Islet Cell Resource Consortium
Administrative and Bioinformatics Coordinating Center

The ICR Newsletter

Volume 2, Issue 3, August 29, 2008

4th Annual ICR Islet Workshop to Be Held in Sunny California

The Islet Cell Resource (ICR) Consortium and its Administrative and Bioinformatics Coordinating Center (ABCC) will proudly be presenting the 4th Annual Islet Workshop at the Hyatt Regency Hotel in Newport Beach, CA on October 3rd, 2008 from 7:30 am until 5:00 pm. Registration forms and a detailed program can be found at http://icr.coh.org/workshops.asp. As at previous ICR sponsored Islet Workshops, the interactive program will feature the world's leading experts on beta cell biology and islet transplantation. Topics this year will include: "Assessing Beta Cells *In Vivo* and *In Vitro"*, "Collagenase", and "New Approaches to Islet Transplantation". Speakers will include experts from 14 different universities and hospitals representing four separate countries. It is the ICR's goal to make this Workshop beneficial to all by encouraging active audience participation and allowing ample time for discussion after each session. Presenters are asked to report on the latest research that is relevant to the field, allowing workshop participants to get first hand knowledge of their most recent findings. The organizers intentionally keep the size of the attendees low (~120) to allow this unique type of professional interaction. The Workshop is funded by the National Center for Research Resources at the National Institutes of Health (NCRR/NIH), the National Institute of Diabetes, Digestive & Kidney Diseases at the National Institutes of Health (NIDDK/NIH) and the Juvenile Diabetes Research Foundation International (JDRFI). The Registration Deadline is September 12th so don't delay, register now at http://icr.coh.org/workshops.asp!

Islet Cell Resource Center

(ICR) Consortium

4th Annual Islet Workshop

Friday, October 3rd, 2008

7:30 AM – 5:00 PM

Counting Workshop 6:00-7:00 PM

Registration Deadline Sept. 12, 2008

Executive Highlights

Congress was successful in overriding President Bush's veto of the Medicare legislation on July 15, 2008, including funding for diabetes research. The legislation includes a two-year extension of the Special Diabetes Program (SDP), providing $300 million for type 1 diabetes research ($150 million per year for two years). This is the second largest influx of federal research dollars ever provided to fight this disease; a multi-year extension of the SDP was JDRF's top legislative priority this year. Passage of the bill avoids a 35 percent cut in federal support for type 1 diabetes research.

Created in 1997, the SDP provides multi-year focused funding that has led to the development of new technologies and therapies that are helping people with diabetes and accelerating the pace of science leading to a cure. The JDRF has been pleased to partner with the NIH on a number of programs funded by the SDP, including the ICR.

We would like to thank our dedicated volunteers for their efforts. For more information on how you can participate in JDRF's advocacy efforts, please follow the link below: http://advocacy.jdrf.org/index.cfm?fuseaction=home.viewPage&page_id=B65C15BF-1279-CFD5A76EA7307F847B80.

For scientists: to apply for JDRF support of research to find a cure for type 1 diabetes and its complications, please visit: http://www.jdrf.org/index.cfm?page_id=103206.

Adrianne Wong,
JDRF Representative to the ICR Steering Committee

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Islet Research History Lessons – Counting

In the 80's when canine islet isolations became the trend for establishing a large animal model for islet transplantation on the road to bringing it to the clinical arena, it became apparent that an "islet" wasn't always an "islet". Dog islets unlike rodent islets were often irregularly shaped and of all different sizes. In 1987, Alderson, *et al* published "Isolation and quantification of canine islet tissue for transplantation" in *Transplantation* establishing for the first time a standard for islet size called Islet Equivalents. In 1990 Ricordi, *et al* published a similar paper in *Acta Diabetologica Latina* stressing the need for consistency among different isolation centers when comparing islet preparations for clinical transplantation. It is a prime objective of the ICR to continue this standardization process both for clinical and basic research isolations. All ICR centers have required their staff members who do the islet counting in their laboratories to complete an ABCC organized Counting Exercise. The results will help individual centers adjust to the consortium standards. The ABCC is also conducting their third Islet Counting Workshop to assist researchers in quantifying the islet preparations that they receive through the distribution program. It is now time for technology to help improve this process. Imaging systems and accompanying software have been out for over 20 years but no one system has been adapted to work with human islet preparations. Hopefully a standardized, widely accepted automated system is in the near future.

ILT3-FC Suppresses T Cell Responses to Allogeneic Human Islet Transplants in HU-NOD/SCID Mice.

Vlad G, D'Agati VD, Zhang QY, Liu Z, Ho EK, Mohanakumar T, Hardy MA, Cortesini R, Suciu-Foca N. Diabetes 2008; 57(7):1878-86.

OBJECTIVE: The aim of our study was to explore the immunomodulatory activity of soluble immunoglobulin (Ig)-like transcript (ILT) 3-Fc in pancreatic islet transplantation and to determine its mechanism of action. RESEARCH DESIGN AND METHODS: NOD/SCID mice in which diabetes was induced by streptozotocin injection were transplanted with human pancreatic islet cells. Mice in which the transplant restored euglycemia were humanized with allogeneic peripheral blood mononuclear cells and treated with ILT3-Fc or control human IgG or left untreated. The blood glucose level was monitored twice a week, and rejection was diagnosed after two consecutive readings >350 mg/dl. Tolerated and rejected grafts were studied histologically and by immunostaining for human T-cells and insulin production. CD4 and CD8 T-cells from the spleen were studied for suppressor activity,*(continued on page 3)*

New Features from the ABCC

✸The Merge ✸ The ABCC has been working for over a year on the merge of the algorithm and the database system. With this change will come many behind the scenes advantages and several that will be evident to the data entry staff at the ICR centers. A major change will be the option to enter data into the system during the isolation process and then broadcast the islets for distribution if they are not used for transplant or center studies. For centers that have internet access in their processing room, isolation data can be entered in the system as it is recorded in the batch records. You will also notice additional enhancements for the database files including an expanded culture page for multiple types of flasks and islet concentrations. *Coming soon to your local website!*

MEET THE STAFF

Barbara Olack
Quality Assurance Administrator

Barbara Olack has been working with islets since 1977 when she married her husband, John, who worked at Washington University Medical School in St. Louis and he saw an ad on a bulletin board looking for someone to take care of diabetic rats. The researcher who placed the ad was Dr. David Scharp, the lab became one of the premier centers in the world working on human islet transplantation and this student, majoring in nursing, biology and journalism was lucky enough to become a Research Associate in Surgery at the prestigious medical center. During her time in the islet lab, she participated in over 30 clinical islet transplants which provided years of insulin free lives to many of the recipients. Barbara ran the islet isolation program at Wash U. until 2003, the last nine years working with the renowned human immunologist, Dr. T. Mohanakumar, during which time she worked on xeno and allo rejection projects involving human and pig islets and humanized SCID mice. Barbara was the ICR representative for Washington University until 2003, when she left the university to manage *DiabetesPortal.com* an interactive website for people with type 1 diabetes to find transplantation help. This allowed her to become familiar with pancreas and islet clinical programs around the world. After working as a consultant for a year and one half she became the Quality Assurance Administrator for the ABCC at the City of Hope. Functioning mainly from her home in Freeburg, IL, 25 miles outside of St. Louis, Barbara travels to the ICR centers performing audits on the database entries, assists in consortium projects, organizes the Counting Workshops and helps in many other ways to make the ICR centers and the ABCC a successful collaborative effort. Her wonderful life is also filled with a loving husband of 31 years, 3 fantastic married children who have given her 5 ½ beautiful grandchildren, 4 dogs, 2 cats, and a comfortable home that welcomes countless friends; all of whom mean the world to her.

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FEATURED ICR:

UNIVERSITY OF WISCONSIN

The University of Wisconsin (UW) at Madison has been involved in the ICR for longer than their official two years as an approved Islet Center. In 2002 and 2003, they sent several pancreata to Washington University in St. Louis, where the ICR center there processed the islets and shipped them back to Madison for clinical transplantation. This makes Madison unique in that they are the only center that participated in the ICR clinical programs as both a recipient center and now as an islet provider. Under the guidance of transplant surgeons, Drs. Luis Fernandez and Jon Odorico and Islet Core Facility Associate Director, Dr. Matt Hanson, the center in Madison has become a leader in the ICR joint projects for islet viability and islet shipping studies. Serving as a core facility for the Consortium project to assess islets pre-shipping, UW assayed hundreds of samples from all the eight ICR centers for DNA content, biochemiluminescence and HPLC for the determination of oxidized and reduced pyridine nucleotides and adenylates. Their specialty has become extended quality control assessment of islet preparations pretransplantation using these sophisticated assays. They recently have moved their workplace to a newly built, state of the art laboratory that will allow this center to perform sophisticated experiments for years to come.

ICR Directors: Luis Fernandez, Jon Odorico **Associate Director:** Matthew Hanson **Distinguished Scientist:** Debra Hullett **Asst. Scientists:** Jamie Sperger, Juan Sebastian Danobetia, Alice Schwaznau, Jolien Connor **Asst. Researcher:** Melissa Barman **Assoc. Research Specialists:** Elisa Park, Mallory Spears **Transplant Nurse Coordinator:** Nancy Radke **Clinical/Laboratory Liaison:** Kristi Schneider

Next Islet Counting Workshop Focuses on Researchers' Needs

The ABCC will be holding their 3rd Counting Workshop following the 4th Annual Islet Workshop on October 3rd, 2008 at the Hyatt Regency Hotel in Newport Beach, California. 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. 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*)
expression of cytokines, and CD40L. RESULTS: Although human T-cell engraftment was similar in all groups, ILT3-Fc-treated mice tolerated the islets for the entire period of observation (91 days), whereas control mice rejected the graft within 7 weeks ($P < 0.0001$). ILT3-Fc treatment suppressed the expression of cytokines and CD40L and induced the differentiation of human CD8(+) T suppressor cells that inhibited Th alloreactivity against graft HLA antigens. T-cells allostimulated in vitro in the presence of ILT3-Fc inhibited CD40L-induced upregulation of CD40 in human pancreatic islet cells. Histochemical studies showed dramatic differences between human pancreatic islets from tolerant, ILT3-Fc-treated mice and control recipients rejecting the grafts. CONCLUSIONS: The data indicated that ILT3-Fc is a potent immunoregulatory agent that suppressed islet allograft rejection in humanized NOD/SCID mice.

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 .

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Coming Events:

ICR Steering Committee Meeting
October 2nd –Hyatt Regency Hotel in Newport Beach, CA

ICR's 4th Annual Islet Workshop
http://icr.coh.org/workshops.asp
October 3rd, 7:30am -5:00pm – Hyatt Regency Hotel in Newport Beach, CA

Islet Counting Workshop
http://icr.coh.org/workshops.asp
After the Islet Workshop: October 3rd, 6:00pm -7:00pm - Hyatt Regency Hotel in Newport Beach, CA

American Society of Human Genetics http://www.ashg.org/
November 11-15, Philadelphia, PA
Stop by the ABCC/ICR booth!

ICR Consortium Statistics

Isolations Reported in the ABCC Database				
To Date	Total	Clinical	Research	Not Used*
2008	165	7	144	14
Cumulative**	1066	201	800	65

IEQs Reported in the ABCC Database				
To Date	Total	Clinical	Research	Not Used*
2008	34,142,850	2,135,310	30,863,274	1,144,266
Cumulative**	289,991,294	93,881,238	188,852,298	7,257,758

ICR Basic Science Distribution Program Activity			
To Date	# Approved Protocols	#Shipments	#IEQs Distributed
2008	16	619	15,630,900
Cumulative**	156	2,536	67,137,259

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

***Cumulative data reported from 12/1/2004 to 8/28/08*

Additional Islets for Basic Research Provided for JDRF-Funded Investigators

The Juvenile Diabetes Research Foundation (JDRF) has developed a new program based on the Administrative and Bioinformatics Coordinating Center (ABCC) algorithm to isolate and distribute islets for basic research necessary for JDRF-funded grants. This new program will increase the number of islet equivalents available to JDRF-funded end-users of islets for basic research, and streamline the process of placing isolated islets.

Distribution of islets from JDRF's six islets for basic research providers will occur via the algorithm successfully developed by the Division of Information Sciences (DIS) at the City of Hope National Medical Center for the Islet Cell Resources Program (ICR).

The same ICR website will be used to accept offers, so all investigators should be aware of which program is offering the islets – there will be a JDRF or an ICR icon on the web page during the alerting process and on the User Feedback Forms in the on-line system. Please note that the DIS provides the JDRF access to the algorithm and provides tracking of islet distribution. However, unlike islets shipped via the ICR program, shipping preferences and choices of quality control assays are determined by the originating center and not by the ABCC. As always, individual investigators may choose which distributing center they would like to accept islets from.

For more information about this program please contact Jessica VanGurp, jvangurp@coh.org, the JDRF Islet Study Coordinator at the City of Hope at 626-256-HOPE Ext. 61600.

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Islet Transplants Affect More than the Recipient

This issue we spotlight not only Timm Gildea, who received his islet transplant at the University of Illinois - Chicago, but also his wife, Pat, and the impact this has had on her life, as well. Their gratitude extends to Dr. Jose Oberholzer and all his staff for making this wonderful change in their lives possible.

University of Illinois-Chicago Islet Transplant Patient Timm Gildea and his wife Pat

Thoughts from Timm…

When I'm asked how the islet cell transplant has changed my life, it's hard to know where to begin. Many things, like after 37 years of taking insulin, attempting to maintain a decent blood sugar level, controlling my diet to have a more normal life are the first few to come to mind. No matter how many reasons I could mention they all narrow down to the most important one – NO MORE LOW BLOOD SUGAR. It's a subject that is at the top of the list to all Type I diabetics and I hope I don't have to deal with it again. Until you've lived the roller coaster ride with the amount of insulin you take, food you eat, and work you do, it's very hard to understand the complications. By now I still can't believe how much I can accomplish without the low or high blood sugars. I will try never to take the transplants for granted, and I would like to thank everyone from Dr. Oberholzer and his entire professional staff to the generous donors and contributions that made this program possible… Thanks again,

Timm

Thoughts from Pat…

If you don't have diabetes or you haven't ever lived with someone that does, you probably don't understand how difficult it can be. Timm is very active. He hasn't ever been the kind of person that can just sit; he enjoys physical labor, such as yard work. Before his transplant, just cutting the grass was next to impossible to get through. He would stop several times to come in the house to eat or drink something in order to bring his blood sugar up. We worried about him when he was driving. I constantly watched him to see if I could see signs of his blood sugar dropping. I would come up with excuses for us not to drive out of town. I pretty much felt like I needed to be with him 24/7, which everyone knows is impossible. When he went on business trips and I couldn't be with him, I would give someone that would be with him instructions such as, "Timm has to eat on time". I would explain to them the signs of low blood sugar and what to do if it happened. I did all of this without Timm knowing because he was embarrassed. He didn't like being different. He would get mad at me if I had to call the EMT's for assistance because he didn't want to admit he needed help. My worry was of what all of this was doing to his health. How long can your body go through the up and down blood sugar levels? Oh, I could go on and on with the woes of diabetes. However, because of the islet cell transplant Timm can be like everyone else. He can eat what he wants, when he wants. As I am typing this, he is mowing the lawn without the worry of his blood sugar dropping. Next week he is going away with our son-in-law to an antique scooter meet and I don't have to tag along for low blood sugar reasons. June 7th he walked our youngest daughter down the isle and we didn't have to worry about blood sugar levels. HE ATE WEDDING CAKE!!! I really can't find the words to explain how much his islet cell transplant has meant to all of us. I hope and pray that more families can experience the life changing benefits of the islet cell transplantation. THANK YOU from the bottom of our hearts.

Pat