

KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

Charting a New Course for Heart Failure: From Discovery to Data (Q8)

Scientific Organizers: Mansoor Husain, Benoit G. Bruneau and Marc Pfeffer

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

New Insights into the Biology of Exercise (Q7)

Scientific Organizers: Sue Bodine, Bret H. Goodpaster and John P. Thyfault

March 1-5, 2020 • Keystone Resort • Keystone, CO, USA

Sponsored by Novo Nordisk A/S

Discounted Abstract & Scholarship Deadline: October 31, 2019 / Abstract Deadline: December 3, 2019 / Discounted Registration Deadline: January 7, 2020

SUNDAY, MARCH 1

Arrival and Registration

MONDAY, MARCH 2

Welcome and Keynote Address (Q8)

Deepak Srivastava, Gladstone Institutes, USA

Cardiac Development: Basis for Disease and Regeneration

Welcome and Keynote Address (Q7)

***Sue Bodine**, University of Iowa, USA

Mark Hargreaves, University of Melbourne, Australia

Exercise and Health: Historical Perspectives and New Insights

Heart Failure and Fibrosis (Q8)

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

New Molecular Mechanisms of Fibrosis in Heart Failure

Michelle D. Tallquist, University of Hawaii, USA

Cardiac Fibroblast Regulation of Matrix Assembly and Inflammation

Eva van Rooij, Hubrecht Institute, Netherlands

Important Regulators of Cardiac Fibrosis during Injury

Nick Quaife, Imperial College London, UK

Short Talk: Novel Small Open Reading Frames Are Regulators of Cardiac Fibrosis

Zachary Kadow, Baylor College of Medicine, USA

Short Talk: Cardiac Pitx2 Deficiency Results in Non-Cell Autonomous Activation of Cardiac Fibroblasts

Translating the Mechanisms Driving Human Exercise Adaptations (Q7)

***Sue Bodine**, University of Iowa, USA

Ruth J.F. Loos, Mount Sinai School of Medicine, USA

Drivers of Physical Activity and Exercise – Insights from Genetic Association Studies

Bret H. Goodpaster, Translational Research Institute for Metabolism and Diabetes, USA

Exercise and Calorie Restriction in Humans: Different Means to the Same End?

Stephen Previs, Merck, USA

Integrative Metabolism in the Search for Drug Targets and Candidates

Jon Woodhead, University of Auckland, New Zealand

Short Talk: MOTS-C Is an Exercise Responsive Peptide That Increases Following Acute High Intensity Exercise and Is Modified by Short-Term Training in Healthy Young Men

Stefan Markus Reitzner, Karolinska Institutet, Sweden

Short Talk: Skeletal Muscle Transcriptomics Following Acute Endurance and Resistance Exercise in Life-Long Trained Males

Cardiovascular Response to Exercise (Joint)

***Jill N. Barnes**, University of Wisconsin-Madison, USA

Daniel P. Kelly, University of Pennsylvania, USA

Feeding the Failing Heart

Julie R. McMullen, Baker Heart and Diabetes Institute, Australia

Molecular Mechanisms of Physiological Cardiac Hypertrophy: Implications for New Heart Failure Therapies, Biomarkers, and Predicting Cardiotoxicity

Douglas R. Seals, University of Colorado, USA

Exercise, Oxidative Stress, and Optimal Vascular Aging

Eric Small, University of Rochester, USA

Short Talk: Differential Regulation of Cardiac Fibroblast Accumulation and Fibrosis in Exercise and Heart Failure

Haobo Li, Massachusetts General Hospital, USA

Short Talk: IncExACT1 Acts as a Pivotal Switch between Physiological and Pathological Cardiac Growth

Jonathan Herrera, University of Michigan, USA

Short Talk: High Intensity Interval Training Increases Cardiorespiratory Fitness and Acceleration Capacity in a Transgenic Mouse Model of HCM

Poster Session 1

TUESDAY, MARCH 3

Learning from Past, Looking at Future (Q8)

Marc A. Pfeffer, Brigham and Women's Hospital, USA

Lessons Learned from Neutral Trials on the Road to Drug Therapy?

Speaker to be Announced

Heather Ross, University Health Network, Canada

Preventing Heart Failure Hospitalization with Artificial Intelligence

Wilson Lek Wen Tan, National University of Singapore, Singapore

Short Talk: Disease and Phenotype Relevant Genetic Variants Identified from Histone Acetylomes in Human Hearts

Alykhan Motani, Amgen, Inc., USA

Short Talk: The Novel Myotrope, AMG 594, Is a Small-Molecule Cardiac Troponin Activator That Increases Cardiac Contractility In Vitro and In Vivo

Fabian Chen, Rocket Pharmaceuticals Inc., USA

Short Talk: Gene Therapy for Male Patients with Danon Disease using RP-A501; AAV9.LAMP2B

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Integrative Metabolic Response to Exercise (Q7)

***Bret H. Goodpaster**, Translational Research Institute for Metabolism and Diabetes, USA

David H. Wasserman, Vanderbilt University School of Medicine, USA
Exercise and Glucose Homeostasis: Push and Pull of Liver and Skeletal Muscle

Monika Fleshner, University of Colorado, USA
Exercise and Prebiotics Optimizes the Gut Microbiota and Promotes Stress Robustness

Marcas M. Bamman, University of Alabama at Birmingham, USA
Inter-Individual Response Heterogeneity: A Window into Molecular Transducers of Exercise Adaptation

Simon Schenk, University of California, San Diego, USA
Regulation of Skeletal Muscle Function and Physiology via Acetylation

Timothy D. Allerton, Pennington Biomedical Research Center, USA
Short Talk: An Ethanolic Extract of Artemisia Dracunculul L. Enhances the Metabolic Benefits of Exercise in Diet-Induced Obese Mice

Gianluca Fulgenzi, National Cancer Institute, National Institutes of Health, USA
Short Talk: Novel Metabolic Role for Skeletal Muscle BDNF in Pancreatic β -Cell Insulin Secretion

Diego Hernandez-Saavedra, Ohio State University Wexner Medical Center, USA
Short Talk: Chronic Exercise Negates Concurrent High-Fat Diet to Improve Inter-Tissue Acylcarnitine Handling and Enhances Hepatic Metabolism

Workshop: In Vitro Models of Heart Failure (Q8)

Michael P. Graziano, TARA Biosystems, USA
Biowire™ II Engineered Human Cardiac Tissues: A Platform for Heart Failure Drug Development

Fereshteh Haghighi, Universitätsmedizin Göttingen, Germany
iPSC-based In Vitro Model of Noonan Syndrome with Multiple Lentiginos Indicates that Proliferation and Dedifferentiation of Cardiomyocytes Significantly Contribute to Dysfunctional Myocardium

Uros Kuzmanov, University of Toronto, Canada
Global Phosphoproteomic Profiling of Signaling Pathway Aberrations in Clinical Samples, Animal and Organ-on-a-Chip Models

Fotios G. Pitoulis, Imperial College London, UK
Myocardial Slices – a Novel Cardiac Model to Study Mechanical Load In Vitro

Andrea Dooley Thompson, University of Michigan, USA
A High-Throughput Screen for Disease Modifying Compounds to Treat Hypertrophic Cardiomyopathy Associated with MYBPC3 Mutations

Jason Maynes, Hospital for Sick Children, Canada
Cardio PyRate: Robust Assessment of Cardiac Myocyte Function Using Computer Vision and Machine Learning

Barbara G. Gonzalez Teran, Gladstone Institute, USA
Integration of Protein Interactome Data with Congenital Heart Disease Variants to Identify Novel Disease Genes

Robert Zweigerdt, Hannover Medical School, Medizinische Hochschule Hannover, Germany
Recapitulating Early Embryonic Heart Development with Human Pluripotent Stem Cells

Workshop 1 (Q7)

***Sean H. Adams**, University of Arkansas for Medical Sciences, USA

Sophie Broome, University of Auckland, New Zealand
Effects of Mitochondria-Targeted Antioxidant Supplementation on the Acute Transcriptional Response to Exercise and Adaptations to High Intensity Interval Training in Middle-Aged Men

Linda A. Buss, University of Otago, New Zealand
Cancer Alters Adaptation of Skeletal Muscle Mitochondria to Exercise

J. Matthew Hinkley, AdventHealth Orlando, USA
Transcriptome Signatures of Skeletal Muscle That Define Sarcopenia and Acute Temporal Response to Endurance Exercise in Older Adults

Malene E. Lindholm, Stanford University, USA
Differential Response Trajectories to Acute Exercise in Blood and Muscle

Regenerative Medicine in Heart Failure (Q8)

Li Qian, University of North Carolina at Chapel Hill, USA
Altering Cardiac Cell Destiny

Stephanie Iris Protze, University Health Network, Canada
Human Pluripotent Stem Cells as Source for Biological Pacemakers

Michael A. Laflamme, University Health Network, Canada
Pluripotent Stem Cells for Heart Failure

James F. Martin, Baylor College of Medicine, USA
Short Talk: Hippo Signaling in Heart Regeneration

Lay Ping Ong, Wellcome Trust-MRC Stem Cell Institute, UK
Short Talk: Cellular Therapy for the Chronically Failing Heart?

Adipose and Liver Adaptations to Exercise (Q7)

***John P. Thyfault**, University of Kansas Medical Center, USA

Matthew Watt, University of Melbourne, Australia
Exercise, Hepatokines, and Metabolic Homeostasis

Kristin I. Stanford, Ohio State University, USA
Brown Adipose Tissue Mediates Cardiac Function

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Lauren M. Sparks, Translational Research Institute, USA
Exercise Treats Metabolic Dysfunction by Improving Adipose Metabolism

Hongji Zhang, Ohio State University, USA
Short Talk: Preoperative Exercise Protects the Liver from Surgical Stress by Altering the Immune Environment

Rory Cunningham, University of Missouri, USA
Short Talk: Deletion of Hepatocellular eNOS Impairs Exercise-Induced Improvements in Hepatic Mitochondrial Function

Poster Session 2

WEDNESDAY, MARCH 4

Special Session: Behind the Curtain on Industry Decisions (Q8)

Martin Lefkowitz, Novartis Pharmaceuticals Corporation, USA

Heart Repair and Immunity (Q8)

Hesham A. Sadek, University of Texas Southwestern Medical Center, USA
Hypoxia Regulated Heart Regeneration

Kory J. Lavine, Washington University School of Medicine, USA
Understanding Heart Failure through Macrophage Biology

Benoit G. Bruneau, Gladstone Institutes, USA
Gene Regulatory Networks in Heart Development

Sarah A. Dick, University Health Network, Canada
Short Talk: Using Single Cell Genomics and Genetic Fate Mapping to Define Cardiac Macrophage Heterogeneity and Cardioprotective Functions

Andy Yu, Massachusetts General Hospital, USA
Short Talk: Increased Activin-A Signaling Is Associated with Endothelial Senescence and Inflammation

Exercise and the Brain (Q7)

***Frank W. Booth**, University of Missouri, USA

Henriette van Praag, Florida Atlantic University, USA
Exercise-Induced Brain Plasticity

Michelle Voss, University of Iowa, USA
Exercise Effects on the Human Brain and Cognition Across the Lifespan

Julie A. Christianson, University of Kansas Medical Center, USA
Early Life Stress, Chronic Pain, and Modulation by Exercise

Jill N. Barnes, University of Wisconsin-Madison, USA
Exercise, Cerebral Perfusion, and Cerebral Vascular Function

Constanza J. Cortes, University of Alabama at Birmingham, USA
Short Talk: Enhanced Skeletal Muscle Proteostasis as a Modulator of CNS Aging and Alzheimer's Disease

Nathan Kerr, University of Missouri, USA
Short Talk: LPS-Induced Mild Cognitive Impairment Displays an Age-Dependent Effect on Cognition That Is Ameliorated by Resistance-Training Exercise

Workshop 2: MoTrPAC (Q7)

***Scott Trappe**, Ball State University, USA

Bret H. Goodpaster, Translational Research Institute for Metabolism and Diabetes, USA
Overview of MoTrPAC Clinical Protocol

Sue Bodine, University of Iowa, USA
Overview of MoTrPAC Preclinical Animal Study Protocol

Nicole R. Gay, Stanford University, USA
Acute Endurance Exercise Induces Widespread Transcriptional Changes across Tissues

Weijun Qian, Pacific Northwest National Laboratory, USA
Proteomic and Phosphoproteomic Changes in Rat Skeletal Muscle Induced by Acute Endurance Exercise

Exercise as a Treatment for Heart Failure (Joint)

***Julie R. McMullen**, Baker Heart and Diabetes Institute, Australia

Anthony Rosenzweig, Massachusetts General Hospital, USA
Can Exercise Teach Us How to Treat Heart Failure?

Craig A. Emter, University of Missouri, USA
Exercise and Heart Failure with Preserved Ejection Fraction

Jane EB Reusch, Rocky Mountain Regional VA Medical Center/ University of Colorado, Denver, USA
Diabetes, Exercise Intolerance and Incipient Heart Failure: Systemic Microvascular Dysfunction

Bliss Chang, Harvard, Massachusetts General Hospital, USA
Short Talk: Exercise Training Reverses Cardiac Aging Phenotypes Associated with Heart Failure with Preserved Ejection Fraction

Isabel Witvrouwen, Antwerp University Hospital, Belgium
Short Talk: Vascular Function and Skeletal Muscle Function Associated miR-23a, a Biomarker of VO₂peak Trainability in Patients with Heart Failure with Reduced Ejection Fraction?

Poster Session 3

THURSDAY, MARCH 5

Targeting Metabolism in Heart Failure (Q8)

J. Travis Hinson, The Jackson Laboratory, USA
Development of a Human Sarcomere Functional Assay to Enable Precise and Scalable Functional Interrogation and Reclassification of Heart Failure-Associated Genetic Variants

Lisa Mielniczuk, University of Ottawa Heart Institute, Canada
Right Ventricular Adaptation to Pressure Overload: The Role of Metabolism and Neurohormonal Activation

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Mansoor Husain, Ted Rogers Centre for Heart Research, Canada
Preventing Heart Failure through Metabolic Modulation of Vascular Cells

Ferhaan Ahmad, University of Iowa, USA
Sodium Glucose Co-Transporter 1 (SGLT1) as a Novel Mediator of Heart Failure

Tsune-hisa Yamamoto, University of Pennsylvania, USA
Short Talk: Targeting RIP140 to Modulate Energy Metabolism in the Failing Heart

Maria Papadaki, Loyola University Chicago, USA
Short Talk: Methylglyoxal Modifications on Myofilament Proteins Caused by Diabetes Block Heart Failure Drug Targets through Changing Tropomyosin Position

Anna C. Calkin, Baker Heart & Diabetes Institute, Australia
Short Talk: Induction of Cardiac-Specific Dominant Active IDOL is Associated with Improved Cardiac Function in the Setting of a High Fat Diet

Molecular Response of Skeletal Muscle to Exercise and Inactivity (Q7)

***Simon Schenk**, University of California, San Diego, USA

John P. Thyfault, University of Kansas Medical Center, USA
Lost in Translation: Barriers in Translating Rodent Exercise Models to Human Health

Scott Trappe, Ball State University, USA
Molecular Transducer Responses to Acute and Chronic Exercise Effects

Sue Bodine, University of Iowa, USA
Molecular Mechanisms Underlying the Differential Response of Young and Old Skeletal Muscle to Inactivity and Reloading

Charlotte Suetta, University of Copenhagen, Denmark
Differential Anabolic Response to Loading in Young and Old Muscle following Disuse

Ola A. Hansson, Lund University, Sweden
Short Talk: Genetic Variation in RAB3GAP2 Promotes Capillary Formation and Athlete Performance via Stimulation of Weibel-Palade Body Release

Maria J. Torres, Duke University, USA
Short Talk: The Chemotherapeutic Agent Docetaxel Disrupts Mitochondrial and Contractile Function in 3D Human Bioengineered Myobundles

Emerging Concepts in Heart Failure (Q8)

Kenneth Walsh, University of Virginia School of Medicine, USA
Clonal Hematopoiesis and the Failing Heart

Javid Moslehi, Vanderbilt University Medical Center, USA
Immune Checkpoint Inhibitor-Associated Cardiotoxicities: Learning from Mice and Humans

Michael Alexanian, Gladstone Institute, USA
Short Talk: Dynamic Epigenetic Shifts in Myofibroblast Cell State Drive Reversibility of Heart Failure

Kathryn N. Ivey, Tenaya Therapeutics, USA
Short Talk: Developing a Clinical Cardiac Reprogramming Gene Therapy

Austin Hsu, University of California, San Francisco, USA
Short Talk: Salt-Inducible Kinase 1 Maintains HDAC7 Stability to Promote Pathologic Cardiac Remodeling

Mitochondrial Adaptations to Exercise (Q7)

***Lauren M. Sparks**, Translational Research Institute, USA

Andrea L. Hevener, University of California, Los Angeles, USA
Exercise and Mitochondrial Quality Control

Benjamin F. Miller, Oklahoma Medical Research Foundation, USA
Exercise and Metformin Interactions in Skeletal Muscle

Makoto Kashiwa, Astellas Pharma, Inc., Japan
Potential Pharmacological and Non-Pharmacological Approaches in Patients Who have Difficulty in Physical Exercise

Timothy M. Moore, University of California, Los Angeles, USA
Short Talk: Leveraging the Exercise Hybrid Mouse Diversity Panel to Understand Mitochondrial DNA

Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (Q8)

Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (Q7)

FRIDAY, MARCH 6

Departure