering stem cells into the affected limb could help regenerate new vessels to support blood flow.



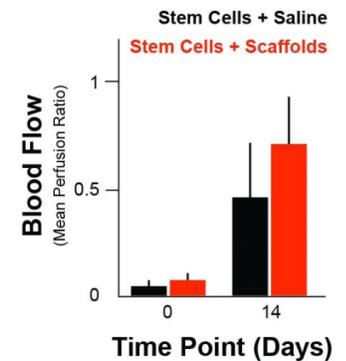
Caroline Hu



Ngan Huang, PhD

One challenge holding back the deployment of stem cells to treat PAD is their poor initial survival when they are delivered into tissue. First author Caroline Hu and senior author Ngan Huang, PhD recently investigated the use of a novel delivery mechanism: nanofibrillar scaffolds. As their recent paper in *Frontiers in Bioengineering and Biotechnology* describes, the authors delivered a cocktail of stem cells into mice exhibiting PAD using either saline or nanofibrillar scaffolds as the vehicle. The researchers found that using nanofibrillar scaffolds to deliver stem cells into the limbs of PAD-like mice resulted in a significantly higher blood perfusion in the affected limbs. This study therefore shows that using nanofibrillar scaffolds to deliver stem cells into tissue with reduced blood flow is an extremely promising method to improve stem cell-based treatments for PAD.

https://med.stanford.edu/cvi/mission/news_center/articles_announcements/an-improved-stem-cell-based-treatment-for-peripheral-arterial-disease.html



Blood flow in the affected limbs of mice treated with stem cells and saline or stem cells with nanofibrillar scaffolds at day 0 and day 14 post-treatment.

Enabling Maturation for Improved Heart Cell Modeling By Amanda Chase, PhD



Fourteen years ago, groundbreaking work showed that the development clock could be turned back on adult skin and blood cells to make stem cells that could be turned into any other kind of cell. These cells, called induced pluripotent stem cells (iPSCs), opened the door for improved, personalized patient health by creating an ideal model for studying disease, drug development, and the opportunity to one day do tissue and cell transplants with patient-derived cells to eliminate the risk of rejection. Cardiovascular medicine is one of the many fields that continues to benefit from iPSCs; the ability to produce human cardiomyocytes (heart muscle cells) from iPSCs (iPSC-CMs) has allowed an unprecedented ability to model human heart disease. Current ways of making iPSC-CMs result in a more fetal-like cardiomyocyte, making it harder to model diseases that usually occur in older adults. Having the ability to make more mature iPSC-CMs is crucial for accessing the full potential of iPSC-CMs and the chance to create better therapeutics for CVD.



Wesley McKeithan, PhD



Dries Feyen, PhD



Mark Mercola, PhD

A team of CVI-affiliated researchers, led by first authors Dries Feyen, Wesley McKeithan, and Arne Bruyneel and senior author Mark Mercola, recently described a new way to enable maturation of iPSC-CMs in *Cell Reports*. Cells, including iPSC-CMs, are maintained by carefully providing the ideal environment for growth, which requires the correct media formulation to provide nutrients and other supplements. Dr. Mercola and his team created a new media that is better adapted to the needs of cardiomyocytes to allow maturation of iPSC-CMs. They were able to show that the iPSC-CMs in their newly developed maturation media had hallmarks of more mature adult CMs. The findings presented in this paper have the ability to significantly improve iPSC-CMs as a model for cardiovascular diseases. The ability to have more mature iPSC-CMs will allow researchers to study CVD, usually associated with adults, in a more relevant model, and has the potential to be widely applied for both basic and translational research goals.

https://med.stanford.edu/cvi/mission/news_center/articles_announcements/enabling-maturation-for-improved-heart-cell-modeling.html

Staff Spotlight

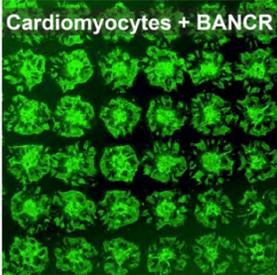
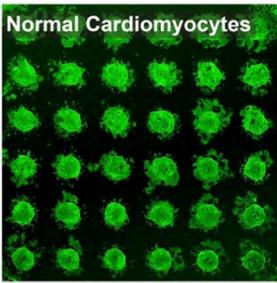


Ying Wong recently celebrated her 5th anniversary at Stanford. At CVI, she monitors grant spending, provides financial projections for future planning, and helps her teammates to support CVI's PIs.

One of her favorite parts of working at CVI is being able to work hard while maintaining balance. CVI trusts her to produce high-quality work, and maintaining that trust keeps her engaged and excited. At the same time, she loves that her job enables her to take good care of her family and to enjoy her other passions in life.

Little known fact about Ying? She needs to sleep at least 9-10 hours a night in order to feel alert.





BANCR boosts migration of human cardiomyocyte stem cells.



Kitchener D. Wilson, MD, PhD



Mohamed Ameen



Hongchao Guo, PhD

When Viruses Give Back: How BANCR Helps Hearts Develop

By Adrienne Mueller, PhD



Endogenous retroviruses (ERVs) are viruses that incorporated themselves into our genome so long ago that our systems now consider them part of us. Almost all of the research we perform is on the 2% of our genome that is made up of protein-coding DNA, not the 98% of our genome that is comprised of non-coding DNA, including ERVs. ERVs can often be harmful—studies have linked them to cancer, schizophrenia, diabetes, and multiple sclerosis. But sometimes ERVs are integrated to such an extent that our cells are now using them as part of their own machinery. Joining this latter group of co-opted viruses is one that entered our genome tens of millions of years ago: BANCR.

A group of scientists led by first authors Kitchener D. Wilson, MD, PhD, Mohamed Ameen and Hongchao Guo, PhD, and senior author Joseph C. Wu, MD, PhD recently demonstrated how endogenous retrovirus-derived BANCR contributes to primate heart development. In their recent report in *Developmental Cell*, Wilson et al first showed that retrovirus-derived BANCR is specifically present in human fetal heart muscle cells (cardiomyocytes), as well as the cardiomyocytes of other large non-human primate species' such as gorilla, chimpanzee and rhesus macaques. The fact that BANCR was specifically present in fetal heart muscle cells suggested that it was important for heart development. The scientists then showed that BANCR actually helps heart muscle cells to move and migrate across a petri dish. Lastly, they introduced BANCR into rodents that do not normally have

this gene and found that it enlarges their hearts. These results, combined with their findings that children with enlarged hearts have high expression of BANCR, and also the fact that only larger primate species have BANCR, led the authors to hypothesize that BANCR promoted increased heart size during primate evolution.

As Dr. Wilson states, "It is likely that many more examples of viruses impacting evolution are yet to be discovered. Recent technologies such as stem cells and genomics will help us understand just what exactly this 'viral' genome is doing in human health and disease."

https://med.stanford.edu/cvi/mission/news_center/articles_announcements/when-viruses-give-back-how-ban-cr-helps-hearts-develop.html

Calcineurin Bound: A New Mechanism to Help Explain Heart Failure

By Adrienne Mueller, PhD

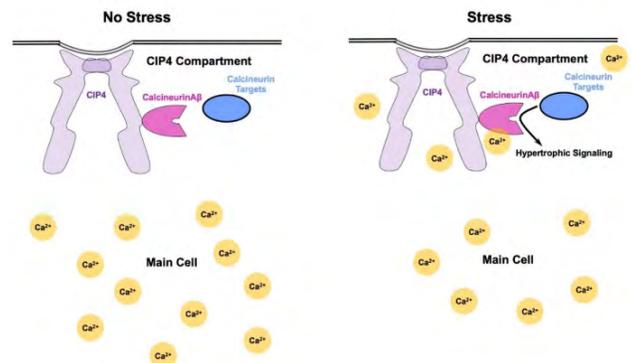


Chronic stress can ultimately lead to heart failure. One explanation for this is that stress-related signals trigger an unwarranted and pathological growth of our heart cells. These pathologically enlarged (hypertrophic) heart cells do not function well, which causes the heart to pump blood poorly, eventually resulting in heart failure.

A protein that plays a central role in this pathological heart cell enlargement is the Ca²⁺-activated protein Calcineurin Aβ. Once activated by Ca²⁺, Calcineurin Aβ causes a cascade of signals that lead to hypertrophy. What is perplexing about this is that heart cells are flooded with calcium all the time—with every heartbeat. A group of CVI-affiliated researchers, including co-first author Jinliang Li, PhD, and senior author Michael Kapiloff, MD, PhD, uncovered not only an explanation for this conundrum, but also a mechanism for how stress could lead to heart failure and a potential means of preventing it.

In their recently published paper in *Circulation*, Li & Li et al demonstrate that in heart cells, Calcineurin Aβ is restricted to cellular "compartments" that shield it from the large Ca²⁺ transients that occur when our heart beats. When the system is pathologically stressed, Ca²⁺ may break into these compartments, activating Calcineurin Aβ, leading to hypertrophy. Li & Li et al not only showed that Calcineurin Aβ is localized to these compartments, but also that stopping the tethering of Calcineurin Aβ in the compartments reduced pathological heart cell enlargement both in cultured heart cells and in living mice. Their results suggest that therapies that disrupt Calcineurin Aβ CIP4-tethering are a promising avenue to help prevent heart failure.

https://med.stanford.edu/cvi/mission/news_center/articles_announcements/calcineurin-bound-a-new-mechanism-to-help-explain-heart-failure.html



Our heart cells use molecular compartments to keep Ca²⁺ away from Calcineurin Aβ, which would normally elicit a cascade of signals resulting in hypertrophy. When the system is pathologically stressed, Ca²⁺ may enter these compartments, activating Calcineurin Aβ, leading to hypertrophy.



Jinliang Li, PhD



Michael Kapiloff, MD, PhD

Treating the Heart of the Matter: Learning How to Prevent Plaque Formation By Amanda Chase, PhD

Heart disease is the leading cause of death in the US for both men and women. Heart disease generally involves narrowed or blocked blood vessels that ultimately restrict blood flow. The narrowing of vessels is caused by a build-up of fats and cholesterol, as well as inflammatory cells, that result in plaque formation, a process called atherosclerosis. Risk factors for atherosclerosis include high cholesterol, high blood pressure, smoking, and diabetes, among others. To date, there are no therapies directly targeting the cells responsible for plaque formation, which could significantly reduce cardiovascular risk beyond what is possible with current therapies.



Ying Wang, PhD



Nicholas Leeper, MD

A team of Stanford researchers, led by first author Ying Wang, PhD, and senior author Nicholas Leeper, MD, aimed to address this unmet need. Previous work has suggested that vascular smooth muscle cells (SMCs), which line the blood vessels, can lose specialized characteristics and can express stem cell markers. These cells give rise to the majority of cells within the plaque and could therefore be a therapeutic target. The therapeutic potential of these atherosclerotic stem cells relies on an understanding how the cell promotes plaque formation and how it escapes the immune system. In a paper recently published in *PNAS*, Dr. Leeper and his team were able to address those questions and to propose a novel approach for lessening plaque burden.

Dr. Leeper and his team found that a defect in macrophages makes them unable to correctly see the atherosclerotic stem cells as a threat, and they also found that there is an increase in the presence of a “don’t eat me” signal (CD47) on the cells, providing further protection from macrophages. Combined, this results in a survival advantage for atherosclerotic stem cells, explaining their ability to form plaques. Dr. Leeper and his team were able to show that blocking CD47 restored macrophage function, reduced the continued expansion of the number of cells, and resulted in a decreased chance of plaque formation. The results of this work suggest, therefore, that therapies targeting CD47 could provide treatment to reduce plaque formation by directly treating cells responsible for forming plaques and reducing cardiovascular risk to a level not possible with current methods.

https://med.stanford.edu/cvi/mission/news_center/articles_announcements/treating-the-heart-of-the-matter-learning-how-to-prevent-plaque.html

Understanding Emphysema: The Role of HIF-2α By Adrienne Mueller, PhD

Pulmonary diseases like emphysema are the third leading cause of death in the US and the fourth leading cause worldwide. Emphysema occurs when air sacs in the lungs are damaged; such as after exposure to smoke, air pollution, or chemical fumes and dust. As emphysema gets worse, the walls of the air sacs weaken and rupture, creating larger air spaces inside the lungs. Despite emphysema’s broad prevalence and severe outcomes, current treatment methods target symptom relief – not prevention or reversal of the disease itself.



Shravani Pasupneti, MD



Xinguo Jiang, MD, PHD



Mark Nicolls, MD

Smoke inhalation, one of the primary causes of emphysema, has been shown to cause a decrease in the expression of a particular protein that is enriched in the lungs: HIF-2α. Given the facts that 1) smoke inhalation triggers a decrease in HIF-2α, and 2) HIF-2α has a known important role in oxygen processing and maintaining lung air sac architecture, a group of scientists including first author Shravani Pasupneti, MD, senior authors, Xinguo Jiang, MD, PHD and Mark Nicolls, MD of Stanford University and Nobel-Laureate Gregg Semenza, MD, PhD of Johns Hopkins, chose to investigate whether changes in HIF-2α levels could be directly responsible for emphysema. In their study, recently published in the *American Journal of Respiratory and Critical Care Medicine*, the authors used genetic manipulations to both decrease and increase HIF-2α levels. When they decreased HIF-2α levels in mice, they were able to recreate the lung pathology of emphysema. They also demonstrated that the presence of HIF-2α is protective. Increasing levels of HIF-2α in mice prevented the animals from the pathological air sac enlargement and cell death that is typical in emphysema. Combined, Pasupneti et al’s results show that loss of HIF-2α function could be directly responsible for the symptoms seen in individuals with emphysema. Identifying ways to preserve HIF-2α function is therefore a promising opportunity for therapies that would limit emphysema progression – or even prevent emphysema in at-risk patients.

https://med.stanford.edu/cvi/mission/news_center/articles_announcements/understanding-emphysema-role-of-hif-2a.html

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Sacubitril/Valsartan Act on Exosomes to Facilitate Heart Repair By Adrienne Mueller, PhD



Heart failure is a major source of hospitalizations and deaths worldwide. When heart cells, or cardiomyocytes, are damaged due to heart failure, cellular signaling pathways are activated to help repair the damage. The drug sacubitril/valsartan (Entresto™) acts on two major pathways involved in cardiomyocyte health and significantly increases survival of heart failure patients. What is the molecular mechanism that mediates sacubitril/valsartan's effects? A novel possibility is that sacubitril/valsartan could influence cardiomyocyte health through cardiomyocyte exosomes. Exosomes are vesicles, filled with small molecules such as microRNAs, that cells release to communicate with other nearby cells.



Evgeniya Vaskova, PhD



Phillip Yang, MD

A team of scientists led by first-author Evgeniya Vaskova, PhD, and senior-author Phillip Yang, MD, addressed the question of whether exosomes were involved in mediating the therapeutic effects of sacubitril/valsartan in a recent study published in the *Journal of the American Heart Association*. They tested the effects of sacubitril/valsartan on stem cell-derived cardiomyocytes that either had or had not been deprived of oxygen. They also looked at the effect of the drug on cardiomyocyte health in rodents with heart attacks. In both experiments, treatment with sacubitril/valsartan improved cardiomyocyte function and reduced scarring and hypertrophy. They also determined that treatment with sacubitril/valsartan caused heart cells to release significantly more exosomes and that these exosomes had a reduced amount of specific microRNA: miR-181a. The authors went on to show that inhibiting the expression of miR-181a in rodents with heart attacks led to healthier hearts. This study therefore demonstrated a novel molecular mechanism underlying sacubitril/valsartan's therapeutic effects: 1) increased exosome release and 2) reduced microRNA miR-181a in the exosomes.

Not only does this study show a novel mechanism for drug action that will inform development of future pharmacotherapies, but it indicates that miR-181a specifically, which is detectable in circulating blood, could be used as a biomarker to indicate heart failure progression and to predict drug response.

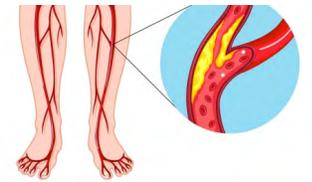
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Scaffolds Instead of Solutions: A Safe and Effective RNA Therapy for Peripheral Arterial Disease

By Adrienne Mueller, PhD



Peripheral arterial disease (PAD) is a disorder that affects a significant proportion of the population. PAD occurs when the vessels that carry blood to your arms and legs narrow or become blocked, which is often the result of plaque buildup. Although PAD can cause debilitating pain, limit your ability to walk, and even result in tissue death.



Peripheral artery disease (PAD) is caused by plaque build-up in arteries that carry blood to your head and limbs.

One of the most promising new strategies to treat PAD is to improve vascular growth to help keep your tissue supplied with blood. Arteries regenerate in response to molecules called growth factors. Modified mRNA (mmRNA) is new method for promoting growth factor signaling in tissue. Currently, mmRNAs are delivered in a lipid-based solution, which is both non-specific and transient. Using a biomaterial, like a scaffold, instead of a solution, could overcome these drawbacks. Firstly, mmRNAs embedded in a scaffold cannot spillover to adjacent tissues. Secondly, scaffolds also allow the slow release of mmRNA, as the scaffold material slowly degrades. An additional benefit of scaffolds is that they closely mimic the structure of existing tissue, which helps tissue regenerate.



Ngan Huang, PhD

In their recent study, first author Tatiana Zaitseva, PhD, of Fibralign Corporation and Stanford senior author Ngan Huang, PhD, report on a scaffold they developed to help deliver mmRNA to limbs with PAD. The researchers loaded mmRNA for a growth factor that promotes new blood vessel formation into a new, slow-releasing scaffold. As reported in *Regenerative Medicine*, the authors found that five weeks after implanting scaffolds in pigs with simulated PAD, the tissue showed significant regeneration of new vessels. Use of scaffolds to deliver mmRNAs promises to be a safer and more effective method to treat PAD than traditional gene therapy. This novel approach could also improve treatments for other disorders of soft tissue that have used gene therapy approaches in the past.

https://med.stanford.edu/cvi/mission/news_center/articles_announcements/scaffolds-instead-of-solutions-safe-and-effective-rna-therapy.html



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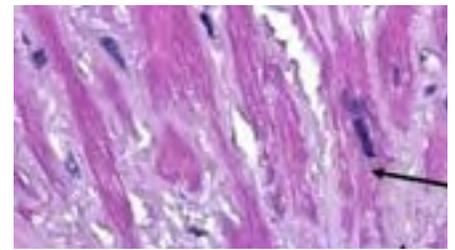
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Change in Protocol? Heart Transplants for Amyloidosis Patients By Adrienne Mueller, PhD



In the US, at any point in time, there are about 4,000 people on the waiting list to receive donor hearts. Because of this incredibly high demand and the life-or-death nature of the need, when a heart becomes available, the procedure for allocating it is an extremely thorough one. Because the tissue is so precious, the number of reasons that can disqualify someone from receiving a donor heart is a very long list. For most medical centers, having a condition called cardiac amyloidosis is one of those reasons.



In this heart biopsy sample, amyloid deposits are stained light pink. Notice how the amyloid deposits are seen everywhere and encircle each heart cell.

Amyloidosis occurs when proteins accumulate in our tissue. These accumulated proteins, called amyloid deposits, are toxic and eventually cause organ dysfunction. The two most common forms of amyloidosis that affect the heart are light chain amyloidosis (AL) and transthyretin amyloidosis (ATTR). Both forms of cardiac amyloidosis cause significant morbidity and mortality.



Ronald Witteles, MD

Because amyloidosis is a chronic disorder individuals with amyloidosis are typically rejected as candidates for new hearts. Between 2004 and 2017, 31 patients—13 with AL and 18 with ATTR—received heart transplants at Stanford. These surgeries provided data for a group of researchers, led by first author Christopher Barrett, MD and Stanford Cardiovascular Institute-affiliated senior author Ronald Witteles, MD, to perform one of the largest single-center studies reported to date to determine whether individuals with amyloidosis do in fact have worse outcomes than other heart transplant recipients. In their paper, recently published in the *Journal of the American College of Cardiology: Heart Failure*, the researchers showed that immediately after the transplant, there were no differences between amyloidosis patients and patients with other heart conditions in terms of their post-operative bleeding, renal failure, rates of infection, or tissue rejection. And eight years later there was also no difference in mortality.

What this study from the Stanford Amyloid Center shows is that we have come a long way in the treatment of amyloidosis and that, if you are careful about the patients you select to receive a heart transplant, you can have outcomes that are every bit as successful as patients with other causes of heart failure.

https://med.stanford.edu/cvi/mission/news_center/articles_announcements/change-in-protocol-heart-transplants-for-amyloidosis-patients.html

Plant-Based Meat Lowers Some Cardiovascular Risk Factors Compared with Red Meat, Study Finds

By Hanae Armitage



Swapping out red meat for plant-based meat alternatives can lower some cardiovascular risk factors, according to a new study by researchers at Stanford Medicine. “There’s been this sort of backlash against these new meat alternatives,” Gardner said. “The question is, if you’re adding sodium and coconut oil, which is high in saturated fat, and using processed ingredients, is the product still actually healthy?”



A pair of uncooked vegan burgers. Participants in a new study ate plant-based meat alternatives for eight weeks and regular meat for eight weeks. Kristi Blokhin/Shutterstock.com

To find out, Gardner and his team gathered a group of more than 30 individuals and assigned them to two different diets, each one for eight weeks. One diet called for at least two daily servings of meat—the options available were primarily red meat—and one called for at least two daily servings of plant-based meat. A paper describing the results of the study was published in the *American Journal of Clinical Nutrition*.

The main outcome the team was interested in tracking, Gardner said, was the level of TMAO. In the past few years, studies have shown that high levels of TMAO are consistent with increased inflammation and blood clotting, among other health concerns. In Gardner’s study, the researchers observed that participants who ate the red-meat diet during the first eight-week phase had an increase in TMAO, while those who ate the plant-based diet first did not. Outside of TMAO, health benefits conveyed from plant-based alternatives extended to weight and levels of LDL cholesterol—or “bad” cholesterol. No matter which diet was first, participants’ levels of LDL cholesterol dropped on average 10 milligrams per deciliter, which is not only statistically significant, but clinically significant too, Gardner said. In addition, participants lost 2 pounds, on average, during the plant-based portion of the diet.



Christopher Gardner, PhD

Gardner hopes to continue studying the relationship between health and plant-based meat alternatives, particularly as it pertains to changes in the microbiome. “Maybe next we’ll look at a combination of dietary factors on health — perhaps alternative meat combined with alternative dairy products,” he said.

<https://med.stanford.edu/news/all-news/2020/08/plant-based-meat-versus-animal-meat.html>

Tracking Down Unhealthy Heart Rhythms: Introducing the Elastrode By Adrienne Mueller, PhD



Atrial fibrillation is a heart condition that affects more than 2.2 million people in the U.S. Atrial fibrillation is usually treated by surgically removing the small piece of tissue that causing the heart to beat irregularly. Clinicians identify which piece of heart to remove by feeding a small sensor into the heart chambers and detecting which specific region is the source of the disorganized signals. Unfortunately, these surgeries have variable outcomes. One reason why surgeries may not be as successful as they could be, is that our sensor technology.



Jia Liu, PhD



Xinyuan Zhang



Yuxin Liu

Current sensor technology is limited in at least two ways. First, conventional sensors have limited spatial resolution — they can only coarsely describe which part of the heart is damaged. Better spatial resolution would help ensure that all damaged tissue can be removed and that no healthy tissue is targeted. Second, conventional sensors cannot access all regions of the heart. Both these issues can be addressed by creating a sensor with more, and smaller, contacts. The challenge with creating heart sensors is that the heart is incredibly hard to take readings from: every heart beat can move tissue away from the sensor's contacts.

A group of CVI-affiliated investigators, led by first co-first authors Jia Liu, PhD, Xinyuan Zhang, and Yuxin Liu, as well as co-senior authors Anson Lee, MD and Zhenan Bao, PhD, recently developed a new sensor that promises to overcome these technical challenges. How? They made it intrinsically stretchable—so the sensor could move with the heart. Their newly-developed elastic electrode, or “elastrode”, is a wafer-thin array of sensors that can map large tissue surfaces. Their recent paper in the *Proceedings of the National Academy of Sciences* describes not only how they developed this new sensor, but how well it works. Comparing the performance of the elastrode to conventional sensors shows that the elastrode is able to capture signals at over 100 times higher spatial resolution, access more regions of the heart, and collect more accurate data.

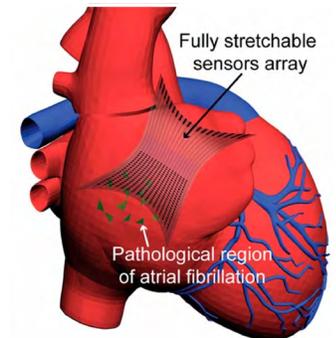
The elastrode promises to significantly improve current treatment of atrial fibrillation. Further, it will lead to an improved understanding of the mechanisms underlying heart rhythm disorders and the development of better therapies with which they can be treated.



Anson Lee, MD



Zhenan Bao, PhD



Application of a fully stretchable elastrode array to the heart surface to identify the pathological regions in atrial fibrillation. Liu, Zhang & Liu et al (2020) PNAS, 117 (26) 14769-14778

http://med.stanford.edu/cvi/mission/news_center/articles_announcements/tracking-down-unhealthy-heart-rhythms.html

Stanford Cardiovascular Data Integration Lab

The Stanford Cardiovascular Data Integration Lab (SCDIL) brings together cardiologists, cardiovascular surgeons, radiologists, and information technology experts with the objective to facilitate cardiovascular data science research. SCDIL aims to:

- Facilitate data integration from different data sources
- Make a data science analytic pipeline accessible for researchers
- Facilitate and prioritize clinical or data science research projects
- Facilitate imaging and clinical Artificial Intelligence research projects

Significant clinical insights can be gained by integrating clinical, laboratory, imaging, and outcome data. SCDIL has been working on this front for several years: contributing to the transcatheter aortic valve replacement (TAVR) database, surgical aortic disease dataset, the inherited cardiovascular disease databases, the heart transplant and LVAD databases, the South Asian Initiative datasets, the Insulin resistance network datasets, and several other heart failure and pulmonary disease datasets. Support has been provided to the IT group by the Department of Cardiothoracic Surgery and the Stanford Cardiovascular Institute.

The Stanford Cardiovascular Data Integration Lab is eager to form collaborations with and support cardiovascular clinicians and scientists in the Stanford community. <https://med.stanford.edu/cvdi.html>



Cardiovascular Clinical Trials at Stanford

Cardiovascular research at Stanford University is diverse and spans over 240 clinical research studies in the division of Cardiovascular Medicine alone. Stanford faculty physicians and scientists, many of whom are recognized internationally for their contributions to advancing science and knowledge of cardiac disease, conduct research aimed to treat patients suffering from a wide variety of cardiovascular issues. Cardiovascular researchers have made significant progress towards the understanding of coronary and vascular disease, endothelial function, cardiac mechanics and heart failure. There are opportunities for patients to participate in studies that may change cardiovascular care for millions.

[Cardiovascular Medicine's Clinical Research Office](https://med.stanford.edu/cvmedicine/research/clinicaltrials.html) and the [Cardiovascular Institute's Clinical Trials Core](http://med.stanford.edu/cvi/translational-research/clinical-trials.html) support faculty with teams of talented Clinical Research Coordinators to move the trials and research forward in the most compliant and efficient way for the benefit of patients, and to ensure research goals are met even in the midst of COVID-19 pandemic. For more information, visit <https://med.stanford.edu/cvmedicine/research/clinicaltrials.html> and <http://med.stanford.edu/cvi/translational-research/clinical-trials.html>.

Introduction to the Khush Research Team: The Research Team of [Kiran Khush, MD](#), including Helen Luikart RN Research Manager, Kian Waddell ACRC, and Dave Morales ACRC, focuses on clinical research studies broadly related to the field of heart transplantation. They are leading the first prospective multi-center study of donor heart utilization in the United States, with a goal of developing risk models to guide donor heart utilization. They are currently collaborating with Interventional Cardiology colleagues to conduct a clinical trial to ameliorate chronic rejection after heart transplantation. They are also involved in several multi-center clinical trials of novel strategies for immunomodulation to prevent short- and long-term complications after heart transplantation.

Introduction to the Cardiovascular Regeneration and Restoration Research Program: During the last eight years, the Cardiovascular Regeneration and Restoration Program, led by [Phillip Yang, MD \(PI\)](#), [David Lee, MD \(Co-PI\)](#), [Fouzia Khan CRC2](#), and [Banu Rajaskeran ACRC](#), has conducted over 10 clinical trials. The NIH/NHLBI has funded over \$70M to the Cardiovascular Cell Therapy Research Network of seven leading US academic sites and completed TIME, LATE-TIME, FOCUS, PACE, SENECA, and CONCERT Trials to study acute myocardial infarction, heart failure, and peripheral vascular disease patients. Industry support completed MEMRI (FDA IND), DREAM, and CAPACITY trials to study heart failure patients. Currently, ACT, CardiAMP and DCM II trials are on-going or preparing to start.

Introduction to the Computational Arrhythmia Research Laboratory: The laboratory focuses on bringing together clinicians, bioengineers and computer scientists to solve important problems in heart rhythm disorders. The lab has been NIH funded since 2001 and is directed by [Sanjiv Narayan, MD, PhD](#) and coordinated by Kathleen Mills Research Lab Manager, Sarah Magee CRCA and Kian Waddell ACRC. They focus on methods to detect and prevent sudden cardiac death, to phenotype and personalize therapy for atrial fibrillation, and to map and ablate atrial fibrillation. Their research has resulted in novel mapping systems translated to clinical use, machine learning to risk stratify patients, new device technology and clinical trials of these approaches. Their outstanding lab members and fellows have recently been awarded several grants and research prizes.

Stanford Hospital Receives Mitral Valve Repair Reference Center Recognition Award

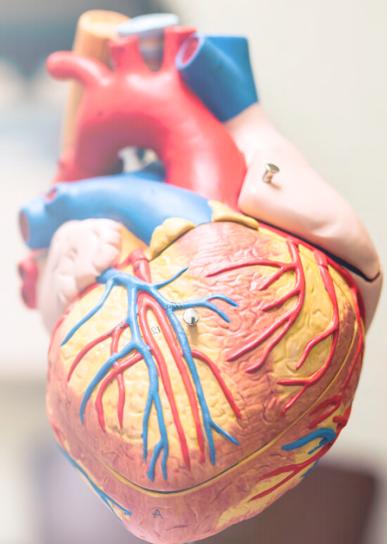


Y. Joseph Woo,
MD

Mitral valve disease is a serious condition often requiring surgical valve replacement or repair. Stanford has dedicated research laboratories continually evaluating the best surgical techniques and equipment for mitral valve surgery.

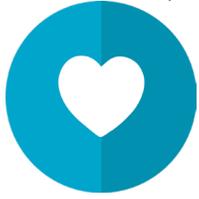
The Mitral Foundation, in partnership with the American Heart Association created the Mitral Valve Repair Reference Center Award to recognize centers in the United States that have a demonstrated record of superior clinical outcomes in degenerative mitral valve repair resulting from evidence-based guideline treatment.

Congratulations to Y. Joseph Woo, MD and his team for receiving this prestigious award, which recognizes Stanford Hospital's contribution to advancing best practice in the surgical treatment of mitral valve disease.



Courses in Cardiovascular Science and Medicine

MED223 | Cardiovascular and Pulmonary Sciences Seminar



The purpose of this course is to familiarize students with the spectrum of basic, clinical and translational CVP research beyond their specific area of chosen investigation. After a Tuesday seminar, students will meet informally with the seminar speaker. Examples of thematic topics that will be covered include how genetics and developmental biology address mechanisms of congenital heart disease, the rationale for new drug development in atherosclerosis and cardiac protection, principles of biomechanics and computer technology in device and biomaterial development, ion channel physiology leading to anti arrhythmic agents and the design of clinical trials, use of epidemiological studies, evidence based medicine, and design of new treatment or diagnostic algorithms. **Fall and Winter Quarter - Tuesdays and Thursdays, 1:00 - 2:00 pm | 2 credits**

Course Directors: Ngan Huang, PhD; Vinicio de Jesus Perez, MD; Edda Spiekerkoetter, MD; Ioannis Karakikes, PhD
<https://med.stanford.edu/cvi/education/cvi-courses/med223.html>

CTS 225 | Stem Cells in Cardiovascular Regenerative Medicine



This cardiovascular course focuses on the basic principles and translational applications of stem cells for treatment of cardiovascular diseases. Topics include the genetic modification of stem cells for precision medicine, as well as the science underlying how stem cells can be applied to regenerative medicine and drug development. Students will have the opportunity to develop their scientific reasoning and presentation skills as well as expand their professional portfolios through student-led journal club presentations and the development of a research proposal. After completion of this course, students should expect to get broad exposure to basic and translational applications of stem cell research to cardiovascular medicine, a key focus of many initiatives in both academia and the biotech industry. This course is open to graduate students, medical students, and upper-division undergraduates. **Spring Quarter - Tuesdays and Thursdays, 2:00-3:00 pm | 2 credits**

Course Director: Ngan Huang, PhD
<https://med.stanford.edu/cvi/education/cvi-courses/cts225.html>

MED 225 | Drug Development: From a Concept to the Clinic



CVI is launching a new course for the 2020-2021 academic year that is designed for medical students, trainees, basic scientists, clinicians and clinician-scientists to provide an educational and practical perspective on the essential issues in drug development. Using a blend of seminars and dynamic workshops, the curriculum is focused on educating the audience on all stages of drug development and related research and business processes – from discovery and translational science and how to launch new projects to analyzing data, communication and interpretation of results of clinical trials, regulatory issues and commercial considerations in product development. The emphasis will be on cardiovascular applications. Proposed seminar topics include How Drugs Are Discovered and Developed, Case Studies of the various challenges in Drug Development, Cardiac Safety, and the FDA Advisory Committee Process. **Winter and Spring Quarter - Tuesdays, 4:00 - 5:30 pm | 1 credit**

Course Directors: Peter DiBattiste, MD; Jonathan Fox, MD, PhD; Alexander Gold, MD; Jaykumar Rajadas, PhD; Philip Sager, MD

Cardiovascular Medicine Fellowship Program

Our mission is to train future academic leaders in Cardiovascular Medicine through a tripartite commitment to clinical care, research, and education.

"The Cardiovascular Medicine Fellowship Program at Stanford University offers a rigorous but collegial training environment for individuals with an interest in developing an academic career. Intensive, individually tailored training in invasive and noninvasive clinical cardiology as well as in basic and/or clinical cardiovascular research prepares each fellow to pursue their career at the forefront of cardiology. **Come train with us!**" --Joshua Knowles, MD, PhD, Program Director

<https://med.stanford.edu/cvmedicine/education/gen-cardiology-fellowship.html>



Recruitment for R38 StARR Resident Fellowship

R38 Stanford Integrated Cardiovascular/Pulmonary Residency Research Training Program

The R38 StARR (Stimulating Access to Research in Residency) program is a multi-disciplinary program funded by the NHLBI of the NIH. The program is designed to recruit and train resident-investigators in cardio-pulmonary research and to accelerate their development into independent clinician-investigators. This program is designed for individuals who have completed a significant portion of their clinical training and have developed a clinical and research focus. Stanford residents will be selected from Internal Medicine, Radiology, Pediatrics, and Cardiothoracic Surgery residency programs.

This program is directed by Joseph Wu, MD, PhD, Marlene Rabinovitch, MD and Michael Fischbein MD, PhD.

Application deadline January 15th, 2021, for a July 1, 2021, start date.

<https://med.stanford.edu/cvi/education/resident-education/resident-fellowship.html>

Recruitment for T32 Postdoctoral Training 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 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.

This program is directed by Joseph Wu, MD, PhD, John M. Pauly, PhD and Koen Nieman MD, PhD.

Currently accepting applications.

<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.

This program is directed by Philip Tsao, PhD and Nick Leeper, MD.

Currently accepting applications.

<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 multi-disciplinary training.

This program is directed by Daniel Bernstein, MD, Thomas Quertermous, MD and Euan Ashley, MRCP, DPhil.

<http://med.stanford.edu/cvmedicine/education/timbs.html>

Grants and Awards



Abdominal aortic aneurysm (AAA) disease is a common cause of premature death in adult Americans. To date, no medical (e.g., non-surgical) therapies have proven effective at limiting AAA disease progression or reducing the risk of AAA rupture or aneurysm-related sudden death. Recent retrospective studies suggest that metformin, the world's most commonly prescribed oral hypoglycemic agent, may be associated with reduced rates of AAA enlargement. **Ronald Dalman, MD**, Walter Clifford Chidester and Elsa Rooney Chidester Professor of Surgery, was recently awarded an R61/R33 NIH clinical trial grant to determine if metformin therapy will safely suppress AAA disease progression in non-diabetic patients. The LIMIT (LIMITing AAA with meTformin) trial will enroll 480 participants to advance the understanding of AAA disease and the translational utility of metformin therapy to treat cardiovascular disease in non-diabetic patients.



Alison Marsden, PhD, Associate Professor of Pediatrics (Cardiology) and of Bioengineering, was invited to join the Additional Ventures Foundation Cures Collaborative, which will fund research in identifying functional cures for single ventricle congenital heart disease patients. Dr. Marsden also joins **David Rosenthal, MD** as an advisory board member of the Additional Ventures Foundation, which uses a venture philanthropy approach to seed high-impact research in congenital heart defects.



Mark Skylar-Scott, PhD, a new Basic Science and Engineering (BASE) Initiative faculty member, received a grant from the Alternatives Research & Development Foundation (ARDF) to develop non-animal methods to bio-fabricate microvascularized human cardiac tissue for use in drug screening. Dr. Skylar-Scott was also invited to join the Additional Ventures Foundation Cures Collaborative, which will fund research in identifying functional cures for single ventricle congenital heart disease patients.



Koen Nieman, MD, PhD, Associate Professor of Medicine (Cardiovascular Medicine) and of Radiology, was awarded an R01 research project grant for an "International consortium for multimodality phenotyping in adults with non-compaction", in collaboration with Cleveland Clinic (Wilson Tang, co-MPI), University of Pennsylvania, Erasmus University, and Seoul National University. This multimodality imaging study will help characterize non-compaction cardiomyopathies and improve risk stratification. **Matt Wheeler, MD, PhD**, **June-Wha Rhee, MD**, **Francois Haddad, MD** and **Daniel Rubin, MD** are Stanford co-investigators on this grant.

Koen Nieman, MD, PhD was also named the new President of the Society of Cardiovascular Computed Tomography in July. <http://www.SCCT.org>

Connect with CVI on LinkedIn



<https://www.linkedin.com/company/stanfordcvi>



Jointly with three other academic medical centers, Stanford has been awarded \$14 million by the American Heart Association to form a new strategically focused research network devoted to health technologies and innovation applied to heart and brain health. The four institutions will devote \$4 million to form a national health technology research collaborative. Each institution has its own project for which it receives \$2.5 million; the overall goal of these projects will be to reduce health care disparities, empower people to better manage their own health and wellness, and enhance patient/provider connectivity.

The Stanford project is entitled Innovation to Implementation: Technology-Enabled Management of Hypertension in Underrepresented Communities and in the Gig Economy. The team is led by **Mintu Turakhia, MD**, Associate Professor of Cardiovascular Medicine and Executive Director of the Center for Digital Health, and includes **Paul J. Wang, MD**, Professor of Cardiovascular Medicine, **Fatima Rodriguez, MD**, Assistant Professor of Cardiovascular Medicine, **Vivek Bhalla, MD**, Assistant Professor of Nephrology, and **Tara Chang, MD**, Associate Professor of Nephrology.



Andrew Sweatt, MD, Clinical Assistant Professor with expertise in pulmonary hypertension, was awarded an NIH Mentored Patient-Oriented Research Career Development Award K23 Award! Roham Zamanian, MD will be serving as his Mentor for this award.

Dr. Sweatt also recently authored an already highly-cited *Circulation Research* study which effectively illustrates how machine-learning approaches can be used to organize complicated data sets to classify pulmonary hypertension phenotypes in an unprecedented manner.



Kevin Alexander, MD, Assistant Professor of Medicine (Cardiovascular Medicine), co-authored an article with Chin-Hong P, Haynes N, Albert MA and the Association of Black Cardiologists in *Nature Reviews Cardiology* titled "Pulling at the heart: COVID-19, race/ethnicity and ongoing disparities."



Jesse Engreitz, PhD, a new Basic Science and Engineering (BASE) Initiative faculty member, received one of the 2020 NHGRI Genomic Innovator Awards to "Apply CRISPR tools to understand gene regulation related to common, complex diseases." <https://www.genome.gov/news/news-release/NHGRI-announces-2020-genomic-innovator-awards>



Christopher Almond, MD, Professor of Pediatrics (Cardiology), was recently awarded the following grant: "Creating a Framework for a National Adaptive Platform Trial to Evaluate Pediatric Medical Devices." It will be funded by the FDA through the UCSF-Stanford CERSI program. The \$85,000 award supports a multidisciplinary project to explore the use of adaptive clinical trials to support FDA review of pediatric medical devices.



Mark Mercola, PhD, Sanford and Joan Weill Scholar and Professor of Cardiovascular Medicine, was awarded a National Institute of Health R21 exploratory research grant for his project "Platform for high-throughput biomechanical measurements using metallic islands on boron nitride nanosheets."

Grants and Awards



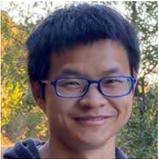
Stephanie Lindsey, PhD was recently granted a Career Awards at the Scientific Interface (CASI) award from the Burroughs Wellcome Fund for her project "Quantitation of early great vessel growth and remodeling", as well as an American Heart Association Career Development Award for her project on "Growth and remodeling of the pharyngeal arch arteries."



Jessica Brodt, MD has received an SCA-IARS Mid-Career Research Grant to support her project "Enhanced recovery after cardiac surgery with erector spinae plane catheters: A prospective, randomized, placebo-controlled trial." Dr. Brodt is specifically examining whether this novel anesthetic technique may reduce opioid requirements, provide better analgesia, and improve clinical recovery.



Melissa Vogelsohn, MD, a recent fellowship graduate and now junior faculty in cardiac anesthesia and critical care, was recently elected to the American Heart Association Emergency Cardiovascular Care Science Committee. This committee is responsible for overseeing AHA scientific statements and guidelines, including the adult life support guidelines. Her clinical research interests in mechanical circulatory support and long-term outcomes address important topics in cardiovascular disease and resuscitation.



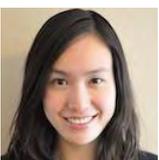
Hongchao Guo, PhD was recently awarded a K99 Career Development Award from the National Heart, Lung and Blood Institute for his project "Delineating the genetic susceptibility of smoking-induced vascular dysfunction."



William Goodyer, MD, PhD was awarded an NHLBI K08 Mentored Clinical Scientist Research Career Development Award for his project "Elucidation of the development and function of the cardiac conduction system."



Ian Williams, PhD was awarded an F32 postdoctoral fellowship from the National Heart, Lung and Blood Institute for his project "Investigating the role of shear stress in coronary artery development."



Han Zhu, MD was appointed as a new Assistant Editor for the Journal of American College of Cardiology (JACC): CardioOncology.



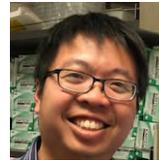
Paul Pang, PhD was recently awarded an F32 postdoctoral fellowship from the National Heart, Lung and Blood Institute for his project "Single-cell splicing analysis of the heart in myotonic dystrophy."



Myriam Amsallem, MD, PhD has been awarded a Translational Research and Applied Medicine (TRAM) Pilot Grant Award for her proposal entitled "Integrated 4-dimensional blood flow magnetic resonance imaging and transcriptomics profiling of right heart adaptation to pulmonary hypertension." Dr. Amsallem will be collaborating with Roham Zamanian, MD, Kevin Contrepois, PhD and Jennifer Arthur Ataam, PhD and co-supervised by Mike Snyder, PhD and Alison Mardsen, PhD.



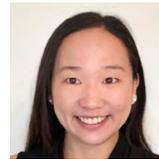
Han Zhu, MD recently received the competitive Sarnoff Scholar Award, designed to support junior faculty who are committed to pursuing a career in cardiovascular research during the early years of faculty appointment.



Paul Cheng, MD received a National Institute of Health K08 Clinical Scientist Research Career Development Award for the project "From locus to function: Role of zeb2 in human risk of coronary artery disease."



Alex Sandhu, MD received an K23 Mentored Patient-Oriented Research Career Development Award for from the National Heart, Lung and Blood Institute for his project "The effect of value-based payment on heart failure quality of care (Value-HF)."



June-Wha Rhee, MD was awarded a K08 Mentored Clinical Scientist Research Career Development Award for her project "Patient-specific modeling of metabolic dysfunction in statin-induced myopathy using iPSC-derived myocytes."



Jennifer Woo, MD was awarded an F32 postdoctoral fellowship to study abnormal myocardial shape, strain and contraction and determine role of exercise testing in Tetralogy of Fallot patients. Her project is titled "Novel computational methods for detecting early right ventricular failure in the tetralogy of fallot population." Dr. Woo will be collaborating with Myriam Amsallem, MD, PhD.



Andrew Young Chang, MD was selected to join the American Heart Association's Scientific Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease as a Fellow Member.



Ananya Chakraborty, PhD received an Maternal & Child Health Research Institute (MCHRI) award to study pulmonary hypertension. The topic of her study is "ROR2 signaling in the pathogenesis of adult and pediatric pulmonary arterial hypertension."

Appointments and Promotions



Meaghan Beattie, MD is joining the Fetal Cardiology team as faculty. She received her MD at UCLA and completed her residency at UCSF. After a year as a CVICU hospitalist at Stanford, she completed her pediatric cardiology fellowship and fellowship in cardiac imaging in Boston.



Rebecca Johnson Kameny, MD is joining the Pediatrics Cardiology CVICU faculty. She completed her medical school and residency in Boston, followed by a PICU fellowship at UCSF and a 4th year CVICU fellowship at Stanford.



Ian Rogers, MD, MPH was promoted to Clinical Associate Professor in the Division of Cardiovascular Medicine.



Anjali Sinha, MD is joining the Pediatrics Cardiology CVICU faculty. She completed medical school at Case Western Reserve University and her residency in Philadelphia (CHOP). She completed her Pediatric Cardiology Fellowship in Boston and Pediatric Critical Care fellowship at CHOP.



David Lee, MD was promoted to Professor in the Division of Cardiovascular Medicine.



Chiu-Yu Chen, MD, PhD was appointed to Instructor in Pediatric Cardiology. She is interested in caring for children with heart failure, studying patient-reported outcome measures and applying innovative approaches to circulatory support and heart transplantation.



Shoa Clarke MD, PhD was appointed to Instructor in the Division of Cardiovascular Medicine.



Paul Cheng MD, PhD was appointed to Instructor in the Division of Cardiovascular Medicine.



Theodore Hart, MD was appointed as a new Vascular Surgery Fellow.



Dries Feyen, PhD has received a position as a Scientific Group Leader at Glaxo Smith Kline.



Elianne Rojas, DO was appointed as a new Vascular Surgery Fellow.



Kevin Alexander, MD was appointed to Assistant Professor in the Division of Cardiovascular Medicine.



Rajesh Dash, MD, PhD was promoted to Associate Professor in the Division of Cardiovascular Medicine.



Gurpreet (Gary) Dhillon, MD is joining the Pediatrics Cardiology CVICU faculty after completing his pediatrics residency and pediatric cardiology fellowship at Texas Children's Hospital. He completed his pediatric critical care fellowship in Boston and recently finished his ICU fellowship.



Abha Khandelwal, MD was promoted to Clinical Associate Professor in the Division of Cardiovascular Medicine.



Kiran Khush, MD was promoted to Professor in the Division of Cardiovascular Medicine.



Mirela Tuzovic, MD was appointed to Clinical Assistant Professor in the Division of Cardiovascular Medicine.



Tom Alsaigh, MD was appointed as a new Vascular Medicine Fellow.



William Goodyer, MD, PhD was promoted to Instructor in Pediatric Cardiology. He will be pursuing both clinical Pediatric Electrophysiology and basic science research focused on Cardiac Conduction System development and disease.



Michael Paisley, MD was appointed as a new Vascular Surgery Fellow.



Alexander Perino, MD was appointed to Instructor in the Division of Cardiovascular Medicine.



Alexander Sandhu, MD was appointed to Instructor in the Division of Cardiovascular Medicine.



Han Zhu, MD was appointed as Clinical Scholar in the Division of Cardiovascular Medicine and will be starting a new appointment as Instructor.

Funding Opportunities

For more information about funding opportunities or grant application support, please contact our Office of Research Development: cvi_grants@stanford.edu.

SEPTEMBER 2020

American Heart Association and Children's Heart Foundation Congenital Heart Defects Research Awards. Deadline: September 22, 2020.

NIH - R01 Large scale mapping and/or molecular profiling of ensembles and/or cell-types mediating opioid action in the rodent brain. Letter of Intent Deadline: September 30th, 2020. Deadline: October 30th, 2020 PAR-20-182

OCTOBER 2020

American Heart Association and Enduring Hearts Research Awards in Pediatric Heart Transplantation. Letter of Intent Deadline: October 1, 2020. Deadline: January 15, 2021.

American Heart Association Merit Award. Letter of Intent Deadline October 1, 2020. Deadline: November 10, 2020.

NIH R01 Research Project Grant (Parent R01 Clinical Trial Not Allowed). New application Deadline: October 5, 2020. PA-20-185

NIH R01 Research Project Grant (Basic Experimental Studies with Humans Required). New application Deadline: October 5, 2020. PA-20-184

NIH R01 Research Project Grant (Parent R01 Clinical Trial Req). New application Deadline: October 5, 2020. PA-20-183

NIH R01 Improving Outcomes in Cancer Treatment Related Cardiotoxicity. Deadline: October 5, 2020. PA-19-112

NIH R01 The Mechanistic Role of the Microbiome in the Pathobiology of Heart, Lung, Blood, and Sleep Diseases. Deadline: October 5, 2020. PA-18-784

NIH R01 Research Project Grant (Parent R01 Clinical Trial Not Allowed). New application Deadline: October 5, 2019. PA-19-056

NIH R01 Research Project Grant (Parent R01 Clinical Trial Req). New application Deadline: October 5, 2019. PA-19-055

NIH K99/R00 Pathway to Independence Award (Parent K99/R00 - Independent Clinical Trial Req). Deadline: October 12, 2020. PA-20-187

NIH K99/R00 Pathway to Independence Award (Parent K99/R00 Independent Clinical Trial Not Allowed). Deadline: October 12, 2020. PA-20-188

NIH K99/R00 Pathway to Independence Award (Parent K99/R00 Indep Basic Exp Studies with Humans Req). Deadline: October 12, 2020. PA-20-189

NIH K08 Mentored Clinical Scientist Research Career Development Award. Deadline: October 12, 2020. PA-20-203

NIH K18 Career Enhancement Award. Deadline: October 12, 2020. PAR-20-226

NIH K24 Midcareer Investigator Award in Patient-Oriented Research. Deadline: October 12, 2020. PA-20-186

American Heart Association Established Investigator Award. Letter of Intent Deadline: October 14, 2020. Deadline: January 14, 2021.

NIH R21 Improving Outcomes in Cancer Treatment-Related Cardiotoxicity. Deadline: October 16, 2020. PA-19-111

NOVEMBER 2020

NIH Toward Translation of Nanotechnology Cancer Interventions (TTNCI). Deadline: November 19th, 2020. PAR-20-116

DECEMBER 2020

NIH F32 Ruth L. Kirschstein National Research Service Award (NRSA) Individual Postdoctoral Fellowship. Deadline: December 8th, 2020. PA-19-188

ROLLING DEADLINE

NIH Research Supplements to Promote Re-Entry into Biomedical and Behavioral Research Careers. PA-18-592

Mackay California-Pacific Rim Tobacco Policy Scholar Award. \$250K/yr x 3 yrs. Build leadership among mid-career researchers to foster evidence-based tobacco control policy with relevance to California and the Pacific Rim. Eligibility: mid-career faculty with PI eligibility and mid-career CE faculty. No citizenship requirement.



National and Global Cardiovascular Conferences

Please note: some events may be canceled or postponed due to COVID-19. Please check directly with event organizers.

SEPTEMBER 2020

CSI Education: CSI Frankfurt. September 16-19, 2020. Congress Center Messe Frankfurt, Frankfurt am Main, Germany. <https://www.csi-congress.org/frankfurt>

Congenital Cardiology Today - 10th Annual Multimodality Cardiovascular Imaging for the Clinician. September 19-20, 2020. <https://congenitalcardiologytoday.com/event/10th-annual-multimodality-cardiovascular-imaging-for-the-clinician/>

Keystone Symposia - RNA Editing and Modifications: From Biology to Therapy. September 20 - October 2, 2020. https://www.keystonesymposia.org/ks/Online/Conferences/Online/Events/All_Events.aspx

Congenital Cardiology Today - Advanced Symposium on Congenital Heart Disease in the Adult. September 21-22, 2020. <https://congenitalcardiologytoday.com/event/achd-virtual-2020-advanced-symposium-on-congenital-heart-disease-in-the-adult/>

Keystone Symposia - Myeloid Cells and Innate Immunity in Solid Tumors. September 21-23, 2020. https://www.keystonesymposia.org/ks/Online/Conferences/Online/Events/All_Events.aspx

Keystone Symposia - Genomic Stability and DNA Repair. September 21-23, 2020. https://www.keystonesymposia.org/ks/Online/Conferences/Online/Events/All_Events.aspx

Keystone Symposia - Proteomics in Cell Biology and Disease. September 21-23, 2020. https://www.keystonesymposia.org/ks/Online/Conferences/Online/Events/All_Events.aspx

5th International Conference on Cardiovascular Medicine and Cardiac Surgery. September 23-24, 2020. <https://cardiovascular.cardiologymeeting.com/>

World Academy of Science, Engineering and Technology: International Conference on Clinical Cardiology, Cardiovascular Medicine and Conditions. September 24-25, 2020. Virtual. <https://waset.org/clinical-cardiology-cardiovascular-medicine-and-conditions-conference-in-september-2020-in-san-francisco>

Outpatient Endovascular and Interventional Society: 7th Annual National Scientific Meeting. September 25-27, 2020. Loews Portofino Bay Hotel, Orlando, Florida. <https://oeisociety.com/meetings/2020-annual-meeting/>

Heart Rhythm Congress - HRC 2020. September 27-30, 2020. <http://www.heartrhythmcongress.org/>

Heart Failure Society of America - HFSA Virtual Annual Scientific Meeting 2020. September 30-October 6, 2020. <https://hfsa.org/annualscientificmeeting>

OCTOBER 2020

American College of Cardiology - Core Curriculum for the Cardiovascular Clinician. October 1-31, 2020. <https://www.acc.org/education-and-meetings/meetings/meeting-items/2019/11/18/12/20/2020-core-curriculum>

Keystone Symposia - Tissue Plasticity: Preservation and Alteration of Cellular Identity. October 5-7, 2020. https://www.keystonesymposia.org/ks/Online/Conferences/Online/Events/All_Events.aspx

Keystone Symposia - Autophagy: Mechanisms and Disease. October 5-8, 2020. https://www.keystonesymposia.org/ks/Online/Conferences/Online/Events/All_Events.aspx

Congenital Cardiology Today - 30th Annual International Symposium on Adult Congenital Heart Disease. October 5-10, 2020. <https://congenitalcardiologytoday.com/event/30th-annual-international-symposium-on-adult-congenital-heart-disease/>

CV TransForum: Fall 2020 Conference. October 8-10, 2020. Austin, Texas. <http://cvtransforum.com/>

Cardiovascular Research Foundation: Transcatheter Cardiovascular Therapeutics 2020. October 14-18, 2020. Virtual. <https://www.crf.org/tct>

World Congress on Cardiology and Cardiovascular Disorders. October 14-15, 2020. <https://cardiac.healthconferences.org/>

Cedars Sinai: Controversies & Advances in the Treatment of Cardiovascular Disease. October 15-16, 2020. The Maybourne Beverly Hills, Beverly Hills, CA. <https://www.controversiesincardiology.com/>

Cleveland Clinic - Unpartitioned Atrioventricular Connection: From Simple to Complex: 5th Annual Advances in Congenital Heart Disease Virtual Summit. October 16-17, 2020. <http://www.clevelandclinicmeded.com/live/courses/pediatricheart/>

Keystone Symposia - Optimizing Nutrition for Maternal, Newborn and Child Health. October 21-23, 2020. https://www.keystonesymposia.org/ks/Online/Conferences/Online/Events/All_Events.aspx

Mayo Clinic: Cases in Echocardiography, Cardiac CT, and MRI Course 2020. October 21-24, 2020. The Meritage Resort and Spa, Napa Valley, California. <http://emedevents.com/c/medical-conferences-2020/cases-in-echocardiography-cardiac-ct-and-mri-course-2020>

NAVBO - Vascular Biology. October 26-29, 2020. <http://www.navbo.org/events/vb2020/>

Congenital Cardiology Today - 38th Annual Echocardiography and Structural Heart Symposium. October 28-29, 2020. <https://congenitalcardiologytoday.com/event/38th-annual-echocardiography-and-structural-heart-symposium/>

Baptist Health South Florida: Echocardiography and Structural Heart Symposium, 38th Annual. October 29-30, 2020. Virtual. <http://cme.baptisthealth.net/echo/pages/index>

NOVEMBER 2020

World Academy of Science, Engineering and Technology - International Conference on Clinical Cardiology, Cardiovascular Medicine and Conditions. November 2-3, 2020. San Francisco, CA. <https://waset.org/advances-in-cardiovascular-pharmacology-conference-in-november-2020-in-san-francisco>

31st Annual Cardiovascular Interventions. November 10 – 13, 2020. Hilton La Jolla Torrey Pines, La Jolla, CA. <https://www.cvinterventions.com/>

American Heart Association - Scientific Sessions 2020. November 13-17, 2020. <https://professional.heart.org/en/meetings/scientific-sessions>

American Heart Association - Resuscitation Science Symposium. November 14-16, 2020. <https://professional.heart.org/en/meetings/resuscitation-science-symposium>

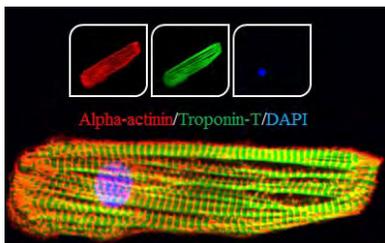
DECEMBER 2020

Keystone Symposia Tuberculosis: Science Aimed at Ending the Epidemic. December 2-4, 2020. https://www.keystonesymposia.org/ks/Online/Conferences/Online/Events/All_Events.aspx

American College of Cardiology - New York Cardiovascular Symposium. December 12-13, 2020. <https://www.acc.org/education-and-meetings/meetings/meeting-items/2020/07/07/13/51/2020-new-york-cardiovascular-symposium>



Stanford CVI Human iPSC Biobank Service



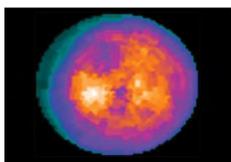
Normal and patient-derived reprogrammed cardiomyocytes are a tremendous resource for researchers and physicians here at Stanford and around the country. Understanding the disease process directly at the population level and observing these cells as surrogates under a myriad of conditions has the potential 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, CVI 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 the National Heart, Lung and Blood Institute (NHLBI) and the Stanford Cardiovascular Institute (CVI).

Contact: Joseph Wu, MD, PhD / joewu@stanford.edu
or Biobank manager, **Yan Zhuge, PhD** / yanzhugue@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, 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 a full spectrum of support to CVI members and their clinical trials. The coordinator 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, efinn@stanford.edu



Cardiovascular Pharmacology (ADD-ReB)

The Advanced Drug Delivery & Regenerative Biomaterials (ADD-ReB) 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.

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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

Communication is at the heart of scientific advancement and innovation. Between June 15th and August 31st, Stanford Cardiovascular Institute members published **519** original manuscripts and reviews, further contributing to our understanding of cardiovascular biology and disease. Here, we highlight selected manuscripts by our members.

June 16-30

Clinical photoacoustic imaging. Manohar S, Gambhir SS. *Photoacoustics*. 2020 Jun 17;19:100196. doi: 10.1016/j.pacs.2020.100196. PMID: 32612928

Verification of the machine delivery parameters of treatment plan via deep learning. Fan J, Xing L, Ma M, Hu W, Yang Y. *Phys Med Biol*. 2020 Jun 30. doi: 10.1088/1361-6560/aba165. PMID: 32604082

Trends in Readmission and Mortality Rates Following Heart Failure Hospitalization in the Veterans Affairs Health Care System From 2007 to 2017. Parizo JT, Kohsaka S, Sandhu AT, Patel J, Heidenreich PA. *JAMA Cardiol*. 2020 Jun 17:e202028. doi: 10.1001/jamacardio.2020.2028. PMID: 32584921

The effects of combination canagliflozin and glucagon-like peptide-1 receptor agonist therapy on intermediate markers of cardiovascular risk in the CANVAS program. Arnott C, Neuen BL, Heerspink HJL, Figtree GA, Kosiborod M, Lam CS, Cannon CP, Rosenthal N, Shaw W, Mahaffey KW, Jardine MJ, Perkovic V, Neal B. *Int J Cardiol*. 2020 Jun 20:S0167-5273(20)33389-1. doi: 10.1016/j.ijcard.2020.06.011. PMID: 32569700

Toward the Clinical Development and Validation of a Thy1-Targeted Ultrasound Contrast Agent for the Early Detection of Pancreatic Ductal Adenocarcinoma. Bam R, Daryaei I, Abou-Elkacem L, Vilches-Moure JG, Meuillet EJ, Lutz A, Marinelli ER, Unger EC, Gambhir SS, Paulmurugan R. *Invest Radiol*. 2020 Jun 18. doi: 10.1097/RLI.0000000000000697. PMID: 32569010

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Opportunities and challenges of implementing computed tomography fractional flow reserve into clinical practice. Nazir MS, Mittal TK, Weir-McCall J, Nieman K, Channon K, Nicol ED. *Heart*. 2020 Jun 19;heartjnl-2019-315607. doi: 10.1136/heartjnl-2019-315607. PMID: 32561589

The American Heart Association COVID-19 CVD Registry powered by Get With The Guidelines®. Alger HM, Rutan C, Williams IV JH, Walchok JG, Bolles M, Hall JL, Bradley SM, Elkind MSV, Rodriguez F, Wang TY, Morrow DA, Das SR, de Lemos JA. *Circ Cardiovasc Qual Outcomes*. 2020 Jun 17. doi: 10.1161/CIRCOUTCOMES.120.006967. PMID: 32546000

July

Quadrupling the N95 Supply during the COVID-19 Crisis with an Innovative 3D-Printed Mask Adaptor. Imbrie-Moore AM, Park MH, Zhu Y, Paulsen MJ, Wang H, Woo YJ. *Healthcare (Basel)*. 2020 Jul 23;8(3):E225. doi: 10.3390/healthcare8030225. PMID: 32717841

Resilience and CVD-protective Health Behaviors in Older Women: Examining Racial and Ethnic Differences in a Cross-Sectional Analysis of the Women's Health Initiative. Springfield S, Qin F, Hedlin H, Eaton CB, Rosal MC, Taylor H, Staudinger UM, Stefanick ML. *Nutrients*. 2020 Jul 16;12(7):E2107. doi: 10.3390/nu12072107. PMID: 32708626

Sufficiency for inducible Caspase-9 safety switch in human pluripotent stem cells and disease cells. Nishimura T, Xu H, Iwasaki M, Karigane D, Saavedra B, Takahashi Y, Suchy FP, Monobe S, Martin RM, Ohtaka M, Nakanishi M, Burrows SR, Cleary ML, Majeti R, Shibuya A, Nakauchi H. *Gene Ther*. 2020 Jul 23. doi: 10.1038/s41434-020-0179-z. PMID: 32704085

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Metabolic Maturation Media Improve Physiological Function of Human iPSC-Derived Cardiomyocytes. Feyen DAM, McKeithan WL, Bruyneel AAN, Spiering S, Hörmann L, Ulmer B, Zhang H, Briganti F, Schweizer M, Hegyi B, Liao Z, Pölönen RP, Ginsburg KS, Lam CK, Serrano R, Wahlquist C, Kreymerman A, Vu M, Amatya PL, Behrens CS, Ranjbarvaziri S, Maas RGC, Greenhaw M, Bernstein D, Wu JC, Bers DM, Eschenhagen T, Metallo CM, Mercola M. *Cell Rep*. 2020 Jul 21;32(3):107925. doi: 10.1016/j.celrep.2020.107925. PMID: 32697997

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