Advances in research and technology now afford us the unique opportunity to develop and test novel diagnostics and therapeutics. This conference takes advantage of the collective experience and expertise of our speakers in drug discovery. A broad range of policy, research, and venture topics are covered. The 2021 virtual Stanford Drug Discovery Symposium will include presentations from leaders of major pharmaceutical companies, federal and foundation policy makers, and scientists making groundbreaking advances in drug discovery.

This symposium is an extraordinary platform for inspiring interdisciplinary exchange at the forefront of drug research and provides an invaluable forum for the open exchange of ideas between academia, industry, government, and non-profits. In addition to the outstanding line-up of speakers, the conference will feature a panel discussions including a panel discussion with leading journal editors, a panel discussion with venture capitalists, and a series of short presentations and interactive discussions with recently established companies. For more information on the speakers, please see page 2 and visit our website (http://tinyurl.com/SDDS2021) for free registration.

Hannah Valantine Elected to National Academy of Medicine

The latest cohort of elected National Academy of Medicine members includes Hannah Valantine, MD, MRCP, FACC, professor of cardiovascular medicine. Election to the NAM is considered one of the highest honors in health and medicine. “This distinguished and diverse class of new members is a truly exceptional group of scholars and leaders whose expertise in science, medicine, health, and policy will be integral to helping the NAM address today’s most pressing health challenges and inform the future of health and health care for the benefit of everyone around the globe,” said National Academy of Medicine President Victor J. Dzau, MD. Dr. Valantine, the former chief officer of scientific workforce diversity for the National Institutes of Health and senior investigator of the National Heart, Lung, and Blood Institute, was recognized, “for her national leadership in both scientific workforce diversity and cardiac transplantation research.” We congratulate our colleague on this honor.


13 CVI Members Are Among the World's Most Highly Cited Researchers in 2020

The Cardiovascular Institute is delighted to recognize the inspirational Stanford scientists who have been included in the Clarivate Analytics Web of Science 2020 Highly Cited Researcher list. Inclusion in this list is a testament to these scientists’ exceptionally broad and impactful contributions, and the significant influence they have had in their fields. We congratulate Drs. Russ Altman, Zhenan Bao, Howard Chang, Hongjie Dai, Mark Davis, Jesse Engreitz, Sanjiv Sam Gambhir, Mark Hlatky, John Ioannidis, Brian Kobilka, Kenneth Mahaffey, Irving Weissman and Joseph C. Wu.

PARTICIPANTS INCLUDE:

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

Douglas Lowy, MD
Director, National Cancer Institute

Michael Basson, PhD
Senior Editor, Nature Medicine

Carmen Chang, MA, JD
General Partner, Head of Asia New Enterprise Associates

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

Anne Heatherington, PhD
Senior Vice President, Head of Data Sciences Institute, Takeda

Peter Kim, PhD
Virginia and D.K. Ludwig Professor of Biochemistry, Stanford

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

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

Lloyd Minor, MD
Carl and Elizabeth Naumann Professorship for the Dean, Stanford School of Medicine

Andrew Plump, MD, PhD
President, Research & Development Takeda Pharmaceutical Company Limited

Mark Smith, MD, MBA
Founding President and CEO California Healthcare Foundation

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

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

LIFETIME ACHIEVEMENT Awardees

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

Douglas Lowy, MD
Director, National Cancer Institute

SDDS takes advantage of the collective experience of our participants to cover a wide range of policy, research, and venture topics. It provides an invaluable forum for interdisciplinary exchange at the forefront of drug research.

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The Institute currently consists of over 240 faculty members representing physicians, surgeons, engineers, basic and clinical researchers. The Institute’s mission is integrating fundamental research across disciplines and applying technology to prevent and treat cardiovascular disease.

To support cardiovascular research and education at CVI, please contact: Joseph C. Wu, MD, PhD, CVI Director at joewu@stanford.edu or Cathy Hutton, Senior Associate Director, Medical Center Development at cathy.hutton@stanford.edu.

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Host: Joseph C. Wu, MD, PhD
Email: joewu@stanford.edu

January 5, 2021
ÅSA GUSTAFSSON, PHD
Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, Department of Pharmacology, UCSD School of Medicine

January 12, 2021
MICHAEL REGNIER, PHD
Director, UW Center for Translational Muscle Research, and Professor of Bioengineering, School of Medicine & College of Engineering, University of Washington

January 19, 2021
JOAN HELLER BROWN, PHD
Distinguished Professor and Chair, Department of Pharmacology, UCSD School of Medicine

January 26, 2021
TEJAL DESAI, PHD
Department Chair and Professor, Department of Bioengineering and Therapeutic Sciences, UCSF School of Pharmacy

February 2, 2021
CATHERINE BOILEAU, PHARMD, PHD
Chair of the Genetics Department, Bichat Hospital

February 9, 2021
KATHERINE YUTZEY, PHD
Professor of Molecular Cardiovascular Biology, The Heart Institute, Cincinnati Children’s Medical Center, Cincinnati Children's Hospital

February 16, 2021
HANNAH VALANTINE, MD, MRCP
Professor of Medicine, Division of Cardiovascular Medicine and Senior Associate Dean for Diversity and Faculty Development, Stanford University School of Medicine

February 23, 2021
NAOMI CHESLER, PHD
Professor of Biomedical Engineering and Director of the Edwards Lifesciences Center for Advanced Cardiovascular Technology, UCI Samueli School of Engineering

March 2, 2021
SUMANTH D. PRABHU, MD
Professor of Medicine, Mary G. Waters Chair of Cardiovascular Medicine, and Director of the Division of Cardiovascular Disease, University of Alabama at Birmingham

March 9, 2021
STAVROS G. DRAKOS, MD, PHD
Professor of Medicine & Nora Eccles Treadwell Scholar, Division of Cardiology Research Director, Co-Chief of Heart Failure & Transplant, and Medical Director of Mechanical Circulatory Support, Nora Eccles Harrison Cardiovascular Research and Training, University of Utah

March 16, 2021
AIKATERINI KONTROGIANNI-KONSTANTOPOULOS, PHD
Professor of Biochemistry and Molecular Biology, Director of Interdisciplinary Training Program in Muscle Biology, Marlene and Stewart Greenebaum Comprehensive Cancer Center, University of Maryland School of Medicine

March 23, 2021
CHARLES C. HONG, MD, PHD
Dr. Melvin Sharoky Professor of Medicine and Director of Cardiology Research, University of Maryland School of Medicine

March 30, 2021
ARJUN DEB, MD
Professor of Cardiology; Molecular, Cell and Developmental Biology; and Director of the UCLA Cardiovascular Medicine Research Theme, UCLA

CVI Represents at #AHA20 Scientific Sessions

DCRI News @DCRINews · Nov 17
@FaRodriguezMD of @StanfordMed is now presenting on racial disparities seen within the AHA COVID Registry. This study, which incl. DCRI’s @TYWangMD as senior author, found that Black and Hispanic patients were overrepresented in the registry. #AHA20 #AHAMeetings #COVID19

Joseph C Wu, MD, PhD @Joseph_C_Wu · Nov 13
Please join #AHA20 and hear about the exciting research @StanfordCVI faculty are doing. Link: professional.heart.org/ls/meetings/sc...
@StanfordDepMed @Stanfordvasc @StanfordCTSurg @StanCVFellows @Stanford_CEmH @BCVSearleyCareer @joshuazkowles @SeanM_Wu @HeartBobH @AHACalifornia @StanfordPulm

DCRI News @DCRINews · Nov 17
@FaRodriguezMD flawlessly presenting her first late breaker at 7am after finding out power was out and needing to urgently relocate to a place with power and wifi! #graceunderfire #Shero @WomenAss @StanfordMed

DCRI News @DCRINews · Nov 17
The amazing @FaRodriguezMD showed us important data that says we need to do better in #Covid19 hospitalizations in both white and non-white patients. Black and Hispanic patients are disproportionately hospitalized and dying. Asians have the worst disease severity. twitter.com/DCRINews/status...

Tracy Wang @TYWangMD · Nov 17
Congrats to Louis N. and Arnold M. Katz Basic Research Prize Glynnis Garry, William Goodyear, Ningxia Ou, Manuel Rosa-Galindo, Joshua Travis. @glynnsicarry @Transactivator @SeanM_Wu @MingxiaGu @Josh/JTravely @AHA_Research #AHAScience

Ngan F Huang, PhD @NganHuang · Nov 17
Awesome times with these stellar ladies of the AHA Women’s Leadership Committee! Moderating roundtable discussions on Navigating Academic Paths for Women and Minorities: We need this now more than ever! @AppliedCVB @StanfordCVI @StanfordCTSurg #AHA20 #AHA2020 #AHAMeetings

Robert Harrington @HeartBobH · Nov 13
And so it begins....@MitchElkind launching #AHA20 Great few days of science, networking and mentoring. @American_Heart @AHAMeetings @AHAScience

Robert Harrington @HeartBobH · Nov 18
Agree! Great to have the option of toggling from talk to talk w/o leaving your seat @ #AHA20 yet missing out on F2F mentoring & chat w friends/colleagues, I’d volunteer 2 organize a mt where talks r virtual but small group, meals & social r in-person @ hotel. Bonus if nice locale.

Eldrin Lewis @EldrinL · Nov 15
I am so excited to attend and participate in #AHA20. Back stage with first LBCT session starting in 5 minutes.

Eldrin Lewis @EldrinL · Nov 15
I am enjoying the session on A primer on diabetes at #AHA2020. 2 1/2 days left of great science and education!
More Than Half of In-hospital Deaths from COVID-19 Among Black, Hispanic Patients, Study Finds By Tracy White

Researchers found that Black and Hispanic people made up 58% of all patients hospitalized for COVID-19 and 53% of those who died from the disease. More than half of all in-hospital deaths due to COVID-19 during the first six months of 2020 were among Black and Hispanic patients, according to a new study led by researchers at the Stanford University School of Medicine and Duke University School of Medicine. The researchers did not find any racial or ethnic differences in mortality rates among people hospitalized with the disease. Yet a disproportionate number of Black and Hispanic people became sick enough to require hospitalization, and they made up 53% of inpatient deaths.

Fatima Rodriguez, MD, assistant professor of cardiovascular medicine at Stanford, is the lead author of the study, which was published Nov. 17 in Circulation. Tracy Wang, MD, professor of medicine at Duke University, is the senior author. “The COVID-19 pandemic has shown a spotlight on racial and ethnic disparities in health care that have been happening for years,” said Rodriguez, an expert in health disparities in cardiovascular medicine. “Our study shows an over-representation of Black and Hispanic patients in terms of morbidity and mortality that needs to be addressed upstream before hospitalization.”

Researchers examined a sample of 7,868 patients hospitalized with the coronavirus at 88 hospitals across the country between Jan. 17 and July 22. The data was collected from the American Heart Association’s COVID-19 Cardiovascular Disease Registry. The average mortality rate for all patients was 18.4%. The researchers found that white patients accounted for 35.2% of the sample, Hispanic patients for 33%, Black patients for 25.5% and Asian patients for 6.3%. The U.S. Census Bureau estimates that white people make up 60% of the nation’s population, Hispanic people 18.5%, Black people 13.4% and Asian people 5.9%. “Interestingly, more of the variations in mortality were explained by the site of the care than by race or ethnicity,” Rodriguez said. “We need to understand more about differences between hospitals. Is it different treatment protocols that are rapidly evolving during the pandemic? Or perhaps minority-serving hospitals have different resources? This is an active area of research within the registry used for this study as we enroll more sites across the country.”

The study had some limitations, Rodriguez said, including an overrepresentation of urban and large academic teaching hospitals in the data sample, but the findings remain startling. “My work focuses on preventing chronic disease before patients are hospitalized,” Rodriguez said. “We need to invest in communities to increase opportunity for healthy lifestyles and good health care. Structural racism, we know, is a major roadblock for preventing good health.”


NASA Takes 3D Engineered Heart Tissue into Space

Earlier this month, NASA flew a cargo resupply rocket to the International Space Station carrying research payloads that included 3D Engineered Heart Tissue developed by Stanford CVI scientists in the lab of Dr. Joseph C. Wu, MD, PhD. The Cardinal Heart program studies how gravity affects heart tissue at the cellular and molecular leve. “For this particular study, we’re sending a piece of human heart tissue that has the cardiomyocytes, the fibroblasts, and the endothelial cells. We put the three cells together to form what we call a 3D Engineered Heart Tissue and our plan is to send this contracting tissue into space so we can understand the effect of microgravity on cardiac function in human heart tissue,” shared Dr. Wu. A researcher on the project, Dilip Thomas, PhD added, “We are confident that our science is going push the frontier of cardiovascular research to the next level.”


Video: https://images.nasa.gov/details-SpX-21_Whats_On_Board

CVI Virtual Tour

Explore the Stanford Cardiovascular Institute’s website to learn more about its history, opportunities, and initiatives - and have the chance to win a prize!

Insights from Cells of Patients with Birth Defects of the Heart

By Amanda Chase, PhD

Hypoplastic left heart syndrome (HLHS) is a severe birth defect of the heart that disrupts normal blood flow. Left untreated, HLHS is fatal. Treatment includes a series of surgeries to redirect blood flow so the right ventricle pumps blood to compensate for the underdeveloped left side. Many patients still require a heart transplant due to unexplained right ventricular (RV) failure. Understanding why there is early RV failure for some patients, and how to prevent or treat that failure, is an important step to improving care for HLHS patients.

Sharon Paige, MD, PhD, and senior author Sean Wu, MD, PhD, used HLHS patient-derived induced pluripotent stem cell cardiomyocytes (iPSC-CMs) to better understand HLHS in a recent *Circulation* paper. They showed that contraction force and acceleration were reduced in HLHS iPSC-CMs, mirroring what was seen in patients. They also showed that genes that were expressed differently in HLHS patients, compared to healthy individuals, were mostly defined as heart failure coordinators. Importantly, the authors also showed that mitochondrial dysfunction contributes to the reduced ability to pump. This dysfunction may underlie early RV failure seen in some HLHS patients, and provide a novel therapeutic target for intervention.


A Molecular Switch Governing Pathological Changes in Heart Muscle Cell Shape

By Adrienne Mueller, PhD

Because heart muscle cells are responsible for the contractions that pump our blood, their shape is very important. Having the right shape allows them to move blood effectively. Stressing heart muscle cells can cause them to change their shape in a way that impairs heart function. One common source of stress is an obstruction to the outflow of the heart, which exposes heart muscle cells to excessive pressure, to which they respond by growing wider. Another source of stress is caused by heart chamber enlargement, which often occurs as a result of a heart attack, to which they respond by growing longer. Both of these changes in heart muscle cell shape—growing wider in response to pressure overload and growing longer in response to volume overload—spell trouble for heart function and increase your risk of heart failure.

A group of investigators led by co-first author Jinliang Li, PhD and co-senior author Michael Kapiloff, MD, PhD, examined the role of the serum response factor (SRF) protein in this process. In their study, recently published in *Circulation*, they discovered that SRF acts as a switch that determines whether heart muscle cells grow predominantly in width or in length. As Dr. Kapiloff describes, "Stress often causes heart muscle cells to grow, but what is especially exciting about this result is that we have identified a molecular switch that specifically directs growth in one direction versus another." Identifying ways to prevent SRF from being switched too far in either direction, therefore, has significant therapeutic potential.


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Exposure to Air Pollution Can Put Adolescents at Risk for Cardiovascular Disturbances

By Amanda Chase, PhD

With the increasing number of wildfires, more people are becoming familiar with air quality and the idea of PM 2.5 (particulate matter 2.5). PM 2.5 is a measure of particulate matter (PM) that is small enough to bypass the body's filtration system and enter into the respiratory tract, which can lead to damage of other parts of the body. PM 2.5 refers to not only particulate released from wildfires, but also from all other pollutants, including from vehicles or burning of fuels. Together, PM 2.5 air pollutants are known to be related to negative health effects, including respiratory disease and increasing symptoms of respiratory disease, and cardiovascular effects. The link between PM 2.5 and cardiovascular disease (CVD) is well established in adults; however, few studies have looked at the impact in children and adolescents. Mary Prunicki, MD, PhD, and Kari Nadeau, MD, PhD, addressed this critical need in their recent publication in *Environmental Health*.

Dr. Nadeau’s team recruited a cohort of 100 adolescents from Fresno, California, an area with high levels of air pollution. They were able to perform proteomic analysis and complex characterization of immune cell populations to identify immune markers linking air pollution exposure and blood pressure. They showed, for the first time in adolescents, that air pollution levels were associated with oxidative stress, inflammation, and endothelial dysfunction. Importantly, they were also able to use human stem-cell-derived cardiomyocytes (heart muscle cells) to show that air pollutants can induce cardiovascular toxicity. Together, these findings suggest that air pollution adversely affects cardiovascular health in adolescents.


Improving Heart Health, Decreasing Tobacco Use in Alaska By Cassie Myers

The COVID-19 pandemic provided the first taste of telemedicine for many people, but Jodi Prochaska, PhD, has been harnessing the benefits of virtual health care for several years. Prochaska, a researcher at the Stanford Prevention Research Center who specializes in tobacco reduction, is one of the leaders of the Healing and Empowering Alaskan Lives Toward Healthy Hearts, known as HEALTHHH, project in Alaska. The project examines how telemedicine can improve heart health for Alaska Native men and women who use tobacco. There’s a high prevalence of smoking in Alaska particularly among the Native population. About half of Alaska Native men and a third of Alaska Native women smoke—rates that haven’t been seen in the continental United States since the 1960s. "It's a very high smoking prevalence in a remote location, without easy access to treatment. Developing partnerships and trust is critical," Prochaska said. To that end, the study team partnered with the tribal council in the Norton Sound region.

Prochaska’s incredibly multidisciplinary team created the HEALTHHH study: a two-group randomized controlled trial. One group is focused on tobacco and physical activity, the other is focused on Native diet and heart medication compliance. The project aims to examine changes in individual behaviors such as smoking and in overall quality of life over 18 months. These interventions are largely delivered by telemedicine. The results of the project haven’t been published yet, but receptivity was high among participants, Prochaska said. "You guys really helped me with trying to quit smoking," one participant said. "There was a lot of different opportunities to quit and that helped me out a lot."

https://scopeblog.stanford.edu/2020/10/16/improving-heart-health-decreasing-tobacco-use-in-alaska/

MAVENS provides a unique opportunity to inspire, empower, and support women in academic medicine throughout their career to create an integrated community of scientists. Junior faculty are invited and encouraged to join.

Program Directors: Cornelia Weyand, MD, PhD; Patricia Nguyen, MD; Amanda Chase, PhD
Cancer Survivors and Lymphedema By Adrienne Mueller, PhD

Lymphedema is a challenging condition that affects 100–250 million individuals globally, including 2–5 million cancer survivors. It is characterized by a buildup of fluid in the lymphatic system, which normally distributes fluid and cells throughout the body to help fight infection. The reason why lymph fluid buildup occurs is unknown.

The circulatory system also uses vessels to distribute fluid throughout the body. Among the molecules that shape our blood vessels are a family of proteins called hypoxia inducible factors (HIFs). Given their influence on vessel remodeling, HIF proteins seemed a promising candidate for understanding lymph vessel blockage in lymphedema. Co-first authors Xinguo Jiang, MD, PhD, Wen Tian, PhD, Eric J. Granucci, and Allen B. Tu, as well as senior author Mark Nicolls, MD, therefore investigated the role of HIF proteins in lymphedema. Described in their recent article in the Journal of Clinical Investigation, the team first looked for the presence of HIF proteins in tissue with lymphedema. They discovered that, indeed, a class of specialized lymphatic cells had an abundance of one HIF protein (HIF-1α), but significantly reduced levels of another HIF protein, HIF-2α. Using genetic manipulations to restore HIF-2α to lymphatic cells alleviated lymphedema and restored lymphatic function. This study points the way towards targeting HIF-2α for the development of new therapies.


Leveraging Innovation to Solve a Medical Mystery By Amanda Chase, PhD

Dilated cardiomyopathy (DCM) is a common cause of heart failure in children, and of heart transplantation for both adults and children. DCM occurs when heart muscle cells are damaged and it results in a worsened ability to pump blood. Understanding the cause of a DCM can improve care for patients and decrease the need for transplantation.

This critical need was recently addressed by a group of investigators led by first author Aviva Levitas and senior author Ioannis Karakikes, PhD, and published in PLOS Genetics. Several years ago, all five children from one family were diagnosed with early-onset, severe DCM, and eventually succumbed to the disease. However, the affected children did not carry any mutations in the 50 plus known genes associated with DCM. By employing innovative technologies, such as human induced pluripotent stem cells (iPSCs) and CRISPR/Cas9-based genome editing technologies, the team developed a platform to assess whether genetic mutations cause childhood cardiomyopathy and death. They found that a specific mutation found in the SPEG protein of the children disrupted normal physiology and function of iPSC-derived cardiac cells.


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Using Artificial Intelligence to Predict Arrhythmia and Sudden Death

By Adrienne Mueller, PhD

If you’ve had a heart attack, you may think the worst is behind you, but heart attack survivors can also develop a condition called ventricular arrhythmia which can lead to sudden cardiac death. Currently, it is very hard to predict whether a given heart attack survivor is likely to develop ventricular arrhythmia. Traditional clinical markers are, at best, only 64% accurate as predictors for developing the condition. Notably, many potential causes have been shown at the cellular level, but these cannot currently be used to predict sudden cardiac death in patients.

In their study, recently published in *Circulation Research*, co-first authors Albert J. Rogers, MD and Anojan Selvalingam, and senior author Sanjiv Narayan, MD, used a machine learning approach based on cell-level data to improve our ability to predict which heart attack survivors are likely to develop sudden death. Their team collected almost 6,000 electrical recordings from the hearts of 42 heart attack survivors who had never had ventricular arrhythmias, and trained a machine learning model to identify which patterns in the recordings were predictive of either: 1) developing sudden death from ventricular arrhythmia or, 2) dying within three years. Their machine learning-derived “computational phenotype” vastly outperforms existing clinical marker models—predicting the development of ventricular arrhythmia with 90% accuracy, and fatality with 91% accuracy. In the future, computational phenotypes that predict a defined outcome may allow better personalized therapy. The success of this study suggests that artificial intelligence-derived computational phenotypes could be considered for the diagnosis of other cardiac and non-cardiac disorders.


New Insights in Vascular Biology

By Amanda Chase, PhD

Precision medicine is an exciting, emerging approach that considers an individual patient’s genes, lifestyle, and environment in disease treatment. Targeted treatment, which can also be called precision drugs, is the chance to provide effective (higher) drug concentrations at the specific areas in the body (tissues) that are diseased, while the rest of the body receives less or none of the drugs.

A key to implementing precision drugs is in understanding what makes each tissue unique, or identifiable. In a recent paper in *Circulation*, a team of researchers from Stanford Cardiovascular Institute, led by first authors David Paik, PhD, Lei Tian, PhD, and Ian Williams, PhD, and senior author Joseph Wu, MD, PhD, looked at what made endothelial cells from different tissues unique. Endothelial cells (ECs) line blood vessels and help regulate blood flow, among many other important functions. The team used novel techniques to look at markers, pathways, or other unique features of ECs in 12 different mouse organs, including the kidney, brain, heart, liver, lung, and pancreas. They identified signature markers that were enriched in ECs from different mouse tissues, and found that some of those markers are the same as in humans. The markers, therefore, could be targets for tissue-specific drug delivery.


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Heart Cells Speak a Common Language with Different Accents by Adrienne Mueller, PhD

Cells communicate with each other in many different ways, one of which is the release of small vesicle packets called exosomes. Exosomes are filled with tiny molecules such as microRNA. The collection of molecules released by secreted exosomes can influence nearby cells’ behavior, function, development, and even identity. What co-first authors Mark Chandy, MD, PhD, June-Wha Rhee, MD and Mehmet Ozen, PhD and co-senior authors Edward Lau, PhD, Utkan Demirci, PhD and Joseph C. Wu, MD, PhD wanted to find out is what different types of heart cells are saying to each other via exosomes.

The investigators used human induced pluripotent stem cells to create three different lineages of heart cells: heart muscle cells, endothelial cells, and fibroblasts. They then went on to collect the exosomes from these three different cell types using a unique tool, ExoTIC, developed at Stanford and compared their microRNA contents. As they report in their recent paper in Circulation, the exosomes of these three different cells possess a shared set of microRNAs, but each cell also releases a specific subset of microRNAs that the other cell types do not. The authors were also able to create an interactive atlas of exosomal microRNAs that allows anyone to explore the relative abundance of particular microRNAs in different tissues. http://med.stanford.edu/cvi/mission/news_center/articles_announcements/heart-cells-speak-a-common-language-with-different-accents.html

Tiny Bits of RNA Give Window into Adult Congenital Heart Disease in Stanford Study by Erin Digitale

Measuring tiny bits of genetic material in blood can provide a unique view into the development of heart failure, according to new Stanford Medicine research. The technique also has the potential to help scientists identify new targets for drugs that treat problems with the muscle on the right side of the heart, which existing heart medications do not help. The study, published recently in PLOS ONE, focused on adults with tetralogy of Fallot, a form of congenital heart disease. Born with a combination of four structural heart defects, these patients generally receive cardiac repair surgeries early in childhood. Though very effective, the surgeries are not perfect.

In the new study, Weldy and his colleagues measured tiny pieces of genetic material called microRNA in patients’ blood, in an effort to secure more information about the development of problems in the right ventricle. The patients’ microRNA profiles correlated with the amount of right ventricular enlargement. The microRNA profiles also held clues as to which metabolic pathways go awry in patients whose right ventricles fail. For instance, the new data showed that molecular pathways that regulate how the right ventricle processes fatty acids were not working correctly. The molecular changes could provide a starting point for designing new drugs that target right ventricular problems, Weldy said, concluding, “It’s exciting that, through a noninvasive test, we now have a potential method that could give insight into biology of what’s going on in someone’s heart.” https://scopeblog.stanford.edu/2020/11/16/tiny-bits-of-rna-give-window-into-adult-congenital-heart-disease-in-stanford-study/

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Tiny Bits of RNA Give Window into Adult Congenital Heart Disease in Stanford Study

Chad Weldy, MD, PhD
June-Wha Rhee, MD
Mehmet Ozen, PhD
Edward Lau, PhD
Utkan Demirci, PhD

Tiny Bits of RNA Give Window into Adult Congenital Heart Disease in Stanford Study

Chandy, Rhee & Ozen et al created a "secretome": an interactive atlas of exosomal microRNAs. https://tinyurl.com/secretome

Sushma Reddy, MD

Chandy, Rhee & Ozen et al created a "secretome": an interactive atlas of exosomal microRNAs. https://tinyurl.com/secretome
How Oxygen Hurts Our Hearts by Adrienne Mueller, PhD

Congenital heart disease, a condition which approximately 1% of children in the US are born with, often causes a chamber of the heart called the right ventricle to fail. The standard therapies we deploy for left heart failure—beta blockers, and ACE-inhibitors—do not work for right ventricular failure. We therefore need better therapies that target the underlying problem in these patients, which means we need a better understanding of the mechanisms causing our hearts’ right ventricles to fail.

Heart cells are extremely energy intensive. Because heart cells consume so much oxygen to produce energy, they are especially vulnerable to oxidative stress. First author HyunTae Hwang, PhD, and senior author Sushma Reddy, MD, therefore investigated how oxidative stress impacts heart cells. In a paper recently published in Circulation, Hwang et al showed that the heart cells of individuals with right ventricular failure do indeed exhibit oxidative stress, particularly of lipid membranes. When lipids are oxidated they create a product called 4HNE. Hwang et al showed that there is more 4HNE being produced in patients with right ventricular failure and that mitochondria, which are extremely lipid-rich, are especially sensitive to 4HNE damage. Antioxidative therapies are thus a promising avenue to preventing right ventricular failure in at-risk patients. This study sheds light on a new mechanism to help explain right ventricular failure.


Learning from 3D Engineered Heart Tissue by Amanda Chase, PhD

A heart attack occurs when blood flow to the heart is blocked, resulting in oxygen loss and damage to the heart muscle due to loss of heart muscle cells (cardiomyocytes). In turn, the damaged heart muscle can disrupt the ability of the heart to pump blood, resulting in heart failure. Despite the high prevalence of heart attacks and heart failure, most treatment options are focused on prevention and reducing known risk factors. Cell therapy, in comparison, has the potential to offer a treatment that can restore heart function by regenerating the damaged heart tissue.

Induced pluripotent stem cells-derived cardiomyocytes (iPSC-CMs) are a potential source of cells to improve damaged heart tissue that results from heart attacks. A team of researchers led by first authors Huaxiao Yang, PhD, and Ningyi Shao, PhD, and senior author Joseph Wu, MD, PhD recently published a study in Cardiovascular Research that evaluated the best way to look at how heart cell therapy, or regenerative therapy, may work. Work with iPSC-CMs is historically done in a single 2D layer in a dish. More recently, work has moved into a 3D model, which allows for more tissue-level interactions. The research team carried out a direct comparison of the two models, subjecting both to decreased oxygen, similar to what is experienced during a heart attack. The team then looked for known identifiers of heart attacks to determine which model best represented heart conditions post-attack. The answer: the 3D model. “Profiling of the iPSC-CMs under different conditions improves our understanding of the mechanism of injury that leads to decreased oxygen to the heart tissue and the chance for heart failure,” says Dr. Joseph Wu, “this may prove useful for advancing cell therapy delivery approaches in the future.”


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Or visit: https://med.stanford.edu/cvi/translational-research/memberpubs.html
Shedding Light on Pulmonary Arterial Hypertension By Amanda Chase, PhD

Translational science is affording us an era of improved understanding and treatment of many diseases, including fatal ones. Recent work led by first authors Lea Steffes, MD, and Alexis Froistad, and senior author Maya Kumar, PhD, highlights how new models and innovative technologies can combine to uncover disease mechanisms of pulmonary arterial hypertension (PAH). PAH is a fatal disease that is characterized by progressive narrowing of the arteries in the lungs. Narrowing is a result of abnormal cells (neointima cells) accumulating in the vessel, and it causes the heart to work harder to pump blood through the lungs. This leads to the heart muscle weakening and, eventually, failing.

In their recent Circulation publication, the team used novel tools to address several unknowns critical to understanding underlying mechanisms of PAH to lead to potential treatments. First, the team demonstrated that the abnormal cells originated from vascular smooth muscle cells of the artery wall, not from the endothelium. The researchers were also able to define both temporally and spatially distinct steps in the development of pulmonary artery formation. Finally, they showed that cells expressing a gene called Notch3 were the major subset of cells that abnormally migrated to result in a narrowed vessel. This finding provides a potential target for treatments to prevent vessel thickening characteristic of PAH. Together, this team of researchers was able to open the door for future studies to offer new avenues for therapy development.


Taking a Closer Look at our Lungs: Discovery of Two Capillary Cell Types By Adrienne Mueller, PhD

"Alveoli, and the surrounding capillaries, were first described by Malpighi more than 350 years ago. The kind of heterogeneity we discovered, where two capillary cell types with distinct functions are part of the same vessel, was unexpected. It had not been described for any organ," shared Ross Metzger, PhD regarding the surprising findings that he recently helped bring to light. The incredibly thin alveolar walls are comprised of two layers: an outer epithelial layer, separating air from the capillary vessels, and an inner endothelial layer, forming the blood vessel walls. A team of primarily Stanford investigators, led by first author Astrid Gillich, PhD and co-senior authors Dr. Metzger and Mark Krasnow, MD, PhD, recently released a paper in Nature in which they systematically investigated the understudied capillary vessels and identified two new, molecularly distinct populations of cells that serve different roles in our lungs.

The first cell type that Gillich et al describe is a huge, complex cell with pores that give them a Swiss cheese-like appearance. These cells are also closely associated with cells in the alveolar layer close to the air, reflecting a specialized role in gas exchange. The second cell type that the investigators discovered are much smaller and more numerous, and the authors named them "general capillary" cells. By closely studying both cell types over time, the investigators discovered that general capillary cells act as progenitors and help repair lung damage.

New Abdominal Aortic Aneurysm Genes Identified, Could Help Pinpoint Those at Risk

American Heart Association News Release

A veteran’s study identified more than a dozen genes associated with abdominal aortic aneurysm (AAA) that could be used to better identify people at risk for the often-deadly condition. Abdominal aortic aneurysm is a bulging or weakening of the aorta—the largest blood vessel in the body. Only about 20% of patients survive the rupture of an abdominal aortic aneurysm. Previous studies have detected 10 locations in the human genome associated with potential risks, however, those genes account for only a fraction of the causes for developing the condition. “This study has doubled the number of genetic associations with abdominal aortic aneurysm,” said corresponding author Philip S. Tsao, PhD, “This new information can enhance screening protocols and help identify individuals at risk for the condition.”

Using the Million Veteran Program database, researchers performed a genome-wide association study in veterans of European ancestry, testing roughly 18 million DNA sequence variants among more than 7,500 abdominal aortic aneurysm cases and 172,000 veterans without abdominal aortic aneurysms. They examined the effects of blood pressure on abdominal aortic aneurysms using Mendelian randomization – a technique that leverages genetic variation to study the causal relationship between traits. Throughout the testing, researchers created a “polygenic risk score” to help identify subsets of the population who are more likely to develop abdominal aortic aneurysms. The analysis found: 14 previously unidentified genetic locations associated with abdominal aortic aneurysm development (bringing the total number of known gene associations to 24), that a genetic increase in diastolic blood pressure increased the risk of developing abdominal aortic aneurysm, and that the polygenic risk score was strongly associated with abdominal aortic aneurysm, regardless of known risk factors, including smoking and family history.


Not All Grafts Are Created Equal: Improving Valve-sparing Aortic Root Surgery

By Amanda Chase, PhD

Aneurysm. A word with big implications for the patient. An aneurysm is an outward bulging of an abnormal, weak spot on a blood vessel wall. Aneurysms can occur in any blood vessel, including the aorta, the largest artery in the body that carries blood from the heart to the rest of the body. Aneurysms are usually asymptomatic, found during routine testing for other medical conditions or when the aneurysm has ruptured and resulted in more severe complications. Despite the implications of an aortic aneurysm, there are no non-surgical treatments, and aneurysms can only be treated with surgery after they have reached a certain size.

A specialized surgery for treating a specific aortic aneurysm is called a valve-sparing aortic root repair. In this surgery, pioneered 28 years ago, the patient’s native aortic valve is spared and reconnected to a graft. In the years since, there have been modifications to the procedure, especially in the choice of graft used. However there is no consensus on which graft choice is ideal. In their recently published manuscript in Circulation, a team of clinician-scientists, led by first author Michael Paulsen, MD, and senior author Y. Joseph Woo, MD, compared several graft options for the operation. The team used an innovative 3D-printed heart simulator that mimics flow, pressures, and other factors of normal heart function. Surprisingly, they found that the original cylindrical graft without modifications to mimic nature, termed a Straight Graft, appeared to act most like a patient’s own aortic root. The observed benefits of the Straight Graft in both simulated heart and clinical data, combined with its relatively lower cost and wide availability world-wide, make this particular surgical graft option preferred by this research team.


Cvi.Stanford.edu

CVI Staff Spotlight

Kari Costa recently celebrated her 20th anniversary at Stanford. Since joining CVI in 2016, she has been supporting research faculty and staff with everything from grant submission, to finance, to helping HR with new hires and more.

One of her favorite parts of working at CVI is hearing about all the exciting research and meeting scientists from around the world. When she’s not supporting CVI’s research, she loves hiking, riding motorcycles, and doing arts and crafts with her 13 grandchildren.

cvi.stanford.edu
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 of patients.

Cardiovascular Medicine’s Clinical Research Office and the Cardiovascular Institute’s Clinical Trials Core 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.

Overcoming Obstacles of ACHD, Uduak Osom-Richardson Runs

Mrs. Uduak Osom-Richardson was told at the age of nine that due to a congenital heart condition, she would likely not be able to lead an active life, bear children, or survive much past her early 40’s. This fall, at the age of 52, Uduak ran a full marathon of 26 miles and had her eldest of three children join her for the last three miles of the race. Undeterred by fires which delayed the race date, or by social distancing requirements imposed due to COVID-19, Uduak was determined to participate in the race to honor the one year anniversary of undergoing her most recent heart surgery.

When asked what inspired her to mark the occasion this way, Uduak responded with spirit and grit, “I mentally wanted to prove to myself I am the same person I was before my surgery. This was the third major surgery on my heart. Though I was born with a heart condition, I have always been determined to decide the direction of my own life. I do not want my health struggles to define me.”

Uduak, her husband and family, and 20 friends raised charitable gifts for the Stanford Adult Congenital Heart Program in association with the run. “Doing this was my way of saying thank you to Dr. George Lui and Dr. Joe Woo for giving me a second chance to enjoy a quality of life and to raise awareness of the great work and care being provided to patients like me by their teams.”
Courses in Cardiovascular Science and Medicine

MED 223 | 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

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 Challenges in Drug Development, Cardiac Safety, and the FDA Advisory Committee Process. Spring and Fall 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 National Heart, Lung, and Blood Institute of the National Institute of Health. 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 from Internal Medicine, Radiology, Pediatrics, and Cardiothoracic Surgery residency programs are especially encouraged to apply for this funding.

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 Vascular 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
Casey Gifford, PhD - New Assistant Professor in Pediatrics: Cardiology and the Basic Science and Engineering (BASE) Initiative

Casey Gifford, PhD, recently joined the Department of Pediatrics and, by courtesy, Genetics, as Assistant Professor. Dr. Gifford is also one of the three scientists recruited to inaugurate the Basic Science and Engineering (BASE) Initiative of the Moore Children’s Heart Center. Her research will further the mission of the BASE in merging scientific discovery and innovation to improve care of children with heart disease.

Prior to joining Stanford, Dr. Gifford was an HHMI fellow of the Damon Runyon Cancer Research Foundation at the Gladstone Institutes and UCSF in the lab of Deepak Srivastava, MD. While at the Gladstone Institutes, she employed recent advances in gene editing and gene expression technologies to study cardiovascular development and disease. She earned her BS in Biochemistry from Simmons University and her PhD from Harvard University and the Broad Institute where she studied the epigenomic mechanisms that underlie pluripotent stem cell differentiation in the lab of Alex Meissner, PhD.

Research in her lab will be focused on defining the complex genetic and molecular mechanisms associated with congenital heart disease using both rodent and stem cell experimental models. Ultimately, she hopes to make personalized medicine a reality for those who suffer from cardiovascular anomalies.

Joseph M. DeSimone, PhD - Inaugural Recipient of 'The Sanjiv Sam Gambhir Professorship in Translational Medicine'

Joseph M. DeSimone, PhD, was announced by the Stanford Department of Radiology as the inaugural recipient of the newly established “Sanjiv Sam Gambhir Professorship in Translational Medicine”, a permanent endowed professorship at the School of Medicine established in honor of Dr. Gambhir, former Chair of Radiology, to support a faculty member conducting translational research in the Department of Radiology. Recruited to Stanford by Dr. Gambhir who saw the enormous potential to foster new opportunities to advance human health, Dr. Joseph (Joe) M. DeSimone joined the department September 1, 2020, with a joint appointment in the Department of Chemical Engineering. He also holds a courtesy appointment in the Stanford Graduate School of Business (GSB).

A shining example of achievement, Dr. DeSimone has been described as “an igniter of innovation”. His work as a chemist and expert in polymeric materials has merged life, physical, and engineering sciences with the goal of fostering innovation in how things are made in order to improve the human condition. This has led to revolutionary discoveries and opened up entirely new fields of study. He has received international recognition as a scientist, inventor, and entrepreneur, earning major accolades including the U.S. Presidential Green Chemistry Challenge Award, the 2017 Heinz Award, and the Lemelson-MIT Prize. He is one of only 25 individuals elected to all three U.S. National Academies—the National Academy of Sciences, Medicine, and Engineering. In 2016, President Obama presented him with the National Medal of Technology and Innovation, the highest honor in the U.S. for achievement and leadership in advancing technological progress. Dr. DeSimone and his lab have made significant scientific breakthroughs in science and medicine including next-generation approaches to cancer treatment and diagnosis, implantable drug delivery devices, green chemistry, and most recently in 3D printing technology for medical devices tailored to an individual patient’s needs.


Stanford Cardiovascular Institute (SCVI) Biobank

Human iPSCs have revolutionized disease modeling, drug screening, and therapeutic research. The Stanford Cardiovascular Institute Biobank serves as a resource that provides iPSC lines to the scientific community. Researchers are encouraged to request SCVI Biobank iPSC lines from healthy controls and various cardiovascular diseases. Additionally, our Biobank also hopes to promote iPSC research and can create specific patient iPSC lines of interest.

If you are interested in creating an iPSC line for a particular patient, our study coordinator can arrange for a blood draw at Stanford or external institutions can send us their samples. To include your patients in our Biobank efforts, your patients must agree to join our Biobank project and sign our Stanford Informed Patient Consent form. When we receive both the patient sample and consent, we will include this sample in our reprogramming pipeline. Please visit the SCVI Biobank website to request cells and find additional information.

https://med.stanford.edu/scvibiobank.html
Nicholas Leeper, MD, is the recipient of the 2020 Falk Medical Research Trust Transformational Award. The $1M in funding from Health Resources in Action will fund Leeper’s project “Precision Nanotherapies for Cardiovascular Disease” through November 2022. “The award is designed to catalyze bench-to-bedside translation of biomedical discoveries,” said Leeper. "The Leeper Lab was awarded this grant to develop new ‘Trojan horse’ nanoparticles that ‘home’ to diseased blood vessels. This project will test whether these ‘precision therapies’ can reanimate immune surveillance pathways and begin to reverse atherosclerotic plaque accumulation.” Leeper, a professor in the Division of Vascular Surgery, says the ultimate goal is to develop a new treatment for heart attack and stroke. Leeper et al published a paper in Nature Nanotechnology earlier this year showing that drug-coated nanoparticles limit the development of atherosclerosis in mice, without side effects.

Sushma Reddy, MD, was awarded a Single Ventricle Research Fund from Additional Ventures in the focus area of "Early Detection: End Organ Trajectory Mapping & Biomarkers" for her project "A Liquid Biopsy of Myocardial Signaling in Children with Single Ventricle Heart Failure".

Alison Marsden, PhD, Associate Professor of Pediatrics and of Bioengineering, has been honored as a 2020 American Physical Society Fellow. Dr. Marsden was nominated by the APS Division of Fluid Dynamics for “the development of numerical methods for cardiovascular blood flow simulation and their application to cardiovascular surgery and congenital heart disease.” The APS Fellowship Program was created to recognize members who have made advances in physics through original research and publications or made significant innovative contributions in the application of physics to science and technology. They may also have made significant contributions to the teaching of physics or service and participation in the activities of the society. This fellowship is a distinct honor signifying recognition by one’s professional peers. Each year, no more than 0.5% of the society’s membership (excluding student members) is recognized for election to the status of Fellow of the American Physical Society.

Tushar Desai, MD, Associate Professor of Medicine (Pulmonary, Allergy & Critical Care Medicine) will serve as the Stanford Pulmonary, Allergy & Critical Care Medicine (PACCM) Director of Translational Lung Biology. Dr. Desai is an emerging international leader in basic and translational lung biology and has become a highly effective mentor and guiding force for academic endeavors. In this role, Dr. Desai will continue to co-organize the Divisional PACCM Grand Rounds series (with Angela Rogers) and engage the trainees in the Pulmonary Biology T32 seminar series to provide scientific mentoring. He will also launch a regular series for fellows and instructors engaged in lab research to foster a community in which topical workshops and seminars will help facilitate their scientific and career development.

Sharon Paige, MD, PhD; Sean M. Wu, MD, PhD; and Tahmina Samad, MD, were awarded a Single Ventricle Research Fund from Additional Ventures in the focus area of "Substrate-Outcome Relationships" for their project "Targeting Mitochondrial Dysfunction to Prevent Heart Failure in Single Ventricle Congenital Heart Disease".

**2020 CVI Seed Grant Award Recipients**

**Research Co-Funded by MCHRI**

[https://med.stanford.edu/mchri.html](https://med.stanford.edu/mchri.html)

- **Development of Optogenetic Thrombin for Light-directed Hemostasis During Unifocalization Surgery**
  - Mark Skylar-Scott, PhD
  - Assistant Professor, Bioengineering

- **The Heart of the Matter: Functional Impact of Prenatal Nicotine Exposure**
  - Ronglih Liao, PhD
  - Professor of Medicine (Cardiovascular Medicine)

**Research Funded by the Steven M. Gootter Foundation**

- **Human Bone Marrow Derived Bilayer Smooth Muscle-endothelial Progenitor Cell Sheets Augment Post-infarction Ventricular Function: Implication for Multi-lineage Cellular Tissue Engineering Clinical Translation**
  - Yasuhiro Shudo, MD
  - Clinical Assistant Professor, Cardiothoracic Surgery
Ananya Chakraborty, PhD, postdoc in the lab of Dr. Vinicio de Jesus Perez, was recognized as a finalist for the AHA Cournand and Comroe Award for her project "Loss of Wnt7a is Associated with Reduced VEGF-A/VEGFR2 Mediated Endothelial Tip Cell Formation and Angiogenesis in Pulmonary Arterial Hypertension."

Seema Dangwal, PhD, was awarded the Stanford Diabetes Research Center Pilot and Feasibility Grant ($50,000), with Co-Investigators Kari Nadeau, PhD, and Ronglih Liao, PhD.

William Goodyer, MD, PhD, instructor in the lab of Dr. Sean Wu, is one of the finalists for the Louis N. and Arnold M. Katz Basic Research Prize competition at the annual American Heart Association Scientific Sessions.

A.J. Rogers, MD, resident-researcher in the lab of Dr. Sanjiv Narayan, was a finalist for the 2020 Young Investigator Award Competition of the Heart Rhythm Society.

Alex Sandhu, MD was awarded a Gordon & Betty Moore Foundation Grant for Development of Clinical Quality Measures to Improve Diagnosis for his project "Missed Diagnosis of New-Onset Heart Failure."

Ken Tran, MD won the 2021 Vascular & Endovascular Surgery Society Resident Research Award for his project "Patient-specific Computational Fluid Dynamics Modeling for Assessing the Hemodynamic Performance of Complex Endovascular Aneurysm Repair."

Prash Ganesan, PhD, recently joined Dr. Sanjiv Narayan's Computational Arrhythmia Research Laboratory as a Postdoctoral Research Fellow. His research interest is studying atrial fibrillation substrate mechanisms using novel mapping approaches of signal processing and machine learning.

Ronald Witteles, MD, and team at the Stanford Multidisciplinary Sarcoidosis Program have received official recognition as a Sarcoidosis Center of Excellence by World Association for Sarcoidosis and Other Granulomatous Disorders.

Euan Ashley, MD, Associate Dean of the School of Medicine and Professor of Medicine, was appointed to AstraZeneca's Board as Non-Executive Director and member of the Science Committee.

Alison Marsden, PhD, was promoted to Professor of Pediatrics (Cardiology).

Phillip Yang, MD, was promoted Oct 1, 2020 to Professor of Medicine (Division of Cardiovascular Medicine).

Myriam Amsallem, MD, PhD, former instructor in Medicine and Associate Director of the Clinical Biomarker and Phenotype Core Laboratory, has accepted a position as Clinical Lead at Facebook.

Zeinab Jahed, PhD, formerly a postdoc in the lab of Dr. Bianxiao Cui, recently accepted an assistant professor position at the nanoengineering department at UCSD.

Owais Khan, PhD, former postdoc in the lab of Dr. Alison Marsden, will be starting a faculty position at Ryerson University in Toronto, Canada starting February, 2021.

Ju Liu, PhD, former postdoc in the lab of Dr. Alison Marsden, started a faculty position at Southern University of Science and Technology in Shenzhen, China, in November, 2020.

2020 CVI Boring Trust Research Award Recipients

Functional Characterization of Cpne5 in the Murine Cardiac Conduction System In Vivo
Sruthi Mantri, Third Year MD Student
Lab of Sean Wu, MD, PhD

Vascular1 - Using Artificial Intelligence (AI) to Develop a Virtual Reality (VR) Ultrasound Guided Vascular Access Training Module
Suleman Khan, Third Year MD Student
Lab of Oliver Aalami, MD
Funding Opportunities

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

JANUARY 2021

American Heart Association Institutional Award for Undergraduate Student Training. Deadline: January 14th, 2021

NHLBI Program Project Applications (P01 - Clinical Trial Optional). The proposed programs may address scientific areas relevant to the NHLBI mission including the biology and diseases of the heart, blood vessels, lung, and blood; blood resources; and sleep disorders. Due Date: January 25, 2021

Stephen I. Katz Early Stage Investigator Research Project Grant (R01 Clinical Trial Not Allowed). Deadline: January 26th, 2021. PAR-21-038

Stephen I. Katz Early Stage Investigator Research Project Grant (R01 Basic Experimental Studies with Humans Required). Deadline: January 26th, 2021. PAR-21-039

FEBRUARY 2021


NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed). New application Deadline: February 5th, 2021. PA-19-056

NIH Research Project Grant (Parent R01 Clinical Trial Required). New application Deadline: February 5th, 2021. PA-19-055


ISHLT/O.H. Frazier Award in MCS Translational Research (Sponsored by Medtronic). Deadline: February 8th, 2021.

NIH Single-Site Investigator-Initiated Clinical Trials (R61/R33 Clinical Trial Required). Deadline: February 11th, 2021. PAR-19-328

NIH Mentored Career Development Award to Promote Faculty Diversity in Biomedical Research (K01 Independent Clinical Trial Required). Deadline: February 11th, 2021. RFA-HL-19-025

NIH Mentored Career Development Award to Promote Faculty Diversity in Biomedical Research (K01 Independent Clinical Trial Not Allowed). Deadline: February 11th, 2021. RFA-HL-19-026

NIH Mentored Research Scientist Development Award (Parent K01 - Independent Clinical Trial Not Allowed). Deadline: February 12th, 2021

NIH Pathway to Independence Award (Parent K99/R00 Independent Clinical Trial Not Allowed). Deadline: February 12th, 2021. PA-20-188

Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) Postdoctoral Career Transition Award to Promote Diversity (K99/R00 - Independent Clinical Trial Not Allowed). Deadline: February 12th, 2021. PAR-19-343


NHLBI Outstanding Investigator Award (OIA) (R35 Clinical Trial Optional). Deadline: February 15th, 2021. RFA-HL-20-011


NHLBI Clinical Trial Pilot Studies (R34 Clinical Trial Optional). Deadline: February 16th, 2021. PAE-21-079

NIH T32 Training Program for Institutions That Promote Diversity (T32 – Clinical Trial Not Allowed). Deadline: February 26th, 2021. Letter of Intent due 30 days prior to the application due date.

MARCH 2021

NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed). Renewal, Revision, Resubmission Deadline: March 5th, 2021. PA-19-056

NIH Research Project Grant (Parent R01 Clinical Trial Required). Renewal, Revision, Resubmission Deadline: March 5th, 2021. PA-19-055

NIH Pathway to Independence Award (Parent K99/R00 - Independent Clinical Trial Required). Renewal, Revision, Resubmission Deadline: March 12th, 2021. PA-19-129

NIH Pathway to Independence Award (Parent K99/R00 Independent Basic Experimental Studies with Humans Required). Renewal, Revision, Resubmission Deadline: March 12th, 2021. PA-19-090

NIH Mentored Patient-Oriented Research Career Development Award (Parent K23 Independent Clinical Trial Required). Renewal, Revision, Resubmission Deadline: March 12th, 2021. PA-19-118

NIH Mentored Patient-Oriented Research Career Development Award (Parent K23 – Independent Clinical Trial Not Allowed). Renewal, Revision, Resubmission Deadline: March 12th, 2021. PA-19-119

NIH Mentored Clinical Scientist Research Career Development Award (Parent K08 Independent Clinical Trial Not Allowed). Renewal, Revision, Resubmission Deadline: March 12th, 2021. PA-19-117

NIH Mentored Clinical Scientist Research Career Development Award (Parent K08 Independent Clinical Trial Required). Renewal, Revision, Resubmission Deadline: March 12th, 2021. PA-19-116

NIH Exploratory/Developmental Research Grant Program (Parent R21 Clinical Trial Not Allowed). Deadline: March 16th, 2021. PA-19-053

NIH Exploratory/Developmental Research Grant Program (Parent R21 Clinical Trial Required). Deadline: March 16th, 2021. PA-19-054

NIDDK Small Grants for New Investigators to Promote Diversity in Health-Related Research (R21 Clinical Trial Optional). Deadline: March 16th, 2021. PAR-19-222


ROLLING DEADLINES

Urgent Phase I/II Clinical Trials to Repurpose Existing Therapeutic Agents to Treat COVID-19 Sequelae (U01 Clinical Trial Required). RFA-TR-20-003. The purpose of this urgent funding opportunity announcement is to invite applications to repurpose existing therapeutic agents to treat Coronavirus Disease 2019 (COVID-19) sequelae and associated complications that result from Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infections. The therapeutic agent must have already completed at least a Phase I clinical trial for a different indication, and not require additional regulatory studies for the new indication prior to starting a clinical trial.

Research Supplements to Promote Re-Entry into Biomedical and Behavioral Research Careers (Admin Supp - Clinical Trial Not Allowed). PA-18-592

Research Supplements to Promote Diversity in Health-Related Research (Admin Supp - Clinical Trial Not Allowed). PA-21-071

Research Supplements to Promote Diversity in Health-Related Research (Admin Supp - Clinical Trial Not Allowed). PA-20-166
Please note: some events may be canceled or postponed due to COVID-19. Please check directly with event organizers.

**JANUARY 2021**


ACC Advancing the Cardiovascular Care of the Oncology Patient. January 25th–April 25th, 2021. Virtual


**FEBRUARY 2021**


ACC Cardiovascular Summit. February 1st – April 30th, 2021. Virtual


Mayo Clinic Cardiovascular Conference at Snowbird. February 9th-12th, 2021. Live Stream


SCA 2021 Annual Echo Week. February 26th-28th, 2021. Virtual

**MARCH 2021**

ASE Advanced Echo: Virtual Experience. February 27th-28th, 2021. Virtual


**SDDS 2021**

Stanford Drug Discovery Symposium

April 19-20, 2021

http://tinyurl.com/SDDS2021

Connect with CVI on LinkedIn

https://www.linkedin.com/company/stanfordcvi
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 / yanzhuge@stanford.edu with any questions.

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

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

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 September 1st and November 30th, Stanford Cardiovascular Institute members published 549 original manuscripts and reviews, further contributing to our understanding of cardiovascular biology and disease. Here, we highlight selected manuscripts by our members.

**September**

- **Hydroxychloroquine, Coronavirus Disease 2019, and QT Prolongation.** Bonow RO, Hernandez AF, Turakhia M. *JAMA Cardiol*. 2020 Sep 1;5(9):2195-2211. doi: 10.1136/JP136542. PMID: 32692882
Leadership

**Joseph C. Wu, MD, PhD**  
Director, Stanford Cardiovascular Institute  
Simon H. Stettzer, MD, Professor of Medicine and Radiology

**Robert A. Harrington, MD**  
Arthur L. Bloomfield Professor of Medicine  
Chair, Dept. of Medicine

**Ronald L. Dalman, MD**  
Walter C. and Elsa R. Chidester  
Professor of Surgery  
Chief, Division of Vascular Surgery

**Stephen J. Roth, MD, MPH**  
Professor and Chief, Pediatric Cardiology  
Director, Children’s Heart Center

**Dominik Fleischmann, MD**  
Professor, Dept. of Radiology  
Chief, Cardiovascular Imaging

**Michael Snyder, PhD**  
Stanford W. Ascherman, MD, FACS, Professor in Genetics  
Chair, Department of Genetics  
Director, Stanford Center for Genomics and Personalized Medicine

**Eldrin Lewis, MD, MPH**  
Professor of Medicine and Division Chief, Cardiovascular Medicine

**Y. Joseph Woo, MD**  
Norman E. Shumway Professor in Cardiothoracic Surgery  
Chair, Dept. of Cardiothoracic Surgery

**Kenneth Mahaffey, MD**  
Professor, Dept. of Medicine  
Vice Chair of Medicine for Clinical Research

**Paul Yock, MD**  
Martha Meier Weiland Professor, Bioengineering and Medicine; and Professor, by courtesy, of Mechanical Engineering, Director, Byers Center for Biodesign

**Ronald L. Dalman, MD**  
Walter C. and Elsa R. Chidester  
Professor of Surgery  
Chief, Division of Vascular Surgery

**Mark Nicolls, MD**  
Professor of Pulmonary, Allergy & Critical Care Medicine, Dept. of Medicine; Chief, Division of Pulmonary, Allergy & Critical Care Medicine

**Marlene Rabinovitch, MD**  
Dwight and Vera Dunlevie Professor in Pediatric Cardiology, Director of BASE Program