



The ICR Newsletter

Volume 2, Issue 1, February 29, 2008

ABCC Sponsors First ICR Consortium Counting Workshop

On January 15th, during the stimulating presentations at the Annual Rachmiel Levine Symposium, thirty one researchers took a break from the talks and attended the first Counting Workshop sponsored by the Administrative Bioinformatics Coordinating Center (ABCC) and the Islet Cell Resource Consortium (ICR). The hour long interactive seminar was attended primarily by representatives of the eight ICR Centers in an effort to standardize the methods of islet counting and sizing. Attendees received a copy of the *Potency Subcommittee Protocol for Assessing Islet Number and Purity* Manual which consists of background on the history of islet sizing, details of the ABCC sponsored study for confirming standardized counting, practice photos of pre-sized islets and 24 separate exercises that the participants can size and email into the ABCC for evaluation. The Manual also explains how the ABCC will evaluate the islet scoring and provide statistical analysis of all results. Additionally, the Workshop provided handouts of the visual presentation that focused on methods of mixing the islet suspension and accurate sampling techniques. Proper mixing and sampling of an islet suspension is more difficult and in many ways, more important than the counting and sizing. Overall, this first Counting Workshop was considered a great success and an excellent dry run for the larger venue planned for the American Diabetes Association's 68th Scientific Sessions in San Francisco this coming June.

Executive Highlights

I would like to bring attention to three important aspects of the ICR Consortium:

- 1) Each ICR laboratory has considerable expertise in islet isolation, culture, and shipping and together the eight ICR islet processing laboratories are supplying high quality, human islets to more than 120 investigators who are conducting a wide range of research.
- 2) The laboratories of the ICR Consortium are working collaboratively to standardize procedures for shipping islets and for assessing islet potency.
- 3) A group of basic science researchers who study human islets provides regular advice and feedback to the ICR about all aspects of the human islet distribution process. This working group is chaired by Andrew Stewart from the University of Pittsburgh and includes Debbie Thurmond, John Hutton, Jerry Nadler, Chris Rhodes, and Alberto Hayek. The ICR Consortium thanks these scientists for their valuable advice. Feedback from this group and from individual investigators (via the forms that accompany each islet shipment) are crucial in improving the islet distribution process.

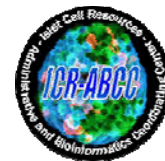
The availability of human islets from the ICR Consortium is critical to improving our understanding of human islet physiology and pathophysiology. The ICR Consortium welcomes your ideas, suggestions, and comments.

Alvin C. Powers, M.D.
Vanderbilt University
Chair, Steering Committee of the ICR Consortium

First ABCC / ICR Counting Workshop in Newport Beach during the Levine Symposium

Photos Courtesy of Jinq Wang of the University of Pennsylvania and Janice Sowinski of the ABCC





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Islet Research History Lessons – Purification

Although looking through a microscope and hand dissecting islets from a pancreas was probably the first type of islet purification, the published procedure for an islet purification after collagenase digestion using density gradients and centrifugation was developed at Washington University in St. Louis in 1972 by Drs. Walter Ballinger and Paul Lacy. Improvement of isolation procedures and purification methods continued to be a focus at Wash U for decades, and through the 80's many researchers around the world tried variations of islet purification through such methods as sedimentation, elutriation, lectins bound to magnetic microspheres and even the mechanical use of Velcro to remove exocrine tissue. Still, density gradients, first sucrose and then Ficoll with centrifugation remain the most effect methods for human islet purification. The introduction of the Gambro BCT COBE 2991 Cell Processor, originally designed to separate different types of blood cells, published by Lake et al in 1989 became a basis for large scale purification of human islets. Although modifications in the density gradients continue to improve as the islet digestion methods change, this basic process has allowed islet transplantation to continue into the 21st century.

Magnetic resonance-guided, real-time targeted delivery and imaging of magnetocapsules immunoprotecting pancreatic islet cells. [Barnett BP](#), [Arepally A](#), [Karmarkar PV](#), [Qian D](#), [Gilson WD](#), [Walczak P](#), [Howland V](#), [Lawler L](#), [Lauzon C](#), [Stuber M](#), [Kraitchman DL](#), [Bulte JW](#) Nature Medicine 2007 Aug;13(8):986-91

In type I diabetes mellitus, islet transplantation provides a moment-to-moment fine regulation of insulin. Success rates vary widely, however, necessitating suitable methods to monitor islet delivery, engraftment and survival. Here magnetic resonance-trackable magnetocapsules have been used simultaneously to immunoprotect pancreatic beta-cells and to monitor, non-invasively in real-time, hepatic delivery and engraftment by magnetic resonance imaging (MRI). Magnetocapsules were detected as single capsules with an altered magnetic resonance appearance on capsule rupture. Magnetocapsules were functional in vivo because mouse beta-cells restored normal glycemia in streptozotocin-induced diabetic mice and human islets induced sustained C-peptide levels in swine. (*Continued on page 3*)

NEW FEATURES FROM THE ABCC

- ***IA Improvements – New User Feedback Forms on line*** Beginning March 1st the database will now require electronic feedback by all islet users in order to continue receipt of islets for basic science research projects. User Feedback Forms have always been a requirement but in order to become “more Green” and to improve the efficiency of our tracking system, the database now requires all users to complete the form on line and copies will automatically be sent to the providing ICR center and the ABCC.
- ***Change in Algorithm's “24 hour rule”*** As of January 28th the ABCC has made a change in the MAID System in the way distributions are handled. See article, “Unique Distribution Scenarios Lead to Algorithm Modifications at ABCC” on pages 3 & 4 for details.

MEET THE STAFF



Martha “M” Antler
Data Manager

M, as she prefers to be called, has been working for the ABCC at COH since 2005 when there were only 26 ICR approved investigators in the program. Before that she worked for Baxter Bioscience as a Clinical Project Coordinator on pediatric hemophilia studies, a job that she loved. About that time her daughter, Jodi was diagnosed with type 1 diabetes and since M has been taking insulin since she was young, she wanted to be near to those who are working on finding a cure. Although M always seems to be available for anyone who needs assistance in the ICR, she has many other interests. When she is not flying across the country to visit her children Jodi, 22, and Bryan, 24, and her granddog, Winston, an adorable 3 year old pug, in Washington DC, she might be found working with Adelante Mujer Latina, a group of professional Latina women who put together a career and educational conference for young Latina women and their mothers, to help them get ahead in the world. She has recently gotten involved with the NAMI (National Alliance on Mental Illness) organization and has been a volunteer marshal at the Champions Tour and LPGA pro golf tournaments for the past five years. Although M often is the person that ends up with the tedious jobs of trying to schedule meetings among incredibly busy doctors, sending countless emails to hundreds of people involved in the ICR and organizing the meetings and workshops sponsored by the ABCC, in reality she is the glue that keeps the ABCC and the ICR together.



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FEATURED ICR:

UNIVERSITY OF MIAMI – DIABETES RESEARCH INSTITUTE

The Diabetes Research Institute (DRI) at the University of Miami in Miami, FL is one of the original ten ICR centers that received funding in 2001 and then qualified for continued funding again in 2006. Led by the renowned investigator and a Distinguished Professor of Medicine, Dr. Camillo Ricordi, the DRI is a world leader in cure-focused diabetes research through cell-based therapies to restore insulin production. The DRI's research agenda is all-inclusive but islet transplantation has been a major focus of the U of Miami's repertoire for over 30 years. Since becoming a part of the ICR Consortium, the DRI have transplanted 38 patients with 71 infusions, have reported to the ICR database that they have performed 26 clinical isolations, 95 basic science isolations, and have provided 8,523,367 million islet equivalents to approved ICR researchers for basic science studies. Dr. Ricordi's philosophy has always been one of openness and sharing when it comes to research techniques and methods that have proven successful in Miami's program therefore the DRI is a leader in international training of isolation, transplantation and other islet research methods. For more information on the Diabetes Research Institute in Miami, you can browse through their website at <http://www.diabetesresearch.org/DiabetesResearchInstitute.htm>.

ICR Director: Camillo Ricordi **Co-Investigators:** Rodolpho Alejandro, Luca Inverardi, Hirohito Ichii, Alejandro Caicedo, Antonello Pileggi **Research Associate:** Chris Fraker
Biostatistician: Shari Messinger Cayetano **Director, cGMP Processing Facility:** Aisha Kahn
Quality Assurance Manager: Elina Linetsky **Cell Transplant Specialists:** Jorge Montelongo, Omais Hanif, Ross Haertter, Xiaojing Wang **Organ Procurement Technician and Preservationist:** Joel Szust

Next Islet Counting Workshop Focuses on Researchers' Needs

The ABCC will be holding their 2nd Counting Workshop at the 68th Scientific Sessions of the ADA on June 7th and 9th 2008 at 6:30pm at the Moscone Center. Two sessions are being offered during the ADA meeting so all those interested will be able to find a convenient time to attend. Although all investigators are welcome, this interactive workshop will focus on the needs of the researchers that receive human islets from the ICR centers. Many of you have worked for years with rodent islets and have recently applied your work to human islets. We hope that we can help you with this transition. Not only will registrants receive an ICR Counting Manual that includes exercises with sized photos of human islets and the opportunity to have your counts compared to those of experts in the field, but the ABCC will present methods for mixing your preparations to insure a homogenous suspension of islets, techniques for sampling islet preparations, and tips on equipment that might make your counting simpler and more accurate. We will also supply you with an instructional CD that you can take back to your laboratory and use as a teaching tool for those technicians at your center that were not able to attend our seminar. Registration for the upcoming workshop can be made at <http://icr.coh.org/workshops.asp>. There is no fee for attending this teaching workshop but we do require registration prior to the event. We encourage all to participate!

Research Paper

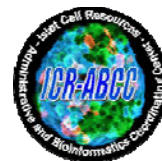
(Continued from page 2)
In this large-animal model, magnetocapsules could be precisely targeted for infusion by using magnetic resonance fluoroscopy, whereas MRI facilitated monitoring of liver engraftment over time. These findings are directly applicable to ongoing improvements in islet cell transplantation for human diabetes, particularly because our magnetocapsules comprise clinically applicable materials.

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.

Unique Distribution Scenarios Lead to Algorithm Modifications at ABCC

On Friday, January 25th, the ICR Matching Algorithm Islet Distribution (MAID) system encountered difficulty in distributing a very large amount of islets (503K Islet Equivalents (IEQs) produced by the Universities of Pennsylvania and Minnesota. The isolation from Pennsylvania contained 3 purity batches of 155K, 155K and 80K IEQs. While the system placed the first batch with no problem, there were not enough respondents on a Friday afternoon to place the islets from the 2nd and 3rd batches. About the same time, two additional batches of islets totaling 113K IEQs were broadcast from U. M., thus "flooding the market" even further.

The MAID system includes a "24 hour rule" such that once an investigator has accepted an open offer shipment, he/she cannot receive another open offer shipment within 24 hours (either from the same or different isolations). We felt that this rule was restricting these islets from being placed, and so the ABCC database personnel temporarily inactivated the 24 hour rule and reran the algorithm allowing 19 investigators to accept a total of 362K (93%) IEQs from the Pennsylvania isolation and 9 to accept offers 60K (53%) of the available IEQs for the Minnesota isolation, all by about 5:30 pm EST. (In this instance we still were unable to place 81K IEQs, or 16% of the total IEQs offered, probably due to the late Friday timeframe and the huge amount of available islets). *(Continued on page 4)*



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Coming Events:

Islet & Beta Cell Biology-Keystone Symposium

[www.keystonesymposia.org/Meetings/ViewMeetings.cfm?](http://www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=920)

[MeetingID=920](http://www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=920) April 6th – 11th, Snowbird, UT

American Transplant Congress 2008

<http://www.atcmeeting.org/2008/> May 31st – June 4th, Toronto, Ont. Canada

68th Scientific Sessions of the American Diabetes Association

[http://professional.diabetes.org/Congress_Display.aspx?](http://professional.diabetes.org/Congress_Display.aspx?TYP=9&CID=58000)

[TYP=9&CID=58000](http://professional.diabetes.org/Congress_Display.aspx?TYP=9&CID=58000) June 6th-10th, San Francisco, CA

ICR Sponsored Counting Workshop for Islet Researchers At the ADA

Registration at: <http://icr.coh.org/workshops.asp>

June 7th and 9th, Moscone Center, San Francisco, CA

Algorithm Modifications (Continued)

(Continued from page 3) As a result of this experience, the ABCC has modified the algorithm permanently as of Monday, January 28th to relax the “24 hour rule”. Now when a new offer comes in, those investigators who have already received islets within 24 hours (either from a targeted or open offer shipment) will be eligible to receive another islet shipment, however with lower priority than other users whose requirements match the offer but have not received recent shipments.

From all accounts, the allocation system has been working very well since its implementation in May of 2007, but when unusual situations such as this one arises, the ABCC will try to continually improve the underlying rules, to optimize fair and complete islet distribution. Any suggestions for further improvements are always welcome and can be sent to Janice Sowinski at the ABCC. jsowinski@coh.org

ICR Consortium Statistics

Isolations Reported in the ABCC Database

To Date	Total	Clinical	Research	Not Used*
2008	44	0	40	4
Cumulative	979	206	714	59

IEQs Reported in the ABCC Database

To Date	Total	Clinical	Research	Not Used*
2008	6,938,045	0	6,173,055	764,990
Cumulative	261,723,276	91,745,928	163,041,899	6,935,449

Cumulative data reported from 12/1/2004 to 2/22/08

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

ICR Basic Science Distribution Program Activity (2/1/2004 to 2/22/2008)

To Date	# Approved Users	#Shipments	#IEQs Distributed
2008	5	172	4,033,000
Cumulative	147	2090	59,139,239

“You Mean I Can Eat Anything?”



Wisconsin Islet Transplant Patient Helen Miller

At first not taking my insulin was a little overwhelming. I kept asking my doctor ‘you mean I can eat anything?’ For 45 years I lived with diabetes. During that time, my life revolved around an often worrisome and always painful routine. Everyday I checked my blood sugar seven times and injected myself with insulin up to five times. I never imagined that I could break free from the relentless schedule that had defined my life in so many ways. That began to change in 2004, after diabetes eventually weakened my kidneys and I received an organ transplant at the University of Wisconsin in Madison.

While I recovered from the successful operation, Dr. Luis Fernandez, my transplant surgeon, began to discuss the islet process and my eligibility for the procedure. At 58 years old, I was one of the oldest patients to be considered. However, after many tests I was offered the chance and jumped at the possibility of finding independence after more than four decades.

After only two infusions in 2006, I found myself free to expand my horizons and embrace the hope of a life without diabetes. I didn’t realize until after the procedure, how much of my time had been spent worrying about eating the right foods and about how I could avoid complications from this disease. With the help of Dr. Fernandez and other staff at the University of Wisconsin, I have embraced my new life. Being free from diabetes means more than just the liberty to eat whatever you want. It has given me the chance to enjoy a more productive life and to dedicate myself to enjoying the company of my two daughters and grandchildren.