

# KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

## Pulmonary Hypertension: State of the Art and Therapeutic Opportunities (Z8)

Scientific Organizers: Marlene Rabinovitch and Kurt R. Stenmark

Sponsored by Ionis Pharmaceuticals, Inc. and Merck & Co., Inc.

## Heart Failure: All Cells Considered (Z7)

Scientific Organizers: Merry L. Lindsey, Crystal Ripplinger and Zamaneh Kassiri

June 25-28, 2023 • Eldorado Hotel & Spa • Santa Fe, NM, USA

Sponsored by AstraZeneca, Ionis Pharmaceuticals, Inc., Merck & Co., Inc. and Novo Nordisk A/S

Scholarship Deadline: April 19, 2023 / Abstract Deadline: April 19, 2023 / Discounted Registration Deadline: April 25, 2023

### SUNDAY, JUNE 25

#### Arrival and Registration

### MONDAY, JUNE 26

#### Welcome and Keynote Address (Joint)

\***Merry L. Lindsey**, Meharry Medical Center, USA

\***Marlene Rabinovitch**, Stanford University, USA

**Elizabeth M. McNally**, Northwestern University, USA  
*Genetic Determinants of Heart Failure*

#### The Metabolic Basis of Pulmonary Arterial Hypertension Beyond Glycolysis (Z8)

\***John Shyy**, University of California, USA

\***David Fulton**, Augusta University, USA

**Marlene Rabinovitch**, Stanford University, USA  
*Integrating Pathways in Pulmonary Hypertension*

**Sadis Matalon**, University of Alabama at Birmingham, USA  
*Oxidative Mitochondrial DNA Injury is a Key Contributor to the Development of Chemical Lung Injury*

**Stephen L. Archer**, Queen's University, Canada  
*The Role of Altered Mitochondrial Dynamics and Metabolism in Pulmonary Hypertension*

**Michela Nosedà**, Imperial College London, UK  
*Single Cell and Spatial Transcriptomics State-of-the-heart*

#### Cell-Cell Cross-Talk (Z7)

\***Merry L. Lindsey**, Meharry Medical Center, USA

\***Uendra Chalise**, University of Nebraska Medical Center, USA

**Gillian A. Gray**, University of Edinburgh Centre for Cardiovascular Science, UK  
*Intracellular Glucocorticoid Regeneration as a Novel Target to Regulate Infarct Repair and Progression to Heart Failure*

**Karin Sipido**, KU Leuven, Belgium  
*Cellular Cross-talk in Ischemic Cardiomyopathy*

**Jennifer E. Van Eyk**, Cedars-Sinai, USA  
*Harnessing Proteomics for Novel HF Diagnostics and Therapies*

**Jason Maynes**, Hospital for Sick Children, Canada  
*Short Talk: Inherent Inflammatory Characteristics Determine Repair and Transferable Benefit of Cardiac Progenitor Cells in Patients with Congenital Heart Disease*

#### Workshop 1: Imaging and Biomarkers of Disease Altering Therapies (Z8)

\***Christopher Rhodes**, Imperial College London, UK

**S M Riajul Wahab**, University of Texas at El Paso, USA  
*Identifying the Role of Prion-like Protein Doppel as a Novel Mediator of Pulmonary Arterial Hypertension*

**Claudia Mickael**, University of Colorado Denver, USA

*Classical Dendritic Cells Drive and Maintain Hypoxia-Induced Pulmonary Hypertension*

**Micheala A. Aldred**, Indiana University, USA  
*Cybrid Analysis Delineates Nuclear and Mitochondrial Contributions to Oxidative Stress in Pulmonary Arterial Hypertension*

**Cassidy Delaney**, University of Colorado, USA  
*Platelets Participate in Regulation of the Early Immune Response in Experimental PH*

**Slaven Crnkovic**, Medical University of Graz, Austria  
*Defining Cell-type Specific Disease States in Pulmonary Hypertension*

**Jingbo Dai**, Northwestern University, USA  
*The RNA m6A Demethylase, FTO, Regulates Vascular Remodeling in the Pathogenesis of Pulmonary Arterial Hypertension*

**Bin Liu**, University of Arizona, USA  
*Fatty Acid-binding Proteins Promote Pulmonary Arterial Hypertension via Glycolysis*

**Caitlin Lewis**, University of Colorado, USA  
*Extracellular Superoxide Dismutase Affects Interstitial Macrophage Accumulation, Reprogramming and Hyaluronan Binding during Pulmonary Hypertension*

#### Workshop 1 (Z7)

\***Nicholas W. Chavkin**, University of Virginia, USA

\***Mikito Takefuji**, Nagoya University School of Medicine, Japan  
**Preethy Parthiban**, University of Minnesota- Twin Cities, USA  
*Macrophage-derived CCL24 Worsens Cardiac Dysfunction by Promoting Fibrosis and Impeding Compensatory Adaptation during Heart Failure*

**Uendra Chalise**, University of Nebraska Medical Center, USA  
*Big Data Guided Analysis Reveals Unique Cardiac Remodeling Trajectories by Sex After Myocardial Infarction*

**Benjamin D. McNair**, University of Wyoming, USA  
*Distinct Mechanisms of Aging in the Right and Left Ventricles*

**Bryana N. Harris**, University of Virginia, USA  
*Dynamic Map Illuminates Hippo Module Crosstalk Driving Cardiomyocyte Proliferation*

**Karin J. Bosma**, Vanderbilt University Medical Center, USA  
*Modulation of Prostaglandin E2 Receptors EP3 and EP4 as a Novel Therapeutic Strategy to Improve Cardiac Function in Type 2 Diabetes*

**Alexa Corker**, Medical University of South Carolina, USA  
*PTSD has a Negative Impact on Cardiac Homeostasis*

**Abraham L. Bayer**, Tufts Graduate School of Biomedical Sciences, USA  
*T-Cell MyD88 is a Novel Regulator of Cardiac Fibrosis through Modulation of T-cell Activation*

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### How Epigenetic Changes and RNA Translation Govern Disease Susceptibility (Z8)

\***Ke Yuan**, Boston Children's Hospital, USA

\***Scott Barman**, Augusta University, USA

**Sebastien Bonnet**, Université Laval, Canada  
*Epigenetics Targets in PAH: BRD4 and ACLY Novel's Targets for Vascular Remodeling*

**Soni Savai Pullamsetti**, Max-Planck-Institute for Heart and Lung Research, Germany

*The Suppressor Function of lnc RNAs in Pulmonary Hypertension*

**Chen-Shan Julia Woodcock**, University of Pittsburgh, USA  
*Short Talk: RNA Editing Deficiency Induces Pulmonary Endothelial Pathophenotypes and Drives Pulmonary Hypertension*

**Cheng-Jun Hu**, University of Colorado Denver, USA  
*Short Talk: Pulmonary Vascular Fibroblasts Are Epigenetically Primed for Inflammatory Responses*

**YouYang Zhao**, Northwestern University-Lurie Children's Hospital of Chicago, USA

*Short Talk: Endothelial Cell-targeted Nanoparticle Delivery of CRISPR/Cas9 Plasmid DNA Disrupts Endothelial HIF-2 $\alpha$  in Adult Rats and Inhibits Experimental PAH: Towards Genome Editing Therapy of PAH*

**Jingbo Dai**, Northwestern University, USA

*Short Talk: Therapeutic Genome Editing of Endothelial Fabp4 Inhibits Pulmonary Arterial Hypertension in Rats*

### Cell Heterogeneity in Heart Failure (Z7)

\***Gillian A. Gray**, University of Edinburgh Centre for Cardiovascular Science, UK

\***Preethy Parthiban**, University of Minnesota- Twin Cities, USA

**Amy D. Bradshaw**, Medical University of South Carolina, USA  
*Fibroblast Activation Profiles in Pressure Overload*

**Jennifer Davis**, University of Washington, USA  
*Mechanical Signaling Networks that Program Fibroblasts*

**Taben Hale**, University of Arizona, USA  
*Sub-Populations of Resident Cardiac Fibroblasts in Hypertension: Taking a Census*

**Alessandra Pasut**, KULeuven, Belgium  
*Short Talk: Metabolic Heterogeneity of Endothelial Cells in HFpEF*

**Richard Keith Babbs**, Keros Therapeutics, USA  
*Short Talk: RKER-012, A Novel Modified ActRIIB Ligand Trap, Attenuated Cardiac Hypertrophy, Fibrosis, and Cardiovascular Remodeling in a Transaortic Constriction Model of Heart Failure*

### Poster Session 1

TUESDAY, JUNE 27

### Cardiopulmonary Crossroads (Joint)

\***Zamaneh Kassiri**, University of Alberta, Canada

\***Gaurav Choudhary**, Alpert Medical School of Brown University, USA

**Tim Lahm**, National Jewish Health, USA  
*Sex as a Determinant of Right Ventricular Dysfunction in Pulmonary Hypertension*

**Tami Martino**, University of Guelph, Canada  
*Circadian Rhythms and HF Chronotherapy*

**Bradley Maron**, University of Maryland School of Medicine, USA  
*Individualized Interactomes Advance Precision Medicine in Heart Failure Syndromes*

**Crystal Ripplinger**, University of California, Davis, USA  
*The Nervous Heart: Autonomic Remodeling Post-MI*

**Yongneng Zhang**, University of Alberta, Canada  
*Short Talk: A Critical Contribution of Cardiac Myofibroblasts in RV Failure and the Role of a UCP2 SNP as a Biomarker Identifying PAH Patients Predisposed to RV Decompensation*

**Kenzo Ichimura**, Stanford University, USA  
*Short Talk: 3D Deep Tissue Imaging Reveals Complex Remodeling of the Microvasculature in Right Heart Failure*

### Poster Session 2

### Workshop 2: Narrowing the Gap Between Discovery and Therapy in Pulmonary Hypertension (Z8)

\***Stephen L. Archer**, Queen's University, Canada

\***Chanil Valasarajan**, Centre for Infection and Genomics of Lung, Justus Liebig University, Germany

**Ke Yuan**, Boston Children's Hospital, USA  
*Deficiency of Smooth Muscle ADAR1 RNA Editing Exacerbates Vascular Remodeling and Pulmonary Hypertension*

**Sarasa Isobe**, Stanford University, USA  
*Loss of BMPR2 Links Unrepaired DNA Damage to Reduced FOXF1 and Pulmonary Arterial Hypertension*

**Tamanna Islam**, University of Texas at El Paso, USA  
*Bioengineering Models to Study Cell-Specific Durotaxis in Pulmonary Arterial Hypertension*

**Emily J. Tsai**, Columbia University Vagelos College of Physicians & Surgeons, USA

*In vivo Cardiac Myocyte-specific Knockdown of Wipi1 Prevents Decompensation of the Pressure-overloaded Right Ventricle*

**Yingjie Chen**, University of Mississippi Medical Center, USA  
*Natural Killer Cells Regulate Heart Failure-induced Cardiopulmonary Inflammation, Pulmonary IFN- $\gamma$  Production, and Pulmonary Remodeling*

**Pontian Adogamhe**, Indiana University School of Medicine, USA  
*NAMPT Overexpression Decreases Sirt 3 Deacetylase Activity in Human Pulmonary Artery Endothelial Cells*

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**Olin Liang**, Brown University, USA

*Targeting RUNX1 as a Novel Treatment Modality for Pulmonary Arterial Hypertension*

### Workshop 2 (Z7)

\***Thomas Martin**, University of Colorado Boulder, USA

\***Alexa Corker**, Medical University of South Carolina, USA

**Thirupura Sundari Shankar**, University of Utah, USA

*Adipocyte Enhancer Binding Protein 1 as a Novel Therapeutic Target to Combat Fibrosis in Heart Failure*

**Mikito Takefuji**, Nagoya University School of Medicine, Japan

*Cardiac Atypical Kinase Improves Left Ventricular Diastolic Dysfunction in Heart Failure with Preserved Ejection Fraction*

**Mohit Kumar**, Regeneron Pharmaceuticals, Inc., USA

*Characterization of Right Ventricle Involvement in MYBPC3-linked Hypertrophic Cardiomyopathy*

**Patricia Perez-Bonilla**, Pfizer Inc., USA

*Heart Rate Variability and Chronotropic Incompetence as Prognostic Markers in a HFpEF Preclinical Model*

**Nicholas W. Chavkin**, University of Virginia, USA

*Hematopoietic Loss of the Y Chromosome Promotes Cardiac Fibrosis through Epigenetic Regulation of Autosomal Genes in Monocytes and Macrophages*

**Thomas Martin**, University of Colorado Boulder, USA

*Activation of FOXO1-dependent Autophagy Mediates Regression of Cardiac Hypertrophy*

### Using Big Data to Understand Complex Disease (Z8)

\***Micheala A. Aldred**, Indiana University, USA

**Christopher Rhodes**, Imperial College London, UK

*The Significance of Noncoding Variants in Pulmonary Hypertension*

**Wendy K. Chung**, Columbia University, USA

*Penetrance of Mutations in Pediatric Pulmonary Hypertension*

**Jose Gomez-Arroyo**, University of Cincinnati, USA

*Role of FOXF1 in the Pathobiology of Pulmonary Arterial Hypertension*

**Gabriel Maldonado-Velez**, Indiana University School of Medicine, USA

*TBX4 Loss-of-function within the Embryonic Lung Mesenchyme Disrupts Lung Alveolar Development and Increases Susceptibility to Pulmonary Hypertension*

### Cell Responses to Myocardial Injury and Growth (Z7)

\***Taben Hale**, University of Arizona, USA

\***Chi Fung Lee**, Oklahoma Medical Research Foundation, USA

**Leslie A. Leinwand**, University of Colorado Boulder, USA

*The Sarcomere is a Very Busy Place: From Bench to Bedside in Myosin Myopathies*

**Kristine Deleon-Pennell**, Medical University of South Carolina, USA

*T Cell Regulation of MI Remodeling*

**Kathleen Woulfe**, University of Colorado Anschutz Medical Campus, USA

*Short Talk: Age-specific Decreases in Sarcomeric Acetylation Modulates Myofilament Function in Skeletal and Cardiac Muscle*

**Ann Chiao**, Oklahoma Medical Research Foundation, USA

*Short Talk: Aging Exacerbates Diastolic Dysfunction and Proteostatic Imbalance in Heart Failure with Preserved Ejection Fraction*

### WEDNESDAY, JUNE 28

#### Using Biology to Guide Vascular Regeneration (Z8)

\***James Klinger**, Alpert Medical School of Brown University, USA

\***YouYang Zhao**, Northwestern University-Lurie Children's Hospital of Chicago, USA

**Vinicio de Jesus Perez**, Stanford University, USA

*Restoring Normal Microvessels in Pulmonary Hypertension*

**Rubin M. Tuder**, University of Colorado Hospital - Anschutz, USA  
*Disease Heterogeneity and the Challenges in Evaluating Therapies for a Complex Disease*

**David B. Frank**, Children's Hospital of Philadelphia, USA

*Ontogeny and Cellular Heterogeneity in Pulmonary Vascular Development and Disease*

**Akiko Mammoto**, Medical College of Wisconsin, USA

*Short Talk: Endothelial Senescence in Pulmonary Hypertension*

#### Cardiometabolic Aspects of HF (Z7)

\***Ann Chiao**, Oklahoma Medical Research Foundation, USA

\***Abraham L. Bayer**, Tufts Graduate School of Biomedical Sciences, USA

**Rebecca Ritchie**, Monash Institute of Pharmaceutical Sciences, Australia

*Diabetic Effects on Cardiac Remodeling*

**Susan E. Howlett**, Dalhousie University, Canada

*The Many Effects of Aging and Frailty on the Heart*

**Helen E. Collins**, University of Louisville, USA

*Mechanisms Contributing to Pregnancy-Induced Cardiac Growth*

**Chi Fung Lee**, Oklahoma Medical Research Foundation, USA

*Short Talk: SARM1 Deficiency Prevents NAD Decline, Improve Mitochondrial and Cardiac Function in Cardiometabolic Disease*

**Kayla J. Rayford**, Meharry Medical College, USA

*Short Talk: Trypanosoma Cruzi Alters Expression of piRNAs That Target Profibrotic and Inflammatory Molecules During Acute Infection of Primary Human Cardiac Fibroblasts*

**Kenneth Rockwood**, Dalhousie University, Canada

*Short Talk: Assessing Frailty-related Mortality Risk in Older Adults Hospitalized with and without Congestive Heart Failure*

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**Adaysha Williams**, Medical College of Wisconsin, USA  
*Short Talk: High Inorganic Phosphate Treatment Reduces Rat Neonatal Cardiomyocyte Viability*

### Departure

### Career Roundtable (Joint)

**Vinicio de Jesus Perez**, Stanford University, USA  
**Michael Dunn**, Regeneron Pharmaceuticals, USA  
**Chi Fung Lee**, Oklahoma Medical Research Foundation, USA

### The Inflammatory Basis of Pulmonary Hypertension (Z8)

\***Thomas Resta**, University of New Mexico HSC, USA  
\***Andrew Bryant**, University of Florida College of Medicine, USA  
**Harry Karmouty-Quintana**, University of Texas Health Science Center, USA  
*RNA Translation and the Proteome of Pulmonary Hypertension*  
**Kurt R. Stenmark**, University of Colorado Denver, USA  
*The Interplay Between Fibroblasts and Monocytes in Pulmonary Hypertension*  
**Simon Bousseau**, National Jewish Health, USA  
*Short Talk: 17 $\beta$ -estradiol Regulates Angiogenesis and Right Ventricle Endothelial Cell Metabolism in Pulmonary Arterial Hypertension*  
**Benjamin Korman**, University of Rochester, USA  
*Short Talk: Single Cell RNA Sequencing of Mice with TNF-mediated Pulmonary Hypertension Demonstrates Marked Changes in Endothelial and Mesenchymal Cell Populations and Aberrant BMP Signaling*

### Pharma Targets for Heart Failure (Z7)

\***Helen E. Collins**, University of Louisville, USA  
\***Yongneng Zhang**, University of Alberta, Canada  
**Zamaneh Kassiri**, University of Alberta, Canada  
*Metalloproteases Make It or Break It*  
**Rachel J. Roth Flach**, Pfizer Inc., USA  
*Metabolic Targets for Heart Failure*  
**Michael Dunn**, Regeneron Pharmaceuticals, USA  
*Sustained Vasodilation in Preclinical Species and Humans by an Investigational Agonist Monoclonal Antibody to a Membrane-bound Guanylate Cyclase Receptor, Natriuretic Peptide Receptor 1*  
**Aina Hirofuji**, Asahikawa Medical University, Japan  
*Short Talk: Mycn Induces Cardiomyocyte Mitosis in Adult Mice*

### Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (Z8)

### Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (Z7)

THURSDAY, JUNE 29