



## Islet Communication Network

Volume 1, Issue 2, November 30, 2007

### Successful ICR 3rd Annual Islet Workshop Provided Intellectual Sharing

The ICR 3rd Annual Islet Workshop hosted by the University of Illinois – Chicago ICR and Dr. Jose Oberholzer, appeared to be the most successful held so far. ***“Can we overcome the obstacles that limit the use of clinical islet transplantation?”*** was the title of this year’s workshop. The full day event featured eight sessions each chaired by distinguished leaders in the field and featured well-known speakers from Europe, Australia and North America. There were 115 participants at this year’s Workshop including 31 speakers and chairs. The experts presented two fifteen minute presentations on their topics during each session followed by a round table discussion with audience participation. This interaction among junior and senior scientists was a key feature of this sized venue.

The morning sessions focused on the human islet as a cell source and included presentations on beta cell development, growth factors, and the human cell cycle as well as the challenges of islet shipping. The afternoon sessions concentrated on the problems and solutions of islet cell loss with presentations featuring methods for the prediction of graft function, islet neogenesis, islet pathology and encapsulation.

The workshop was followed by an elegant dinner at the UIC Dean’s Room, part of the old campus at the university. The magnificent dining hall provided a perfect atmosphere to continue the scientific discussions and productive dialogue that was fueled by the day’s presentations at the well attended ICR workshop.

### Executive Highlights

*As the Program Officer at the National Center for Research Resources who is responsible for the Islet Cell Resource Consortium (ICRC), I would like to underscore my enthusiasm for the potential of this newsletter to introduce new communication opportunities to the sites distributing islets and the recipients of the islets and to improve upon our distribution algorithm at the Administrative and Bioinformatics Coordinating Center at the City of Hope in Duarte. Over the past year, under the leadership of Dr. Alvin Powers, chair of the Steering Committee of the ICRC, we have introduced an advisory committee composed of recipients of islets for basic research. The exchange between the advisory and steering committees has opened up a range of questions that have motivated the ICRC to move forward to explore conditions of shipping and storage and to evaluate methods of islet assessment in order to provide our recipients with better products.*

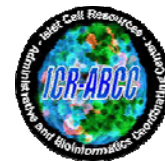
*In turn, the recipients have learned that, even though the ICRC has been distributing islets without charge for several years, these products remain an expensive product for which funding has become scarce as the number of users expands. The ICRC islet sites are grateful to the NIDDK, JDRFI, and NCRR for providing \$0.10/Islet Equivalent in reimbursement. For many recipients, their generosity defrays thousands of dollars of potential costs for pancreata and purified islets. To help garner continued support for the resource, it will be most helpful if each of the recipients takes care to provide appropriate attribution in any publications based on use of the islets.*

*Dan Rosenblum*

### Photos from the ICR 3rd Annual Islet Workshop and Dinner

*Photos courtesy of Dr. Jing Wang of U Penn*





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## Islet Research History Lessons – The Breakdown

Once it was established that the organelles discovered by Langerhans were the source of life saving insulin and organ transplantation became a reality, naturally scientists tried to establish a viable way to use islets as a transplant source. In 1964 Hellerstrom published a microdissection of rodent islets followed shortly by the use of an enzymatic release of the islets from the surrounding exocrine tissue using collagenase. Lacy's group improved this technique in rodent pancreata using Hank's solution to distend the tissue, manual chopping and agitation of the tissue in collagenase. However this method did not prove efficient for large animal islet isolation. The pancreatic tissue of higher mammals was much more fibrous and compact; it had exponentially greater volume as well as islets so methods of automation and ductal collagenase injection were investigated. After several attempts to improve the tissue processing including chopping machines, sieves, homogenizers and even velcro, several flow through systems using a two stage process with collagenase infused pancreatic tissue contained in a screened section were developed. As the tissue digested, islet sized pieces were released through the screen and collected in cold, protein containing solutions. Today, variations of the Ricordi Chamber Method, which uses this premise, are the most popular techniques for human islet isolation.

## MEET THE STAFF



**James Cravens**  
Study Coordinator

James is probably the best known person at the ABCC to both ICR staff and investigators. He is the one that you go to for most questions, the trainer for the IA distribution system and the man that gets the calls when almost anything breaks down. Officially James is the ABCC Study Coordinator but his Masters in epidemiology and biostatistics from George Washington University and BS in mathematics from Georgetown University give him the needed background to coordinate and analyze data from all the ICR systems for presentations, troubleshoot new database structures before launching, and manage the data-sharing with Collaborative Islet Transplant Registry (CITR), the project he worked on for the Emmes Corporation before coming to the ABCC over a year ago. James is originally a California boy and after several years on the East Coast for school and his first job with Emmes, the position with the ABCC brought him back home to Orange County. According to James, "Islets are my first love...other than music, family, movies, dating, investing, traveling, money, beer, and beer."

ICR Contributes to Islet Research: Limited capacity of human adult islets expanded in vitro to redifferentiate into insulin -producing beta-cells *Diabetes* 56(3):703-8, 2007 Kayali AG, Flores LE, Lopez AD, Kutlu B, Baetge E, Kitamura R, Hao E, Beattie GM, Hayek A

Limited organ availability is an obstacle to the widespread use of islet transplantation in type 1 diabetic patients. To address this problem, many studies have explored methods for expanding functional human islets in vitro for diabetes cell therapy. We previously showed that islet cells replicate after monolayer formation under the influence of hepatocyte growth factor and selected extracellular matrices. However, under these conditions, senescence and loss of insulin expression occur after >15 doublings. In contrast, other groups have reported that islet cells expanded in monolayers for months progressed through a reversible epithelial-to-mesenchymal transition, and that on removal of serum from the cultures, islet-like structures producing insulin were formed. (Continued on page 3.)

## New Features from the ABCC

- ★You Have Islets!★ Busy on your computer but don't want to miss the chance to get islets for your research? The ABCC has now made it hard to miss! When your name comes up as an islet distribution recipient, there can be a widget alert in the bottom right hand corner of your computer screen to remind you to log on and accept your islets! Be expecting an email soon from James Cravens to down load this application and instructions on how get high tech!



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## FEATURED ICR:

### SOUTHERN CALIFORNIA ISLET CONSORTIUM - SCIC

The SCIC, headquartered on the beautiful campus of the City of Hope (COH) Medical Center in Duarte, CA. is one of the four original ICR centers that survived the second round of funding and remains a leader in islet distribution as well as clinical transplantation. Under the guidance of Dr. Fouad Kandeel, a renowned diabetologist and islet researcher, the COH ICR has processed 46 pancreata so far in 2007, distributed 3.9 million islets to ICR researchers and performed one clinical transplant. The staff consists of many experienced islet researchers including Dr. Yoko Mullen who has devoted over 40 years to islet studies, now in charge of the ICR's Quality Assurance Program. An annual event sponsored by COH and Dr. Kandeel is the Rachmiel Levine Symposium, next year being held January 13<sup>th</sup> through 16<sup>th</sup> at the Newport Beach Marriott Hotel in Newport Beach, CA. **"Translational Research in Type 1 Diabetes: Beyond Insulin and the Edmonton Protocol"** will feature distinguished speakers from around the globe. ([www.cityofhope.org/levinesymposium](http://www.cityofhope.org/levinesymposium))

**Program Director:** Fouad Kandeel

**Program Manager:** Jeannette Hacker

**Isolation Teams:** **A.**-Ismail Al-Abdullah, Kwamina Bentsi-Barnes, Elena Forouhar, Itzia Iglesias-Meza, Chikodili Umeadi **B.** Willem Kuhlreiber, Lam Ho, Patricia Kao, Tania Urrutia, Emily Zebadua;

**Islet Distribution:** Noe Gonzales, Autumn Tate;

**Organ Procurement:** Donald Dafoe, Alina Oancea

**QA/QC:** Yoko Mullen, Yasmine Shad, Ivan Todorov, Karen Ramos, Indu Nair, Noe Gonzales, Keiko Omori, Jeffrey Rawson, Sherri Stinson, Luis Valiente, Doreen Ligot, Alina Oancea

**Clinical Transplant Team:** Fouad Kandeel, Donald Dafoe, Mohamed El-Shahawy, Alice Peng, Jasmine Zain, Mohamad Al-Sayed, Howard Marx Julie Ressler, Lisa Huntsinger, Brenda Williams, Ammar Aboul-Saoud, Doreen Ligot, KD Shiang, Jeannette Hacker

## Research Paper

(continued from page 2): The aim of the current study was to compare the two methods for islet expansion using immunostaining, real-time quantitative PCR, and microarrays at the following time points: on arrival, after monolayer expansion, and after 1 week in serum-free media. At this time, cell aliquots were grafted into nude mice to study in vivo function. The two methods showed similar results in islet cell expansion. Attempts at cell differentiation after expansion by both methods failed to consistently recover a beta-cell phenotype. Redifferentiation of beta-cells after expansion is still a challenge in need of a solution. [\[PUBMED abstract\]](#)

*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](mailto:abcc@coh.org).*

## Open Islet Allocation System: The Tortoise and the Hare Have Equal Chances to Win

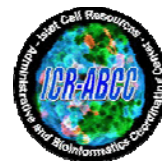
In our on-going effort to make islet acquisition easy and efficient, the ABCC recently completed a major change to the online ICR Islet Allocation System. The new open offer system eliminates the old, frustrating mass offer system. In the past, when there were fewer than 30 minutes or there weren't any eligible matches for targeted offers, all investigators in the system would receive a notification of a mass offer and a mad dash to the computer would ensue. The only way to get islets from a mass offer was to beat your fellow ICR-approved investigators to the draw. Now, the open offers will be triggered under the same circumstances as before, but only a small number of investigators will be notified for each open offer. All of these selected investigators will have until the stated deadline to respond. This eliminates the first come, first served method. When the offer has expired, the system will rank the respondents according to offer history and priority level, and the available islets will be assigned to the optimal recipients. This ensures that the islets are distributed to the most worthy recipients every time. Ultimately, each investigator will receive fewer open offers, but it will be much easier to obtain islets from the offers that actually do show up. This will eliminate any bias and maximize the fair distribution of islets for basic science research within the ICR.

## ICR Consortium Standardized Shipping Containers Now in Use



Photo courtesy of Chris Groh of UIC

The ICR Consortium has been working to improve the quality of the islets upon arrival at the investigators' laboratories through the standardization of the shipping containers. Based on results from several previous studies, the ICR centers are now using a standardized shipping box that is well marked to assure the recipient is aware that their islets have arrived. In addition, we have replaced the "fly-away", static noodles with reusable bubble-wrap, enlarged the absorbent material to surpass all federal guidelines, and have included disposable indicators that allow the user to know immediately if the shipment has been challenged by high or low temperatures. The most important and definitely the most expensive additions are the 6 ambient gel packs included in every shipment to ensure proper temperature control. It is critical that all investigators promptly return all shipping equipment to the providing ICR and complete and return the new User Feedback Forms that will be included in every package. The form can be found on our website at <http://icr.coh.org/docs/UserFeedbackForm.doc>



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## Coming Events:

### Rachmiel Levine Symposium

January 13<sup>th</sup>-16<sup>th</sup>, Newport Beach, CA

[www.cityofhope.org/levinesymposium](http://www.cityofhope.org/levinesymposium)

### ICR Islet Counting Workshop

January 15<sup>th</sup>, 12:30 -2:00pm at the Levine Symposium

Register on line at:

<https://stage.coh.org/icr/workshops.asp>

### ICR Steering Committee Meeting

February 28<sup>th</sup> – 29<sup>th</sup>, Miami, FL

### Islet & Beta Cell Biology-Keystone Symposium

April 6<sup>th</sup> – 11<sup>th</sup>, Snowbird UT

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

## Islet Counting Workshop

The ABCC will be hosting the first of several Islet Counting Workshops to be held during the Rachmiel Levine Symposium on Tuesday, January 15<sup>th</sup> at 12:30 pm in the Avalon East Room at the Newport Beach Marriott Hotel. The goal of this workshop is to standardize the counting of human islets among the ICR centers as well as the ICR approved investigators that receive the islets through the distribution program with the sizing and purity of isolated human islets. The ABCC has designed a Counting Manual that has 16 photographs depicting the microscopic field of purified human islets and a grid that mimics a 50µm graded reticle which is customarily used for sizing the islets in the microscope eyepiece. The manual comes with a practice sheet of 67 numbered islets with a corresponding Islet Equivalent size to familiarize the counters with the standard sizing protocol. The Consortium is requesting that at least one representative from each ICR attend this free session during the Symposium and also welcome any investigators that would like to improve their assessment of human islet size and purity. Registration for this free workshop can be made online at: <https://stage.coh.org/icr/workshops.asp>. A discount for the Levine Symposium is also available for those registering for the ABCC workshop. The deadline for registration is December 15, 2007. Hope to see you all there or at one of our future Islet Counting Workshops!

My Road through Life Has  
Gotten a Little Straighter



Islet Transplant Patient Irene Bumann Lyon

## ICR Consortium Statistics

### Isolations Reported in the ABCC Database

To Date	Total	Clinical	Research	Not Used*
2007	201	6	185	10
Cumulative	918	206	656	56

### IEQs Reported in the ABCC Database

To Date	Total	Clinical	Research	Not Used*
2007	41,448,184	1,477,013	39,065,875	905,296
Cumulative	246,538,612	90,758,161	149,548,505	6,321,946

*Cumulative data reported from 12/1/2004 to 11/27/07*

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

### ICR Basic Science Distribution Program Activity

*(2/1/2004 to 11/27/2007)*

To Date	# Approved Users	#Shipments	#IEQs Distributed
2007	19	719	19,552,504
Cumulative	122	1,848	53,265,239

"Everyday is a winding road, I get a little high, I get a little low. These are the days when anything goes." These lyrics from Cheryl Crow's song describe my life prior to my islet cell transplant. My husband constantly reminded my daughters they had "Mommy duty" anytime he had to leave for coaching and officiating duties. I missed observing many of my daughters' sport and school activities in addition to holiday and family events due to the unexpected hypoglycemic episodes I experienced. One of the most humiliating experiences I remember was the time I was shopping at a discount center and left the store, but I couldn't find my car. I stood next to someone else's vehicle and wouldn't leave. They called the police, who administered a breath analysis. After seeing my emergency awareness card in my billfold indicating I was diabetic, the paramedics were notified. They administered tests, followed with glucose. The police called my home, where my daughter answered and literally ran a half mile to the high school to get her father who was coaching baseball to come pick me up. Thanks to Dr. Hering, Jamen Parkey, the transplant team, nursing staff members and medical personnel involved with my care at the Diabetes Institute at Fairview Hospital of the University of Minnesota, I've been able to return to a normal life with my family, co-workers, and friends. I no longer worry about needing to be rescued from hypoglycemic episodes.