



# Molecular Mechanisms of Heart Development

March 26–30, 2017 | Keystone Conference Center | Keystone, Colorado | USA

## Scientific Organizers:

**Benoit G. Bruneau**, Gladstone Institute of Cardiovascular Disease, USA

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

**Margaret E. Buckingham**, Institut Pasteur, France

## Joint with the meeting on *RNA-Based Approaches in Cardiovascular Disease*

*The heart is the first organ to form in the embryo, and its development and function is essential for life. Defects in heart formation result in congenital heart disease, which affects at least 1% of live births. The lessons learned from heart development are also critical for the development of strategies aimed at regenerating diseased adult hearts. This meeting will address advances in our understanding of cellular and molecular mechanisms of heart development, with a view toward congenital heart disease and cardiac regeneration. It will bring together developmental biologists, cardiologists, geneticists and basic scientists from many disciplines to discuss current findings and to promote multi-disciplinary collaborations. The pairing with the Keystone Symposia meeting on “RNA-Based Approaches in Cardiovascular Disease” presents an opportunity to bridge exciting fields in cardiovascular biology.*


## Session Topics:

- Common RNA-Based Mechanisms in Cardiovascular Development and Pathology (Joint)
- Workshop 1: Gene Regulatory Mechanisms
- Cardiac Lineages
- Epicardium and Coronaries
- Gene Regulatory Mechanisms
- Congenital Heart Disease: Genes and Pathways
- Mechanisms of Cardiac Growth and Morphogenesis
- Mechanisms of Cardiovascular Regeneration (Joint)
- Workshop 2: Cardiovascular Repair Mechanisms
- Modeling Human Heart Development

**Scholarship Application & Discounted Abstract Deadline: November 30, 2016**

**Abstract Deadline: December 11, 2016**

**Discounted Registration Deadline: January 26, 2017**



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

Upper image of heart embryo courtesy of Vincent M. Christoffels, Academic Medical Center, Amsterdam

Meeting Hashtag: #KScardiodev

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# KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

## Molecular Mechanisms of Heart Development (X7)

Scientific Organizers: Benoit G. Bruneau, Brian L. Black and Margaret E. Buckingham

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## RNA-Based Approaches in Cardiovascular Disease (X8)

Scientific Organizers: Thomas Thum and Roger J. Hajjar

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### SUNDAY, MARCH 26

#### Arrival and Registration

### MONDAY, MARCH 27

#### Welcome and Keynote Address (Joint)

\***Benoit G. Bruneau**, Gladstone Institute of Cardiovascular Disease, USA

\***Thomas Thum**, Medical School Hannover, Germany

**Eric N. Olson**, University of Texas Southwestern Medical Center, USA  
*Following the Heart*

#### Common RNA-Based Mechanisms in Cardiovascular Development and Pathology (Joint)

\***Benoit G. Bruneau**, Gladstone Institute of Cardiovascular Disease, USA

\***Thomas Thum**, Medical School Hannover, Germany

**Stefanie Dimmeler**, University of Frankfurt, Germany  
*Non-coding RNAs in Cardiovascular Repair and Aging*

**William C. Sessa**, Yale University School of Medicine, USA  
*Vascular Therapeutics Approaches using miRNAs*

**Laurie A. Boyer**, Massachusetts Institute of Technology, USA  
*Long Noncoding RNAs in Heart Development and Differentiation*

**Tilman Ziegler**, Klinikum rechts der Isar der TU München, Germany  
*Short Talk: LNA Mediated Inhibition of miR-132 Prevents Hypertrophy Induced Cardiomyopathy in Pigs*

#### Workshop 1: Gene Regulatory Mechanisms (X7)

\***Eric Small**, University of Rochester, USA

**Nicole Schlüßler**, Goethe University Frankfurt, Germany  
*A LncRNA Locus in the Genomic Region of Hand2 is Essential for Cardiac Development*

**Alexandre R. Colas**, Sanford-Burnham Medical Research Institute, USA  
*Id Genes Are Essential For Early Heart Formation*

**Sunil K. Verma**, University of Texas Medical Branch, USA  
*Role of the RNA Binding Protein Rbfox2 in Hypoplastic Left Heart Syndrome*

**Christian Mosimann**, University of Zürich, Switzerland  
*An Ancient Regulatory Program Controls the Emergence of Cardiogenic Lateral Plate Mesoderm*

**Li Qian**, University of North Carolina at Chapel Hill, USA  
*Single Cell Transcriptomics Reveals a Deterministic Trajectory of Cell Fate Conversion during Direct Cardiac Reprogramming*

**Min Zhang**, Shanghai Children's Medical Center, China  
*Atrial Fibrillation-Associated Functional Element Regulates Pitx2 Expression via CTCF-Mediated Long-Range Interaction*

#### Workshop 1: Basic and Novel Tools for RNA Research (X8)

\***Carlos Fernandez-Hernando**, Yale School of Medicine, USA

\***Leon Johannes De Windt**, Maastricht University, Netherlands

**Esther E. Creemers**, Academic Medical Center, Netherlands  
*Circular RNA Profiling and Implications for Cardiac Disease*

**Mark Mercola**, Stanford University, USA

*High Throughput Screening as a Massive Omics Approach to Understand the Heart*

**Lior Zangi**, Icahn School of Medicine at Mount Sinai, USA

*Gene Therapy Approach for Cardiac Regeneration using Modified mRNA*

**Cristina Espinosa-Diez**, Oregon Health and Science University, USA  
*A MicroRNA Regulated Incoherent Feedforward Loop Drives Vascular Senescence*

#### Cardiac Lineages (X7)

\***Kristy Red-Horse**, Stanford University, USA

**Margaret E. Buckingham**, Institut Pasteur, France  
*Cardiac Cell Lineages and the Second Heart Field*

**Lionel Christiaen**, New York University, USA  
*Regulation of Cardiopharyngeal Multipotency and Early Fate Specification in a Simple Chordate*

**Caroline E. Burns**, Harvard Medical School, Massachusetts General Hospital, USA

*Development of the Cardiopharyngeal Lineage in Zebrafish*

**Nicole Dubois**, Icahn School of Medicine at Mount Sinai, USA  
*Short Talk: Foxa2 Marks a Ventricular Progenitor Population during Heart Development*

#### Fundamentals in RNA Diagnostics and Paracrine Effects (X8)

\***Manuel Mayr**, King's College, University of London, UK

\***Susmita Sahoo**, Icahn School of Medicine at Mount Sinai, USA

**Carlos Fernandez-Hernando**, Yale School of Medicine, USA  
*Noncoding RNAs as Paracrine Players in Vascular Inflammation and Lipid Metabolism*

**Denise Hilfiker-Kleiner**, Medizinische Hochschule Hannover, Germany

*Pathophysiology of Peripartum Cardiomyopathy Links Prolactin to the PAI-1/uPAR System: Modulation of NF- $\kappa$ B Signaling and miR146a as Therapeutic Options*

**Paula da Costa Martins**, Maastricht University, Netherlands  
*Short Talk: Cardiomyocyte-Derived Exosomes Mediate Pathological Cardiac Microvascular Remodeling*

**Yuri D'Alessandra**, Centro Cardiologico Monzino, Italy  
*Short Talk: Circulating MicroRNAs as Biomarkers of Long-Term Doxorubicin-Induced Cardiotoxicity*

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**Stefanie Novakowski**, University of British Columbia, Canada  
*Short Talk: Engineering Platelets for the Delivery of RNA*

**Christa L. Trexler**, University of Colorado Boulder, USA  
*Short Talk: Cardiomyocyte Function and Gene Expression are Influenced by Biological Sex*

### Poster Session 1

#### TUESDAY, MARCH 28

##### Keynote Address (X8)

- \***Roger J. Hajjar**, Mount Sinai School of Medicine, USA
- \***Gerald W. Dorn, II**, Washington University School of Medicine, USA
- Manuel Mayr**, King's College, University of London, UK  
*A Systems Biology Approach: Circulating Noncoding RNAs as Innovative Diagnostic and Prognostic Markers of Cardiovascular Disease*

##### Epicardium and Coronaries (X7)

- \***Kelly Smith**, University of Queensland, Australia
- Kristy Red-Horse**, Stanford University, USA  
*Cell Fate Decisions during Coronary Artery Development*
- Kenneth D. Poss**, Duke University Medical Center, USA  
*Cardiac Regeneration*
- Bin Zhou**, Albert Einstein College of Medicine, USA  
*Developmental Mechanisms of Coronary Artery Formation*
- Paul R. Riley**, University of Oxford, UK  
*Developmental Programming of the Cardiac Lymphatics*
- Michael A. Trembley**, University of Rochester Medical Center, USA  
*Short Talk: Novel Mechanisms of Epicardial-Derived Cell Mobilization*

##### Noncoding RNA Therapeutics: What Have We Learned? (X8)

- \***Roger J. Hajjar**, Mount Sinai School of Medicine, USA
- \***Gerald W. Dorn, II**, Washington University School of Medicine, USA
- Susmita Sahoo**, Icahn School of Medicine at Mount Sinai, USA  
*Exosomes as a Diagnostic and Therapeutic Tool in Cardiovascular Disease*
- Eva van Rooij**, Hubrecht Institute, Netherlands  
*Advances in Targeting miRNAs in the Heart*
- Gianluigi Condorelli**, Humanitas University, Italy  
*Chheaf1: A Novel lncRNA Regulating Cardiac Hypertrophy and Failure*
- Elizabeth M. McNally**, Northwestern University, USA  
*Targeting Muscular Dystrophy*
- Robin Verjans**, Maastricht University, Netherlands  
*Short Talk: Downregulation of the microRNA-221/222 Family Upon Heart Failure Contributes to Adverse Cardiac Fibrotic Remodeling*

**Christine Wahlquist**, Stanford University, USA  
*Short Talk: Modulation of Cardiomyocyte Physiology by Stretch-Induced miRNAs*

##### Gene Regulatory Mechanisms (X7)

- \***Laurie A. Boyer**, Massachusetts Institute of Technology, USA
- Vincent M. Christoffels**, Academic Medical Center, Netherlands  
*Transcriptional Regulation of the Electrical Activity Pattern of the Heart*
- Benoit G. Bruneau**, Gladstone Institute of Cardiovascular Disease, USA  
*Transcriptional Regulation of Heart Development*
- Brian L. Black**, University of California, San Francisco, USA  
*Cooperative Activation of Cardiac Transcription through Myocardial Bridging of Paired MEF2 Sites*
- Rangarajan Nadadur**, University of Chicago, USA  
*Short Talk: Differential Enhancer Transcription Defines a Disease-Associated Gene Regulatory Network*

##### Novel Approaches in RNA Detection and Networks (X8)

- \***Gianluigi Condorelli**, Humanitas University, Italy
- \***Christian Kupatt**, Technical University Munich, Germany
- Stefan Engelhardt**, Institut für Pharmakologie & Toxicologie der TUM, Germany  
*Approaches to Identify Crucial miRNA Mechanisms of Action*
- Arthur A. Levin**, Avidity Biosciences, USA  
*Toxicological Considerations in Oligonucleotide Therapeutics Development*
- Anne Katrine Johansen**, Hubrecht Institute, Netherlands  
*Short Talk: CRISPR/Cas9-based Postnatal Gene Editing to Study Cardiac Gene Function in vivo*
- Prabhu Mathiyalagan**, Icahn School of Medicine at Mount Sinai, USA  
*Short Talk: Dynamic Regulation of m6A RNA methylation is a Novel Remodeling Mechanism of the Ischemic Heart*

### Poster Session 2

#### WEDNESDAY, MARCH 29

##### Congenital Heart Disease: Genes and Pathways (X7)

- \***Vincent M. Christoffels**, Academic Medical Center, Netherlands
- Christine E. Seidman**, Harvard Medical School, USA  
*Steps and Missteps in Building the Heart*
- Ivan P. Moskowitz**, University of Chicago, USA  
*A Timing Switch for Cardiac Progenitor Differentiation*
- William T. Pu**, Children's Hospital, Harvard Medical School, USA  
*iPSC-CM Models of Congenital Heart Disease*

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**Richard P. Harvey**, University of New South Wales, Victor Chang Cardiac Research Institute, Australia

*Transcriptional Targets and Off-Targets in Congenital Heart Disease*

**Zhe Han**, Children's National Medical Center, USA

*Short Talk: High Throughput in vivo Functional Validation of Candidate Congenital Heart Disease Genes in Drosophila*

### Non-Coding RNAs Going Looooong.... (X8)

\***Stefan Engelhardt**, Institut für Pharmakologie & Toxicologie der TUM, Germany

**Gerald W. Dorn, II**, Washington University School of Medicine, USA  
*Orchestration of Smoothed/Hedgehog/GATA Transcriptional Activity by GRKs 2, 5, and 6 in Developing Mouse Hearts*

**Yibin Wang**, University of California, Los Angeles, David Geffen School of Medicine, USA

*A lncRNA-Dependent Epigenetic Check-Point for Cardiac Hypertrophy and Remodeling*

**Thomas Thum**, Medical School Hannover, Germany  
*lncRNAs in Cardiac Remodeling*

**Venkata Naga Srikanth Garikipati**, Temple University, USA  
*Short Talk: Long Noncoding Circular RNA mmu\_circ\_008396 Modulates Cardiac Repair After Myocardial Infarction*

**Da-Zhi Wang**, Children's Hospital Boston, USA  
*Short Talk: Genome-Wide Identification and Characterization of Cardiac Hypertrophy-Related Long Noncoding RNAs*

**Samir Ounzain**, University of Lausanne, Switzerland  
*Short Talk: Transposable Elements Contribute to the Functional and Regulatory Characteristics of Cardiovascular lncRNAs*

### Mechanisms of Cardiac Growth and Morphogenesis (X7)

\***Caroline E. Burns**, Harvard Medical School, Massachusetts General Hospital, USA

**Anthony B. Firulli**, Wells Center for Pediatrics Research, USA  
*Characterization of a Hand1 Left Ventricular Enhancer and Development of a Left Ventricular Specific Cre Driver*

**Katherine E. Yutzey**, Cincinnati Children's Hospital Medical Center, USA

*Developmental Mechanisms of Heart Valve Disease*

**James F. Martin**, Baylor College of Medicine, USA  
*The Hippo Pathway in Heart Development and Regeneration*

**Daniela Panakova**, Max Delbrück Center for Molecular Medicine, Germany

*Short Talk: Planar Cell Polarity Pathway Links Mechanosensitive Feedback between Cardiac Remodeling and Muscle Differentiation*

### Preclinical Approaches Using RNA Therapeutics (X8)

\***Yibin Wang**, University of California, Los Angeles, David Geffen School of Medicine, USA

\***Patrick Most**, University of Heidelberg, Germany

**Rusty Montgomery**, miRagen Therapeutics, Inc., USA  
*Pharmacokinetic/Dynamic Aspects of Oligonucleotide Therapeutics*

**Christian Kupatt**, Technical University Munich, Germany  
*Micro-RNAs based Therapeutics in Porcine Cardiac Disease Models*

**Rabea Hinkel**, Klinikum rechts der Isar, TUM, Germany  
*Short Talk: Cardio-Protective Potential of miR-92a Inhibition in Myocardial Ischemia*

**Dongtak Jeong**, Ichan School of Medicine at Mount Sinai, USA  
*Short Talk: AAV9 miR-25 Tough Decoy Transfer Improves Cardiac Function in HF and Aged MDX/UTRN KO Mice*

**Adam E. Mullick**, Ionis Pharmaceuticals, Inc., USA  
*Short Talk: Characterization of Cardiac Gen 2.5 Antisense Oligonucleotide Activity*

**Deepak Prabhu Ramanujam**, Institute of Pharmakologie und Toxikologie, Technische Universität München, Germany  
*Short Talk: Inhibition of microRNA-21 Prevents Myocardial Remodeling in a Pig Model of Ischemia/Reperfusion Injury*

### Poster Session 3

#### THURSDAY, MARCH 30

### Mechanisms of Cardiovascular Regeneration (Joint)

\***Mauro Giacca**, International Center for Genetic Engineering, Italy

**Deepak Srivastava**, Gladstone Institute of Cardiovascular Disease and University of California, San Francisco, USA  
*Cellular Reprogramming Approaches for Cardiovascular Disease*

**Nadia Mercader**, Institut of Anatomy, University of Bern, Switzerland  
*Plasticity of Cardiomyocyte Fate during Heart Regeneration in Zebrafish*

**Leon Johannes De Windt**, Maastricht University, Netherlands  
*Fetal miRNAs Play Large at Heart Failure*

**Andrew H. Baker**, University of Edinburgh, UK  
*Non Coding RNA Therapeutics in Cardiovascular Pathophysiology*

**Chen Gao**, University of California, Los Angeles, USA  
*Short Talk: Cytosolic RBFOX1 In Cardiac Fibrosis Regulation*

### Workshop 2: Cardiovascular Repair Mechanisms (Joint)

\***Masaki Ieda**, Keio University School of Medicine, Japan

\***Eva van Rooij**, Hubrecht Institute, Netherlands

**Monika M. Gladka**, Hubrecht Institute, Netherlands  
*Zeb2 Protects the Heart from Ischemic Damage*

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**Ajit Magadum**, Icahn School of Medicine, Mount Sinai Hospital, USA  
*Cardiomyocyte-Specific Expression of Cell Cycle Inducer modRNA Induces Cardiac Regeneration*

**FRIDAY, MARCH 31**

**Departure**

**Shin Watanabe**, Icahn School of Medicine at Mount Sinai, USA  
*miR-146a Regulates Cardiac Function by Targeting SUMO1/SERCA2a Pathway*

**Lina A. Shehadeh**, University of Miami Miller School of Medicine, USA  
*Osteopontin RNA Aptamer Can Prevent and Reverse Pressure Overload-Induced Heart Failure*

**C. Geoffrey Burns**, Harvard Medical School, Massachusetts General Hospital, USA  
*Cardiomyocyte Polyploidization Creates a Barrier to Heart Regeneration in Zebrafish*

**Honghai Liu**, Children's Hospital of Pittsburgh of UPMC, USA  
*Repression of Epithelial Cell Transforming 2 (Ect2) Induces Binucleation of Cardiomyocytes*

**Thomas J. Cahill**, University of Oxford, UK  
*Macrophages Activate Distinct Programs of Regeneration and Scar Formation to Direct Repair following Myocardial Infarction*

**Hamid el Azzouzi**, Maastricht University, Netherlands  
*Targeted Deletion of ADAR1 in the Adult Heart Causes Severe Cardiac Dysfunction and Increased Lethality*

### Modeling Human Heart Development (X7)

\***Benoit G. Bruneau**, Gladstone Institute of Cardiovascular Disease, USA

**Christine L. Mummery**, Leiden University Medical Center, Netherlands  
*Developmental Patterning of Human Pluripotent Stem Cells: From Beating Cardiomyocytes to Heart Disease Models*

**Charles E. Murry**, University of Washington, USA  
*Networks Underlying Human Cardiovascular Differentiation*

**Gordon M. Keller**, University Health Network, MaRS Centre, Canada  
*Modeling Cardiovascular Development with Human Pluripotent Stem Cells*

### RNA Therapeutics in Clinical Translation (X8)

\***Wolfram Hubertus Zimmermann**, University Medical Center Göttingen, Germany

**Roger J. Hajjar**, Mount Sinai School of Medicine, USA  
*Gene Therapy and Genome Editing for Heart Failure*

**Patrick Most**, University of Heidelberg, Germany  
*Development of Nucleic-Acid Therapeutics for Cardiac and Vascular Disorder Treatment*

**Mauro Giacca**, International Center for Genetic Engineering, Italy  
*Small RNA Therapy for Cardiac Regeneration*

**Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (X7)**

**Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (X8)**