

# Mitochondria, Metabolism and Heart

May 8–12, 2017 | Eldorado Hotel & Spa | Santa Fe, New Mexico | USA

## Scientific Organizers:

**Junichi Sadoshima**, Rutgers New Jersey Medical School, USA

**Toren Finkel**, National Heart, Lung, and Blood Institute, National Institutes of Health, USA

**Åsa B. Gustafsson**, University of California, San Diego, USA

## Joint with the meeting on *Angiogenesis and Vascular Disease*

*Mitochondria play a central role in regulating energy metabolism, redox status and cell death. The homeostasis of mitochondrial function is maintained by multiple mechanisms, collectively called mitochondrial quality control mechanisms. During the past decade, we have witnessed an explosion of research identifying novel mechanisms by which mitochondria control various cellular functions and cells maintain the homeostasis of mitochondria and metabolism in various cell types. Mitochondria are particularly abundant in the heart, and mitochondrial dysfunction and changes in cellular metabolism are commonly observed in failing or stressed hearts. However, there is a significant gap in our understanding of these mechanisms in cardiomyocytes and those in other cell types. The overall learning objectives of this meeting are to: 1) Understand how the novel functions of mitochondria contribute to the development or the prevention of myocardial injury and heart failure, and 2) Discuss how the quality of mitochondria is maintained in adult cardiomyocytes, whose mitochondrial dynamics are quite distinct from other commonly investigated cell types. Special emphasis will be placed on discussing the function and the mechanism of mitophagy; a novel mechanism of cell death mediated through autophagy; interaction between mitochondria dynamics and mitophagy; mitochondrial unfolded protein response (UPR) controlling aging, stress resistance and longevity; the role of metabolic intermediates as signaling mechanisms; and novel biomarkers identified through metabolomics analyses. Overall, the audience will obtain better understanding regarding how the function of mitochondria is regulated in the heart, how it affects the overall function of the cardiovascular system, and how one intervenes with mitochondria and metabolism to achieve better treatment for heart failure and other cardiovascular diseases.*

## Session Topics:

- Metabolism and Disease (Joint)
- Mitochondria Quality Control
- Autophagy and Metabolism
- Epigenetic Regulation of Vascular Growth
- Hypoxia Sensing Mechanism and Mitophagy (Joint)
- Metabolic Regulation of Cell Signaling
- Regulation of mPTP Opening
- Metabolism and Heart Failure

**Scholarship Application & Discounted Abstract Deadline: January 11, 2017**

**Abstract Deadline: February 8, 2017**

**Discounted Registration Deadline: March 8, 2017**



Note: Scholarships are available for graduate students and postdoctoral fellows and are awarded based on the abstract submitted.

Meeting Hashtag: #KSmitometa

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# KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

## Mitochondria, Metabolism and Heart (Z4)

Scientific Organizers: Junichi Sadoshima, Toren Finkel and Åsa B. Gustafsson

Supported by Bayer HealthCare Pharmaceuticals

## Angiogenesis and Vascular Disease (Z3)

Scientific Organizers: Luisa Iruela-Arispe, Timothy T. Hla and Courtney Griffin

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### MONDAY, MAY 8

#### Arrival and Registration

### TUESDAY, MAY 9

#### Welcome and Keynote Session (Joint)

\***Luisa Iruela-Arispe**, University of California, Los Angeles, USA

\***Junichi Sadoshima**, Rutgers New Jersey Medical School, USA

**Kari K. Alitalo**, University of Helsinki, Finland  
*Therapeutic Potential of Vascular Growth Factors*

**David C. Chan**, California Institute of Technology, USA  
*Mitochondria Dynamics*

#### Metabolism and Disease (Joint)

**Robert E. Gerszten**, Beth Israel Deaconess Medical Center, USA  
*Metabolic Profiles and the Risk of Cardiometabolic Diseases*

\***Andrew G. Dillin**, University of California, Berkeley, USA  
*Mitochondria Mitokines and Aging*

**Peter F. Carmeliet**, University of Leuven, VIB, Belgium  
*Angiogenesis Revisited: Role and (Therapeutic) Implications of Endothelial Metabolism*

**Arpita Chowdhury**, Universitätsmedizin Göttingen, Germany  
*Short Talk: Oxidative Stress and Altered Mitochondrial Signaling in Barth Syndrome Models*

**Nicholas Sibinga**, Albert Einstein College of Medicine, USA  
*Short Talk: Control of Mitochondrial Function by Atypical Cadherins*

#### Workshop 1: How to Evaluate Metabolism in the Heart: From the Langendorff Perfusion to Metabolome Analyses (Z4)

\***Toren Finkel**, University of Pittsburgh/UPMC, USA

**Larissa Pfisterer**, Frankfurt University, Germany  
*Regulation of Endothelial Cell Metabolism by Long Noncoding RNA Incf2*

**Jessica M. Pflieger**, Temple University, USA  
*Bioenergetics as a Tool for Assessing Cardiomyocyte Response to  $\beta$ -Adrenergic Stimulation and Insulin Resistance*

**Paul T. Schumacker**, Northwestern University, USA  
*Mitochondrial Complexes I and III Regulate Cardiomyocyte Proliferation in Adult Mouse Hearts*

**Junco Shibayama Warren**, University of Utah, USA  
*The Histone Methyltransferase Smyd1 Regulates Mitochondrial Energetics in Cardiomyocytes*

**Yuan Zhang**, University of Iowa, USA  
*Ketogenic Diet Rescues Cardiac Hypertrophy and Heart Failure Induced by Loss of the Mitochondrial Pyruvate Carrier 1*

**Dan Shao**, University of Washington, USA  
*Glucose Promotes Cell Growth by Suppressing Branched-Chain Amino Acid Degradation*

#### Workshop 1: Current Strategies for Funding Angiogenesis and Vascular Disease Research (Z3)

\***Luisa Iruela-Arispe**, University of California, Los Angeles, USA

**Yunling Gao**, NHLBI, National Institutes of Health, USA  
*Angiogenesis Research: The Extramural Portfolio Supported by the National Heart, Lung, and Blood Institute, 2008-2015*

**Morris J. Birnbaum**, Pfizer Inc., USA

**Philip Tagari**, Amgen, Inc., USA  
*Amgen – Funding External Innovation*

**Courtney Griffin**, Oklahoma Medical Research Foundation, USA  
*Updates on the American Heart Association Research Funding Portfolio*

**Christer Betsholtz**, Uppsala University, Sweden

#### Mitochondria Quality Control (Z4)

**Gerald W. Dorn, II**, Washington University School of Medicine, USA  
*The Cardiomyopathy of Defective Mitochondrial Fusion*

\***Junichi Sadoshima**, Rutgers New Jersey Medical School, USA  
*Mitophagy in the Heart*

**R. Luke Wiseman**, The Scripps Research Institute, USA  
*Stress-Responsive Regulation of Mitochondria Inner Membrane Proteostasis*

**Ana Victoria Lechuga Vieco**, Spanish National Center for Cardiovascular Research, Spain  
*Short Talk: Conflict between Mitochondrial DNA Variants*

#### Metabolite Signaling in Angiogenesis and Vascular Disease (Z3)

\***William C. Sessa**, Yale University School of Medicine, USA

**Morris J. Birnbaum**, Pfizer Inc., USA  
*Control of Hepatic Lipid Metabolism*

**Christer Betsholtz**, Uppsala University, Sweden  
*Pericytes as Regulators of Vascular Stability*

**J. David Symons**, University of Utah, USA  
*Short Talk: Endothelial Cell Autophagy Maintains Shear-Stress-Induced Nitric Oxide Generation via Glycolysis-Dependent Purinergic Signaling to eNOS*

**Andreas M. Beyer**, Medical College of Wisconsin, USA  
*Short Talk: Autophagy is a Novel Regulatory Mechanism in the Human Microcirculation*

#### Poster Session 1

### WEDNESDAY, MAY 10

#### Autophagy and Metabolism (Z4)

**Heidi M. McBride**, McGill University, Canada  
*Emerging Functions of Mitochondrial-Derived Vesicles in Health and Disease.*

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\***Ana Maria Cuervo**, Albert Einstein College of Medicine, USA

*Control of Metabolism by Chaperone-Mediated Autophagy*

**Daniel P. Kelly**, University of Pennsylvania, USA

*Mitochondrial Remodeling in the Developing and Diseased Heart*

**E. Dale Abel**, University of Iowa, Carver College of Medicine, USA

*Myocardial Autophagy and Metabolic Regulation*

**Helena C. Kenny**, University of Iowa, USA

*Short Talk: Inducible Deletion of OPA1 Causes Heart Failure in Part*

*by mTOR - Mediated Suppression of Autophagy*

**Iain Scott**, University of Pittsburgh, USA

*Short Talk: Acetylation of Mitochondrial Proteins by Gcn5l1 Promotes*

*Enhanced Fatty Acid Oxidation in the Heart*

### Transcriptional Control of Endothelial Fate (Z3)

\***Courtney Griffin**, Oklahoma Medical Research Foundation, USA

**William T. Pu**, Children's Hospital, Harvard Medical School, USA

*Transcriptional and Epigenetic Regulation of Endothelial Gene Expression*

**Michael Potente**, Max Planck Institute for Heart and Lung Research, Germany

*EMBO Young Investigator Lecture: Metabolism, Metabolites and Endothelial Plasticity*

**Brian L. Black**, University of California, San Francisco, USA

*Identification of Injury- and Regeneration-Responsive Cardiac Endothelium Enhancer Elements*

**William C. Sessa**, Yale University School of Medicine, USA

*New Insights into Endothelial Lipid Metabolism*

**Manu Beerens**, Brigham and Women's Hospital, Harvard Medical School, USA

*Short Talk: Prdm16 Modifies the Canonical Notch Output to Establish Proper Arterial Development*

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

*Short Talk: YAP1 in Angiogenesis and Lung Regeneration*

### Cell Signaling and Metabolism (Z4)

**Pinchas Cohen**, University of Southern California, USA

*Mitochondrial-Derived Peptides and their Role in Vascular Disease*

**Xiang-Dong Fu**, University of California, San Diego, USA

*A Novel Strategy to Inhibit Angiogenesis in Cancer*

**Arieh Moussaieff**, Hebrew University of Jerusalem, Israel

*The Metabolic Switch of Cells Exiting Pluripotency*

\***Lorrie A. Kirshenbaum**, University of Manitoba, Canada

*Short Talk: Alternative Spliced Form of Bnip3 Preferentially Interacts with Mitofusion2 and Endoplasmic Reticulum for Cell Survival*

### Epigenetic Regulation of Vascular Growth (Z3)

\***Brian L. Black**, University of California, San Francisco, USA

**Stefanie Dimmeler**, University of Frankfurt, Germany

*Function of Long Noncoding RNAs in the Regulation of the Vasculature*

**Philip Tagari**, Amgen, Inc., USA

*Pharmacological and Genetic Inhibition of Hypoxia-Inducible Factor Prolyl Hydroxylases*

**Courtney Griffin**, Oklahoma Medical Research Foundation, USA

*Chromatin Remodeling and Vascular Development*

**Federico Bussolino**, University of Torino, Italy

*Short Talk: Transcription Factor EB Regulates VEGFR2 Function*

### Poster Session 2

#### THURSDAY, MAY 11

### Hypoxia Sensing Mechanism and Mitophagy (Joint)

\***Stefanie Dimmeler**, University of Frankfurt, Germany

**Åsa B. Gustafsson**, University of California, San Diego, USA

*Parkin-Dependent Degradation of Mitochondria by a Rab5 Endosomal Pathway*

\***Kenneth Walsh**, University of Virginia School of Medicine, USA

*Clonal Hematopoiesis and Cardio-metabolic Disease: New Mechanisms, New Therapeutic Opportunities*

**Marlene Rabinovitch**, Stanford University, USA

*A BMP-Notch Axis Coordinates Mitochondrial Function, Chromatin Remodeling and Gene Regulation to Regenerate Endothelium in Response to Injury*

**M. Celeste Simon**, University of Pennsylvania, USA

*Balancing Cell Growth with Homeostasis in the Tumor Microenvironment*

**Ivan Menendez-Montes**, Fundacion CNIC, Spain

*Short Talk: Cardiac HIF/VHL Signaling Regulates Glycolytic and Oxidative Metabolic Programs and Is Essential for Myocardial Maturation during Heart Development*

**Erin Reineke**, Houston Methodist Research Institute, USA

*Short Talk: Coordination of Cellular Function by Steroid-Receptor Coactivator 2 in Stress-Induced Cardiac Angiogenesis*

### Workshop 2: Intracellular Signaling and Vascular Function (Z3)

\***George E. Davis**, University of Missouri School of Medicine, USA

**Christopher D. Kontos**, Duke University Medical Center, USA

*Caskin2: A Novel Regulator of Endothelial Cell Quiescence*

**Qing Robert Miao**, Medical College of Wisconsin, USA

*Ras Signaling Is Required for Preventing Cerebrovascular Malformation*

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**Sarah J. Parker**, Cedars Sinai Medical Center, USA  
*Proteomics Reveals Context-Dependent Shifts in Mitochondrial Protein Expression and Novel Non-Canonical TGF $\beta$  Signaling Activation in the Aorta of Marfan Syndrome Mice*

**Vivek Venkataramani**, University Medical Center Göttingen, Germany  
*CD31 Expression Determines Redox Status and Chemoresistance in Human Angiosarcomas*

**Ruowen Ge**, National University of Singapore, Singapore  
*Extracellular Antiangiogenic Proteins Target Mitochondria through a Novel Route of Protein Trafficking via Endocytosis and Direct Endosome-Mitochondrion Fusion*

### Metabolic Regulation of Cell Signaling (Z4)

\***Guido Kroemer**, Cordeliers Research Center, France  
*Metabolic Regulation of Autophagy*

**Michael N. Sack**, NHLBI, National Institutes of Health, USA  
*Nutrient Sensing, Mitochondria and the Inflammasome*

**Stephen Y. Chan**, University of Pittsburgh School of Medicine, USA  
*The Emerging Nexus between Matrix Stiffness and Cellular Metabolism in the Diseased Pulmonary Vasculature: New Targets for Treating Pulmonary Hypertension*

**Jianhua Xiong**, NHLBI, National Institutes of Health, USA  
*Short Talk: Fatty Acid Oxidation Regulates Endothelial Cell Fate*

### Vascular Stability and Cell-Cell Interactions (Z3)

\***Ralf H. Adams**, Max Planck Institute for Molecular Biomedicine, Germany

**Harry (Hal) C. Dietz**, Johns Hopkins University School of Medicine, Blade Therapeutics, USA  
*TGF $\beta$  in Inherited Vasculopathies: A Matter of Aneurysmic Proportions*

**George E. Davis**, University of Missouri School of Medicine, USA  
*Molecular Determinants Governing EC-Pericyte Tube Co-Assembly and Stability*

**Luisa Iruela-Arispe**, University of California, Los Angeles, USA  
*Vascular Stability and Cell-Cell Interactions during Endothelial Regeneration*

**Arie Horowitz**, Thomas Jefferson University, USA  
*Short Talk: Dynamic Equilibrium of Endothelial Cell Junctions Is Required for Vascular Morphogenesis*

### Poster Session 3

#### FRIDAY, MAY 12

### Regulation of mPTP Opening (Z4)

**Toren Finkel**, University of Pittsburgh/UPMC, USA  
*Mouse Models of the Mitochondrial Calcium Uniporter Complex*

**Elizabeth A. Jonas**, Yale University, USA  
*The Mitochondrial Permeability Transition Pore: Molecular Structure and Function in Health and Disease*

**John W. Elrod**, Temple School of Medicine, USA  
*Mitochondrial Calcium Exchange in Heart Disease*

\***Jeffery D. Molkentin**, Cincinnati Children's Hospital Medical Center, USA

*Mitochondrial Calcium Regulated by MCU Underlies Skeletal Muscle Adaptation*

**Amit U. Joshi**, Stanford University SOM, USA  
*Short Talk: Mitochondrial Dynamics in Neurodegeneration in Patient-Derived Cells and in Animal Models*

**Vivian Werloger Rodrigues de Moraes**, The Scripps Research Institute, USA

*Short Talk: PERK Activation Regulates Mitochondrial Quality Control during Endoplasmic Reticulum Stress*

### Organ Specific Vasculature (Z3)

\***Kathleen M. Caron**, University of North Carolina at Chapel Hill, USA

**Ralf H. Adams**, Max Planck Institute for Molecular Biomedicine, Germany

*Organ-Specific and Functional Specialization of Blood Vessels*

**Susan Quaggin**, Northwestern University, USA

*Unique Molecular and Functional Requirements of the Renal Vasculature*

**Anne C. Eichmann**, Yale University School of Medicine, USA  
*Cross-Talk between Vessels and Nerves*

**Paul S. Frenette**, Albert Einstein College of Medicine, USA  
*Bone Marrow Vascular Niche*

**Lisandra Vila Ellis**, MD Anderson Cancer Center, USA

*Short Talk: Investigating Alveolar Angiogenesis in the Developing Mouse Lung*

**Ching-Ling Ellen Lien**, Saban Research Institute, Children's Hospital, USA

*Short Talk: Coordinated Development of Coronary Vessels, Cortical Cardiomyocytes and Cardiac Lymphatics Supports Heart Morphogenesis and Regeneration*

### Workshop 2: How to Evaluate Mitophagy and Mitochondrial Function in the Cardiovascular System (Z4)

\***Åsa B. Gustafsson**, University of California, San Diego, USA

**Brian Glancy**, NHLBI and NIAMS, National Institutes of Health, USA  
*The Mitochondrial Reticulum of the Heart*

**Knut Lauritzen**, Oslo University Hospital, Norway  
*Impaired Dynamics and Function of Mitochondria Caused by mtDNA Damage Leads to Heart Failure*

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**Xiyuan Lu**, University of California, Davis, USA

*Mitochondrial Subpopulations and Heterogeneity in Adult Cardiac Myocytes Revealed by Confocal Imaging*

**Liming Pei**, Children's Hospital of Philadelphia/University of Pennsylvania, USA

*A Heart-Derived Hormone that Regulates Body Growth*

**Venkatesh Sundararajan**, Rutgers New Jersey Medical School, USA

*Mitochondrial Lon Protease Protects the Heart in vivo Against Ischemia-Reperfusion Injury by Reducing Oxidative Damage*

**Nuo Sun**, NHLBI, National Institutes of Health, USA

*Measuring Cardiac Mitophagy and the Role of USP30 in Heart Failure*

### Metabolism and Heart Failure (Z4)

\***Richard N. Kitsis**, Albert Einstein College of Medicine, USA

*Chaperone-Mediated Autophagy in the Regulation of Mitochondrial Function and Heart Failure*

**Rong Tian**, University of Washington, USA

*The Signaling Role of Branched Chain Amino Acids*

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

*Role of Acquired Abnormalities in Mitochondrial Dynamics and the Mitochondrial Calcium Uniporter (MCU) in Pulmonary Hypertension*

**Katsuhito Fujii**, University of Tokyo, Japan

*Short Talk: Cardiac Macrophage Is Required to Avoid Heart Failure and Cardiac Sudden Death after Pressure Overload*

### Lymphangiogenesis (Z3)

\***Anne C. Eichmann**, Yale University School of Medicine, USA

**Tsutomu Kume**, Northwestern University, USA

*Regulation of Postnatal Lymphatic Vessel Development by Foxc1 and Foxc2*

**Tatiana V. Petrova**, CHUV, University of Lausanne, Switzerland

*Mechanisms of Lymphatic Vessel Specialization*

**Kathleen M. Caron**, University of North Carolina at Chapel Hill, USA

*Lymphatics in Myocardial Injury and Repair*

### Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (Z4)

### Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (Z3)

**SATURDAY, MAY 13**

Departure