13TH ANNUAL SYMPOSIUM

Cardiovascular Research Institute

APRIL 8, 2026

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ABOUT THE **CVRI**

CVRI MISSION

The Cardiovascular Research Institute was established in 2012 to enhance collaborative opportunities for research, promote the development of new cardiovascular technologies, and to expand training programs in cardiovascular sciences. The CVRI aims to provide administrative and research support to promote synergy for interdisciplinary basic, translational, and clinical research.

SYMPOSIUM & SEMINAR COMMITTEE CHAIR

Lilei Zhang, M.D., Ph.D.
Associate Professor
Molecular and Human Genetics
Baylor College of Medicine

SYMPOSIUM & SEMINAR COMMITTEE

David Durgan, Ph.D.
Mirza Umair Khalid, M.D.
Riyad Kherallah, Ph.D.
William Lagor, Ph.D.
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Na Li, Ph.D.
Xiao Li, Ph.D.
A.J. Marian, M.D.
James Martin, M.D., Ph.D.
Azeez Mulli, Ph.D.
Jack Price, M.D.
Xander Wehrens, MD., Ph.D.
Richelle Ouch
Tyler Robinson

SESSION CHAIRS

Session I: Diwakar Turaga, M.D., Ph.D.
Session II: Xander Wehrens, M.D., Ph.D.
Session III: Lilei Zhang M.D., Ph.D.
Session IV: Jessica Karch, Ph.D.

FROM THE DIRECTOR

Dear Colleagues,

It is with great pleasure that I welcome you to the 13th Annual Symposium of the Cardiovascular Research Institute (CVRI) at Baylor College of Medicine.

The CVRI at Baylor College of Medicine was founded in 2012. One of its core missions is to promote innovative research by facilitating new collaborations across the various BCM departments and affiliated hospitals as well as throughout other institutions in the Texas Medical Center.

This year CVRI is honored to feature two distinguished keynote speakers, Alfred L. George Jr., M.D., and James F. Martin, M.D., Ph.D.

Dr. George serves as the A.N. Richards Professor and Chair of the Department of Pharmacology at the Northwestern University Feinberg School of Medicine. Dr. George has been a pioneer in elucidating the genetics and pathogenesis of channelopathies - disorders caused by mutations in ion channel genes. His work focuses on genetic disorders of membrane excitability, including diseases affecting muscle, heart, and brain that result in abnormal muscle contraction, cardiac arrhythmias, sudden death, epilepsy, and related neurodevelopmental disorders.

Dr. Martin is an internationally recognized physician-scientist who has made fundamental contributions to our understanding of cardiac development, disease, and regeneration. His research focuses on understanding how signaling pathways are connected to adult tissue regeneration to develop treatments for congenital diseases and to regenerate heart muscle and other adult tissues.

On behalf of the organizing committee, I hope you enjoy the symposium and that it provides a great opportunity to meet and network with colleagues and trainees interested in cardiovascular research.

Sincerely,

Xander Wehrens, M.D., Ph.D.
Director, Cardiovascular Research Institute
Baylor College of Medicine

DR. MARK L. ENTMAN AWARD FOR EXCELLENCE IN CARDIOVASCULAR EDUCATION

Mark L. Entman, M.D.
Distinguished Professor
Emeritus of Medicine,
Biochemistry and Pathology
Baylor College of Medicine

The Dr. Mark L. Entman Award for Excellence in Cardiovascular Education was established in 2021 by the Cardiovascular Research Institute (CVRI) at Baylor College of Medicine to recognize faculty members for outstanding teaching and service in the graduate school curriculum.

In honor of Dr. Entman's extensive contributions to cardiovascular education and research at Baylor College of Medicine, the CVRI will present these prestigious awards at the annual symposium.

Dr. Entman was recruited to Baylor as an Assistant Professor in 1970. He was a Howard Hughes Medical Investigator from 1971-1979. In 1977, Dr. Entman became the Chief of the Section of Cardiovascular Sciences and the Director of the Division of Research of the NHLBI National Research and Demonstration Center (now the DeBakey Heart Center) at Baylor College of Medicine and The Methodist Hospital from 1976-1985. Dr. Entman has been an inspirational leader whose research has spanned a range of topics, including the role of myocardial calcium and sarcoplasmic reticulum function, acute inflammation and myocardial injury, and the chronic inflammatory response in cardiac repair and remodeling.

Before joining Baylor faculty, Dr. Entman's training at Duke University involved matriculation in the highly innovative Research Training Program designed to promote the proper background for cellular and molecular research for M.D.'s seeking a career in academic medicine. In 1974, his former mentor at Duke, Dr. Salih Wakil, joined the Baylor faculty as Chairman of Biochemistry and the two collaborated in writing the NIH training grant to establish the M.D./Ph.D. Program at Baylor, of which Dr. Entman was a co-director until 1980. In 1978, Dr. Entman became the Director of the Section of Cardiovascular Sciences in the Department of Medicine and he was paramount in the new development of that program. The core curriculum for the DeBakey Heart Center Graduate Program arose from those efforts and was funded for many years by an NIH training grant which supported an independent graduate program directed by his colleague and close friend, Dr. Julius Allen. The resources of this program also provided the structure of a Basic Science Training program in Pediatric Cardiology at Texas Children's Hospital which was financed by an independent NIH training program.

Dr. Entman has given countless lectures to trainees on the Cardiovascular Sciences Ph.D. Track and has been dedicated to furthering the educational mission at Baylor College of Medicine. Dr. Entman has mentored over 50 physician-scientists and researchers, many of whom are now leading cardiology departments and research programs across the US and world. His enthusiasm and commitment to the educational programs at Baylor College of Medicine is revered among his trainees and peers.

SPEAKERS

Michael Bround, Ph.D.

Assistant Professor
Department of Intergrative Physiology
Baylor College of Medicine

Mark A. Herman, M.D.

E.L. Wagner, M.D., Chair of Internal Medicine
Section Chief of Endocrinology, Diabetes and Metabolism
Associate Professor
Baylor College of Medicine

Gabriel Loor, M.D.

Surgical Director of Lung Transplantation
Baylor St. Luke's Medical Center
Associate Professor
Department of Surgery
Baylor College of Medicine

Bradley McConnell, Ph.D.

Professor of Pharmacology and Assistant Chair
Department of Pharmacological
and Pharmaceutical Sciences
University of Houston

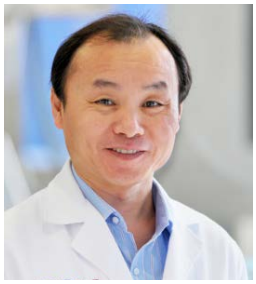
Francesca Polverino, M.D., Ph.D.

Lester and Sue Smith Professor
Department of Medicine
Baylor College of Medicine

SPEAKERS

Christina Tringides, Ph.D.

Assistant Professor
Department of Materials Science and Nanoengineering
Rice University



Huaizhu Wu, M.D.

Professor
Department of Medicine
Baylor College of Medicine

Bing Yu, Ph.D.

Professor
JLH Foundation Distinguished Chair in Transplant Prevention
Co-Director of Human Genetics Center
Department of Epidemiology
School of Public Health, University of Texas Health Science Center at Houston

13TH ANNUAL SYMPOSIUM
Cardiovascular Research Institute

8 – 8:30 a.m.	**REGISTRATION**
8:30 – 8:40 a.m.	**WELCOME & OPENING REMARKS** **Xander Wehrens, M.D., Ph.D.** Professor, Department of Integrative Physiology, Medicine/Cardiology Director, Cardiovascular Research Institute Baylor College of Medicine
8:40 – 10 a.m.	**SESSION I**
	Moderator: Diwakar Turaga, M.D., Ph.D. Assistant Professor, Department of Pediatrics Texas Children's Hospital/Baylor College of Medicine
8:40 – 9 a.m.	**"Precision Modulation of Cardiac Stress Pathways Through AKAP-Directed Signaling."** **Bradley McConnell, Ph.D.** Professor of Pharmacology and Assistant Chair Department of Pharmacological and Pharmaceutical Sciences College of Pharmacy University of Houston
9 – 9:20 a.m.	**"The Role of Pulmonary Endothelium in Lung Transplant Outcomes"** **Gabriel Loor, M.D.** Surgical Director, Baylor St. Luke's Medical Center Lung Transplantation Associate Professor Department of Surgery Baylor College of Medicine
9:20 – 10 a.m.	**KEYNOTE** **"Hippo Signaling in Heart Regeneration"** **James F. Martin, M.D., Ph.D.** Vivian L. Smith Chair of Regenerative Medicine Department of Integrative Physiology Director, Cardiomyocyte Renewal Laboratory, Texas Heart Institute at Baylor College of Medicine
10 – 11 a.m.	**POSTER SESSION I**

11 a.m. – Noon	**SESSION II**
	Moderator: Xander Wehrens, M.D., Ph.D. Professor Department of Integrative Physiology, Medicine/Cardiology Director, Cardiovascular Research Institute Baylor College of Medicine
11 a.m. – Noon	**KEYNOTE** **"Calmodulinopathy: A Genetic Trilogy"** **Alfred L. George, Jr, M.D.** A.N. Richards Professor and Chair of Pharmacology Northwestern University, Feinberg School of Medicine
Noon - 1:20 p.m.	**POSTER SESSION II & LUNCH**
1:20 – 2:20 p.m.	**SESSION III**
	Moderator: Lilei Zhang, M.D., Ph.D. Associate Professor Department of Molecular and Human Genetics Baylor College of Medicine
1:20 – 1:40 p.m.	**"Developing in vitro and in vivo platforms to interface with electrically active systems"** **Christina Tringides, Ph.D** Assistant Professor of Materials Science and Nanoengineering Rice University
1:40 – 2 p.m.	**"Beyond Single Genes: Polygenic Risk and Heart Failure"** **Bing Yu, Ph.D.** Professor JLH Foundation Distinguished Chair in Transplant Prevention Co-Director of Human Genetics Center Department of Epidemiology School of Public Health, University of Texas Health Science Center at Houston
2 – 2:20 p.m.	**"Autoimmunity in Pulmonary Emphysema"** **Francesca Polverino, M.D., Ph.D.** Lester and Sue Smith Professor Department of Medicine Baylor College of Medicine

AGENDA

2:20pm - 3:20pm	**POSTER SESSION III**
3:20 – 4:20 p.m.	**SESSION IV**
	Moderator: Jessica Karch, Ph.D. Assistant Professor Department of Integrative Physiology Baylor College of Medicine
3:20 – 3:40 p.m.	**"What Fructose Metabolism Teaches Us About Cardiometabolic Disease"** **Mark Herman, M.D.** E.L. Wagner, M.D., Chair of Internal Medicine Section Chief of Endocrinology, Diabetes and Metabolism Associate Professor Department of Medicine Baylor College of Medicine
3:40 – 4 p.m.	**"The Role of LETM1 in Cardiac Mitochondrial Ca^{2+} Homeostasis"** **Michael Bround, Ph.D.** Assistant Professor Department of Integrative Physiology Baylor College of Medicine
4 – 4:20 p.m.	**"Inflammation and Atherosclerosis in Hypertriglyceridemia"** **Huaizhu Wu, M.D.** Professor Department of Medicine Baylor College of Medicine
4:20 – 4:40 p.m.	**AWARDS CEREMONY & CLOSING REMARKS** **Lilei Zhang, M.D., Ph.D and Xander Wehrens, M.D., Ph.D.**
4:40pm – 5:15pm	**POSTER VIEWING**

KEYNOTE SPEAKER
ALFRED L. GEORGE, JR., M.D.

A.N. Richards
Professor and Chair,
Department of Pharmacology
Northwestern University
Feinberg School of Medicine

Dr. George is the A.N. Richards Professor and Chair of the Department of Pharmacology at the Northwestern University Feinberg School of Medicine.

Dr. George received his medical education at The University of Rochester (M.D. 1982) followed by residency training at Vanderbilt University and a clinical fellowship at University of Pennsylvania. He developed expertise in the molecular genetics of ion channels initially as a research fellow in Lausanne, Switzerland, then later as a fellow in the Departments of Medicine, Biochemistry & Biophysics and Institute for Neurological Sciences at University of Pennsylvania.

Dr. George joined the faculty of Vanderbilt University in 1992, and was promoted to the rank of full Professor 6 years later. In 1999, he was named the Grant W. Liddle Professor of Medicine and established the Division of Genetic Medicine serving as inaugural Division Chief until 2014. He also founded then led the Physician-Scientist Training Program and Harrison Society for the Department of Medicine. He left Vanderbilt in 2014 to become Chair of the Department of Pharmacology at the Northwestern University Feinberg School of Medicine.

Dr. George was elected to the American Society of Clinical Investigation in 1998 and to the Association of American Physicians in 2001. He served as ASCI Councilor from 2000 to 2003. Dr. George was a recipient of the Lucille P. Markey Scholar Award in Biomedical Sciences, American Heart Association Established Investigator Award, the Javits Neuroscience Investigator Award from the National Institute of Neurological Diseases and Stroke, and he was elected as Fellow of the American Association for the Advancement of Science. He has co-authored 340 peer-reviewed publications and 78 reviews, editorials, book chapters, and books (Google Scholar h-index = 108).

Dr. George has been a pioneer in elucidating the genetics and pathogenesis of channelopathies - disorders caused by mutations in ion channel genes. His work focuses on genetic disorders of membrane excitability including diseases affecting muscle, heart and brain that result in abnormal muscle contraction, cardiac arrhythmias, sudden death, epilepsy and related neurodevelopmental disorders. Dr. George has been involved from the beginning of the channelopathy field making enduring contributions to revealing the molecular genetic basis for several disorders, elucidating the functional consequences of hundreds of mutant ion channels and helping to translate discoveries into new therapeutic strategies for these orphan diseases.

KEYNOTE SPEAKER
JAMES F. MARTIN, M.D., PH.D.

Vivian L. Smith
Chair in Regenerative Medicine
Department of Intergrative Physiology
Director, Cardiomyocyte Renewal Laboratory
Baylor College of Medicine

Dr. Martin is an internationally recognized physician-scientist who has made fundamental contributions to our understanding of development, disease, and regeneration. His research focuses on understanding how signaling pathways are connected to adult tissue regeneration to develop treatments for congenital diseases and to regenerate heart muscle and other adult tissues. Dr. Martin holds the Vivian L. Smith Chair and Fertitta Chair in Regenerative Medicine at Baylor College of Medicine (BCM), where he serves as Vice Chairman of the Department of Integrative Physiology. He also directs the Cardiomyocyte Renewal Laboratory at Texas Heart Institute at BCM. Dr. Martin has authored over 215 peer-reviewed papers in top-tier journals, with an H-index of 96 on Google Scholar. His pioneering studies are highly cited and frequently reported by the lay media.

His landmark studies on the Hippo pathway's role in heart size regulation revealed that Hippo signaling inhibits adult heart muscle regeneration, opening new avenues for treating human heart failure. His group demonstrated that Hippo pathway deficiency reverses established systolic heart failure and that the Hippo downstream effector, Yap, directly interacts with the dystrophin-glycoprotein complex. His team found that Yap increases chromatin accessibility for fetal gene expression, promoting the reprogramming of somatic cells into a primitive, fetal-like proliferative state. His group completed a pivotal study demonstrating that Hippo deficiency improves functional outcomes in a swine heart failure model, advancing these discoveries toward clinical translation. Dr. Martin's lab has transitioned into single-cell genomics and computational biology to interrogate complex biological systems.

Their most recent landmark study investigated human congenital heart disease using single-cell multi-omics approaches, providing unprecedented resolution of disease mechanisms. Dr. Martin is a founder of Medley Therapeutics, which has launched a groundbreaking Phase I/II clinical trial investigating gene therapy for heart regeneration following myocardial infarction. This innovative approach aims to stimulate cardiomyocyte renewal by targeting the Hippo signaling pathway, translating decades of basic science discoveries into potential clinical therapies.

SPEAKER BIOGRAPHIES

Michael Bround, Ph.D.

Assistant Professor
Department of Intergrative Physiology
Baylor College of Medicine

Dr. Michael Bround is currently an Assistant Professor in the Department of Integrative Physiology at Baylor College of Medicine. As a scientist he is interested in how molecular biology controls cell function and effects whole body physiology in health and disease. His research focuses on the mitochondria, an important cellular organelle that is the site of high energy biochemistry in cells. Mitochondria are responsible for generating the majority of cellular ATP, the energy currency of the cell, as well as producing the reducing potential and molecular building blocks that underpin biosynthesis. His goal is to understand the molecular biology of mitochondrial signaling to maximize energy metabolism and mitochondrial quality control, while preventing pathogenic cell death processes. The hope is this research will lead to new treatments strategies for diseases such as cardiac ischemia reperfusion injury, muscular dystrophy, and Alzheimer's disease.

Mark A. Herman, M.D.

E.L. Wagner, M.D., Chair of Internal Medicine
Section Chief of Endocrinology, Diabetes and Metabolism
Associate Professor
Department of Medicine
Baylor College of Medicine

Dr. Mark A. Herman is the E.L. Wagner, M.D., Chair in Internal Medicine and Chief of the Section of Endocrinology, Diabetes, and Metabolism in the Department of Medicine at Baylor College of Medicine. He also serves as the Director of the NIH-funded Houston Nutrition and Obesity Research Center. Dr. Herman has made important contributions in the field of metabolic diseases, including his discovery of a new isoform of Carbohydrate Responsive-Element Binding Protein, a novel class of endogenous lipids with anti-diabetic and anti-inflammatory properties, and mechanisms by which sugar metabolism contributes to metabolic diseases. He was elected as a member of the American Society of Clinical Investigation in 2021. Dr. Herman is committed to education, having taught medical students, and supervised internal medicine residents, endocrine fellows, and research trainees. He has received multiple awards for excellence in teaching. In addition to his administrative and research roles, Dr. Herman remains committed to his clinical practice in endocrinology, diabetes, and lipid management.

SPEAKER BIOGRAPHIES

Gabriel Loor, M.D.

Surgical Director of Lung Transplantation
Baylor St. Luke's Medical Center
Associate Professor
Department of Surgery
Baylor College of Medicine

Dr. Gabriel Loor is a tenured Professor in the Michael E. DeBakey Department of Surgery and Surgical Director of the Baylor St. Luke's Medical Center (BSLMC) Lung Transplantation. He is credited with the first "breathing lung transplantation" in the Midwest performed in 2014 and in Texas in 2018. Dr. Loor was the first surgeon in the US to utilize portable ex vivo lung perfusion (EVLP) for a donation after cardiac death (DCD) lung transplantation in 2015. This set a new paradigm for the conduct of DCD lung and heart transplants. In his eight-year tenure at Baylor, he has grown our lung transplant program to a total annual case volume of over 100 cases over the past year – the highest ever for Baylor or BSLMC and currently the largest volume lung transplant program in Texas.

Bradley McConnell, Ph.D.

Professor of Pharmacology and Assistant Chair
Department of Pharmacological and Pharmaceutical Sciences
College of Pharmacy
University of Houston

Dr. Bradley McConnell is a Professor of Pharmacology and Assistant Chair of Pharmacological and Pharmaceutical Sciences in the College of Pharmacy at the University of Houston. His research focuses on translational cardiac biology to improve heart function and enable myocardial repair through a collaborative, team-based approach. Dr. McConnell's group studies cardiac signaling and physiology in health and disease, with current projects examining AKAP signalosomes and biased β-adrenergic receptor signaling, as well as developing reprogrammed cardiac conduction cells for cardiac repair. Building on these insights, they are engineering aptamer-conjugated lipid nanoparticles for targeted RNA delivery to enhance contractility and promote myocardial repair after infarction. Dr. McConnell is an elected Fellow of the American Heart Association and the American Physiological Society (Cardiovascular Section), and his research is supported by the NIH/NHLBI, VA, and AHA. Dr. McConell has mentored over 50 undergraduates, 12 primary graduate students, and numerous trainees at other levels, many of whom have progressed to advanced training and academic or clinical careers.

SPEAKER BIOGRAPHIES

Francesca Polverino, M.D., Ph.D.

Lester and Sue Smith Professor
Department of Medicine
Baylor College of Medicine

Francesca Polverino, M.D., Ph.D., is an endowed Lester and Sue Smith Full Professor of Medicine with tenure at Baylor College of Medicine, where she leads the COPD Translational Research Program. A physician–scientist, her clinical and research interests center on the pathogenesis and developmental origins of chronic airway diseases, with a focus on the genetic, genomic, and developmental determinants of individual susceptibility to cigarette smoke.

After completing medical school and residency in Italy, she joined Harvard Medical School in 2010, where she earned her Ph.D. and later joined the faculty in 2015. Over the course of her career, she has received numerous prestigious honors, including the COPD Gold Medal from the European Respiratory Society, the Medal of Honor for Scientific Merit from the President of the Italian Republic, and the Parker B Francis Award from the American Thoracic Society.

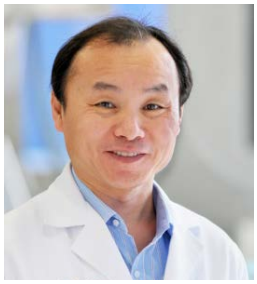
Dr. Polverino has published over 140 peer-reviewed papers and serves as Principal Investigator on several NIH and foundation-funded projects. She is also a national medical spokesperson for the American Lung Association, where she advocates for awareness, prevention, and treatment of chronic lung diseases.

Christina Tringides, Ph.D.

Assistant Professor
Department of Materials Science and Nanoengineering
Rice University

Christina M. Tringides is a tenure-track assistant professor in Materials Science and NanoEngineering, and a core member of the Neuroengineering Initiative (NEI) at Rice, and joined July 2024. She earned her B.S. degrees in physics and in materials science and engineering from the Massachusetts Institute of Technology (MIT) in 2015, and spent one year as a Fulbright Scholar and Swiss Government Excellence Scholar at the Ecole Polytechnique Federale de Lausanne before starting her Ph.D. in 2016. Her Ph.D. work was done in the laboratory of Professor David Mooney (Harvard, School of Engineering and Applied Sciences), and her degree came from Harvard Biophysics and the Medical Engineering Medical Physics program between Harvard and MIT in May 2022. Afterwards, Christina moved to ETH Zürich, where she was an ETH Postdoctoral Fellow, with Professor Janos Vörös (D-ITET, Institute of Biomedical Engineering). Her research focuses on developing new materials and neurotechnologies to interface with the nervous system, from the cell to organ levels, and for both in vivo and in vitro applications.

SPEAKER BIOGRAPHIES



Huaizhu Wu, M.D.

Professor
Department of Medicine
Baylor College of Medicine

Huaizhu Wu received his M.D. degree from Weifang Medical College, China, and Master of Science from Peking Union Medical College. Then, he received postdoctoral training in Dr. Ballantyne's lab at Baylor College of Medicine and was promoted to a faculty member and is now professor of Medicine at Section of Cardiovascular Research, Department of Medicine, at BCM. His research has been focused on the role of immune cells and inflammation in atherosclerosis and obesity. Working with Dr. Ballantyne, they were the first group to report "foamy monocytes" in the circulation of mice and people with hyperlipidemia and their contributions to atherosclerosis and also one of the first groups to report T cells in adipose tissue and skeletal muscle and effects of T cells on adipocyte and myocyte metabolism in obesity.

Bing Yu, Ph.D.

Professor
JLH Foundation Distinguished Chair in Transplant Prevention
Co-Director of Human Genetics Center
Department of Epidemiology
School of Public Health, University of Texas Health Science Center at Houston

Dr. Bing Yu is a tenured Professor in the Department of Epidemiology at The University of Texas Health Science Center at Houston (UTHealth Houston) School of Public Health. She holds the JLH Foundation Distinguished Chair in Transplant Prevention and serves as Co-Director of the Human Genetics Center. Dr. Yu is an epidemiologist with expertise in medicine, biostatistics, and genetics. Her research focuses on identifying novel molecular biomarkers and elucidating the biological pathways underlying cardiopulmonary diseases. She has established a molecular epidemiology program that integrates genomics, proteomics, and metabolomics, and has received numerous awards from the American Heart Association (AHA) and the National Institutes of Health (NIH) to support her work. Dr. Yu's contributions to epidemiology and public health are multifaceted. She has served as a convener for working groups in large consortia, including the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium, the Trans-Omics for Precision Medicine (TOPMed) Program, and the Consortium of Metabolomics Studies (COMETS). In addition, she has served as a member of NIH and AHA study sections and as a member of an Observational Study Monitoring Board (OSMB) for an NIH-funded cohort. Dr. Yu is deeply committed to advancing cardiovascular research, improving public health, and training the next generation of epidemiologists.

POSTER SESSION SCHEDULE

SESSION I — 10 – 11 a.m.

1	Adult cardiac deletion of MYC- associated factor X (MAX) leads to cardiac hypertrophy and dysfunction
2	Cardioprotective Roles of Mas and MrgD Axis Activation by Angiotensin-(1–7) and Alamandine in Cardiac Remodeling
3	Insulin Induces Cardiac Chrono via a Posttranscriptional Regulatory Mechanism
4	The Epigenetic Regulator Histone Demethylase KDM5A is Activated and Pathogenic in a Mouse Model of Heart Failure
5	Treatment with β Nicotinamide Mononucleotide Replenishes the Depleted NAD+ Levels but Fails to Rescue the Phenotype in Mouse Models of Heart Failure
6	Early Renal Denervation Improves Structural and Functional Remodeling after Acute Myocardial Infarction
7	p90RSK–KCNK6 Signaling Drives Radiation-Induced Genomic Instability and Endothelial Senescence
8	LETM1 deficiency in heart is lethal due to reduced mitochondrial Ca^{2+} efflux
9	Targeting ALDH2: Colchicine Directly Activates ALDH2 to Protect Against Radiation-Induced Senescence and Atherosclerosis
10	Loss of Bcl-Rambo Protects the Heart from Ischemic-Reperfusion Injury by Limiting Mitochondrial ROS
11	Cysteine and Glycine-Rich Protein 3 (CSRP3) Inhibits adult Cardiomyocyte Cell Cycle Entry Through Regulating YAP
12	Notch inhibition with IMR-1 improves cardiac regenerative potential
13	YAP Creates a Distinct Metabolic State to Regenerate the Heart
14	Hippo Pathway Deficiency Drives Post-Injury Cardiac Lymphatic remodeling to Support Heart Failure Recovery
15	Ubiquitin-conjugating enzyme E2C gene (Ube2c) is a novel post-translational modification driver that regulates cardiomyocyte cell cycle through regulation of RhoA activity
16	METABOLIC IMBALANCE IN TANGO2 DEFICIENCY-INDUCED ARRHYTHMOGENESIS
17	Recapitulation of tissue-scale ventricular tachyarrhythmic mechanisms in human engineered heart tissues
18	ELECTROCARDIOGRAPHIC CHANGES AND ATRIAL FIBRILLATION IN A MURINE MODEL OF FOLIC-ACID INDUCED ACUTE KIDNEY INJURY
19	Cis-regulatory Enhancer Variation Modulating QT Interval
20	MGP Limits Stress-Induced Atrial Structural Remodeling in Atrial Fibrillation
21	Chronic dietary stress drives early cardiac dysfunction and progressive MASH through systemic inflammation and fibrosis
22	A Novel JPH2 E169K Knock-in Mouse Model of Cardiac Hypertrophy and Atrial Fibrillation
23	Decoding Chamber-Specific Cardiac Microenvironments and Macrophage Heterogeneity
24	Integrated profiling of hepatic and cardiac remodeling during metabolic disease
25	Polycystin-1 deficiency increases the β-Adrenergic Signaling response in cardiomyocytes through impaired PP2A activity

POSTER SESSION SCHEDULE

SESSION II — Noon – 1:20 p.m.

26	BDH1–OCT4 Signaling Orchestrates Metabolic Rewiring to Suppress Endothelial Senescence in Hutchinson–Gilford Progeria Syndrome
27	Macrophage PARP1 Orchestrates DNADamage and Inflammatory Protein Signaling in PD1 Blockade–Induced Cardiovascular Injury
28	PKCζ-TERF2IP S205 Phosphorylation Promotes LATS1/2 Degradation and Endothelial Pro-inflammatory Senescence Phenotype in Disturbed Flow–Induced Atherosclerosis
29	CD38 NADase Suppresses Sulfite Oxidase (SUOX) and Activates Reverse Complex V to Promote Metabolic Remodeling in Endothelial Cells (ECs) Under Disturbed Flow
30	Immune checkpoint inhibition augments smooth muscle cell phenotypic modulation and promotes atherosclerosis
31	Lipid Nanoparticle-based In Vivo Delivery of Sting siRNA Mitigates Aortic Dissection
32	Investigating Cellular Mechanisms of Fibrotic Remodeling in Functional Mitral Regurgitation
33	Biomechanics of Functional Mitral Regurgitation: Using the RUFLS Bioreactor to Model Mitral Valve Hemodynamics
34	PRKG1 R177Q Mutation Disrupts Mechanotransduction and Mitochondrial Function in Aortic Smooth Muscle Cells
35	Burst Wave Laser Lithotripsy of Calcified Heart Valves
36	Overactivation of ATP-sensitive K channel and Kv7.1 dysfunction contribute to lethal cardiac arrhythmias in TANGO2 deficiency disorder
37	Bilateral Renal Ischemia Reperfusion Injury (IRI) promotes Atrial Fibrillation in mice
38	Prediction of Candidate Causal Cis-Regulatory Variants Underlying 35 QT Interval Variation GWAS Loci
39	LOX-1 ACTIVATION MEDIATES ATRIAL FIBRILLATION DEVELOPMENT IN CHRONIC KIDNEY DISEASE
40	Inflammasome activation contributes to sinus node dysfunction
41	A membrane bioreactor for the mechanically biomimetic culture of heart slices
42	TYK2 AS A NOVEL GENETIC DETERMINANT OF HYPERTROPHIC CARDIOMYOPATHY
43	Plasma MicroRNA Signature for the Prediction of Early Stroke in Patients with Left Ventricular Assist Devices
44	The Impact of HeartLogic on Heart Failure Events and Guideline-Directed Medical Therapy in the Veterans Affairs Health System: A Pre-Post Analysis
45	A Qualitative Study of Health Priorities Among Hospitalized Patients Admitted for Heart Failure
46	Mitral Repair Durability is Preserved in Heritable Thoracic Aortic Disease Patients After Concomitant Mitral and Proximal Aortic Surgery
47	Multi-Biobank Gene-Based Rare Variant Burden Analysis Identifies Novel High-Risk Genes for Thoracic Aortic Disease
48	Severe Ocular Manifestations in Neonatal Marfan Syndrome: Case Series and Literature Review
49	A Bicuspid Aortic Valve Hydrogel Model of Various Age and Disease Related States.
50	Identification and characterization of cardiac enhancers of NOTCH1 identified from a CHD patient cohort

POSTER SESSION SCHEDULE

SESSION III — 2:20 – 3:20 p.m.

51	Targeting Integrin Signaling in Atherosclerotic Cardiovascular Disease (ASCVD)
52	Targeting CTLA-4 with Small Molecules to Modulate T-Cell Responses in Cardiovascular Injury
53	THE ROLE OF A DOMAIN OF VON WILLEBRAND FACTOR IN INFLAMMATION DURING RHEUMATOID ARTHRITIS
54	Developing Disease-Targeted Anti-Angiogenic Therapy Against Thrombospondin-4 via Ligandomics.
55	Vascular Smooth Muscle Cells-Specific Adenosine Kinase Deficiency Attenuates Vascular Calcification Through Histone Methylation–Dependent Epigenetic Reprogramming
56	A circadian lncRNA Circa gates MI recovery by modulating hnRNPA1–RPA–R-loop dynamics
57	Mitral annular disjunction is associated with markers of cardiomyopathy in pediatric Marfan syndrome.
58	Midwall Late Gadolinium Enhancement Predicts Adverse Outcomes in Pediatric Myocarditis
59	Calciprotein Particles Induce Endothelial Mitochondrial Dysfunction and AVF Maturation Failure in CKD
60	Adipocyte NPC1 regulates cholesterol homeostasis and systemic glucose metabolism
61	Notch2 regulates nuclear dynamics in cardiomyocytes promoting a hypertrophic cardiomyocyte state
62	Combinatorial Gene Therapy Completely Recovers the Cardiac Functions After Myocardial Infarction
63	YAP Activation in Cardiomyocytes Orchestrates a Regenerative Niche by Limiting Fibrosis and Expanding the Lymphatic Vasculature
64	Optogenetic mapping of embryonic cardiac pacemaker cells
65	Frequency and Diagnostic Yield of Genetic Testing in Patients with Ebstein Anomaly
66	Neutrophil-derived miR-223 attenuates cardiac injury by suppressing endothelial RhoB
67	c-Rel–Mediated Lipid Accumulation and Inflammatory Activation in Monocytes in Hypertriglyceridemia
68	Glycocalyx Mimetic Hydration Layers Prevent Thrombosis in Small-Diameter Vascular Grafts Without Anticoagulation
69	Hypoxia-inducible Factor-2a Stabilization in Regulatory T Cells Promotes Cardioprotection after Myocardial Ischemia and Reperfusion Injury
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Poster 1

ADULT CARDIAC DELETION OF MYC- ASSOCIATED FACTOR X (MAX) LEADS TO CARDIAC HYPERTROPHY AND DYSFUNCTION

Amin Al-Awar[1], Amin Al-Awar[1], Yuanbiao Zhao[1], Andrea Wilderman[1], Lilei Zhang[1]

[1]Molecular and Human Genetics, Baylor College of Medicine, Houston, TX

Background:
MYC-associated factor X (MAX) is a protein in the basic helix-loop-helix leucine zipper (BHLHLZ) family. MAX acts as a transcriptional activator when binding to other BHLHLZ proteins, in particular, oncoprotein MYC. Its role in cancer is well established. However, whether it is involved in cardiovascular disease has not been studied yet.
Materials/Methods:
Cardiomyocyte-specific deletion of Max was induced by 5 days of tamoxifen injection (25mg/kg) of MAXflox/flox Cre-expressing mice (MAXfl/fl, Cre^{+}). Cardiomyocytes were isolated by Langendorf, and MAX deletion was confirmed by western blot. To study changes in cardiac phenotype, echo analysis was performed at baseline and different time points after tamoxifen injection on control (MAXfl/fl, Cre-) and MAX-cKO (MAXfl/fl, Cre^{+}) mice, followed by up to 18 weeks.
Results:
MAX-cKO mice exhibited reduction in ejection fraction overtime compared to controls. Left ventricular mass and diastolic wall thickness were significantly increased at 10 and 18 weeks in MAX-cKO mice compared to controls. We also found an increase in cardiomyocyte cell size and fibrosis and 18 weeks in MAX-cKO mice compared to controls. No difference in inflammatory response, cell death and cell proliferation was seen in both groups.
Conclusions:
Obtained results indicate that MAX deletion in the heart plays a role in development of cardiac hypertrophy. Mechanisms underlying its effect are under investigation. Also, we further plan to study the gene's deleterious effect in a disease condition, using a transverse aortic constriction (TAC) surgical model.

Poster 2

CARDIOPROTECTIVE ROLES OF MAS AND MRGD AXIS ACTIVATION BY ANGIOTENSIN-(1–7) AND ALAMANDINE IN CARDIAC REMODELING

Tabish K. Ali[1], Dinakar Iyer[1], Cleva Villanueva-Lopez[1], Bradley McConnell[1]

[1]PPS, University of Houston, Houston, TX

Background:
Pathological cardiac hypertrophy is a leading cause of heart failure and remodeling. Angiotensin II (Ang-II), a key effector of the renin–angiotensin system (RAS), promotes hypertrophic remodeling and fibrosis by activating maladaptive transcriptional and metabolic programs in cardiomyocytes. In contrast, the non-canonical RAS peptides Angiotensin-(1–7) and Alamandine exert cardioprotective effects through activation of the Mas and MrgD receptors, respectively. However, the molecular mechanisms underlying their protective actions remain incompletely understood.

Materials/Methods:
In vitro experiments were performed using AC16 cells and human induced pluripotent stem cell-derived cardiomyocyte. Pathological hypertrophy was induced by Ang-II stimulation, after which cells were treated with Alamandine, Angiotensin-(1–7), or their combinations with Ang-II. These cellular models enabled evaluation of molecular pathways for hypertrophic and fibrotic remodeling, including changes in gene expression and downstream signaling mechanisms regulated by Mas and MrgD activation. To validate these findings in vivo, cardiac hypertrophy was induced in mice through Ang-II infusion for 14 days using ALZET 1002 osmotic pumps. Mice were subsequently treated with Alamandine or Angiotensin-(1–7) to assess their therapeutic and preventive potential. Cardiac structure and function were assessed using Echocardiography, while histological and molecular analyses were performed to quantify hypertrophy and fibrosis.

Results:
Our results show that treatment with Alamandine or Angiotensin-(1–7) prevented Ang-II–induced hypertrophy and fibrosis, demonstrating the protective role of Mas and MrgD axis activation.

Conclusions:
This study aims to define the distinct and overlapping roles of Mas and MrgD receptor signaling in regulating cardiac remodeling and downstream effector pathways. Elucidating these mechanisms may identify novel therapeutic targets within the protective arm of the RAS for the prevention and treatment of heart failure.

Poster 3

INSULIN INDUCES CARDIAC CHRONO VIA A POSTTRANSCRIPTIONAL REGULATORY MECHANISM

Ekenedilichukwu C Anekwe[1], Connor Madalo[2], Mason Wheeler[3], Jamie Renick[3], Roslyn Fawbush[3], Jessica Karch[1]

[1]Integrative Physiology, Baylor College of Medicine; [2]Carilion School of Medicine, Virginia Tech; [3]Fralin Biomedical Research Institute, Virginia Tech

Background:
Circadian rhythms are endogenous, ~24-hour cycles that enable tissues to anticipate daily environmental changes. Exogenous cues, such as light and feeding, synchronize these cycles, aligning internal biological processes with environmental conditions. Importantly, while light-dependent circadian entrainment is well-studied, feeding-dependent entrainment remains poorly defined. In response to feeding, insulin is the main entrainment stimulus. Our goal is to elucidate the molecular mechanisms of insulin-mediated circadian entrainment in the heart.

Materials/Methods:
Our data demonstrate that cardiac 'ChIP-derived repressor of network oscillator' (Chrono), a repressor of core circadian transcription factor heterodimer, Clock/Bmal[1], is increased with insulin. We also performed RNA polymerase (Pol) II ChIP-Seq and RNA-Seq in the hearts of mice following insulin stimulation versus vehicle control. We observe that insulin does not alter Pol II density across the Chrono gene, however we observe increases in its mRNA levels.

Results:
Together, these data suggest a post-transcriptional regulatory mechanism for Chrono. Furthermore, analysis of the human and murine Chrono 3' UTRs (78% homology) reveal 9 and 18 predicted binding sites for 'human antigen R' (HuR), an RNA binding protein that stabilizes mRNAs. Importantly, HuR is stabilized with insulin treatment, and its deletion causes insulin resistance (IR) in other tissues

Conclusions:
Based on these observations, we hypothesize that insulin induces Chrono expression via a post-transcriptional mechanism and that this may be HuR-dependent. Such a study is critical to understanding the mechanisms of feeding-dependent entrainment of cardiac circadian rhythms and has implications for their disruption in IR and type II diabetes.

Poster 4

THE EPIGENETIC REGULATOR HISTONE DEMETHYLASE KDM5A IS ACTIVATED AND PATHOGENIC IN A MOUSE MODEL OF HEART FAILURE

Manisha Deogharia[1], Chitra Lekha Reddy Reddy[1], Ritapa Chaudhuri[1], Manogna Chirasani[1], Abhinav K Jain[2], Leila Rouhi[1], Ali J Marian[1], Priyatansh Gurha[1]

[1]Center for Cardiovascular Genetics, UT Health Science Center, Houston, TX; [2]Epigenetics and Molecular Carcinogenesis, Center for Cancer Epigenetics, The University of Texas MD Anderson Cancer Center

Background:
The KDM5 family of histone demethylases regulates chromatin state by removing trimethyl groups from histone H3 lysine 4 (H3K4me3). We previously showed that KDM5 proteins regulate maturation of iPSC-derived cardiomyocytes (CMs) by controlling genes involved in oxidative phosphorylation (OXPHOS) and fatty acid oxidation (FAO). Although KDM5 levels decline during CM maturation, KDM5A is aberrantly upregulated in human and murine heart failure, including Lamin A/C dilated cardiomyopathy (LMNA-DCM). The objective of this study is to determine the role of KDM5A in LMNA-DCM.

Materials/Methods:
We used a CM-specific Lmna knockout mouse model (Myh6-Cre:LmnaF/F), which develops DCM with contractile dysfunction, increased apoptosis, and shortened lifespan. To determine the functional role of KDM5A, we generated double-knockout mice (Myh6-Cre:LmnaF/F:Kdm5aF/F). CMs from wild-type, Lmna knockout, and double-knockout mice were analyzed by RNA sequencing to assess transcriptional changes. Genome wide H3K4me3 profiling was performed using CUT&RUN to evaluate KDM5A dependent chromatin remodeling.

Results:
KDM5A protein levels were elevated in LMNA-deficient cardiomyocytes. The deletion of the Kdm5a gene improved cardiac function, prolonged survival, attenuated fibrosis, and reduced cell death in LMNA-DCM mice. Kdm5a deletion restored the expression of over 1,400 dysregulated genes, including those involved in FAO, myogenesis, and OXPHOS in the Myh6-Cre:LmnaF/F:Kdm5aF/F mice. CUT&RUN analysis revealed that loss of Kdm5a partially restored H3K4me3 enrichment at loci encoding cardiac transcription factors and metabolic regulators, including Tbx5 and Esrrg, accompanied by rescue of their downstream targets.

Conclusions:
Kdm5a deletion in LMNA-DCM restores gene programs required for mitochondrial metabolism and sarcomere function, partly through remodeling of H3K4me3 chromatin states, attenuating cardiac dysfunction and improving survival in LMNA-DCM.

Poster 5

TREATMENT WITH B NICOTINAMIDE MONONUCLEOTIDE REPLENISHES THE DEPLETED NAD+ LEVELS BUT FAILS TO RESCUE THE PHENOTYPE IN MOUSE MODELS OF HEART FAILURE

Weiyue Wang[1], Priyatansh Gurha[1], Junji Chen[1], Leila Rouhi[1], Nickan Poshtkoohi[1], Quoc Nguyen[2], Ali Marian[1]

[1]Center for Cardiovascular Genetics, UT Health Science Center, Houston, TX; [2]Medicine, Baylor College of Medicine, Houston, TX

Background:
Nicotinamide adenine dinucleotide (NAD^+) is a multifunctional coenzyme involved in cellular energy homeostasis, genomic stability, and epigenetic regulation of gene expression. NAD^+ levels decline with aging and in pathological conditions such as heart failure, prompting interest in therapeutic strategies to raise cellular NAD^+ levels. Several studies have reported beneficial effects of NAD^+ supplementation on intermediary phenotypes in heart failure; however, these findings are limited by small sample sizes, lack of blinding, and incomplete knowledge of the expression of key enzymes involved in NAD^+ biosynthesis.

Materials/Methods:
Two established mouse models of heart failure, Myh6-McmTam:DspF/F and Myh6-McmTam:LmnaF/F, were studied. Total NAD, NADH, and NAD^+ levels were measured spectrophotometrically. β-nicotinamide mononucleotide (βNMN) was administered intraperitoneally at four doses daily for 1–4 weeks to assess cardiac phenotypes and for 180 days to evaluate survival. Survival was analyzed using K-M plots; cardiac function by echocardiography; cardiac rhythm by electrocardiography; gene expression by RNA-seq; protein expression and PARylation by immunoblotting; cell death by TUNEL assay and immunoblotting; and myocardial fibrosis by collagen volume fraction.

Results:
Cardiac NAD^+ levels were depleted in both mouse models and restored in a dose-dependent manner by βNMN administration, accompanied by recovery of suppressed protein PARylation. However, βNMN did not improve survival, cardiac conduction abnormalities, arrhythmias, cardiac function, gene expression, cell death pathways, including parthanatos, or myocardial fibrosis. Preliminary data show that restoring the NAD^+ levels activated the DNA damage pathways, negating its potential beneficial effects.

Conclusions:
βNMN restored depleted NAD^+ levels and protein PARylation in two mouse models of heart failure but did not improve major cardiac outcomes. Administration of NAD^+ may not be beneficial in heart failure.

Poster 6

EARLY RENAL DENERVATION IMPROVES STRUCTURAL AND FUNCTIONAL REMODELING AFTER ACUTE MYOCARDIAL INFARCTION

Haoran Guo[1], Suiyong Du[1], Wenfeng Hu[1], Dongze Zhang[1]

[1]Anesthesiology, Critical Care & Pain Medicine, UT Health Science Center, TX

Background:
Acute myocardial infarction (AMI) leads to adverse left ventricular remodeling characterized by myocardial fibrosis and infarct expansion, which further contributes to progressive cardiac dysfunction. Although renal denervation (RDN) has emerged as an effective therapeutic strategy in cardiovascular diseases, it remains unclear whether RDN immediately after AMI has protective effects on cardiac remodeling and functional recovery.

Materials/Methods:
AMI was induced by permanent surgical ligation of the left anterior descending coronary artery in rats. RDN was performed immediately after AMI by surgically cutting all the visible renal sympathetic nerves around the renal vessels. Angiotensin II (Ang II,1.44mg/kg/day) was infused into sham rats and continued for 14 days. Cardiac function was evaluated by transthoracic echocardiography at 14 days post-AMI.

Results:
Data from Masson staining revealed decreased collagen deposition in RDN-treated AMI rats compared with AMI rats. TTC staining showed that early RDN reduced the infarct size of the AMI heart. Western blot analysis showed that early RDN not only reduced alpha-smooth muscle actin (α-SMA) levels but also decreased transforming growth factor-β1 (TGF-β1) expression in the border zone of the AMI heart, indicating attenuation of myofibroblast activation and inhibition of fibrosis-related signaling pathways. Ang II infusion in sham rats also increased protein expression of α-SMA and TGF-β1 in the LV, accompanied by mild cardiac fibrosis. Importantly, early RDN improved AMI-reduced cardiac performance and cardiac contractility.

Conclusions:
Early renal denervation reduces myocardial fibrosis by suppressing Ang II-promoted fibrotic signaling, thereby further limiting infarct expansion and improving AMI-induced cardiac dysfunction. These findings suggest that early RDN could be a potential strategy to mitigate adverse cardiac remodeling and promote functional recovery after AMI.

Poster 7

P90RSK–KCNK6 SIGNALING DRIVES RADIATION-INDUCED GENOMIC INSTABILITY AND ENDOTHELIAL SENESCENCE

Kun Yuan Chu[1], Venkatasubrahman Kumar Samanthapudi[1], Jun-ichi Abe[1], Sivareddy Kotla[1]

[1]Cardiology/Division of Internal Medicine, MD Anderson Cancer Center

Background:
Ionizing radiation (IR) promotes long-term cardiovascular disease by inducing endothelial genomic instability, telomere dysfunction, and senescence. Although p90RSK is activated by radiation-induced stress signaling, its role in sustaining chromosomal damage and vascular injury after exposure remains incompletely defined. Radiation-activated p90RSK promotes persistent genomic instability and endothelial senescence through induction of the potassium channel KCNK6, and post-exposure p90RSK inhibition restores genomic integrity and vascular function.

Materials/Methods:
Endothelial cells exposed to ionizing radiation were treated with selective p90RSK inhibitors (FMK-MEA, BI-D1870) after irradiation. Genomic instability was assessed by comet assay, dicentric chromosome analysis, micronuclei quantification, telomere CO-FISH, and TIF imaging. RNA-seq identified p90RSK-dependent genes. Therapeutic efficacy was tested in a radiation-accelerated atherosclerosis mouse model.

Results:
Radiation induced acute DNA double-strand breaks followed by persistent chromosomal instability, including dicentrics, micronuclei, and telomere sister chromatid exchanges, accompanied by mitochondrial ROS and endothelial senescence. Post-irradiation p90RSK inhibition markedly reduced both early DNA damage and chronic cytogenetic abnormalities and suppressed senescence phenotypes. Transcriptomics identified KCNK6/TWIK-2 as the dominant p90RSK-dependent gene induced by radiation. KCNK6 depletion prevented telomere damage and senescence, whereas p90RSK overexpression enhanced these effects. In vivo, delayed p90RSK inhibitor therapy attenuated radiation-accelerated atherosclerosis, demonstrating therapeutic benefit after exposure.

Conclusions:
Radiation-activated p90RSK drives endothelial genomic instability and senescence through a KCNK6-dependent pathway. Pharmacologic p90RSK inhibition restores chromosomal stability and limits vascular injury even when administered after radiation, identifying a potential clinically relevant strategy.

Poster 8

LETM1 DEFICIENCY IN HEART IS LETHAL DUE TO REDUCED MITOCHONDRIAL CA^{2+} EFFLUX

Ta'Aliyah Jones[1], Michael Bround[1]

[1]Integrative Physiology, Baylor College of Medicine, Houston, TX

Background:
During ischemia-reperfusion (I/R) injury, excessive mitochondrial calcium (mCa^{2+}) uptake causes sustained activation of the mitochondrial permeability transition pore (mPTP) which triggers necrotic cell death of cardiomyocytes. I/R injury accounts for up to 50% of the total infarct size in myocardial infarction and increases the risk for chronic heart-failure in patients. To mitigate I/R injury, we aim to characterize mechanisms of mCa^{2+} transport that might be leveraged to reduce mCa^{2+} overload. In this study we test the hypothesis that LETM1 mediates mitochondrial $H+/Ca^{2+}$exchange and is required for cardiac mCa^{2+} efflux.

Materials/Methods:
We demonstrate that cardiac-specific deletion of Letm1 in the heart is perinatal lethal, while Letm1 deletion in adult hearts induces heart failure, cardiomyocyte necrosis, and premature death in mice.

Results:
Letm1-KO cardiac mitochondria were shown to exhibit elevated mCa^{2+} content and reduced oxidative phosphorylation indicating impairments in mitochondrial function. Likewise, Letm1-KO cardiac mitochondria were found to display an increase in swelling and reduced calcium retention capacity, however, Ppif (CypD) deletion partially rescued lethality in Letm1-KO hearts, validating that the loss of LETM1 increased mPTP activation in cardiomyocytes. Furthermore, Letm1-KO cardiac mitochondria demonstrated a decrease in Na^{+}-independent mCa^{2+}efflux compared to control mitochondria, consistent with a role in $H+/Ca^{2+}$ exchange. Over-expression of Mcub, the inhibitory subunit of the MCU-complex, was sufficient to reduce cardiac dysfunction and extend the lifespan of cardiacLetm1-KO mice whereas Mcu over-expression enhanced cardiac dysfunction and accelerated lethality in these mice, confirming that perturbations in mCa^{2+} handling drives dysfunction in Letm1-KO hearts.

Conclusions:
Collectively, this work establishes the essential role of LETM1 in mediating mCa^{2+} efflux in the heart and suggests LETM1 is a primary mediator of mCa^{2+} homeostasis.

Poster 9

TARGETING ALDH2: COLCHICINE DIRECTLY ACTIVATES ALDH2 TO PROTECT AGAINST RADIATION-INDUCED SENESCENCE AND ATHEROSCLEROSIS

Venkatasubrahman Kumar Samanthapudi[1], Kun Yuan Chu[1], Sivareddy Kotla[1], Jun-ichi Abe[1]

[1]Cardiology/Division of Internal Medicine, MD Anderson Cancer Center, Houston, TX

Background:
Ionizing radiation (IR) accelerates atherosclerosis by inducing oxidative stress, macrophage senescence, and loss of clonal hematopoiesis (CH) regulators, but mechanisms linking radiation injury to vascular inflammation remain unclear. Although colchicine reduces cardiovascular events in atherosclerosis, its molecular targets in radiation-associated cardiovascular disease are unknown. We hypothesized that colchicine protects against radiation-induced vascular injury by activating aldehyde dehydrogenase 2 (ALDH2), restoring mitochondrial redox balance, and limiting macrophage senescence.

Materials/Methods:
Bone marrow–derived macrophages were pretreated with low-dose colchicine and exposed to 2 Gy IR. RNA sequencing and Western blotting assessed molecular changes. Oxidative stress, senescence, and CH driver expression were measured using transcriptomic and biochemical analyses. ALDH2 dependence was tested using pharmacologic modulation, siRNA knockdown, molecular docking, and recombinant enzyme assays. In vivo effects were examined using a partial carotid ligation model with spatial proteomic analysis.

Results:
Radiation suppressed ALDH2 and CH drivers TET2 and DNMT3A while increasing mitochondrial ROS, lipid peroxidation, and macrophage senescence. Colchicine restored ALDH2 activity, reduced 4-HNE accumulation, preserved CH driver expression, and reversed senescence-associated transcriptional programs. ALDH2 inhibition abolished these effects. Docking and enzymatic assays showed direct activation of ALDH2 by colchicine. In vivo, IR increased macrophage p16 and p21 levels correlating with Ki67, suggesting senescence-associated stemness. Colchicine reduced senescence and proliferation and attenuated radiation-accelerated plaque growth. Human macrophages after radiotherapy showed similar ALDH2 loss and oxidative stress.

Conclusions:
Colchicine activates ALDH2 to interrupt radiation-induced oxidative stress and macrophage senescence, limiting atherosclerosis progression, identifying ALDH2 as a potential target.

Poster 10

LOSS OF BCL-RAMBO PROTECTS THE HEART FROM ISCHEMIC-REPERFUSION INJURY BY LIMITING MITOCHONDRIAL ROS

Marque R Villareal[1], Jason Karch[1]

[1]Integrative Physiology, Baylor College of Medicine, Houston, TX

Background:
Myocardial infarction (MI) is a leading cause of mortality and results in cardiomyocytes (CMs) death. A major contributor to CM death during MI is ischemia-reperfusion injury (I/R) injury, causing mitochondrial dysfunction, excessive reactive oxygen species (ROS), and necrotic cell death. Identifying regulators that of these processes during I/R injury is integral. The Bcl-2 family are established regulators of both apoptotic and necrotic cell death.

Materials/Methods:
To determine the Bcl-2 family members expressed in the heart, we performed quantitative mass spectrometry on mouse heart mitochondria. We found Bcl-Rambo to be the highest expressed member by 10-fold higher than all others. Bcl-Rambo has been implicated in apoptosis and mitophagy, but its role in the heart is undefined. To investigate its function, we generated Bcl-Rambo knockout (KO) mice. Bcl-Rambo KO CMs and mouse embryonic fibroblasts (MEFs) displayed hyperfused mitochondria, and mitophagy/autophagy regulators were down regulated.

Results:
These MEFs were resistant to oxidative stress and ferroptosis. Bcl-Rambo KO mice subjected to I/R injury had significantly reduced infarct size compared to controls. To determine the mechanism of protection, we subjected cardiac mitochondria to swelling assays and found that Bcl-Rambo KO mitochondria are resistant to iron-induced swelling but not calcium-induced swelling. Suggesting Bcl-Rambo is a driver of ferroptosis, not mitochondrial permeability transition pore-dependent necrosis. Consistent with this, crossing Bcl-Rambo KO on to the Ppif null background, Ppif encodes the mPTP regulator cyclophilin D (CypD), resulted in additive protection against I/R injury. However, treatment with the mitochondrial antioxidant MitoQ did not further reduce infarct size in Bcl-Rambo KO, indicating that Bcl-Rambo drives injury through a mitochondrial ROS-dependent mechanism.

Conclusions:
Together, these findings identify Bcl-Rambo as a regulator of mitochondrial dynamics and oxidative damage during I/R injury.

Poster 11

CYSTEINE AND GLYCINE-RICH PROTEIN 3 (CSRP3) INHIBITS ADULT CARDIOMYOCYTE CELL CYCLE ENTRY THROUGH REGULATING YAP

Kamal Abou Farraj[1], Abou Bakr M. Salama[1], Joern Huelsmann[1], Pretty Rose Matthew[1], Rebecca Liu[1], Sara Taha[1], Todd K. Rosengart[1], Tamer MA Mohamed[1], Riham Abouleisa[1]

[1]Surgery, Baylor College of Medicine, Houston, TX

Background:
Adult cardiomyocytes (CMs) have limited proliferative capacity after injury, unlike neonatal CMs, which can regenerate, eventually leading to heart failure after myocardial injury. We previously showed that overexpression of four cell cycle regulators, Cdk1, Cdk4, Ccnb, and Ccnd (collectively 4F), induces adult CM proliferation accompanied by sarcomere disassembly. Here, we aimed to identify the sarcomeric protein regulating this process during CM mitosis.
Materials/Methods:
Temporal and ubiquitin-linked proteomic analyses were performed on 60-day-old human iPSC-derived CMs transduced with control or 4F adenovirus at 24 h, 48 h, and 72 h. Cysteine- and glycine-rich protein 3 (Csrp3), a Z-disk–associated protein interacting with T-Cap and α-actinin, was the most downregulated sarcomeric protein at 24–48 h, returning to baseline at 72 h. Ubiquitination at lysines K119 and K113 increased at 24 h, indicating active degradation of Csrp3 during mitosis. Csrp3 KO mice was used to confirm the role of Csrp3 in CM cell cycle
Results:
Csrp3 knockdown (KD) in neonatal mouse CMs (NMCMs) enhanced 4F induced PHH3-positive (G2/M phase) and mononucleated CMs without affecting EdU incorporation, suggesting increased G2/M transition. In vivo, Csrp3 knockout (Csrp3KO) mice at postnatal day 21 (P21) exhibited sarcomere disorganization, elevated heart weight-to-body weight ratio, and more PHH3- and Aurora B positive CM nuclei. Transcriptomic and RT-PCR analyses confirmed upregulation of cell cycle genes. Similarly, Csrp3 KD in human heart slices increased PHH3-positive nuclei and cell cycle gene expression.
Mechanistically, Adult Csrp3 KO showed a significant activation of YAP which led to its translocation to the nucleolus and activation of cell cycle machinery
Conclusions:
Csrp3 is a key regulator of sarcomere disassembly during CM proliferation. Its degradation facilitates mitotic entry and CM cell cycle reactivation through modulation of YAP pathways.

Poster 12

NOTCH INHIBITION WITH IMR-1 IMPROVES CARDIAC REGENERATIVE POTENTIAL

Nathan Giang[1], Wyatt Paltzer[1], Elizabeth Straight[2], Yuka Morikawa[2], James Martin[1],

[1]Integrative Physiology, Baylor College of Medicine; [2]Cardiomyocyte Renewal Laboratory, Texas Heart Institute

Background:
Adult cardiomyocytes possess limited regenerative ability, especially after an ischemic injury such as myocardial infarction (MI). Recent studies have uncovered that promoting cardiomyocyte proliferation is an effective method to regenerate damage myocardial tissue after ischemic injury. We have preliminary data demonstrating that Notch signaling inhibits cardiomyocyte proliferation, instead promoting cardiomyocyte nucleation and ploidy increase. Thus, we hypothesized that Notch inhibition may promote cardiomyocyte proliferation and regeneration after cardiac injury.

Materials/Methods:
In our study, we examined whether the next generation Notch inhibitor IMR-1 could promote cardiomyocyte cell cycling and regeneration.

Results:
Adult mice that were treated with IMR-1 for 7 days showed increases in cell cycle proteins CCNA and CCND, along with Yap1, a known driver of cardiomyocyte proliferation. Furthermore, IMR-1 treatment led to functional recovery and reduced scar size after adult MI, demonstrating that Notch inhibition is an effective method to promote cardiac regeneration.

Conclusions:
Future experiments will examine what cell types are most responsive to the IMR-1 treatment and whether those cells could be targeted with more specific treatments to promote improved recovery after cardiac injury.

Poster 13

YAP CREATES A DISTINCT METABOLIC STATE TO REGENERATE THE HEART

Lin Liu[1], Jeffrey Steimle[2], Chang-Ru Tsai[2], Xiao Li[1], James Martin[2]

[1]Texas Heart Institute, Baylor College of Medicine, Houston, TX; [2]Integrative Physiology, Baylor College of Medicine

Background:
Cardiomyocytes (CMs) are highly specialized somatic cells with minimal self-renewal capacity. Cardiac regenerative ability diminishes as CMs undergo metabolic maturation. During which, mitochondrial metabolism transitions toward OXPHOS and fatty acid oxidation (FAO) to meet increasing ATP demands, which inadvertently limits regenerative potential. Notably, mitochondria also sustain reductive biosynthetic pathways alongside oxidative metabolism.

Materials/Methods:
To elucidate YAP's role in CM metabolic reprogramming, we employed an integrative multi-omics approach that included single-nucleus RNA sequencing (snRNA-seq), CM-specific mitochondrial proteomics, and metabolomic profiling in mice. Lipidomic analysis was performed alongside [^{13}C]-glucose and [^{13}C]-palmitate tracing to examine the shift between fatty acid breakdown and phospholipid biosynthesis. We further conducted DNA footprinting, ATAC-seq, and bulk RNA-seq to uncover transcription factors disrupted by YAP and their roles in modulating cardiac metabolic programs.

Results:
Our results reveal that YAP reprograms mitochondrial metabolism, promoting a neonatal-like metabolic state in mature CMs that favors regeneration. YAP suppresses FAO while enhancing fatty acid anabolism and phospholipid synthesis, thereby facilitating CM proliferation. YAP was found to inhibit retinoid X receptor (RXR) signaling, an effect reversed by γ-linolenic acid (GLA). RXR also functioned with MEF2A, whose activity was suppressed following YAP activation. Targeting MEF2A helps restore regenerative potential.

Conclusions:
Our findings identify YAP as a central regulator of CM metabolic remodeling, orchestrating the balance between fatty acid catabolism and phospholipid biosynthesis. Through coordinated interactions with RXR and MEF2A, YAP drives a metabolic shift that reverts mature CMs toward a more regenerative, neonatal-like phenotype. This work provides a mechanistic framework for understanding how metabolic plasticity underlies cardiac regeneration.

Poster 14

HIPPO PATHWAY DEFICIENCY DRIVES POST-INJURY CARDIAC LYMPHATIC REMODELING TO SUPPORT HEART FAILURE RECOVERY

Renhao Lu[1], Chang-Ru Tsai[1], Yuka Morikawa[2], James Martin[1,]

[1]Integrative Physiology, Baylor College of Medicine, Houston, TX; [2]Texas Heart Institute, Baylor College of Medicine

Background:
Heart failure has a high prevalence and significant clinical burden, partially due to our limited understanding of how cardiac tissues adapt to a chronically inflamed and fluid-overloaded microenvironment. Cardiomyocyte-specific deletion of Sav1, a scaffold protein within the Hippo pathway, improves cardiac recovery in the chronic post-MI stage, providing a promising therapeutic approach for heart failure patients. Recently, we found that cardiac regeneration in Sav1 CKO mice is highly correlated with cardiac lymphatic density, yet the role of the cardiac lymphatic system in the ischemic heart failure context is unknown.
Materials/Methods:
Hence, we aim to investigate how Sav1 deficiency influences lymphatic function and cardiomyocyte-lymphatic endothelial cell (CM-LEC) crosstalk to support cardiac repair with in vivo mouse model and in vitro organ-on-chip platform.
Results:
To investigate this topic in a human-relevant system, we developed a cardiac lymphatic-on-a-chip platform that integrates iPSC-derived human cardiomyocytes with engineered lymphatic vessels. In this system, the human LECs and iPS-CMs exhibit high viability and robust spontaneous beating. Notably, Sav1 knockdown led to significant LEC channel dilation on the chip. This dilation suggests improved lymphatic drainage capacity and highlights active LEC-CM communication. Alongside our in vitro models, we performed bulk RNA sequencing on mediastinal lymph nodes from mice with and without MI. This in vivo analysis demonstrated distinct immune cell trafficking profiles between the two groups, indicating an active role for the lymphatic system in the post-infarction immune response.
Conclusions:
Our data indicate that Sav1 modulation affects cardiomyocyte gene expression and induces lymphatic vessel dilation, which may collectively enhance drainage and alter immune cell trafficking to support post-MI recovery.

Poster 15

UBIQUITIN-CONJUGATING ENZYME E2C GENE (UBE2C) IS A NOVEL POST-TRANSLATIONAL MODIFICATION DRIVER THAT REGULATES CARDIOMYOCYTE CELL CYCLE THROUGH REGULATION OF RHOA ACTIVITY

Rebecca Liu[1], Kamal Faraj[1], Abou Bakr Salama[1], Sara Taha[1], Tamer Mohamed[1], Riham Abouleisa[1]

[1]Surgery/Division of Cardiothoracic Surgery, Baylor College of Medicine, Houston, TX

Background:
Adult cardiomyocytes (CMs) exhibit minimal proliferative capacity, severely limiting cardiac regeneration following ischemic injury. In contrast, fetal and neonatal CMs display robust cell-cycle activity but permanently exit the cell cycle within 5–7 days after birth. This transition is tightly coupled to post-translational modifications (PTMs), including ubiquitination, which regulate protein expression to meet the demands of CM maturation. Identifying PTM regulators that control neonatal CM cell cycle exit may uncover therapeutic targets to promote adult CM regeneration.
Materials/Methods:
Through screening a PTM-focused small molecule library in naturally proliferative postnatal day 1 neonatal mouse CMs (P1 NMCMs), we identified the ubiquitin-conjugating enzyme (Ube2c) as a key regulator of CM cell cycle exit.
Results:
Ube2c knockdown (KD) in P1 NMCMs promoted premature cell cycle exit, whereas Ube2c overexpression under the CM-specific TNNT2 promoter reactivated the cell cycle in adult human heart slices and in mice. Proteomic analysis of Ube2c KD P1 NMCMs revealed altered expression of postnatal maturation-associated proteins, including sarcomeric, lipid metabolism, developmental, and cell cycle regulators. Notably, Ube2c KD increased expression of the Rho GTPase activators ARHGEF10L and FARP2, accompanied by enhanced RhoA GTPase activity. Pharmacological inhibition of RhoA reversed the Ube2c KD phenotype, demonstrating that Ube2c acts upstream of RhoA signaling to regulate the cell cycle in CM. Consistently, Ube2c KD increased activation of the RhoA downstream effector serum response factor (SRF), a central transcriptional regulator of CM maturation.
Conclusions:
Ube2c functions as a critical PTM mediator that modulates Rho GTPase signaling through ARHGEF10L and FARP2, enhancing RhoA–SRF dependent transcriptional programs that initiate and reinforce cell cycle exit to activate CM maturation. Overexpression of Ube2c is a promising approach to induce CM regeneration post-myocardial infarction (MI).

Poster 16

METABOLIC IMBALANCE IN TANGO2 DEFICIENCY-INDUCED ARRHYTHMOGENESIS

Adeniyi G Adeleye[1], Haydee Montemayor[1], William Whitfield[1], Lilei Zhang[2], Christina Miyake[3], Na Li[1]

[1]Medicine/Cardiovascular Research, Baylor College of Medicine, Houston, TX; [2]Molecular and Human Genetics, Baylor College of Medicine; [3]Pediatrics, Baylor College of Medicine

Background:
TANGO2 deficiency disease (TDD) causes metabolic crises and cardiac arrhythmias, but its arrhythmogenic mechanism remains unclear. Clinical data suggest vitamins B5 and B9 may reduce cardiac crises through their roles in lipid metabolism and bioenergetics. We sought to test the hypothesis that the loss of TANGO2 triggers ventricular arrhythmias by disrupting mitochondrial function and lipid homeostasis in cardiomyocytes.
Materials/Methods:
Cardiac phenotype was assessed in Tango2-/- knockout (KO) mice using programmed electrical stimulation, optical mapping, calcium imaging, and telemetry after a vitamin B-deficient diet (VBD). To evaluate the impact of TANGO2 levels on cellular and molecular stress, we assessed cell stress (pERK), autophagic (LC3a and LC3b), and lipid droplet (PLIN5) markers in TANGO2 deficiency models. Cellular ultrastructure and mitochondrial function were determined via transmission electron microscopy (TEM) and Seahorse assay.
Results:
Compared with WT littermates, KO mice developed prolonged QTc intervals and were more prone to pacing-induced ventricular tachycardia (VT) after VBD ($p<0.05$). Supplementation of B5 or B9 in drinking water during VBD challenges reduced VT inducibility in KO mice. Telemetry ECG recordings revealed increased heart rate variability during a 10-hour fasting period in KO mice compared with WT controls, which were restored with B9-supplemented water. TEM revealed increased lipid droplets in the cardiac tissue of KO mice compared with WT mice. Western blot analysis revealed elevated levels of pERK, LC3a, and PLIN5, indicative of metabolic distress. In line with this, Seahorse showed defects in mitochondrial function in TANGO2-deficient AC16 cells.
Conclusions:
Our findings suggest that TANGO2 is involved in lipid homeostasis and mitochondrial/metabolic stress responses. TDD causes arrhythmias via mitochondrial dysfunction, and it is partly rescued by B5/B9. Future work will test how impaired lipid turnover disrupts ion-channel trafficking and drives arrhythmias.

Poster 17

RECAPITULATION OF TISSUE-SCALE VENTRICULAR TACHYARRHYTHMIC MECHANISMS IN HUMAN ENGINEERED HEART TISSUES

Matthew W Fiedler[1], Alejandra Vasquez Limeta[1], Leah Carter[1], Ernesto Reyes Sanchez[1], Francisco Altamirano[1]

[1]Cardiovascular Sciences, Houston Methodist Research Institute

Background:
Human iPSC-derived engineered heart tissues (EHT) are increasingly being used to model cardiac electrophysiology and pharmacologic sensitivity. However, the tachyarrhythmia susceptibility of these models remains unclear. Detailed electrophysiological characterization has been limited by the lack of compatible optical mapping frameworks.

Materials/Methods:
To address this gap, we developed a reproducible high-resolution (22μm spatial, <1ms temporal) workflow for simultaneous voltage/Ca^{2+} mapping with open-source EHTs. We modeled ventricular tachycardia (VT) with an established acquired long-QT model of hERG blockade (E-4031) with extracellular low K+/$Mg^{2+,}$ electrolyte imbalances common in clinical practice.

Results:
Baseline recordings showed physiologic rate-dependent restitution action potential duration (APD) and Ca2+ transient duration (CaD) curves, AP-Ca^{2+} activation latency, and sensitivity to pharmacological hERG inhibition. Beat-resolved optical mapping revealed progressive diastolic interval shortening, APD dispersion and long-short APD zones, forming spatial conduction barriers and wavebreak/reentry exclusively under VT-condition. Early afterdepolarizations generated triggered activity at long-short APD zones, creating localized repolarization barriers facilitating reentry and rotor formation. Phase-singularity tracking identified short-lived rotors predominately in EHT head-neck regions. A minority of VT-condition EHTs exhibited brief periods of multiple simultaneous rotors and wavelets arising from chaotic activation patterns before renormalizing.

Conclusions:
While VT-condition spontaneous tissue acceleration was common and precipitated rotor formation, the brief nature of rotor events likely reflects spatial limitations (e.g., critical mass hypothesis).
We demonstrate that iPSC-derived EHTs under basal conditions exhibit adult-like human ventricular electrophysiology, susceptibility to selective hERG inhibition, and inducibility of tissue-scale VT mechanisms under an acquired long-QT syndrome.

Poster 18

ELECTROCARDIOGRAPHIC CHANGES AND ATRIAL FIBRILLATION IN A MURINE MODEL OF FOLIC-ACID INDUCED ACUTE KIDNEY INJURY

Daniel F Hutchison[1], Alberto Navarro-Garcia[1], Alexandra Osborne[1], Xander Wehrens[1]

[1]Cardiovascular Research Institute, Baylor College of Medicine, Houston, TX

Background:
Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia. Chronic kidney disease (CKD) is a well-established risk factor for AF; however, the impact of acute kidney injury (AKI) on AF susceptibility is less understood. Like CKD, AKI disrupts electrolyte balance and increases circulating uremic toxins, which may impair cardiac electrical conduction. Drug-induced nephrotoxicity is a recognized cause of AKI, and folic acid–induced AKI (FA-AKI) is one widely used experimental model for studying kidney injury in mice.

Materials/Methods:
Mice received a single intraperitoneal injection of folic acid (250 mg/kg) to induce AKI or vehicle (0.3 M $NaHCO_3$) as control. Baseline electrocardiograms (ECGs) were obtained prior to injection. Pacing electrical stimulation (PES) studies were performed at either 30, 36, or 48 hours to assess conduction changes and AF inducibility. Serum kidney function markers, creatinine and phosphorus, were assessed, and heart and kidney tissues were harvested for subsequent analysis.

Results:
FA-AKI mice at 30, 36, and 48 hours showed a 3-fold increase in circulating phosphate (23.6±1.4 mg/dL, 29.0±3.0 mg/dL, and 22.9±6.6 mg/dL versus 7.8±0.4 mg/dL in controls, $P<0.01$) and serum creatinine (5.1±0.4 mg/dL, 6.4±1.4 mg/dL, and 4.7±1.4 mg/dL versus 1.5±0.1 mg/dL in controls, $P<0.05$). The 36- and 48-hour FA-AKI mice demonstrated increased P-wave duration (19.6±2.9 ms and 22.8±2.8 ms versus 11.9±0.3 ms in controls, $P<0.05$ and $P<0.01$) and prolonged QT (57.7±3.5 ms and 69.2±6.7 ms versus 41.1±0.8 ms in controls, $P<0.05$ and $P<0.001$). QRS duration was significantly prolonged in all AKI groups (30, 36, and 48 hours, 32.6±3.0 ms, $P<0.05$; 33.9±4.3 ms, $P<0.05$; and 46.8±8.6 ms, $P<0.001$). FA-AKI mice showed increased AF inducibility (75% of 48-hr FA-AKI versus 10% of controls, $P<0.01$).

Conclusions:
Folate-induced AKI promotes cardiac electrical instability and increases susceptibility to AF in mice. Future studies are needed to elucidate the possible pathways responsible for AF onset in AKI.

Poster 19

CIS-REGULATORY ENHANCER VARIATION MODULATING QT INTERVAL

Cassandra Ratliff[1], Kyla Vickery[1], Ashish Kapoor[1]

[1]IMM - Human Genetics, UT Health Science Center, Houston, TX

Background:
Electrocardiographic QT interval (QTi), the time taken by cardiac ventricles to de- and repolarize in every heartbeat, is a clinically relevant heritable complex trait associated with an increased risk of arrhythmias. Genome-wide association studies (GWAS) of QTi variation have identified significant associations with common noncoding variants at loci encompassing the three major long QT syndrome genes, SCN5A, KCNQ1 and KCNH2, as well as NOS1AP, all of which are known to regulate QTi, thereby highlighting their role in trait variation in the general population. However, the causal variants underlying these GWAS loci remain largely unknown.

Materials/Methods:
Following a cis-regulatory hypothesis for GWAS signals in the noncoding genome, we performed enhancer-based screens for all QTi-associated variants at these four major loci.

Results:
We have previously reported on the identification of five and six enhancer variants at the SCN5A and NOS1AP QTi GWAS loci, respectively. Here we report that of the 104 KCNQ1 and 57 KCNH2 variants evaluated using variant-centered test elements in luciferase reporter-based enhancer assays in mouse cardiomyocyte HL-1 cells, we identified 16 and 10 enhancer variants, respectively. Using the GTEx database, we found four of the KCNQ1 and six of the KCNH2 enhancer variants are correlated with gene expression in human cardiac tissues. Validation reporter assays with variant-centered small deletion constructs (±5 bases) demonstrated that the identified variants and their flanking sequences are critical, and likely act as transcription factor (TF) binding sites. In silico TF binding predictions identified 40 and 34 unique candidate TFs with predicted allelic binding at 14 KCNQ1 and 6 KCNH2 enhancer variants, respectively.

Conclusions:
We have identified a total of 37 enhancer variants at SCN5A, KCNQ1, KCNH2 and NOS1AP QTi GWAS loci that likely underlie the observed genetic associations via regulating expression of these critical genes.

Poster 20

MGP LIMITS STRESS-INDUCED ATRIAL STRUCTURAL REMODELING IN ATRIAL FIBRILLATION

Shuai Zhao[1], Jose Alberto Navarro-Garcia[1], Satadru Lahiri[1], Mohit Hulsurkar[1], Elda Munivez[1], Alexandra Osborne[1], Siena Bush[1], Sarah Woodfield[2], Svetlana Reilly[3], Xander Wehrens[1]

[1]Integrative Physiology, Baylor College of Medicine, Houston, TX; [2]Pediatrics, Baylor College of Medicine; [3]Cardiovascular Medicine, University of Oxford

Background:
Therapies targeting atrial fibrosis in atrial fibrillation (AF) are lacking due to incomplete understanding of anti-fibrotic mechanisms. We previously showed cardiomyocyte-derived calcitonin (CT) reduces atrial fibrosis and AF susceptibility, yet key downstream effectors remain elusive. Proteomics and transcriptional analysis identified Matrix Gla Protein (MGP) as a CT-responsive target in atrial cardiac fibroblast (ACF). The objective of this study is to determine how CT regulates MGP expression and whether MGP independently alters fibroblast activation and AF-related remodeling.

Materials/Methods:
MGP expression was analyzed in human atrial single-cell RNA sequencing datasets and CREM-Tg atria (a spontaneous AF model). CT-induced MGP regulation was examined by qPCR and immunoblotting. PKA–PBX1 signaling was assessed using pharmacologic inhibition, immunostaining, and CUT&RUN-qPCR. The role of MGP in fibrotic activation was tested by lentiviral knockdown or overexpression in ACFs and 3T3 fibroblasts. Atrial remodeling and AF phenotypes were assessed in fibroblast-specific Mgp-knockout mice following Angiotensin (Ang) II infusion.

Results:
MGP was enriched in ACFs and reduced in human AF. In CREM-Tg atria, MGP levels declined with AF progression and inversely correlated with fibrotic markers. CT upregulated MGP via PKA-dependent PBX1 nuclear translocation and promoter binding. MGP suppressed fibroblast migration, proliferation, and TGFβ-induced fibrotic activation. In vivo, MGP loss did not affect baseline cardiac structure or AF inducibility but exacerbated Ang II-induced remodeling, with greater atrial enlargement, enhanced atrial fibrosis, and worsened diastolic dysfunction. AF duration was prolonged in cKO mice under Ang II stress.

Conclusions:
CT–PKA–PBX1 signaling regulates MGP expression to restrain fibroblast activation. Fibroblast-specific MGP loss exacerbates Ang II-induced atrial remodeling and enhances arrhythmogenic substrate, suggesting MGP modulation as a therapeutic strategy in AF.

Poster 21

Chronic dietary stress drives early cardiac dysfunction and progressive MASH through systemic inflammation and fibrosis

Saima Shakil[1], Hua Mao[2], Xinchun Pi[2], Liang Xie[2]

[1]Medicine, Baylor College of Medicine, Houston, TX; [2]Medicine, Cardiovascular Research Institute, Baylor College of Medicine

Background:
Animal models of cardiac dysfunction leading to heart failure (HF) are important tools in preclinical research and drug discovery. Cardiovascular disease and metabolic dysfunction associated steatohepatitis (MASH) are closely associated metabolic disorders that frequently coexist in individuals with obesity and metabolic syndrome. However, the mechanisms linking diet-induced metabolic stress to concurrent liver and cardiac dysfunction remain incompletely understood.

Materials/Methods:
Animals were divided into normal chow and high-fat, high-fructose, high-cholesterol diet groups (40% fat, 22% fructose, 2% cholesterol) and monitored for six months. Cardiac function was assessed by echocardiography, while serum cholesterol, triglycerides, and liver function tests (LFTs) were measured using commercial kits. Histopathological analysis of heart and liver tissue was performed using standard staining methods.

Results:
Early manifestations were observed at 2 months, characterized by cardiac dysfunction with reduced ejection fraction (EF) and hepatic steatosis, accompanied by elevated total cholesterol (TC) levels. By 4 months, disease progression was evident with increased cardiac inflammation, further reduction in EF, and impaired diastolic function as indicated by increased E/A and E/E′ ratios. These changes were paralleled by worsening hepatic pathology, including elevated TC and LFTs. At 6 months, mice developed pronounced fibrotic remodeling in both the heart and liver, with persistent reduction in EF, increased TC, and elevated LFTs. Histopathological analyses confirmed significant fibrosis and inflammatory infiltration in cardiac and hepatic tissues, consistent with advanced disease progression.

Conclusions:
Our findings demonstrate for the first time that chronic dietary stress induced by a high-fat, high-fructose, high-cholesterol diet leads to early cardiac dysfunction accompanied by progressive MASH, driven by systemic inflammation and fibrotic remodeling in both the heart and liver.

Poster 22

A NOVEL JPH2 E169K KNOCK-IN MOUSE MODEL OF CARDIAC HYPERTROPHY AND ATRIAL FIBRILLATION

Alfonso J Godínez Aguilar[1], Mara Turkieltaub Paredes[1], Satadru Lahiri[1], Alberto Navarro-Garcia[1], Xander Wehrens[1]

[1]Integrative Physiology, Baylor College of Medicine, Houston, TX

Background:
Junctophilin-2 (JPH2) stabilizes sarcoplasmic reticulum Ca^{2+} channel RyR2 and sarcolemmal interactions for cardiac excitation–contraction coupling. Disruptions promote Ca^{2+} release and arrhythmias. We identified the JPH2 mutation E169K in hypertrophic cardiomyopathy (HCM) and early-onset atrial fibrillation (AF) patients. A pseudo-knock-in mouse model showed impaired JPH2–RyR2 binding and increased Ca^{2+} release events leading to AF, but true knock-in effects remain unclear.
Materials/Methods:
JPH2 E169K knock-in mice were generated via CRISPR. Cardiac structure and function were assessed using echocardiography with Doppler to evaluate diastolic function. Programmed electrical stimulation (PES) was performed to assess AF incidence.
Results:
E169K knock-in mice developed cardiac hypertrophy with increased wall thickness from 3 months, progressing to systolic dysfunction. Mutant mice showed atrial enlargement and diastolic impairment (elevated mitral valve early-to-atrial flow ratio (MV E/A) at 12 months. Surface ECG recordings showed no significant differences between groups. However, PES at 12 months showed a trend toward increased AF inducibility and duration in mutant mice. Histology confirmed an increase in cardiomyocyte size by WGA staining. No significant increase in cardiac fibrosis was observed in mutant hearts. JPH2 protein expression was comparable between mutant and WT hearts, suggesting the phenotype results from functional impairment of mutant JPH2 rather than altered expression.
Conclusions:
These findings show that the JPH2 E169K mutation promotes cardiac remodeling and dysfunction. Ongoing studies will establish this knock-in model as a novel preclinical platform to study how disrupted JPH2-mediated calcium handling contributes to cardiomyopathy and atrial arrhythmogenesis.

Poster 23

DECODING CHAMBER-SPECIFIC CARDIAC MICROENVIRONMENTS AND MACROPHAGE HETEROGENEITY

Xin Wang[1], Chang-Ru Tsai[2], Yi Zhao[3], Fansen Meng[3], Yue Yuan[5], Jeffrey Steimle[3], Na Li[4], Jun Wang[5], James Martin[1], Xiao Li[2]

[1]Texas Heart Institute, Baylor College of Medicine, Houston, TX; [2]The Texas Heart Institute; Molecular and Human Genetics, Baylor College of Medicine; [3]Integrative Physiology, Baylor College of Medicine; [4]Medicine, Section of Cardiovascular Research; Cardiovascular Research Institute, Baylor College of Medicine; [5]Pediatrics, McGovern Medical School, The University of Texas Health Science Center at Houston

Background:
Left and right atria (LA and RA) experience distinct hemodynamic and biochemical environments, yet how these differences shape chamber-specific cardiac microenvironments remains unclear.

Materials/Methods:
Here, we combined integrative single-nucleus RNA sequencing and spatial transcriptomics to define cellular heterogeneity and immune specialization across atrial chambers.

Results:
Comparative analysis of adult mouse atria revealed transcriptionally distinct stromal and immune states between LA and RA. Stromal populations in the RA—including fibroblasts, endothelial, and epicardial cells—shared a convergent transcriptional program enriched for oxidative phosphorylation, protein translation, and stress-response pathways, suggesting a metabolically active niche. Macrophages displayed pronounced chamber specificity: RA macrophages were enriched for monocyte-derived macrophage (MoMP) signatures with elevated inflammatory and antigen-presentation programs, whereas LA macrophages preferentially exhibited tissue-resident macrophage (TRMP) signatures associated with anti-inflammatory functions. Reanalysis of published human single-nucleus heart datasets confirmed conserved enrichment of MoMP signatures in the RA. Single-cell–resolved spatial transcriptomics further mapped these immune states in situ, revealing preferential localization of MoMP-enriched immune niches within the RA and validating asymmetric macrophage distribution across atrial chambers.

Conclusions:
Our findings suggest that postnatal pulmonary circulation drives asymmetric metabolic stress in atrial macrophages, shaping chamber-specific transcriptional programs. This conserved immune asymmetry provides a framework for understanding macrophage–stromal interactions in atrial physiology and disease.

Poster 24

INTEGRATED PROFILING OF HEPATIC AND CARDIAC REMODELING DURING METABOLIC DISEASE

Maaria K Saeed[1], Kang Ho Kim[1], Hyun-Jung Jung[1], Bo Ryung Lee[1], Matthew DeBerge[1]

[1]Anesthesiology, UT Health Science Center, Houston, TX

Background:
Metabolic dysfunction, including obesity, hypertension, and type 2 diabetes, drives both cardiovascular and hepatic disease, yet mechanisms linking systemic stress to cardiac dysfunction remain poorly understood. Heart failure with preserved ejection fraction (HFpEF), the most common form of heart failure, lacks effective disease-modifying therapies and is often accompanied by metabolic dysfunction–associated steatotic liver disease (MASLD), with MASLD present in up to 50% of HFpEF patients. This comorbidity suggests a multi-organ axis in which hepatic dysfunction worsens cardiac remodeling and diastolic dysfunction, highlighting the heart-liver axis as a potential therapeutic target.

Materials/Methods:
Three preclinical models were used to assess this axis: HFpEF (high-fat diet with L-NAME), CDAHFD (choline-deficient, L-amino acid-defined high-fat diet), and Western Diet (high-fat, high-sucrose, and high-cholesterol diet). Cardiac function was evaluated using echocardiography, transcriptional changes by bulk RNA sequencing and PCR, and tissue morphology by histology.

Results:
Cardiometabolic stress induced diastolic dysfunction in all three models and increased cardiac fibrosis, indicating a consistent impact on myocardial remodeling. Hepatic inflammation and fibrosis were most pronounced in CDAHFD mice, reflecting the pronounced liver-directed injury. Bulk RNA sequencing of the heart revealed both divergent and shared transcriptional pathways across models. Among the conserved pathways was Serpine1, which encodes PAI-1. This protein is upregulated in HFpEF patients and associated with increased mortality, prompting us to target it therapeutically. In HFpEF mice, pharmacologic inhibition of PAI-1 ameliorated diastolic dysfunction, supporting a causal role for this pathway in HFpEF.

Conclusions:
Together, these findings suggest a conserved pathogenic axis underlying heart-liver dysfunction and identify PAI-1 as a potential therapeutic target in HFpEF.

Poster 25

POLYCYSTIN-1 DEFICIENCY INCREASES THE B-ADRENERGIC SIGNALING RESPONSE IN CARDIOMYOCYTES THROUGH IMPAIRED PP2A ACTIVITY

Alejandra Vasquez Limeta[1], Ernesto Reyes Sanchez[1], Leah Carter[1], Matthew Fiedler[2], Francisco Altamirano[1]

[1]HMRI/Cardiovascular Sciences, Houston Methodist, Houston, TX; [2]Cardiology (Weill Cornell)/Program in Physiology, Biophysics & Systems Biology, Weill Cornell Medicine /Houston Methodist

Background:
Cardiovascular disease is the leading cause of death in individuals with Autosomal Dominant Polycystic Kidney Disease (ADPKD). While these complications are often attributed to ADPKD-related hypertension, cardiac alterations are also present in normotensive ADPKD patients with preserved renal function, suggesting a direct role of Polycystin-1 (PC1) in cardiac cells.

Materials/Methods:
To clarify the mechanisms of PC1 in the heart, we performed RNA-seq in cardiac tissues and isolated adult ventricular cardiomyocytes from WT (F/F) and a cardiomyocyte-specific PC1 knockout mouse model (CKO; F/F αMHC-Cre).

Results:
Bulk RNA-seq of heart tissue revealed modest changes in gene expression, primarily affecting β-adrenergic and cAMP signaling pathways, as identified with Ingenuity Pathway Analysis (IPA) software (Qiagen). RNA-seq of isolated CKO cardiomyocytes revealed many more differentially expressed genes with cardiac β-adrenergic signaling, cAMP/PKA, and the apelin cardiomyocyte signaling as the most upregulated pathways. To assess if β-adrenergic signaling was affected, we conducted functional studies in WT and CKO adult cardiomyocytes. CKO cardiomyocytes had impaired Ca^{2+} transients and reduced contractility. Isoproterenol increased Ca^{2+} transient amplitude and contraction peak in both WT and CKO cells, restoring CKO function to WT-comparable levels. RNA-seq validation revealed low PPP2R3A protein levels, a regulatory subunit of protein phosphatase 2A (PP2A). Phosphorylation of phospholamban (PLN), a PKA and PP2A target, was altered in CKO cardiomyocytes after isoproterenol stimulation, suggesting impaired PP2A activity.

Conclusions:
Our data indicate that increased β-adrenergic signaling response can temporarily restore functionality in PC1-deficient cardiomyocytes, but potentially at the expense of cardiac reserve. Over time, such adaptations may lead to detrimental remodeling. PC1 seems to fine-tune the β-adrenergic response by regulating the expression of key pathway components, more specifically, PPP2R3A.

Poster 26

BDH1–OCT4 SIGNALING ORCHESTRATES METABOLIC REWIRING TO SUPPRESS ENDOTHELIAL SENESCENCE IN HUTCHINSON–GILFORD PROGERIA SYNDROME

Kun Yuan Chu[1], Venkatasubrahman Kumar Samanthapudi[1], Jun-ichi Abe[1], Sivareddy Kotla[1], Masaki Osawa[2], Nhat-Tu Le[2]

[1]Cardiology/Division of Internal Medicine, MD Anderson Cancer Center; [2]Cardiovascular Sciences, Houston Methodist

Background:
Hutchinson–Gilford progeria syndrome (HGPS) causes premature vascular aging driven by endothelial senescence and metabolic dysfunction. How altered energy metabolism contributes to endothelial aging remains unclear. We hypothesize that loss of β-hydroxybutyrate dehydrogenase-1 (BDH1)–mediated ketone metabolism promotes endothelial senescence through metabolic imbalance and oxidative stress, whereas restoration of the BDH1–3-hydroxybutyrate (3-HB)–OCT4 axis preserves endothelial metabolic homeostasis

Materials/Methods:
Endothelial cells derived from HGPS patient–specific induced pluripotent stem cells and age-matched controls were analyzed using metabolomics, transcriptomics, and metabolic-flux tracing. BDH1 and OCT4 signaling were genetically manipulated, and effects on glycolytic and mitochondrial metabolism, ATP production, mitochondrial ROS, pyrimidine metabolism, DNA-damage responses, and senescence were assessed. Ionizing radiation–induced endothelial senescence served as a complementary stress model.

Results:
Multi-omics analyses showed increased glucose flux in HGPS endothelial cells but reduced steady-state levels of downstream glycolytic intermediates and decreased pentose phosphate pathway flux, indicating rapid carbon turnover. Pyrimidine metabolism was upregulated, consistent with increased DNA-repair demand. Integration identified BDH1 and its product 3-HB as metabolic regulators linked to OCT4 expression. BDH1 overexpression increased OCT4 levels, enhanced glycolytic and TCA-cycle flux, restored ATP production, reduced mitochondrial ROS, suppressed senescence, and improved DNA-repair capacity. BDH1 depletion impaired mitochondrial metabolism and promoted senescence and apoptosis. Ionizing radiation suppressed BDH1–OCT4 signaling and induced senescence, whereas restoration of BDH1 or OCT4 rescued metabolic flux and reversed senescence.

Conclusions:
The BDH1–3-HB–OCT4 axis coordinates cellular metabolism to maintain mitochondrial function, support DNA repair, and restrain endothelial senescence.

Poster 27

MACROPHAGE PARP1 ORCHESTRATES DNA-DAMAGE AND INFLAMMATORY PROTEIN SIGNALING IN PD-1 BLOCKADE–INDUCED CARDIOVASCULAR INJURY

Kun Yuan Chu[1], Venkatasubrahman Kumar Samanthapudi[1], Jonghae Lee[1], Sivareddy Kotla[1], Jun-ichi Abe[1]

[1]Cardiology/Division of Internal Medicine, MD Anderson Cancer Center

Background:
Immune checkpoint inhibitors (ICIs) have transformed cancer therapy but can cause cardiovascular immune-related adverse events, including myocarditis, pericarditis, heart failure, and accelerated atherosclerosis. Macrophage dysfunction and inflammatory remodeling are implicated, yet the molecular mechanisms linking PD-1 blockade to cardiovascular injury remain unclear. This study examined whether PD-1 blockade alters macrophage stress responses and whether PARP1 activation in macrophages drives immunosenescence and inflammatory remodeling in ICI-associated cardiovascular disease.

Materials/Methods:
A multimodal mouse model combining anti–PD-1 therapy with hypercholesterolemia and pressure overload was used to reproduce ICI-associated cardiovascular pathology. Macrophage-specific PARP1 deletion (LysM Parp1) tested the role of macrophage PARP signaling. Mitochondrial assays, metabolic flux tracing, RPPA proteomics, and telomere/senescence analyses defined molecular mechanisms, while histology, echocardiography, and vascular imaging assessed cardiac and vascular injury.

Results:
Anti–PD-1 therapy under metabolic and hemodynamic stress produced myocarditis, pericarditis, left ventricular systolic dysfunction, macrophage infiltration, and accelerated coronary atherosclerosis. RPPA proteomics revealed activation of macrophage stress pathways including DNA damage, replication stress, chromatin remodeling, NF-κB inflammatory signaling, and cell-cycle arrest. These changes coincided with telomere dysfunction and senescence-associated remodeling. Macrophage-specific PARP1 deletion suppressed these proteomic alterations and attenuated cardiac dysfunction, inflammatory infiltration, and coronary atherosclerosis progression.

Conclusions:
PD-1 blockade activates macrophage PARP1-dependent DNA damage, chromatin remodeling, and inflammatory signaling networks that promote immunosenescence and drive ICI-associated cardiovascular disease, with accelerated coronary atherosclerosis as a central manifestation.

Poster 28

PKCZ–TERF2IP S205 PHOSPHORYLATION PROMOTES LATS1/2 DEGRADATION AND ENDOTHELIAL PRO-INFLAMMATORY SENESCENCE PHENOTYPE IN DISTURBED FLOW–INDUCED ATHEROSCLEROSIS

Venkatasubrahman Kumar Samanthapudi[1], Kun Yuan Chu[1], Sivareddy Kotla[1], Jun-ichi Abe[1]

[1]Cardiology/Division of Internal Medicine, MD Anderson Cancer Center

Background:
Atherosclerotic plaques preferentially form in arterial regions exposed to disturbed flow (d-flow), where endothelial cells (ECs) develop a proinflammatory senescence phenotype. Loss of Hippo kinases LATS1/2 promotes this response, but mechanisms linking hemodynamic stress to LATS1/2 degradation remain unclear. We hypothesize that disturbed flow activates mitochondrial ROS–dependent PKCzeta signaling that phosphorylates TERF2IP, promoting MKRN1-mediated LATS1/2 degradation and endothelial senescence driving atherosclerosis.

Materials/Methods:
Endothelial responses to laminar versus disturbed flow were studied in cultured ECs and mouse models. EC-specific PKCzeta knockout and TERF2IP S205A knock-in mice were examined in partial carotid ligation and PCSK9-AAV hypercholesterolemia models. LATS1/2 regulation, senescence, NAD metabolism, and plaque phenotypes were analyzed by RNA sequencing, spatial proteomics, imaging mass cytometry, and biochemical assays.

Results:
Disturbed flow reduced LATS1/2 protein without altering mRNA and increased TEAD transcriptional activity. LATS1/2 knockdown amplified TEAD activation, EC proliferation, inflammation, senescence, and apoptosis, whereas overexpression reversed these effects. MKRN1 was identified as an E3 ligase promoting LATS1/2 degradation through TERF2IP interaction. Phosphorylation of TERF2IP at S205 was required for MKRN1-mediated LATS1/2 degradation and activation of senescence pathways. PKCzeta, but not p90RSK, mediated this phosphorylation. Disturbed flow–induced mitochondrial ROS activated PKCzeta, and NAD precursors suppressed ROS generation. Deletion of EC PKCzeta or the TERF2IP S205A mutation reduced SASP markers and plaque formation.

Conclusions:
Disturbed flow promotes endothelial senescence and atherosclerosis through a PKCzeta–TERF2IP–MKRN1 pathway that drives LATS1/2 degradation and Hippo dysregulation, identifying a potential therapeutic target.

Poster 29

CD38 NADASE SUPPRESSES SULFITE OXIDASE (SUOX) AND ACTIVATES REVERSE COMPLEX V TO PROMOTE METABOLIC REMODELING IN ENDOTHELIAL CELLS (ECS) UNDER DISTURBED FLOW

Venkatasubrahman Kumar Samanthapudi[1], Kun Yuan Chu[1], Sivareddy Kotla[1], Jun-ichi Abe[1]

[1]Cardiology/Division of Internal Medicine, MD Anderson Cancer Center, Houston, TX

Background:
Atherosclerotic lesions preferentially develop in arterial regions exposed to disturbed flow (DF), where endothelial cells undergo mitochondrial dysfunction, metabolic reprogramming, and senescence. Hippo kinases LATS1/2 regulate endothelial homeostasis, but mechanisms linking DF-mediated suppression of LATS1/2 to metabolic remodeling remain unclear. We hypothesized that DF activates CD38, causing mitochondrial dysfunction and metabolic reprogramming that drive endothelial senescence and proliferation through inhibition of LATS1/2 signaling.

Materials/Methods:
Endothelial Lats1/2 knockout mice were generated using tamoxifen-inducible Cre, and disturbed flow was induced by partial carotid ligation. Murine and human plaques were analyzed by immunofluorescence and spatial metabolomics. Bioenergetic profiling included Seahorse analysis and isotope tracing with pharmacologic modulation of CD38 and mitochondrial pathways.

Results:
Complete endothelial LATS1/2 deletion caused fatal edema, whereas partial loss promoted fragile neovascularized plaques. Spatial proteomics identified a CD38-driven senescence phenotype under LATS1/2 deficiency. Metabolomics revealed sulfite and taurine accumulation consistent with sulfite oxidase insufficiency. Mechanistically, CD38 suppressed SUOX, induced reverse-mode ATP synthase activity, increased succinate flux, and accelerated ATP consumption. Despite ATP depletion, glycolytic and TCA flux increased, supporting endothelial proliferation under energetic stress. LATS1/2 loss reduced mitochondrial respiration and shifted metabolism toward glycolysis. CD38 inhibition restored mitochondrial respiration and corrected metabolic defects induced by DF and LATS1/2 loss.

Conclusions:
Partial LATS1/2 deficiency promotes fragile plaque formation through a CD38-dependent metabolic–senescence program. Targeting CD38 restores mitochondrial function and limits endothelial senescence in disturbed-flow regions.

Poster 30

IMMUNE CHECKPOINT INHIBITION AUGMENTS SMOOTH MUSCLE CELL PHENOTYPIC MODULATION AND PROMOTES ATHEROSCLEROSIS

Abhijnan Chattopadhyay[1], Darshan Reddy[1], Aminat Dosunmu[1], Sree Dharma[1], Natasha Biswas[1], Callie Kwartler[1], Dianna Milewicz[1]

[1]Internal Medicine/Medical Genetics, The University of Texas Medical School at Houston

Background:
Immune checkpoint inhibitors (ICIs), including the monoclonal antibody nivolumab, which blocks the interaction between the programmed death 1 (PD-1) receptor on immune cells and its ligands PD-L1/PD-L2 on cancer cells, have revolutionized the treatment of many cancers, and indications for ICI use is increasing. However, the use and success of ICIs have been increasingly linked to cardiovascular disease, including a ~3-fold higher risk of coronary artery disease within 2 years of treatment. During atherogenesis, smooth muscle cells (SMCs) undergo complex phenotypic modulation (PM): they de-differentiate and variably express markers of other cell types. We have established that cholesterol-induced endoplasmic reticulum stress, particularly PERK signaling, drives atherosclerosis-associated PM of SMCs. We additionally discovered that activation of heat shock factor 1 (HSF1) due to inherited genetic variants in SMCs that predispose to early onset atherosclerosis can increase intracellular cholesterol levels by increasing HMG-CoA reductase (HMGCR) activity, which then augments PERK signaling and promotes SMC PM.
Materials/Methods:
We exposed explanted human SMCs to sub-therapeutic levels of nivolumab and performed molecular assays to determine its effect on SMC PM.
Results:
Nivolumab exposure increases SMC migration, activates HSF1 and upregulates HMGCR, resulting in elevated levels of intracellular cholesteryl esters, increased PERK signaling and augmented SMC PM. Furthermore, nivolumab-induced SMC PM was reversed by either treatment with the HMGCR inhibitor pravastatin or SMC-specific deletion of Perk. Collectively, our results identify a novel atherogenic effect of nivolumab on SMCs, resulting in activation of HSF1-HMGCR-PERK signaling and PM.
Conclusions:
These data suggest that targeting cholesterol biosynthesis or PERK signaling might offer viable therapeutic strategies to prevent or treat ICI-associated atherosclerosis without compromising anti-tumor efficacy.

Poster 31

LIPID NANOPARTICLE-BASED IN VIVO DELIVERY OF STING SIRNA MITIGATES AORTIC DISSECTION

Sanjib Sarkar[1], Chen Zhang[1], Yanming Li[1], Bowen Li[1], Fuhai Li[1], Hernan Vasquez[1], Lin Zhang[1], Ghanashyam Acharya[2], Rohan Bhavane[3], Ketankumar Ghaghada[3], Joseph Coselli[1], Scott LeMaire[4], Ying Shen[1]

[1]Cardiothoracic Surgery, Baylor College of Medicine, Houston, TX; [2]Surgery, Baylor College of Medicine; [3]Radiology, Baylor College of Medicine; [4]Investigational Medicine, Geisinger College of Health Sciences

Background:
Aortic aneurysm and dissection (AAD) is a life-threatening condition marked by progressive aortic dilation, dissection, and rupture. There is no effective pharmacological therapy to halt its progression. We evaluated LNP-mediated delivery of Sting siRNA, targeting a key mediator of aortic inflammation and destruction, as a potential therapy for AAD.

Materials/Methods:
LNPs encapsulating Cy3-scrambled siRNA and labelled with fluorescent dye, DiD (Cy3-siRNA-DiD-LNP), control siRNA (control siRNA-LNP), or Sting siRNA (Sting siRNA-LNP) were formulated using an ionizable lipid, cholesterol, helper phospholipids, and PEGylated lipids and were characterized. LNP delivery in aortic wall, STING expression, and AAD incidence were assessed in wild-type mice challenged with angiotensin II (Ang II) infusion for 7 days and treated with either control siRNA-LNP or Sting siRNA-LNP.

Results:
Formulated LNPs showed favorable properties including a hydrodynamic size of 156 nm, a zeta potential of −4 ± 2 mV, a polydispersity index of 0.15 ± 0.05, and ~85% siRNA encapsulation, with negligible cytotoxicity and minimal hemolysis. Ex vivo imaging confirmed the presence of DiD-LNP and Cy3-siRNA in the aortic wall of Ang II-challenged mice, whereas no signal was detected in aortas of saline control mice. Immunofluorescence analysis further localized DiD-LNP and Cy3-siRNA to endothelial cells, smooth muscle cells, and macrophages within the aortic wall. In Ang II–challenged mice, treatment with Sting siRNA-LNPs significantly reduced the incidence of aortic dissection ($p = 0.03$) compared with control siRNA-LNPs. This protective effect correlated with a marked reduction in STING protein expression in the aortic wall.

Conclusions:
The study demonstrates successful LNP formulation and delivery of Sting siRNA to the aorta, with effective STING suppression and reduction of AAD in vivo. This work provides proof-of-concept for LNP-based RNA therapeutics for the treatment of AAD and supports further optimization and preclinical evaluation.

Poster 32

Investigating Cellular Mechanisms of Fibrotic Remodeling in Functional Mitral Regurgitation

Inioluwa Ojediran[1], Jane Grande-Allen[1]

[1]Bioengineering, Rice University, Houston, TX

Background:
Among patients with advanced congestive heart failure (CHF), approximately 50% develop functional mitral regurgitation (FMR) of at least mild severity, significantly worsening their prognosis. Fibrotic remodeling further exacerbates this dysfunction, highlighting the need to investigate fibrosis-driven mechanisms at the cellular level. The mitral valve consists primarily of valve endothelial (VECs) and interstitial (VICs) cells. Making up the valve endothelium, mitral VECs are the first to encounter the pro-inflammatory and pro-fibrotic CHF environment, suggesting their role in fibrotic remodeling.

Materials/Methods:
MVEC isolation begins with removing the mitral valve leaflets from freshly dissected porcine hearts, before washing, digesting, and sorting them using magnetic activated cell sorting (MACS) to positively select for $CD31^+$ valve cells. Culture optimization showed that sorting at least 3x yielded the purest population of VECs. Flow cytometry and immunofluorescent staining were used to validate the VEC and VIC phenotype using αSMA (mesenchymal marker) and CD31(endothelial marker).

Results:
It is anticipated that exposure to CHF-associated pro-inflammatory and pro-fibrotic factors will induce a phenotypic transition consistent with fibrotic remodeling and a loss of endothelial markers. Endothelin is a vasoactive cytokine that is increased in plasma levels of patients with CHF and has been shown to contribute to fibrosis. Mitral VECs were treated with endothelin-1 in dosages ranging from 0nM to 30nM to observe a possible dose-dependent response after 24 and 48 hours. Results from immunofluorescence showed higher mesenchymal expression in the 20nM and 30nM groups, compared to the 0nM and 10nM groups.

Conclusions:
This study plays a role in understanding the behavior of mVECs in the context of CHF and FMR-associated fibrotic remodeling. Further treatment with vasoactive hormones and inflammatory cytokines will elucidate the effect of the pathological FMR environment on valve cells.

Poster 33

Biomechanics of Functional Mitral Regurgitation: Using the RUFLS Bioreactor to Model Mitral Valve Hemodynamics

Jessica Wang[1], K. Jane Grande-Allen[1]

[1]Bioengineering, Rice University, Houston, TX

Background:
Functional mitral regurgitation (FMR) is caused by underlying heart disease that distorts the geometry of the mitral valve (MV) annulus and/or papillary muscles. These structural changes increase tensile forces throughout the leaflets and chordae tendineae, impairing coaptation during systole and resulting in regurgitation. FMR is the least studied form of MV disease, particularly from a biomechanical perspective.

Materials/Methods:
To study the effects of altered MV geometry on mitral valve tissue, our group has developed a pseudo-physiological flow loop system, RUFLS, that is capable of sterile, long-term culture of porcine mitral valves. By mimicking FMR hemodynamics and valve geometry (5mm apical + 5mm lateral displacement, 65% larger annular area), our group has previously shown that FMR-conditioned MVs became stiffer, more brittle, and less extensible after 1 week. These prior studies have provided broad insights into the MV remodeling process in FMR, but more work is needed to further understand MV responses to mechanical changes. To address this gap and some design limitations, we have recently been improving upon the RUFLS design and reestablishing its full functionality.

Results:
For example, we have incorporated 3D printing using a Formlabs printer and BioMed Clear resin, an autoclavable and biocompatible material well suited for RUFLS applications. We have also characterized fluid flow through the updated system using both mechanical and porcine MVs. Once RUFLS is fully updated and reestablished, the system will be used to determine the effect of mechanical and chemical stimulation on the production of inflammatory and pro-fibrotic mediators in FMR-conditioned MVs.

Conclusions:
Results from this research will provide investigators with new avenues for studying fundamental aspects of mitral valve disease as well as directions for the pursuit of medical treatments that can improve health outcomes in patients with FMR who do not yet qualify for, or cannot tolerate, more invasive interventions.

Poster 34

PRKG1 R177Q MUTATION DISRUPTS MECHANOTRANSDUCTION AND MITOCHONDRIAL FUNCTION IN AORTIC SMOOTH MUSCLE CELLS

Xiaoli Cai[1], Dianna Milewicz[1]

[1]Internal Medicine, UT Health Science Center, Houston, TX

Background:
Mutations in PRKG1, encoding cGMP-dependent protein kinase I (PKG1), cause familial thoracic aortic aneurysm and dissection (TAAD). The PRKG1 R177Q mutation (R192Q in mice) results in constitutive PKG1 activation, but how this mutation alters smooth muscle cell (SMC) function remains unclear. Because cytoskeletal organization and focal adhesion complexes are central to SMC mechanosensing, we hypothesized that constitutive PKG1 activation disrupts mechanotransduction signaling and mitochondrial function in aortic SMCs.

Materials/Methods:
Primary aortic SMCs were isolated from Prkg1R192Q/+ and wild-type mice. Cytoskeletal organization and focal adhesions were analyzed by immunofluorescence staining of actin and focal adhesion proteins. Activation of mechanotransduction pathways was assessed by Western blotting for phosphorylated MYPT1 and FAK. YAP/TAZ signaling was evaluated by immunostaining. Mitochondrial structure and function were examined using mitochondrial network imaging and Seahorse extracellular flux analysis.

Results:
Prkg1R192Q/+ SMCs displayed disorganized actin stress fibers and uneven focal adhesion distribution compared with wild-type cells. Mutant SMCs showed increased activation of mechanotransduction pathways, including elevated phosphorylation of MYPT1 and FAK, indicating enhanced RhoA–ROCK and integrin–FAK signaling. YAP/TAZ signaling was also activated, suggesting altered mechanosensitive transcription. In addition, mutant SMCs exhibited abnormal mitochondrial organization and impaired mitochondrial respiratory capacity, indicating mitochondrial dysfunction.

Conclusions:
These findings suggest that constitutive PKG1 activation alters mechanotransduction signaling and mitochondrial function in aortic SMCs, providing insight into cellular mechanisms that may contribute to vascular remodeling in PRKG1-associated aortic disease.

Poster 35

BURST WAVE LASER LITHOTRIPSY OF CALCIFIED HEART VALVES

Nitesh Katta[1], Anh Nguyen[1], Kenneth Liao[1], Thomas Milner[1]

[1]Surgery, Baylor College of Medicine, Houston, TX

Background:
Calcific aortic and mitral valve disease creates rigid, irregular leaflets and annuli that are difficult to suture or cross with transcatheter devices. Effective intraoperative fracture of valvular calcium can restore compliance, enable secure suturing, and reduce risk of peri-valvular leaks. Current electric intravascular lithotripsy (E-IVL), optimized for arteries, may be insufficient for thick valvular calcium. In contrast, our novel burst wave laser lithotripsy (BWLL) approach delivers high-repetition-rate, directed pressure waves via small optical fibers without electromagnetic interference, offering potential compatibility with surgical and catheter-based valve therapies.

Materials/Methods:
Hydroxyapatite phantoms were assessed with EIVL and with our BWLL device prototype visually and by micro-CT. Under an approved IRB protocol, calcified human valve specimens were obtained from four surgical patients (3-5 samples per subject). Human aortic samples were exposed to BWLL over a range of energies. Calcium fracture and soft tissue integrity were evaluated by micro-CT and histology.

Results:
In phantoms, E-IVL produced 0 fractures after 80 pulses (device limit), while BWLL fractured all phantoms (N=5), generating >5 cracks/sample with fragments of ~0.1–5 mm. In human valves (14 samples, 4 patients), BWLL achieved fracture in 11/11 calcified samples (100%) with 0/3 soft tissue controls fractured. Median shots delivered: 1,125 (range 1,000–2,000). Fragment sizes: ≤2 mm in 5/11 (45%), >2 mm in 4/11 (37%), residual plates >10 mm in 2/11 (18%). Micro-CT confirmed intralesional cracks of 0.2–2 mm in 3 pre/post samples; no gross tears in soft tissue controls (N=3). Effective fragmentation required 1,000–2,000 shots at >100 atm/shot—far exceeding E-IVL's practical limit of ~80–120 pulses.

Conclusions:
Unlike E-IVL, BWLL achieves reliable calcium fragmentation in phantoms and ex vivo human valves while preserving soft valvular tissue, supporting it as a promising candidate for treatment for valvular heart disease.

Poster 36

OVERACTIVATION OF ATP-SENSITIVE K CHANNEL AND KV7.1 DYSFUNCTION CONTRIBUTE TO LETHAL CARDIAC ARRHYTHMIAS IN TANGO2 DEFICIENCY DISORDER

Weiyi Xu[1], Yingqiong Cao[1], Frank T. Horrigan[2], Lilei Zhang[1]

[1]Molecular and Human Genetics, Baylor College of Medicine, Houston, TX; [2]Integrative Physiology, Baylor College of Medicine, Houston, TX

Background:
TANGO2 (Transport and Golgi Organization 2 Homolog) is a novel player in fatty acid metabolism. Loss-of-function (LoF) in TANGO2 causes a rare recessive multiorgan genetic disease named TANGO2 deficiency disorder (TDD). Upon metabolic stresses such as fasting, TDD patients often present with life-threatening metabolic crisis where cardiac arrhythmias are the leading cause of death. These lethal arrhythmias are recalcitrant to standard antiarrhythmic treatment. The etiology remains elusive.

Materials/Methods:
Ion channel activity was studied by thallium flux assay and SyncroPatch. Metabolic study was performed with Seahorse assay and lipidomics.

Results:
TDD-associated arrhythmias are marked by long QTC (LQT), which serves as an arrhythmic substrate. While most LQT syndrome-associated ion channels showed normal activity, Kv7.1 activity was reduced by one-third in TDD iPSC-CMs, indicating that LQT in TDD is caused by Kv7.1 dysfunction. Mechanistically, TDD iPSC-CMs showed impaired production of ATP, which is an activator for Kv7.1, suggesting that Kv7.1 dysfunction may be caused by reduced ATP level.
Moreover, we assessed another important cardiac ion channel, ATP-sensitive K channel (KATP), and found it was aberrantly activated in TDD iPSC-CMs. KATP is inhibited at physiological ATP level, as was observed in WT iPSC-CMs. Overactivation is known to increase the risk of cardiac arrhythmias thus may underline the trigger mechanism. Mechanistically, a potent KATP activator, long chain fatty acyl (LCFA)-CoA was found accumulated in TDD iPSC-CMs. Therefore, the elevated LCFA-CoA together with the reduced ATP level jointly induce KATP overactivation.

Conclusions:
Our study suggests multiple K channel defects secondary to metabolic dysregulation underline the pathogenesis of TDD-associated arrhythmias, which can be further exploited for developing targeted therapy. These findings also have implications for arrhythmias observed in other metabolic disorders especially fatty acid oxidation disorders.

Poster 37

BILATERAL RENAL ISCHEMIA REPERFUSION INJURY (IRI) PROMOTES ATRIAL FIBRILLATION IN MICE

Alexandra Osborne[1], Jose Alberto Navarro-Garcia[1], Xander Wehrens[1]

[1]Integrative Physiology, Baylor College of Medicine, Houston, TX

Background:
Acute kidney injury (AKI) is defined by the KDIGO as any of the following increase in serum creatinine ≥ 0.3 mg/dl (≥26.5 lmol/l) within 48 hours; or ≥ 1.5 times that of a known baseline within the previous 7 days; or a decrease in urine volume < 0.5ml/kg/h for 6 hours. The risk of developing cardiovascular disease in AKI, such as arrhythmias, heart failure, acute coronary syndrome, or other major cardiac events, is high. Death has been described to occur in 16% to 49% of ICU patients. Arrhythmias are a typical complication of AKI. The most common arrhythmia seen in AKI patients is atrial fibrillation (AF).

Materials/Methods:
AKI was induced surgically in mice by bilateral ischemia-reperfusion injury (IRI). Heart function was monitored daily by surface electrocardiogram (ECG) recordings for 3 days after surgery. Pacing electrical stimulation studies were used 72 hours after surgery to assess AF inducibility in AKI mice. Serum, atrial, ventricular, and kidney samples were collected. Kidney dysfunction was confirmed by circulating phosphate and creatinine levels.

Results:
Kaplan–Meier analysis showed higher mortality in AKI vs Sham mice ($P<0.001$) and reduced body weight ($P<0.001$). No cardiac hypertrophy was observed at 72 hours; however, AKI mice that died at 48 hours had increased heart weight to tibial length (HW/TL) vs Sham and surviving AKI ($P<0.001$). KW/TL was elevated in both AKI groups ($P<0.01$ and <0.001). ECG showed prolonged P wave in deceased AKI mice ($P<0.05$). Surviving AKI mice had greater AF inducibility ($P<0.09$) and duration. SNRT and AERP were unchanged. AKI-SR mice showed increased serum phosphate ($P<0.01$) and creatinine ($P<0.01$), suggesting delayed disease progression.

Conclusions:
In conclusion, we demonstrated for the first time that the experimental murine model of AKI bilateral ischemia reperfusion injury (IRI) promotes AF. Future studies should address the possible mechanisms underlying the development of AF as a consequence of an abrupt loss of kidney function.

Poster 38

PREDICTION OF CANDIDATE CAUSAL CIS-REGULATORY VARIANTS UNDERLYING 35 QT INTERVAL VARIATION GWAS LOCI

Atsuko K Price[1], Ashish Kapoor[2]

[1]Physics and Biosciences, Rice University, Houston, TX; [2]Institute of Molecular Medicine, McGovern Medical School, UTHealth Houston

Background:
Prolongation of the QT interval, an index of ventricular depolarization and repolarization, is a known risk factor for certain cardiac arrhythmias. Genome-wide association studies have identified many loci associated with QT interval variation, yet most variants lie in noncoding regions, making identification of causal variants and their target genes difficult. Since many noncoding GWAS variants are hypothesized to act through cis-regulatory mechanisms, using functional genomic data can help us prioritize candidate regulatory variants.
Materials/Methods:
We performed regulatory fine-mapping across 35 QT interval GWAS loci. All common (minor allele freq. >1%) genome-wide significant variants ($P < 5\times10^{-8}$) were collected and integrated with functional genomic annotations. Variants were assessed for overlap with chromatin accessibility datasets (like DNase-seq and ATAC-seq peaks from human left and right ventricle tissues), predicted enhancer–promoter contacts using Activity-by-Contact (ABC) models in left ventricle tissue, and expression quantitative trait loci (eQTL) from GTEx cardiac tissues.
Results:
Across the 35 loci, 14,512 associated variants were identified. Of these, 1690 and 865 overlapped DNase-seq peaks in left and right ventricle tissues, respectively, while 1449 and 1879 overlapped ATAC-seq peaks. In total, 2568 variants overlapped at least one open chromatin region. Additionally, 181 variants overlapped ABC-predicted enhancer regions. eQTL analysis identified 4111 variants associated with gene expression in left ventricle tissue and 4514 associated with atrial appendage expression.
Conclusions:
Integration of regulatory datasets prioritized 149 variants that satisfied all filtering criteria, representing a high-confidence set of candidate causal cis-regulatory variants underlying QT interval GWAS data. Even though experimental studies to validate their functional effects are warranted, these analyses are critical in prioritizing candidate causal variants among a large set of associated variants.

Poster 39

LOX-1 ACTIVATION MEDIATES ATRIAL FIBRILLATION DEVELOPMENT IN CHRONIC KIDNEY DISEASE

Jose Alberto Navarro-Garcia[1], Shuai Zhao[1], Alexandra Osborne[1], Satadru Lahiri[1], Issam Abu-Taha[2], Gema Ruiz-Hurtado[3], Dobromir Dobrev[2], Xander Wehrens[1]

[1]Integrative Physiology, Baylor College of Medicine, Houston, TX; [2]IntInstitute of Pharmacology, University Duisburg-Essen; [3]Hypertension, Hospital Universitario 12 de Octubre

Background:
Atrial fibrillation (AF) is the most common sustained arrhythmia. AF risk is increased in chronic kidney disease (CKD). CKD is associated with increased oxidative stress, a risk factor for AF. Oxidized low-density lipoprotein (oxLDL) is a marker of lipid oxidative damage. Lectin-like oxLDL receptor-1 (LOX-1) is expressed in macrophages and cardiomyocytes. We aimed to determine whether LOX-1 activation contributes to AF onset in CKD.

Materials/Methods:
Blood samples from dialysis patients were used to measure oxLDL. Human atrial samples were used to assess LOX-1 expression. AF incidence in mice was assessed by pacing stimulation. Single-nuclei RNA sequencing (snRNA-seq) was performed in atria from sham, CKD-SR and CKD-AF mice. Atrial size was assessed by echocardiography. Serum oxLDL was measured in all mouse groups. Western blotting assessed LOX-1 and pSTAT3 in human and mouse atria. Confocal microscopy analyzed spark-mediated diastolic Ca^{2+} leak in atrial cardiomyocytes (ACM). LOX-1 was inhibited with BI-0115 or genetically using AAV9-ANF-Cre and AAV9-CAG-floxSTOP-shLOX1.

Results:
CKD-AF patients showed higher serum oxLDL ($P<0.001$) and OXY-Score ($P<0.001$) than CKD-SR. Serum oxLDL was also higher in CKD-AF than sham mice ($P=0.025$). LOX-1 expression increased in atria from CKD-AF patients ($P<0.05$) and mice ($P<0.05$). snRNA-seq did not show differential fibroblast or macrophage activation in CKD-AF versus sham mice, prompting cardiomyocyte analysis. KEGG revealed cardiac contraction and calcium signaling as the most dysregulated pathways. CKD-AF mice showed atrial enlargement. Diastolic Ca^{2+} leak increased in ACM from CKD-AF versus CKD-SR and sham ($P<0.001$). pSTAT3 was also increased ($P<0.01$). LOX-1 blockade prevented AF development and reduced Ca^{2+} leak ($P<0.05$) and pSTAT3 ($P<0.001$).

Conclusions:
In conclusion, CKD promotes atrial enlargement and Ca^{2+} mishandling leading to AF. LOX-1 blockade prevented these changes and reduced AF inducibility, identifying LOX-1 as a potential therapeutic target for AF in CKD.

Poster 40

INFLAMMASOME ACTIVATION CONTRIBUTES TO SINUS NODE DYSFUNCTION

Anna K Shinohara[1], Tingting Li[1], Luge Li[1], Enrique Martinez[1], Yue Yuan[1], Mihail Chelu[3], Na Li[2]

[1]Medicine (Section of Cardiovascular Research), Baylor College of Medicine, Houston, TX; [2]Medicine (Section of Cardiovascular Research), Cardiovascular Research Institute, Baylor College of Medicine; [3]Medicine (Section of Cardiovascular Research), Baylor College of Medicine, Texas Heart Institute at Baylor St. Luke's Medical Center

Background:
Pacemaker cell function in the sinoatrial node (SAN) controls rhythmic heart beats. Disruptions of the SAN can lead to irregularities in cardiac rhythm, or sinus node dysfunction (SND), which often results in heart failure. The development of SND could be due to fibroinflammatory remodeling within the SAN. The NOD-, LRR- and pyrin domain-containing protein 3' (NLRP3) inflammasome is a canonical signaling pathway that plays a critical role in innate immunity. Our prior research has indicated that enhanced activity of this pathway in cardiomyocytes and cardiac fibroblasts promotes atrial fibrillation (AF). Given that SND frequently coexists with AF, we hypothesized that enhanced NLRP3 activity may also contribute to SND.
Materials/Methods:
To investigate the canonical function of NLRP3 inflammasome activation within the SAN, a cardiac conduction system (CCS)-specific NLRP3 activation mouse model (CCS-KI) was developed by crossing Hcn4iCre and Nlrp3NeoRA350V alleles. Electrophysiological studies were conducted to analyze heart rate and susceptibility to atrial arrhythmias. Ca^{2+} imaging was performed to examine SAN pacemaker cell automaticity. Immunofluorescence staining and Masson's Trichrome staining were conducted to evaluate NLRP3 inflammasome pathway activation and fibrosis in the SAN.
Results:
NLRP3 inflammasome activation in the SAN was validated by Caspase-1 overexpression in the SAN of CCS-KI mice. Compared with control littermates, CCS-KI mice displayed features of SND, including bradycardia, sinus block, and prolonged sinus node recovery time. Reduced SAN pacemaker cell automaticity, along with increased fibrosis and collagen I deposition surrounding the SAN, was observed in the CCS-KI mice, accompanied by increased heart mass.
Conclusions:
These results suggest that NLRP3 inflammasome signaling pathway activation within CCS exerts adverse effects on SAN function, contributing to SND pathogenesis. This finding may contribute to potential therapeutic approaches for patients with SND.

Poster 41

A MEMBRANE BIOREACTOR FOR THE MECHANICALLY BIOMIMETIC CULTURE OF HEART SLICES

Joern Huelsmann[1], Beatriz Mayol[2], Abhijeet Kumar[1], Sairam Pasam[1], Angel Moctezuma-Ramirez[3], Mir Timo Nazari Shafti[1], Rose Mathew[1], Emmanuel Camors[1], Abou Bakr Salama[1], Kamal Abou Farraj[1], Riham Abouleisa[1], Juliane Sempionatto[2], Tamer Mohamed[1]

[1]Surgery, Baylor College of Medicine, Houston, TX; [2]Electrical and Computer Engineering, Rice University; [3]Surgery, The Texas Heart Institute at Baylor College of Medicine

Background:
We are developing a bioreactor for the ex-vivo culture of precision-cut human myocardium (heart slices), aiming to predict drug effects on the heart and to model biomechanical pathologies. Therefore, we designed a model to mimic the native mechanical environment of the myocardium with two major elements. The first one (i) is a smart membrane that subjects the Heart Slices to fully controlled organ level diastolic deformation dynamics. The second one (ii) is two-dimensional contraction resistance to mimic also the systolic mechanical environment.
Materials/Methods:
For (i), we assessed the directional composition of the tensile mechanical properties of the myocardial wall by subjecting tangential left-ventricular vibratome slices of varying thicknesses to tensile testing in anatomical axial vs. circumferential orientation. In parallel, we designed an anisotropic reinforcement structure and matched it mechanically to the found tissue values. For (ii), we designed a contraction resistance for the Heart Slices, matched it to myocardial contraction forces and tested the functionality with mounted slices under electrical field stimulation.
Results:
For (i), we observed a highly pronounced mechanical Anisotropy for the myocardium at organ level thickness, with altering mechanical properties at decreasing thickness. Mechanically matched reinforcement structures could reflect the found organ-level Anisotropy. For (ii), slices that were mounted to the contraction resistances showed physiological contraction dynamics and calcium handling.
Conclusions:
Our membrane aims to restore organ-level biomechanics to heart slices by compensating for mechanical alterations of thin slices. In the next steps, we will integrate strain sensors to enable control of the deformation dynamics. With (i) and (i) combined, we will model healthy and pathological infill stresses at varying afterloads at the same time.

Poster 42

TYK2 AS A NOVEL GENETIC DETERMINANT OF HYPERTROPHIC CARDIOMYOPATHY

Azeez Muili[1], Andrew Bigler[1], Weiyi Xu[1], Yingqiong Cao[1], Olivier Lichtarge[1], Lilei Zhang[1]

[1]Molecular and Human Genetics, Baylor College of Medicine, Houston, TX

Background:

Hypertrophic cardiomyopathy (HCM) affects 1 in 500 individuals and is the leading cause of sudden cardiac death (SCD) in young adults. HCM is a genetic disease characterized by thickening of the left ventricle. This makes it difficult for the heart to contract and to pump blood, causing complications such as atrial fibrillation and cardiac arrest. Although pathogenic variants in sarcomeric genes account for a subset of cases, less than half of HCM patients carry a known causal mutation, limiting opportunities for precision medicine. Thus, it is critical to determine potential genetic signs of HCM for early detection.

Materials/Methods:

To expand the spectrum of HCM genes, we applied *MEVA*, a machine learning ensemble of evolutionary action–based algorithms, to a UK Biobank cohort of HCM patients and controls. *MEVA* highlighted five genes including *TYK2* (Tyrosine Kinase 2), as candidate genes. While *TYK2* is well characterized in cytokine signaling via STAT proteins in immune and neuronal contexts, its role in the heart remains unexplored. We used CRISPR-Cas9 systems to knock out *TYK2* in human-induced pluripotent stem cells (hiPSCs), then differentiated these cells into cardiomyocytes. We then used their relative size, heartbeat amplitude, and mitostress seahorse assay to determine if these cells displayed signs of HCM compared to positive and negative controls. In this way, we evaluate *TYK2* relationship with HCM.

Results:

We found similar to prototypical HCM model (MYH7 R403Q), homozygous deletion of *TYK2* leads to hypercontractility, cell hypertrophy, and mitochondria dysfunction of cardiomyocytes compared to its isogenic controls, which is considered the key driver of concentric hypertrophy. We also see a reduction in STAT1 and STAT3 phosphorylation, suggesting that the phenotype is dependent on alteration of the STAT pathway.

Conclusions:

Combining novel machine learning tools, large dataset, and invitro hiPSC-cardiomyocyte model, we were able to identify and confirm *TYK2* novel genetic causes for HCM.

Poster 43

PLASMA MICRORNA SIGNATURE FOR THE PREDICTION OF EARLY STROKE IN PATIENTS WITH LEFT VENTRICULAR ASSIST DEVICES

Christopher Bi[1], Nikita Singh[1], Shiyi Li[1], Iván Murrieta-Álvarez[1], Kenneth Liao[1], Nandan Mondal[1]

[1]Surgery/Cardiothoracic Transplantation and Circulatory Support, Baylor College of Medicine, Houston, TX

Background:
Stroke is a devastating complication after Left Ventricular Assist Device (LVAD) implantation. Predictive biomarkers are needed to identify at-risk patients and enable preventive strategies. This exploratory study aimed to identify plasma microRNA (miRNA) signatures associated with the development of stroke following LVAD implantation.

Materials/Methods:
We studied 20 heart failure patients undergoing LVAD implantation, of whom 10 developed a stroke (Stroke Group) at a median of 293 days (range: 14–596 days) post-implantation, and 10 did not (No-Stroke Group). High-throughput plasma miRNA sequencing was performed on day 0 (Pre-LVAD) and at day 7 (Post-LVAD) in all patients. Differential expression analysis was conducted to compare Stroke vs. No-Stroke groups at both Pre-LVAD and Post-LVAD time points.

Results:
A distinct baseline miRNA signature was identified in Pre-LVAD samples from patients who later suffered a stroke compared to those who did not. This signature included the significant upregulation of neuronal injury and ischemia-associated miRNAs, specifically miR-9-5p, miR-124-3p, let-7c-5p, and miR-129-5p, suggesting a pre-existing vulnerability or ongoing subclinical pathology. At the Post-LVAD time point, the Stroke group continued to exhibit elevated levels of brain-enriched miRNAs (miR-9-5p, miR-128-3p) compared to the No-Stroke group, alongside a distinct downregulation of miRNAs involved in vascular health, inflammation, cardiac hypertrophy, and heart failure progression, such as miR-331-3p, let-7b-3p, and miR-195-5p. KEGG analysis showed enrichment of neurotrophin signaling Pre- and Post-LVAD.

Conclusions:
This study identifies a key baseline plasma miRNA signature that may predict the risk of Post-LVAD stroke. The upregulation of neuron-derived miRNAs prior to a clinical event warrants further investigation as a predictive biomarker. If validated, this signature could lead to targeted prophylactic interventions and improve outcomes for LVAD patients.

Poster 44

THE IMPACT OF HEARTLOGIC ON HEART FAILURE EVENTS AND GUIDELINE-DIRECTED MEDICAL THERAPY IN THE VETERANS AFFAIRS HEALTH SYSTEM: A PRE-POST ANALYSIS

Aryan Rezvani[1], Miguel Garza[1], Jaiza Vanegas[2], Dzung Quach[2], Savitri Fedson[2], Steve Antoine[2]

[1]Internal Medicine, Baylor College of Medicine, Houston, TX; [2]Cardiology, Michael E. DeBakey Veterans Affairs Medical Center

Background:
HeartLogic is a multisensor algorithm that uses physiologic trends to calculate an index value to predict heart failure (HF) decompensation. A nurse practitioner-driven protocol using HeartLogic was instituted at a tertiary Veterans Affairs hospital in 2023. The protocol involved contacting patients with abnormal indices and adjusting their guideline-directed medical therapy (GDMT). The objective was to investigate the impact of remote monitoring on HF events (HFE) and GDMT.

Materials/Methods:
A retrospective chart review was performed. Fifty-one patients met inclusion criteria. The primary outcome was HFE – a composite of HF hospitalizations, emergency room visits, and unscheduled clinic visits. Secondary outcomes were GDMT scores (calculated with the modernized Heart Failure Collaboratory system); the proportion of patients on each GDMT pillar; and the number of patients reengaged in cardiology clinic after being lost to follow-up. Outcomes were compared one year before and after initiation of remote monitoring.

Results:
There was no significant difference in HFE (sign test, 11 events, $p=1$). Patients were more likely to have an improvement in their GDMT score on HeartLogic (sign test, 20 positive, 2 negative, $p<0.0005$). There was a higher likelihood that patients would be on mineralocorticoid receptor antagonists (MRA) (McNemar test, $p<0.05$) and sodium-glucose cotransporter-2 inhibitors (SGLT2i) ($p<0.05$) after intervention. There was a positive trend for β-blockers (McNemar test, $p=0.25$) and angiotensin neprilysin inhibitors ($p=0.13$), although not statistically conclusive. Thirty percent (15) of patients had previously been lost to follow-up; all of them were reengaged for ≥2 visits.

Conclusions:
There were no significant changes in the number of HFE. However, HeartLogic patients were more likely to have positive GDMT score changes. All patients previously lost to follow-up reestablished care. These findings suggest that HeartLogic is a promising tool for HF therapy optimization and patient engagement.

Poster 45

A QUALITATIVE STUDY OF HEALTH PRIORITIES AMONG HOSPITALIZED PATIENTS ADMITTED FOR HEART FAILURE

Shreya Tamma[1], Annika Bhananker[3], Jose Ramirez[1], Biykem Bozkurt[4], Elizabeth Schoenfeld[5], Adrian Haimovich[6], Kenneth Lam[7], Aanand Naik[3], Anita Chary[2]

[1]School of Medicine, Baylor College of Medicine; [2]Emergency Medicine, Baylor College of Medicine; [3]Center for Innovations in Quality, Effectiveness and Safety, Michael E. DeBakey VA Medical Center; [4]Medicine, Baylor College of Medicine; [5]Emergency Medicine, UMass Chan; [6]Emergency Medicine, Beth Israel Deaconess Medical Center; [7]Medicine-Geriatrics, University of Colorado Anschutz

Background:
As of 2025, the Centers for Medicare and Medicaid Services (CMS) require hospitals to elicit patients' goals of hospitalization under the Age-Friendly Health Systems initiative. Heart failure (HF), a leading cause of hospitalization and readmission among older adults, presents an opportunity to examine how patients articulate goals in acute care settings. Patient Priorities Care (PPC), an outpatient framework designed to align care with patients' values and health outcome goals, has not been applied to understand goal-setting during hospitalization. We explored how patients admitted for HF describe their goals for hospitalization and broader health outcome goals.
Materials/Methods:
We conducted semi-structured qualitative interviews with adults aged ≥50 admitted for HF at two academic hospitals. Participants had at least one HF admission in the prior year. Interviews, informed by the PPC framework, explored goals of hospitalization, health outcome goals, and prior experiences. Transcripts were analyzed using a mixed deductive-inductive thematic approach.
Results:
We interviewed 24 patients (mean age 68; 58% female). Three themes emerged. First, goals of hospitalization centered on acute symptom relief—particularly dyspnea, edema, and fatigue—with the primary aim of returning home. Second, health outcome goals reflected values of mobility, independence, and social connection, including the ability to work, care for family, and participate in community life. Third, participants described frustration with recurrent hospitalizations that provided temporary symptom improvement but failed to restore valued activities, contributing to resignation and diminished quality of life.
Conclusions:
For patients hospitalized with HF, immediate goals focus on symptom relief, while broader goals center on independence and meaningful activity. Goal elicitation in acute care should explicitly connect hospitalization to patients' longer-term values and realistic health trajectories to better support shared decision-making.

Poster 46

MITRAL REPAIR DURABILITY IS PRESERVED IN HERITABLE THORACIC AORTIC DISEASE PATIENTS AFTER CONCOMITANT MITRAL AND PROXIMAL AORTIC SURGERY

Stacey Chen[1], Susan Green[1], Veronica Glover[1], Subhasis Chatterjee[1], Joseph Coselli[1], Marc Moon[1]

[1]Cardiothoracic Surgery, Baylor College of Medicine, Houston, TX

Background:
Patients with heritable thoracic aortic disease (HTAD) often present with concomitant mitral valve (MV) and aortic pathology requiring complex surgery. It is unclear whether HTAD independently increases operative mortality or compromises MV repair durability. We evaluated outcomes following combined MV and proximal aortic surgery in patients with and without HTAD.
Materials/Methods:
We retrospectively studied patients undergoing proximal aortic replacement (root, ascending, or arch) with MV surgery at a high-volume aortic center from 1991–2025. HTAD was defined as documented heritable aortic disease or early-onset aortopathy requiring surgery before age 50, reflecting limited historical genetic testing. The primary endpoint was operative mortality defined as death ≤30 days or during the index hospitalization. Multivariable logistic regression evaluated the association between HTAD and operative mortality adjusting for age, arch replacement, and renal dysfunction. Secondary endpoints included MV repair failure and long-term survival.
Results:
A total of 126 patients underwent proximal aortic replacement with MV surgery, of whom 54 (43%) had HTAD. HTAD patients were younger (median age 44 versus 67 years, $p<0.001$) with fewer cardiovascular comorbidities. MV repair was performed in 74 (59%) patients and was favored over replacement in both HTAD and non-HTAD patients (52% versus 64%, $p=0.2$). Overall operative mortality was 18% (13% HTAD versus 21% non-HTAD, $p=0.3$). After multivariable adjustment, HTAD was not independently associated with operative mortality. Among operative survivors, MV repair failure was rare and occurred at similar rates in HTAD and non-HTAD patients (1.9% versus 1.4%, $p=0.8$). Long-term survival was also comparable between cohorts.
Conclusions:
Combined MV and proximal aortic surgery carries substantial risk. However, clinical outcomes appear to be driven primarily by operative complexity and comorbidities rather than connective tissue pathology.

Poster 47

MULTI-BIOBANK GENE-BASED RARE VARIANT BURDEN ANALYSIS IDENTIFIES NOVEL HIGH-RISK GENES FOR THORACIC AORTIC DISEASE

David R Murdock[1], Pujun Guan[1], Dongchuan Guo[1], Francisca Bermudez[2], John DePaolo[2], John Cabot[3], Sumaiya Nazeen[4], Habib Nasir[4], Rajat Gupta[5], Alok Jha[6], John Elefteriades[6], Bobbi McGivern[7], Kirsty McWalter[7], Samantha Anderson[8], Carolyn Jones[8], Scott Damrauer[2], Han Chen[9], Dianna Milewicz[1]

[1]Internal Medicine, Medical Genetics, The University of Texas Medical School at Houston, Houston, TX; [2]Surgery, University of Pennsylvania; [3]Surgery, Stanford University; [4]Biomedical Informatics, Harvard Medical School; [5]Cardiovascular Medicine, Harvard Medical School; [6]Surgery, Yale University School of Medicine; [7]GeneDx; [8]Pediatrics, Rush University; [9]Epidemiology, UTHealth Houston

Background:
Thoracic aortic disease (TAD) is a major cause of morbidity and mortality. Despite routine clinical genetic testing for suspected heritable TAD (HTAD), diagnostic yield remains low, leaving most patients without an identifiable pathogenic variant in known disease genes. We therefore applied genome-wide rare variant burden analyses across large biobanks to identify novel high-risk genes.
Materials/Methods:
We developed a scalable, genome-wide gene-based rare variant burden framework to detect ultrarare predicted damaging missense and loss-of-function (LOF) variants in constrained genes using large population-based biobanks. Discovery meta-analyses were performed in the UK Biobank and All of Us, followed by replication and meta-analysis across five biobanks using harmonized filtering and statistical approaches, with additional evaluation in independent TAD cohorts. Biological relevance was assessed using single-cell transcriptomic data from healthy and diseased human thoracic aortas.
Results:
In discovery analyses, 80 genes reached study-wide significance, conferring an average 25-fold increased risk for TAD and including most established HTAD genes. Meta-analysis across >10,000 TAD cases and 880,000 controls confirmed an excess burden of ultrarare variants in 14 genes (6 established and 8 novel), including FNDC3B, with effect sizes comparable to known HTAD genes. Seven genes remained study-wide significant in missense-only analyses. Single-cell transcriptomic data supported biologically relevant roles for implicated genes in aortic cell populations.
Conclusions:
Genome-wide gene-based rare variant burden analysis identifies ultrarare damaging variants in novel genes, including FNDC3B, that confer clinically actionable risk for TAD and expand its genetic architecture. This framework is broadly applicable to other cardiovascular diseases.

Poster 48

SEVERE OCULAR MANIFESTATIONS IN NEONATAL MARFAN SYNDROME: CASE SERIES AND LITERATURE REVIEW

Christopher M Spence[1], Emmanuel Chang[2], Taylor Beecroft-Dawson[1], Chandni Bhagtaney[1], Shaine Morris[1]

[1]Pediatric Cardiology, Baylor College of Medicine; [2]Ophthalmology, Baylor College of Medicine

Background:
Although rare, neonatal Marfan Syndrome (nMFS) is the most severe presentation of Marfan Syndrome (MFS) with cardiac and systemic manifestations present from birth. Cardiovascular manifestations are the primary contributors to the high rates of morbidity and mortality. With improved survival beyond the neonatal period, management of extra-cardiac manifestations, such as ocular disease, becomes increasingly important. Severe myopia, megalocornea, astigmatism, glaucoma, retinal detachment, microspherophakia, cataracts, and coloboma have been reported previously.

Materials/Methods:
We present two cases of nMFS with aniridia, coloboma, and congenital aphakia, not previously described.

Results:
1. 13-year-old female with nMFS with severe mitral valve prolapse (MVP) and regurgitation (MR), and aortic root dilation. Severe ocular disease was present from birth, including glaucoma. Ultrasound biomicroscopy (UBM) demonstrated minute iris stumps in keeping with aniridia. Crystalline lenses were never demonstrated on physical exam, ultrasound or MRI confirming congenital aphakia. Initial genetic panel sequencing was negative, but later whole genome sequencing confirmed a chromosome 15 deletion encompassing FBN1.
2. 21-month-old female with nMFS and severe MVP, MR, aortic root dilation, and tricuspid valve prolapse. Eye disease was noted in the neonatal period, including anterior segment dysgenesis with elevated intra-ocular pressure and corneal haziness. There was also right corneal edema, optic nerve coloboma, aniridia, and complete luxation of the lens into the mid-vitreous. Genetic testing revealed a likely mosaic multi-exon intragenic deletion of FBN1.

Conclusions:
As survival of patients with nMFS extends beyond the first few years of life, the recognition and management of the associated ocular conditions become paramount. Screening of all ocular segments and components should be carefully and regularly performed with consideration of early intervention to optimize vision and quality of life and minimize morbidity.

Poster 49

A BICUSPID AORTIC VALVE HYDROGEL MODEL OF VARIOUS AGE AND DISEASE RELATED STATES.

Nathan Almeida[1], Isha Murugesan[1], Eric Garcia Huitron[1], Jane Grande-Allen[1]

[1]Bioengineering, Rice University, Houston, TX

Background:
Bicuspid aortic valve (BAV) is the most common congenital heart disease impacting about 1-2% of the population. Typically, aortic valves contain 3 leaflets, but in BAV the aortic valve contains 2 often unevenly sized leaflets. This creates increased wall shear stress with downstream effects such as increased inflammation, fibrosis, and endothelial to mesenchymal transition (EndMT). This can alter endothelial cell behavior and contribute to diseases such as aortic aneurysms, endocarditis, and aortic valve stenosis. Several studies have been conducted showing the relationship between matrix stiffness and its contribution to EndMT and valvular diseases. However, these studies have not investigated how the stiffness of aortic valves at various stages of development or disease impact the development of this process. We hypothesize increasing matrix stiffness related to age and diseases related to BAV drives increased EndMT, inflammation and fibrosis in VECs.

Materials/Methods:
To investigate this hydrogels matching tissue relevant stiffnesses of 5, 25, 50, and 100 kPa will be created using PEGDA. These will then be functionalized using PEG-PQ, PEG-RGDS, and RKR. These gels will be created in transwells and VECs will be cultured on the top layer of them. Experimental groups will be stimulated with TGF-B to induce migration. Comparisons will also be made between degradable and non-degradable gels to determine if these impacts signaling. Soft hydrogels will be created with varying levels of collagen and hyaluronan to determine the effects of ECM composition on cell phenotype.

Results:
PEGDA hydrogels matching stiffnesses of 5, 25, 50, and 100 kPa have been successfully created. Soft hydrogels with varying ECM components have also been successfully created. Functionalized hydrogels at soft stiffnesses have been shown to support both cell adhesion and migration.

Conclusions:
PEG hydrogels are a viable model for the impact of cell stiffness and composition on VEC behavior. More work is needed to characterize these gels.

Poster 50

IDENTIFICATION AND CHARACTERIZATION OF CARDIAC ENHANCERS OF NOTCH1 IDENTIFIED FROM A CHD PATIENT COHORT

Andrea Wilderman[1], Keyang Yu[1], Haoquan Zhao[1], Shaine Morris[2], Aleksandar Milosavljevic[1], Lilei Zhang[1]

[1]Molecular and Human Genetics, Baylor College of Medicine, Houston, TX; [2]Pediatrics-Cardiology, Baylor College of Medicine

Background:
Congenital heart defects (CHD) affect approximately 1% of newborns, with most cases thought to have a genetic basis. Current methods for genetic analysis (whole exome sequencing, chromosomal microarrays and whole genome sequencing) have identified causal mutations for 45% of CHD cases. 90% of currently unexplained CHD cases are expected to have genetic causes, with the majority of variants appearing in non-coding sequences. Whereas the impact of coding variants can often be inferred from protein structure and function, translating non-coding variants into clinically interpretable effects remains challenging.

Materials/Methods:
Epigenetic signatures can act as indicators of enhancer function but must be confirmed experimentally. We present the initial steps in a platform to identify putative cardiac enhancers that contain CHD patient mutations and assign specific cardiac function to the enhancer and variant. Screening a cohort of 1,844 CHD patients, we identified de novo non-coding variants in putative cardiac enhancer regions proximal to NOTCH1. These regions are predicted to interact with the NOTCH1 promoter and bear enhancer epigenetic signatures in human adult and embryonic cardiac tissue. While mutations in the NOTCH1 gene are associated with structural heart defects including severe defects like hypoplastic left heart syndrome (HLHS) and tetralogy of Fallot (TOF), no cardiac enhancers in human or mouse have been experimentally validated.

Results:
Deletion of a 600bp putative cardiac enhancer does not impede differentiation to cardiomyocytes (CM) and gene expression indicates a shift in CM differentiation away from ventricular type towards atrial type, similar to a published model of NOTCH1 gene KO.

Conclusions:
Together with characterizing the effects of patient variants we will advance our ability to predict the effects of non-coding variants for CHD in NOTCH1 and enable future high-throughput screening of the full spectrum of CHD-associated non-coding variants.

Poster 51

TARGETING INTEGRIN SIGNALING IN ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD)

John W Craft[1], Amy Caivano[2], Anna Kazansky[3], Shahrzad Abbasi[2], Reiko Chamberlain[2], Qian Xiang[2], Anuj Kurella[1], Elizabeth Merlinskey[1], Yi Zhao[2], Frederick Meece[2], Darren Woodside[2]

[1]Biology and Biochemistry, University of Houston, Houston, TX; [2]The Texas Heart Institute at Baylor College of Medicine, Baylor College of Medicine

Background:
Cardiovascular disease remains the leading cause of death, worldwide. The most common underlying cause of ischemic heart disease and stroke is atherosclerosis. Recent clinical studies have demonstrated that atherosclerosis is an inflammatory disease, and that targeting mechanisms of inflammation can reduce major adverse cardiac events independent of lipid lowering.

Materials/Methods:
Here we describe a drug discovery program designed to address residual inflammatory risk in patients with ASCVD. Inflammatory cells like activated monocytes and macrophage are a significant source of pro-inflammatory cytokines, such as IL-1β, in ASCVD. In monocytes, integrin cell adhesion molecule signaling via the tyrosine kinase Syk is a very early event leading to expression of IL-1β. This occurs through the direct interaction between integrin β-chain cytoplasmic domains and the tandem SH2 domains of Syk. To identify regulators of the integrin/Syk signaling axis, a structure-based computational screen of over 15 million compounds was performed to identify small molecules that may bind to Syk SH2 domains and inhibit integrin signaling.

Results:
From this virtual screen, >1000 compounds were identified with favorable pseudo ΔGs, and were clustered into five major families based on functional group similarity scoring. A prevalent number of compounds were predicted to interact with SYK ARG45 and GLU242 along a proposed locus of interface residues. Current lead compounds demonstrate inhibition of integrin-dependent phosphorylation of Syk, monocyte chemotaxis, and integrin-dependent expression of pro-inflammatory cytokines like IL-1β and MCP-1. Our most active lead, from a medicinal chemistry campaign that has tested over 400 compounds, demonstrated an IC50 of 6.8 ± 3.5 nM in integrin signaling assays.

Conclusions:
The Integrin/Syk signaling axis is amenable to regulation by small molecules. Future work will involve improving drug-like characteristics of leads and testing in animal models of acute inflammation and atherosclerosis.

Poster 52

TARGETING CTLA-4 WITH SMALL MOLECULES TO MODULATE T-CELL RESPONSES IN CARDIOVASCULAR INJURY

Zaniqua N Bullock[1], William Decker[1], Damian Young[1]

[1]Pathology & Immunology, Baylor College of Medicine, [2]Biochemistry & Molecular Pharmacology, Baylor College of Medicine, Houston, TX

Background: T-cell activation plays a critical role in the fibrotic and inflammatory responses following cardiovascular injury. CTLA-4, a key T cell inhibitory receptor, has been implicated in modulating post-injury immune responses, with its dysregulation contributing to maladaptive fibrosis and chronic inflammation. While antibody-based immune checkpoint inhibitors for CTLA-4 have been extensively explored in oncology, their application in cardiovascular disease remains under investigated. In addition, antibody-based CTLA-4 inhibitors carry significant risks, including systemic toxicities. To develop a safer and more precise therapeutic approach, we aimed to identify small-molecules that could modulate T-cell activation in a controlled manner via CTLA-4 interaction.

Materials/Methods: We expressed and purified the extracellular domains of CTLA-4 and its ligands, CD86 and CD80, in human cells. The stability and functionality of these proteins were confirmed via dendritic cell binding assays and thermal shift analyses. To identify potential small-molecule modulators, we utilized a DNA-encoded library (DEL) comprising over four billion unique compounds. Candidate molecules were synthesized through a multi-step process involving repeated purification and rigorous structural validation to confirm their purity and identity. Biophysical assays were conducted to assess the binding interactions of these compounds with CTLA-4, CD80, and their complex.

Results: Enrichment analysis revealed a subset of compounds preferentially enriched in the presence of the protein complex. Selected compounds were synthesized off DNA and evaluated using biophysical assays. Binary binding analysis demonstrated weak binding to CTLA-4 (~84 μM) and CD80 (~250 μM). The truncated analog, Z2T1, exhibited improved binding to both CTLA-4 (~24 μM) and CD80 (~96 μM). Although the screen was designed with the purpose of identifying competitive inhibitors, Time-Resolved Fluorescence Resonance Energy Transfer (TR FRET) analysis demonstrated that Z2 and selected analogs enhanced CD80–CTLA-4 proximity by ~20% and reduced the activity of a known inhibitor by ~30%, consistent with glue like stabilization rather than competitive inhibition.

Conclusions: These findings underscore the potential of small-molecule checkpoint modulators as novel therapeutic agents for cardiovascular disease.

Poster 53

THE ROLE OF A DOMAIN OF VON WILLEBRAND FACTOR IN INFLAMMATION DURING RHEUMATOID ARTHRITIS

Jorie D Fleischman[1], Stephanie Rivera[1], Miguel Cruz[1], Nick Elston[1], Madilyn Brandt[1], Lauren Snyder[1], Joel Yearick[1], Robia Pautler[1], Jenna Nimri[2], Sandeep Agarwal[2], Christine Beeton[1]

[1]Integrative Physiology, Baylor College of Medicine, Houston, TX; [2]Medicine, Baylor College of Medicine, Houston, TX

Background:
Rheumatoid arthritis (RA) is one of the most common autoimmune diseases, affecting 18 million people worldwide as of 2019. This disease occurs when immune cells attack the lining of the joints and cause joint damage and systemic inflammation that increases thrombosis and can lead to major cardiovascular events such as myocardial infarction and stroke. Current therapeutics for RA are immunosuppressive and/or include the risk of cardiovascular complications. The recombinant A2 domain of the blood-clotting protein von Willebrand Factor (VWF) has recently been shown to reduce thrombosis without causing bleeding in mouse models with coagulopathies.

Materials/Methods:
I will identify the effects of A2 on the function of T cells and the efficacy of using A2 as a treatment for rodent models of arthritis.

Results:
I have preliminary data demonstrating that rats with the pristane-induced arthritis model of RA treated with the A2 protein have both reduced blood clots and reduced disease severity. Under further investigation, I found that treatment with A2 inhibits the proliferation of human T cells in vitro. These cells are central to the pathogenesis of RA by recognizing autoantigens and producing pro-inflammatory cytokines. I hypothesize that the recombinant A2 domain of von Willebrand Factor reduces inflammation by modulating the pathogenic functions of T cells in RA while also decreasing thrombosis.

Conclusions:
Experiments uncovering the effects of the A2 protein on T cells and rodent models of RA are highly significant for finding a therapeutic that reduces both inflammation and thrombosis to help the millions of patients with this debilitating disease.

Poster 54

DEVELOPING DISEASE-TARGETED ANTI-ANGIOGENIC THERAPY AGAINST THROMBOSPONDIN-4 VIA LIGANDOMICS.

Avinash Kaur[1], Chengchi Huang[1], Prabuddha Waduge[1], Liyang Ji[1], Chang Dai[1], Bojun Zhang[1], Elizabeth Zuniga-Sanchez[1], Hong Tian[2], Keith A Webster[1] Wei Li[1]

[1]Ophthalmology, Baylor College of Medicine, TX; [2]LLC, Everglades Biopharma

Background:
Disease-targeted anti-angiogenic therapy is a highly desirable strategy for treating neovascular disorders with improved safety; however, no approved therapy currently offers selective suppression of pathological angiogenesis. This study aims to develop a novel therapeutic approach that specifically targets disease-specific vasculature.
Materials/Methods:
Comparative ligandomics profiling in mouse models of diabetic retinopathy (DR) and choroidal neovascularization (CNV) identified thrombospondin-4 (THBS4/TSP-4) as a disease-restricted endothelial ligand. THBS4 was independently validated as a disease-selective angiogenic factor using in vivo ligand binding (IVLB), functional immunohistochemistry (FIHC), and therapy-first validation assays. IVLB mapping of its disease-specific receptor-binding domain guided the development of THBS4-neutralizing monoclonal antibodies (mAbs), which were evaluated for therapeutic efficacy in DR, CNV, and oxygen-induced retinopathy (OIR) models.
Results:
IVLB and FIHC demonstrated selective THBS4 binding to diseased, but not healthy, vasculature across all models. Therapy-first validation confirmed THBS4 as a disease-specific angiogenic driver. Mapping of the disease-relevant receptor-binding domain enabled generation of neutralizing anti-THBS4 mAbs. These mAbs significantly reduced pathological angiogenesis in CNV mice and decreased vascular leakage in DR mice. In neonatal OIR mice, anti-THBS4 mAbs selectively inhibited pathological neovascularization while sparing physiological angiogenesis, demonstrating high disease-targeting specificity.
Conclusions:
The anti-THBS4 mAbs developed in this study represent promising candidates for clinically translatable, disease-targeted anti-angiogenic therapy for ocular vascular diseases. More broadly, these findings highlight comparative ligandomics as a powerful platform for discovering disease-restricted ligands and advancing disease-targeted therapeutic development.

Poster 55

VASCULAR SMOOTH MUSCLE CELLS-SPECIFIC ADENOSINE KINASE DEFICIENCY ATTENUATES VASCULAR CALCIFICATION THROUGH HISTONE METHYLATION–DEPENDENT EPIGENETIC REPROGRAMMING

Dingwei Zhao[1], Qian Ma[1], Yongfeng Cai[1], Shengnan Mou[1], Yuqing Huo[1]

[1]Ophthalmology, Baylor College of Medicine, Houston, TX

Background:
Vascular calcification (VC) is a prevalent and clinically consequential complication of chronic kidney disease, diabetes, aging, and atherosclerosis, and a major contributor to cardiovascular morbidity and mortality. VC is an active, cell-driven process dominated by osteogenic trans-differentiation of vascular smooth muscle cells (VSMCs). Adenosine kinase (ADK), a key phosphotransferase, converts adenosine into AMP, which is highly expressed in vascular cells and has been linked to human coronary artery calcification, but whether ADK causally drives VSMC osteogenic switching and VC—and thus represents a tractable therapeutic target—remains unknown.
Materials/Methods:
VSMCs and mouse aortic rings were cultured in osteogenic medium to establish in vitro and ex vivo models. VC in mice was induced by a vitamin D3 (VD3) injection model. The effects of ADK on vascular calcification were evaluated by calcium deposition, alkaline phosphatase (ALPL) activity, and changes in osteogenic markers and vascular phenotypic markers.
Results:
ADK expression was significantly upregulated in calcified murine aortic tissues and in VSMCs under osteogenic conditions. Genetic deletion of Adk (global or VSMC-specific) markedly attenuated aortic calcification and osteogenic marker expression in vivo. Consistent findings were observed in in vitro and ex vivo models. Mechanistically, ADK promoted VSMC osteogenic differentiation by enhancing transmethylation and H3K4me3-mediated epigenetic reprogramming, thereby increasing ALPL activity and promoting subsequent mineralization. Conversely, ADK inactivation mitigates VSMC osteogenic differentiation and aortic calcification by downregulating histone methylation.
Conclusions:
In summary, our study employed a comprehensive set of in vitro, ex vivo, and in vivo VC models and demonstrated that ADK inhibition suppresses vascular osteogenesis and subsequent VC by reducing methyltransferase reactions. Thus, our findings support ADK as a potential therapeutic strategy for treating VC.

Poster 56

A CIRCADIAN LNCRNA CIRCA GATES MI RECOVERY BY MODULATING HNRNPA1–RPA–R-LOOP DYNAMICS

Yuanbiao Zhao[1], Chih-Liang Tien[1], Lei Qi[1], Hui Li[1,] Andrea Graves[1], Muge Kuyumcu-Martinez[3], David Mitchell[2], Anne Caitlin Starner[2], Eric Lyman Van Nostrand[2], Anthony McDowell Mustoe[2], Zhishi Chen[4] Jiang Chang[4], Lilei Zhang[1]

[1]Molecular and Human Genetics, Baylor College of Medicine, Houston, TX; [2]Biochemistry and Molecular Biology, Baylor College of Medicine; [3]Molecular Physiology and Biological Physics, University of Virginia School of Medicine; [4]Institute of Biosciences and Technology, Texas A&M University Health Science Center

Background:
Disruption of circadian rhythm is associated with cardiovascular diseases, but the exact molecular mechanism remains elusive.
Materials/Methods:
Via transcriptional profiling of murine hearts, we discovered a cardiac-specific circadian lncRNA Circa, which is uniquely expressed in the cardiomyocytes (CM) of the adult mouse heart. Circa expression is increased postnatally and diminished after stress such as myocardial infarction (MI). Circa null mice exhibit exaggerated infarct and reduce cardiac function after MI. Ectopic expression of Circa reversed the exaggerated MI phenotype in Circa null mice and improved the post-MI recovery of the wildtype animal from HF development.
Results:
Mechanistically, we found that Circa is primarily localized in the nuclei where it associates with chromatin and RNA binding proteins, including hnRNPA1(A1). Under hypoxia, there is increased A1 translocation to the cytosol, which leads to a concomitant increased cytosolic export and degradation of Circa. The nuclear Circa is critical in reducing the hypoxia stress induced R-loop structure, R-loop associated RPA foci and DNA damage formation (both DSB/SSB) by reducing the A1 and RPA interaction. The down-regulated R-Loop and RPA signal in the MI border zone by Circa is associated with less DNA damage and less sustained immune cell infiltration during the recovery stage, which may limit infarct expansion.
Conclusions:
In conclusion, our study suggests that LncRNA Circa may regulate DNA damage response and reduce the immunogenic signaling produced from the R-loop structure to down-regulate inflammation level and enhance the ability of the heart to recover from the MI induced damage.

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MITRAL ANNULAR DISJUNCTION IS ASSOCIATED WITH MARKERS OF CARDIOMYOPATHY IN PEDIATRIC MARFAN SYNDROME.

Khanh-Linh K Doan[1], Tam Doan[1], Ricardo Pignatelli[1]

[1]Cardiology, Texas Children's Hospital, Houston, TX

Background:
Cardiomyopathy in pediatric Marfan syndrome (MFS) is defined as left ventricular (LV) dilation and dysfunction independent of volume loading. Mitral annular disjunction (MAD) is linked to adverse outcomes in pediatric MFS. We examined whether MAD was associated with LV dilation and systolic dysfunction in children with MFS.
Materials/Methods:
In this retrospective cross-sectional study, we included patients age 1 to <21 years with MFS (2010 Ghent criteria plus a pathogenic FBN1 variant or ectopia lentis). On the initial echocardiogram, LV end-diastolic and end-systolic volumes (LVEDV, LVESV) and ejection fraction (LVEF) were measured by the 5/6 area-length method; indexed values and Boston Z scores were derived (dilation: Z≥+2) and abnormal LVEF as <55%. MAD was defined as LV-mitral valve separation ≥2 mm. Mitral and aortic regurgitation were graded (0-5) and summed. Analyses of LV size/function excluding patients with ≥moderate combined regurgitation to minimize volume loading.
Results:
Among 152 patients with MFS (median age 11.1 years), MAD was present in 93 (61%). Age and sex were similar between groups. Combined regurgitation ≥moderate was more frequent with MAD (10.8% vs 0%, p=0.007). After excluding 10 patients with ≥moderate combined regurgitation (all with MAD), MAD patients (83/142) remained with higher LVEDV index (79.4 mL/m² vs 76.4, p=0.025) and Z score (0.8 vs 0.1, p<0.001), higher LVESV index (32.3 mL/m² vs 26.1, p=0.002) and Z score (1.4 vs 0.1, p<0.001), and lower LVEF (59% vs 62%, p=0.016). LVESV Z score ≥+2 was more common with MAD (24.7% (20/81) vs 3.7% (2/54), p=0.001). While LVEDV Z≥+2 and LVEF <55% were higher among MAD, they did not reach statistical significance (17.3% vs 7.4%, p=0.214 and 16.9% vs 8.5%, p=0.148, respectively).
Conclusions:
In pediatric MFS without significant valve-related volume loading, MAD is associated with larger LV volumes and lower ejection fraction, suggesting an early cardiomyopathy phenotype.

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MIDWALL LATE GADOLINIUM ENHANCEMENT PREDICTS ADVERSE OUTCOMES IN PEDIATRIC MYOCARDITIS

Alexandra Dennee[1], Alexander Kiener[2], Hanna Tadros[2], Tam Doan[2]

[1]Pediatric Cardiology, Other; [2]Pediatric Cardiology, Baylor College of Medicine/Texas Children's Hospital

Background:
Pediatric acute myocarditis is associated with variable recovery and risk of adverse cardiac outcomes. Late gadolinium enhancement (LGE) detected by cardiac magnetic resonance (CMR) plays an important diagnostic role, but the prognostic significance of specific LGE patterns in children remains uncertain. Purpose: To evaluate whether midwall LGE on early CMR is associated with long-term adverse outcomes in pediatric myocarditis.
Materials/Methods:
A retrospective cohort study was conducted, including patients <21 years old with myocarditis determined by Lake Louise criteria on CMR performed within 30 days of clinical diagnosis. Midwall LGE was defined as mid-myocardial LGE on visual assessment. A composite adverse endpoint was defined as the diagnosis of dilated cardiomyopathy (DCM), arrhythmogenic cardiomyopathy (ACM), or recurrent myocarditis. Associations between Midwall LGE and adverse outcomes were evaluated using univariate Cox proportional hazards regression. Event-free survival was assessed using Kaplan–Meier analysis (time 0 = date of diagnosis) with log-rank testing.
Results:
A total of 81 patients met inclusion criteria with the initial CMR performed at a median age of 14.8 years (IQR 11.8-16.6), and 23 (28%) were female. Midwall LGE was present in 25 patients (31%). Over a median follow-up period of 2.2 years (IQR 0.7-4.3), 14 patients (17%) experienced a composite adverse endpoint, including DCM (n=6; 1 death), ACM (n=6; 2 heart transplants), and recurrent myocarditis (n=2). This occurred more frequently among patients with Midwall LGE (32% vs 11%, p=0.03). Event-free survival was lower among patients with Midwall LGE with a nearly threefold increased hazard of adverse outcome (HR 2.9, 95% CI 1.0-8.4, p=0.047).
Conclusions:
In pediatric CMR-confirmed myocarditis, Midwall LGE on early CMR is associated with an increased risk of adverse outcomes. Initial CMR findings may provide prognostic value and aid risk stratification.

Poster 59

CALCIPROTEIN PARTICLES INDUCE ENDOTHELIAL MITOCHONDRIAL DYSFUNCTION AND AVF MATURATION FAILURE IN CKD

Owen H Cheng[1], Tae Hoon Lee[1], Qingtian Li[1], David Sheikh-Hamad[1], Eric Peden[2], Jizhong Cheng[1],

[1]Selzman Institute for Kidney Health, Section of Nephrology, Medicine, Baylor College of Medicine, Houston, TX; [2]Surgery, Houston Methodist Hospital

Background:
Chronic kidney disease (CKD) is a long-term condition where the kidneys cannot properly filter waste. Patients with end-stage renal disease (ESRD) often require hemodialysis through an arteriovenous fistula (AVF), though many factors undermine AVF maturation and function. Calciprotein particles (CPPs), which are present at elevated levels in ESRD patients, may contribute to this failure, though their role in AVF dysfunction remains unclear.

Materials/Methods:
In this study, we created a mouse CKD model with elevated CPP levels and examined AVF remodeling in CKD mice and mice treated with synthesized CPPs, while investigating the mechanisms underlying CPP-induced AVF dysfunction.

Results:
In ESRD patient serum, we detected larger CPP sizes and shortened CPP2 formation time, both associated with AVF maturation failure. Similarly, CKD mice showed increased CPP2 formation relative to sham controls. AVFs in CKD mice displayed neointimal calcification, increased RUNX2, and decreased α-SMA expression, indicating vascular smooth muscle cell dedifferentiation into osteoblast-like cells. Mice treated with synthesized CPPs also showed delayed endothelial regeneration and neointimal calcification. Mechanistically, CPPs impair endothelial integrity by inducing mitochondrial superoxide accumulation and mitochondrial dysfunction. Immunofluorescence showed elevated 4-HNE levels, indicating lipid peroxidation, and increased MitoSOX signals reflecting mitochondrial superoxide production. Mitochondria in CPP-treated cells appeared smaller and fragmented, consistent with mitochondrial fission. Seahorse XF assays showed reduced mitochondrial respiration and ATP production. CPP exposure also suppressed EC migration and reduced expression of junction proteins VE-cadherin and Occludin.

Conclusions:
These CPP-induced abnormalities impair EC function, enhance CPP deposition in AVFs, promote neointima formation, and ultimately contribute to AVF failure, thereby increasing mortality risk for ESRD patients undergoing dialysis.

Poster 60

Adipocyte NPC1 regulates cholesterol homeostasis and systemic glucose metabolism

Hua Mao[1], Saima Shakil[1], Bing Sun[1], Liang Xie[1], Sean Hartig[1], Pandit Lavannya[3], Xinchun Pi[1]

[1]Medicine, Baylor College of Medicine, Manvel, TX; [2]Pulmonary, Critical Care, Sleep Section, BCM

Background:
Niemann–Pick type C1 (NPC1) is a lysosomal membrane protein essential for intracellular cholesterol trafficking. Mutations in NPC1 cause Niemann–Pick disease type C, a fatal lysosomal storage disorder characterized by cholesterol accumulation and progressive neurodegeneration. Although NPC1-mediated cholesterol transport has been extensively studied in neurons and hepatocytes, its physiological role in adipose tissue remains poorly understood.

Materials/Methods:
Here we generated adipose-specific NPC1 knockout mice (NPC1-AdiKO) using Adipose-Cre+ to investigate the role of NPC1 in adipocyte lipid homeostasis and systemic metabolic regulation.

Results:
Male adipose-specific NPC1 knockout mice displayed significantly increased body weight, adipose weight (Inguinal and epididymal white adipose tissue) compared with littermate controls and exhibited pronounced glucose intolerance and insulin resistance. Hyperinsulinemic-euglycemic clamp studies revealed profound metabolic abnormalities in NPC1-AdiKO mice, including increased basal glucose production, reduced glucose infusion rate, and decreased glucose disposal rate, indicating systemic insulin resistance. In contrast, hepatic glucose production was not significantly altered. Importantly, glucose metabolism in white adipose tissue was significantly impaired, suggesting that adipose tissue dysfunction contributes to the observed metabolic phenotype.

Conclusions:
Together, these findings identify adipose NPC1 as a critical regulator of cholesterol homeostasis and systemic glucose metabolism, revealing a previously unrecognized role for lysosomal cholesterol trafficking in adipose tissue insulin sensitivity. Loss of NPC1 in adipose tissue promotes obesity and systemic insulin resistance, potentially through lysosomal cholesterol accumulation, impaired autophagy-lysosomal function, and disruption of lipid handling pathways.

Poster 61

NOTCH2 REGULATES NUCLEAR DYNAMICS IN CARDIOMYOCYTES PROMOTING A HYPERTROPHIC CARDIOMYOCYTE STATE

Wyatt G. Paltzer[1], Jeffrey Steimle[2], Jong Kim[1], Nathan Giang[1], Elizabeth Straight[3], Yuka Morikawa[3], James Martin[1]

[1]Integrative Physiology, Baylor College of Medicine, Houston, TX; [2]Molecular Cardiovascular Biology, Cincinnati Children's Hospital Medical Center; [3]Cardiomyocyte Renewal Laboratory, Texas Heart Institute

Background:

Previous studies have focused on the mechanisms driving cardiomyocyte proliferation, however, the biological mechanisms that act as barrier to entry for cardiomyocyte proliferation remain under characterized.

Materials/Methods:

To identify potential pathways inhibiting cardiomyocyte proliferative potential, we drove a proliferative cardiomyocyte state using YAP5SA (a continuously active form a Yap1, previously demonstrated to promote proliferation). Using single nuclei RNAseq (snRNAseq), we then examined proliferative and non-proliferative cardiomyocytes.

Results:

Finding that non-proliferative cardiomyocytes were defined by high Notch transcriptional activity, with all cardiomyocytes exhibiting higher levels of Notch2 compared to other Notch receptors. To determine whether Notch activity can promote cardiomyocyte maturation, we overexpressed Notch2 intracellular domain (N2ICD) in cardiomyocytes via AAV9 in postnatal mice. We observed that N2ICD increased the number of cardiomyocytes in M-phase while also increasing binucleation state. Furthermore, N2ICD increased the individual ploidy count of cardiomyocyte nuclei, observing reduced 2n and higher 4n, 8n, and high n nuclei populations in N2ICD treated hearts compared to controls. To examine how these changes in nuclear and ploidy number impacted cardiomyocyte state, we conducted snRNAseq on N2ICD and control hearts. In the snRNAseq data, we found an N2ICD exclusive cardiomyocyte subcluster that was elevated in Notch targets and known hypertrophic markers such as Slit3. To examine how this N2ICD specific cardiomyocyte state impacts the local microenvironment, we conducted Xenium spatial transcriptomic analysis comparing N2ICD and control treated mice.

Conclusions:

We demonstrated that Notch activity regulates cardiomyocyte nuclear dynamics facilitating a pro-hypertophic cardiomyocyte and surrounding microenvironment state.

Poster 62

COMBINATORIAL GENE THERAPY COMPLETELY RECOVERS THE CARDIAC FUNCTIONS AFTER MYOCARDIAL INFARCTION

Abou Bakr M. Salama[1], Kamal Abou Farraj[1], Sara Taha Taha[1], Rebecca Liu[1], Pretty Rose Mathew[1], Joern Huelsmann[2], Riham Abouleisa[1], Todd Rosengart1, Tamer MA Mohamed[1]

[1]Surgery, Baylor College of Medicine

Background:
Ischemic heart failure is driven by irreversible cardiomyocyte loss, fibrotic scar formation, and impaired perfusion. Single-pathway regenerative strategies have yielded limited functional recovery. We evaluated a first-in-class combinatorial gene therapy that simultaneously induces cardiomyocyte proliferation, reprograms resident cardiac fibroblasts, and promotes angiogenesis, and report the results of phase 1 preclinical testing in rats.
Materials/Methods:
Adult rats underwent myocardial infarction via left anterior descending coronary artery ligation and received intramyocardial injection of a triple gene therapy cocktail or control vectors either acutely (at infarction) or subacutely (7 days post-MI). Cardiac function was serially assessed by echocardiography over 3 months. Myocardial scar size was quantified using Masson's trichrome staining. Safety was evaluated by serum toxicity and oncogenic markers, along with assessment of viral gene expression in remote organs.
Results:
In the acute setting, triple therapy resulted in complete recovery of systolic function, with ejection fraction comparable to non-infarcted myocardium (EF 63.9 ± 7.7% vs 33.1 ± 6.0% in controls; $p < 0.0001$; $n = 8–10$/group) and minimal residual scar. In the subacute setting, treatment normalized systolic function (EF 58.0 ± 7.3% vs 29.8 ± 5.8%; $p < 0.0001$) and significantly reduced scar size. Left ventricular remodeling indices showed concordant improvement. No evidence of systemic toxicity, organ dysfunction, carcinogenesis, or off-target viral expression was observed.
Conclusions:
Combinatorial regenerative gene therapy enables robust functional recovery and scar reduction after myocardial infarction without detectable safety concerns. These results establish a strong translational foundation for advancement to large-animal studies and clinical development.

Poster 63

YAP Activation in Cardiomyocytes Orchestrates a Regenerative Niche by Limiting Fibrosis and Expanding the Lymphatic Vasculature

Chang-Ru Tsai[1], Xin Wang[2], Yuka Morikawa[3], Bing Xie[1], Rich Gang Li[3], Lin Liu[3], Hanna J Tadros[4], Yi Zhao[3], Elizabeth Straight[1], Mohamed Shehata[6], Andrew Switala[6], Rita Schack[1], Ayman El-Baz[6], Robia Pautler[1], Xiao Li[2], James Martin[1]

[1]Integrative Physiology, Baylor College of Medicine, Houston, TX; [2]Molecular and Human Genetics, Baylor College of Medicine; [3]The Texas Heart Institute, Baylor College of Medicine; [4]Division of Pediatric Cardiology, Texas Children's Hospital; [5]Bioengineering, University of Louisville

Background:
Ischemic heart failure (iHF) involves irreversible remodeling, microvascular rarefaction, and a stiff extracellular matrix (ECM) that often resists conventional revascularization. We previously showed that cardiomyocyte (CM)-specific deletion of the Hippo component Sav1 promotes cardiac recovery. This study investigates the non-cell-autonomous mechanisms—specifically crosstalk with fibroblasts (FBs) and lymphatic endothelial cells (LECs)—driving this regeneration.

Materials/Methods:
Sav1 was deleted in cardiomyocyte (Sav1CKO) in mice three weeks post-myocardial infarction (MI). Cardiac recovery was assessed via cardiac magnetic resonance imaging and echocardiography. We employed single-nucleus RNA sequencing (snRNA-seq), single-nucleus assay for transposase-accessible chromatin sequencing (snATAC-seq), and spatial transcriptomics (ST) at 6 and 9 weeks post-MI, alongside ligand-receptor analysis and VEGFR3 immunofluorescence to profile the myocardial microenvironment.

Results:
Sav1CKO hearts showed reduced end-systolic/diastolic volumes and improved ejection fraction. YAP activation in CMs restored oxidative phosphorylation and contractile gene expression while reducing stress markers (Nppa, Nppb). ST revealed that Sav1 deletion restricted the expansion of highly fibrotic FBs (FB1: Hif1a^{+}, Col11a1^{+}) in the border zone, shifting the landscape toward a pro-reparative/resting state (FB6: Inmt^{+}, C3^{+}). Furthermore, Sav1CKO hearts exhibited a significant expansion of LEC in the ischemic zone. This enhanced lymphangiogenesis correlated with functional recovery and was likely driven by CM-derived signals including Wnt5b, Vegfa, and Angpt1.

Conclusions:
YAP activation in CMs orchestrates a coordinated reparative program that extends beyond myocyte-specific renewal. By suppressing the expansion of fibrotic fibroblast states and inducing lymphangiogenesis, Sav1-deleted cardiomyocytes non-cell-autonomously remodel the chronic ischemic microenvironment to drive heart regeneration.

Poster 64

OPTOGENETIC MAPPING OF EMBRYONIC CARDIAC PACEMAKER CELLS

Guzel Musina[1], Nanbing Jade Li-Villarreal[2], Deirdre Scully[3], Andrew Lopez III[1], Irina Larina[2]

[1]Biomedical Engineering, University of Houston, Houston, TX; [2]Integrative Physiology, Baylor College of Medicine; [3]Reproductive Biology, Case Western Reserve University

Background:
Congenital heart defects (CHD) affect over 1% of newborns and remain a major health challenge. To improve CHD management, it is crucial to understand how molecular, genetic, mechanical, and electrical processes interact during early development. While genetic and molecular factors governing heart development and disease have been extensively studied, the role of the early heartbeat and conduction is less understood due to the lack of tools for imaging and controlling cardiodynamics in mouse embryos. Therefore, we are developing a novel optogenetic platform to control cardiodynamics and map pacemaker regions ex vivo in real time.

Materials/Methods:
We generated mouse embryos to ubiquitously express ChR2 and eNpHR3.0 in all cells through CMV-cre cross. Embryos, at embryonic day 8.5, were imaged in static culture with a color camera under controlled conditions. For optogenetic stimulation, 473 nm and 594 nm lasers were used.

Results:
Efficient optogenetic pacing of embryonic hearts was achieved using both continuous wave and pulsed light stimulation techniques. The cardiac responses varied by region and were influenced by the intensity of the light used. We defined a range of parameters for real-time functional identification of embryonic cardiac pacemakers and implemented automated scanning for spatial mapping of pacemaker regions. Using this technique, we mapped pacemaker clusters within embryonic hearts across developmental stages.

Conclusions:
This study establishes a platform for investigating conduction system development and the interplay of electrical, mechanical, and structural factors during cardiogenesis under both normal and pathological conditions. Ultimately, it may contribute to a deeper understanding of the mechanisms underlying CHDs.

Poster 65

Frequency and Diagnostic Yield of Genetic Testing in Patients with Ebstein Anomaly

Shelby Walcott[1], Abigail Yesso[2], Emily Soludczyk[2], Taylor Beecroft-Dawson[2], Hanna J. Tadros[2], Shaine Morris[2]

[1]Pediatrics, Other; [2]Division of Pediatric Cardiology, Texas Children's Hospital and Baylor College of Medicine

Background:
Ebstein anomaly is a rare congenital heart defect (CHD) associated with variants in the MYH7, NKX2.5, and TPM1 genes, among others. While chromosomal microarray (CMA) is widely considered the first-line genetic test for patients with CHD, its usefulness in Ebstein anomaly is unclear. A better understanding of the genetic basis of Ebstein anomaly is needed to guide optimal test selection.

Materials/Methods:
In total, 302 patients with Ebstein anomaly were identified by the echocardiographic database at Texas Children's Hospital from 2010-2025. 37 had congenitally corrected transposition of the great arteries (ccTGA). Genetic test results were analyzed including CMA, whole exome and whole genome sequencing (WES, WGS), karyotype, fluorescence in situ hybridization (FISH), and gene panels.

Results:
Of 92 patients (7 of which had ccTGA) who underwent genetic testing, a diagnosis was found in 19 (20.7%). CMA was performed in 70 patients, with a diagnostic yield (apart from detecting aneuploidy) of 5.7% (4/70: 1p36 deletion syndrome, n=2; 22q11.2 duplication syndrome, n=1; 3q29 deletion syndrome, n=1). The most common diagnosis was Trisomy 21 (n=4, 4.3%). The only other aneuploidy was Turner syndrome (n=1, 1.1%). Although gene sequencing was performed in a minority (WES: 10.9%, n=10; WGS: 8.7%, n=8; Panels: 20.7%, n=19), it had the highest yield (11/37, 29.7%) with most single gene variants isolated in cardiomyopathy and cardiac development genes (MYH7 n=2 and 1 each in TPM1, PKP2, TNNT2, EPHB4, NKX2.5, CHD7, NODAL, MED13L). Identical variants were found in 2 unrelated children (MYH7 c.698C>T, p.Ala233Val). Of those with ccTGA, 1/7 (14%) had diagnostic testing (NODAL variant).

Conclusions:
In our cohort, CMA was the most common genetic test performed but had much lower yield than gene sequencing, suggesting that evaluating for both copy number variants and single gene variants should be standard for patients with Ebstein anomaly. The most common genetic findings were Trisomy 21 and variants in cardiomyopathy genes.

Poster 66

NEUTROPHIL-DERIVED MIR-223 ATTENUATES CARDIAC INJURY BY SUPPRESSING ENDOTHELIAL RHOB

Xinxin Ma[1], Cong Luo[1], Jiwen Li[1], Inhyuk Bang[1], Fang Du[1], Katherine Figarella[1], Jihoon Tak[1], Fenfen Wang[1], Yang Yang[1], Songjian Lu[2], Wankun Deng[2], Zhongming Zhao[2], Ragini Nair[1], Paul A J Krijnen[3], Ingeborg S E Waas[3], Hans W M Niessen[3], Dongze Zhang[1], Cristian, Rodriguez-Aguayo[4], Gabriel Lopez-Berestein[4], Anil K. Sood[4], Yu A An[1], Xiaoyi Yuan[1], Cynthia Ju[1], Jagat Narula[5], Matthew DeBerge[1], Wei Ruan[1], Holger K. Eltzschig[1]

[1]Anesthesiology, Critical Care and Pain Medicine, The University of Texas Health Science Center at Houston, McGovern Medical School, Houston, TX; [2]Center for Precision Health, McWilliams School of Biomedical Informatics, The University of Texas Health Science Center at Houston, Houston, TX; [3]Pathology and Cardiac Surgery, Amsterdam Cardiovascular Sciences, Amsterdam UMC, VU Medical Center, Amsterdam, The Netherlands; [4]Departmental of Experimental Therapeutics and Center for RNA Interference and Non-Coding RNA, The University of Texas MD Anderson Cancer Center, Houston, TX; [5]Division of Cardiology, Medicine, The University of Texas Health Science Center at Houston, McGovern Medical School, Memorial Hermann Hospital, Houston, TX

Background:
Neutrophils are traditionally viewed as drivers of tissue injury after myocardial ischemia-reperfusion, but emerging evidence suggests they can also activate endogenous mechanisms that limit cardiac damage and promote repair. The mechanisms regulating the shift between pathogenic and protective neutrophil functions remain unclear. Since microRNAs (miRNAs) are potent post-transcriptional regulators of neutrophil activity and intercellular communication, we hypothesized that neutrophil-derived miRNAs contribute to cardioprotective signaling after myocardial injury.

Materials/Methods:
Using a mouse model of myocardial ischemia-reperfusion and human postmortem hearts, we identified neutrophil-derived miRNAs in the myocardial area at risk by miRNA sequencing. Candidates were validated by miRNAscope, flow cytometry, cell isolation, and exosome profiling. Neutrophil-endothelial co-culture assessed intercellular transfer, while in vivo genetic and pharmacologic models evaluated functional roles and therapeutic potential.

Results:
miRNA-seq identified miR-223-3p as the leading neutrophil-derived miRNA after myocardial injury, a pattern conserved in human postmortem infarcted hearts. Neutrophil-specific deletion of miR-223-3p worsened cardiac injury and systolic function, revealing a new protective program induced by neutrophils. Mechanistically, neutrophil-derived exosomes delivered miR-223-3p to endothelial cells, where suppression of the direct target Rhob attenuated inflammatory activation and preserved barrier integrity. Modulation of this axis through miR-223-3p mimics, Rhob-deficiency or pharmacologic inhibition reduced infarct sizes, preserved endothelial function, and improved cardiac function.

Conclusions:
These findings identify neutrophil-derived miR-223-3p as an endogenous cardioprotective signal and support therapeutic targeting of immune-endothelial crosstalk to limit myocardial injury.

Poster 67

c-REL–MEDIATED LIPID ACCUMULATION AND INFLAMMATORY ACTIVATION IN MONOCYTES IN HYPERTRIGLYCERIDEMIA

Jing Xiao[1], Veronica O'Brien[1], Benjamin Litchfield[1], Feng Gao[1], Bing Sun[1], Xiaoyuan Dai Perrard[1], Xinyi Xi[1], Arsalan Hamid[1], Yakubu Bene-Alhasan[1,2], Yanming Li[3], William R. Lagor[4], Ying H. Shen[3], Xinchun Pi[1,2], Chao Cheng[1], Iris A. K. Lähdeniemi[5], Tamara Alagirova[5], Ron C. Hoogeveen[1], Christie M. Ballantyne[1,2], Simon G. Pfisterer[5], Huaizhu Wu[1,2]

[1]Medicine, Baylor College of Medicine, [2]Center for Cardiometabolic Disease Prevention, Baylor College of Medicine, Houston, TX; [3]Surgery, Baylor College of Medicine, Houston, TX; [4]Integrative Physiology, Baylor College of Medicine, Houston, TX; [5]MONCYTE Health, Helsinki, Finland.

Background:
Hypertriglyceridemia (HTG) promotes atherosclerotic cardiovascular disease, but the mechanisms remain incompletely defined. We investigated whether triglyceride-rich lipoproteins drive lipid accumulation and inflammatory activation in circulating monocytes.
Materials/Methods:
Ldlr−/− mice with or without human Apoc3 transgene expression and human subjects with or without severe HTG were studied. Monocytes were analyzed by flow cytometry, automated confocal microscopy, and single-cell RNA sequencing. In vitro, primary mouse and human monocytes and THP-1 cells were treated with VLDL from HTG subjects, with or without the c-Rel inhibitor IT-901.
Results:
Compared with controls, A3LDLRKO mice and subjects with HTG showed increased lipid droplet accumulation in intermediate/nonclassical monocytes. Single-cell RNA-seq identified an HTG-responsive monocyte cluster enriched for lipid metabolic and inflammatory pathways, including Rel. In vitro, VLDL increased lipid droplet accumulation and inflammatory markers in primary monocytes and THP-1 cells. RNA-seq showed induction of genes involved in lipid uptake and inflammation. Pharmacologic inhibition of c-Rel reduced VLDL-induced lipid accumulation and inflammatory gene expression.
Conclusions:
HTG-derived VLDL drives lipid accumulation and inflammatory activation in intermediate/nonclassical monocytes, with c-Rel acting as a key regulator. These findings identify c-Rel as a potential therapeutic target for monocyte-driven inflammation and atherosclerosis in HTG.

Poster 68

GLYCOCALYX MIMETIC HYDRATION LAYERS PREVENT THROMBOSIS IN SMALL-DIAMETER VASCULAR GRAFTS WITHOUT ANTICOAGULATION

Nitisha Mehrotra[1], Angel Ramirez[3], Abdelmotagaly Elgalad[3], Xiaoxiao Zhang[3], Suran Somawardana[4] Nitesh Katta[4], Abhijit Biswas[1], Kirti Mhatre[4], Chih-Wei Hsu[5], Bijay Dhungana[6], Peyton Carrol[7], Ramyar Gilani[4], Sung Park[7], Sudipta Seal[6], Thomas Milner[4], Pulickel Ajayan[1], Crystal Shin[4], Ghanashyam Acharya[2]

[1]Material Science and Nanoengineering, Rice University, Houston, TX; [2]Surgery, Baylor College of Medicine; [3]Center for Preclinical Surgical & Interventional Research in Cardiothoracic Surgery, Texas Heart Institute; [4]Surgery, Baylor College of Medicine; [5]Optical Imaging and Vital Microscopy core, Baylor College of Medicine; [6]Advanced Materials Processing and Analysis Center, University of Central Florida; [7]Molecular Vista, Molecular Vista

Background:
Thrombosis remains the principal failure mechanism of small-diameter (<6 mm) synthetic vascular grafts, with patency rates below 30% at one year for coronary and below-knee applications. Current synthetic materials lack intrinsic antithrombotic properties of native endothelium, leading rapid platelet activation and occlusive thrombus formation. We hypothesized that hierarchically organized interfacial water layers could mimic the antithrombotic glycocalyx of vascular endothelium by creating a dynamic barrier against blood component adsorption.

Materials/Methods:
We fabricated hierarchically assembled anisotropic microfilamentous (HAM) membranes from poly(vinyl alcohol) through solvent-exchange-driven molecular self-assembly. Hydrogen-bonded water layer was characterized by PI-AFM, XPS, and XRD. Thromboresistance was evaluated using human PRP, porcine blood ex vivo perfusion, and microscopy for platelet markers. We fabricated 4-mm pulsatile HAM grafts with tunable mechanical properties and evaluated performance in a porcine carotid artery replacement model with Doppler analysis.

Results:
Spectroscopic analyses confirmed the formation of 2–3 nm thick hydrogen-bonded intermediate water layer on HAM surfaces. Ex vivo studies demonstrated prevention of platelet adhesion and activation on HAM compared to platelet deposition on polypropylene carbonate. HAM grafts exhibited mechanical properties matching native carotid artery, yield strength of HAM graft 2.35 MPa vs. carotid artery 1.8-1.9 MPa. In vivo porcine carotid artery replacement study demonstrated normal blood flow by Doppler ultrasound. Explanted HAM graft lumen showed complete absence of thrombus formation, platelet deposition, or fibrin accumulation by immunofluorescence and IR spectroscopy, while ePTFE grafts showed extensive blood component adsorption.

Conclusions:
First demo of hierarchically organized hydrogen-bonded water barrier providing thromboresistance in small-diameter synthetic vascular grafts without anticoagulation or endothelialization.

Poster 69

HYPOXIA-INDUCIBLE FACTOR-2A STABILIZATION IN REGULATORY T CELLS PROMOTES CARDIOPROTECTION AFTER MYOCARDIAL ISCHEMIA AND REPERFUSION INJURY

Cong Luo[1], Xinxin Ma[1], Matthew DeBerge[1], Holger Eltzschig[1]

[1]Anesthesiology, Critical Care and Pain Medicine, The University of Texas Medical School at Houston, Houston, TX

Background:
Ischemic heart disease is a leading cause of mortality worldwide. Myocardial injury after noncardiac surgery occurs in approximately 20% of patients undergoing major surgery and is associated with significant morbidity and mortality, yet effective preventive strategies remain limited. Myocardial ischemia leads to tissue hypoxia and activation of hypoxia-inducible factors (HIFs), which regulate adaptive responses to hypoxic stress. Regulatory T cells (Tregs) have recently been implicated in promoting cardiac repair after myocardial ischemia–reperfusion (I/R) injury; however, the role of HIF signaling in regulating Treg-mediated cardioprotection remains unclear.

Materials/Methods:
A murine model of myocardial I/R injury was used to examine changes in Treg accumulation and HIF stabilization in the injured heart. Functional studies were performed using adoptive transfer of wild-type Tregs or Tregs selectively deficient in Hif1α or Hif2α. The effects of pharmacologic HIF stabilization were evaluated using the clinically approved HIF activator vadadustat.

Results:
Cardiac Treg accumulation and HIF stabilization peaked three days after myocardial I/R injury. Adoptive transfer of wild-type Tregs significantly reduced infarct size and preserved systolic function. In contrast, these protective effects were abolished when Tregs lacked Hif2α but were preserved in Hif1α–deficient Tregs. Mechanistically, Hif2α selectively regulated amphiregulin production in Tregs, which was required for Treg-mediated cardioprotection. Pharmacologic HIF stabilization with vadadustat enhanced Treg accumulation and HIF signaling in cardiac Tregs, attenuated adverse ventricular remodeling, and prevented progression to heart failure.

Conclusions:
HIF2α in regulatory T cells is critical for cardioprotection after myocardial I/R injury. Therapeutic stabilization of HIF signaling enhances Treg-mediated cardiac repair and may represent a promising strategy for reducing myocardial injury.

Poster 70

IDENTIFYING A NOVEL MOLECULAR MECHANISM FOR CORONARY ARTERIOLAR CONSTRICTION TO ENDOTHELIN-1 GUIDES DRUG DEVELOPMENT FOR CLASSIFICATION AND THERAPY OF CORONARY MICROVASCULAR DYSFUNCTION

Guangrong Lu[1], Robert Widmer[3], Travis Hein[2], Lih Kuo[2]

[1]NA, Other; [2]Medical Physiology, Texas A&M Health Science Center; [3]Cardiology, Baylor Scott & White Health

Background:
Elevated plasma levels of potent vasoconstrictor endothelin-1(ET-1) are associated with coronary microvascular dysfunction (CMD) in myocardial ischemic patients. Recent randomized controlled trials with endothelin receptor antagonist zibotentan (NCT04097314) or L-type calcium channel (LTCC) blocker diltiazem (NCT04777045) failed to improve clinical outcomes, partly due to limited understanding of mechanistic signaling underlying coronary microvascular constriction. Herein, we probed the molecular mechanisms responsible for coronary arteriolar constriction at clinically relevant ET-1 concentrations to identify potential new targets amenable to CMD management.
Materials/Methods:
The vasoconstrictor response and signaling pathway of isolated, pressurized (at 44 mmHg) porcine coronary arterioles to ET-1 and protein kinase C (PKC) activator phorbol 12,13-dibutyrate (PDBu) were studied using videomicroscopic and pharmacological tools.
Results:
Coronary arterioles developed basal tone with a resting diameter (40±4 μm) about 50% of the maximal diameter (73±3 μm). ET-1 caused concentration-dependent vasoconstriction with a threshold at 0.1 pM and an EC50 at 10 pM. A clinical level of ET-1 (100 pM) caused sustained vasoconstriction to 20-25 μm (~25% of maximal diameter) for over 2 hours. The ETA receptor antagonist BQ123 (1 μM) prevented but failed to reverse vasoconstriction to ET-1. Rho kinase (ROCK) inhibitor H-1152 (3 μM) and the conventional PKC inhibitor Ro 32-0432 (1 μM) prevented and reversed arteriolar constrictions to 100 pM ET-1 and 0.1 μM PDBu, respectively. LTCC blocker nifedipine (1 μM) prevented and reversed vasoconstriction to PDBu but not to ET-1.
Conclusions:
A clinical level of ET-1 caused profound and long-lasting narrowing of coronary arterioles and was reversed by blockade of ROCK but not of PKC, ETA receptors, or LTCC. Thus, the current data may explain why zibotentan or diltiazem failed to show clinical benefit for CMD. A new drug target, i.e., ROCK, might be a solution for managing CMD.

Poster 71

IV FOLATE AS A LIFE-SAVING ACUTE ANTIARRHYTHMIC IN MANAGEMENT OF TORSADE DE POINTES AND LETHAL CARDIAC ARRHYTHMIAS IN TANGO2 DEFICIENCY DISORDER

Sergio A Espinosa Alvarez[1], Svjetlana Tisma-Dupanovic[3], Kathleen Pope[4], Ozlem Turan[5], Lilei Zhang[6], Christina Miyake[2]

[1]Cardiology, Baylor College of Medicine; [2]Cardiovascular Genetics Arrhythmia, Texas Children's Hospital; [3]Cardiology, Nemours Children's Hospital; [4]Pediatrics / Genetics, University of South Florida; [5]Pediatrics, Nemours Children's Hospital; [6]Molecular and Human Genetics, Baylor College of Medicine

Background:
TANGO2 deficiency disorder (TDD) is a recessive disease characterized by neurodevelopmental delays (NDD), seizures, hypothyroidism, episodic ataxia, and acute life-threatening metabolic crises. During crises, marked QT prolongation rapidly progresses to torsade de pointes (TdP) and cardiac arrest with high mortality. Lidocaine and esmolol will worsen arrhythmias and can trigger arrest. We report the use of IV bolus folate to acutely suppress and treat TdP and frequent PVCs. We also describe how current genetic testing can miss the diagnosis and how to avoid this.
Materials/Methods:
Data obtained through chart review.
Results:
14-year-old male with 22q11.2 deletion syndrome (DS), NDD, hypothyroidism, ataxia, seizures, presented with altered mental status and rhabdomyolysis. At 6AM he had TdP that spontaneously resolved. Over several hours, he had frequent PVCs and a second episode of TdP. An ECG revealed a QTc of 619 msec. Historically, TDD patients in this situation have a 50% chance of death. Electrophysiology was consulted. TDD was suspected and a 1mg IV bolus of folate was given over 30 minutes. No other antiarrhythmic was used. Within 10 minutes, all ventricular ectopy (prior PVCS happened every 10 seconds) completely suppressed, and the patient had not a single PVC or TdP. IV folate was continued 1mg every 6 hours along with magnesium and IV multivitamins. QTc normalized within 7 days. Genetic testing through PreventionGenetics identified the known heterozygous deletion of 22q11.2 and no additional variant for TDD. Due to high clinical suspicion, a second genetic test was sent to Baylor Genetic Laboratory, which confirmed TDD diagnosis.
Conclusions:
IV folate is a therapeutic option for life-threatening TdP in TDD crisis. This case also highlights the importance of recognizing risk of TDD in 22q11.2DS. Clinicians must recognize the clinical markers of TDD because high suspicion is crucial and diagnosis should be pursued with a different genetic laboratory, even when initial genetic testing is negative.

Poster 72

DIAGNOSTIC PERFORMANCE OF FETAL AND POSTNATAL ECHOCARDIOGRAPHY FOR RIGHT AORTIC ARCH ANATOMY COMPARED WITH COMPUTER TOMOGRAPHY

Mary C Jenkins[1], Tam Doan[1], Betul Yilmaz Furtun[1], Heidi Ostler[2], Lacey Schoppe[3], Jianhong Zhang[3], Maggie Zhang[3], Shaine Morris[1]

[1]Pediatric Cardiology, Baylor College of Medicine; [2]Pediatric Cardiology, University of Utah Health; [3]Pediatric Cardiology, Texas Children's Hospital

Background:
Right aortic arch (RAA) is increasingly identified on fetal echocardiography (FE), enabling early counseling and perinatal planning for vascular ring anatomy and associated genetic conditions. However, the diagnostic performance of FE and postnatal echocardiography relative to computed tomography (CT), the anatomic reference standard, remains incompletely defined.

Materials/Methods:
We conducted a retrospective cohort study of fetuses with suspected right aortic arch (RAA), including those with other congenital heart disease, who underwent both postnatal transthoracic echocardiography and cardiac CT at our institution from 2016–2025. Arch anatomy was classified by fetal echocardiography, postnatal echocardiography, and CT. CT studies with equivocal interpretations or discordant findings were reviewed by a pediatric cardiovascular imager for adjudication. Cases in which anatomy could not be defined by CT were excluded. Diagnostic accuracy of fetal and postnatal echocardiography was assessed using CT as the reference standard and agreement evaluated using Cohen's kappa (κ). Equivocal fetal or postnatal studies were classified as inaccurate.

Results:
Among 247 FE with suspected RAA, 52 lacked postnatal echo, 74 had echo without CT, and 2 CTs were equivocal, leaving 121 patients. FE detected RAA in 100% and vascular rings with 83% accuracy; exact branching accuracy was 65% (κ=0.53). Postnatal echo detected RAA in 96% with 74% vascular ring accuracy and 71% branching accuracy (κ=0.60). In the two eras, FE vascular ring detection improved from 74% to 95% and branching accuracy from 49% to 82% over time.

Conclusions:
FE demonstrated excellent detection of RAA and higher overall accuracy for vascular ring identification, while postnatal echocardiography showed modestly stronger agreement for detailed branching characterization. Diagnostic performance for both modalities improved over time, with the greatest gains seen in FE.

Poster 73

MARGINAL HEARTS WITHOUT PROLONGED ISCHEMIA DO NOT INCREASE THE RISK OF PROLONGED HOSPITALIZATION AFTER ADULT HEART TRANSPLANTATION

Anirudha R Karla[1], Gwendolyn Henry[1], Matthew Stout[1], Michael Tyler Guinn[2], Abbas Rana[2]

[1]Student Affairs, Baylor College of Medicine; [2]Division of Abdominal Transplantation, Michael E. DeBakey Surgery, Baylor College of Medicine

Background:
The persistent shortage of donor hearts has driven increased use of “marginal” allografts. However, concerns remain regarding their impact on postoperative outcomes, particularly prolonged length of stay (PLOS). We sought to evaluate the association between marginal allograft use and PLOS following adult orthotopic heart transplantation (OHT).
Materials/Methods:
In this study, 16,301 adult patients who underwent first-time, single-organ OHT between October 2018 and May 2024 were retrospectively analyzed with data from the UNOS/OPTN database. Marginal allografts were defined as those with donor age >55 years, total ischemia time >6 hours, donation after circulatory death, or structural abnormalities. The primary outcome of interest was PLOS, defined as postoperative length of stay >30 days. Analyses included multivariable, criterion-specific, and mixed-effects logistic regression, as well as sensitivity analyses using log-adjusted LOS. Secondary outcomes included 1-year survival, analyzed with Cox proportional-hazard modeling.
Results:
In multivariable logistic regression, marginal allografts were associated with increased odds of PLOS (adjusted odds ratio [aOR] 1.16 [1.02-1.31], P<.001), an effect primarily driven by prolonged ischemia time and structurally abnormal hearts. However, when prolonged ischemia was excluded, marginal status was not associated with PLOS (aOR 1.04 [0.91-1.19], P=.55). Sensitivity and mixed-effects analyses mirrored these results. Additionally, marginal transplants were not associated with worse 1-year survival (adjusted hazard ratio 1.07 [0.87-1.32], P=.53).
Conclusions:
Use of marginal donor hearts was not independently associated with PLOS once prolonged ischemia was excluded from the marginal definition. These findings suggest that “marginal” allografts without prolonged ischemia do not increase the odds of PLOS, and that strategies to minimize allograft ischemic time may help to enable safe expansion of the donor pool without prolonging postoperative recovery.


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