ALBERTA TRANSPLANT INSTITUTE

Research Day

2022

June 20-21

Register Here

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Table of Contents

Message from the Director: Year in Review

Welcome to ATI Research Day 2022!

Dr. Lori West, OC, MD, DPhil, FRSC, FCAHS, FRCPC

This past year has been a year of revitalization, community engagement, and increasing momentum for the ATI. The relaunch of key activities and an ongoing governance reboot has been a driving force for strengthened community connections and advances for the Institute. Beginning in 2021 with a single part-time Operations Manager (Patricia Gongal), we have added a full-time Research and Education Program Manager (Saeideh Davoodi) and a part-time Administrative Assistant (Diana Tertzakian). While a still very lean team, these complementary roles have allowed significant progress in the development of activities for ATI members, strategic planning, and establishing a path to sustainability.

Over the last two years, the ATI has been in the process of setting its forward-looking strategy. A key focus in 2021-2022 was synthesizing all the information necessary to be able to make strategic choices. We developed a comprehensive map of the key stakeholders and players in the ATI ecosystem and identified their needs, challenges in addressing those, and opportunities they see for greater collaboration. The good news is that ATI is recognized as an agent of positive change in the Alberta donation and transplantation research ecosystem. However, to realize its full potential, one important next step is to refine and communicate the value of being an ATI member. You can expect to hear more about this at the June 20 Town Hall and in the coming year. In addition, significant discussions have taken place regarding improved collaboration between ATI and the clinical programs, which has been a longstanding challenge. We've also made progress in updating Institute governance, including a new Research Committee, which has helped plan this fantastic Research Day.

Communication with our membership is a critical area of focus, and in 2021-2022, we refreshed existing channels and created a few new ones:

· Our weekly newsletter, The Transplant Times;
· Our website (www.ualberta.ca/alberta-transplant-institute);
· Our Twitter account (@AB_OTDT); and
· Our Youtube channel, which hosts recordings of all ATI seminars.

Education activities

The relaunched virtual ATI seminar series has hosted 35 sessions, with local, national and international speakers in medicine, nursing, philosophy, law, social sciences, humanities; from sectors including academia, health care, and not-for-profit; 8 speakers with lived experience (patients, family, or donors); and several trainees. The series received accreditation from the Royal College in April and the ATI Youtube channel has grown quickly in popularity! Our community has already logged 1400 views and 252 hours of watch time. We are particularly proud of connecting the seminar series to timely issues for the donation and transplantation community, including urgent issues around COVID for transplant patients and recent legislative changes for donation in Alberta.

Advocacy activities

A key focus of our community partners and patient, family, and donor groups this year was around legislative reforms to the Alberta donation system. ATI worked to connect research, evidence, and international best practices to community advocates, members of the civil service, and Members of the Legislative Assembly to inform the development of Bill 205, which was passed in May 2022. ATI's work took the form of direct meetings with advocacy groups, AHS leadership, MLA RJ Sigurdson (Bill 205's sponsor), and making connections between advocates and policymakers to national experts, identified by ATI leveraging the national Canadian Donation and Transplantation Research Program (CDTRP) network. Knowledge translation work from the International Legislation and Policy Forum (hosted by Transplant Quebec, co-hosted by CDTRP) directly informed the legislative debate, in the form of Fast Facts documents on the topics of Mandatory Referral and Data and Public Reporting. Multiple MLAs drew directly from these documents in their speeches during debate on the bill. Notably, individuals from government and the opposition attended seminars, and during Third Reading of Bill 205, MLA Sigurdson specifically cited the value of the ATI Seminar Series for the development of the bill.

Support for Research

The CDTRP provides a highly developed structure for research development support, which many ATI members leveraged this year. The very design of the CDTRP is intended to promote and support collaborative research across the country and around the world, and it is a place where large team research projects are continuously arising. All ATI members are eligible to join the CDTRP and 37 Alberta researchers are active members. This year, we welcomed 4 new Alberta-based patient, family or donor partners to the CDTRP Patient, Family, and Donor Partnership Platform, which provides training, support, and funding.

A notable leveraging success was support committed to two research proposals led by Dr. Puneeta Tandon (Dept of Medicine) for economic, legal, ethics and social analysis, access to a Data Safety Monitoring Board, support for patient, family and donor partnerships and trainees, and knowledge translation support. Dr. Tandon was awarded a $1.2M CIHR Project grant and $600K from Alberta Innovates on virtual pre-habilitation and health monitoring technologies. Congratulations Dr. Tandon!

There have been Alberta researchers awarded seed grants through the CDTRP's Research Innovation Grant program every year since 2015, and this year was no exception. Dr. Michael Khoury (Dept of Pediatrics) was awarded $30,000 for his project "The MedBIKE™: Evaluating a Novel Telemedicine and Video Game-Linked Exercise Platform for Pediatric Heart Transplant Recipients". Congratulations Dr. Khoury!

Looking forward to 2022-2023, we are very excited to build on these successes as we continue strategic planning and find the right areas of focus for the Institute. Enhancing the connectivity of the donation and transplantation ecosystem and leading the community into the future requires broad collaboration. We are thrilled to continue building connections within and between our communities at Research Day 2022, and have no doubt that the excellence that will be showcased provides a strong foundation for our collective future success.

Program at a glance

June 20, 2022

1:00–1:15 Welcome
Dr. Lori West, ATI Director
Dr. Brenda Hemmelgarn, Dean, Faculty of Medicine and Dentistry

1:15–2:15 Keynote: Dr. Beth Foster
Age-dependent sex and gender differences in organ transplant outcomes
Moderator: Dr. Sarah Forgie

2:15–2:30 Break

2:30–3:30 ATI Town Hall

3:30–4:30 Concurrent professional development session (graduate)
Breakout Room 1: *Careers Beyond Academia*

3:30–4:30 Concurrent professional development session (clinical)
Breakout Room 2: *COVID-19 in SOT: Beyond Vaccination*

June 21, 2022

8:30–9:30 Concurrent Abstract Presentations - Session I

9:30–9:45 Break

9:45–10:45 Concurrent Abstract Presentations - Session II

10:45-11:00 Break

11:00-12:00 Patient and Family Panel: Mental health in transplant patients

12:00-12:30 Closing remarks and award announcements

June 20, 1:15-2:15 pm (Hybrid)
Keynote Speaker: Dr. Beth Foster

Beth Foster, MD

Chair, Department of Pediatrics
McGill University

Age-dependent sex and gender differences in organ transplant outcomes

Dr. Bethany Foster is a Professor of Pediatrics and a clinical epidemiologist with a primary research interest in the long-term outcomes of children and young adults with kidney transplants at McGill University. Dr. Foster has played an important leadership role in promoting child health research, clinical practice and education, locally, nationally and internationally. Her work on medication adherence in young transplant patients has led to a major multi-site North American trial, as well as to a Canadian national observational study involving transplant investigators from over two dozen pediatric and adult transplant programs. She has recently determined that girls and young women have higher risks of graft failure than boys and young men, a discovery which has transformed our understanding of the impact of developmental changes on graft outcomes. Dr. Foster has a phenomenal publication record (over 100 publications) with recent papers published in Transplantation, Pediatric Transplantation, and the American Journal of Transplantation.

Supported by the Walter Mackenzie Visiting Speaker Fund

UNIVERSITY OF ALBERTA
FACULTY OF MEDICINE & DENTISTRY

June 20, 2:30-3:30 pm (Hybrid)
ATI Town Hall

JOIN US IN A CONVERSATION ABOUT HOW THE ATI CAN BEST LEAD THE DONATION & TRANSPLANTATION ECOSYSTEM IN 2022 AND BEYOND

Vision

The ATI is a hub to lead the Alberta donation and transplantation ecosystem to excellence in research, education, and advocacy

Mission

- Improve outcomes for patients, families and donors (living and deceased) by supporting ATI members in achieving internationally-recognized excellence in donation and transplantation research
- Train and promote the next generation of donation and transplantation specialists
- Support patient, family, and donor-led advocacy in donation and transplantation

Success is

- Increased collective research output and impact of ATI members
- Educational opportunities being available to all learners in the ATI community to support their professional achievements
- ATI being an essential resource and partner for patients, families, and donors

The ultimate impact of all of the above successes will be improved long-term health and wellness for transplant recipients and a strengthened donation system in Alberta.

June 20, 2:30-3:30 pm (Hybrid)
ATI Town Hall

ATI ACTION PLAN: 2022-2023

PRIORITY 1 IN RESEARCH

Increasing the capture of funding for donation and transplantation research by aligning ecosystem needs with funding opportunities

How we get there:

- An effective mechanism to identify and prioritize top research needs across the ecosystem
- Facilitation of connections amongst researchers to align research questions with system needs

ACTIONS for 2022-2023

- Community engagement drive: articulate and promote the benefits of ATI membership, map researchers' expertise, and highlight the expertise and excellence of the clinical teams
- Establish an effective mechanism to prioritize top research needs and connect research expertise across the community, delivering a publication entitled “Alberta’s Research Priorities in Donation and Transplantation” that will represent the ATI’s programmatic and fundraising priorities for the next 5-10 years
- Develop and initiate a strategy to resource the research priorities identified

PRIORITY 1 IN EDUCATION

Accelerate the inclusion of research innovations within clinical practice by acting as a hub for professional development within the clinical community

How we get there:

- Knowledge and an understanding of current research that is most applicable to clinical care
- The ability to effectively deliver educational activities through relevant channels

ACTIONS for 2022-2023

- Engage the newly Royal College-approved Area of Focused Competency program in Solid Organ Transplantation as a key mechanism for clinical education, delivering a plan for how the ATI and the AFC program interact
- Deliver the weekly accredited ATI seminar series that connects to clinical professional development needs by expanding the clinical representation on the planning committee

PRIORITY 1 IN ADVOCACY

Influence donation and transplantation policy decisions by acting as a resource for research for patient, family, and donor-led advocacy

ACTIONS for 2022-2023

- Strengthen relationships with patient-facing associations and foundations, and connect research and researchers to inform advocacy work driven by patients, families and donors

June 20, 3:30-4:30 pm (Zoom Room 1)
Concurrent Professional Development Session

Careers Beyond Academia

In this discussion, we will be learning from invited panelists about their career paths. Undergraduate, graduate and post-doctoral trainees from all departments at the University of Alberta are welcome to attend!

Andrews Tawiah, PhD
Career Advisor (Graduate Students & Post Doctoral Fellows), University of Alberta

Angela Zhang, PhD
Senior Product Manager
Precision NanoSystems

Moderator:
Mykhaylo Bodnar, CCDP
Career Advisor
University of Alberta

Sanil Sansar, PhD
Medical Science Liaison
US Transplantation, Sanofi

Brittany Umer, PhD
Associate Science and Strategy Consultant, Sixsense Strategy Group

June 20, 3:30-4:30 pm (Zoom Room 2)
Concurrent Professional Development Session

COVID-19 in SOT: Beyond Vaccination

Dima Kabbani, MD, MSc
Assistant Professor
Education Lead, Transplant Infectious Diseases
University of Alberta

Learning Objectives:

- Illustrate the changing epidemiology of COVID-19 in SOT
- Discuss prophylaxis and early therapy (antivirals and monoclonal antibodies)
- Describe the use of SARS-CoV-2 positive donors in organ transplant

****Accreditation pending**

June 21, 11:00 am-12:00 pm (Zoom)
Patient and Family Panel: Mental health in transplant patients

In this panel discussion, transplant recipients and families will be speaking about their transplant journeys, share their thoughts on mental health issues faced by patients and families and discuss unmet research needs related to improving mental health in transplantation.

Moderator:

Flavia Robles
Executive Director, Kidney Foundation
Northern Alberta & The Territories Branch

Panelists:

Lindsey Kemp
Mother of George (two-time heart recipient)

Manuel Escoto
Kidney recipient

Chantel Esak-Stumpf
Double lung recipient

Abstracts Session I: June 21, 8:30 to 9:30 am
Room 1, Chair: Dr. Simon Urschel

8:30-8:45 am

"Anti-Neu5Gc Antibodies as a Potential AT1R ELISA Assay Interference: Sugar Sprinkled Interference?"

Anne M. Halpin, Kelley M. Hitchman, Bruce Motkya, Simon Urschel, Lori J. West

8:45–9:00 am

"A role for ABO antibodies in the association between ABO blood group and COVID-19 susceptibility"

Bushra Anjum, Anne Halpin, Jean Pearcey, Tess Ellis, John S. Klassen, Bruce Motyka, Lori J. West

9:00–9:15 am

"The role of sex and the microbiome in production of 'natural' antibodies: impact on ABO antibodies in a mouse model"

Bushra Anjum, Ibrahim Adam, Jean Pearcey, Kesheng Tao, Bruce Motyka, Lori J. West

9:15 – 9:30 am

"Preliminary results of the first clinical trial to prevent graft rejection in heart transplant children employing a cellular therapy with autologous Treg obtained from thymic tissue (thyTreg)"

Esther Bernaldo-de-Quirós, Manuela Camino, Juan Miguel Gil-Jaurena, Nuria Gil, Rocío López-Esteban, Marta Martínez-Bonet, Diana Hernández-Flórez, Mª Eugenia Fernández-Santos, Laura Butrageño, Megan K Levings, Esme I Dijke, Lori J West, Marjorie Pion, Rafael Correa-Rocha

Abstracts Session I: June 21, 8:30 to 9:30 am
Room 2, Chair: Dr. Gregory Korbutt

8:30-8:45 am

"Leveraging continuous 3D suspension culture systems over 2D planar platforms for scale up and efficiency of human pluripotent stem cells"

Ila Jasra, Nerea Cuesta Gomez, Kevin Verhoeff, Sandhya Sapkota, Rena Pawlick, Nidheesh Dadheech, James Shapiro

8:45–9:00 am

"Normothermic Machine Perfusion in Liver Transplantation – Seven Year Experience at a Single North American Centre"

Joshua Hefler, Dayne Leon-Izuierdo, Mariusz Bral, Glenda Meeberg, Blaire Anderson, Khaled Dajani, Norman Kneteman, David L. Bigam, A.M. James Shapiro

9:00–9:15 am

"Optimization of the differentiation protocol for the generation of autologous pluripotent stem cell-derived islet-like clusters for the treatment of diabetes"

Nerea Cuesta-Gomez, Ila Jasra, Kevin Verhoeff, Rena Pawlick, Braulio Marfil-Garza, Haide Razavy, Nidheesh Dadheech, AM James Shapiro

9:15–9:30 am

"POLY(N-vinylpyrrolidone) and tannic acid (PVPON/TA) conformal coating preserves human and mouse islets in vitro and in vivo functional potency"

Kateryna Polishevska, Sandra Kelly, Purushothaman Kuppan, Karen Seeberger, Saloni Aggarwal, Joy Paramor, Gregory S. Korbutt, Andrew R. Pepper

Abstracts Session II: June 21, 9:45 to 10:45 am, Room 1, Chair: Dr. Esme Dijke

9:45-10:00 am

"Natural vs induced ABO antibodies in a murine model: Role of sex and T cells"

Ibrahim Adam, Bruce Motyka, Kesheng Tao, Lori West

10:00–10:15 am

"Neonatal Tolerance Induction: Behaviours of Adult Allogeneic Spleen and Bone Marrow Inocula in Neonatal Mice Are Largely Determined By the Nature of their CD8 T Cells"

Roger Bascom, KeSheng Tao, Lori West

10:15–10:30 am

"HLA Sensitization within One-Year of VAD Implantation: Prospective Study in Adults and Pediatrics"

Madeleine Townsend, Tara Pidborochynski, Patricia Campbell, Anne Halpin, Simon Urschel, Daniel Kim, Susan Nahirniak, Lori West, Holger Buchholz, Jennifer Conway

10:30–10:45 am

"Neurodevelopmental and clinical outcomes of infants and children with end-stage liver disease awaiting liver transplantation"

Andrea Razcon Echeagaray, Amber Hager, Thomas Snyder, Vera Mazurak, Susan Gilmour, Diana Mager

Abstracts Session II: June 21, 9:45 to 10:45 am
Room 2, Chair: Dr. Soroush Shojai

9:45-10:00 am

"Pre-transplant medications and primary graft dysfunction risk in lung transplant recipients"

Amanda Stanton, Rhea Varughese, Alim Hirji, Justin Weinkauf, Dale Lien, David Li, Jayan Nagendran, Kieran Halloran

10:00–10:15 am

"Lung transplantation from donors with prior substance use"

David Li, Alim Hirji, Justin Weinkauf, Rhea Varughese, Dale Lien, Jayan Nagendran, Kieran Halloran

10:15–10:30 am

"Long-term outcomes for living kidney donors with early guideline-concordant follow-up care"

Anisha Dhalla, Anita Lloyd, Krista Lentine, Amit Garg, Robert Quinn, Pietro Ravani, Scott Klarenbach, Brenda Hemmelgarn, Uchenna Ibelo, Ngan Lam

10:30–10:45 am

"Risk Factors for Developing Low eGFR and Albuminuria in Living Kidney Donors"

Anisha Dhalla, Huda Al-Wahsh, Ngan Lam

Abstracts

Anti-Neu5Gc Antibodies as a Potential AT1R ELISA Assay Interference: Sugar Sprinkled Interference?

Anne M. Halpin [1,2,3,4,5] , Kelley M. Hitchman [6], Bruce Motkya [1,4,5] , Simon Urschel [1,4,5] , Lori J. West[1,3,4,5]

1.Pediatrics, University of Alberta, Edmonton, AB, Canada.
2.Histocompatibility Laboratory, Alberta Precision Laboratories, Edmonton, AB, Canada.
3.Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB, Canada.
4.Alberta Transplant Institute (ATI)
5.Canadian Donation and Transplantation Research Program (CDTRP)
6.Pathology and Laboratory Medicine, University of Texas Health San Antonio, San Antonio, TX, United States.

Aim
A commercial angiotensin II type 1 receptor (AT1R) ELISA is used for AT1R antibody (AT1R-Ab) assessment; AT1R antigens are from AT1R-overexpressing Chinese hamster ovary (CHO) cells. Neu5Gc antibodies (Neu5Gc-Ab) have been proposed as a potential assay interference. CHO cells are decorated with Neu5Gc sialic acid. Humans cannot produce endogenous Neu5Gc glycans thus have anti-Neu5Gc-Ab. This could result in false positive results for AT1R-Ab, especially in absence of "no antigen" controls. Adsorb Out™ (AdsOut) decreases non-specific reactivity in HLA assays and has been reported to reduce AT1R-Ab detection. Our aim was to investigate whether true AT1R-Ab were removed by AdsOut and if this product has Neu5Gc glycans.
Method
AT1R ELISA was performed as recommended. Assay provided positive control, 20, and 40 U/mL calibrators were treated with Adsorb Out™. Neu5Gc on AdsOut beads was measured by flow cytometry with chicken anti-Neu5Gc-Ab and FITC-labelled anti-chicken antibody. Negative control human albumin-coated latex beads were included.
Results
The AdsOut treatment did not remove AT1R-Ab reactivity from positive control or calibrators. Although Neu5Gc glycans were not detected on the human albumin coated beads, they were detected on AdsOut.
Conclusion
It is essential that assays demonstrate specificity. This AT1R-Ab assay lacks a 'no antigen' control making it difficult to rule out non-specificity. The AdsOut product is described as antigen-free microparticles treated with 'blocking solution'. Most blocking solutions contain bovine serum antigen, which is reported to have Neu5Gc. Thus the finding that Neu5Gc is detected on AdsOut but not human albumin beads is unsurprising and identifies anti-Neu5Gc-Ab as a possible source of false positive AT1R-Ab. Use of AdsOut mitigates interference of anti-Neu5Gc-Ab and could be used to improve assay specificity.

Abstracts

A role for ABO antibodies in the association between ABO blood group and COVID-19 susceptibility

Bushra Anjum [1], Anne Halpin [1,2,3,4], Jean Pearcey [1,2,3], Tess Ellis [1,2,3], John S. Klassen [5], Bruce Motyka [1,2,3], Lori J. West [1,2,3,4,6,7]

1. Department of Pediatrics
2. Canadian Donation and Transplantation Research Program
3. Alberta Transplant Institute
4. Department of Laboratory Medicine & Pathology
5. Department of Chemistry
6. Department of Surgery
7. Department of Medical Microbiology & Immunology

Background: Blood group A (ABO-A) individuals have been shown to be more susceptible, and ABO-O individuals less susceptible, to COVID-19. Antibodies to blood group A glycans are produced naturally in ABO-O but not in ABO-A individuals. Here we explored the hypothesis that anti-A antibodies may bind A/A-like glycotopes on the heavily glycosylated SARS-CoV-2 spike protein (SP), resulting in viral neutralization.

Methods: A 'direct' and an 'indirect/inhibition' binding assay was used to examine ABO- and SP-antibody binding to soluble recombinant SP (produced in Sf9 cells). COVID-19 convalescent (CCP) and pre-pandemic plasma from ABO-O individuals was tested. IgG antibodies to ABO glycans and SARS-CoV-2 targets, and SP binding to ACE2 beads, were assessed using a multiplex bead-based assay developed in our laboratory.

Results: In a direct binding assay, incubation of pre-pandemic plasma with soluble SP resulted in a 27% decrease in SP binding to ACE2-beads. In an inhibition binding assay, as a positive control, incubation of CCP with soluble SP resulted in a dose-dependent decrease (up to 90%) in detection of IgG anti-SP antibodies. Incubation of ABO-O CCP or pre-pandemic plasma resulted in a dose-dependent decrease (up to 20-25%) in IgG anti-A and anti-B.

Conclusion: Our preliminary observations of decreased binding of SP to ACE2 by ABO-O pre-pandemic plasma and decreased detection of IgG anti-A/B antibodies following incubation of ABO-O CCP/pre-pandemic plasma with soluble SP is suggestive of ABO antibody binding to SP. Studies are ongoing to investigate binding of ABO antibodies to SP produced in ABO-O vs ABO-A cells.

Abstracts

The role of sex and the microbiome in production of 'natural' antibodies: impact on ABO antibodies in a mouse model

Bushra Anjum[1], Ibrahim Adam[1,2,3,4], Jean Pearcey[1,2,3], Kesheng Tao [1,2,3], Bruce Motyka [1,2,3], Lori J. West [1,2,3,4,5,6]

1.Department of Pediatrics
2.Alberta Transplant Institute
3.Canadian Donation and Transplantation Research Program
4.Department of Medical Microbiology & Immunology
5.Department of Surgery
6.Department of Laboratory Medicine & Pathology

Background: ABO histo-blood group incompatibility is a barrier in solid organ transplantation due to 'natural' preformed ABO antibodies. Here we assessed the hypothesis that natural ABO antibodies may develop due to cross-reactive gut microbiome components by examining serum ABO antibody levels in germ-free and conventionally-housed male and female mice of different ages.
Methods: Germ-free and conventionally-housed mice included the inbred strains C57BL/6 (females/males, n=10 /10) and BALB/c (females/males, n=10/10), and the outbred strain Swiss Webster (females/males, n=4/6). Plasma at different ages was assessed by ABH glycan microarray for ABO antibody isotype (IgM/IgG) and ABH subtype specificity (subtypes I-VI).
Results: Anti-A and anti-B antibodies were present in all germ-free mice at levels similar to conventionally-housed mice. At 4-weeks of age, IgG (but not IgM) anti-A antibodies were detected in both sexes at levels similar to that of 12-week females. At >8-weeks, IgM anti-A antibodies were present at higher levels in females vs males. In females, anti-A antibodies were mostly IgG at 4-weeks, predominately IgM at 8-weeks, and shifted to mostly IgG by 12-weeks. By 8-weeks anti-B antibodies, mostly IgM and at lower levels compared to anti-A antibodies, were detectable in both sexes. Most anti-A antibodies, in germ-free or conventionally-housed mice, were specific to subtypes III/IV while specificity to subtype II antigens were low/absent.
Conclusion: Detection of natural anti-A antibodies in germ-free mice combined with higher levels of natural anti-A antibodies in females vs males suggests a unique sex-dependent, alternative mechanism of natural ABO antibody production than cross-reactivity with gut microbiome antigens.

Abstracts

Preliminary results of the first clinical trial to prevent graft rejection in heart transplant children employing a cellular therapy with autologous Treg obtained from thymic tissue (thyTreg)

Esther Bernaldo-de-Quirós [1], Manuela Camino [2], Juan Miguel Gil-Jaurena [3], Nuria Gil [2], Rocío López-Esteban[1], Marta Martínez-Bonet[1], Diana Hernández-Flórez[1], Mª Eugenia Fernández-Santos[4], Laura Butrageño [5], Megan K Levings[6], Esme I Dijke[7], Lori J West[7], Marjorie Pion [1], Rafael Correa-Rocha[1]

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2.Pediatric Cardiology Unit, Hospital Gregorio Marañón, Madrid, Spain
3.Pediatric Cardiac Surgery Unit, Hospital Gregorio Marañón, Madrid, Spain
4.GMP Cell Production Unit, Instituto de Investigación Sanitaria Gregorio Marañón (IISGM), Madrid, Spain
5.Pediatric Intensive Care Unit, Hospital Gregorio Marañón, Madrid, Spain
6.Childhood Diseases Research Theme, BC Children's Hospital, Vancouver, BC, Canada
7.Alberta Transplant Institute, University of Alberta, Edmonton, AB, Canada.

Due to their suppressive capacity, regulatory T cell (Treg) therapy is a very promising alternative to prevent rejection and achieve indefinite graft survival. Clinical trials conducted in adults with peripheral blood Treg demonstrate the safety of the therapy, although its efficacy seems to be limited. To overcome these limitations, we have developed a novel GMP-compatible protocol to obtain Treg from thymuses routinely discarded during pediatric cardiac surgeries (thyTreg). After receiving the approval by the Spanish Drug Agency (AEMPS), we have started the first worldwide phase I/IIa clinical trial (NCT04924491) that evaluates the autologous use of thyTreg in preventing rejection in children undergoing heart transplantation. A single dose of fresh thyTreg is administered to the patient intravenously at day +8±2 post-transplant and the remaining thyTreg are cryopreserved. To date, 4 patients have received a thyTreg dose. The four thyTreg products infused showed very high viability (>94%) and purity (CD25+FOXP3+) ≥85% in all cases. The procedure's safety is confirmed, and the preliminary results obtained in the children treated suggest that with a single thyTreg infusion it is possible to maintain the reserve of Treg cells, even in these patients who have undergone thymectomy and treated with immunosuppressive therapy. So far, we have yet recruited six more patients in the trial who are still on the heart transplant waiting list, completing the 10 patients planned for this clinical trial.ThyTreg cell constitutes a new therapeutic strategy to induce graft tolerance that could establish a new paradigm in the context of solid organ transplantation.

Abstracts

Leveraging continuous 3D suspension culture systems over 2D planar platforms for scale up and efficiency of human pluripotent stem cells

Ila Jasra [1], Nerea Cuesta Gomez [1], Kevin Verhoeff [1], Sandhya Sapkota [1], Rena Pawlick [1], Nidheesh Dadheech[1], James Shapiro[1]

1.Department of Surgery, Faculty of Medicine and Dentistry, University of Alberta.

Background: Recent technologies for human induced pluripotent stem cells (iPSC) scaling show advantage over 2D planar systems. Transition of human iPSC from 2D planar to 3D continues suspension cultures may leverage scale-up and long-term efficiency.
Methods: We used vertical-wheel (VW)-based bioreactor system to comparison to planar methods for morphological and physiological parameters using established iPSC line. Cells were assessed for growth kinetics, viability, genetic/genomic integrity (RT-PCR), pluripotency makers (FACS), and mitochondrial function (OCR/DNA).
Results: We found 3D suspension systems more advantageous over 2D matrix-dependent cultures. iPSC using 0.1L VW-based bioreactor show optimal growth rate and high-throughput scale-up production of stem cells. Nearly 100-fold expansion per week was recorded with bioreactors compared to 18-fold expansion with 2D plates. Cells cultured in bioreactors preserved epiblastic morphology, promoted cell proliferation while maintaining maximum viability (~90%) and minimal sheer-stress injury with minimum 200ml batch-feed media requirement per week. Real-time PCR confirmed uncompromised genetic stability and genomic integrity in long-term (>20) passaged iPSC. 3D organization enhanced pluripotency markers (70% Oct4+, 80% Nanog+, 90% Sox2+, and membrane markers >90% Tra1-60 and Tra1-81) compared to 2D cultured cells (<30% Oct4, Nanog, Sox2; and 60% Tra1-60, Tra 1-81). OCR measurements of 30nmol/min/mgDNA in 3D culture were recorded.
Conclusion: 200 million in 0.1L and over 1 billion cells in 0.5L bioreactors can be obtained per week using minimal media consumption. 3D expansion promotes higher yield, improved viability, stable genomic integrity, and enhanced cellular metabolism. Bioreactor-based scale-up of iPSC is ideal to mass manufacturing cells for cell therapy application.

Abstracts

Normothermic Machine Perfusion in Liver Transplantation – Seven Year Experience at a Single North American Centre

Joshua Hefler [1], Dayne Leon-Izuierdo[2], Mariusz Bral[1,3], Glenda Meeberg [3], Blaire Anderson[1,3], Khaled Dajani [1,3], Norman Kneteman[1,3], David L. Bigam[1,3], A.M. James Shapiro [1,2,3]

1.Division of General Surgery, Department of Surgery, Faculty of Medicine & Dentistry, University of Alberta, Edmonton, Canada
2.Clinical Islet Transplant Program, University of Alberta, Edmonton, Canada
3.Division of Transplantation Surgery, Department of Surgery, Faculty of Medicine & Dentistry, University of Alberta, Edmonton, Canada

Machine perfusion for preservation of liver grafts before transplantation has risen in prominence over the past decade. Normothermic machine perfusion (NMP), in particular, has been bolstered by a multicentre, randomized control trial published in 2018 by Nasralla et al., which showed decreased graft injury, despite a greater than 50% increase in graft utilization. The liver transplant program at the University of Alberta Hospital in Edmonton, Canada was one of the first North American centres to adopt this technology. Herein, we describe the 7-year outcomes from our centre, part of an open-label, non-randomized clinical trial. Between January 1, 2015 and December 31, 2021, 79 livers were transplanted after undergoing NMP on the OrganOx metra® device. These grafts had an average NMP time of 528±24 minutes and an average static cold storage (SCS) time of 350±12 minutes, which was significantly longer than the cold storage time of 383 livers transplanted after only SCS (300±8 minutes) during the same period (p=0.005). Despite significantly prolonged overall preservation time (p<0.0001), we found no difference in the majority of early outcomes, including early allograft dysfunction and 1 year patient survival (p=0.718 and 0.458, respectively), and even significantly improved 30-day graft survival (p=0.042). Our extensive, early experience with NMP technology confirms the major finding of the larger clinical trial by Nasralla et al. that NMP is a safe means of preserving liver allografts for extended periods of time. Confirming safety and efficacy of this technology in the North American setting is an essential step in the development of protocols to assess and optimize liver grafts, with the ultimate goal of improving organ utilization and clinical outcomes for liver transplant recipients.

Abstracts

Optimization of the differentiation protocol for the generation of autologous pluripotent stem cell-derived islet-like clusters for the treatment of diabetes

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Generation of autologous pluripotent stem cell (PSC)-derived islets capable to reverse diabetes have the potential for PSC-islet transplantation for a cell-based cure for all forms of diabetes. However, the major limitation of this approach is the presence of undifferentiated proliferating cells that produce cysts or teratomas. Hence, development of methods to selectively eliminate contaminating proliferating cells would enable to translate this approach into the clinic.

We tested both chemical and physical approaches in an established 7-stage (S1-7) islet differentiation protocol to eliminate residual off-target cells. Flow cytometry was used to compare the cell composition during the differentiation protocol upon addition of replication fork inhibitor Aphidicolin, oleic acid synthesis inhibitor PluriSln1(chemical) in parallel to dissociation and re-aggregation of the clusters (physical).

Aphidicolin at the terminal stage of differentiation resulted in absolute removal of undifferentiated cells and promoted endocrine cell maturation with 55% Pdx1+GP2+ and 84% ChrgA+ Nkx6.1+ cells, compared to conventional differentiation with <20% Pdx1+ChrgA+ Nkx6.1+. Addition of PluriSln, however, showed a reduction in PSCs but also affected pancreatic progenitor cell population. On the other hand, physical disaggregation and reaggregation modestly eliminated residual contaminating off-target cells but compromised cell yield. Since aphidicolin generated islet-like clusters with mature endocrine cells without affecting the yield, we studied the insulin secretion and observed improved dynamic glucose stimulated insulin release and higher exocytosis than with other methods.

Implementation of chemical and physical approaches into current differentiation protocols to remove off-target cells may deliver a method to manufacture safe and mature autologous PSC-islets for cell therapy.

Abstracts

Poly(n-vinylpyrrolidone) and Tannic Acid (pvpon/ta) conformal coating preserves human and mouse islets in vitro and in vivo functional potency

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Background:
Pancreatic islet transplantation represents a proven therapeutic strategy to restore physiologic glycemic control for patients with T1DM who suffer from life-threatening severe hypoglycemia unawareness. However, limiting factors prevent islet transplantation from replacing insulin therapy, including donor shortage and lifelong immunosuppression. Islet encapsulation has the potential to reduce the immune reaction. We hypothesize that conformal islet coating with poly(N-vinylpyrrolidone) (PVPON) and tannic acid (TA) PVPON/TA will increase the engraftment efficacy of human islet xenografts as well as murine islet allografts.
Methods:
Human and murine islets were coated with PVPON and TA to form 3.5 deposit bilayers. Confirmation that PVPON/TA does not hinder islet function was examined by the in vitro function of coated and non-coated human islets and confirmed in vivo function by transplanting these human islets (1500IEQ) into diabetic immunodeficient Rag-/- mice. Subsequently, the immunoprotective properties of PVPON/TA coating were examined by transplanting coated and non-coated islets in our well-established murine islet allograft model.
Results: Both control and coated islets exhibited similar results in all in vitro assays performed. Human islet recipients transplanted with PVPON/TA coated islets reversed diabetes, proving this coating technique is non-toxic. Data from allograft recipients demonstrate that PVPON/TA coating reduces intragraft inflammation and delays allograft rejection.
Conclusions:
The present study demonstrates that PVPON/TA coated islets retain their in vitro and in in vivo functional potency. This transplant approach has the potential to decrease post-transplant inflammatory responses, high possibility of translation to clinical investigation, improve islet allograft survival, and eliminate the need for toxic systemic immunosuppression.

Abstracts

Natural vs induced ABO antibodies in a murine model: Role of sex and T cells

Ibrahim Adam[1], Bruce Motyka[1], Kesheng Tao[1], Lori West[1]

1.Alberta Transplant Institute and Canadian Donation and Transplantation Research Program

Introduction: Interaction of 'natural' ABO antibodies (nAbs) with their cognate AB(H)-antigens (Ags) poses a high risk of rapid rejection of ABO-incompatible (ABOi) organ transplants. We previously demonstrated that a clear understanding of factors influencing ABO nAbs is crucial for successful ABOi heart transplantation. Here we investigated anti-A nAbs vs. intentionally-induced Abs (iAbs) with regard to role of sex and T cell requirement.
Methods: Adult wild-type (WT) and CD4 T cell knock-out (CD4KO) mice (C57BL/6 (B6) background) received weekly i.p. injection x3 of human ABO-A blood cell membranes (Hu-A BCM; 100ul of 10% v/v) or left untreated. Serum anti-A Ab was measured by hemagglutination assay using ABO-A erythrocytes from our A-transgenic mouse line. To test for T cell help and/or suppression, sex-matched CD4+ T cells (8-12×106/mouse) or CD4+CD25+ T cells (1.7-2.8×106/mouse) from spleens of WT mice were transferred to CD4KO mice. After adoptive transfer, CD4+ T cell reconstitution in peripheral blood was confirmed and mice were left untreated or challenged with Hu-A BCM and assessed for anti-A Ab.
Results: In contrast to WT mice, untreated CD4KO females produced dramatically more anti-A than males, rising substantially with puberty, and this was significantly suppressed in both sexes by adoptive transfer of sex-matched CD4+ T cells. Unlike WT mice, attempted sensitization of CD4KO mice with Hu-A BCM failed to induce additional anti-A beyond the already high levels in either sex; CD4+ T cell adoptive transfer rendered CD4KO mice responsive to A-sensitization. CD4+CD25+ T cell transfer into CD4KO mice neither suppressed anti-A nAbs nor rendered them responsive to A-sensitization (Figure).
Conclusions: When ABO 'natural' antibodies are discriminated from intentionally induced Abs, several important findings emerge: 1) Anti-A nAbs are produced without CD4+ T cell help in a sex- and age-dependent manner, suggestive of a role for sex hormones in regulating anti-A nAbs. 2) CD4+ T cells, but not CD4+CD25+ regulatory T cells, down-regulate anti-A nAb production. 3) In contrast to anti-A nAbs, production of anti-A iAbs was CD4+ T cell-dependent without a sex bias.

Abstracts

Neonatal Tolerance Induction: Behaviours of Adult Allogeneic Spleen and Bone Marrow Inocula in Neonatal Mice Are Largely Determined By the Nature of their CD8 T Cells

Roger Bascom[1,2], KeSheng Tao[1,2], Lori West[1,2]

1.Alberta Transplant Institute
2.Department of Pediatrics, University of Alberta

Introduction: Interaction of 'natural' ABO antibodies (nAbs) with their cognate AB(H)-antigens (Ags) poses a high risk of rapid rejection of ABO-incompatible (ABOi) organ transplants. We previously demonstrated that a clear understanding of factors influencing ABO nAbs is crucial for successful ABOi heart transplantation. Here we investigated anti-A nAbs vs. intentionally-induced Abs (iAbs) with regard to role of sex and T cell requirement.
Methods: Adult wild-type (WT) and CD4 T cell knock-out (CD4KO) mice (C57BL/6 (B6) background) received weekly i.p. injection x3 of human ABO-A blood cell membranes (Hu-A BCM; 100ul of 10% v/v) or left untreated. Serum anti-A Ab was measured by hemagglutination assay using ABO-A erythrocytes from our A-transgenic mouse line. To test for T cell help and/or suppression, sex-matched CD4+ T cells (8-12×106/mouse) or CD4+CD25+ T cells (1.7-2.8×106/mouse) from spleens of WT mice were transferred to CD4KO mice. After adoptive transfer, CD4+ T cell reconstitution in peripheral blood was confirmed and mice were left untreated or challenged with Hu-A BCM and assessed for anti-A Ab.
Results: In contrast to WT mice, untreated CD4KO females produced dramatically more anti-A than males, rising substantially with puberty, and this was significantly suppressed in both sexes by adoptive transfer of sex-matched CD4+ T cells. Unlike WT mice, attempted sensitization of CD4KO mice with Hu-A BCM failed to induce additional anti-A beyond the already high levels in either sex; CD4+ T cell adoptive transfer rendered CD4KO mice responsive to A-sensitization. CD4+CD25+ T cell transfer into CD4KO mice neither suppressed anti-A nAbs nor rendered them responsive to A-sensitization (Figure).
Conclusions: When ABO 'natural' antibodies are discriminated from intentionally induced Abs, several important findings emerge: 1) Anti-A nAbs are produced without CD4+ T cell help in a sex- and age-dependent manner, suggestive of a role for sex hormones in regulating anti-A nAbs. 2) CD4+ T cells, but not CD4+CD25+ regulatory T cells, down-regulate anti-A nAb production. 3) In contrast to anti-A nAbs, production of anti-A iAbs was CD4+ T cell-dependent without a sex bias.

Abstracts

HLA Sensitization within One-Year of VAD Implantation: Prospective Study in Adults and Pediatrics

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Background: Ventricular assist devices (VAD) have improved survival to heart transplant (HTx). However, VADs have been associated with development of human leukocyte antigen antibodies (HLA-Ab) which may limit the donor pool and increase risk for worse outcomes post-HTx. Since HLA-Ab development after VAD insertion is poorly understood, the aim of this prospective study was to quantify the incidence of and risk factors for HLA-Ab development post-VAD insertion across the age spectrum.

Methods: Adult and pediatric patients who were undergoing durable VAD placement between 5/2016 and 7/2020 were enrolled. HLA-Ab were assessed pre-VAD and at approximately 1-, 3-, and 12-months post-implant. HLA-Ab were measured by Luminex screen and confirmed by Luminex single antigen beads. Regression models were used to evaluate factors associated with HLA-Ab development post-VAD.

Results: The study cohort included 41 adult and 17 pediatric patients. Following implant, 37% adults and 41% pediatric patients developed new HLA-Ab. Majority of patients (19/22) developed HLA-Ab within two months of implant. Of those that developed HLA-Ab, class I antibody development was most common (87% adult, 86% pediatric). Factors associated with HLA-Ab development included female sex and pre-VAD HLA-Ab.

Conclusion: More than one-third of adult and pediatric VAD patients developed new HLA-Ab early after implant with majority class I. HLA-Ab development was associated with female sex and pre-VAD HLA sensitization. Further studies evaluating persistence of HLA-Ab over time in VAD patients, risk factors specific for HLA-Ab development in adults vs pediatrics, and clinical impact of HLA-Ab on long-term outcomes are in progress.

Abstracts

Neurodevelopmental and clinical outcomes of infants and children with end-stage liver disease awaiting liver transplantation

Andrea Razcon Echeagaray [1] , Amber Hager [1], Thomas Snyder [3], Vera Mazurak [1], Susan Gilmour [2,3], Diana Mager [1,2]

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INTRODUCTION: Pediatric end-stage liver disease (ESLD) patients are at high risk for neurodevelopmental delay (NDD) due to malnutrition, hyperammonemia and other medical complications before and after liver transplantation (LTx). The study aimed to determine NDD prevalence and its associations with pre-and-post LTx outcomes.
METHODS: A retrospective chart review of infants and children who attended the Pediatric LTx Clinic at the Stollery Children's Hospital (2009-2019) was conducted. NDD was assessed at LTx assessment using the Vineland Adaptive Behaviour Scales (motor skills, socialization, communication, adaptive behavior composite ABC scores). Clinical outcomes (encephalopathy, Intensive Care Unit [ICU] and total hospital length of stay [LOS], ventilation dependence, mortality) were collected at LTx assessment, LTx, ICU and hospital discharge, 6- and 12-months post-LTx.
RESULTS: 48 patients (0.58 [0.4 -1] years at LTx assessment; 20M/28F) were included. 67% lacked age-appropriate gross motor skills. Most prevalent ABC score was adequate (64%) and moderately low (28%). A motor skill score ˂83 (median[IQR]: 83 [76 – 95]) was associated with higher incidence of pre-LTx encephalopathy (15.8% vs 0%, p=0.02), increased post-LTx ICU LOS (15 [8 – 47] vs 8 [4 – 21] days, p=0.04); longer ventilator dependency (8 [3 – 33] vs 3 [1 – 13] days, p=0.02), and higher mortality rate (26.3% vs 6.4%, p=0.04). Longer LTx waitlist time was associated with higher socialization, motor skill and ABC scores (p<0.05).
CONCLUSION: Pediatric ESLD patients have high rates of NDD, particularly in motor skills. Worse scores are associated with adverse clinical outcomes in the perioperative period. NDD is an important consideration when developing intervention strategies pre- and post-LTx.

Abstracts

Pre-transplant medications and primary graft dysfunction risk in lung transplant recipients

Amanda Stanton[1], Rhea Varughese[1], Alim Hirji[1], Justin Weinkauf[1], Dale Lien[1], David Li[1], Jayan Nagendran[2], Kieran Halloran[1]

1. Department of Medicine, University of Alberta, Edmonton, Canada
2. Department of Surgery, University of Alberta, Edmonton, Canada

Introduction: Primary graft dysfunction (PGD) is a serious complication of lung transplantation marked by acute lung injury and reperfusion edema in the immediate post-transplant period, but the effect of pretransplant medication use on PGD risk is not known. We hypothesized that some pretransplant medications could be associated with PGD risk, particularly those with anti-inflammatory activity (macrolide antibiotics, statins) and vasoactives (anti-hypertensives, pulmonary vasodilators).

Methods: We reviewed a previously published cohort of adult patients who underwent lung transplant in our program between 2004 and 2016. The primary outcome was the development of grade 3 PGD (PGD3) at 48- or 72-hours post-transplant. We assessed use of medication classes from listing records, with a sample of these verified against transplant admission records. We evaluated the relationship between pretransplant medication class and PGD3 using Fisher's exact testing and multivariable logistic regression, adjusting for known PGD risk factors including recipient pulmonary diagnosis, body mass index, mean pulmonary arterial pressure, donor age and donor smoking status.

Results: 19% of 330 patients who underwent lung transplant during the study timeframe developed PGD3. Phosphodiesterase inhibitor (PDE5i), endothelin receptor antagonist, proton pump inhibitor, and beta-blocker (BB) use showed unadjusted associations with PGD3 risk. PDE5 and BB use remained associated after adjustment, with BB use significantly associated after further correction for left ventricular end diastolic pressure.

Conclusion: Our exploratory analysis showed no association between pretransplant use of medications with anti-inflammatory properties, including macrolides and statins, and PGD3 risk, but PDE5i and BB use increased PGD risk despite adjustment, suggesting vasoactive medications may play a role in PGD pathogenesis. These associations would benefit from further study.

Abstracts

Lung transplantation from donors with prior substance use

David Li[1], Alim Hirji[1], Justin Weinkauf[1], Rhea Varughese[1], Dale Lien[1], Jayan Nagendran[2], Kieran Halloran[1]

1. Department of Medicine, University of Alberta, Edmonton, Canada
2. Department of Surgery, University of Alberta, Edmonton, Canada

Substance use is common among lung transplant donors, but the implications have not been well studied aside from donor smoking. We sought to characterize donor substance use at our center and evaluate the associations with overall survival as well as post-transplant graft function.

We studied all double lung transplants at UAH between 2004-2016. We reviewed donor substance use histories for the following: heavy smoking, heavy drinking, cannabis smoking, ecstasy, benzodiazepines, cocaine, crack cocaine, methamphetamine, crystal methamphetamine, and opiates. We used proportional hazards modelling to evaluate the association between each drug and overall survival as well as chronic lung allograft dysfunction (CLAD) development. We used Fisher's Exact test to evaluate the association between drug use and grade 3 primary graft dysfunction (PGD3) in addition to baseline lung allograft dysfunction (BLAD).

Of 473 recipients studied, 186 (39%) received lungs from a donor with a history of drug use in at least one of the 9 categories defined. Donor heavy smoking (n=65) was associated with lower overall survival (HR1.47; 95%CI 1.03-2.10; p=0.032). Donor crack cocaine use (n=24) was also associated with impaired overall survival even after adjustment for donor heavy smoking (HR1.99; 95% CI: 1.13-3.50; p=0.017). No other history of donor substance use was associated with post-transplant survival, CLAD, PGD3, or BLAD.

History of substance use was common in our cohort of lung donors. Donor crack cocaine use in addition to donor heavy smoking were associated with impaired post-transplant survival while donor use of other substances does not appear to affect outcomes post-transplant.

Abstracts

Risk Factors for Developing Low eGFR and Albuminuria in Living Kidney Donors

Anisha Dhalla[1], Huda Al-Wahsh[1], Ngan Lam[1]

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Background: Chronic kidney disease is associated with significant morbidity and mortality in the general population, but little is known about the incidence and risk factors associated with developing kidney dysfunction in living donors following nephrectomy.
Methods: We conducted a retrospective, population-based control study using linked healthcare databases in Alberta, Canada to identify 590 donors who underwent nephrectomy between May 2001 and December 2017. The primary outcome was evidence of sustained kidney dysfunction following nephrectomy, defined as either 2 estimated glomerular filtration rate (eGFR) measurements <45 mL/min/1.73 m2 or 2 measurements of moderate or severe albuminuria that were at least 90 days apart. We used Cox proportional hazard regression analyses to examine the association between potential risk factors and the outcome of post-donation kidney dysfunction.
Results: Over a median follow-up period of 8.6 years (interquartile range [IQR]: 4.7-16.9 years), 47 donors (8.0%) developed sustained kidney dysfunction, with an incidence rate of 9.2 per 1,000 person-years (95% confidence interval: 6.6-11.8). The median time for development of kidney dysfunction beyond the first year after nephrectomy was 2.9 years (IQR: 1.4-8.0 years). Donors who developed kidney dysfunction after donation were more likely to be older, male, have lower pre-donation eGFR, have evidence of pre- or post-donation hypertension, and post-donation diabetes.
Conclusion: A small proportion of kidney donors will develop post-donation kidney dysfunction. Donors with risk factors associated with sustained kidney dysfunction may benefit from more diligent follow-up care.

Abstracts

Long-term outcomes for living kidney donors with early guideline-concordant follow-up care

Anisha Dhalla[1], Anita Lloyd [2], Krista Lentine [3], Amit Garg [4], Robert Quinn[1], Pietro Ravani [1], Scott Klarenbach [2], Brenda Hemmelgarn[2], Uchenna Ibelo [1], Ngan Lam [1]

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4.Western University Schulich School of Medicine, Division of Nephrology, London, ON, Canada

Background: Current guidelines recommend that living kidney donors receive lifelong annual follow-up care. In the United States, the reporting of complete clinical and laboratory data for kidney donors has been mandated for the first two years post-donation to improve adherence with follow-up; however, the long-term impact of early guideline-concordant care remains unclear.
Methods: We conducted a retrospective, population-based cohort study using linked healthcare databases in Alberta, Canada to compare long-term post-donation follow-up care and clinical outcomes of living kidney donors with and without early guideline-concordant care. The primary outcome was receipt of annual follow-up at 5 and 10 years after donation (adjusted odds ratio with lower and upper 95% confidence limits, aOR [LCL, UCL]).
Results: Of the 460 donors included in the study, 187 (41%) had clinical and laboratory evidence of guideline-concordant follow-up care throughout the first two years post-donation. The odds of receiving annual follow-up for donors without early guideline-concordant care were 76% lower at 5 years (aOR 0.24 [0.18, 0.32]) and 68% lower at 10 years (aOR 0.32 [0.23, 0.46]) compared to donors with early care. The odds of continuing follow-up remained stable over time for both groups. Early guideline-concordant follow-up care did not appear to substantially influence estimated glomerular filtration rate (eGFR) or hospitalization rates over the longer term.
Conclusion: Although policies directed towards improving early donor follow-up may encourage continued follow-up, additional strategies may be necessary to mitigate long-term donor risks.

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