Islet Cell Resource Consortium
Administrative and Bioinformatics Coordinating Center

Islet Communication Network

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Two Consortium Joint Projects Making Progress

The ICR Consortium is currently conducting two projects orchestrated to help improve research islets for approved investigators, a Shipping Study working towards standardization of the shipment of islets and a Viability Study to establish routine protocols that could be adopted by ICR centers as well as research investigators to verify islet viability. The Shipping Study has concluded Phase I of the project where temperature and pressure were monitored in multiple shipments for all centers using a standard shipping container. The consortium is currently working to establish a standardized container with packing supplies based on the results of that study. Phase II of the Shipping Study will consist of mini-studies to test the effects of pressure on islet viability as well as testing different types of islet vessels that will maintain the best oxygen supply for cultured and shipped islets. These studies will be carried out by both the University of Wisconsin and Minnesota in a joint effort to improve the quality of islets distributed. The Viability Study is being conducted jointly by all 8 ICR centers and monitored closely by the ABCC. Individual centers are conducting FACS analysis, ADP/ATP ratio, DNA content, and Cellular Composition assays on 4 separate islet isolations. Results will be analyzed by the ABCC and statistical analysis will hopefully determine the most reliable assessment of islet viability.

Executive Highlights

As Director of the Administrative and Bioinformatics Coordinating Center (ABCC) for the Islet Cell Resource Center, it is with great pleasure that I introduce the newest method proposed by the ICR Steering Committee to enhance communication among the ABCC, ICRs, funding organizations (NIH,NCRR,NIDDK, JDRFI), resource users, and support staff. In an effort to foster better communication, we are launching our first web-based quarterly newsletter. The intent of this newsletter is 1) to keep both centers and researchers abreast of new developments within the islet cell resource, 2) to highlight patients who have benefited from islet cell research and transplant, 3) to present some historical background on islet cell research, 4) to feature high impact papers of interest to the community, 5) to provide quarterly statistical program updates, 6) to serve as a bulletin board for upcoming scientific conferences and other relevant events and, 7) to introduce program staff and feature the ICR centers, their work and their staff. The ICRs as well as resource users will be encouraged to offer suggestions for future articles.

In this first issue you will find information on the ICR Shipping and Potency Studies, meet the new ABCC Project Administrator, Janice Sowinski, and read about the featured ICR center, the University of Illinois at Chicago and more.

I hope the launching of this quarterly newsletter will provide a medium for enhanced communications, foster the exchange of information, and build stronger associations among all individuals associated with this islet cell resource. The ABCC looks forward to its role in providing this forum for information exchange.

Joyce Niland

Islet Allocation System Is Making Fair Islet Distribution for All

Distribution Parameters	Number of IEQs		
	Total	Targeted	Open
Offered by Web System	10,525,573	9,477,600	4,954,973
Accepted by Investigators	10,147,173	5,248,700	4,898,473
Actually Shipped	9,335,090	4,897,300	4,437,790

The numbers in this table reflect shipments between 3/7/2007 to 8/30/07 distributed through the new Islet Allocation System. This distribution mechanism is being continually revised by ABCC staff to accommodate new found challenges and increase proficiency. SEE NEW FEATURES from the ABCC!

The new Islet Allocation (IA) System has officially been distributing islets through its web-based system for 5 months and the numbers show the success. After a preliminary 6 month testing period conducted by the ABCC and led by John Kaddis, the program was made available to both ICR centers and approved investigators in March. Extensive training of the ICRs and the research recipients was conducted by James Cravens prior to the launching of the system. Like all new programs, a few unexpected problems occurred but the ABCC database staff has continued to repair and improve the system, which is now working error free. The algorithm designed, by Drs. Joyce Niland, Dajun Qian and John Kaddis[1], of the ABCC matches the islet preparations to the researchers' requests, considering waiting time, purity, viability, culture time and IEQs. We have documented several issues that may give answers to the problems some users may have. Please see the ***Most Frequently Asked Questions*** continued on page three.

1. Qian D, Kaddis J, Niland JC. A matching algorithm for the distribution of human pancreatic islets, Computational Statistics & Data Analysis: 51(2007) 5494-5508.

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Islet Research History Lessons

Although clinical islet transplantation has only been successful for a few decades, the idea for using pancreatic tissue to stop the ravages of the "sugar disease" has been around for a century longer. In 1892, P. Watson Williams, a Senior Assistant Physician in Bristol Royal Infirmary in London attempted the transplantation of a few pieces of freshly slaughtered sheep pancreas under the skin of a 15 year old end-stage diabetic boy. The child's condition actually improved for a few days after which he died of infection and the disease. Frederick Pybus described patients transplanted under the skin with sliced human pancreata in an article published in Lancet 1924. Since the microscopic identification of "irregular, polygonal structures" by Paul Langerhans described in a paper published 1896 and coined "ilots de Langerhans" by Edouard Laguesse in 1892, the elusive islet is still the holy grail of many researchers today and the hope of millions of people with diabetes around the world.

This section of the ICR_ICN newsletter will feature interesting tidbits about islet research from the past. If anyone has an interesting fact or story to pass along, please feel free to send it to bolack@coh.org .

ICR Contributes to Islet Research: **Melanin Concentrating Hormone Is a Novel Regulator of Islet Function and Growth** Diabetes 56(2):311-9, 2007

Pissios P, Ozcan U, Kokkotou E, Okada T, Liew CW, Liu S, Peters JN, Dahlgren G, Karamchandani J, Kudva YC, Kurpad AJ, Kennedy RT, Maratos-Flier E, Kulkarni RN

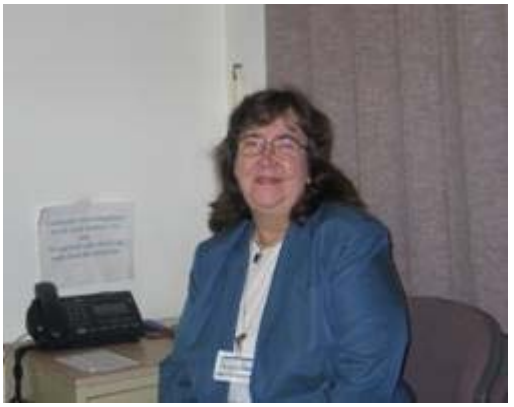
Melanin concentrating hormone (MCH) is a hypothalamic neuropeptide known to play a critical role in energy balance. We have previously reported that overexpression of MCH is associated with mild obesity. In addition, mice have substantial hyperinsulinemia and islet hyperplasia that is out of proportion with their degree of obesity. In this study, we further explored the role of MCH in the endocrine pancreas. Both MCH and MCHR1 are expressed in mouse and human islets and in clonal beta-cell lines as assessed using quantitative real-time PCR and immunohistochemistry. Mice lacking MCH (MCH-KO) on either a C57Bl/6 or 129Sv genetic background showed a significant reduction in beta-cell mass and complemented our earlier observation of increased beta-cell mass in MCH-overexpressing mice. Furthermore, the compensatory islet hyperplasia secondary to a high-fat diet, which was evident in wild-type controls, was attenuated in MCH-KO. Interestingly, MCH enhanced insulin secretion in human and mouse islets and rodent beta-cell lines in a dose-dependent manner. Real-time PCR analyses of islet RNA derived from MCH-KO revealed altered expression of islet-enriched genes such as glucagon, (continued on page 3)

New Features from the ABCC

✸ICP Database Improvements✸ - While entering new data in the database you will see subtle improvements to make questions more clear. Also new icons for the edit and delete buttons on the Purification Sections – No more accidental deletions of data!

✸Widget Alerts for Islet Distribution✸ Coming Soon! – When your name comes up as an islet distribution recipient, there will be a little alert in the bottom right hand corner of your computer screen to remind you to log on and accept your islets!

MEET THE STAFF



Janice Sowinski New ABCC Project Administrator

The new fiscal year has brought a change to the ABCC administration. Dr. Joyce Niland announced at the Spring Steering Committee Meeting that Janice Sowinski, MS would be joining the ICR as the new ABCC Project Administrator. Janice comes to the ABCC from the University of Maryland where she was a clinical research supervisor for a multi- hospital trial where she was responsible for IRB submission, protocol development, data collection, data entry and data quality control. Before that she was the Division Director for the Human Biological Data Interchange in Philadelphia. Janice and her husband have a personal reason for being excited about moving to sunny California, they are now closer to their daughter and grandchild. "I am delighted to have joined the ABCC team and to have an opportunity to make a contribution to diabetes research," Janice reports. Ms Sowinski has replaced John Kaddis who is pursuing his PhD studies but remains as a Support Scientist with the ABCC.

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FEATURED ICR:

UNIVERSITY OF ILLINOIS—CHICAGO

The windy city hosts two ICR sponsored centers but this Newsletter feature's Dr. Jose Oberholzer's group at the University of Illinois – Chicago. This center has made an impressive start to their contributions to the ICR Consortium. Since their approval by the NCRR as a qualified, active center in November of 2006, UIC has distributed almost 3 million IEQs to well over 30 different investigators. The center has been focusing on improvement of the isolation process and a major project has centered on the enhancement of oxygenation of the pancreatic tissue prior to, during, and following the isolation. UIC has also contributed to the Consortium spirit, most recently by sharing a purification protocol that has been successful in their hands with all the other ICR centers. This new method of Ficoll purification can reduce processing time, yield pure islets and reduce the overall cost of isolating islets. **On October 18th UIC will be hosting the ICR Consortium's 3rd Annual Islet Workshop (http://icr.coh.org/workshops.asp *for more information*) at which all investigators are welcome to attend.**

Jose Oberholzer	*ICR Director*	*Research Scientists and Specialists*		
Travis Romagnoli	*Asst. Director*	Meirigeng Qi	Barbara Barbaro	Moolky Nagabhushan
Mike Hansen	*Lab Manager*	Payam Salehi	Lisette Rodriguez	Shusen Wang
Joan Martellotto Elaine Shestokas	*Nurse Coordinators*	Yong Wang	Chris Groh	Joe Kuechle

Research Paper

(continued from page 2): forkhead homeobox A2, hepatocyte nuclear factor (HNF)4alpha, and HNF1alpha. Together, these data provide novel evidence for an autocrine role for MCH in the regulation of beta-cell mass dynamics and in islet secretory function and suggest that MCH is part of a hypothalamic-islet (pancreatic) axis. [PUBMED abstract]

This section of the ICR-ICN will feature an abstract from a peer-reviewed paper reporting scientific studies conducted using islets received through the ICR Human Islet Distribution system. To alert us to a recently published paper that fits this profile, please contact us at abcc@coh.org .

Islet Allocation System: *Most Frequently Asked Questions* (continued from page 1)

1. I accepted the islets, where are they? If you received and accepted an islet offer always make sure you log into the IA system and view your "History of Islet Offers" table to check your "Status" and "IEQs Shipped". This will tell you if the islets have been shipped by the ICR center and soon will display the Fed EX tracking number in case your islets do not arrive at the time expected.

2. Why is the interval between my islet shipments so long? If you are not receiving islets as often as expected, please check your "Human islet Request Form" in your original application to see if the time requested for islet shipments still matches your research needs. Also, if you chose to receive islets from specific Islet Centers, please be certain they are still active participants in our program. If you are unable to identify a reason for a prolonged interval between shipments or wish to revise the information in our system, please contact Martha Antler mantler@coh.org or James Cravens jcravens@coh.org for revisions.

3. Why does it sometimes say there are no islets available when I log in for an Open Islet offer? In the initial operation of the Islet Allocation system, open offers were extended to all investigators simultaneously and offered on a first come, first served basis. We have become aware that the system should be revised to take waiting time and other matching factors into account. We expect to complete the revisions to our system in the coming weeks. In addition, please check with your institutional Information Technology Department to determine whether you are receiving our messages "instantaneously."

4. Why am I not receiving my text messages? Some ATT subscribers have reported having problems receiving IA text messages. Be sure and check with your service provider to make sure there is not a spam block on your phone.

If you are still having problems with the system or have new staff, please contact James Cravens at jcravens@coh.org.

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Coming Events:

CTS-IPITA-IXA-2007 Joint Conference
September 15-20th, Minneapolis, MN
info@cts-ipita-ixa-2007.org

ICR Consortium's 3rd Annual Workshop
October 18th, Chicago IL
http://icr.coh.org/workshops.asp

The workshop will provide a forum for addressing user's concerns as well as the science of islet procurement and processing. The topics include islet expansion, designing a "super media", the problems with shipping islets, islet function predictors, and more. Please click on the website above and checkout the detailed agenda as well as the list of guest speakers.

"In their last moments donors give a lifetime..."

Islet Transplant Patient Cyndi Smart-Williams

ICR Consortium Statistics

The Administrative and Bioinformatics Coordinating Center (ABCC) oversees the data management for the Islet Cell Resource Consortium (ICR). The information entered in the Islet Cell Processing Database (ICP) consists of data involved in the pancreas procurement and islet isolation since 2001, the year the ICR Consortium was established. Both clinical and research isolations have been tracked through this system that requires the entry of detailed information by each of the centers and is reviewed for quality assurance by the ABCC. Research islets are used for the improvement of islet isolation techniques, culture protocols and unique experiments at each center that were outlined in the center's application for their ICR grant. In 2003, the ICR's also began distributing islets to approved investigators for NIH or JDRF funded projects. This system has been monitored by the ABCC and has recently been improved by the use of the automated Islet Allocation system. (See previous article) The following table will be a highlighted in every Newsletter with updated data to show the progress of the ICR in both clinical and research islets produced.

This first table shows the accumulative numbers collected by the ABCC for isolations reported since 2001 and for islets distributed for basic research since 2003 to date as well as those reported in 2007 to date. (8/30/07)

ICP Database Isolations Reported

To Date	Total	Clinical	Research	Not Used*
Acc.	860	203	603	54
2007	143	3	132	8

ICP Database IEQs Reported

To Date	Total	Clinical	Research	Not Used*
Acc.	230,470,094	90,756,85	133,500,440	6,212,804
2007	25,857,448	1,477,044	23,584,250	796,154

To Date	# Approved Users	#Shipments	#IEQs Distributed
Acc.	119	1659	48,945,047
2007	16	532	15,064,312

** Not Used-Poor quality pancreata and/or islets; or no permission for research*

"The day starts out like any other day; check your sugar, get in the car and head off to work. Except you don't make it to work, you're in the driver's seat of the car, the airbag has exploded and you are covered in blood. You have no idea what's happened or how it happened. Welcome to *one* of my many low blood sugar experiences. My daughters, family and friends were babysitters on constant vigil. Telephone numbers of every local family member were posted on the refrigerator with instructions to 'call 911 only if mommy is unconscious.' That was my life prior to the islet cell transplant. For the first time in my adult life, I am in control. It is wonderful to know that I can go from point A to B without a low sugar. I will no longer come out of stupor and wonder where I have been, what I have said or done. The islet cell program has not only changed my life, it has made life better for everyone in my circle."

These are the heartfelt words of islet transplant patient, Cyndi Smart-Williams. Her life changed dramatically after she received three islet infusions at the Diabetes Research Institute, ICR Center in Miami. The final infusion coming one and a half years ago, she has had little problems with her immunosuppression and loves her new freedom from fear. She expressed her gratitude to Drs. Gaston Ponte, Aleida Saenz, and Tatiana Froud for their care and patience as well as Dr. Camillo Ricordi and Rudolfo Alejandro for their vision to make her transplant possible.