IIDP
INTEGRATED ISLET DISTRIBUTION PROGRAM

The Newsletter

A Quarterly Update of IIDP Activities of Interest

May 3, 2019 Volume 10, Issue 2 Spring

Non-Islet Pancreatic (Acinar) Tissue Soon to Be Offered through IIDP

By mid-May 2019, the IIDP will launch a new program to allow for the distribution of the non-islet pancreatic tissue (NIPT) that remains after the isolation and purification process. Commonly known as "acinar" tissue, in reality these samples contain not only the acinar tissue but also connective tissue, blood vessel fragments, ductal fragments as well as imbedded islets. The offers for NIPT will be made prior to the islet broadcasts and will not be contingent or otherwise linked to the islets from the same donor. The NIPT will be available as both freshly isolated and flash frozen samples, in most cases.

If interested in registering for this tissue, and if the acinar research falls under the auspices of the current approved islet study, one can do so by clicking on Study Details **(Figure 1)** and clicking Non-Islet Biomaterials Profile on the navigation drop down list and confirm the interest in acinar tissue. Those investigators who have already indicated interest in receiving NIPT will automatically get these alerts. If the acinar use will be for a different type of research than the approved islet study, then one must apply under a separate study approval by completing a brief application form which can be obtained through the investigator dashboard under add a new study **(Figure 1).**

Investigators who register their interest in acinar tissue will receive an automated query on the day of isolation asking of their interest in the available NIPT. Interested investigators will have a short deadline of a few hours to decide if they would be interested in this tissue. They can choose an amount between 0.5mL-5.0mL of freshly isolated tissue to be sent within 24 hours of the isolation and between 1.0mL-4.0mL of flash frozen tissue if that is preferred.

The cost for each sample requested will be $250.00 per sample plus the cost of the FedEx shipment. Fresh tissue will be sent cold in standard IIDP Islet shipping containers, and flash frozen samples will be sent on dry ice in insulated boxes. Fees for the tissue will be deducted automatically from the investigator's existing total subscription. A unique view by IIDP Co-Principal Investigator, Dr. Carmella Evans-Molina, of the importance of this new IIDP offering can be read in the *Executive Highlights* section of this Newsletter, located on page 2.

Inside this Issue

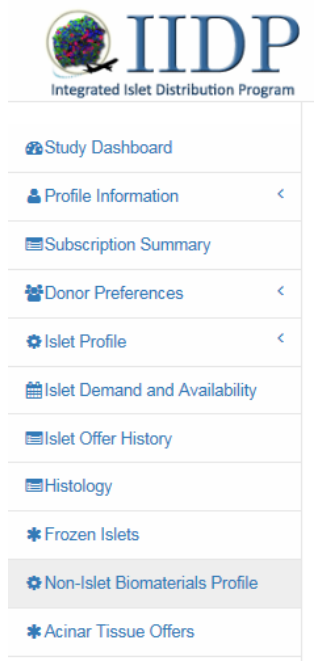

Figure 1B.

Figure 1: From the new Investigator Dashboard (**Figure 1A.** available 5/13/19) one can navigate to add acinar tissue to the current study by clicking on the Study Details link (red oval), to the navigation pane (**Figure 1B.**), to confirm the acinar need (**Figure 1C.**) The red arrow in **Figure 1A.** indicates where investigators can add a new study for acinar tissue.

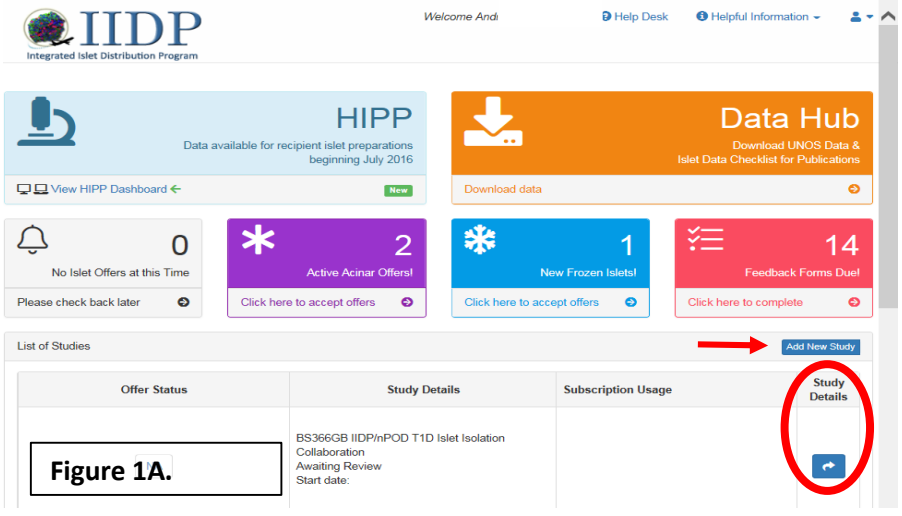

Figure 1A.

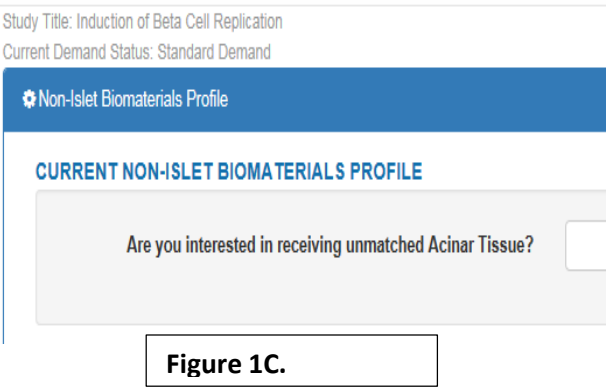

Figure 1C.

New IIDP Features

The IIDP is dedicated to facilitating and supporting leading edge diabetes research which is reliant on human islets. Here are our latest updates:

Distribution of Non-Islet Pancreatic (Acinar) Tissue: *Beginning in mid-May, the IIDP isolation centers will begin the distribution of the tissue left after the islet purification in the isolation process to all interested investigators. Update your profile for Non-Islet Biomedical Materials if applicable in your current approved study or apply for a new study for acinar tissue.*

Center Secure Website Enhancements: *Center Isolation Staff, enjoy the updated website for your broadcast pleasure!*

Islet Award Initiative: *Next application deadline is August 1st! Go to https://iidp.coh.org/ for more details.*

IIDP Holds Informational Sessions for Both Isolation Centers and Investigators

The IIDP Coordinating Staff held informational sessions in the past few weeks to update IIDP participants of program updates. On Tuesday, April 23rd and Thursday April 25th, all center staff were invited to a Webex call to view the new enhancements for the center's secure site including new navigation panels and color-coded alerts, and to engage in the demonstration of the new Non-Islet Pancreatic Tissue (NIPT-acinar) process for broadcasting, confirmation of tissue acceptance, and online preparation for shipping. All centers were represented on the calls.

On the following week, all current IIDP investigators and their lab contacts were invited to attend one of two calls scheduled for Wednesday, May 1st and Friday May 3rd to introduce researchers to the new acinar distribution program. After a few overview slides noting the reasoning behind the program and outlining the process presented by Research Coordinator, Barbara Olack, a live demonstration of an NIPT broadcast, mock acceptance as an interested investigator, and presentation of all new alerts was conducted by Project Administrator, James Cravens. Instructions were given as to how to register for acinar tissue in order to receive future email notices, similar to the islet broadcast emails. The calls were well attended, however if more information is needed, please contact either James or Barbara through the iidp-email@coh.com or by their private emails.

Executive Highlights

From IIDP Co-Principal Investigator,
Carmella Evans-Molina, M.D., Ph.D.

Announcing the new IIDP Non-Islet Pancreatic Tissue Program (NIPT): You asked, and we listened!

In this month's newsletter, we are pleased to announce a new initiative for IIDP investigators that will allow researchers to receive fresh and frozen non-islet pancreatic tissue that is generated from the process of pancreatic digestion and islet isolation. This new IIDP Non-Islet Pancreatic Tissue Program (NIPT) program, beginning May 13th, 2019, was developed in response to an articulated need from the community and has been shaped by input from IIDP investigators.

Several recent papers have highlighted previously unappreciated roles for exocrine dysfunction as part of diabetes pathogenesis. Martha Campbell-Thompson and colleagues at the University of Florida have shown that pancreatic size is reduced in type 1 diabetes, largely due to loss of exocrine mass (PMID 26358584). In parallel, Xia Li and Mark Atkinson have shown that serum trypsinogen levels (a read-out of pancreatic exocrine function) were reduced in persons with multiple autoantibodies and established type 1 diabetes compared to controls (PMID 28115475).

Emerging data also suggest acinar tissue may be utilized in β cell replacement and differentiation strategies. Qiao Zhou's group has shown that expression of *Ngn3*, *Mafa* and *Pdx1* (referred to as "M3 factors") in mice was sufficient to convert acinar cells into insulin positive cells *in vivo* (PMID 25402613).

In aggregate, these findings have raised a number of questions, and IIDP investigators are keen to address them through assessment of human acinar tissue. To address this need, we convened a small working group to gain insight into the specific types of questions investigators are interested in addressing and also to understand the types and quantities of tissues needed.

The accompanying article, *"Non-Islet Pancreatic Tissue Soon Being Offered through IIDP," (page 1 of this Newsletter)* provides details of the types of samples available and discusses the logistics of how investigators can request this tissue. We would like to thank IIDP Investigators, Bridget Wagner, Martha Campbell Thompson, and Amelia Linnemann for their participation in the working group calls and their input into this new program.

As always, we welcome feedback from investigators. The IIDP team looks forward to our continued partnership with the research community and the persistent development of programs which allow investigators to suggest innovative research inquiries.

Hope all who attended the recent Human Islet Research Network (HIRN) Annual Investigator Meeting had a wonderful, scholarly, and productive time!

FEATURED IIDP ISLET ISOLATION CENTER:

DIABETES RESEARCH INSTITUTE, UNIVERSITY OF MIAMI

The Islet Isolation Group at the University of Miami has been part of the islet distribution team at City of Hope since the program's inception in 2002. Camillo Ricordi, M.D., the Stacy Joy Goodman Professor of Surgery, Distinguished Professor of Medicine, Professor of Biomedical Engineering, and Microbiology and Immunology at the University of Miami (UM), Florida, serves as Director of the Diabetes Research Institute (DRI) and the Cell Transplant Program. Dr. Ricordi began his interest in human islet isolation in the research lab of Paul E. Lacy, M.D., Ph.D. where, working with the human isolation team of David Scharp, M.D. at Washington University Medical School in St. Louis, developed the Ricordi chamber for large animal and human islet isolation, of which a variation of the device is in use by most islet isolation facilities world-wide. Dr. Ricordi honed his transplantation skills working in Pittsburgh under the mentorship of Dr. Thomas Starzl, a pioneer in organ transplantation. He has served as the head of the Islet Isolation cGMP Processing Facility at the DRI at UM since 1993. Dr. Ricordi and his team continue to produce high quality human islets for clinical transplantation in their diabetic patients, while providing the IIDP with research islets for the IIDP family of investigators. Thank you for your enduring support to find the cure!

Meet the IIDP

Shaunna Spears
IIDP Senior Project Manager

Thousands of payments have been sent from hundreds of institutions to compensate for the millions of islets sent to investigators over the past years for islet subscriptions, and someone has to make certain that all of those checks, credit card transactions and purchase order numbers get to the right place in a timely manner. It is a part of Senior Project Manager, Shaunna Spears' responsibility to bring them all to their rightful home. Since Shaunna started in August, 2016, she has worked to establish new strategies to modernize the financial structure of the IIDP. From single payments for islet subscriptions, as mentioned above, to overseeing the administration of grant funds, to balancing multi-million dollar budgets for several grants directed by Dr. Joyce Niland, Shaunna values her education and experience in business management. She also works closely with Project Administrator, James Cravens, Program Manager, Janice Sowinski, as well as Principal Investigator, Dr. Niland to assure financial stability for the IIDP. And when she is not buried in the books, Shaunna can usually be found hiking in the mountains or playing on the beach with her four legged best buddy, Jacques, her scruffy terrier mix.

Miami Islet Isolation Team: *(from left to right)* **Pix 1** – *A dedicated group of human islet researchers at the UM DRI:* Xiaojing Wang, Luis Roque, Simona Corrora, Elina Linestsky, Ph.D., Facility Manager, Alejandro Alvarez, Carmen Castillo; **Pix 2** - *Prepped for the cGMP environment* – Xiaojing Wang, Elina Linetsky, Simona Corrora; **Pix 3** – *Elina Linetsky and Camillo Ricordi carrying their precious cargo to an awaiting islet transplant recipient.*

Featured Investigator Research Publication

Utilizing Human Islets Provided through the IIDP

Connecting pancreatic islet lipid metabolism with insulin secretion and the development of type 2 diabetes.

Yumi Imai, Ryan S. Cousins, Siming Liu, Brian M. Phelps, Joseph A. Promes

Ann N Y Acad Sci (2019) April 2. Epub
https://doi.org/10.1111/nyas.14037

Abstract: Obesity is the major contributing factor for the increased prevalence of type 2 diabetes (T2D) in recent years. Sustained positive influx of lipids is considered to be a precipitating factor for beta cell dysfunction and serves as a connection between obesity and T2D. Importantly, fatty acids (FA), a key building block of lipids, are a double-edged sword for beta cells. FA acutely increase glucose-stimulated insulin secretion through cell-surface receptor and intracellular pathways. However, chronic exposure to FA, combined with elevated glucose, impair the viability and function of beta cells in vitro and in animal models of obesity (glucolipotoxicity), providing an experimental basis for the propensity of beta cell demise under obesity in humans. To better understand the two-sided relationship between lipids and beta cells, we present a current view of acute and chronic handling of lipids by beta cells and implications for beta cell function and health. We also discuss an emerging role for lipid droplets (LD) in the dynamic regulation of lipid metabolism in beta cells and insulin secretion, along with a potential role for LD under nutritional stress in beta cells, and incorporate recent advancement in the field of lipid droplet biology. *Click here for the full paper.*

Program Statistics

2019	Cumulative
# Subscribers*	
149	364
# Shipments*	
408	12,884
# IEQs Distributed*	
3.5 Million	252.3 Million
# Publications**	
23	685

***Since 2004** ****Since 2002**

Check out more recent publications using IIDP Islets!

- Lo CW, Kryvalap Y, Sheu TJ, Chang CH, Czyzyk J. Cellular proliferation in mouse and human pancreatic islets is regulated by serpin B13 inhibition and downstream targeting of E-cadherin by cathepsin L. *Diabetologia*, 2019 May, 62(5): 822-34.
- Jiang K, Chaimov D, Patel SN, Liang JP, Wiggins SC, Samojlik MM, Rubiano A, Simmons CS, Stabler CL. 3-D physiomimetic extracellular matrix hydrogels provide a supportive microenvironment for rodent and human islet culture. *Biomaterials*, 2019 Apr, 198: 37-48. PMCID: 6397100.
- Li J, Rawson J, Chea J, Tang W, Miao L, Sui F, Li L, Poku E, Shively JE, Kandeel F. Evaluation of [(68)Ga]DO3A-VS-Cys(40)-Exendin-4 as a PET Probe for Imaging Human Transplanted Islets in the Liver. *Sci Rep*, 2019 Apr, 9(1): 5705.
- Pecic S, Milosavic N, Rayat G, Maffei A, Harris PE. A novel optical tracer for VMAT2 applied to live cell measurements of vesicle maturation in cultured human beta-cells. *Sci Rep*, 2019 Apr, 9(1): 5403. PMCID: 6443945.

For a complete list of publications that utilized human islets provided through the IIDP, go to https://iidp.coh.org/Publications.

IIDP Publication Reminders:

1. Please remember to submit all publications generated from IIDP islets, to *Carol Swanson* at *cswanson@coh.org* for cataloging on our website.
2. The following acknowledgement should be documented in all publications where IIDP human Islets were used:
   Human pancreatic islets were provided by the NIDDK-funded Integrated Islet Distribution Program (IIDP) at City of Hope, NIH Grant # 2UC4DK098085.
3. **RRID** is an asset to your current and future experiments; be sure to include in all future publications!

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