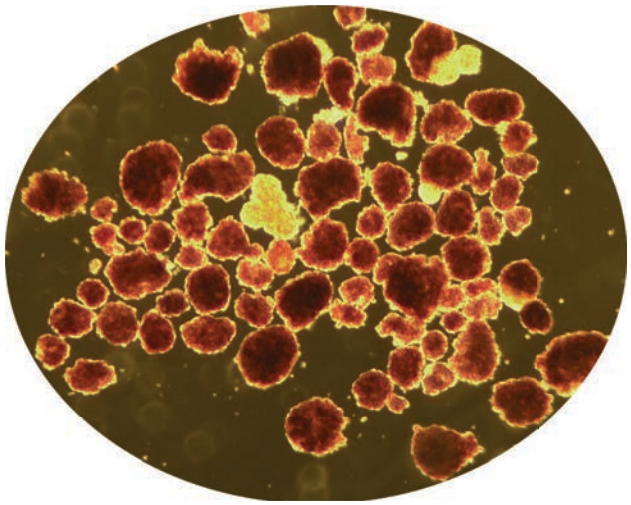
Centre universitaire de santé McGill

McGill University Health Centre

HUMAN ISLET TRANSPLANT LABORATORY

Suite 4100, McGill University and Genome Quebec Innovation Centre, 740 Ave. Dr. Penfield, Montreal, QC, H3A 0G1
Tel: 514-398-4400 ext. 00938, Fax: 514-398-6422

Human Islet Distribution Proposal



Created by Marco Gasparrini, Craig Hasilo, Alissa Rutman, Sarita Negi, Dr. Steven Paraskevas

Introduction

The McGill University Health Centre Human Islet Transplant Laboratory (MHITL) is a Government of Canada registered cell therapeutics program. Located in the Genome Québec Innovation Centre at McGill University in Montréal, Québec, this state-of-the-art, GMP designed facility, provides highly purified preparations of insulin-producing Islets of Langerhans from donated human pancreases under expressed clinical and research consent. This vital material is used in novel clinical applications for the treatment of type 1 diabetics, as well as for fundamental research projects studying all forms of diabetes.

In today's competitive scientific environment, there is an urgent need to obtaining human islets from cadaveric donors. This increase in demand is the result of grant review committees and scientific journals requesting data from human subjects. In addition, testing on human tissue, rather than just using animal models, increases efficacy and safety which in turn lowers long term costs. However, the availability, quality and affordability of human islets, remain limiting factors for many researchers. Since the MHITL can overcome these limiting factors, we are proposing to become a human islet supplier for your laboratory.

Approach

All of our islet isolations are performed in compliance with GMP, Health Canada and CSA strict regulatory requirements. The 2200 sq. ft. facility is fully self-sufficient, with its own environmental systems, instrument sterilization, and water purification. Research isolations are performed with the same methodology, supplies, reagents and animal-free media as clinical islet isolations designated for transplant. Briefly, human pancreases are retrieved from brain dead cadaveric multi-organ donors under the coordination of the local organ procurement organization (OPO). Donors are from local area hospitals located in the Montréal and Québec City regions in order to reduce the cold ischemia time. Serology testing is conducted on all organ donors and only those pancreases from donors suitable for clinical solid organ transplant are retrieved. Research consent is obtained prior to the initiation of pancreas retrieval under the direct supervision of the OPO. All steps are carried out aseptically in our cleanroom facility. After inspection and surface decontamination of the pancreas, the spleen, duodenum and extraneous tissues are removed. The pancreas is loaded intraductally with cold collagenase and neutral protease enzymes, cut into pieces and then transferred to a digestion chamber and warmed to 37°C in a closed loop circuit. Digestion is stopped using ice-cold solution containing 10% normal human AB serum once 50% free, intact islets are identified. The digest is collected, centrifuged, washed and then purified in a COBE 2991 Cell Processor on a continuous density gradient. Purified fractions are collected, washed and quantified prior to culture in separate 175cm^2 cell culture flasks with vented caps. The isolation procedure is referred to as being "minimally manipulated", as the process does not alter the biological characteristics of the islets. After an overnight culture of 12 hours, the islets are assessed for purity, viability, sterility and function. Once islets meet our strict release criteria, they are distributed for research, stored in our biorepository or transplanted.

The laboratory's success in isolating high-quality islets from clinical grade donors is summarized in the table below which represents isolation data from the last four years:

Parameter	Mean ± SD
Age (years)	48.5 ± 10.9
Cold Ischemic Time (hours)	6.83 ± 2.65
Yield (IE)	341 960.8 ± 219 583.2
Viability (%)	95.1 ± 3.0
Purity (%)	76.8 ± 10.2
GSIS	3.8 ± 4.0
BMI	27.8 ± 4.2
Gender	85% are Male
OPO pancreas donor requests received per month	1.1
Number of publications from islets distributed	6
Number of isolations	20
Number of islet recipient laboratories under contract (North America, Europe and Asia)	24

The MHITL has a great standing reputation with our OPO, from which we receive research donor pancreas availability requests at least once a month. Therefore, the availability of organ donors is not an issue. Unfortunately, we cannot isolate all the research pancreases that we receive. Instead, we generate pancreas biopsies for our biobank. The MHITL biorepository currently has over 3 000 samples of islets and whole pancreas biopsies snap frozen for DNA, RNA and Protein studies. Formalin fixed or frozen blocks and sections from both islets and pancreatic tissues are also available from over 100 different donors, both normal and diabetic. These samples as well as corresponding donor information are available to researchers at any time.

Management and Qualifications

The MHITL has been isolating research islets since 2010 and in 2015 began transplanting type 1 diabetic patients. It is composed of a skilled technical team with a long history of isolating islets for both clinical and research purposes:

Steven Paraskevas, MD, PhD

Dr. Steven Paraskevas is Associate Professor of Surgery and Director of the Pancreas and Islet Transplant Program at McGill University Health Centre. He received a BSc in Biology at Harvard in 1988, and completed medical school and surgical residency at McGill University. He received a PhD from McGill in 2003, on cell survival in isolated human islets. His interest in transplantation and the treatment of diabetes led him to a transplant surgery fellowship at the University of Minnesota, where he trained under pancreas and islet transplant pioneer Dr. David Sutherland and Dr. Bernhard Hering, director of one of the world's most successful islet transplant programs. He has been a staff surgeon at the Royal Victoria Hospital since 2002 and is director of the Human Islet Transplant Laboratory at the MUHC. Dr. Paraskevas is past President of the Canadian Society of Transplantation and an expert advisor to Canadian Blood Services on the Canadian organ donation and transplantation system. His ongoing research work includes beta-cell survival and the signals released by ischemic tissues which provoke an immune response.

Marco Gasparrini, MSc

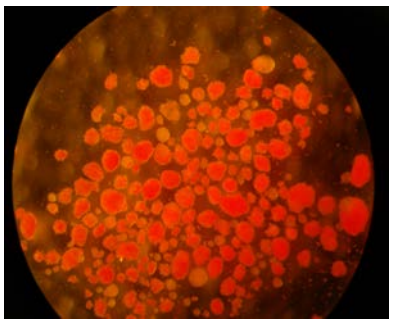
Mr. Marco Gasparrini is an Islet Specialist and Project Manager of the MUHC Human Islet Transplant Laboratory. Originally from Montréal, QC, Mr. Gasparrini obtained his BSc in Physiology at McGill University in 2008. His research focus on discovering novel therapeutic approaches to the development of beta-cells lead him to obtain a Master of Science degree in Experimental Medicine at McGill University in 2010. He has worked at the MHITL since 2011 and has been responsible for SOP development, lab certification and islet isolations. In addition, Mr. Gasparrini is responsible for islet evaluation and maintenance of the MHITL's own biorepository, which is funded partly by the Canadian National Transplant Research Program. He is now overseeing the clinical and islet distribution programs.

Craig Hasilo, MSc

Mr. Craig Hasilo is the Technical Consultant of the McGill University Health Centre Human Islet Transplant Laboratory. Originally from Brantford, ON, Mr. Hasilo obtained a BSc in Biology at the University of Western Ontario in 2001 and obtained his MSc in the departments of Physiology and Zoology at UWO. After graduation, he was hired as the Clinical Research Manager and Research Associate to initiate the Islet Transplant Program at the London Health Sciences Centre, London, ON, in 2005. Based on this work, Mr. Hasilo was trained by many experts in the field of Islet Isolation and Transplantation, including Dr. Jonathan Lakey and Dr. James Shapiro in Edmonton, Dr. Bernhard Hering in Minnesota, Dr. Shinichi Matsumoto from Baylor in Dallas, TX, and Dr. Steven Paraskevas from McGill.

Cost Recovery

The cost recovery per Islet Equivalent (IE) has been established at $0.13 Canadian. The $0.13/IE price, includes all expenses incurred during the retrieval, processing, culture and release of islets for distribution. It does not include shipment costs. Unlike our competitors, there are no subscription fees or mandatory purchases that need to be made. There is also the possibility to purchase an entire islet isolation preparation for $18 000 Canadian. At which point, we would be able to distribute to your lab all the islets isolated from a single donor pancreas with a minimum quantity of islets of 150 000IE provided. Researchers wanting to reserve defined quantities of serial isolations in advance may do so. In addition, we allow cost splitting/sharing of islet preparations among multiple researchers. Purchases of entire isolation worth of islets can be negotiated depending on yield and frequency needed.



Upon the establishment of a Material Transfer Agreement (MTA), the MHITL will generate a private laboratory members space on our website (http://www.isletlab.org/). Once islets become available, automatic email notifications will be send to researchers displaying detailed donor information. Researchers can then decline the islet offer or accept it by requesting the number of islets needed. All of which is competed online. Once requests are received and the islets pass release testing, they are packaged in a media-filled, air permeable, cell culture bag. The islets are then shipped in a temperature regulated Styrofoam box using FedEx Express. The islet shipment is usually received the following business day. Since we are flexible with shipping, islet preparations can be shipped to individual labs or to one institutional lab for further distribution to other colleagues.

Contact Information

Our facility is committed to providing researchers all over the world with clinical grade human islets. If you would like to join our islet distribution network, don't hesitate to contact us.

Marco Gasparrini, MSc.

Human Islet Transplant Laboratory Manager
McGill University Health Centre
Suite 4100 McGill University and Genome Quebec Innovation Centre
740 Avenue Docteur-Penfield
Montreal, QC, H3A 0G1
Tel: 514-398-4400 ext. 00938
Fax: 514-398-6422
Email: research@isletlab.org
Website: isletlab.org