

KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

Islet Biology: From Gene to Cell to Micro-Organ (J6)

Scientific Organizers: Patrick MacDonald, Wen-hong Li, Anna Gloyn and Anette-Gabriele Ziegler

Sponsored by Novo Nordisk A/S

Diabetes: Glucose Control and Beyond (J5)

Scientific Organizers: Alan D. Attie and Deborah M. Muoio

January 27-31, 2020 • Santa Fe Community Convention Center • Santa Fe, NM, USA

Sponsored by Novo Nordisk A/S

Discounted Abstract & Scholarship Deadline: October 2, 2019 / Abstract Deadline: October 30, 2019 / Discounted Registration Deadline: December 3, 2019

MONDAY, JANUARY 27

Arrival and Registration

TUESDAY, JANUARY 28

Welcome and Keynote Address (Joint)

*Patrick MacDonald, University of Alberta, Canada

*Alan D. Attie, University of Wisconsin-Madison, USA

Morris J. Birnbaum, Pfizer Inc., USA

The Development of Therapeutics for T2DM and Related Diseases

All About Insulin: Signaling, Secretion, and Action (Joint)

*Patrick MacDonald, University of Alberta, Canada

*Barbara B. Kahn, Beth Israel Deaconess Medical Center, Harvard Medical School, USA

Michael P. Czech, University of Massachusetts Medical School, USA
Molecular Mechanisms of Insulin Resistance

Maureen Anne Gannon, Vanderbilt University Medical Center, USA
Promoting β -cell Survival and Preserving Functional β -cell Mass by Targeting PGE2 Receptors

Morris F. White, Boston Children's Hospital, Harvard Medical School, USA

The Systemic Integration of Hepatic Insulin Resistance

Arya Mani, Yale University, USA

Short Talk: Mutations in the Celsr2 Gene Unravel the Function of the Encoded Protein as a Novel Incretin

Amelia K. Linnemann, Indiana University School of Medicine, USA
Short Talk: IFN- α Mediates Heterogenous ROS Accumulation in Human Islet Beta-Cells

Poster Session 1

Workshop 1: What Do GWAS Genes Do in Islets? (J6)

*Karen L. Mohlke, University of North Carolina at Chapel Hill School of Medicine, USA

*James D. Johnson, University of British Columbia, Canada

Joseph Angleson, University of Denver, USA

Melanocortin Receptor-4 Regulates α -Cell Function and the Counter-Regulatory Response to Insulin-Induced Hypoglycemia in Mice

Malin Fex, Lund University, Sweden

Loss of Melatonin Type 1A Receptor Results in Dysregulated Whole-Body Metabolism Characterised by Hyperglucagonemia, Glucose Intolerance and Enhanced Insulin Secretion

YongKyung Kim, University of Colorado Anschutz Medical Campus, USA

PTPN2 Plays a Novel Role in the Beta Cells to Regulate Mitochondrial Function in Type 1 Diabetes Progression

Taiyi Kuo, Columbia University, USA

Identification of C2CD4A as a Human Diabetes Susceptibility Gene with a Role in β -Cell Insulin Secretion

Haopeng Lin, Alberta Diabetes Institute, Canada

SEN1 in Compensation and Failure of Insulin Secretion with High-Fat Diet

Depeng Yang, Memorial Sloan Kettering Cancer Center, USA

Sequential CRISPR Screening Uncovers a Novel Role of HHEX in Specifying Human Pancreatic Differentiation

Taylor S. Morriseau, University of Manitoba, Canada

New Insights into the HNF-1 α G319S Variant in Early-Onset T2D Among Manitoba Indigenous Youth

Workshop: Therapeutic Strategies for Targeting Insulin Action (J5)

*Silvia Corvera, University of Massachusetts Medical School, USA

Thiago M. Batista, Joslin Diabetes Center, USA

Dissection of Protein Phosphorylation Networks Underlying Muscle Insulin Resistance in Type 2 Diabetes

Jaroslawna Meister, NIH-NIDDK, USA

Role of β 2-adrenergic Receptor Signaling in Skeletal Muscle Glucose Metabolism

Paul M. Titchenell, University of Pennsylvania, USA

Regulation of Skeletal Muscle Metabolism by Insulin Signaling

Jacqueline Stoeckli, University of Sydney, Australia

ABHD15: A Novel Player in Insulin Regulation of Lipolysis in Adipocytes

Panel Discussion (J5)

*David E. James, University of Sydney, Australia

*Deborah M. Muoio, Duke University Medical Center, USA

Morris J. Birnbaum, Pfizer Inc., USA

Michael P. Czech, University of Massachusetts Medical School, USA

Peter A. Crawford, University of Minnesota, USA

Daniel P. Kelly, University of Pennsylvania, USA

Barbara B. Kahn, Beth Israel Deaconess Medical Center, Harvard Medical School, USA

Islet Plasticity (J6)

*Jean Buteau, University of Alberta, Canada

*Bridget Wagner, Broad Institute, USA

George K. Gittes, Children's Hospital of Pittsburgh of UPMC, USA
Beta Cell Neogenesis and Protection

Julie B. Sneddon, University California, San Francisco, USA
Elucidating Human Endocrine Cell Fate Selection

Seung K. Kim, Stanford University, USA

Alternative Systems to Study Pancreatic Islet Development and Function

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Christine A. Beamish, Houston Methodist Research Institute, USA

Short Talk: Loss of Endocrine Cell Identity Correlates with Pre-Surgical HOMA- β in Patients with Chronic Pancreatitis Undergoing Islet Auto-Transplantation

Mathieu Latreille, Imperial College London, UK

Short Talk: Beta-Cell Dedifferentiation Is Associated with Epithelial-Mesenchymal Transition In Diabetes

Novel Approaches for Monitoring Carbon Traffic Control (J5)

***Peter A. Crawford**, University of Minnesota, USA

Joshua D. Rabinowitz, Princeton University, USA
Isotope Tracing for Deciphering Metabolic Network Usage

David H. Wasserman, Vanderbilt University School of Medicine, USA
Extracellular Barriers to Insulin-Stimulated Muscle Glucose Uptake

Barbara M. Bakker, University Medical Center Groningen, Netherlands
Modeling for Young and Old: Tackling the Complexity of Fatty Acid Oxidation in Metabolic Disease

Maciek R. Antoniewicz, University of Delaware, USA
Short Talk: Metabolite Cross-Feeding Interactions in Adipocyte-Hepatocyte Co-Cultures Elucidated with a Novel ^{13}C -Metabolic Flux Analysis Technique

Jose M. Orozco, Whitehead Institute for Biomedical Research/MIT, USA
Short Talk: Dihydroxyacetone Phosphate Signals Glucose Availability to mTORC1

WEDNESDAY, JANUARY 29

Visualizing Islet Function in vitro, in situ, and in vivo (J6)

***Amelia K. Linnemann**, Indiana University School of Medicine, USA

***Wen-hong Li**, University of Texas Southwestern Medical Center, USA

Sebastian Barg, Uppsala University, Sweden
Exocytosis of Insulin and Glucagon Granules in Type-2 Diabetes

Joana Almaca, University of Miami, USA
Control of Islet Hormone Secretion by Vascular Pericytes

Robin A. Kimmel, University Innsbruck, Austria
In Vivo Imaging of Pancreatic Islet Morphogenesis in Zebrafish

Stephan Speier, Helmholtz Zentrum München, Germany
Imaging Islet Physiology in situ and in vivo

Yu Hsuan Carol Yang, Max Planck Institute for Heart and Lung Research, Germany
Short Talk: Innervation Modulates the Functional Connectivity between Pancreatic Endocrine Cells

Nicole Hallahan, University of Sydney, Australia

Short Talk: Reconstruction of the Polar Domains of Pancreatic Beta-Cells Affects Synaptic Protein Localisation and GSIS

Barak Blum, University of Wisconsin, USA

Short Talk: Roundabout Receptors Regulate Three-Dimensional Architecture and Facilitate Synchronized Ca^{2+} Oscillations In Vivo in the Islet of Langerhans

Ketones and Ketogenesis; Super-Fuel or Nuclear Signal? (J5)

***Judith A. Simcox**, University of Wisconsin, Madison, USA

Richard Veech, NIAAA, National Institutes of Health, USA
The Effects of Ketone Body Metabolism on the Great Controlling Nucleotide Couples and their Application to Common Diseases

Peter A. Crawford, University of Minnesota, USA
Tracing the Role of Intrahepatic Ketone Turnover in Fatty Liver Disease

Daniel P. Kelly, University of Pennsylvania, USA
Ketones and Heart Failure

Eric M. Verdin, Buck Institute for Research on Aging, USA
Ketones as a Nuclear Signal

Justin Lengfeld, University of Minnesota, USA
Short Talk: Chronic Low-Dose Ethanol Intake Exacerbates High-Fat Diet Induced Hepatic Fibrosis

Meilian Liu, University of New Mexico Health Sciences Center, USA
Short Talk: Adipocyte COX-2/PGE2 Pathway is Required for Intermittent Fasting-Induced Treg Development and Improvement of Insulin Sensitivity

Molecular and Functional Analysis of Islet Cell Heterogeneity (J6)

***Claes B. Wollheim**, University of Geneva Medical Centre, Switzerland

***Maureen Anne Gannon**, Vanderbilt University Medical Center, USA

Wen-hong Li, University of Texas Southwestern Medical Center, USA
Functional Heterogeneity of Islet beta Cells

Richard KP Benninger, University of Colorado, USA
Imaging Islet Heterogeneity and Connectivity

Anna Martinez Casals, Science for Life Laboratories, Sweden
Single Cell Protein Variability in Pancreas by CODEX Highly-Multiplexed Imaging

James C. Lo, Weill Cornell Medicine, USA
Short Talk: Adipsin Blocks Beta Cell Failure in Diabetic Mice and Associates with Protection from Diabetes in Humans

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Lydia Amanda Farack, Weizmann Institute of Science, Israel
Short Talk: Transcriptional Heterogeneity of Beta Cells in the Intact Pancreas Reveals Division of Labor between 'Basal Secretor' Extreme Beta Cells and 'Glucose Responder' Non-Extreme Beta Cells

Supercomplexities of Mitochondrial Dynamics and Bioenergetics (J5)

***Dave Pagliarini**, Morgridge Institute for Research at University of Wisconsin-Madison, USA

Jared Rutter, University of Utah, USA
Metabolism and Cellular Decisions

Orian S. Shirihai, University of California, Los Angeles, USA
Mitochondrial Heterogeneity in the Adipocyte

Deborah M. Muoio, Duke University Medical Center, USA
Understanding and Preventing Lipid-Induced Mitochondrial Stress

Ayon Ibrahim, University of Pennsylvania, USA
Short Talk: Mitochondrial ATP Production Drives Endothelial Fatty Acid Uptake and Transport

Heather A. Lawson, Washington University in Saint Louis, USA
Short Talk: Natural Brown Adipose Expansion and Remission of Hyperglycemia in Obese SM/J Mice

Poster Session 2

THURSDAY, JANUARY 30

Stem Cells and Micro-Organs (J6)

***Malin Fex**, Lund University, Sweden

***Jochen Lang**, Université de Bordeaux, France

Jennifer E. Bruin, Carleton University, Canada
Environmental Toxins and Embryonic Pancreas Development

Burcak Yesildag, InSphero AG, Switzerland
Biomimetic Microtissues: Novel Methods for Studying Islet Biology in Health and Disease

Anne Grapin-Botton, University of Copenhagen, Denmark
Three Dimensional Models of Human Pancreas Organogenesis to Understand Diabetes

Mark D. Ungrin, University of Calgary, Canada
Generation and Characterization of Human Pseudoislets

Phillip L. Lewis, Cincinnati Children's Hospital Medical Center, USA
Short Talk: Development of a Fluidic Platform to Study Insulin Secretion from Pluripotent Stem Cell-Derived Human Insulin-Secreting Cells

Ali Hasan Shilleh, University of Colorado, Anschutz Medical Campus, Barbara Davis Center, USA
Short Talk: Determining the Fate of Stem Cell Derived Pancreatic β -like Cells (sBCs) Upon Transplantation Using Genetic Lineage Tracing

Katharina Scheibner, Helmholtz Zentrum Munich, Germany
Short Talk: New Approaches to Produce Beta Cells from Human Stem Cells

Molecules Mediating Tissue Crosstalk (J5)

***Mark A. Herman**, Duke University Medical Center, USA

Joseph A. Baur, University of Pennsylvania, USA
Mitochondrial NAD Transport

Mark A. Febbraio, Monash Institute of Pharmaceutical Sciences, Australia
Extracellular Vesicles Mediating Cross-Talk during Exercise

Judith A. Simcox, University of Wisconsin, Madison, USA
Role of Acylcarnitines as Peripheral Metabolic Signals

Barbara B. Kahn, Beth Israel Deaconess Medical Center, Harvard Medical School, USA

Lipokines as Nutrient Sensors and Signals

Silvia Corvera, University of Massachusetts Medical School, USA
Short Talk: A Placenta to Adipose Tissues Signaling Axis Controls IGF-1 Availability and Insulin Sensitivity in Pregnancy

Peter K. Jackson, Stanford University, USA
Short Talk: Omega-3 Fatty Acids Activate Ciliary FFAR4/GPR120 to Trigger cAMP-Dependent Differentiation of Preadipocytes

Inflammation, Killing, and Islet Dysfunction (J6)

***Bruce Verchere**, University of British Columbia, Canada

***Rebecca Hull**, University of Washington, USA

Anette-Gabriele Ziegler, Helmholtz Zentrum München, Germany
Islet Autoimmunity

Irina Maria Stefana, University of Oxford, UK
Hyperphosphorylated Tau is Expressed in Human Pancreatic Islets and Accumulates in the β -cell Cytoplasm During Ageing

Rebecca Hull, University of Washington, USA
Islet Inflammation in CFRD

Mollie Huber, University of Florida, USA
Short Talk: Investigating Type 1 Diabetes Pathogenesis Using Live Pancreas Tissue Slices

Diane C. Saunders, Vanderbilt University Medical Center, USA
Short Talk: Macrophages Are a Prominent Immune Cell Population in the Developing Human Pancreas

Gut Control of Metabolism (J5)

***Kristina Schoonjans**, École Polytechnique Fédérale de Lausanne – EPFL, Switzerland

Darleen A. Sandoval, University of Michigan, USA
Using Bariatric Surgery to Understand the Regulatory Role of the Gut in Metabolism

Mark A. Herman, Duke University Medical Center, USA
Molecular Aspects of Fructose-Induced Metabolic Dysregulation

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Eric Yen, University of Wisconsin-Madison, USA
Intestinal Lipid Processing and Pancreatic Islet Function: A Gut Reaction?

Marc Liesa, University of California, Los Angeles, USA
Short Talk: Mitochondrial ABCB10 Increases Bilirubin Actions on the Redox State to Promote Insulin Resistance and Steatosis in Liver

Sophie L. Lewandowski, University of Wisconsin-Madison, USA
Short Talk: Additive Effects of β -Cell Pyruvate Kinase Activation and GLP-1 Receptor Signaling on Insulin Secretion

Poster Session 3

FRIDAY, JANUARY 31

Keynote Address (Joint)

***Maureen Anne Gannon**, Vanderbilt University Medical Center, USA

***Anna Louise Gloyn**, University of Oxford, UK

Maike Sander, University of California, San Diego, USA
Metabolic Influences on Pancreatic Beta Cells

Genetics/Genomics of T2D (Joint)

***Maureen Anne Gannon**, Vanderbilt University Medical Center, USA

***Anna Louise Gloyn**, University of Oxford, UK

Unravelling Mechanisms for Pancreatic Islet Dysfunction from GWAS

Karen L. Mohlke, University of North Carolina at Chapel Hill School of Medicine, USA

Adipose Tissue Genomics and Type 2 Diabetes

Alan D. Attie, University of Wisconsin-Madison, USA

Genetics of Insulin Secretion

Marcus M. Seldin, University of California, Irvine, USA

Short Talk: Systems Genetics Approaches to Dissect Inter-tissue Communication

Christopher Emfinger, University of Wisconsin-Madison, USA

Short Talk: Zfp148 Regulates a Transcriptional Network Suppressing Insulin Secretion

Workshop 2: The Human Islet Research Network - Human Pancreas Analysis Programs (J6)

***Marcela Brissova**, Vanderbilt University, USA

***Nicolai M. Doliba**, University of Pennsylvania, USA

Catherine Lee May, University of Pennsylvania, USA
The Human Pancreas Analysis Program – Type 1 Diabetes

Alvin C. Powers, Vanderbilt University School of Medicine, USA
The Human Pancreas Analysis Program - Type 2 Diabetes

Xiaoqing Dai, University of Alberta, Canada
Pancreatic α -cell Function and Identity in Type 1 Diabetes Mellitus

Matthew Haemmerle, Perelman School of Medicine at the University of Pennsylvania, USA

The PCBP RNA Binding Proteins as Post-Transcriptional Regulators of β Cell Identity

Tiffany Richardson, Vanderbilt University, USA

Pancreatic Islet and Exocrine Tissue Innervation is Not Altered in Type 1 Diabetes

Rafael Arrojo e Drigo, The Salk Institute, USA

Aging of Human Endocrine Pancreatic Cell Types Is Heterogeneous and Sex-Specific

Novel Approaches to Single Cell Biology (J6)

***Mathieu Latreille**, Imperial College London, UK

***Julie B. Sneddon**, University California, San Francisco, USA

Heiko Lickert, Institute of Diabetes and Regeneration, Germany
Deciphering Mechanisms of β -Cell Failure and Regeneration by Single Cell RNA Sequencing

Diego Balboa, Centre for Genomic Regulation, Spain
Improving Diabetes Disease Modelling with Single Cell RNA Sequencing of Stem Cell Derived Pancreatic Cells

Patrick MacDonald, University of Alberta, Canada
Connecting Single-Cell Function and Transcriptomics

Rachel E. Jennings, University of Manchester, UK
Short Talk: A Single Cell Atlas of the Developing Human Pancreas

From Systems Biology to Metabolic Physiology (J5)

***Barbara M. Bakker**, University Medical Center Groningen, Netherlands

Kristina Schoonjans, École Polytechnique Fédérale de Lausanne – EPFL, Switzerland

Emerging Roles of Bile Acid Signaling in Metabolism and Stemness

Dave Pagliarini, Morgridge Institute for Research at University of Wisconsin-Madison, USA

Regulation of Mitochondrial Metabolism by Reversible Phosphorylation

David E. James, University of Sydney, Australia

The Role of Reactive Oxygen Species in Insulin Resistance

Takumi Kitamoto, Columbia University, USA

Short Talk: The Genomic Architecture of the FoxO1 Response to Fasting and Refeeding in Liver

Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (J6)

Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (J5)

SATURDAY, FEBRUARY 1

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