



Join Keystone Symposia
for the 2016 conference on:

Stem Cells & Regeneration in the Digestive Organs

March 13–17, 2016

Keystone Resort | Keystone, Colorado | USA

Scientific Organizers:

Linheng Li, Martín G. Martín, James M. Wells and Markus Grompe

Joint with the conference on Islet Biology: From Cell Birth to Death

The gastrointestinal, pancreatic and hepatobiliary systems serve many essential functions, and stem cell (SC)-based tissue regeneration holds promise for treating diseases of the digestive system (DS). Recent advances include differentiation of pluripotent SCs (ESCs, iPSCs) into intestinal, pancreatic and hepatic cells that may someday be used to replace defective cell types. However, a gap remains between these achievements in basic research and translation into clinical treatment. This meeting will be the first to bring together a broad representation of scientists researching SC from the interrelated fields of the DS. With open and vigorous discussion, the meeting will “cross boundaries” and capitalize on the common principles and unique features of the three systems. Specific aims of the meeting are to: 1) Facilitate characterization of the properties of DS SC in vivo; 2) Address how the heterogeneity of the microenvironment influences the state and fate of SCs/PCs; 3) Narrow the gap between findings of in vitro and in vivo identification; and 4) Explore applications for converting stem into functional DS cell systems to overcome disease. The meeting should result in new scientific methods, insights, collaborations and technical capabilities for the entire DS, and facilitate further clinical advances.

Session Topics:

- GI Lineages from Pluripotent Stem Cells
- Workshop and Panel Discussion: Tissue Engineering
- Disease Modeling
- Identity and Function of GI Stem and Progenitor Cells
- Programmed or Reprogrammed Regeneration
- Adult Pancreatic Stem Cells (Joint)
- Stem and Progenitor Cells in Homeostasis and Diseases
- Developmental Origin of Stem Cells
- Workshop and Panel Discussion: Hurdles to Translation
- Translational and Clinical Applications



Submitting an abstract is a great way of participating in the conference through poster presentation and possible selection for a short talk.

Scholarship & Discounted Abstract Deadline: Nov 12, 2015

Abstract Deadline: Dec 15, 2015

Discounted Registration Deadline: Jan 14, 2016

For additional details, visit www.keystonesymposia.org/16X6.

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KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

Stem Cells and Regeneration in the Digestive Organs (X6)

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Islet Biology: From Cell Birth to Death (X5)

Scientific Organizers: Klaus H. Kaestner, Christopher J. Rhodes and Yuval Dor

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SUNDAY, MARCH 13

Arrival and Registration

MONDAY, MARCH 14

Welcome and Keynote Address (Joint)

***Klaus H. Kaestner**, University of Pennsylvania School of Medicine, USA

***Linheng Li**, Stowers Institute for Medical Research, USA

Hiroimitsu Nakauchi, Stanford University, USA

Interspecific Blastocyst Complementation: Can Patient-Specific Islets of Langerhans Be Generated in Pigs?

GI Lineages from Pluripotent Stem Cells (X6)

***Stephen A. Duncan**, Medical University of South Carolina, USA

Gordon M. Keller, University Health Network, MaRS Centre, Canada
Patterning Human Pluripotent Stem Cell-Derived Endoderm

Paul Gadue, Children's Hospital of Philadelphia, USA

GATA6 Regulation of Endoderm and Pancreatic Development from Human Pluripotent Stem Cells

James M. Wells, Cincinnati Children's Hospital Research Foundation, USA

Human Pluripotent Stem Cell-Derived Tissues as New Models to Study Development and Disease of the Digestive Tract

Alexander Kleger, Ulm University, Germany

Short Talk: Human Pluripotent Stem Cell-Derived Pancreatic Organoids to Study Cystic Fibrosis in a Dish

Developmental and Regenerative Biology of the Endocrine Pancreas (X5)

***Lori Sussel**, University of Colorado Anschutz Medical Campus, USA

Anne Grapin-Botton, University of Copenhagen, Denmark

Progenitor Heterogeneity as a Driver of Pancreas Development

Chris Wright, Vanderbilt University Medical Center, USA

Intra-Islet Endocrine-Cell Communication and the Control of Beta-Cell Number and Replication State

Seung K. Kim, Stanford University, USA

Signaling Regulation of Islet Morphogenesis

Caitlin Braitsch, University of Texas Southwestern Medical Center, USA

Short Talk: Hippo-Warts Pathway Regulation of Pancreatic Epithelial Architecture and Progenitor Cell Fate

Alireza Rezania, CRISPR Therapeutics, USA

Short Talk: In vitro Generation of Insulin-producing Cells with Insulin Secretion Dynamics and Mitochondrial Metabolism Similar to Adult Human Islets

Workshop and Panel Discussion 1: Tissue Engineering (X6)

***Mo Ebrahimkhani**, Arizona State University, USA

Engineering Self-Organization of Human Pluripotent Stem Cells to a Fetal Liver-Like Tissue

Bruce M. Wang, Stanford University, USA

Self-Renewing Diploid Axin2+ Cells Fuel Homeostatic Renewal of the Liver

Joseph J. Lancman, Sanford Burnham Presbys Medical Discovery Institute, USA

Induced in vivo Cell Reprogramming of Muscle into Endoderm Lineages

Kay Wiebrands, Hubrecht Institute, Netherlands

Single-Cell RNA Sequencing Reveals Divergence of Lgr5+ Stem Cells during Development of the Gastrointestinal Tract

Alan C. Mullen, Harvard Medical School, USA

DIGIT is a Conserved Long Noncoding RNA that Regulates Goosecoid Expression to Control Endoderm Differentiation of Human Embryonic Stem Cells

***Jan Jensen**, Lerner Research Institute, USA

Understanding Multi-Lineage Differentiation of Endodermal Progenitor Cells using a Systems Developmental Biology Approach

Workshop 1: Pancreatic Islet Cell Development, Growth and Regeneration (X5)

***Doris A. Stoffers**, Perelman School of Medicine, University of Pennsylvania, USA

Yunus Alpogu, IMB-ASTAR, Singapore

Modelling Mitchell-Riley Syndrome in vitro using iPS Cells Derived from a RFX6 Mutant Patient

Caitlin Collin, University of Copenhagen, Denmark

The Function of Notch Ligands in Pancreas Development

Nidheesh Dadheech, University of Alberta, Canada

GLP-1 Induces Neurog3 Re-expression and Beta-Cell Neogenesis in Adult Mice

Benjamin Neal Ediger, University of Pennsylvania, USA

Ldb1 Maintains the Terminally Differentiated State of Pancreatic Beta-cells through a Functional Interaction with Isl-1

Katie L. Sinagoga, Cincinnati Children's Hospital Medical Center, USA

mTOR Regulates Postnatal Morphogenesis, Maturation, and Function of Murine Islets

Francesca M. Spagnoli, Max Delbrück Center for Molecular Medicine, Germany

Axon Guidance Signaling Controls Pancreatic Cell Identity

Amita Tiyaboonchai, University of Pennsylvania, USA

GATA6 in Human Endoderm and Pancreatic Development from Human Pluripotent Stem Cells

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Pei Wang, University of Texas Health Science Center at San Antonio, USA

Investigating the Role of the Hippo Signaling Pathway in Pancreatic Endocrine Cell Development and Beta Cell Proliferation

Disease Modeling (X6)

***Gordon M. Keller**, University Health Network, MaRS Centre, Canada

Frederic J. de Sauvage, Genentech, Inc., USA

Targeting Intestinal Stem Cells in Cancer

Stephen A. Duncan, Medical University of South Carolina, USA

Disease Modeling with ESC/iPSCs-Derived Hepatocyte-Like Cells

Holger Willenbring, University of California, San Francisco, USA

Liver Cell Therapy with Hepatocytes Derived from Pluripotent Stem Cells

Tobias Cantz, Hannover Medical School, Germany

Short Talk: Patient-Specific iPSC Cell-Based Hepatic Cells Allow Modeling of Transthyretin-Related Familial Amyloid Polyneuropathy

Controlling Beta-Cell Function (X5)

***Alvin C. Powers**, Vanderbilt University School of Medicine, USA

Doris A. Stoffers, Perelman School of Medicine, University of Pennsylvania, USA

Mining the Pdx1 Cistrome for Novel Insights into Diabetes

Christopher J. Rhodes, AstraZeneca, USA

CNS Control of Pancreatic Islet-Cell Function

Cristina M. Rondinone, Cellarity Inc., USA

Novel Direct and Indirect Ways to Improve Beta Cell Health

Poster Session 1

TUESDAY, MARCH 15

Identity and Function of GI Stem and Progenitor Cells (X6)

***Hans C. Clevers**, Hubrecht Institute, Netherlands

Frédéric Lemaigre, de Duve Institute and Université Catholique de Louvain, Belgium

Dynamics of Hepatic Cell Differentiation Depend on microRNA-Dependent Regulatory Motifs

Stuart J. Forbes, University of Edinburgh, UK

The Role of Hepatic Progenitor Cells in Liver Regeneration

Timothy C. Wang, Columbia University, USA

Gastric Stem Cells and Their Niches

Linheng Li, Stowers Institute for Medical Research, USA

Characterization of Drug-resistant Quiescent Stem Cells in Intestine

Nicholas R. Smith, Oregon Health & Science University, USA

Short Talk: Bmi1-Expressing Intestinal Stem Cells Drive Emergency Re-Epithelialization

Beta-Cell Growth and Proliferation (X5)

***Andrew F. Stewart**, Mount Sinai School of Medicine, USA

Yuval Dor, Hebrew University-Hadassah Medical School, Israel
The Genetic Program of Replicating beta Cells

Heiko Lickert, Institute of Diabetes and Regeneration, Germany
Identification of Proliferative and Mature B-cells in the Islet of Langerhans

Klaus H. Kaestner, University of Pennsylvania School of Medicine, USA

The Epigenome during Beta-Cell Maturation

Jorge Ferrer, Imperial College London, UK

Long Noncoding RNAs in Beta-Cells

Justin P. Annes, Stanford University, USA

Short Talk: Multi-ligand Targeting of DYRK1A/B and Casein Kinase1gamma2 Promotes beta-cell Replication

Bethany A. Carboneau, Vanderbilt University, USA

Short Talk: Regulation of Beta-Cell Mass Expansion by Prostaglandin E2 Signaling

Workshop 2: Pancreatic Beta-Cell Death and Survival (X5)

***Guy A. Rutter**, Imperial College London, UK

Michal Aharoni-Simon, University of British Columbia, Canada
Anti-Apoptotic Bcl-2 Regulates Reactive Oxygen Species Signaling and a Redox-Sensitive Mitochondrial Proton Leak in Mouse Pancreatic beta-Cells

Lukas Adrian Berchtold, University of Copenhagen, Denmark
Pannexin-2 is an Anti-Apoptotic Protein in Pancreatic beta-Cells

Anne Close, University of Alberta, Canada

The Nuclear Receptor Nor1/Nr4a3 Mediates Cytokines-induced beta-cell Apoptosis and Regulates beta-cell Mass

Yong Kyung Kim, University of Colorado, Anschutz Medical Campus, USA

Disruption of Mitochondrial Crif1 (CR6-interacting factor-1) in Mouse beta Cells Leads to Diabetes with Progressive beta Cell Failure

Amelia K. Linnemann, University of Wisconsin-Madison, USA
Interleukin-6 Stimulates Autophagy in Pancreatic beta-cells and Protects against Apoptosis

Michelle E. Kimple, University of Wisconsin, Madison, USA
G-protein-mediated Mechanisms Linking Beta-cell Death, Dysfunction, and Decompensation in Diabetes

Jason M. Tonne, Mayo Clinic, USA

Nestin-positive Pericytes Facilitate beta-cell-protection through Prevention of Excessive beta-cell-targeted Immune Reactions and Promotion of beta-cell Regeneration in Insulinitis

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Brett S. Peterson, Duke University, USA

Delayed Apoptosis Allows Islet beta-cells to Implement an Autophagic Mechanism to Promote Cell Survival

Programmed or Reprogrammed Regeneration (X6)

***Holger Willenbring**, University of California, San Francisco, USA

Lijian Hui, Shanghai Institutes of Biological Sciences, China
Direct Reprogramming of Human Fibroblasts to Functional Hepatocyte-Like Cells

Louise Laurent, University of California, San Diego, USA
Using Single-Cell Transcriptomics to Discover Cellular Reprogramming Factors for Autologous Cell Replacement Therapy for Type 1 Diabetes

Markus Grompe, Oregon Health & Science University, USA
Tissue Regeneration in Liver: Plasticity or Stem Cells?

Claude Gérard, Université Catholique de Louvain, Belgium
Short Talk: A Mathematical Model for the Transcription Factor Network Driving Hepatocyte Differentiation

Other Islet Cell Types: Major Contributor to Glucose Homeostasis and Health? (X5)

***Nils Billestrup**, University of Copenhagen, Denmark

Alvin C. Powers, Vanderbilt University School of Medicine, USA
Interactions of Endothelial Cells, Macrophages, and Islet Cells

Patrik Rorsman, Oxford Centre for Diabetes, Endocrinology and Metabolism, UK
ATP-Regulated Potassium Channels in the Regulation of Glucagon Secretion

Per-Olof Berggren, Karolinska Institutet, Sweden
Insight Into Pancreatic Islet Cell Physiology/Pathology

Guy A. Rutter, Imperial College London, UK
Short Talk: Deletion of the Type 2 Diabetes-associated Gene StarD10 in Mice Impairs Insulin Secretion and Action

Poster Session 2

WEDNESDAY, MARCH 16

Adult Pancreatic Stem Cells (Joint)

***Catherine Lee May**, University of Pennsylvania, USA

***Markus Grompe**, Oregon Health & Science University, USA

Matthias Hebrok, University of California, San Francisco, USA
Cellular Plasticity in the Adult Pancreas

Joe Q. Zhou, Weill Cornell Medical College, USA
Renewable Generation of Functional Insulin+ Cells from Gastric Tissues

Lori Sussel, University of Colorado Anschutz Medical Campus, USA
Regulation of Pancreatic Beta Cell Identity

Maik Sander, University of California, San Diego, USA

Chromatin State in Beta cell Development and Function

Stephanie A. Campbell, Child and Family Research Institute, Canada
Short Talk: Trithorax Group Complexes are Essential for Pancreatic Endocrine and Exocrine Cell Specification

Stem and Progenitor Cells in Homeostasis and Diseases (X6)

***Linheng Li**, Stowers Institute for Medical Research, USA

Maureen Anne Gannon, Vanderbilt University Medical Center, USA
Expansion of Functional Pancreatic beta-Cell Mass Using Connective Tissue Growth Factor (CTGF)

Calvin Kuo, Stanford University, USA
Regulation of Intestinal Stem Cell Self-Renewal

Ben Z. Stanger, University of Pennsylvania, USA
Cellular Plasticity in the Liver

Mark Lewis, Washington University in St. Louis, USA
Short Talk: The Role of IFRD1 in Reprogramming Secretory Cells

Beta-Cell Stress (X5)

***Ernesto Bernal-Mizrachi**, University of Miami Miller School of Medicine, USA

Miriam Cnop, Universite Libre de Bruxelles, Belgium
Mechanisms of Pancreatic Beta-cell Death in Type 2 Diabetes

Marc Y. Donath, University Hospital Basel, Switzerland
Physiology of Pro-Inflammatory Cytokines in Metabolism: Therapeutic Consequences

Roland W. Stein, Vanderbilt University Medical Center, USA
Examining How the MAFA and MAFB Transcription Factors Regulate Human Islet Beta Cell Function

Maria S. Remedi, Washington University Medical School, USA
Short Talk: Plasticity of Pancreatic beta-cells: Dedifferentiation in Diabetes and Re-differentiation after Insulin Therapy

Poster Session 3

THURSDAY, MARCH 17

Keynote Address (X6)

***Markus Grompe**, Oregon Health & Science University, USA

Hans C. Clevers, Hubrecht Institute, Netherlands
Lgr5 Stem Cell Organoids and Disease

Developmental Origin of Stem Cells (X6)

***James M. Wells**, Cincinnati Children's Hospital Research Foundation, USA

Jason R. Spence, University of Michigan Health System, USA
Pluripotent Stem Cell Derived Organoid Models to Study Human Development

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Atsushi Suzuki, Medical Institute of Bioregulation, Kyushu University, Japan

Stem Cell Systems in the Liver

Olivia G. Kelly, Viacyte, Inc., USA

Stem-Cell Derived, Macroencapsulated Islet Replacement for Type 1 Diabetes

Somdutta Mukherjee, University of Pennsylvania, USA

Short Talk: Investigating the Role of TBX3 in Endodermal Progenitor Cell Maintenance and Differentiation

Targeting Novel Drugs to the Islet (X5)

***Carina Ammala**, AstraZeneca, Sweden

Shalev Itzkovitz, Weizmann Institute of Science, Israel

EMBO Young Investigator Lecture: Single Molecule Approaches for Studying Gene Expression in Intact Mammalian Tissues

Andrew F. Stewart, Mount Sinai School of Medicine, USA

Progress and Hurdles in Human Beta Cell Regeneration for Diabetes

Robert A. Sreaton, Sunnybrook Research Institute, Canada

Functional Genomics and the Human Pancreatic Beta Cell

Jesper Gromada, Regeneron Pharmaceuticals, USA

Single Islet Cell RNAseq for Target Discovery

Christian Helker, Max Planck Institute for Heart and Lung Research, Germany

Short Talk: Whole Organism Secretome-wide Screen to Identify Novel Regulators of Pancreatic Beta-Cell Function

Samuel B. Stephens, Duke University Medical Center, USA

Short Talk: Loss of the Pro-hormone VGF Decreases beta-cell Function via Reduced Insulin Secretory Granule Biogenesis

Workshop and Panel Discussion 2: Hurdles to Translation (X6)

***Martín G. Martín**, David Geffen School of Medicine at UCLA, USA

Shinichiro Ogawa, McEwen Centre for Regenerative Medicine, Canada

Modeling Cystic Fibrosis Biliary Disease with hPSC-Derived Cholangiocyte

Casey Allison Rimland, Cambridge University, UK

Progenitor Cells in the Human Extrahepatic Biliary Tree and Gallbladder

Ken Woo, University of Western Australia, Australia

Liver Progenitor Cells Derived from Pluripotent Stem Cells

Christopher Heinen, University of Connecticut Health, USA

The DNA Mismatch Repair-Dependent Damage Response in Human Embryonic Stem Cell-Derived Intestinal Organoids

Maelle Lorvellec, University College London, UK

Differentiation of human Embryonic Stem Cells and Induced Pluripotent Stem Cells into Hepatocytes-like Cells in a Mouse Decellularized Liver Scaffold

Li-Fang Chu, University of Wisconsin-Madison, USA

Single-cell RNA-seq Reveals Novel Regulators of Human Embryonic Stem Cell Differentiation to Definitive Endoderm

Workshop 3: Novel Insight into Beta-Cell Functions and Dysfunctions (X5)

***Chris Wright**, Vanderbilt University Medical Center, USA

Aimee Bastidas Ponce, Helmholtz Zentrum Munich, Germany

Analysis of the Role of Synaptotagmin 13 in Pancreatic Beta-cell Function and Islet Architecture

Esther Marie Bolanis, Indiana University School of Medicine, USA

Posttranslational Modification of the Factor eIF5A is Required for the Adaptive Response of the Islet Beta Cell During Insulin Resistance

Gitte Lund Christensen, University of Copenhagen, Denmark

Pancreatic beta-cells Dysfunction Induced by Prolonged Exposure to Low Dose IL1beta or Bmp2 is associated with beta-cell De-differentiation

Jennifer L. Estall, Institut de Recherches Cliniques de Montréal, Canada

Pgc-1 Coactivators in beta-cells are Essential for Glycerolipid Metabolism and Insulin Secretion Coupled to Fatty Acids

Amanda M. Ackermann, Children's Hospital of Philadelphia, USA

Integration of ATAC-seq and RNA-seq Identifies Human Alpha Cell and Beta Cell Signature Genes

Aharon Helman, Harvard University, USA

p16Ink4a-induced Senescence of Pancreatic beta-cells Enhances Insulin Secretion

Aida Martinez-Sanchez, Imperial College London, UK

Disallowance of Acot7 in Beta-cells is Required for Normal Insulin Secretion and Glucose Tolerance

Lu Zhu, NIDDK, National Institutes of Health, USA

Beta-Arrestin-2 is an Essential Regulator of Pancreatic beta-cell Function

Translational and Clinical Applications (X6)

***Jill L. Carrington**, National Institute of Diabetes and Digestive and Kidney Diseases, USA

Tsutomu Chiba, Kyoto University, Japan

Double Cortin-Like Kinase 1 (Dclk1) Marks PanIN-initiating Cells in Acinar-to-Ductal Metaplasia (ADM)

William Proctor, Genentech, Inc., USA

Role of PI3Kalpha and mTOR Inhibition in Endoderm Differentiation as a First Step toward

***Miriam**

Cnop,

Universite

Libre de

Bruxelles,

Belgium

Mark A.

Atkinson,

University of

Florida, USA

The

Pathogenesis

of Human

Type 1

Diabetes - A

Disease of the

Immune

System, Beta

Cells and

Pancreas

Carla J.

Greenbaum,

Benaroya

Research

Institute at

Virginia

Mason, USA

T1D

Therapeutic

Approaches

Rene Maehr,

University of

Massachusetts

Medical

School, USA

Towards a

Human

Pluripotent

Stem

Cell-Based

Disease Model

for

Autoimmune

Diabetes

Meeting

Wrap-Up:

Outcomes and

Future

Directions

(Organizers)

(X6)

Meeting

Wrap-Up:

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Personalized Toxicology

Martín G. Martín, David Geffen School of Medicine
at UCLA, USA

*Intestinal Stem Cells - Bench to Bedside, and
Future Challenges*

**Type-1 Diabetes: The Beta-Cell Immune System
Interface (X5)**

**Outcomes and
Future
Directions
(Organizers)
(X5)**

**FRIDAY,
MARCH 18**

Departure