WRISG 2021 PROGRAM

November 3-5, 2021

Skamania Lodge, Stevenson, WA

Welcome to WRISG!

Welcome and thank you for attending the 2021 meeting of the Western Region Islet Study Group. We are very excited to be able to meet in person!

Over the next few days, we look forward to continuing the WRISG tradition of trainee presentations with outstanding islet science and lively discussions in an interactive and inclusive forum.

Hosts: (from *University of Washington and VA Puget Sound Health Care System)*

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Laura Crisa
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Steven Kahn
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Territory Acknowledgement

Skamania is Chinookian for “swift water” and is home to the Nez Perce, Umatilla, Warm Springs tribes, and the Yakama Nation. We would like to acknowledge that we are holding our meeting on traditional land of these tribes and thank them for allowing us to work and play on their lands. We give thanks to their leaders and ancestors for cultivating and looking after the resources of this land.

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Organizing Sponsor: University of Washington Diabetes Research Center

For additional information of the University of Washington Diabetes Research Center, visit www.depts.washington.edu/diabetes/ or contact drc@medicine.washington.edu

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Conference Overview

Day 1: Wednesday, November 3

12:00-2:00	Arrivals and Check-in
2:00-3:30	Registration and Presentation Uploads
3:30-4:00	Welcome and Introduction - WRISG 2021 Organizing Committee
4:00-5:00	Hutton Keynote Lecture Kyle Gaulton, PhD, University of California San Diego
5:30-6:15	Cocktail Hour
6:30-8:00	Dinner

Day 2: Thursday, November 4

7:00-8:00	Breakfast
8:00-10:00	Scientific Session A: Novel Mechanisms of Insulin Secretion Chairs: Sangeeta Dhawan and Patrick Fueger
10:00-10:30	Morning Break
10:30-12:30	Scientific Session B: Non-Beta Cells in Health and Disease Chairs: Rocky Baker and Sakeneh Zraika
12:30-1:30	Lunch
1:30-3:15	Scientific Session C: Beta-Cell Dysfunction and Type 2 Diabetes Chairs: Andrew Templin and Luke Wander
3:15-3:45	Afternoon Break
3:45-6:00	Scientific Session D: Beta-Cell Death and HNF1A-MODY Chairs: Thomas Delong and Christine Doucette
7:00-9:30	Dinner with Grodsky Keynote Lecture Steven Kahn, MB, ChB, University of Washington & VA Puget Sound Health Care System

Day 3: Friday, November 5

7:00-8:00	Breakfast
8:00-10:00	Scientific Session E: Strategies for Beta-Cell Replacement Chairs: Senta Georgia and Zong Wei
10:00-10:30	Morning Break
10:30-12:15	Scientific Session F: New Technologies and Disease Models Chairs: Holger Russ and Hung Ping Shih
12:15-12:30	Afternoon Break
12:30-12:45	Trainee Awards Presentation
12:45-2:00	Lunch To-Go
2:00	Departures

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John C. Hutton Award

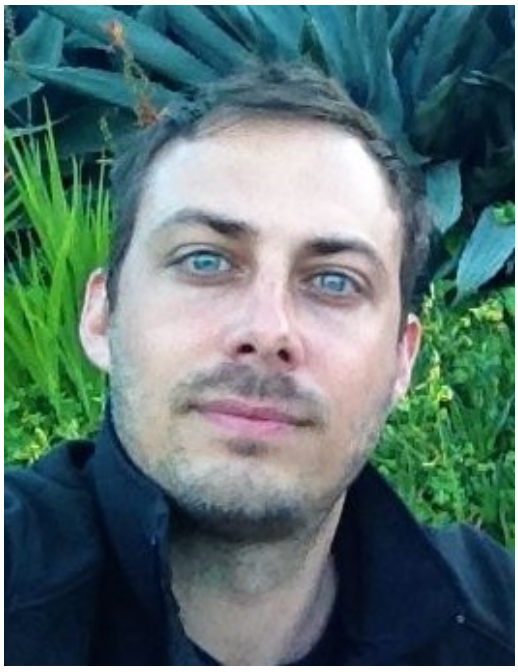
John C. Hutton, PhD. was an internationally acclaimed leader in diabetes research. He trained in labs all over the world including Bolivia, Brussels and Cambridge. Upon joining the faculty at the University of Cambridge in 1979 his research moved to the molecular cell biology of insulin secretion and the discovery of biomarkers of ß-cell function and disease. In 1996 John joined the Barbara Davis Center as its Research Director and expanded his research program to include human immunology and translational diabetes research. His laboratory was responsible for the discovery of many of the new β-cell targets of diabetic autoimmunity, including Imogen 38, phogrin (IA2-ß), IGRP, and ZnT8 (SLC30A8). Using a combination of genetically-manipulated animal models and studies in human subjects, he increased our understanding of pancreatic islet biology in the context of T1D. Shortly after he moved to Denver, John catalyzed the establishment of the West Coast Regional Islet Study Group meeting to promote interactions between islet biologists and their trainees. Unfortunately, in 2012, at the height of his career, John died of cancer. In 2019, the WRISG John Hutton award for a promising early stage investigator was established to honor John's memory.

The John C. Hutton award is supported by the Barbara Davis Center for Diabetes

2021 John C. Hutton Awardee:

Kyle Gaulton, Ph.D.

The Islet Epigenome and Genetic Risk of Diabetes



Dr. Gaulton is an Assistant Professor in the Department of Pediatrics at the University of California San Diego. He received a BAS in computer science from the University of Pennsylvania and a PhD in genetics from the University of North Carolina and did postdoctoral training at Oxford University and Stanford University. A primary interest of his research group is defining the epigenome and gene regulatory programs of pancreatic cell types and characterizing the effects of non-coding genetic variation on pancreatic cell type-specific gene regulation and function. In recent work his group has generated pioneering single cell epigenome maps in the pancreas which combined with genetic association data revealed novel insight into the genes, pathways, and cellular origins of diabetes risk. His group has also developed collaborative platforms for diabetes-relevant genomics data (www.cmdga.org) for the research community.

Gerold M. Grodsky Award

Gerry Grodsky has been a central figure in the islet field for many decades. After completing his postdoctoral work at Cambridge in 1955, he joined the faculty at UCSF, where he has remained since. He was a pioneer in the development of the insulin radio immunoassay. His group has contributed a great deal to our understanding of mechanisms involved in the synthesis, storage and secretion of insulin, with emphasis on the kinetics and quantitative relationships of these mechanisms. From these studies came the description of the fast and slow phases of insulin release and the hypothesis that insulin is stored in compartments of differing availability for release. The rapid phase of insulin release was shown to be vital in the maintenance of glucose homeostasis and this discovery has been critical for the design of the closed-loop artificial pancreas, as well as faster acting beta-cell secretagogues, and fast absorbing insulin preparations. Gerry has received numerous awards over his career and several award lectures have been named for him, including this WRISG award recognizing a leader in the islet biology field. He has been a constant presence at WRISG since its inception, and we are delighted to have him here again this year.

The Gerold M. Grodsky award is supported by the UCSF Diabetes Center

2021 Gerold M. Grodsky Awardee:

Steven Kahn, M.B., Ch.B.

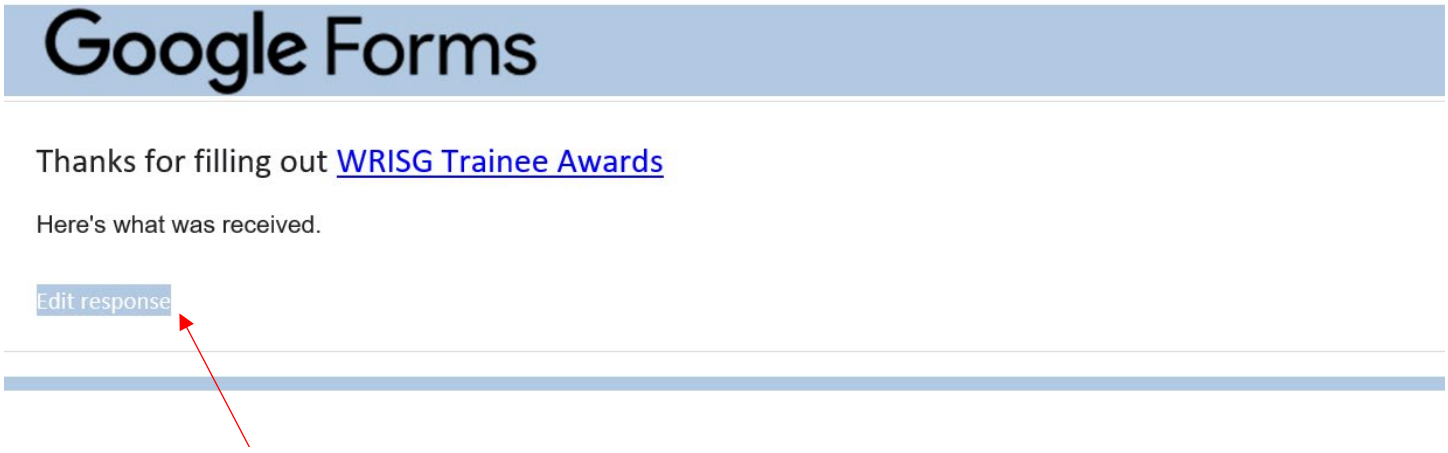
Clinical Observations and Science: Including Some Lessons Gerry Taught Me

Steven Kahn is a Professor of Medicine at the VA Puget Sound Health Care System and University of Washington in Seattle, Washington. He holds the Leonard L. Wright and Marjorie C. Wright Chair and directs the Diabetes Research Center at the University of Washington. His research interests include the role of the β-cell in the pathogenesis and treatment of prediabetes and type 2 diabetes. He has performed physiological studies and actively participates in a number of large multicenter clinical trials to prevent and treat type 2 diabetes, which includes studies comparing youth and adults. Aside from his clinical studies, he has an extensive basic research program examining the loss of β-cells in type 2 diabetes. He has received numerous awards including the Endocrine Society Clinical Investigator Award, Department of Veterans Affairs John B. Barnwell Award, European Association for the Study of Diabetes Albert Renold Award and Claude Bernard Award, and the American Diabetes Association Outstanding Achievement in Clinical Diabetes Research Award.

Voting Instructions for Trainee Awards

Please go to the following link to vote for the WRISG Trainee Awards, sponsored by the Diabetes Research Connection.

This form can be edited by utilizing the email link that will be sent to you once you submit the form the first time.



Click Here in Confirmation Email to Edit Response

Diabetes Research Connection

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Meeting Agenda

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12:00-2:00	Arrivals and Check-in
2:00-3:30	Registration and Presentation Uploads
3:30-4:00	Welcome and Introductory Remarks - WRISG Organizing Committee
4:00-5:00	Hutton Keynote Lecture Kyle Gaulton, PhD, Assistant Professor, University of California San Diego *The Islet Epigenome and Genetic Risk of Diabetes*
5:30-6:15	Cocktail Hour
6:30-8:00	Dinner

Day 2: Thursday, November 4

7:00-8:00		Breakfast	
8:00-10:00		Scientific Session A: Novel Mechanisms of Insulin Secretion Chairs: Sangeeta Dhawan and Patrick Fueger	
8:00-8:15	**A1**	**Diti Chatterjee Bhowmick** *DOC2b Enhances β-Cell Function Via A Novel Tyrosine Phosphorylation-Dependent Mechanism*	City of Hope
8:15-8:30	**A2**	**Jennifer Ngo** *Promoting Mitofusin 2 Activity Mediates Hyper Basal Secretion Induced by Mitochondrial Proton Leak*	University of California Los Angeles
8:30-8:45	**A3**	**Chelsea Garcia** *Changes in Peri-islet Extracellular Matrix Stiffness Regulate Insulin Secretion Via Mechanotransduction Signaling*	Colorado School of Mines
8:45-9:00	**A4**	**JeaAnn Dwulet** *What Role Do Highly Functional β-cell Subpopulations Play in Islets? A Theoretical Study*	University of Colorado
9:00-9:15	**A5**	**Anirudh Gaur** *Effects of Naturally Occurring Genetic Variations in Incretin Receptors on Glucose Homeostasis*	University of California Davis
9:15-9:30	**A6**	**Ryan Hart** *Somatostatin Signaling Drives Filamentous-Actin Reorganization in Primary Mouse Beta Cells*	University of California Davis
9:30-9:45	**A7**	**Vira Kravets** *Spatial Organization of First Phase Calcium Response to Glucose in Mouse and Human Pancreatic Islets*	University of Colorado
9:45-10:00	**A8**	**Michelle Chan** *Heterogeneity in Incretin Responses within Pancreatic Islets*	University of Colorado Davis
10:00-10:30		Morning Break	
10:30-12:30		Scientific Session B: Non-beta Cells in Health and Disease Chairs: Rocky Baker and Sakeneh Zraika	
10:30-10:45	**B1**	**Elliott Brooks** *NKX2.2 Maintains α Cell Identity by Directly Regulating Cell Specific Gene Transcription*	University of Colorado
10:45-11:00	**B2**	**Vy Nguyen** *Identifying the Role of RFX6 in Human Alpha Cell Function*	Stanford University
11:00-11:15	**B3**	**Jessica Huang** *Contribution of δ Cells to the Glucose Set Point*	University of California Davis

		Scientific Session B (continued)	
11:15-11:30	**B4**	**Mohammad Pourhosseinzadeh** *Coordination Between Beta and Delta Cells Is Not Mediated by Gap Junctions*	University of California Davis
11:30-11:45	**B5**	**Marcus Flisher** *Delta Cell Mediated Inhibitory FFAR4 Signaling Potentiates Insulin and Glucagon Secretion*	University of California Davis
11:45-12:00	**B6**	**Rene van Tienhoven** *Presence of Alternatively Spliced Insulin Gene Product in Human Pancreatic Delta Cells*	City of Hope
12:00-12:15	**B7**	**Samantha Crawford** *Determination of Hybrid Insulin Peptide Mechanism of Formation in Type 1 Diabetes*	University of Colorado
12:15-12:30	**B8**	**James Dilisio** *NOD Mouse CD4 T Cells Recognize a Novel Insulin B-chain Hybrid Peptide*	University of Colorado
12:30-1:30		Lunch	
1:30-3:15		Scientific Session C: Beta-cell Dysfunction and Type 2 Diabetes Chairs: Andrew Templin and Luke Wander	
1:30-1:45	**C1**	**Dayoung Oh** *Unlocking the Therapeutic Potential of GPR92 to Combat Diabetes*	UT Southwestern Medical Center
1:45-2:00	**C2**	**Jacob Herring** *Sex Specific Effects of Nr4a1 in the Beta Cell*	Brigham Young University
2:00-2:15	**C3**	**Rehana Akter** *Cholesterol Accumulation in Islets Upregulates Expression of the Mitochondrial Cholesterol Transporter*	University of Washington
2:15-2:30	**C4**	**Mark Andrade** *Unlocking β-cell Replication Through the Manipulation of αE-catenin Function*	University of Washington
2:30-2:45	**C5**	**Joseph Castillo** *Islet Amyloid Formation is Associated with Increased Islet Capillary Diameter and Increased Pericyte Density in a Transgenic Mouse Model*	University of Washington
2:45-3:00	**C6**	**Holger Russ** *Transplantation of Stem Cell Derived Beta-like Cells (sBCs) Triggers a Senescence Associated Secretory Phenotype (SASP) Marked by CD9*	University of Colorado
3:00-3:15	**C7**	**Donghan Shin** *Correlation Between Perturbed β-cell Intracellular Calcium Dynamics and Maturity Marker Expression After Prolonged Exposure to Hyperglycemia*	University of California Davis
3:15-3:45		Afternoon Break	
3:45-6:15		Scientific Session D: Beta-cell Death and HNF1A-MODY Chairs: Thomas Delong and Christine Doucette	
3:45-4:00	**D1**	**Joanna Filipowska** *Membrane-bound LGR4 and its Soluble Form (LGR4-ECD) as Novel Regulators of β-cell Survival and Proliferation*	City of Hope
4:00-4:15	**D2**	**Meghana Shivananda Murthy** *Laminin Interactions with the Islet Protect Against Cytokine-mediated β-cell Death via Protein Kinase C δ Downregulation*	Colorado School of Mines
4:15-4:30	**D3**	**Jillian Collins** *Cleavage of Protein Kinase C δ by Caspase-3 Mediates Cytokine-Induced β-Cell Death*	Colorado School of Mines
4:30-4:45	**D4**	**Andrew Templin** *TNFα-Induces RIPK3 Mediated β-Cell Necroptosis When Caspases Are Inhibited*	Indiana University
4:45-5:00	**D5**	**Kevin Chi** *Inflammatory Stress-induced Endogenous-dsRNAs Drive β-cell to IFN-I State*	City of Hope

		Scientific Session D (continued)	
5:00-5:15	**D6**	**Roberto Castro Gutierrez** *Genetic Engineering of Stem Cell Derived Pancreatic Beta-like Cells Confers Protection from Autoimmune*	University of Colorado
5:15-5:30	**D7**	**Taylor Morriseau** *The HNF-1aG319S Variant Shifts Beta-Cell Metabolism Towards Fat Oxidation in MIN6 Beta-Cells and Mouse*	University of Manitoba
5:30-5:45	**D8**	**Kim-Vy Nguyen-Ngoc** *A Human Pluripotent Stem Cell Model of HNFα/MODY1 Provides Mechanistic Insights into Disease Phenotypes*	University of California San Diego
5:45-6:00	**D9**	**Mollie Friedlander** *A Primary Human Model of HNF1α Deficiency Recapitulates HNF1A-MODY Phenotypes*	Stanford University
7:00-9:30		Dinner with Grodsky Keynote Lecture Steven Kahn, MB, ChB, Professor, University of Washington *Clinical Observations and Science: Including Some Lessons Gerry Taught Me*	

Day 3: Friday, November 5

7:00-8:00		Breakfast	
8:00-10:00		Scientific Session E: Strategies for Beta-cell Replacement Chairs: Senta Georgia and Zong Wei	
8:00-8:15	**E1**	**Han Zhu** *Multiomic Single Cell Analysis Identifies Mechanisms of Human Pancreatic Endocrine Cell Specification and Beta Cell Maturation*	University of California San Diego
8:15-8:30	**E2**	**Alexandra Theis** *Groucho Co-repressor Proteins Regulate β Cell Development and Proliferation by Repressing Foxa1 in the Developing Pancreas*	University of Colorado
8:30-8:45	**E3**	**David Vaisar** *Integrin-linked Kinase (ILK) Regulates β-cell Mass Development and Function*	University of Washington
8:45-9:00	**E4**	**Samanda Valente** *Control of Pancreatic Islet Cell Identity and Function by Tissue Macrophages*	University of Washington
9:00-9:15	**E5**	**Nazia Parveen** *Early De Novo DNA Methylation Patterning Regulates Beta Cell Function and Survival Programs*	City of Hope
9:15-9:30	**E6**	**Christopher Schaaf** *The Roles NKX2.2 and NKX6.1 in Human Islet Cell Fate Determination*	University of Colorado
9:30-9:45	**E7**	**Nicole Krentz** *Type 2 Diabetes-Associated Gene PAX4 Is Required for Human Endocrine Cell Development*	Stanford University
9:45-10:00	**E8**	**Connor Littlefield** *Identifying the Nkx6.1 Interactome in Beta Cells*	Brigham Young University
10:00-10:30		Morning Break	
10:30-12:15		Scientific Session F: New Technologies and Disease Models Chairs: Holger Russ and Hung Ping Shih	
10:30-10:45	**F1**	**Wilma Tixi** *ECM Signaling and Cell-Cell Adhesion Coordinate the Development of Islet Architecture and Functional*	City of Hope
10:45-11:00	**F2**	**J. Quinn Matuschek** *Elucidating the Role of PTPN2 in Human Pancreatic Beta Cells*	University of Colorado

		Scientific Session F (continued)
11:00-11:15	**F3**	**Hannah Mummey** — University of California San Diego *Defining Genetic Effects on Cell Type-Specific Cis-Regulatory Programs and Function in Pancreatic Islets Using Single Cell Multimodal Profiling*
11:15-11:30	**F4**	**Zong Wei** — Mayo Clinic Arizona *Vitamin D-Dependent Chromatin Accessibility Dynamics in Pancreatic Islet Dysfunction*
11:30-11:45	**F5**	**Maria Hansen** — University of Colorado *The Role of UCP2 in the Maturation of Stem Cell-Derived Beta-like Cells*
11:45-12:00	**F6**	**Janielle Cuala** — University of Southern California *Utilizing Multimodal Imaging Techniques to Investigate Beta Cell Structure and Function During the Pathogenesis of COVID-19*
12:00-12:15	**F7**	**Sudipta Ashe** — University of California San Francisco *Alleviating SARS-CoV2 Infection in Beta Cells with ER Stress Pathway Antagonists*
12:15-12:30		Afternoon Break
12:30-12:45		Diabetes Research Connection Awards Presentation
12:45-2:00		Lunch
2:00		Departures

Skamania Lodge

Skamania Lodge was established as a part of a 1986 resolution passed by congress creating a Columbia River Gorge National Scenic Area. This lodge was designed to be similar to the rustic feeling of lodges in the early 1900's including wood paneling, large columns, and native stone. Skamania Lodge first opened in 1993 and lies on 175 acres overlooking both the Cascade Mountains and the Columbia River Gorge. The lodge is surrounded by beautiful scenery and is located near several hikes, wineries, and other attractions.

Things To Do In and Around Stevenson, WA

Columbia Gorge Interpretive Center – Learn about the history of the Columbia River Gorge and Skamania County. Open daily from 9:00 am to 5:00 pm with a $10 admission for adults.

Maryhill Winery and Amphitheater – Award-winning winery with beautiful views and a great place to relax, have a picnic, and enjoy some wine.

Bridge of the Gods – A natural dam created by the Bonneville Slide (a landslide that dammed the Columbia River) which has sense washed away but is remembered by Native Tribes through legends. Now a manmade bridge connecting between Oregon and Washington.

Crown Point Observatory – Natural area and designated National Natural Landmark shaped by volcanic lava, flood waters, and winds.

Beacon Rock – An 848-foot-tall (258 m) basalt monolith, formed from the core of an extinct volcano. A mile-long switchback trail provides access to outstanding views of the Columbia River and surrounding area.

Multnomah Falls – The tallest waterfall in Oregon, at 620 ft (198 m) in height. Easily accessible from Interstate 84.

Additional attractions can be found on Skamania Lodge's website:
https://www.skamania.com/things_to_do_in_washington_state/washington_state_attractions

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Job Postings

A Postdoctoral Position is available immediately in the laboratory of Dr. Vincenzo Cirulli at the University of Washington (Seattle, WA) to study the role of cell-cell and cell-matrix-dependent signaling in the development, function and regeneration of the pancreatic islet cell lineage. The successful candidate will be required to work with animal models of Cre/Lox-mediated targeted deletion and/or activation of select cell adhesion molecules, or signaling effectors thereof, human islet cell preparations, and with pluripotent stem cells (hESC and iPSC). Requirements for this position include a strong background in cellular and molecular biology. Solid knowledge on computational biology for the analysis of scRNA-seq data sets is also desirable, although not required at the time of recruitment. Excellent communication skills and proficient knowledge of English are also expected. Applicants should send a detailed curriculum vitae, a statement of research interests and postdoctoral training goals, as well as the name and contact information of three references to Vincenzo Cirulli, MD, PhD (email: vcirulli@uw.edu).

The Crisa Laboratory at the University of Washington is seeking a highly motivated Post-Doctoral Fellow to lead pioneering studies investigating pro-regenerative signals imparted by tissue macrophages on pancreatic islets, using models of pancreatic islet development and islet injury. In addition, in collaboration with bioengineering and stem cell programs, the applicant will work to the development of novel transplant scaffolds allowing for immunomodulation and maturation of stem-cell-derived islet progenitors. Candidates must have a Ph.D. relevant to biological science, M.D., or equivalent degree. Excellent verbal and written English communication skills are essential. Proficiency with routine molecular and histological techniques as well as experience in handling of murine animal models are expected. Interested candidates should send their CV and contact the PI's laboratory at lcrisa@uw.edu for details on job application.

The laboratory of Dr. Anna Gloyn at Stanford University is seeking a postdoctoral fellow. We are an inter-disciplinary team of basic and clinical scientists with shared interests in using molecular genetics as a tool to uncover novel biology. We use a variety of different approaches to address important challenges in the field, which range from studies that work genome wide to those which are focused on specific genes and even precise nucleotide changes to understand their impact on pancreatic islet biology. We have developed a series of pipelines that use primary human islets and authentic beta-cell models which allow us to generate and then integrate complex genomic, transcriptomic and cellular datasets. We use state-of-the art genome engineering approaches combined with induced pluripotent stem-cells to study the impact of T2D-associated genetic variants on islet cell development and function. We have a range of project opportunities available supported by our NIDDK UM1 award within the AMP-CMD partnership. For more information, contact Anna Gloyn (agloyn@stanford.edu).

The Hull-Meichle laboratory is looking to recruit a postdoctoral fellow to lead projects in the lab broadly focused on interactions between non-endocrine islet cells and beta cells in diabetes pathogenesis. Ongoing projects are investigating the role of the vasculature in islet dysfunction and determining the importance of pancreatic ductal and vascular pathology in the development of cystic fibrosis-related diabetes. These studies encompass in vitro work using primary islets/cells from humans and animal models, and in vivo physiology studies using rodent models. Experience in working with complex data sets and eligibility for NIH fellowship funding are desirable, but not required. Interested candidates should send their CV, along with a brief statement of research experience to Dr. Rebecca Hull-Meichle at rhull@uw.edu.

Steven Kahn's laboratory at the University of Washington and VA Puget Sound Health Care System in Seattle has a funded post-doctoral fellowship position in islet biology available. New and ongoing studies are addressing the pathophysiology of type 2 diabetes, and specifically the etiology of the islet secretory dysfunction and loss of β-cells that characterize the disease. These studies include the role of islet amyloid and mitochondrial cholesterol accumulation in β-cell dysfunction and loss. Through work on these and an assortment of other ongoing and developing projects in the lab, the fellow will have the opportunity to learn a variety of approaches and methods based in part on in vitro cell systems and animal models of type 2 diabetes. An additional unique feature of the position is the opportunity to interact with clinical researchers in the group who are also studying type 2 diabetes, thereby broadening the fellow's knowledge of the disease. Interested candidates should contact Steven Kahn at skahn@uw.edu sending their CV and any other material they deem would be relevant.

The laboratory of Dr. Lori Sussel at the Barbara Davis Center for Diabetes at the University of Colorado is searching for a postdoctoral fellow to lead new and ongoing research projects in the lab related to transcriptional regulation of islet cell development and function using mice and stem cell-derived islet cells as model systems. The candidate should have a PhD and research publications. Information about the lab can be found here. Qualified candidates are encouraged to contact Dr. Lori Sussel at lori.sussel@cuanschutz.edu with their CV and the names of three references.

The Zraika lab at the University of Washington is seeking postdoctoral fellows interested in studying the pathophysiology of diabetes, with an emphasis on islet dysfunction. Current projects focus on communication between islet cell types, as well as identifying pathways/proteins that may be targeted for therapeutic intervention in diabetes. The latter intersects with mechanisms involved in cardiovascular disease, wherein novel aspects of the renin-angiotensin system and cholesterol metabolism are being studied in the context of islet dysfunction. Another area of interest involves unraveling mechanisms for impaired insulin secretion in cystic fibrosis related diabetes. In vitro and animal models of diabetes are utilized to interrogate various aspects of cell biology and in vivo physiology. Postdoctoral fellows will also have the opportunity to interact with clinical researchers in the group who study diabetes. To find out more, contact Sakeneh Zraika (zraikas@uw.edu).