# Undergraduate Summer Research Program Symposium

**August 9th, 2021**

**Morning Session: 9-11am PT**

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<td>Sameer Sundrani</td>
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<td>Amal Adamu</td>
<td>Lab of Dr. Nazish Sayed</td>
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<td>Parth Amin</td>
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<td>9:55am</td>
<td>Alexander Boakye</td>
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<td>Nickeisha Cuthbert</td>
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<td>Sofia Torres Bigio</td>
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<td>Chisomaga Ekwueme</td>
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<td>Jane Thomas</td>
<td>Lab of Dr. Daniel Bernstein</td>
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<td>10:30am</td>
<td>Rocio Vazquez</td>
<td>Lab of Dr. Vinicio de Jesus Perez</td>
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<td>Natasha Auer</td>
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<td>JooChan Shin</td>
<td>Lab of Dr. Christopher Cheng</td>
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<td>Thinzar Htwe</td>
<td>Lab of Dr. Anson Lee</td>
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**Afternoon Session: 1-3pm PT**

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<td>1:00pm</td>
<td>Aaron Panduro</td>
<td>Lab of Dr. Alison Marsden</td>
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<td>Angel Emodi</td>
<td>Lab of Dr. Mark Skylar-Scott</td>
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<td>Savan Patel</td>
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<td>Celine Escarmant</td>
<td>Lab of Dr. Alison Marsden</td>
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<td>Jamie Bozeman</td>
<td>Lab of Dr. Kristy Red-Horse</td>
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<td>1:35pm</td>
<td>Arely Campos-Melendez</td>
<td>Labs of Drs. Karen Hirsch and</td>
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<td>Britney Joy Sison</td>
<td>Melissa Vogelsong</td>
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<td>Jaylen Sandifer</td>
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<td>Kevin Tan</td>
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<td>Stefan Veizades</td>
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<td>2:20pm</td>
<td>Eileen Tzng</td>
<td>Lab of Dr. Phillip Yang</td>
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<td>Gabriel Heckerman</td>
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<td>Josephine Gollin</td>
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<td>Yuri de Castro</td>
<td>Lab of Dr. Joseph Wu</td>
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<td>2:50pm</td>
<td>Closing Remarks</td>
<td>Dean Lloyd Minor and Dr. Joseph Wu</td>
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Please join us to celebrate the scientific accomplishments of our 2021 cohort of CVI Summer Undergraduate Research students.

**Zoom Link for Live Event**

**View and Comment on the Recordings on August 9th**
Transposons are mobile genetic elements that, like viruses, hold promise for gene therapy delivery. Computational analyses have identified an unusual transposon family called Polintons (from POLymeraseINTegrase) that resemble a family of DNA viruses and may be capable of forming functional virus particles. However, such particles have never been seen, let alone characterized. Here, we describe both an experimental and a computational search for genetic sequence characteristics that demonstrate the evolutionary existence of functional Polinton particles. Our pilot lab-based studies have not yet captured environmental Polintons in real time, but our experiments are ongoing. Computationally, we searched all publicly available genomes of the worm phylum *Nematoda* and found preliminary evidence of functional Polintons in 23 assemblies. Although our search continues, these results strongly suggest Polinton existence in this phylum and are a first step in studying the origin, evolution, and potential gene therapy applications of these elements over time.

**Modeling chemotherapy-induced cardiotoxicity using iPSCs**

*Amal Adamu – Lab of Dr. Nazish Sayed*

Cancer patients treated with anti-cancer drugs often suffer from heart failure. Despite the beneficial effects of these drugs on cancer, many of them are discontinued due to their serious effects on the heart. The emergence of induced pluripotent stem cell (iPSC) technology offers an experimental human-based platform to model chemotherapy-induced cardiotoxicity. It has been shown that doxorubicin disrupts the normal endothelial physiology by damaging endothelial cells (ECs) that can lead to the development of severe chronic vascular diseases, which often leads to cardiac dysfunction. With the knowledge that dysfunctional ECs can have a negative impact on cardiomyocyte function, we need a better understanding of the integral role of ECs in the development of doxorubicin-induced myocardial injury. This project aims to study the role of the endothelium in the pathogenesis of doxorubicin-induced cardiotoxicity using bioengineering tools. Results from this work could lead to new strategies that could lower morbidity and mortality.

**Identifying novel gene targets associated with Diabetic Cardiomyopathy**

*Andreanne Sannajust – Lab of Dr. Joseph Wu*

Individuals with diabetes mellitus (DM) are predisposed to developing diabetic cardiomyopathy (DiCM), a non-ischemic cardiomyopathy accompanied with ventricular hypertrophy.
and diastolic dysfunction. To date, there are no interventions against DiCM and glucose lowering therapies worsen cardiovascular outcomes. To identify novel therapeutic targets against DiCM, I used publicly accessible multi-omics resources, and hypothesized that cardiac-lipotoxicity is an underlying cause of DiCM. A list of 35 genes significantly associated with 5 phenotypes: Type 2 Diabetes adjusted to BMI, fasting insulin adjusted to BMI, Hypertension, Dyslipidemia, and Nonischemic cardiomyopathy was generated. The list of genes was stratified by adding genes within 50 kb of the target genes and excluding genes not expressed in the cardiovascular system. This has generated 9 gene targets (ZBTB4, NUCKS1, NUDT22, TRPT1, ESRRA, TRIM54, UBA7, PCSK7, CYTH1), including 3 novel targets (ZBTB4, NUCKS1, CYTH1). A future mechanistic study on iPSC-derivatives will elucidate the role of these genes in DiCM.

Using hiChIP to identify IncRNAs responsible for immune gene expression
*Parth Amin – Lab of Dr. Kevin Wang*

Innate immune dysregulation is the hallmark of many diseases, such as cancer. Immunotherapy for cancer attempts to stimulate the patient’s immune responses against tumors as treatment. It is used clinically now and will provide many innovative and more effective cancer treatments. Through our interests in chromosomal architecture, chromatin structure, and the interplay between the two in regulating gene expression, we discovered new classes of long noncoding RNAs that work in cis downstream innate immune genes through utilizing HiChIP data. We hope that our work will further understand the innate immune response in an attempt to further immunotherapy.

Classifying arrhythmias using deep learning
*Elsa Lawrence – Lab of Dr. Mark Mercola*

An arrhythmia is a condition where the heart beats abnormally. As there are many causes of arrhythmia, e.g. heart attacks, genetic predispositions, or drug side-effects- about 5% of the population worldwide suffer from some form of arrhythmia. Without proper diagnosis and treatment, arrhythmias can increase risk of stroke or heart failure. Different types of arrhythmia present with different patterns of electrical signals. A key task in the *in vitro* study of arrhythmias is classification of these types from cellular electrical signals; however, human classification is time-consuming, resource-intensive, and often inaccurate. Machine learning models can automate and improve this process. Here, we implemented a deep convolutional neural network to classify traces from patient-derived hiPSC-cardiomyocytes. The network attained 94% accuracy in our validation dataset. This model could be used to study genetic contributions that affect the risk of developing arrhythmias, or as a screening method for new therapeutic targets that prevent arrhythmias.
Cyanobacteria as a photosynthetic symbiotic therapy in ischemic cardiomyocytes

Alexander Boakye - Lab of Dr. Joseph Woo

Ischemic heart disease (IHD) is the leading cause of mortality worldwide – posing a problem across all income levels. IHD results from poor circulation of oxygen and glucose to the heart tissue usually caused by a vascular blockage. To strategically aid oxygen consumption in ischemic sites, we propose harnessing the light-activated properties of *Synechococcus elongatus* (*Synechococcus*), a strain of cyanobacteria, to aid regeneration of cardiomyocytes after ischemia. When introduced into an animal model, *Synechococcus* absorbs carbon dioxide and water from the ischemic environment and synthesizes oxygen and glucose to be metabolized by dying tissue. We quantified the number of cells present in both damaged and undamaged tissue that had been exposed to *Synechococcus*. We found that *Synechococcus* integrates well into the host tissue, elevates oxygen levels by nearly 25-fold, and improves cell proliferation. These results indicate a leap forward in cellular regeneration and the potential reduction of ischemic death.

Regulation of skeletal muscle growth by an adipocyte-secreted polypeptide (Isthmin)

Nickeisha Cuthbert - Lab of Dr. Katrin Svensson

Skeletal muscle growth is regulated by factors like Isthmin that activate the PI3K/AKT pathway. This project’s aim is to understand Isthmin’s effect on skeletal muscle growth by analyzing muscle fiber size in ImageJ software. The significance of this project is to ultimately develop therapeutics to treat muscle loss and degradation. Wild type and Isthmin knockout mice were separated into fast then feed and fast only categories for the 6 weeks of growth. ImageJ was used to measure the area, minimal Feret’s diameter and nuclei location of skeletal muscle fibers from the mice in all categories. In the quadriceps, Isthmin knockout mice had larger muscle fibers than wild type mice. This result differs from a previous investigation, so Isthmin’s effect on muscle fiber size cannot be concluded. The project’s future involves analyzing other muscle locations to determine if the results are location specific and if they are affected by age and sample size.

Using human IPS cells for cardiac muscle modeling in Duchenne Muscular Dystrophy patients

Sofia Torres Bigio - Lab of Dr. Helen Blau

Duchenne Muscular Dystrophy (DMD) is a degenerative muscular X-linked genetic disease that affects approximately 1 in 5,000 boys all over the world. The disease is marked by the absence of dystrophin, a 79 exon-long protein that bridges each muscle cell’s cytoskeleton (structural support) to its extracellular matrix. The lack of this protein induces muscle weakness and slowly causes the deterioration of all types
of muscle, including cardiac. To avoid excessive human testing, animal models have been traditionally employed for the study of cardiac muscle degeneration in Duchenne patients, among them breeds of mice and dogs. However, these fail to accurately reproduce the effect of the disease in humans. The aim of the project is thus to create dystrophin-lacking cardiomyocytes (heart cells) from human induced pluripotent stem cells (iPSC) to provide a more precise alternative to further investigate DMD’s effect on the heart at a cellular level. We expect these findings will help the worldwide aim of finding a cure for DMD.

**Effect of nicotine exposure on induced pluripotent stem cell-derived endothelial cell therapy for peripheral artery disease**

*Chisomaga Ekwueme - Lab of Dr. Ngan Huang*

Peripheral artery disease (PAD) is a serious circulatory condition that affects 8-12 million Americans. The use of human induced pluripotent stem cell-derived endothelial cells (iPSC-ECs) is a promising therapy, however, its efficacy may be diminished in smoker patients because chronic nicotine exposure can impair angiogenesis. This study examines the potential effects of nicotine on the therapeutic potential of iPSC-ECs in PAD. Mice osmotically received nicotine or saline (control). Then, hindlimb ischemia was surgically induced to mimic PAD and iPSC-ECs were injected. All mice were monitored for blood perfusion recovery using laser Doppler imaging and iPSC-ECs survival was tracked by bioluminescence imaging. Post-surgery, all mice were euthanized, and the gastrocnemius muscles were harvested for histological analysis. We then compared angiogenesis processes by assessing capillary and arteriole formation in the surgerized limbs. Understanding how nicotine influences iPSC-ECs through our study will help inform therapies for PAD patients with chronic nicotine exposure.

**Comparison of alpha and beta myosin subpopulations in hypertrophic cardiomyopathy cell lines**

*Jane Thomas - Lab of Dr. Daniel Bernstein*

Hypertrophic cardiomyopathy (HCM) is a disease that affects one in 500 people. HCM causes the heart muscle cells (cardiomyocytes) to enlarge (hypertrophy), which can obstruct blood flow or cause sudden cardiac death. There are over 1000 gene mutations associated with HCM; many in beta-cardiac myosin. Human iPSCs gene-edited with the P710R myosin mutation reflected disease phenotypes including hypertrophy in vitro, but their response to HCM drugs and the influence of population heterogeneity is incompletely understood. I investigated alpha and beta myosin expression in control and mutant cardiomyocytes after treatment with a myosin inhibitor (Mavacamten). Using immunohistochemistry, I quantified cardiomyocyte dimensions and found differences in alpha myosin and beta myosin expression and cell subpopulation elongation. Surprisingly, Mavacamten did not reduce cell area, but further assessment of subpopulations and microenvironment factors could yield new insights. A better understanding of myosin properties will help us understand mechanisms underlying hypertrophy.
Pulmonary Arterial Hypertension (PAH) is a disease characterized by small vessel loss, vascular remodeling, and arterial wall thickening, ultimately leading to right heart failure. The disease involves dysfunction of endothelial and pericyte cells, contributing to the signs of the disease. Endothelial cells lining the lung microvasculature are supported by interactions with pericytes; loss of pericyte coverage leads to vessel instability, a hallmark feature of PAH. Recent studies in pulmonary hypertension and other diseases have identified exosomes as a possible new mechanism of intercellular communication that carry genetic information, namely microRNAs and Long Noncoding RNAs (lncRNAs). With this in mind, we wanted to determine the role of exosomal lncRNA cargo from endothelial cells and pericytes of PAH patients in endothelial-pericyte interaction and lung vascular function.

Exosomes from healthy donor and PAH patient endothelial cells and pericytes were collected and RNAseq analysis was conducted. Based on highest fold change and lowest p-value, the top five lncRNAs for each cell type were selected for annotations and functional information using the bioinformatic databases, Genecards and IncRRIsearch. The association of these lncRNAs with genes or microRNAs involved in signaling pathways relevant to PAH pathology was characterized by STRING network analysis and GO pathway analysis. Out of five lncRNA candidates, one lncRNA from each cell type was selected as they were well-annotated in the databases and determined to possibly be involved in regulating MAPK/ERK cascade signaling pathways or other serine/threonine pathways that have been known to promote vascular remodeling in PAH. Further validation of these lncRNAs will be done by knockout and overexpression studies in human pericytes and microvascular endothelial cells in vitro to assess their contribution in maintaining pericyte-endothelial behavior. Identification of these lncRNAs in exosomes suggest novel mechanisms of endothelial-pericyte interaction and their utility as disease biomarkers as well as potential therapeutic targets in PAH.

The modeling of the thoracic aorta to better understand geometrical changes after thoracic endovascular aortic repair

JooChan Shin – Lab of Dr. Christopher Cheng

The thoracic endovascular aortic repair (TEVAR) has the potential to expand the true lumen region for patients with type B aortic dissection. When patients go through computed tomography angiography before and after TEVAR, the images created are used to...
Ventricular tachycardia (VT) describes an abnormal fast rhythm in the ventricles that disrupts the functions of the heart. One of the treatments for VT is ablation, which is a procedure that scars parts of the heart by burning/freezing to stabilize rhythm. The purpose of this study is to determine if there are differences between VT ablation patients that were referred for a heart transplant evaluation and those that did not. There were 195 patients that underwent VT ablation procedures between 2000 and 2020. These patients were split into two groups: transplant vs non-transplant. We collected information about their medications (beta blockers and AADs), health history, and details of ablation procedures (location of ablation, scar, and type of VT). These variables will be analyzed using independent t-tests, fisher’s exact tests, and chi-square tests of independence. These results will improve protocols and direction for future catheter ablations and patients with VT.
Identifying hemodynamic predictors of cerebral aneurysm growth using computational fluid dynamics

Aaron Panduro – Lab of Dr. Alison Marsden

Cerebral aneurysms are weak or thin areas of an artery wall in the brain that bulge and fill with blood. Aneurysms, whether growing or rupturing, have been the cause of severe health concerns for patients and clinicians. Today, hemodynamic characteristics are believed to be suggestions of the growth or rupture of cerebral aneurysms but current literature are unable to provide known conclusive predictors for clinicians to successfully use. In this study, a safe and efficient in silico methodology was used for patient-specific modeling and hemodynamic simulations of cerebral aneurysms. Results thus far suggest that wall shear stress is higher in growing cerebral aneurysms compared to non-growing cerebral aneurysms. We hope that by the end of the study, there will be new data to suggest hemodynamic predictors to help with faster and preventative treatments to detect the growth of an aneurysm as well as support in vivo procedures.

Computer aided design of trileaflet valves for 3D bioprinting applications

Angel Emodi – Lab of Dr. Mark Skylar-Scott

Single ventricle heart disease is a congenital heart condition in which one of the ventricles in the fetal heart is not properly developed. As a result, one ventricle is forced to do most of the work in the heart, causing oxygenated and deoxygenated blood to mix and hypoperfusion. The Fontan procedure involves grafting the inferior vena cava to the pulmonary artery to increase blood oxygenation. Our lab seeks to incorporate trileaflet valves into an engineered Fontan conduit to promote unidirectional blood flow into the pulmonary circulation. Our current valve design does not provide the optimal strength needed to withstand physiologic blood pressures. We will implement different Computer Aided Design (CAD) modifications in the current valve design in order to explore mechanical strength and create a trileaflet valve that can withstand 10 millimeters of mercury. Furthermore, we will incorporate alterations in our printing process to optimize the 3D printed valve.

Visualization and digital signal analysis of invasive arterial blood pressure data

Savan Patel – Lab of Dr. Anoop Rao

The importance of incorporating invasive arterial blood pressure (IBP) data into patient diagnosis, treatment, and care is unequivocal. However, the post hoc analysis of the patient’s blood pressure over time, as opposed to real-time analysis, requires physicians to take several additional steps to assess.
The present work involves the development of an open-source Python framework for the visualization and digital signal analysis of IBP data. Such analysis includes the estimation of key cardiac parameters such as stroke volume, cardiac output, and heart rate variability. This analysis, consisting of mathematical methods like the Fourier transform, was then applied to a diseased newborn IBP dataset and will be inputted into a machine learning model to identify predictive/diagnostic markers in IBP data. Utilization of this platform would enable physicians to observe patient response to drugs/interventions as well as understand higher-order trends in patient arterial pressure dynamics over the course of their stay.

Optimization of Pott’s Shunt placement in pediatric patients with pulmonary hypertension through patient specific models  
*Celine Escarmant – Lab of Dr. Alison Marsden*  
Pulmonary hypertension is caused by high blood pressure in the arteries of the lungs and could potentially progress in pediatric patients. While drugs and other therapeutic methods are used to treat this disease, the pott’s shunt has been used as a surgical option. This is where a connection between the left pulmonary artery and the descending aorta is formed in order to offset the high pressure pulmonary blood without having to go through damaged lungs. We created a patient specific model to replicate the diseased patient’s pulmonary arteries and aorta using Simvascular. With this, we ran simulations of the cardiac cycle using patient data from catheterization and 4DMRI reports. We found that our model was able to accurately replicate pressure and flow results as shown by patient data. With this, we could use this model and simulations to predict the most optimal placement for the pott’s shunt.

Characterization of collateral coronary arteries in guinea pigs  
*Jamie Bozeman – Lab of Dr. Kristy Red-Horse*  
Coronary artery disease (CAD) is the leading cause of death in the United States, and approximately 805,000 Americans experience a myocardial infarction each year. Unlike humans, guinea pigs, which are from high-altitude environments, have an abundance of collateral coronary arteries (cCA), which connect the main arteries of the heart. Studies show that cCA help guinea pigs to increase O2 delivery and provide protection from myocardial infarction. Since most humans lack cCA, the tissue surrounding an arterial occlusion can quickly undergo necrosis. In this study, we use high-resolution vasculature tracing to quantify the number of cCA in embryonic guinea pig hearts. Furthermore, we will develop 3D models to study the perfusion of blood through cCA. The findings from this study are expected to provide a better understanding of cCA development with the goal of improving preventative and therapeutic strategies for CAD.
In situations when the heart and lungs are severely damaged, Venoarterial (VA) extracorporeal membrane oxygenation (ECMO) can aid in organ recovery by allowing blood to be pumped and oxygenated outside the body. However, following treatment, some patients have suffered from previously unforeseen neurological disorders as a side effect. During ECMO, organs are temporarily hyperoxic – they receive excessive oxygen. In conjunction with Johns Hopkins and the Sung-Min Cho lab, a multicenter retrospective study was launched to analyze the relationship between ECMO-induced hyperoxia neurological outcomes following ECMO treatment. Parallel to the results obtained in the Hopkins study, we expect to find longer durations of hyperoxic states to be associated with an increased probability of a poor neurological outcome. Our goal is to contribute to the development of guidelines for oxygen saturation settings in Venoarterial ECMO to lower the risk of neurological damage for future patients.

Dietary patterns influence gut microbiota composition and dysbiosis, including the loss of gut microbial diversity, has been associated with the pathogenesis of cardiovascular disease and metabolic disorders. A Western diet abundant in fats, proteins, and refined carbohydrates, leads to dysbiosis and higher levels of Bacteroides. In contrast, traditional populations with carbohydrate and fiber-rich diets, like the Hadza, have increased Prevotella species that possess high genetic diversity. To better understand the Prevotella transcriptome, we studied Hadza Bacteroidetes isolates in mice using RNA-seq data. We searched for differentially expressed genes in three strains (Bacteroides thetaiotaomicron 05, Prevotella copri 2477, Prevotella copri 2497). Results show that upregulated genes were involved in carbohydrate metabolism, including polysaccharide utilization loci, which supports the idea that P. copri’s colonization of a host is vulnerable to changes in diet. This provides an insight into the connection between diet and gut microbiota composition at the molecular level.

Transthyretin amyloidosis (ATTR) is a deadly form of heart failure. Transthyretin breaks down, misfolds, and aggregates to form amyloid fibrils that deposit into the organs and tissues. ATTR disproportionately affects older adults and Black
individuals yet remains underdiagnosed particularly among these groups. We sought to better understand these disparities through a retrospective study. We aimed to build a REDCap database from Stanford Amyloid Center clinical data (n=276) and query these data for ethnicity, gender, and insurance status. Designer was used to create a demographic form for each data type. The clinical data were uploaded to REDcap and reports were generated. The data show that the majority of patients had Medicare, were Non-Hispanic, and White. In the future, we seek to analyze more variables and identify correlations. The significance of this study is to provide more insight into barriers to diagnosis in ATTR amyloidosis and potential interventions.

Characterizing the immune signature of cardiovascular remodeling post myocardial infarction

Kevin Tan – Lab of Dr. Patricia Nguyen

Cardiac remodeling is the collection of cellular, molecular, and interstitial disturbances clinically manifested as changes in the geometry and function of the heart after injury. Early in the myocardial infarction (MI) disease process, remodeling can be adaptive, allowing the heart to compensate for damage sustained. But if continued, alterations in ventricular morphology may become exaggerated, resulting in cardiac function deterioration and ensuing heart failure. Whether the heart fully recovers from MI depends on several well-known factors such as the duration of ischemia and door-to-balloon time. However, how the immune system contributes is understudied. This clinical trial involves comparing the blood profile of patients with stable coronary artery disease against those who have recently suffered an MI. Following proteomic and transcriptomic analysis, the immune signature will be correlated with cardiac remodeling measured via imaging. Importantly, a deeper understanding of remodeling post MI may support the development of novel cardiac reparative strategies.

Predicting the reactivity of T cells in coronary atherosclerosis

Stefan Veizades – Lab of Dr. Patricia Nguyen

Atherosclerosis-related diseases are a leading cause of death worldwide. Patients with atherosclerosis are at risk of developing heart attack and stroke, which may result in death. Currently, no treatments directly stabilize plaque. To genotype the CDR3b region of the T cell receptor (TCR), the primary binding site for the MHC-antigen complex, in T cells isolated from coronary atherosclerotic plaque. Plaques sorted into CD8+ T cells and TCRs were sequenced. We compared each clonotype from our data against sequences with known specificities from publicly available databases, restricted for CDR3b regions and HLA alleles. Our analysis showed plaque CD8+ T cells were specific for various Flu, CMV, EBV, and SARS-Cov-2 epitopes, with Flu-M1, CMV-pp65, EBV-BMLF1, and SARS-CoV-2-ORF1ab being the most prevalent. A subset of plaque derived CD8+ T cells show potential to react with viral epitopes, suggesting a potential viral interaction in the pathogenesis of atherosclerosis.
Myocardial infarction (MI), more commonly known as a heart attack, is the leading cause of death worldwide. Treatments using exosomes, or cell secretions that act to communicate among the cells in the body, have been shown to regulate the restoration of heart function after MI. To understand how exosomes improve post-MI heart function, we studied the molecular cargo of exosomes from induced pluripotent and mesenchymal stem cells by gene analysis. To further determine how exosome treatments can become a clinical reality, cardiovascular literature was reviewed. We specifically addressed the potential challenges by clarifying exosome morphology and biology, elucidating the role of exosomes in specific repair processes, and standardizing their therapeutic efficacy. This translational work will identify the main mechanistic pathway(s) to target the exosomes to restore the injured heart.

Exosome treatments show promising potential in improving heart function after myocardial infarction

Eileen Tzng – Lab of Dr. Phil Yang

Hypertrophic cardiomyopathy (HCM) is the most prevalent form of inherited cardiovascular disease and a leading cause of sudden cardiac death. Past research has linked this disease to 1,000+ mutations, roughly a third in β- myosin heavy chain, a primary human ventricular motor protein coded by MYH7 gene. To better understand the implications of MYH7 mutations, such as G256E, we cultured human induced pluripotent stem cells (hiPSCs), differentiated them into cardiomyocytes (CM), introduced the G256E mutation to half using CRISPR-Cas9, and performed single cell transcriptional profiling on, both, mutant and isogenic control cells of day 30. Comparison of G256E and isogenic CM early transcriptional properties revealed mismatched upregulation and downregulation of key markers. Lack of resulting phenotype led to the conclusion the model is not biologically relevant for HCM modeling. Further investigation and exploration of methodology is required to understand the mechanism behind this model.

Hypertrophic cardiomyopathy: Modeling of G256E mutation

Gabriel Heckerman – Lab of Dr. Sean Wu

Dilated cardiomyopathy (DCM) is a cause of debilitating heart disease, and a significant proportion of cases are caused by genetic mutations. Our focus is on the systematic exploration of mechanism-based therapeutic targets. microRNAs (miRNAs) are an ideal tool for target identification, as they inhibit multiple genes

miRNA-Based therapies for PLN mutant dilated cardiomyopathy

Josephine Gollin – Lab of Dr. Mark Mercola
At this time, the clinical burden has become of great concern as patient populations have increased and medical errors remain high. In recent years, medical artificial intelligence (AI) devices developed by predictive algorithms have emerged as tools that can automate clinical tasks effectively. Cardiovascular-focused medical AI devices make up a significant amount of current AI clinical trials as cardiovascular disease is the leading cause of death worldwide. However, recent studies have revealed that AI models can have characteristic biases depending on the degree of diversity included in their training dataset. To evaluate these datasets, a database containing completed cardiovascular-focused AI studies was created and characteristics such as sample size, age, sex, race, and allocation were analyzed. The examination revealed a lack of reporting in all parameters and disproportional distribution of patient demographics. Future implementation of strict reporting guidelines on such dataset demographics shows potential for decreasing biases.

Lack of diversity on datasets used to train cardiovascular focused medical AI devices

Yuri de Castro – Lab of Dr. Joseph Wu

At this time, the clinical burden has become of great concern as patient populations have increased and medical errors remain high. In recent years, medical artificial intelligence (AI) devices developed by predictive algorithms have emerged as tools that can automate clinical tasks effectively. Cardiovascular-focused medical AI devices make up a significant amount of current AI clinical trials as cardiovascular disease is the leading cause of death worldwide. However, recent studies have revealed that AI models can have characteristic biases depending on the degree of diversity included in their training dataset. To evaluate these datasets, a database containing completed cardiovascular-focused AI studies was created and characteristics such as sample size, age, sex, race, and allocation were analyzed. The examination revealed a lack of reporting in all parameters and disproportional distribution of patient demographics. Future implementation of strict reporting guidelines on such dataset demographics shows potential for decreasing biases.
Stanford CVI Undergraduate Program Faculty Mentors

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Vinicio de Jesus Perez, MD  Andrew Fire, PhD  Karen Hirsch, MD  Ngan Huang, PhD
Anson Lee, MD  Alison Marsden, PhD  Mark Mercola, PhD  Patricia Nguyen, MD
Nazish Sayed, MD  Anoop Rao, MBBS  Nazish Sayed, MD  Mark Skylar-Scott, PhD
Kristy Red-Horse, PhD  Michael Snyder, PhD  Katrin Svensson, PhD  Melissa Vogelsong, MD
Sean Wu, MD  Phillip Yang, MD
Stanford CVI Undergraduate Program Mentors
and many more!

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Yuanjia Zhu

Rigor and Reproducibility Project Leads

Danielle Mullis
Carlos Vera, PhD
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**Many Thanks to Our Guest Speakers!**

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