Stanford V Cardiovascular Institute

SEPTEMBER 2021

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Stanford Health Care ranked among top hospitals nationwide by U.S. News &

World Report By Stanford Medicine News Center

For the seventh year running, U.S. News & World Report has ranked Stanford Health Care one of the nation's finest hospitals. Stanford Health Care has been named to U.S. News & World Report's 2021-22 Best Hospitals Honor Roll, which recognizes the 20 highest-performing hospitals nationwide across a variety of medical specialties, procedures and conditions. "During a time of unprecedented challenges in health care and public health, this recognition from U.S. News & World Report is particularly meaningful," said David Entwistle, president and CEO of Stanford Health Care. "I could not be prouder of our faculty and staff at Stanford Health Care for their dedication to providing exceptional patient care and raising the bar in health care delivery."

Stanford Health Care moved up a notch from last year to No. 12 on the honor roll and was ranked No. 4 in California and No. 1 in the San Jose metropolitan area. Stanford Health Care's national rankings rose in eight specialties: cancer, which rocketed from No. 21 to No. 12; cardiology and heart surgery; ear, nose and throat; gastroenterology and gastrointestinal surgery; geriatrics; gynecology; pulmonology and lung surgery; and urology.

Dr. Jason Lee Appointed New Chief of Vascular Surgery

Congratulations to Dr. Jason Lee, newly appointed Chief of the Division of Vascular Surgery. After completing his residency in general surgery at Harbor-UCLA Medical Center in 2004, Dr. Lee came to Stanford for his vascular surgery fellowship before accepting a position on the faculty. He was program director for the vascular surgery residency and fellowship programs from 2011 to 2020 and was recently inducted as president of the Vascular and Endovascular Surgical Society. He also serves in leadership roles for the Society for Clinical Vascular Surgery, National Comprehensive Cancer Network, American Heart Association, and American Board of Surgery. Dr. Lee has a strong "patient first" philosophy of care, is passionate about educating and mentoring tomorrow's vascular surgeons, and champions clinical and translational research. Dr. Lee is assuming this position from Dr. Ron Dalman, who stated, "Dr. Lee is a nationally recognized leader in Vascular Surgery, and eminently qualified to lead the Division."



Faculty Position Open: VA Palo Alto Health Care System and Stanford CVI

The VA Palo Alto Health Care System (VAPAHCS) and the Cardiovascular Institute at Stanford Medicine are seeking to recruit an outstanding academic cardiologist to join their full-time faculties. This



appointment will be at the rank of Assistant Professor in the Medical Center Line at Stanford University School of Medicine. The successful candidate will be expected to lead a prolific research group with a focus on structural heart disease, cardiovascular imaging, or stem cell biology. See page 4 for more information.

Faculty Position Open: Cardio-Oncologist

The Division of Cardiovascular Medicine in the Department of Medicine and the Cardiovascular Institute at Stanford Medicine are seeking a board-certified Cardiologist with expertise in



Cardio-Oncology to join the faculty as Assistant, Associate or Professor in the Medical Center Line or University Tenure Line. Criteria for appointment include a major commitment to research and teaching, excellence in clinical care, scholarly activity that advances clinical medicine, and institutional service. See page 4 for more information.



Inaugural Gambhir Symposium honors, discusses late researcher's work

The Gambhir Symposium, hosted by Stanford Medicine, was developed in honor of radiology professor Sanjiv Sam Gambhir, a pioneer in molecular imaging and early cancer detection who died last July. Gambhir was the former director of Stanford's Canary Center for Early Cancer Detection and served as chair of the radiology department. The conference, which was sponsored by the department of radiology, featured 21 doctors and researchers representing 10 academic institutions who spoke about the future of cancer detection and precision health at Stanford.

Ralph Weissleder, a former mentee of Gambhir and current professor of radiology and systems biology at Harvard Medical School, praised Gambhir's mentorship and support as he pursued research on early detection of pancreatic cancer. "Gambhir applied a mathematical rigor to everything we did," Weissleder said. "His ability to ask the right questions was really uncanny." Michael Phelps, emeritus professor of molecular and medical pharmacology at the University of California, Los Angeles, characterized the symposium as an important interdisciplinary approach to addressing the obstacles in the early detection of cancer. He said that collaboration from multiple fields of medicine and science is crucial in the achievement of a scientific breakthrough. Stanford Medical School dean Lloyd Minor spoke about Gambhir's impact on the field of medicine. "The legacy of Sam Gambhir will drive us today, and for years to come," Minor said.

Q&A: A call to action to end disparities in cardio-oncology research and care By Scott Buzby

Drivers of racial and ethnic disparities in cardio-oncology include increased risk factors among historically underrepresented groups, underrepresentation in clinical trials and socioeconomic barriers, researchers reported. In a call-to-action statement published in *JACC: CardioOncology*, June-Wha Rhee, MD, and colleagues proposed a framework of solutions that address these issues and more. "In oncology, cancer incidence and mortality are generally highest among Black individuals compared with other races. Additionally, although CVD is the leading cause of death in non-Hispanic groups, cancer was the leading cause of death for Hispanic individuals, accounting for 21% of deaths in adult Hispanic individuals in 2016," Rhee and colleagues wrote.

"These differences stem from structural factors such as lower educational attainment, decreased financial security, lack of health insurance and less access to high-quality health care, thus leading to lower rates of preventive health services such as cancer screening and a greater prevalence of cancer risk factors such as obesity and smoking."

What are the main takeaways for cardiologists and oncologists? It is well established that racial and ethnic health care disparities exist in CV outcomes of patients with cancer. These disparities stem from structural racism, which in turn result in higher rates of CV risk factors and reduced access to specialty care among historically underrepresented individuals. A multidisciplinary approach is required to dismantle these disparities and should include key stakeholders, including health care policymakers, scientists and clinicians.

At a policymaking level, what is your call to action? Socioeconomic factors and lack of access to specialty care play important roles in the observed disparities in cardio-oncology. Policy changes to ensure access to affordable and quality care among people from historically marginalized racial and ethnic backgrounds would be critical. Additionally, establishing community health centers and programs in low socioeconomic areas to increase access to specialty care such as cardio-oncology would be necessary. Finally, there needs to be a government-wide, systemic approach to find an innovative solution such as the use of digital and wearable technologies to improve the cardio-oncology quality of care among historically marginalized groups.

Buzby S. Chance for early HF diagnosis in a primary care setting missed for many women, Black patients. Cardiology Today. Published July 27, 2021. https://www.healio.com/news/cardiology/20210727/chance-for-early-hf-diagnosis-in-a-primary-care-setting-missed-for-many-women-black-patients

Donate to the Stanford Cardiovascular Institute

The Institute currently consists of over 240 faculty members representing physicians, surgeons, engineers, basic and clinical researchers. The Institute's mission is integrating fundamental research across disciplines and applying technology to prevent and treat cardiovascular disease. To support cardiovascular research and education at CVI, please contact: **Joseph C. Wu, MD, PhD**, CVI Director at joewu@stanford.edu or **Cathy Hutton**, Senior Associate Director, Medical Center Development at cathy.hutton@stanford.edu.

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



Joseph C. Wu, MD, PhD



June-Wha Rhee, MD



Frontiers in Cardiovascular Sciences Seminar Series

Join us from 1:00 - 2:00 pm PST 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 7, 2021 4th Annual Gootter Foundation Lecture BARBARA CASADEI, MD, DPHIL British Heart Foundation Professor of Cardiovascular Medicine University of Oxford



October 26, 2021 W. ROBB MACLELLAN, MD

Professor of Medicine, Professor of Physiology Director of UW Medicine Heart Institute; Division Head, Cardiology; Robert A. Bruce Endowed Chair in Cardiovascular Research University of Washington Medical Center



September 14, 2021 CHINMAY M. TRIVEDI, MD, PHD Associate Professor, Department of Medicine University of Massachusetts Medical School



September 21, 2021 BRENDA OGLE, PHD

Professor & Head, Department of Biomedical Engineering; Professor, Department of Pediatrics Director, Stem Cell Institute University of Minnesota-Twin Cities



September 28, 2021 JULIE A. PHILLIPPI, PHD

Associate Professor, Vice Chair for Cardiac Research & Director of Postdoctoral Research, Department of Cardiothoracic Surgery University of Pittsburgh School of Medicine Department of Bioengineering McGowan Institute for Regenerative Medicine



<mark>October 5, 2021</mark> E. DOUGLAS LEWANDOWSKI, PHD

Jack M. George Chair in Medicine & Director, Translational Research Dorothy M. Davis Heart & Lung Research Institute Professor, Department of Internal Medicine and Department of Biological Chemistry & Pharmacology The Ohio State University College of Medicine



October 12, 2021 TATIANA BYZOVA, PHD, FAHA

Staff, Canova Chair in Angiogenesis & Director, Angiogenesis Center, Department of Neuroscience Cleveland Clinic Lerner Research Institute



October 19, 2021 DAWOOD DARBAR, MBCHB, MD

Chief, Division of Cardiology Associate Director, Medical Scientist Training Program Co-Director, Center for Cardiovascular Research Professor of Medicine and Pharmacology University of Illinois at Chicago



November 2, 2021 HEMAL H. PATEL, PHD

Professor & Vice-Chair for Research Director, UCSD Cardiac/Neuro Protection Laboratories VA Research Career Scientist, VA San Diego Healthcare System, Department of Anesthesiology University of California, San Diego



November 9, 2021 KORY J. LAVINE, MD, PHD

Associate Professor of Medicine, Center for Cardiovascular Research & Director of Cardiovascular Precision Medicine Research Initiative Washington University School of Medicine in St. Louis



November 23, 2021 JAVIER G. BLANCO, PHD

Professor, Department of Pharmaceutical Sciences School of Pharmacy and Pharmaceutical Sciences University at Buffalo, The State University of New York



November 30, 2021 PATRICK OSEI-OWUSU, PHD Associate Professor of Physiology & Biophysics Case Western Reserve University School of Medicine



December 7, 2021 IVAN MOSKOWITZ, MD, PHD

Professor of Pediatrics, Pathology, and Human Genetics & Vice Chair for Research, Pediatrics The University of Chicago



December 14, 2021 CHRISTOPHER GLEMBOTSKI, PHD

Professor, Department of Internal Medicine Director, Translational Cardiovascular Research Center Associate Dean, Research The University of Arizona

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

Faculty Position Open: Pediatric Cardiology

The Division of Pediatric Cardiology in the Department of Pediatrics at Stanford University seeks a physician scientist with expertise in pediatric cardiology to join the Division and Department as an Assistant or Associate Professor in the University Medical Line, University Tenure Line, or Non-tenure Research Line. Candidates should have clinical training in Pediatrics and Pediatric Cardiology (completed fellowship and be board eligible or board certified), plus training and experience in pediatric cardiovascular research. He/she will have demonstrated outstanding, or the promise of outstanding, laboratory-based and/or patient-based investigative experience studying congenital cardiovascular diseases in children. Preference will be given to candidates who have acquired extramural, peer-reviewed, national research funding.



He/she will be expected to establish, or will already have established, a high quality, independent research program and have a strong track record of, or potential for, outstanding mentorship and teaching. <u>Read the full announcement and apply here.</u>

Faculty Position Open: VA Palo Alto Health Care System and Stanford CVI

The VA Palo Alto Health Care System (VAPAHCS) and the Cardiovascular Institute at Stanford Medicine are seeking to recruit an outstanding academic cardiologist to join their full-time faculties. This appointment will be at the rank of Assistant Professor in the Medical Center Line at Stanford University School of Medicine and jointly supported by the Medical (Cardiology) and Radiology Services at VAPAHCS, Departments of Medicine (Cardiovascular Medicine) and Radiology at Stanford University, and the Stanford Cardiovascular Institute. A major objective of this recruitment is to identify a highly qualified individual with broad experience in clinical cardiology, strong expertise in basic or translational cardiovascular



research, and the potential to stimulate and lead interdisciplinary collaborations among clinicians and scientists from the supporting services/departments, as well as the rest of VAPAHCS-Stanford research communities. The successful candidate will be expected to lead a prolific research group with a focus on structural heart disease, cardiovascular imaging, or stem cell biology. *Read the full announcement*.

Faculty Position Open: Cardio-Oncologist

The Division of Cardiovascular Medicine in the Department of Medicine and the Cardiovascular Institute at Stanford Medicine are seeking a board-certified Cardiologist with expertise in Cardio-Oncology to join the faculty as Assistant, Associate or Professor in the Medical Center Line or University Tenure Line. The predominant criterion for appointment in the University Tenure Line is a major commitment to research and teaching. The major criteria for appointment for faculty in the Medical Center Line shall be excellence in the overall mix of clinical care, clinical teaching, scholarly activity that advances clinical medicine, and institutional service appropriate to the programmatic needs the individual is expected to fulfill.



The candidate should posses an MD or MD/PhD, be board certified in Cardiovascular Disease, and have current basic science/ translational science research expertise in cardio-oncology. Additionally, we are seeking a candidate who is an outstanding clinician and is a nationally recognized or upcoming clinical and academic leader in the field. Applicants should submit a curriculum vitae, statement of research interests, and the names of three references (who will not be contacted without your permission) to search committee chair, Dr. Hannah Valentine at: http://facultyapplication.stanford.edu/.



Chance to win a PRIZE! <u>CVI Virtual Tour</u>

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

https://med.stanford.edu/cvi/cvi-virtual-tour.html

Stanford Presentations at American Heart Association Scientific Sessions

Plasma Proteomic Signature Implicates Impaired Calcium Handling and Cell-Matrix Adhesion in Repaired Tetralogy of Fallot with Right Ventricular Volume and Pressure Overload. Ingrid Lan, et al, **Sushma Reddy**

Spatially Synchronized Electrogram Islands Within Atrial Fibrillation Predict Termination by Ablation. **Prasanth Ganesan**, et al, Sanjiv M Narayan

Spatial Electrical Synchronization in Patients With Atrial Fibrillation and Atrial Tachycardia. **Prasanth Ganesan**, et al, Sanjiv M Narayan

Deep Learning to Identify Atrial Fibrillation Phenotypes in Individual Patientsbased on Rate, Variability, Electrogram Shape. **Brototo Deb**, et al, Miguel Rodrigo

Women, Ethnic, and Racial Groups Are Underreported and Underrepresented in Atrial Fibrillation Clinical Trials. **Paul C Wang**, et al, Paul J Wang

RBM20 Regulation In Healthy And Diseased Cardiomyocytes: A New Opportunity For Targeted Therapeutics. **Francesca Briganti**, et al, Mark Mercola

Zeb2 Shapes the Epigenetic Landscape of Atherosclerosis and Modulates the Risk of Myocardial Infarction. **Paul Cheng**, et al, Thomas Quertermous

Genetic Determinants of Interventricular Septal Anatomy and Risk of Congenital Heart Disease. Mengyao Yu, et al, **James R Priest**

Rural Health, Coronary Heart Disease, Heart Failure, and Stroke Outcomes. Robert A Harrington

Identification of Pathogenic Immune Cell Subsets in Immunotherapy-Induced Myocarditis. **Han Zhu**, et al, Sean M Wu

The Effect of Regionalization on End-of-Life Hospitalizations for Adult Congenital Cardiology Patients. **Christine M Bui**, et al, Susan M Fernandes

Using Data Analytics Toward Precision Warfarin Dosing in Children With Heart Disease. **Claudia Algaze**, et al, Ronnie T Collins II

Fluid-Structure Interaction Simulations of Bicuspid Aortic Valve Disease. Alexander D Kaiser, et al, Alison L Marsden

Extracellular Matrix Signaling in Marfan Syndrome Induced Pluripotent Stem Cell Derived Smooth Muscle Cells. **Alex R Dalal**, et al, Michael P Fischbein

Smooth Muscle Cell Embryologic Origin Does Not Define Propensity for Phenotype Modulation in Murine Marfan Syndrome Aortic Root Aneurysm. **Albert J Pedroza**, et al, Michael P Fischbein

Insulin-Like Growth Factor Binding Protein 2 is a Novel Marker of Early Smooth

Muscle Cell Phenotype Modulation in Thoracic Aortic Aneurysm. Albert J Pedroza, et al, Michael P Fischbein

RF26 - Disrupted N-Cadherin Expression Leads to Sarcomeric Disassembly and Cell Cycle Activation in Human Induced Pluripotent Stem Cell-Derived Cardiomyocytes. **Soah Lee**, et al,Sean M Wu

Lineage Specific Integrin Alpha V Augmentation Promotes Tgf- β Induced Integrin-FAK-Aktthr308 Signaling Pathway. Ken Nakamura, et al, Michael P Fischbein

Effect of Nicotine Exposure to Induced Pluripotent Stem Cell Derived Endothelial Cell Therapy in a Murine Model of Peripheral Artery Disease. **Alex Ho Pang Chan**, et al, Ngan F Huang

Three-Dimensional Deep-Tissue Imaging of the Right Ventricle Reveals Decreased Capillary-Cardiomyocyte Contact Surface in Decompensated Right Heart Failure. **Kenzo Ichimura**, et al, Edda F Spiekerkoetter

TBX5-Based Lineage Tracing Identifies a Propensity for Left Ventricular Cardiomyocyte Differentiation of Human Induced Pluripotent Stem Cells Using Biphasic Modulation of WNT Signaling. **Francisco X Galdos**, et al, Sean M Wu

The Feasibility of a Mail-Out 12-Lead ECG in a Pediatric Cardiac Electrophysiology Telemedicine Environment. **Henry Chubb**, et al, Scott R Ceresnak

Prediction of Pacemaker Implantation in Patients With Postoperative Heart Block: A Data Analytics Approach. **Son Q Duong**, et al, Claudia Algaze

Biomechanical Comparison of Atrioventricular Valve Repair Strategies in Hypoplastic Left Heart Syndrome. **Sumanth Kidambi**, et al, Michael Ma

Statins Improve Endothelial Function via Suppression of Epigenetics Driven-EndMT. **Chun Liu**, et al, Joseph C Wu

Impact of Increased Utilization of Expanded Criteria Donors at a High-Volume Heart Transplant Center: A Quasi-Experimental Analysis. **Brian Wayda**, et al, Kiran K Khush

Cardiothoracic Surgery Research Articles Supported by National Institutes of Health Grant Funding Exhibit Enhanced Scholarly Impact. **Hanjay Wang**, et al, Jack Boyd

Deficiency is Associated With Oxidative Stress and Endoplasmic Reticulum/ Mitochondrial Injury in Pulmonary Endothelial Cells. **Stuti Agarwal**, et al, Vinicio A Dejesus Perez

CVI Seed Grant Awards October 15, 2021



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 strongly encourage proposals that emphasize interdisciplinary collaborations.

2021 Stanford CVI Seed Grant Competition:

Maternal and Child Health

Cardiac Arrhythmia and Sudden Cardiac Death

Eligibility: Stanford CVI member faculty or instructors

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

Stanford Presentations at American Heart Association Scientific Sessions

A Novel Selectively Flexible Mitral Annuloplasty Ring Designed Based on Human Imaging with Superior Performance in Hemodynamics, Biomechanics, and Annular Dynamics - A Comprehensive Bench to in vivo Large Animal Analysis. **Yuanjia Zhu**, et al, Y Joseph Woo

Inventing the Future: Challenges in Image-Based Planning of Transcatheter Valve Therapies. Jody Shen

2021 Honorary Dickinson W. Richards Memorial Lecture Immune Dysregulation and Inflammation in Pulmonary Arterial Hypertension. Mark Nicolls

Cancer and Heart Failure: Novel Chemotherapeutic Agents and their consequences. Han Zhu

Abbreviated Cardiac Magnetic Resonance Imaging versus Echocardiography for Interval Assessment of Systolic Function in Duchenne Muscular Dystrophy: Patient Satisfaction, Clinical Utility and Image Quality. **Hamsika Chandrasekar**, et al, Shiraz A Maskatia

Automated Tracing of Tricuspid Regurgitation Doppler Waveforms. Jonathan Pham, et al, Alison L Marsden

Biomechanical Analysis of Neochordal Mitral Valve Repair Geometry to Quantitate the Impact of Diastolic Phase Inversion During Static Left Ventricular Pressurization. **Matthew H Park**, et al, Y Joseph Woo

Optimal Patient Selection for Simultaneous Heart-Kidney Transplant: A Modified Cost-Effectiveness Analysis. **Brian Wayda**, et al, Kiran K Khush

Patient-Specific Computational Flow Simulation Reveals Differences in Aortic Hemodynamics Between Two versus Four Vessel Fenestrated Endovascular Aneurysm Repair. **Ken Tran**, et al, Jason Lee

E-cigarette Nicotine Vapor Increases Aortic Stiffness in Mice. Pireyatharsheny Mulorz, et al, **YaeHyun Rhee**, et al, Philip S Tsao

Reduced Pulmonary Artery Distensibility: A Predictor of Persistent Pulmonary Hypertension and 2-Year Mortality Post-Transcatheter Aortic Valve Replacement in High-Risk Patients with Severe Aortic Stenosis. **Valery Turner**, et al, Dominik Fleischmann

Cardiomyopathy cell phenotyping and prediction of sudden death. Albert J Rogers

Menopause: Is It Really an Independent Risk Factor for CVD? Marcia L Stefanick

Productivity Targets and Performance Reviews for Cardiology Practices in the Veterans Health Administration: Do They Work? **Neil M Kalwani**, Paul A Heidenreich Machine Learning-Enhanced Determinants of Oral Anticoagulation in Atrial Fibrillation: Findings From the PINNACLE Registry. Fatima Rodriguez, **Andrew Ward**, et al, Rajesh Dash

Arrhythmogenic Cardiomyopathies, so much more than ARVC. Victoria Parikh

Clinical Predictive Tool for Pediatric Cardiac Patients on Extracorporeal Membrane Oxygenation Therapy and Ultrafiltration. Jennifer Sedler, et al, David Kwiatkowski

Deep Learning and Patient-Derived hiPSC Cardiomyocytes to Predict Drug Proarrhythmia. Ricardo Serrano, et al, **Mark Mercola**

Machine learning approaches to mapping: Promises and Limitations. Sanjiv M Narayan

Prevalence and Outcomes of Primary Cardiomyopathy in Marfan Syndrome. Brynn S. Connor, et al, Ronnie T Collins II

Transitions in Academic Cardiothoracic Surgery From 2018 to 2020. Simar S Bajaj, et al, Jack H Boyd

Measuring Cerebrovascular Reactivity in Moyamoya Disease: Insights from Simultaneous PET/MRI. **Yize Y Zhao**, et al, Greg Zaharchuk

Understanding Hospital-Acquired Venous Thromboembolisms in Pediatric Cardiology Patients. **Nancy Song**, et al, David Scheinker

Video-Based Deep Learning Model for Automated Assessment of Ejection Fraction in Pediatric Patients. Bryan He, et al, **Charitha D. Reddy**

Classic Pattern Dyssynchrony Score: A Predictor of Response to Cardiac Resynchronization Therapy in Pediatric and Congenital Heart Disease. **Henry Chubb**, et al, Mark K Friedberg.

Walking Performance, Quality of Life, and Hemodynamic Characteristics in Patients with Peripheral Artery Disease and End-Stage Kidney Disease (PAD-ESKD). **Naomi Hamburg**, et al, Glenn M Chertow

Association of Medical Non-Adherence to Health Status Outcomes in the ISCHEMIA Trial. **R. Angel Garcia**, et al, David J Maron

Automated Assessment of Video Quality and Ejection Fraction in Emergency Department Point-of-Care Echocardiograms. **Bryan He**, et al, James Zou

The Index of Microcirculatory Resistance to Predict Subsequent Acute Cellular Rejection and Cardiac Events After Heart Transplantation. **Jung-Min Ahn**, et al, William F Fearon

Hypertrophic Cardiomyopathy in Infants of Diabetic Mothers is Associated With Significantly Worse In-Hospital Outcomes: A Multicenter Analysis. **Ronnie T Collins II**, et al, Elijah H Bolin

SCVI Biobank

Formed in 2014, the SCVI biobank provides a repository of patient specific, de-identified human induced pluripotent stem cell (iPSC) lines that are distributed to the scientific community. The iPSC lines cover a broad spectrum of cardiac diseases, healthy controls, and non-cardiac disease controls.

Biobankstaffhavevaluabletechnical and operational expertise in iPSC reprograming, culturing, and resource management. With blood from consented patients, both from Stanford and external institutions, the Biobank staff can reprogram the cells and send the iPSC lines back after validation.

The SCVI Biobank places a strong emphasis on recruiting diverse racial and ethnic populations that broadly reflect the contemporary population diversity of the United States. Substantial numbers of unknown disease-causing variants are likely present in the genetic background of the global population, and may present opportunities for the next breakthrough in combating disease progression.

For more information, to request cell lines, or to inquire about SCVI Biobank offerings, please visit our website:

https://med.stanford.edu/scvibiobank/forms.html



ers \$750 of travel expenses and requires presentation of research posters at Car-

affiliations when first submitted

Heart disease is the leading cause of death in the US, contributing to about 655,000 Americans deaths each year. Heart disease refers to several types of heart conditions, including genetic diseases, decreased pumping capacity and heart failure, stroke, and non-fatal heart attack. An individual's atherosclerotic cardiovascular disease (ASCVD) risk is the basis of prevention of cardiovascular disease, and ranges from lifestyle adjustment to therapy treatment (e.g., statins). Randomized cholesterol treatment clinical trials are used to inform treatment guidelines which can guide clinicians into shared treatment decisions based on ASCVD risk.

In a recent <u>Circulation</u> manuscript, first author Ashish Sarraju, MD, and senior author Fatima Rodriguez, MD, MPH, presented the need for NHW indicates non-Hispanic White people.

improved diverse racial and ethnic group representation in high-impact cholesterol treatment trials. There are important racial/ethnic differences in both cardiovascular disease risk and in cholesterol management that should be considered when devising a treatment plan. They found that Black, Hispanic, and Asian participation were significantly underrepresented compared to US Census data. This has critical implications for the real-world applicability and generalizability of both the cholesterol clinical trials and the guidelines. Moving forward, sustained efforts to recruit and retain diverse participants in clinical trials will lead to more generalizable guidelines.

Importance of Diversity in High-impact Cholesterol Treatment Trials By Amanda Chase, PhD

80

70

50 Percentage

40

30

76.5

NHW (Trial N = 41)

Stanford study ties milder COVID-19 symptoms to prior run-ins with other coronaviruses By Bruce Goldman

A study by Stanford University School of Medicine investigators hints that people with COVID-19 may experience milder symptoms if certain cells of their immune systems "remember" previous encounters with seasonal coronaviruses — the ones that cause about a quarter of the common colds kids get. These immune cells are better equipped to mobilize quickly against SARS-CoV-2, the coronavirus responsible for COVID-19, if they've already met its gentler cousins, the scientists concluded. The findings may help explain why some people, particularly children, seem much more resilient than others to infection by SARS-CoV-2, the coronavirus that causes COVID-19. They also might make it possible to predict which people are likely to develop the most severe symptoms of COVID-19.

The immune cells in question, called killer T cells, roam through the blood and lymph,

park in tissues, and carry out stop-and-frisk operations on resident cells. The study, published in Science *Immunology*, showed that killer T cells taken from the sickest COVID-19 patients exhibit fewer signs of having had previous run-ins with common-cold-causing coronaviruses. COVID-19 patients with milder symptoms tended to have lots of killer-T memory cells directed at peptides SARS-CoV-2 shared with other coronavirus strains. Sicker patients' expanded killer T-cell counts were mainly among those T cells typically targeting peptides unique to SARS-CoV-2 and, thus, probably had started from scratch in their response to the virus.

CVI Travel Awards Deadline: September 30, 2021

The Cardiovascular Institute encourages and supports the travel of eligible researchers to conferences dedicated to cardiovascular research. This award covdiovascular related research conferences. To increase diversity in cardiovascular medicine and research we also have an additional "Outreach Travel Award" slot available which is exclusive to candidates from underrepresented groups.

Ashish Sarraju,

MD

Killer T cells from patients with mild cases of COVID-19 show indications of recent encounters Kon/

with other coronaviruses. Kateryna Shutterstock



Requirements

- You must be a Stanford Postdoc, Instructor, Graduate Student, or Nurse
- An accepted abstract to a national or international meeting related to cardiovascular research
- The abstract must list "Stanford Cardiovascular Institute" in the author

Application and more information: https://med.stanford.edu/cvi/funding-opportunities/travel_grant_awards.html







Fatima

Rodriguez, MD

Mark Davis, PhD

16.3 18.3

10.6*

Hispanic (Trial N = 19)

12.6 13.4

5.5*

Black (Trial N = 23)



Asian (Trial N = 11)

What Contributes to Spongy, Thick Heart Muscle: Understanding Non-compaction of the Heart 👔 🕑 💼

By Amanda Chase, PhD

As we all know, the heart muscle (myocardium) is critical for blood flow. The myocardium is a smooth, firm muscle that can contract and relax in a coordinated manner to facilitate the pumping of blood. Left ventricular non-compaction (LVNC) is a rare cardiovascular disease in which the lower part of the heart that helps pump blood does not develop correctly. The myocardium is thick and spongy instead of being smooth and firm, meaning that the heart is unable to fully relax or fully contract and thus there is decreased blood flow. LVNC is the third most common form of congenital cardiomyopathy in the US, and two-thirds of patients develop heart failure. There remains no therapeutic cure to reverse the non-compact phenotype, primarily because the genetic basis of LVNC is both complex and not well understood.

Stanford University researchers, led by first authors Siyeon Rhee, PhD, and David Paik, PhD, and senior authors Ashby Morrison, PhD, Joseph Wu, MD, PhD, and Kristy Red-Horse, PhD, recently published a proposed model of how the non-compact phenotype may occur in European Heart Journal.

In this manuscript, the team explored a novel idea that non-cardiomyocyte cell types may be the culprit. Specifically, the team found that endothelial cells, which compose

the innermost lining of blood vessels, and endocardial cells, which give rise to valves, together secrete a number of paracrine factors (also known as "angiocrine" factors) that dynamically regulate the growth (proliferation) and maturation of the cardiomyocytes during heart development. These critical cellular processes of developing cardiomyocytes are naturally linked to the structural formation and maturation of the ventricular wall, notably in the reduction of trabeculae and generation of compact myocardium. The team identified that dysfunction in



Analysis of a mouse model of LVNC, coupled with in vitro analysis of cardiomyocyte growth, found that endothelial factors expressed during development can contribute to noncompaction.





Red-Horse, PhD

secretion of specific angiocrine factors by these endothelial and endocardial cells lead to LVNC in both mouse and human stem cell models.

Identification of specific factors that impact cardiomyocyte proliferation and maturation during development has the potential to lead to the development of effective, patient-specific therapeutics to treat and correct LVNC.

REGISTER NOW!

CVI Early Career Symposium

Join Stanford CVI early career scientists for a day of cardiovascular and pulmonary science, professional development, networking and fun!

November 3rd, 2021

Register at https://tinyurl.com/cviec2021



Introducing the **CVI Early Career Committee**



Francesca

Briganti, PhD

Marina Codari,

PhD







Alok Jha, PhD





Danielle Mulli:



Carlos Vera, PhD

Domenico Mastrodicasa, MD

Soah Lee, PhD

Guiding, inspiring and creating opportunities for the next generation of cardiovascular scientists!

Mirwais Wardak,



Khadem Ali, PhD

Vedant

Pargaonkar, MBBS

James Jahng,

PhD

Brian Wayda, MD

Treating Heart Failure from the Outside In By Adrienne Mueller, PhD

Heart attacks and heart failure cause damage to heart tissue, which in turn causes heart dysfunction. Because human heart muscle cells do not regenerate, once you lose them, they are lost forever. Previous research from the lab of Phillip C. Yang, MD and others has shown that extracellular vesicles, small bundles of signaling molecules that are present outside the cell, can help repair heart muscle cells. However, in order to develop a treatment that would deploy these extracellular vesicles, or EVs, it is important to know exactly which molecules in the EVs are helping with the repair, and how they are doing so. A recent study by first author Ji-Hye Jung, PhD and senior author Philip C. Yang, MD sought to answer specifically these questions.

In their study, recently reported in *Basic Research in Cardiology*, they compared the EVs of healthy tissue with tissue that has been oxygen-deprived. They hypothesized that the EVs produced by oxygen-deprived heart muscle cells would be more able to help heart cells regenerate than control EVs - and their hypothesis was correct. They then investigated exactly which molecules were enriched in the EVs of oxygen-

deprived tissue and found that they contained higher levels of a specific microRNA cluster: miR-106a-363. They further demonstrated that miR-106a-363 alone was effective at preserving heart muscle cell function and reducing tissue scarring in the injured heart and that key player in the signaling cascade initiated by this microRNA cluster is the Notch3 pathway. This Yang lab study therefore shows that a microRNA cluster never before associated with cardiovascular disease contributes to heart tissue repair through heart muscle cell division.

Damaged heart

Damaged heart cells release exosomes enriched with microRNA cluster miR-106a-363, which then acts via Notch3 to increase cell proliferation and help repair the damaged tissue.



Ji-Hye Jung, PhD

Phillip Yang, MD

Chance for early HF diagnosis in a primary care setting missed for many women, Black patients By Scott Buzby

Women and Black individuals are more likely to be diagnosed with HF in an acute care setting than a primary care setting compared men and white patients, respectively, according to data published in <u>Circulation: Heart</u> <u>Failure</u>. Researchers also reported that low net worth and occupation status ("homemaker" or "retired") were also associated with elevated odds of receiving a first HF diagnosis in an acute setting compared with a primary care setting. "Patients diagnosed with heart failure in the emergency room or during inpatient hospitalization often have more advanced heart failure and complications with worse prognoses than individuals diagnosed with heart failure in a primary care setting," Alexander Sandhu, MD, MS, instructor of medicine in advanced



Sandhu, MD

heart failure in the division of cardiovascular medicine and the Stanford Cardiovascular Institute at Stanford University, said in a press release. Based on diagnostic codes from a large claims database, Sandhu and colleagues identified characteristics that predicted HF diagnosis in the acute care setting compared with the primary care setting.

Researchers reported that women more likely to receive a first HF diagnosis in an acute care setting compared with men (aOR = 1.11; 95% CI, 1.1-1.12) and Black individuals were more likely to be diagnosed in an acute setting compared with white individuals (aOR = 1.18; 95% CI, 1.16-1.19). Researchers also reported that individuals with lower net worth were more like to receive a first HF diagnosis in the acute care setting compared with those with greater net worth (adjusted OR for net worth less than \$25,000 vs. over \$500,000 = 1.39; 95% CI, 1.36-1.41). Patients whose occupation was categorized as "homemaker" or "retired" in the database were also more likely to be diagnosed with HF in the acute care setting compared with those who were marked as professionals (aOR = 1.04; 95% CI, 1.01-1.07). "Further research is needed to better understand the factors influencing these disparities," Sandhu said. "It is important to note that we only analyzed patients with health insurance, raising concerns that inequities may be even larger among people who are uninsured, marginally insured or those who have less access to care."

Buzby S. Chance for early HF diagnosis in a primary care setting missed for many women, Black patients. Cardiology Today. Published July 27, 2021. https:// www.healio.com/news/cardiology/20210727/chance-for-early-hf-diagnosis-in-a-primary-care-setting-missed-for-many-women-black-patients

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Engineered tissue sent into space to test muscle loss drugs By Helen Santoro

As people age, they gradually lose muscle mass and strength because of a condition called sarcopenia, which typically takes decades to progress. For astronauts in space, however, microgravity, or weightlessness, causes them to experience extreme muscle weakness over a significantly shorter period of time. To test whether microgravity can be a tool to better understand sarcopenia, a team of Stanford Medicine researchers sent engineered muscle tissue to the International Space Station. If the experiment works, scientists will be able to rapidly assess potential drugs that diminish muscle loss in advance of launching treatment clinical trials. The tissue was launched into space on Aug. 10.

"If one were to try to develop a drug to treat sarcopenia on Earth, that would be really hard because it would take decades to study the efficacy in patients," said Ngan F. Huang, PhD, principal investigator of this study. "Microgravity has been shown, in a lot of contexts, to accelerate a lot of different diseases. We thought: 'Well, maybe microgravity could be a way to accelerate the process of sarcopenia."

To create the engineered tissue, Huang and her colleagues layered human muscle cells onto scaffolding

made from collagen. The cells fuse into organized strips of myotubes, or primitive muscle fibers. As the muscle cells mature, astronauts onboard the space station will collect microscopic images and tissue samples from them. The astronauts will also test whether two drugs that have been shown to induce the formation of myotubes work efficiently in microgravity. This could allow scientists to identify therapeutics for sarcopenic patients on Earth and for Courtesy of NASA and the National Science Foundation astronauts during long space missions. "Based on what we know from other works

and from the astronauts themselves, we think microgravity will simulate muscle atrophy," said Huang. "If it works, this platform could be used to identify drugs over the course of a week or two."

How A Former Retrovirus Contributes to Pulmonary Arterial Hypertension By Adrienne Mueller, PhD

Pulmonary arterial hypertension (PAH) is a chronic disorder that progressively worsens over time. PAH is caused by narrowing of the arteries that supply blood to the lungs. Having narrower arteries forces the heart to work extremely hard to pump more blood to the lungs and supply more oxygen to our bloodstream. Over time, the heart muscle tires and eventually fails. The vessel narrowing seen in PAH is partly caused by the abnormal expansion of the cells that make up the vessel walls. One cause for this abnormal expansion of cells is the transformation of a specific lung blood vessel cell type - endothelial cells - into a different cell type. The loss of endothelial cells triggers inflammation, further exacerbating PAH. An important question for treating PAH is therefore, what triggers the transformation of endothelial cells?

Some viruses have been embedded in our DNA for so long that they are now an integral part of our genome, producing proteins that our cells have incorporated into their regular functioning. One such protein is HERV-K dUTPase. In a study recently reported in the journal JCI Insight, Shoichiro Otsuki, MD, PhD et al showed that when monocytes, a particular type of immune cell, have an excess of HERV-K dUTPase, they shed the protein via small packets called extracellular vesicles. The investigators further showed that shed HERV-K dUTPase, which mediates gene expression

in lung endothelial cells, initiates signaling cascades that trigger the transformation of endothelial cells into a different cell type This transition provokes inflammation and is therefore likely to ultimately cause the inflammatory responses underlying PAH.

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Otsuki, MD, PhD Rabinovitch, MD

Marlene



UTPase (right) causes lung endothelial cells to

change morphology and lose endothelial cell

Shoichiro





Northrop Grumman CRS-16 search Overview

Cardinal Muscle





Leveraging Pulmonary Arterial Hypertension Patient Cells for Drug Discovery By Amanda Chase, PhD

Pulmonary arterial hypertension (PAH) occurs when the arteries in the lung become narrowed and/or blocked. The exact cause of PAH is unknown, and current treatments for PAH are aimed at managing the condition: improving symptoms and slowing progression. However, there is an unmet medical need to develop a cure for PAH as well as to identify agents that may cause PAH.

Previously, animal models have been used to identify potential therapies. Unfortunately, due to considerable species differences, a majority (90%) of drugs that perform well in animal models fail in clinical trials. To address the need. researchers led by first author Mingxia Gu, currently an Assistant Professor at the Cincinnati Children's Hospital Medical Center, and senior author Marlene Rabinovitch, together with Purvesh Khatri and his team in Biomedical Data Science utilized relatively new tools to identify promising PAH therapies. Their findings, recently published in Science Translational Medicine, share not only a potential candidate for curing PAH, but also describe a workflow to accelerate drug discovery for specific diseases, such as PAH.

In this study, iPSC derived endothelial cells (iPSC-ECs) from PAH patients provided a platform to first determine the effects of different drugs on improving survival and potential for regeneration after injury (drug screening). Intriguingly, they were able to identify a compound, tyrphostin or AG1296, as having the greatest potential as a therapy. With follow-up tests and analyses, they showed that AG1296 performed exceptionally well at improving PAH Mingxia Gu,MD, Marlene vascular function, and the researchers were able to provide an explanation for why AG1296 was



Workflow of the combined drug screen and bioinformatics to accelerate drug discovery. Here, the process identified AG1296 as a potential therapy for PAH



PhD

Rabinovitch, MD

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able to improve PAH cell function. In additoin, this study describes a means to accelerate drug discovery for PAH treatment by combining the use of patient-specific iPSC cells for functional screening with analysis of available drug and PAH datasets.

Climate change linked to longer allergy season in Bay Area, Stanford study finds By Erin Digitale

Bay Area allergy sufferers take note: Climate change has lengthened the local pollen and mold season by eight to nine weeks per year during the past two decades, according to a study from the Stanford University School of Medicine. The study, based on allergen data collected starting in 2002 in Los Altos Hills, California, found that local temperature increases are linked to longer tree and grass pollen seasons, while changes in local precipitation are linked to more mold spores in the air. Tree pollen and mold seasons each grew by about half a week per year from 2002 through 2019, the study found. The research, the first to analyze the effects of climate change on airborne allergens in the San Francisco Bay Area, was published in the journal Scientific Reports.

"Climate change is really a problem for health, and we are living and breathing the effects of climate change now," said the study's senior author, Kari Nadeau, MD, PhD, professor of medicine and of pediatrics at Stanford School of Medicine. Nadeau became interested in the problem

because her patients kept saying their seasonal allergies were getting worse. The researchers analyzed airborne pollen and mold spore data collected at a National Allergy Bureau-certified pollen counting station in Los Altos Hills. Pollen season now starts earlier and ends later for many species of plants and molds, the researchers found. Allergy sufferers and their doctors should note the findings and adjust allergy treatment accordingly, Nadeau said. "It helps patients to know that the reason they're having more allergies is that pollen is in the air longer than in the past."



Changes in temperature and rainfall lengthened allergy season in Bay Area. Elizaveta Galitckaia/Shutterstock



Kari Nadeau, MD, PhD



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The Ticking Clock of Aging By Amanda Chase, PhD

While the immune system is well known to play a critical role in maintaining human health and protection against infections, it has more recently become clear that components of the immune system are chronically elevated in aged individuals and are associated with an increased incidence of cardiovascular disease and others. Therefore, what if inflammation plays a critical role in regulating aging? And what if there could be a way for physicians to detect age-related disease early to allow more preventative care?

A team of researchers from two institutions, Nazish Sayed, MD, PhD (Assistant Professor at Stanford Cardiovascular Institute and Division of Vascular Surgery) and Yingxiang Huang, PhD (co-first authors) and corresponding author David Furman, PhD (Associate Professor at Buck Institute for Research on Aging and Director of the Stanford 1000 Immunomes Project), utilized artificial intelligence to address both questions. Their findings were recently published in *Nature Aging*.

The researchers used machine learning to look for patterns of age-related inflammation and to develop an inflammatory clock of age-related chronic inflammation (iAge) that can predict important aging characteristics, including multiple morbidities, frailty, and cardiovascular

aging. Uniquely, iAGE was associated with exceptional longevity in an independent cohort of individuals over one hundred years of age (centenarians). iAge has the important potential to be used as a diagnostic tool to identify those at risk for both non-communicable and infectious disease, as well as to identify healthy older adults at risk for early cardiovascular aging.

Interestingly, a major contributor to the inflammatory clock was a protein called CXCL9. The researchers were able to validate CXCL9 as an indicator of cardiovascular pathology. In fact, CXCL9 was shown to be the master

regulator of vascular function, suggesting that future therapies targeting CXCL9 could prevent age-related deterioration.

New findings expand hopes for a stem cell cancer 'vaccine' By Krista Conger

In my previous article, I explained how the cells, called induced pluripotent stem cells, or iPS cells, might work to prevent cancer: "The iPS cells work as an anti-cancer vaccine because, like many cancer cells, they resemble developmentally immature progenitor cells, which are free from the growth restrictions built into mature cells that make up the body's tissues. Injecting iPS cells that genetically match the recipient, but that are unable to replicate, can safely expose the immune system to a variety of cancer-specific targets, the researchers found." The researchers, led by Stanford cardiovascular researcher Joseph Wu, MD, PhD,

had found that the injection of iPS cells and an immune-stimulating agent known as an adjuvant into laboratory mice could prevent the formation of cancers when the animals were subsequently injected with mouse breast cancer, skin cancer or mesothelioma cells.

Now, Wu and postdoctoral scholar Xiaoming Ouyang, PhD, have extended this finding to include mice injected with mouse pancreatic cancer cells. (Pancreatic ductal adenocarcinoma, the most common type of pancreatic cancer, is the fourth leading cause of cancer deaths in the United States.) As in the previous study, injecting iPS

cells made from the animals' own tissues, along with an adjuvant, made them resistant to pancreatic cancer tumors that readily formed in control animals without the iPS cells. They published their results recently in Stem Cell Reports. "When we vaccinated the mice, and then challenged them with the pancreatic cancer cells, 75% of the animals that had received iPS cells plus the adjuvant didn't develop any tumors at all," Ouyang said. "In contrast, all of the control animals developed cancers." Amping up the immune system's response to cancer cells might also help to eliminate existing tumors, the researchers believe. They hope to begin testing the approach in people in a clinical trial. Initially, the researchers will use iPS cells that are created directly from each patient's own tissue. They hope that, if the approach proves successful in people, it might one day be possible to have a one-size-fits-all vaccine based on the proteins on the cells that trigger an immune response against these cancers."



https://med.stanford.edu/cvi/translational-research/memberpubs.html



Artist depiction showing the immunological fire throughout humans as the body faces all sorts of challenges.



Nazish Sayed, MD, PhD



Image by LASZLO



Ouyang, PhD



5 Questions: Lisa Patel on California wildfires and school ventilation By Erin Digitale

With the COVID-19 pandemic and the growth of wildfires, California schools need to improve their air quality, according to Stanford pediatrician Lisa Patel. Fortunately, the funds are available. The wildfires that annually burn hundreds of thousands of acres in California don't just scorch the land; they also pump toxic smoke into the air. Pediatrician Lisa Patel, MD, an expert on the health effects of climate change, is worried about that smoke harming children, especially as the peak of wildfire season coincides with the beginning of the school year. But Patel sees an opportunity in the confluence of two public health crises. The global COVID-19 pandemic prompted state and federal governments to fund upgrades to schools' ventilation systems.



Lisa Patel, MD

1. During last year's fire season, California students were learning online due to the global pandemic. This year, they'll return to the classroom just as fire season intensifies. What concerns does that raise? Kids in places like Marin County [north of San Francisco], which was hit by smoke from devastating fires, missed upward of three weeks during the 2018-2019 school year due to wildfire smoke, evacuation orders or power outages. Then the pandemic hit, schools across the state closed, and school district officials have since put a huge amount of time and resources into reopening our schools with an eye to pandemic safety. That's very important, but I'm worried we forgot about this other risk factor, wildfire season, which is also hugely disruptive.

2. Why is wildfire smoke dangerous to children's health? A study that just came out in Pediatrics shows wildfire smoke is 10 times more toxic than other pollution we're used to, which isn't surprising because what's burning includes houses and cars. The smoke includes ultrafine particles, all smaller than 2.5 microns. It's a mixture of solids and liquids that become disbursed in the smoke. Because they're so tiny, the particles can get into the lungs, into the vasculature, and enter our bodies, potentially setting off a cascade of inflammation. That leads, for example, to increased emergency-department visits because of asthma.

3. The COVID-19 pandemic drew attention to indoor air quality and to buildings' heating, ventilation and air conditioning, or HVAC, systems. Why should we upgrade these systems in our schools? From a COVID point of view, we are thinking about fresh air exchange because it's an airborne disease. HVAC systems can bring more air in from outside and facilitate more exchange of air so that respiratory droplets don't linger. HVAC systems can also clean the air of all kinds of pollutants that affect children's educational achievement. If the systems are fitted with highly rated filters, they clean the air of particulate matter pollution made by diesel trucks or gas-powered cars, or the pollutants in wildfire smoke.

4. How are California schools doing in regard to improving their ventilation? Last October, the California state legislature passed a bill allocating up to \$600 million for upgrades, maintenance and repairs to schools' HVAC systems. There are also federal funds allocated through the Coronavirus Aid, Relief, and Economic Security (CARES) Act of 2020, and the Environmental Protection Agency is putting together money to create clean air shelters, some of which may be located at schools, to provide places where people can access clean, filtered air. Even with this funding, we see challenges ahead. Lots of schools don't have HVAC systems, and schools that do often don't maintain them.

5. What else could help schools adjust to longer, more intense wildfire seasons? After more than a year in a global pandemic, the Centers for Disease Control and Prevention has finally come out and said that in-person learning should be our priority for children's health. We should have said this long ago. This generation of kids is going to have a lot to surmount from one year of missed school due to the pandemic, and I'm concerned about what continued disruptions from wildfires mean in terms of children's progress. We can equip schools to monitor their on-site level of air pollution, and we can provide more education to parents and teachers so school communities understand why certain decisions are made and how they help kids stay safe.

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Nazish Sayed Lab

Seeking a postdoctoral researcher with a background in vascular biology and cellular signaling to perform **cutting-edge research on endothelial biology**. The Sayed Lab conducts translational research in vascular biology and aims to understand the role

of the vasculature in the development of cardiac diseases. The lab employs iPSC technology, bioengineering tools and CRISPR to investigate human vascular diseases. Candidates should have past experience in molecular and cellular biology and mouse models. Knowing bioinformatics is a plus.

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Joseph C. Wu Lab

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analytical, organizational, and communication skills. Successful candidates will work independently in a dynamic research team composed of molecular and cell biologists, biochemists, and non-invasive imaging specialists.

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of multi-scale approaches, ranging from single molecule to single myofibril to single and multiple cell platforms. We have also applied a unique multi-omics approach integrating genomics, metabolomics and lipidomics. Candidate must have strong laboratory, analytical, and communication skills and enjoy working in a small but highly collaborative environment.

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Combining "Disease in a Dish" and "Drug Discovery in a Dish" By Amanda Chase, PhD

Almost one million individuals are hospitalized every year in the US for cardiac arrhythmias, or an irregular heartbeat, making cardiac arrhythmias a leading cause of healthcare expenditures. Ventricular cardiac arrhythmia (VA) is when the abnormal heartbeat starts in the ventricles, or lower heart chambers. As the heart beats too fast, it prevents oxygen-rich blood from circulating to the brain and body, which may result in cardiac arrest. About 300,000 individuals die of sudden arrhythmic death syndrome each year.

Although arrhythmias are very common in older adults,

pharmaceutical treatments often have significant side effects. In a recent <u>Journal of Medicinal Chemistry</u> publication, stem cell biologists from the Cardiovascular Institute, medicinal chemists from the Human BioMolecular Research Institute, and cardiovascular pharmacologists from UCLA worked together to create an alternative version of a drug that had decreased severe side effects. Induced pluripotent stem cells (iPSCs) have provided a new way to model and learn about diseases: disease in a dish. The disease-in-a-dish concept allows researchers to test new drugs to determine their effectivitivity and safty. The team, led by Mark Mercola,



Mark Mercola, PhD

PhD and John Cashman, PhD, used iPSC cells from patients with long QT syndrome (LQTS), a type of VA, to design improved drugs similar to mexiletine. Mexiletine is a drug used to treat life-threatening VAs that may to lead to worsened arrythmias. The re-engineered analogues were evaluated for safety in healthy iPSC-derived cardiomyocytes (iPSC-CMs). IPSC-CMs from patients with LQTS were also used to determine how effective the analogues were at improving arrhythmias. This is the first report of using iPSC-CMs from both normal and diseased individuals to re-engineer a drug and evaluate its safety and effectiveness, combining "drug development in a dish" and "disease in a dish" to develop a compound for treating cardiovascular disease.

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A fermented-food diet increases microbiome diversity and lowers inflammation By Janelle Weaver

Stanford researchers discover that a 10-week diet high in fermented foods boosts microbiome diversity and improves immune responses. In a clinical trial, 36 healthy adults were randomly assigned to a 10-week diet that included either fermented or high-fiber foods. The two diets resulted in different effects on the gut microbiome and the immune system. Eating foods such as yogurt, kimchi, and kombucha tea led to an increase in overall microbial diversity. "This is a stunning finding," said Justin Sonnenburg, PhD. "It provides one of the first examples of how a simple change in diet can reproducibly remodel the microbiota across a cohort of healthy adults." In addition, four types of immune cells showed less activation in the fermented-food group. "Microbiota-targeted diets can change immune status, providing a promising avenue for decreasing inflammation in healthy adults," said Christopher Gardner, PhD. By contrast, none of these 19 inflammatory proteins decreased in participants assigned to a high-fiber diet rich in legumes, seeds, whole grains, nuts, vegetables and fruits. On average, the diversity of their gut microbes also remained stable. "We expected high fiber to have a more universally beneficial effect and increase microbiota diversity," said Erica Sonnenburg, PhD, a senior research scientist in basic life sciences, microbiology and immunology. The study was published in <u>Cell</u>. Justin and Erica Sonnenburg and Christopher Gardner are co-senior authors.



"Disease

in a dish

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Cardiomyocytes

Screen for desired decrease in APD

Screen against undesired arrhy

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in a dish

"Disease in a dish" and "drug discovery in a dish" was used to generate a

safter, effective version of Mexiletine - a drug used to treat arrhythmias,

that has severe side effects. Induced pluripotent stem cell-derived

cardiomyocytes (iPSC-CMs) from healthy donors or patients with long QT syndrome (characterized by arrhythmias) were used to test mexiletine

analogues for safety and effectiveness in treating increased heart rates.

Stanford researchers found that eating a diet high in fermented foods such as kimchi increases the diversity of gut microbes, which is associated with improved health. Nungning20/Shutterstock



Erica Justin Christopher Sonnenburg, PhD Sonnenburg, PhD Gardner, PhD

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Innovative Method to Better Understand How Protein Isoforms are Disease-associated



By Amanda Chase, PhD

Proteins are the "work horses" of the body; they are necessary for the structure, function, and regulation of the body's tissues and organs, and are involved in all body functions, both healthy and diseased. The process of creating a protein involves several steps, and starts with DNA, the instructions for how to make protein. The information in DNA is copied, but not understood, into messenger RNA (mRNA) that acts as the messenger to bring the information to the translator. However, extra pieces of information (introns) must first be removed to create mature mRNA that can be used for translating the instructions to create

the protein. After intron removal, the remaining information (exons) are joined together to become the code (information) that translates to protein. The process of differently removing introns and exon joining is referred to as alternative splicing. Dysregulation of alternative splicing is known to be associated with disease, including cardiovascular disease. For example, mutations in a heart-specific alternative splicing regulator, RMB20, leads to dilated cardiomyopathy (DCM), a leading cause of heart failure.



Example of genome-wide measurement of full-length splicing isoforms in iPSC-CMs with a region of chromosome 19, demonstrating the complexity. Known isoforms are in green; previously unidentified isoforms are in red.



Understanding how alternative splicing may be dysregulated during disease would be an important step in finding molecular mechanisms that lead to diseases in which splicing is implicated. The need for improved methods of analyzing alternative splicing was addressed by a group of researchers, led by co-first authors Chenchen Zhu, PhD, and Jingyan Wu, PhD, and senior author Lars Steinmetz, PhD, Professor of Genetics at Stanford and Group Leader at European Molecular Biology Laboratory in Germany. Their method, recently described and published in <u>Nature Communications</u>, establishes a computational method to quantify full-length transcripts and enable the identification of disease-associated transcript isoforms.

The team leveraged the knowledge that a specific mutation in the heart-specific alternative splicing regulator RMB20 can lead to DCM to generate data, develop the method, and identify mis-spliced isoforms in RMB20 mutants. Their innovative method enables analysis of the impact of patient mutations via long-read sequencing. The transcriptome is complex, as demonstrated in the figure that shows a region as an example. The team created a computational method for transcript quantification, FulQuant, that allows de novo transcript annotation and better rules out artifacts and sequencing errors. When this method was first used, it was found that the number and complexity of all alternative splicing isoforms is not fully appreciated yet and RBM20 mutations may generate novel transcripts that have previously been missed. These findings could be used for future diagnostics and drug development. Intriguingly, this new method also provides the opportunity to study differences in protein expression that separate health from disease.

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CVI Staff Spotlight

David Preston will be celebrating eight and a half years with the Stanford Cardiovascular Institute in September! David's main responsibilities at CVI include 1) live-event management, 2) back-



end administration of our T32 and R38 training grants, and 3) everything else others need to help CVI's programs run smoothly!

One little-known fact about David is that he has a diverse collection of musical instruments from all over the world - and he can even play a few! At CVI, he truly appreciates that the people he works with are amazing - from staff to postdocs to faculty - and that they have such a wide range of excellent talent and skills all working towards advancement of cardiovascular medicine.

Discovery of a new biomarker for pulmonary arterial hypertension By Adrienne Mueller, PhD

Pulmonary arterial hypertension (PAH) is a chronic disorder in which the walls of your pulmonary artery progressively thicken, making it harder for blood to reach your lungs and for you to renew the oxygen supply to your body. As your right heart struggles to meet the lung's demands, PAH often culminates in right heart failure and, ultimately, death. A well-recognized feature of PAH is persistent inflammation. Prolonged inflammation can ultimately trigger the release of growth factors that cause vascular cells to grow and multiply. Previous work has shown that some of the immune cells active in the inflammatory response release a protein called neutrophil elastase (NE), a likely candidate for triggering the vascular changes underlying PAH.

If NE is contributing to PAH, blocking it may help relieve symptoms.

Elafin is a protein that does just that – it inhibits NE. In order to understand the relationship between NE, Elafin, and PAH, a collaboration led by Roham Zamanian MD, recently investigated whether circulating NE and Elafin levels are abnormal in individuals with PAH, and, if so, whether the levels are correlated with clinical severity. This study is part of program project grant given to Marlene Rabinovitch, MD as lead PI to bring Elafin to the clinic for pulmonary arterial hypertension. The

findings, first authored by Andrew Sweatt, MD, were recently reported in <u>*Chest*</u> and showed that NE levels are associated with disease severity and progression, making it an ideal candidate as a biomarker, evaluating disease severity, and developing new therapies. The Zamanian and Rabinovitch labs are currently engaged in a phase 1 clinical trial to test Elafin therapy for PAH.

Study shows why second dose of COVID-19 vaccine shouldn't be skipped by Bruce Goldman

Scientists scrutinized Pfizer vaccine recipients' blood samples to learn exactly what effects the vaccine exerts on the body's immune system. The second dose of a COVID-19 vaccine induces a powerful boost to a part of the immune system that provides broad antiviral protection, according to a study led by investigators at the Stanford University School of Medicine. The finding strongly supports the view that the second shot should not be skipped. The study, published in Nature, was designed to find out exactly what effects the vaccine, marketed by Pfizer Inc., has on the numerous components of the immune response. The researchers analyzed blood samples from individuals inoculated with the vaccine. They counted antibodies, measured levels of immune-signaling proteins and characterized the expression of every single gene in the genome of 242,479 separate immune cells' type and status. "The second shot has powerful beneficial effects that far exceed those of the first shot," Pulendran said. "It stimulated a manifold increase in antibody levels, a terrific T-cell response that was absent after the first shot alone, and a strikingly enhanced innate immune response." Unexpectedly, Pulendran said, the vaccine — particularly the second dose — caused the massive mobilization of a newly discovered group of first-responder cells that are normally scarce and guiescent.



Stanford undergraduate student is inoculated with a COVID-19 vaccine. Photo by Steve Fisch

Khatri, PhD



Bali Pulendran,

PhD



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Neutrophil elastase (NE) P<0.0001 P<0.0001 P<0.0001 Healthy PAH controls PAH patients Elafin P<0.0001 P<0.0001 Healthy PAH controls PAH

PAH patients have significantly higher levels of NE (neutrophil elastase) and significantly lower levels of Elafin, an NE inhibitor.

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Andrew Sweatt, Marlene MD Rabinov

Rabinovitch, MD Zamanian, MD

Roham

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.

<u>Cardiovascular Medicine's Clinical Research Office</u> and the <u>Cardiovascular Institute's Clinical Trials Core</u> 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 Stanford Arrhythmia Service: Linda K. Ottoboni, PhD, CNS, founded the Atrial Fibrillation Prevention and Lifestyle Management Program to help individuals reduce their cardiovascular risk. Research has shown that reducing cardiovascular risk improves atrial fibrillation outcomes. Dr. Ottoboni is also testing strategies to help patients manage the unpredictability of arrhythmias. In collaboration with Dr. Paul Wang, Dr. Sanjiv Narayan, Dr. Mintu Turakhia, and the other members of the Stanford Arrhythmia Service, Dr. Ottoboni is pursuing several research projects including: evaluating symptom management strategies that may improve patient quality of life; a multi-center clinical trial on whether bariatric surgeries improve patient outcomes; and an assessment of whether a digital health platform targeting a patient's psychometric profile can help modify behaviors to reduce cardiovascular risk factors and thereby improve access for underrepresented populations.

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.

Clinical hESC-CM Trial for Heart Failure Patients

Heart disease strikes in many forms, but collectively it causes one-third of all deaths in the U.S. An estimated 4.8 million Americans have heart failure (HF), with 400,000 new cases diagnosed each year. Half will die within five years. Current drug- and device-based therapies, while effective, are limited in their ability to address the complex underlying mechanism of this multi-faceted disease.

The California Institute of Regenerative Medicine (CIRM) has recently awarded Dr. Joseph Wu and his team at Stanford University funding to carry out a first-in-man clinical trial in the US to test human embryonic stem cell-derived cardiomyocyte (hESC-CM) therapy. The study is called: A Phase I Pilot Study of Human Embryonic Stem Cell-derived Cardiomyocytes in PaTients with ChrOnic Ischemic Left VentRicular Dysfunction (HECTOR). The study include Drs. Phillip Yang, Kenneth Mahaffey, Manisha Desai, David Lee, Eldrin Lewis, and other members.

The study will recruit participants diagnosed with chronic ischemic cardiomyopathy to evaluate hESC-CMs in a randomized dose-escalation manner. Successful completion of this study will lead to safe and effective stem cell therapy for patients with chronic ischemic cardiomyopathy. For further information, please contact Fouzia Khan (Email: fouziak@stanford.edu) or Evgenios Neofytou (Email: neofytou@stanford.edu).



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, 12:30 - 1:20 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 227 | Drug Development: Key Issues in Regulation, Benefit vs. Risk, and Commercialization



CVI is launching a new course for the 2021-2022 academic year! MED227 is intended to provide an educational and practical perspective of drug development and its incredible potential, as well as challenges. Attendees can expect a blend of seminars, debates, and case study analyses to educate on key regulatory issues and commercial considerations, with an emphasis on cardiovascular applications.

This course is suitable for medical students, graduate students, basic scientists, clinicians, and clinicianscientists to provide an educational and practical perspective on the essential issues in drug development.

Fall Quarter - Mondays, 11:00am - 12:20 pm | 1 credit

Course Directors: Peter DiBattiste, MD; Jonathan Fox, MD, PhD; Alexander Gold, MD; Jayakumar Rajadas, PhD; Philip Sager, MD *https://med.stanford.edu/cvi/education/cvi-courses/med227.html*

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. <u>*Come train with us!*</u> — Joshua Knowles, MD, PhD, Program Director



https://med.stanford.edu/cvmedicine/education/gen-cardiology-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

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, 2022, for a July 1, 2022, start date. *https://med.stanford.edu/cvi/education/resident-education/resident-fellowship.html*

Electrophysiology in the West 2021

The Electrophysiology in the West conference provides a comprehensive overview of the science and therapy of heart rhythm disorders, provided by world-renowned experts in a concise and exciting format.Divided into three parallel tracks, the symposium is designed to meet individual learner needs to improve their base of knowledge and to promote effective management of cardiac arrhythmia by all members of the healthcare team.

Friday, October 8, 2021

8:00 AM - 4:30 PM PST

FREE Registration

Stanford Medicine designates this Live Activity for a maximum of 6.50 AMA PRA Category 1 Credits[™], and a maximum of 6.5 ANCC contact hours.

Find out more!

REGISTER NOW!

RING FOR ADULTS AND TEENS WITH CONGENITAL HEART DISEASE

Thursday, February 17-

Saturday, February 19, 2022 Honolulu, Hawai'i

CATCH Hawai'i 2022

The Seventh CATCH Conference will focus on improving the quality of life of patients with congenital heart disease. We will discuss patient experience during the period of transitioning from childhood to adulthood, discover unique aspects of disease perception and emphasize the benefits of individualized care in a rapidly evolving field of medicine.

Who Should Attend: Physicians including cardiologists, emergency room physicians, internists, family practitioners, pediatricians, anesthesiologist, intensivists, advanced practitioners such as physician assistants and nurse practitioners, nurses working in adult care as well as pediatric settings, cardiac sonographers, cardiac catheterization laboratory technicians and pharmacists. It's also appropriate for any health care professional actively involved in the care of, or interested in, patients with congenital heart disease.

For more information: HawaiiPacificHealth.org/CATCH or Hawai^ci Pacific Health Conference Services at 808-522-346









SDDS 2022 Stanford Drug Discovery Symposium

April 25-26, 2022

View recordings of talks and panel discussions from SDDS 2021!

https://med.stanford.edu/cvi/events/2021-drug-discovery-conference/ event-recordings.html#day1





SDDS

Stanford



Grants, Awards, Appointments and Promotions

Euan Ashley Appointed the Roger W. and Joelle G. Burnell Professor of Genomics and Precision Health

Euan Ashley, MD, PhD, was recently appointed the Roger W. and Joelle G. Burnell Professor of Genomics and Precision Health. The award recognizes Ashley's vast expertise in medicine, including particular focus on cardiology, precision medicine, rare genetic disease and more. His numerous accomplishments include leading the team that carried out the first clinical interpretation of a human genome, co-founding three companies, authoring "The Genome Odyssey" and receiving multiple national recognitions from institutions such as the Obama White House and the American Heart Association. The professorship is made possible through the generous contributions of Roger, a Stanford masters program graduate and founder of Arnell Enterprises, Inc., and his wife, Joelle,

a retired fashion and interior designer. According to Roger, the contribution aims to support "the pursuit of ultimate human wellness [by] maximizing the potential for ideal, integrated physical, mental and spiritual health and well-being in the broadest sense, and for the largest number of human beings to benefit from this knowledge."

Dr. Nick Leeper to Receive 2021 Jeffrey M. Hoeg Arteriosclerosis, Thrombosis, and Vascular Biology Award

Congratulations to Dr. Nick Leeper, who will be awarded the Jeffrey M. Hoeg Arteriosclerosis, Thrombosis, and Vascular Biology Award for Basic Science and Clinical Research. The award recognizes an investigator who has made an outstanding contribution to furthering understanding of the pathophysiology of atherosclerosis and/ or the development of treatment strategies for its prevention through basic science and clinical research efforts.

Congratulations to the AIRHEALTH and SEAL Study Teams!

Kari Nadeau, MD, PhD, recently received a P01 Program Project Grant (PPG) for the project titled, Air pollution disrupts Inflammasome Regulation in HEart And Lung Total Health (AIRHEALTH) for \$10.6m from the NHLBI to study the links between human health issues and molecular mechanisms of exposure to air pollution and to wildfire smoke. The team includes Drs. Joseph Wu, Michael Snyder, Sharon Chinthrajah, Mary Prunicki, Francois Haddad, Holden Maecker, Manisha Desai, PJ Utz, and Brian Kim (pictured from left to right in upper right pannel, starting with row 1.)

Dr. Nadeau (PI), along with Drs. Sharon Chinthrajah, Tina Sindher, Donald Leung, Gideon Lack, Helen Brough, Susan Chan, Tee Bahnson, Julie Parsonnet, Christina Ciacco, Manisha Desai, Scott Boyd, Mark Boguniewicz, Evgeny Berdyshev, Bruce Lanser, Bruce Bender and Elena Goleva as co-investigators, also received an National Institute of Allergy and Infectious Diseases (NIAID) funded multinational study with \$12.1m for the prevention of food allergies on the SEAL (Stopping Atopic dermatitis and ALlergy) Study: Prevent allergy by enhancing the skin barrier. Team pictured in bottom panel.

ACTIV-5 / Big Effect Trial (BET) for the Treatment of COVID-19

The urgent quest for new therapeutics to reduce mortality and outcomes of hospitalized patients with the novel Coronavirus 2019 (COVID-19) continues. Researchers at Stanford partnered with the National Institutes of Health for the ACTIV-5 Big Effect Trials (BET). Researchers at Stanford are participating in the BET-A trial that will compare the efficacy of remdesivir plus an interleukin-23 inhibitor, risankizumab, to placebo for the treatment of COVID-19. Stanford is also participating in the BET-B trial, that will compare the efficacy of remdesivir plus a GM-CSF inhibitor, lenzilumab, to placebo for the treatment of COVID-19. The team includes Nidhi Rohatgi, MD (PI); Co-investigators: Drs. Kari Nadeau, Neera Ahuja, John Kugler, Andre Kumar, and Andra Blomkalns; and Sean N. Parker Center Team: Julia Kang Ye, Olivia Raeber, and Allie Lee.

TRISH Fellow From Stanford Dives Into Space Research and the Mitochondria By Nascha Martinez

The Stanford Daily sat down with James Won Suk Jahng, PhD, a Stanford postdoctoral student, and one of four postdoctoral students in the United States picked for a Translational Research Institute for Space Health (TRISH) fellowship. The fellowship works to collaborate with researchers to design biomedical technology for astronaut safety and apply them for future space missions. Jahng is interested in both space health as well as mitochondria, popularly known as the powerhouse of the cell. He has done research in numerous parts of the

globe from Hong Kong to California, and will be working on creating or finding a medication to help prevent mitochondrial











Grants, Awards, Appointments and Promotions



Shipra Arya, MD, Associate Professor of Surgery (Vascular Surgery), has been chosen to chair the Association of VA Surgeons' (AVAS) new Diversity and Inclusion Committee. She has also been chosen to Chair the Society for Vascular Surgery's VA surgeons committee.

Dr. Arya also received a 5-year Merit Award from the Department of Veterans Affairs (VA) to study frailty with the project "PAtientcentered mUltidiSciplinary care for vEterans undergoing surgery (PAUSE): a hybrid 1 clinical effectiveness-implementation intervention trial."

In addition, Dr. Arya was awarded the Society for Vascular Surgery's E.J. Wylie Traveling Fellowship. The Fellowship pays up to \$12,000, allowing the recipient to visit a number of vascular surgery centers around the world.



Venita Chandra, MD, Associate Professor, Surgery (VascularSurgery)will receive the the Vascular Career Advancement (VCA) Award at the international VIVA (Vascular InterVentional Advances) society conference in October, highlighting that she is one of the top up-and-coming clinical researchers and

vanguards in the specialty.



Christopher Gardner, PhD, Rehnborg Farquhar Professor of Medicine, was appointed co-chair of the Nutrition Committee of the American Heart Association.



Xinguo Jiang, MD, PhD, was awarded a \$2.3M R01 grant to study how hypoxic responses, mediated by hypoxia inducible

factors (HIFs), modulate lymphatic vascular remodeling and metabolic alterations in lymphedema. Amy Tian, PhD, and Mark Nicolls, MD, Professor of Pulmonary, Allergy & Critical Care Medicine, serve as co-investigators of this work. This grant investigates important lymphatic pathologies associated with hypoxia and how these may be driven by inflammation and edema.

Drs. Jiang, Dr. Tian and Nicolls were also awarded two new awards in PAH research including new R01 and VA Merit grant awards for research into how immunity and immune dysregulation contribute to pulmonary vascular remodeling and exploring the possibility of Treg (cell-based) therapy for PAH patients.



Mary Prunicki, MD, and Kari Nadeau, MD, PhD, (PI), Naddisy Foundation Professor of Pediatric Food Allergy, Immunology and Asthma, were will co-lead a recently-awarded National Institute of Environmental Health

Sciences (NIEHS) funded R21 with Dr. Christopher Gardner and Dr. Francois Haddad on the effect of exposures and nutrition on COVID disease outcomes.

Drs. Prunicki and Nadeau (PI) were also awarded an NIEHS R01 for research on pregnancy and exposure to air pollution, studying immune tolerance and disease outcomes.



Elsie Ross, MD, Assistant Professor of Surgery (Vascular Surgery), was awarded the Clinical Scientist Development Award from the Doris Duke charitable foundation for her work on "The Application of Deep Learning for Automated Vascular Imaging Analysis."



Nazish Sayed, MD, PhD, received funding from the Stanford Aging and Ethnogeriatrics Research Center (SAGE) for his research on modeling vascular aging in humans by identifying an inflammatory clock using deep learning and induced pluripotent stem cells (iPSCs).





Sayantani Sindher, MD, Associate Professor of Medicine, will lead a study (\$0.5M) for the NIH PCORI grant awarded

to Stanford PEDS Net - Grace Lee, MD, Professor of Pediatrics (Infectious Diseases), and Bonnie Maldonado, MD, Professor of Pediatrics (Infectious Diseases) - to research asthma in children by working with their pulmonary colleagues at the Lucile Packard Children's Hospital.



Edda Spiekerkoetter, MD, received \$1.7M funding through a new NIH R01 grant to study the molecular and structural mechanisms of right ventricle failure in pulmonary arterial hypertension (PAH). This work focuses on cardiac fibrosis and microvascular pathology and addresses the most important

cause of mortality in PAH. Ross Metzger, PhD, and Sushma Reddy, MD, Assistant Professor of Pediatrics (Cardiology), serve as co-investigators on the grant.



Josh Spin, MD, PhD, Assistant Professor in the Division of Cardiovascular Medicine, was awarded the 2021 CARE Seed Grant from the Stanford Center for Asian Health Research and Education for his project titled "Securinine in Abdominal Aortic Aneurysm." This is a pilot study investigating the

Aneurysm." This is a pilot study investigating the mechanisms and potential efficacy of a traditional Asian herbal medicine in an aneurysm model.



Phillip C. Yang, MD, Professor of Medicine (Cardiovascular Medicine), was awarded Department of Defense funding for "A Phase IIB, randomized, placebo-controlled, multicenter study of the comparative efficacy and safety of transendocardial injection of allogeneic

mesenchymal stem cells versus placebo in patients with nonischemic dilated cardiomyopathy (DCM II Trial)."

Dr. Yang received a CIRM award for "Hypoxia-specific Production of Exosomes from iPSC-derivatives for Myocardial Repair."

Dr. Yang, with Co-PI Hannah Valantine, MD, was also sponsored by the Stanford Innovative Medicine Accelerator Human Experimental Biology RFP. for the "Evaluation of Bioactive Agents to Predict Heart Rejection."

Dr. Yang, with Co-PI Jeffrey Teuteberg, MD, was also sponsored by the Stanford Division of CV Medicine Cost Savings Reinvestment Program for the project "Cloud-based machine learning algorithm for home monitoring of hospital-discharged cardiovascular patients to reduce re-admission."



Roham Zamanian, MD, Associate Professor of Medicine (Pulmonary and Critical Care Medicine), received \$3M funding in a new multi-PI NIH R01 grant working with Steve Kawut (UPENN) and coinvestigator Vinicio de Jesus Perez, MD, Associate Professor of Medicine (Pulmonary and Critical Care

Medicine). They will lead a 10-center initiative to evaluate the link between methamphetamine use and PAH in the United States. The aims of the project to conduct a well-designed prospective case-control study to validate use and quantify characteristics and patterns of methamphetamine use as a risk factor for PAH, determine predictors of clinical worsening in Meth-APAH, and study the role of genetic mutations and activity in this population.

Grants, Awards, Appointments and Promotions



Abha Khandelwal, MD, Associate Professor, of Medicine (Cardiovascular Medicine), was awarded funding from Novartis Pharmaceuticals Corp. for "A randomized double-blind, placebo-controlled, multicenter trial assessing the impact of lipoprotein (a) lowering with TQJ230 on major cardiovascular

events in patients with established cardiovascular disease [CA]."



Anuradha Chirala, MD, was appointed to Clinical Assistant Professor in the Division of Cardiovascular Medicine on July 1, 2021.



William Fearon, MD, Professor of Medicine (Cardiovascular Medicine) was awarded funding from the Cardiac Research Institute for "The PPG Global Registry: Prospective multicenter evaluation of the PPG index."



Guson Kang, MD, was appointed to Clinical Assistant Professor in the Division of Cardiovascular Medicine.



Mena Abdelsayed, PhD, postdoc in the lab of Dr. Mark Mercola, was recently awarded the Wilton W. Webster Fellowship in Pediatric Electrophysiology by the Heart Rhythm Society for his work on cardiac fibrosis.



Tom Alsaigh, MD, was awarded a position on the Mechanisms and Innovation in Vascular Disease T32 Training Program. Dr. Alsaigh will be working in the lab of Dr. Nick Leeper on the project " Precision Nanotherapies for Atherosclerotic Disease."



Kevin Cyr, medical student in the lab of Dr. Paul Wang, was was selected as a Young Investigator Awards finalist at the Heart Rhythm Society Conference.



Alex Dalal, MD, resident in Cardiothoracic Surgery and postdoc in the lab of Dr. Michael Fischbein, was awarded an NIH NHLBI Individual Postdoctoral Fellowship (F32) postdoctoral fellowship for his project, "Extracellular Matrix Biomechanical Properties Contribute to Aneurysm Formation in Marfan Syndrome."



Elizabeth George, MD, was awarded first place at the Association of VA Surgeons (AVAS) meeting for her presentation "Comparing perioperative outcomes after noncardiac surgery across VA and non-VA hospitals."



Urh Groselj, MD, PhD, is joining the lab of Dr. Joshua Knowles on a prestigious Fulbright fellowship for the year. Dr. Groselj will be working on the project "Genetic causes of hypercholesterolemia and their associations with clinical characteristics in children, adolescents and young adults"



Neil Kalwani, MD, was appointed as Clinical Scholar in the Division of Cardiovascular Medicine on June 30, 2021.



Marco Perez, MD, Associate Professor of Medicine (Cardiovascular Medicine), was awarded funding from WearLing, Inc. for the "WearLing Usability and Wearability Validation Study."



Jennifer Tremmel, MD, Associate Professor of Medicine (Cardiovascular Medicine) was awarded funding from the Boston Scientific Corporation for "A Prospective, Randomized (2:1), Multicenter Trial to Assess the Safety and Effectiveness of the AgentTM Paclitaxel Coated PTCA Balloon Catheter

for the Treatment of Subjects with In-Stent Restenosis (ISR)."



Rahul Sharma, MBBS, Associate Professor, of Medicine (Cardiovascular Medicine), was awarded funding from Edwards Lifesciences Corp. for "Edwards EVOQUE Transcatheter Tricuspid Valve Replacement: Pivotal Clinical Investigation of Safety and Clinical Efficacy using a Novel Device Short Title: TRISCEND II Pivotal Trial."



Paul J. Wang, MD, Professor of Medicine (Cardiovascular Medicine), was awarded funding from the Coulter Endowment Program - University Research for the project "High Frequency Ultrasound Myocardial Ablation System."



McKay Mullen, PhD, was awarded a position on the Stanford Propel Postdoctoral Scholars Program. Dr. Mullen will be working in the lab of Dr. Joseph Wu on the project "Evaluating the Impact of Androgen Deprivation Therapy in Mediating Breast and Prostate Cancer Chemotherapy Cardiotoxicity."



Ashish Sarruju, MD, received the Alderman Clinical Research Award in June, 2021.

Dr. Sarruju was also appointed to Clinical Scholar in the Division of Cardiovascular Medicine on July 1, 2021.



Katharina Schimmel, PhD, was awarded a position on the Mechanisms and Innovation in Vascular Disease T32 Training Program. Dr. Schimmel will be working in the lab of Dr. Edda Spiekerkoetter on the project "Elucidating the Pathogenesis of Arteriovenous Malformations."



James Tooley, MD, postdoctoral medical fellow in Cardiovascular Medicine, received the Sharon Hunt and Alan Yeung Outstanding Clinical Fellow Award in June 2021.

Dr. Tooley also received an AHA SFRN Health and Technology Innovation and Center for Digital Health Fellowship Award in July 2021.



Chad Weldy, MD, PhD, fellow in the lab of Dr. Thomas Quertermous, received the Gerald Reaven Awards for Basic Science Research in June 2021.

Dr. Weldy also received the Timothy F. Beckett Jr. Award for Best Clinical Teaching by a Medicine Fellow.

Dr. Weldy also received an NIH Loan Repayment Award from NHLBI for his research project titled "Single cell transcriptomic and epigenomic features of human atherosclerosis."

cvi.stanford.edu

Funding Opportunities

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

SEPTEMBER 2021

AHA/CHF Congenital Heart Defect Research Awards. Postdoctoral Fellowship. Application deadline: September 21, 2021

AHA/Enduring Hearts Research Awards in Pediatric Heart Transplantation. LOI due Sept 30th, 2021. Application Deadline: January 20, 2022

OCTOBER 2021

NIH R01 Research Project Grant (Parent R01 Clinical Trial Req). Application Deadline: October 5, 2021. PA-20-183

NIH R01 Research Project Grant (Basic Experimental Studies with Humans Required). Application Deadline: October 5, 2021. PA-20-184

NIH R01 Research Project Grant (Parent R01 Clinical Trial Not Allowed). Application Deadline: October 5, 2021. PA-20-185

Improving Outcomes in Cancer Treatment-Related Cardiotoxicity (R01). Application Deadline: October 5, 2021. PA-16-035

Improving Outcomes in Cancer Treatment-Related Cardiotoxicity (R01 Clinical Trial Optional). Application Deadline: October 5, 2021. PA-19-112

Cardiovascular and Pulmonary Research on E-Cigarettes (R01). Application Deadline: October 5, 2021. RFA-HL-18-024

NIH R01 Research Project Grant (Parent R01 Clinical Trial Not Allowed). Application Deadline: October 5, 2021. PA-19-056

NIH R01 Research Project Grant (Parent R01 Clinical Trial Req). Application Deadline: October 5, 2021. PA-19-055

NIH K99/R00 Pathway to Independence Award (Parent K99/R00 - Independent Clinical Trial Req). Application Deadline: October 12, 2021. PA-20-187

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

NIH K99/R00 Pathway to Independence Award (Parent K99/R00 Indep Basic Exp Studies with Humans Req). Application Deadline: October 12, 2021. PA-20-189

NIH K08 Mentored Clinical Scientist Research Career Development Award. Deadline: October 12, 2021. PA-20-203

NIH K24 Midcareer Investigator Award in Patient-Oriented Research. Application Deadline: October 12, 2021. PA-20-186

NIH K24 Midcareer Investigator Award in Patient-Oriented Research (Parent K24 Independent Clinical Trial Required). Application Deadline: October 12, 2021. PA-20-193

Understanding and Reducing Cardiovascular Disease in Type 1 Diabetes Mellitus (R01 – Clinical Trial Optional). Application Deadline: October 15, 2021. RFA-HL-21-014

Improving Outcomes in Cancer Treatment-Related Cardiotoxicity (R21). Application Deadline: October 16, 2021. PA-16-036

Improving Outcomes in Cancer Treatment-Related Cardiotoxicity (R21 Clinical Trial Optional). Application Deadline: October 16, 2021. PA-19-111.

Cardiovascular Biorepository for Type 1 Diabetes (U24 Clinical Trial Not Allowed). Application Deadline: October 20, 2021. RFA-DK-21-010

NIH Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) Postdoctoral Career Transition Award **to Promote Diversity (K99/R00 – Independent Clinical Trial Required).** Application deadline: October 27, 2021. PA-21-272

NIH Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) Postdoctoral Career Transition Award to Promote Diversity (K99/R00 – Independent Clinical Trial Not Allowed). Application deadline: October 27, 2021. PA-21-271

NOVEMBER

Toward Translation of Nanotechnology Cancer Interventions (TTNCI) (R01 Clinical Trial Not Allowed). Application Deadline: November 18, 2021. PAR-20-116

DECEMBER

Myocarditis, Heart Failure and Sudden Death Research Grant Program. Application Deadline: December 1, 2021

AHA Career Development Award. Application Deadline: December 6, 2021

NIH F32 Ruth L. Kirschstein National Research Service Award (NRSA) Individual Postdoctoral Fellowship. Application Deadline: December 8th, 2020. PA-20-242.

ROLLING DEADLINES

NIH Research Supplements to Promote Re-Entry and Re-Integration into Health-Related Research Careers. NOT-OD-21-134

Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supplement). PA-20-272

Research Supplements to Promote Diversity in Health-Related Research. PA-21-071

Mackay California-Pacific Rim Tobacco Policy Scholar Award. \$250K/yr x 3 yrs. Build leadership among mid-career researchers to foster evidencebased tobacco control policy with relevance to California and the Pacific Rim. Eligibility: mid-career faculty with PI eligibility and midcareer 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 2021

Internal Medicine review for Nurse Practitioners, Physician Assistants & Primary Care Physicians. September 16-17, 2021. Virtual

UCLA Heart Failure Symposium 2021: State of the Art Updates & Therapies for Advanced Heart Failure. September 18, 2021. Hybrid

AHA Vascular Discovery 2021. September 22-24th, 2021. Virtual

Columbia Medicine- 9th Annual Challenges in Hypertension. September 24, 2021. Virtual

Innovations in Structural Heart Interventions. September 25-26, 2021. Virtual

CIRSE 2021 Summit. September 25-28, 2021. Virtual

AHA Hypertension Scientific Sessions 2021. September 27-29, 2021. Virtual

36th World Cardiology Conference. September 27-28th, 2021. Dublin, Ireland / Hybrid

OCTOBER 2021

11th Annual Women's Heart & Vascular Symposium 2021. October 1, 2021. Virtual

Echo in Congenital Heart Disease. October 1-3, 2021. Hybrid

The VEINS at VIVA. October 3-4th, 2021. Las Vegas, NV

Vascular Interventional Advances - VIVA2021. October 5-7, 2021. Las Vegas, NV

38th Annual MRI of the Body & Heart 2021 National Symposium. October 7-8th, 2021 Las Vegas, NV / Hybrid

2021 SCAI SHOCK Virtual Conference. October 7-8, 2021. Virtual

The genetics of Heart Variation. October 7-9, 2021. Hybrid

Cardiovascular Implant Durability Conference. October 13-15th, 2021. Asilomar Conference Center, Monterey, CA

Harvard Update in Clinical Cardiology. October 13-15th, 2021. Virtual

7th Annual Pulmonary Embolism Symposium. October 14-16th, 2021. Virtual

Artificial Intelligence in Cardiology. October 14-16, 2021. Hybrid

16th Annual Cardiometabolic Health Congress. October 14-17, 2021. National Harbor, MD

Penn Medicine Advanced TAVR, TMVR and Beyond. October 15-16th, 2021. Virtual

Coronary Artery Disease. October 15-17, 2021. Hybrid

George and Angelina Kostas Research Center for Cardiovascular Nanomedicine: Annual International Meeting. October 18, 2021. Virtual

Cases in echo, Cardiac CT, and MRI. October 20-23, 2021. Hybrid

Innovations in Atrial Fibrillation Management. October 23, 2021. Hybrid

International Conference on Applications of Cardiology and Human Anatomy. October 28-29th, 2021. Los Angeles, CA / Hybrid

NOVEMBER

International Conference on Clinical Cardiology, Cardiac Diseases and Conditions. November 1-2nd, 2021. San Francisco, CA / Hybrid

International Conference on Heart Diseases and Clinical Cardiology. November 1-2nd, 2021. San Francisco, CA / Hybrid

NIH Virtual Seminar on Program Funding and Grants Administration. November 1-4th, 2021. Virtual

AHA Resuscitation Science Symposium. November 12-14th, 2021. Boston, MA

AHA Scientific Sessions. November 13-15th, 2021. Boston, MA + Virtual

QCOR Scientific Sessions. November 15, 2021. Virtual

32nd Annual Cardiovascular Interventions. November 16-19th, 2021. La Jolla, CA

Pacific Northwest Vascular Society 2021. November 18-19th, 2021. Portland, Oregon

DECEMBER

Heart Rhythm & ECG: Case Based Approach. December 2-5th, 2021. Hybrid

Innovations in Cardiovascular Interventions 2021. December 5-7th, 2021. Israel / Hybrid

International Conference on Hearth Failure. December 9-10th, 2021. New York, NY / Hybrid

SAVE THE DATE

CATCH - Caring for Adults and Teens with Congenital Heart Disease. February 17-19, 2022. Honolulu, HI

SDDS - Stanford Drug Discovery Symposium. April 25-26, 2022. Stanford, CA

CVI Resources

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 deidentified 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.

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

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 pharmacodynamic and studies, and developing smart materials for biomedical applications. CVI Cardiovascular Pharmacology also offers trainings and lectures.

Contact: Jayakumar Rajadas, PhD jayraja@stanford.edu



3DQ Imaging Laboratory

Stanford's 3DQ Imaging Laboratory develops new approaches to exploration, analysis and quantitative assessments of diagnostic images that result in new and/or more cost-effective diagnostic approaches, and new techniques for the design and monitoring of therapy. The lab processes over 1,200 clinical cases to deliver relevant visualization and analysis of medical imaging data at Stanford. The lab is co-directed by Dominik Fleischmann, MD, Roland Bammer, PhD and Sandy Napel, PhD. **Contact: Dominik Fleischmann, MD** / d.fleischmann@stanford.edu

Member Publications

Communication is at the heart of scientific advancement and innovation. Between June 1st and August 31st, Stanford Cardiovascular Institute members published 629 original manuscripts and reviews, further contributing to our understanding of cardiovascular biology and disease. Here, we highlight selected manuscripts by our members.

June

Biophysical matrix cues from the regenerating niche direct muscle stem cell fate in engineered microenvironments. Madl CM, Flaig IA, Holbrook CA, Wang YX, Blau HM. *Biomaterials*. 2021 Jun 14;275:120973. doi: 10.1016/j. biomaterials.2021.120973. PMID: 34224984

Modest Gains After an 8-Week Exercise Program Correlate With Reductions in Non-traditional Markers of Cardiovascular Risk. Liang G, Huang X, Hirsch J, Mehmi S, Fonda H, Chan K, Huang NF, Aalami O, Froelicher VF, Lee DP, Myers J, Lee AS, Nguyen PK. *Front Cardiovasc Med.* 2021 Jun 17;8:669110. doi: 10.3389/ fcvm.2021.669110. PMID: 34222367

Lung Pericytes in Pulmonary Vascular Physiology and Pathophysiology. Yuan K, Agarwal S, Chakraborty A, Condon DF, Patel H, Zhang S, Huang F, Mello SA, Kirk OI, Vasquez R, de Jesus Perez VA. Compr Physiol. 2021 Jun 30;11(3):2227-2247. doi: 10.1002/cphy.c200027. PMID: 34190345

Monocyte released HERV-K dUTPase engages TLR4 and MCAM causing endothelial mesenchymal transition. Otsuki S, Saito T, Taylor S, Li D, Moonen JR, Marciano DP, Harper RL, Cao A, Wang L, Ariza ME, Rabinovitch M. *JCl Insight*. 2021 Jun 29:146416. doi: 10.1172/jci.insight.146416. PMID: 34185707

A Fetal Risk Stratification Pathway for Neonatal Aortic Coarctation Reduces Medical Exposure. Maskatia SA, Kwiatkowski D, Bhombal S, Davis AS, McElhinney DB, Tacy TA, Algaze C, Blumenfeld Y, Quirin A, Punn R. *J Pediatr.* 2021 Jun 25:S0022-3476(21)00629-6. doi: 10.1016/j.jpeds.2021.06.047. PMID: 34181988

Severe Pulmonary Arterial Hypertension is Characterized by Increased Neutrophil Elastase and Relative Elafin Deficiency. Sweatt AJ, Miyagawa K, Rhodes CJ, Taylor S, Del Rosario PA, Hsi A, Haddad F, Spiekerkoetter E, Bental-Roof M, Bland RD, Swietlik EM, Gräf S, Wilkins MR, Morrell NW, Nicolls MR, Rabinovitch M, Zamanian RT. *Chest.* 2021 Jun 25:S0012-3692(21)01255-1. doi: 10.1016/j.chest.2021.06.028. PMID: 34181952

Cardiovascular Procedural Deferral and Outcomes over COVID-19 Pandemic Phases: A Multi-Center Study. Yong CM, Spinelli KJ, Chiu ST, Jones B, Penny B, Gummidipundi S, Beach S, Perino A, Turakhia M, Heidenreich P, Gluckman TJ. *Am Heart J.* 2021 Jun 25:S0002-8703(21)00167-8. doi: 10.1016/j.ahj.2021.06.011. PMID: 34181910

Immunoglobulin Y for Potential Diagnostic and Therapeutic Applications in Infectious Diseases. Lee L, Samardzic K, Wallach M, Frumkin LR, Mochly-Rosen D. *Front Immunol.* 2021 Jun 9;12:696003. doi: 10.3389/fimmu.2021.696003. PMID: 34177963

On the Periodicity of Cardiovascular Fluid Dynamics Simulations. Pfaller MR, Pham J, Wilson NM, Parker DW, Marsden AL. *Ann Biomed Eng.* 2021 Jun 24. doi: 10.1007/s10439-021-02796-x. PMID: 34169398

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Increases in SARS-CoV-2 Test Positivity Rates Among Hispanic People in a Northern California Health System. Rodriguez F, Coquet J, Harrington R, Hernandez-Boussard T. *Public Health Rep.* 2021 Jun 23:333549211026778. doi: 10.1177/0033549211026778. PMID: 34161176

A protocol for transdifferentiation of human cardiac fibroblasts into endothelial cells via activation of innate immunity. Liu C, Medina P, Thomas D, Chen IY, Sallam K, Sayed D, Sayed N. *STAR Protoc.* 2021 Jun 5;2(2):100556. doi: 10.1016/j.xpro.2021.100556. PMID: 34151292

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Assessment of North American Clinical Research Site Performance During the Start-up of Large Cardiovascular Clinical Trials. Goyal A, Schibler T, Alhanti B, Hannan KL, Granger CB, Blazing MA, Lopes RD, Alexander JH, Peterson ED, Rao SV, Green JB, Roe MT, Rorick T, Berdan LG, Reist C, Mahaffey KW, Harrington RA, Califf RM, Patel MR, Hernandez AF, Jones WS. *JAMA Netw Open.* 2021 Jul 1;4(7):e2117963. doi: 10.1001/jamanetworkopen.2021.17963. PMID: 34297072

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Canagliflozin, serum magnesium and cardiovascular outcomes-Analysis from the CANVAS Program. Wang KM, Li J, Bhalla V, Jardine MJ, Neal B, de Zeeuw D, Fulcher G, Perkovic V, Mahaffey KW, Chang TI. *Endocrinol Diabetes Metab.* 2021 Mar 13;4(3):e00247. doi: 10.1002/edm2.247. PMID: 34277971

Factional flow reserve derived from computed tomography coronary angiography in the assessment and management of stable chest pain: the FORECAST randomized trial. Curzen N, Nicholas Z, Stuart B, Wilding S, Hill K, Shambrook J, Eminton Z, Ball D, Barrett C, Johnson L, Nuttall J, Fox K, Connolly D, O'Kane P, Hobson A, Chauhan A, Uren N, Mccann GP, Berry C, Carter J, Roobottom C, Mamas M, Rajani R, Ford I, Douglas P, Hlatky MA; FORECAST Investigators. *Eur Heart J.* 2021 Jul 16:ehab444. doi: 10.1093/eurheartj/ ehab444. PMID: 34269376

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Safety and Efficacy of B-Cell Depletion with Rituximab for the Treatment of Systemic Sclerosis-associated Pulmonary Arterial Hypertension: A Multicenter, Double-Blind, Randomized, Placebo-controlled Trial. Zamanian RT, Badesch D, Chung L, Domsic RT, Medsger T, Pinckney A, Keyes-Elstein L, D'Aveta C, Spychala M, White RJ, Hassoun PM, Torres F, Sweatt AJ, Molitor JA, Khanna D, Maecker H, Welch B, Goldmuntz E, Nicolls MR. *Am J Respir Crit Care Med*. 2021 Jul 15;204(2):209-221. doi: 10.1164/rccm.202009-34810C. PMID: 33651671

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August

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