ALBERTA TRANSPLANT INSTITUTE

Research Day

2024

May 15

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As we have immune-compromised individuals attending ATI RESEARCH DAY 2024, we are strongly encouraging masking at all times unless you are presenting. Thank you for wearing masks and protecting the very patients we are here to serve.

Message from the Director

Welcome to ATI Research Day 2024!

Lori West, MD, PhD
Professor
ATI director

Every year our annual ATI Research Day marks the milestones of the closing of another academic year, the culmination of many new accomplishments by ATI members, the celebration of our best and brightest new researchers, and also some fond farewells.

As I announced earlier this year, 2024 will be my tenth and final year as Director of the Alberta Transplant Institute; the University of Alberta Faculty of Medicine and Dentistry has been actively recruiting a new leader to take my place. It has been my absolute privilege to see the ATI through some very strong years as well as the challenges of pandemic closures and leaner years. I am very pleased with the state of the ATI upon my departure, with a strong staffing model to help lead us into the future and a fantastic new 10-year Research Priorities plan now published in the Canadian Health Policy Journal to be our 'North Star' for the next phase of your ATI.

The formation of an ATI Advocacy Committee (Chair: Dr. Rhea Varughese) was a welcome new addition to our activities in support of our partners across Alberta who are also allies in keeping both research and education regarding donation and transplantation out in the public eye. Collaborations on Green Shirt Day, promoting each other's events, and creating a table for discussion of emerging opportunities are all part of their monthly priorities. The agencies and contact information for all of our partners can be found on a new page of the ATI website at: Link. Additionally, the ATI has created a new ATI Events Calendar that will highlight not only own seminars/events, but also those of the CDTRP, relevant national/international conferences, AND all of the community outreach and fundraising events of our Alberta partners. We invite you to check them all out, and please submit any relevant and related activities to be added to transplant@ualberta.ca! Several of our partner organizations will also have information tables set up in the foyer at Research Day, so please take a moment to introduce yourselves and become informed about the breadth of amazing work going on in Alberta!

Message from the Director

Lori West, MD, PhD
Professor
ATI director

The ATI education committee has been relaunched (Chair: Dr. Emily Christie) with a mandate to facilitate, support, and promote educational activities for all levels of learners within the ATI to support their professional achievements. As research, education, and advocacy are intertwined and all are ultimately required for success, the ATI is now in a strong position to leverage its interdisciplinary expertise and collaborative networks to drive meaningful change in the field of organ and tissue donation and transplantation.

As you will see from the program and extensive list of abstracts within, the ATI Research Committee members have planned a very full and exciting ATI Research Day 2024, crossing both basic and clinical research, as well as showcasing the brightest new talents who will be showing off their work through oral and poster presentations. Please show your support for our next generation of research leaders and take in all that they have been working on!

Finally, we are honoured to welcome Dr. Marie-Josée Hébert to share her latest research findings as our 2024 ATI Keynote Speaker. Dr. Hébert is the founding Co-Director of the Canadian Donation and Transplantation Research Program and Vice-Rector of Research at the University of Montreal. An extraordinarily talented transplant clinician-scientist, she has played major roles in Canadian research leadership including her current service as the Chair of the Governing Council of the Canadian Institutes of Health Research.

We are excited to see you all! Enjoy the day and thank you for your ongoing support of the Alberta Transplant Institute.

Program at a glance

May 15, 2024

08:15–08:30 Registration

08:30–08:40 Welcome (Bernard Snell Hall and Zoom)
Opening remarks by Drs. Tom Stelfox and Jason Acker

08:40–09:40 Professional Development Session (Bernard Snell Hall and Zoom)
The art of writing a grant: pearls and pitfalls *with Dr. Jason Weatherald*
Essential Components of a Research Presentation: What You Need to Know with Dr. Gina Rayat

09:40-09:50 Break

09:50-10:50 Patient-focused Session (Bernard Snell Hall and Zoom)
Long COVID and Post-COVID Conditions in SOT *with Dr. Dima Kabbani and Donna's Experience: Coping with the Challenges of Long COVID with Ms. Donna Krilow-Lorenz*

10:50-11:00 Break

11:00-12:00 Oral Presentations (Bernard Snell Hall and Zoom)

12:00-13:00 Lunch

13:00-14:15 Royal College of Physicians and Surgeons of Canada Accredited Session
DCD, organ perfusion and ethics considerations with Drs. Dennis Djogovic, Markus Selzner and Michael van Manen

14:15-14:30 Break

14:30-15:30 Poster Presentations

15:30-15:50 Closing Remarks with Dr. Lori West

15:50-16:40 Keynote: Dr. Marie-Josée Hébert (Bernard Snell Hall and Zoom)
"Microvascular reserve in transplantation, the key to long-term allograft function?"

16:40-17:00 Awards for Best Talk/Poster (Bernard Snell Hall and Zoom)

8:40-9:40 am (Bernard Snell Hall & Zoom)
Professional Development Session for Graduate Students

The art of writing a grant: pearls and pitfalls

Jason Weatherald
Associate Professor
Pulmonologist
University of Alberta

Essential Components of a Research Presentation: What You Need to Know

Gina Rayat
Professor
University of Alberta

Moderator:
Margret Michaels
Masters student

9:50-10:50 am (Bernard Snell Hall & Zoom)
Patient-Focused Session

Long COVID and Post-COVID Conditions in SOT

Dima Kabbani
Assistant Professor
Infectious disease specialist
University of Alberta

Donna's Experience: Coping with the Challenges of Long COVID

Donna Krilow-Lorenz
Kidney transplant recipient

Moderator:
Kathy Tachynski
Kidney patient partner

11:00-12:00 pm (Bernard Snell Hall & Zoom)

Abstracts - Oral Presentation

Longer duration of donor ventilation is not associated with long-term lung function after lung transplantation

Samuel Fioretti [1] , David Li [1], Karina Kaur [1], Alisha Rullay [1], Justin Weinkauf [1], Dale C Lien[1]
Rhea Varughese [1], Laura van den Bosch[1] , Jason Weatherald[1] , Kieran Halloran[1], Alim Hirji [1]

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

Background:
Prolonged mechanical ventilation increases the risk of developing ventilator-induced lung injury, but the relationship between duration of donor mechanical ventilation (DDV) and post-lung transplant lung function is not known.

Methods:
We conducted a retrospective analysis of patients undergoing lung transplantation in our program between January 2007 and December 2020. The risk factor of interest was DDV in days prior to organ retrieval. The primary outcome was FEV1% predicted at 1-year post-transplant (1yrFEV1%). We used multiple linear regression to test the association between DDV and 1yrFEV1%, adjusting for known confounders. Secondary outcomes included lung function at 3 months, incidence of primary graft dysfunction, ICU and hospital length of stay, development of baseline and chronic lung allograft dysfunction, and 3-month and 1-year mortality.

Results:
714 patients were eligible for study, 588 of whom had available DDV data. Median DDV was 3 days (range 0-37 days). 336 donors (59%) had bronchial wash cultures positive for clinically relevant organisms. In the multivariate analysis, longer DDV was not associated with a lower 1yrFEV1% (p=0.725) or with other identified secondary outcomes. DDV was however associated with donor bronchial wash culture positivity for clinically relevant organisms (odds ratio [OR] 1.11 per day of ventilation, 95% CI 1.02 – 1.21, p=0.02).

Conclusions:
Duration of donor ventilation prior to procurement was not associated with FEV1 % predicted at 1-year post-transplant, but we noted an increased likelihood of donor bronchial wash culture positivity. This suggests donors with extended ventilation duration prior to offer can be safely considered for lung transplantation.

Abstracts - Oral Presentation

ABO-incompatible transplantation immune risk assessment: expanding horizons with better tools

Francis Leier [1], Anne Halpin[2,3,4,5], Caishun Li [4,5,6], Jean Pearcey[4,5,6] , Esme Djike [2,3,4,5], Simon Urschel[4,5,6], Bruce Motyka[4,5,6], Lori West [1,2,4,5,6]

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2. Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB, Canada
3. Alberta Precisions Laboratories, Calgary, AB, Canada
4. Canadian Donation and Transplantation Research Program, Edmonton, AB, Canada
5. Alberta Transplant Institute, Edmonton, AB, Canada
6. Department of Pediatrics, University of Alberta, Edmonton, AB, Canada

Background:
High waitlist mortality in pediatric heart transplantation (HTx) can be reduced via ABO-incompatible (ABOi) transplantation when ABO antibodies (ABO-Ab) are low. Hemagglutination assays (HA) are the clinical standard of ABO-Ab assessment despite known limitations.such as difficulty in distinguishing IgM from IgG ABO-Abs. Additionally, HA reagent red cells express ABO-A/B subtype glycans absent on cardiac endothelium.

Methods:
Non-transplant pediatric sera were studied (n= 139; ABO-O, n=63; ABO-A, n=50; ABO-B, n=15; ABO-AB, n=11). We used ABO LuminexTM single-antigen beads to measure A,B, and H antibodies to subtype glycans (I-VI) and measured IgG and IgM ABO-Abs. Sera were incubated with these beads coupled to individual subtype A/B glycans then incubated with a secondary fluorescent antibody; IgG and IgM levels specific to each subtype glycan were measured as mean fluorescence intensity (MFI).

Results:
Anti-ABO A-II and B-II antibody increased over time with early production of IgM followed by IgG isotype antibodies with increasing age. ABO-O individuals were found to have higher levels of anti-B-II IgG antibodies than ABO-A patients (p=0.004). Spearman test showed correlation between age and IgG and IgM antibody in ABO-O patients for anti-A-II and anti-B-II (p<0.001) but no significant correlation was found between age and anti-B-II in ABO-A individuals.

Conclusions:
Expansion of ABOi HTx beyond infancy increases access to lifesaving HTx. A precise, standardized ABO-histocompatibility immune risk assessment is needed to support ABOi HTx. The bead-based assay allows accurate characterization of IgM and IgG isotype ABO-Abs with specificity for A-II and B-II glycans, which are the sole endothelial cell targets.

Abstracts - Oral Presentation

Development of an in vitro renal cellular model for characterizing the transporter and metabolism interactions involving mycophenolate

Jinal Adhiya [1], Ala'a Al-Dajani [1], Tony Kiang [1]

1. Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta

Background:
Mycophenolic acid (MPA) is an immunosuppressant which is frequently used in kidney transplant patients to prevent organ rejection. MPA and its major metabolite (MPA-glucuronide, MPAG) undergo further intrinsic clearance and excretion by renal proximal tubule epithelial cells. This study aims to develop an in vitro renal cellular model for characterizing the pharmacokinetic interactions of MPA.

Methods:
Human renal conditionally immortalized proximal tubule epithelial cells overexpressing organic anion transporter 3 (ciPTEC-OAT3) were seeded in 24-well plates. To determine transporter-mediated interactions, cells were exposed to fluorescein (1-15 µM; OAT3 probe) with known OAT3 inhibitors (e.g., probenecid 90 µM or diclofenac 390 µM) or MPA (4 µg/mL, physiological concentration). Fluorescein uptake was measured by microplate reader (excitation 485nm/emission 535nm). The ability of ciPTEC-OAT3 cells to metabolize MPA was determined by exposing cells to MPA (0.4 or 4 µg/mL) up to 72 hours. MPAG formation was quantified by liquid chromatography-tandem mass spectrometry in our lab.

Results:
Fluorescein uptake into ciPTEC-OAT3 cells was concentration-dependent (3 µM over 10 min represented the initial velocity condition). Probenecid, diclofenac, and MPA reduced fluorescein (3 µM) uptake by 41.1±7.7% (p<0.0001), 42.8±1.2% (p<0.0001), and 31.2±5% (p<0.005) respectively. ciPTEC cells exposed to 0.4 µg/mL or 4 µg/mL of MPA generated MPAG in a linear fashion, producing 22.9±7.6 ng/mL and 123.2±8.8 ng/mL of MPAG (in cell supernatant) over 72 hours, respectively.

Conclusions:
We have developed an in vitro renal cellular model suitable for characterizing the pharmacokinetic interactions involving MPA with respect to transporter uptake and intrinsic clearance

Abstracts - Oral Presentation

Repurposing A Standard-of-care Heart Failure Therapy to Alleviate Vascular Injury of Chronic Allograft Vasculopathy in Transplanted Heart Allografts

Andrew G. Masoud [1,2], Jiaxin Lin [2,3], Kesheng Tao [2,4], Zamaneh Kassiri [5] , Lori West [2,4], Colin C. Anderson [2,3], Gavin Y. Oudit [1,6], Allan G. Murray [1,2]

1. Department of Medicine, University of Alberta, Edmonton, Alberta, Canada
2. Alberta Transplant Institute, Edmonton, Alberta, Canada
3. Department of Surgery, University of Alberta, Edmonton, Alberta, Canada
4. Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada
5. Department of Physiology, University of Alberta, Edmonton, Alberta, Canada
6. Mazankowski Alberta Heart Institute, Edmonton, Alberta, Canada

Background:
Heart failure correlates with a high mortality among North Americans. Heart transplantation is the definitive treatment for end-stage heart failure, but the survival of transplanted hearts is limited by Chronic Allograft Vasculopathy (CAV), the leading cause of death among recipients beyond the first year post-transplantation. Pathologically, CAV starts with immune-mediated vascular Endothelial-Cell (EC) injury by encountering infiltrating immune-inflammatory cells with subsequent EC inflammatory activation. Successively, arterial fibro-intimal thickening with progressive luminal obliteration and loss of myocardial microvascular density cause allograft ischemia and loss. Sacubitril, a neutral endopeptidase inhibitor, is standard-of-care therapy in heart failure. We tested Sacubitril's effects on heart transplantation.

Methods:
We exploited mouse minor-histocompatibility-(HY) antigen-mismatched, heterotopically-transplanted heart allografts to model CAV. Daily oral gavage of Sacubitril or vehicle was started at 2 weeks post-transplant when early CAV was established. At 6 weeks post-transplant, we examined coronary arterial neo-intima formation, microvascular density, leukocyte infiltration, cytokine production and vascular response to pro-inflammatory milieus.

Results:
Sacubitril treatment decreased arterial neo-intimal thickness (0.70 vs 0.22%) and preserved microvessel density (52 vs 156 vessels/ HPF; vehicle vs Sacubitril groups). Sacubitril reduced CD4+, CD8+ lymphocytes, and Mac-2+ mononuclear-cell infiltration and reduced aCasp3+ ECs (75%). However, Sacubitril did not consistently reduce arterial pro-inflammatory cytokine abundance. Paradoxically, arterial EC expression of CX3CL1 and VCAM-1 was markedly suppressed (91.77 and 94.48%). Further, Sacubitril reduced arterial Tgfb1 (76.37%) and Tgfb2 expression (73.37%). Similarly, Sacubitril reduced arterial EC FSP-1 expression in early and advanced diseased arteries (96.94 and 82.77%).

Conclusions:
Sacubitril protects heart allografts from vascular injury and subsequent maladaptive endothelial-mesenchymal trans-differentiation.

1:00-2:15 pm (Bernard Snell Hall & Zoom)
Continuing Medical Education Session

Dennis Djogovic, MD
Clinical Professor
University of Alberta

Markus Selzner, MD
Professor of Surgery
University of Toronto

Michael van Manen, MD, PhD
Associate Professor
University of Alberta

DCD, Organ Perfusion, and Ethical Considerations

Learning Objectives:

- **Demonstrate what unique circumstances an individual could become an organ donor via Donation after Cardiac Death (DCD) and how the process of DCD occurs**
- **Identify opportunities and limitations of organ perfusion and determine values of ex vivo assessment criteria**
- **Discuss ethical considerations related to DCD and organ perfusion**

This event is an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada and approved by the University of Calgary Office of Continuing Medical Education and Professional Development. You may claim a maximum of 1.25 hours (credits are automatically calculated).

Moderator:
Rex Townsend, MD
Associate Clinical *Professor*
University of Alberta

2:30-3:30 pm (Bernard Snell Hall Lower Foyer) Abstracts - Poster Presentation

Heart Rate and Oxygen Consumption in Patients Awaiting Liver Transplant During and Following a Six-Minute Walk Test

Thomas McMurtry [1], Stephan Foulkes [1], Christofer Cruz [2], Ana Limon-Miro [2], Carly Mak [2], Corey Tomczak [3], Puneeta Tandon [2], Mark Haykowsky [1], Rachel Skow [1]

1. Faculty of Nursing, University of Alberta, Edmonton, Alberta, Canada
2. Faculty of Medicine & Dentistry, University of Alberta, Edmonton, Alberta, Canada
3. College of Kinesiology, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

Background:
People with liver cirrhosis (LC) awaiting liver transplant have reduced physical function and evidence of poor skeletal muscle oxygen consumption (VO2) recovery kinetics following small muscle mass exercise. Whether this holds true during activities of daily living (e.g., walking) has yet to be determined. We hypothesized that people with LC will have prolonged heart rate (HR) and VO2 recovery kinetics following a six-minute walk test.

Methods:
Fourteen participants with LC (59±7 years, 3 female) and nine healthy adults (HA; 62±8 years, 2 female) were recruited. We measured HR (Polar HR monitor) and VO2 (VO2 Master portable analyzer) during 5 minutes of seated rest, 6-minutes of walking, and 5-minutes of seated recovery. Post-exercise HR and VO2 recovery kinetics were evaluated using monoexponential modelling (OriginLab, 2023b) by calculating the mean response time (MRT = time delay to exponential recovery + time to reach 63% of recovery) immediately following the walking test during seated recovery.

Results:
Resting HR and VO2 were not different between groups. VO2 was higher during exercise in the HA group (19.1±3.6 vs 13.2±3.3 ml/kg/min; p<0.001) owing to a greater total distance walked (622±70 vs 433±117 m; p<0.001). VO2 MRT was slower in LC compared to HA (61±15 vs 78±23 s; p=0.061), but HR MRT was not different (p=0.335).

Conclusions:
These preliminary data suggest that individuals with LC awaiting liver transplant have skeletal muscle metabolic alterations related to reduced VO2 recovery. Interventions to improve fitness and physical function such as pre-habilitation may improve recovery during or following liver transplant.

Abstracts - Poster Presentation

Gastrointestinal Viral Infection in Adult and Pediatric Solid Organ Transplant Recipient: A Retrospective, Single-center Study from 2015 to 2022

Waiva Ann Mancenido Galang - De Leon [1], Dima Kabbani [1], Catherine Burton [2], Pang Xiao-Li [3,4], Varalika Tyagi [1]

1. Division of Infectious Disease, Department of Internal Medicine University of Alberta
2. Department of Pediatrics, University of Alberta
3. Alberta Precision Laboratory
4. Department of Laboratory Medicine and Pathology, University of Alberta

Background:
Gastrointestinal (GI) viruses are common causes of diarrhea in solid organ transplant (SOT). Little is known of the difference in epidemiology and clinical presentation of GI viruses between adult (A) and pediatric (P) SOT.

Methods:
Single-center retrospective study of Pediatric (≤18 y.o) and Adult SOT with a positive gastrointestinal viral Panel (GVP) assay based on RT-qPCR from 2015-2022. The GVP assay detects 5 viruses: Norovirus (NoV), Rotavirus, Sapovirus (SaP), Astrovirus, and Adenovirus (Adv).

Results:
During the study period, 871 (P:8.2%) SOT had at least 1 GVP, and 192 (22%) tested positive for at least 1 virus. 177 SOT had 1 GI virus/GVP and 15 at least 2 viruses/GVP. Pediatrics were more likely to have positive GVP (P:48.6% vs A:16.5%), multiple viruses/GVP (P:18.1% vs A:1.7%), and multiple different viruses during follow-up period (P:26.3% vs A:2.5%). NoV was most common single virus in A (69.2%) and P (26.4%). Chronic diarrhea (>14 days) was common in SOT with SaP (A:76%, P:70%), NoV (A:65.1%, P:42.1%), and Adv (A:47.2%, P:50%). NoV was associated with acute renal failure in (A:80.7%, P:36.8%), weight loss (A:47%, P:31%), and hospitalization (A:41%, P:26.3%). Treatment for NoV included oral immunoglobulin (A:37.3%, P:0), Nitazoxanide (A:9.6%, P:5.3%), and modification of immunosuppression (A:36.2%, P:10.5%).

Conclusions:
Although NoV is the most common cause of GI viral infection in SOT, P-SOT had more diverse and mixed GI viral infections. Chronic diarrhea, weight loss, and modification in immunosuppression are common with NoV. Further studies are needed to assess outcomes of GI viruses in SOT.

Abstracts - Poster Presentation

Assessment of Immunosuppression Induction with Basiliximab compared to Antithymocyte-globulin in Adult Heart Transplant Patients

Theresa E. Eberhardt [1], Daniel H. Kim [2], Shannon Nethersole [3], Glen J. Pearson [2]

1. Pharmacy Services, Alberta Health Services
2. Division of Cardiology, Department of Medicine, University of Alberta
3. Transplant Services, University of Alberta Hospital, Alberta Health Services

Background:
Patients undergoing heart transplant are at risk of rejection which can have significant morbidity and mortality. Induction immunosuppression at the time of transplant reduces the early risk and has additional benefits. The induction agent of choice within our program was changed from rATG to basiliximab, so it was necessary to evaluate whether this had any impact on patient outcomes. Our primary objective was to describe rejection, infection, and other outcomes in adult heart transplant patients at the University of Alberta Hospital in Edmonton, Canada.

Methods:
This study was a non-randomized, retrospective cohort study.

Results:
Sixty-three patients were included with median ages 50 years vs 54 years. More female patients received rATG (20% vs 42.4%). The most common indication for transplant in both cohorts was ICM (63.3% vs 57.6%). Patients who received rATG had significantly higher PRA (0% vs 43%, p<0.001). Acute rejection episodes were similar at 3-months (16.7% vs 15.1%) and 6-months (30.0% vs 18.1%). Infections were more common with rATG (at 3-months, 43.3% vs 63.6%, and at 6-months 60.0% vs 66.7%). There were no fatalities in either group.

Conclusions:
Our study did not demonstrate differences in rejection with basiliximab compared to rATG. Mortality did not differ, but basiliximab-treated patients had fewer infections and infection-related hospitalizations than those treated with rATG. Larger studies with longer duration will more completely describe the differences in rejection and infectious outcomes.

Abstracts - Poster Presentation

NSAID Prescriptions in Living Kidney Donors

Mikayla Laube [1], Robert Quinn [1,2], Pietro Ravani[1,2], Alix Clarke [1], Krista Lentine [3], Rachel Jeong[1,4], Jason Bau [1], Ngan Lam [1,2]

1. Cumming School of Medicine, University of Calgary, Calgary, AB, Canada
2. Department of Community Health Sciences, University of Calgary, Calgary, AB, Canada
3. Center for Abdominal Transplantation, Saint Louis University, St. Louis, MO, USA
4. Department of Critical Care Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

Background:
Current guidelines recommend that living kidney donors should avoid non-steroidal anti-inflammatory drugs (NSAIDs) due to their potential nephrotoxic effects. It is unclear if physicians are adhering to this guideline recommendation.

Methods:
We conducted a population-based, retrospective cohort study of adult living kidney donors in Alberta, Canada, who donated between 2002 and 2019. We identified the proportion of living kidney donors who filled an NSAID prescription at least 1-year beyond date of donation. Of those donors who were prescribed an NSAID, we assessed how many underwent post-prescription laboratory testing for kidney function and potassium within 14 days.

Results:
Our study included 759 living kidney donors with a mean age of 44.5 (SD 11.6) and 65% were female. We found that 273 (36%) donors had at least one NSAID prescription over a median potential follow up of 7.2 years (IQR 3.5-11.5). The proportion of donors with at least one prescription in follow-up remained stable over time (~10% per year). Family physicians accounted for 66% of all NSAID prescriptions. Approximately 10% of donors had measurements of serum creatinine or potassium within 14 days of the first NSAID prescription.

Conclusions:
Over one-third of living kidney donors are prescribed NSAIDs despite current guideline recommendations. Few donors had evidence of post-prescription laboratory testing, but adverse outcomes were uncommon in those who were tested. Further research assessing outcomes following NSAID use is recommended to better inform guidelines for living kidney donors.

Abstracts - Poster Presentation

RIP kinase inhibition improves human marginal mass islet graft survival and function

Nerea Cuesta-Gomez[1,2] *, Saloni Agarwall[1,2]*, Karen Seeberg[1,2], Sandra Kelly[1,2], Jessica Worton[1,2], Joy Paramor[1,2] , Andrew R. Pepper[1,2]
* These authors contributed equally to this work.

1. Alberta Transplant Institute, Department of Surgery, University of Alberta, Edmonton, Canada.
2. Alberta Diabetes Institute, Department of Surgery, University of Alberta, Edmonton, Canada.

Background:
Islet transplantation (ITx) established that cellular therapies can improve glycemic control in a subset of patients with type 1 diabetes. However, cell death in the acute post-transplant period accounts for the loss of up to 80% of the islets, resulting in the requirement of multiple donors per recipient to achieve normoglycemia. Several studies have targeted apoptosis prevention after ITx; our study explores a novel approach by inhibiting necroptosis using Necrostatin-1 (Nec-1), a RIPK1 and RIPK3 inhibitor, to enhance human islet survival, engraftment, and function post-transplant.

Methods:
Human islets were treated for 24h with Nec-1; untreated islets were used as control. Viability, oxygen consumption rate, glucose-stimulated insulin secretion and transcriptomic analysis were used to assess the effect of Nec-1 treatment in vitro, while marginal mass ITx under the kidney capsule of diabetic mice was performed for in vivo functional assessment.

Results:
Nec-1 treatment significantly reduced the expression of RIPK1 ($p=0.0021$) and RIPK3 ($p=0.0042$) resulting in decreased cell death ($p=0.0017$) without affecting basal respiration nor insulin secretion. Nec-1 treatment drastically reduced cytokine ($p=0.0083$), NFκB ($p=0.0179$), TGFβ ($p=0.0015$) and TNF family ($p=0.0010$) signalling pathways at the transcriptional level compared to control. These results correlated with increased diabetes reversal ($p=0.0200$) and decreased reversal time ($p=0.0011$) in the Nec-1 treated group.

Conclusions:
The success of Nec-1 treatment in this study showcases that necroptosis inhibition therapy promotes early marginal mass engraftment post-ITx. In the clinical context, improvement of marginal mass islet function could enable single-donor islet infusion making ITx available to a wider population of individuals suffering from diabetes.

Abstracts - Poster Presentation

Exploring the relationship between hematocrit, oxygen consumption, and functional decline during normothermic ex-situ heart perfusion

Mitchell J. Wagner[1], Guilherme Mainardi [1], Parham Hassanzadeh [1], Sanaz Hatami [1,2], Xiuhua Wang [1], Jayan Nagendran [1], Darren H. Freed [1,3]

1. Department of Surgery, University of Alberta
2. Department of Medicine, University of Alberta
3. Alberta Transplant Institute

Background:
Ex-situ heart perfusion (ESHP) is a method to better preserve donor hearts during transport, however is limited by characteristic functional decline. While mechanisms are unclear, it is known that alongside decline in cardiac output, myocardial oxygen consumption (MVO2) decreases whilst hemolysis proceeds during ESHP; whether hampered oxygen delivery limits MVO2 and precipitates functional decline is yet to be investigated.

Methods:
The hearts of Yorkshire pigs were surgically procured and reconstituted on a custom ESHP apparatus, being perfused for 11 hours. Hearts were allocated to one of three perfusion groups varying in perfusion solution hematocrit: dilute whole blood (1:1 with Krebs-Heinseleit buffer with 8% albumin; DWB, n=4), whole blood (WB, n=6), or concentrated whole blood (CWB, n=4). Functional assessments and perfusate samples were taken once every two hours of perfusion.

Results:
Cardiac index and stroke work declined most from baseline in the CWB group by end perfusion compared to the control DWB group (each p<0.01). MVO2 was initially elevated in CWB group versus DWB group, however declined to a greater extent, with WB group retaining MVO2 into later perfusion versus DWB group (p<0.05 at T7 and T9). Serum potassium rose steadily in each group, with CWB group ending with the highest concentration (in mmol/L, 9.2 CWB vs. 7.6 WB vs. 6.2 DWB, p<0.05).

Conclusions:
Increased hematocrit during ESHP may bolster MVO2, however appears to concomitantly worsen hemolysis that may ultimately cancel out functional benefits.

Abstracts - Poster Presentation

Variability in lung transplant clinical practices in Canada: Preliminary results of a national survey

Margret Michaels[1], Karina Kaur[1], Jason Weatherald[1], Jayan Nagendran[2], Meghan Aversa[3], Roland Nador[4], Charles Poirier[5], Kieran Halloran[1]

1. Deparment of Medicine, University of Alberta, Edmonton, Canada
2. Department of Surgery, University of Alberta, Edmonton, Canada
3. Toronto lung transplant program, University of Toronto, Toronto, Canada
4. Department of Medicine, University of British Columbia, Vancouver, Canada
5. Department of Medicine, University of Montreal, Montreal, Canada

Background:
Long-term survival and meaningful quality of life after lung transplant are possible, but there is great heterogeneity in these outcomes. The management of lung transplant recipients is complex, and the degree to which heterogeneity in clinical practices contributes to outcomes is unknown. We sought to quantify both average practices and variability in practices among all Canadian lung transplant centers via a national survey of physicians and surgeons. Here we present the preliminary results restricted to the four surgical centers.

Methods:
A cross-sectional survey of all Canadian lung transplant centers, including surgical centers (performs transplants and provides care pre- and post-) and non- surgical surgical centers (transplant performed elsewhere, provides care pre- and post-). Survey conduct was administered digitally and circulated via email to a comprehensive list of identified surgeons and physicians. We analyzed data via chi square tests, t-tests, and Wilcoxon rank sum tests.

Results:
55 clinicians across Canada were identified as eligible, and 50 (91%) completed the survey. This analysis was restricted to the 38 respondents from surgical centers, including 22 physicians and 16 surgeons who most frequently: identified as cisgender male (68%); had been in practice for 20+ years; reported lung transplant as the majority of their work (42%); and practiced in an academic setting (100%). Table 1
depicts a selection of responses. Significant variation was noted in: the presence of an upper age limit; the value of the BMI upper limit; performing single lung transplants, deceased donor lobar transplants, heart-lung, combined lung-abdominal organ, and simultaneous CABG; and the presence of a donor age limit. The average rank order of
and variation in allocation priorities is depicted in figure 1.

Conclusions:
Substantial variation was observed in some basic aspects of lung transplant clinical practice. We plan to expand our analysis to include all survey elements for a comprehensive overview of Canadian clinical practice, responses from non-surgical sites, and within-center variation.

Abstracts - Poster Presentation

Priorities for future lung transplant research: a preliminary report from a James Lind alliance priority setting partnership

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Background:
Lung transplantation is an important therapy for end-stage lung disease, but further research and improvement are needed to improve outcomes. The research priorities of lung transplant candidates, recipients, caregivers, and clinicians for future research are unknown. The aim of the Lung Transplantation Priority Setting Partnership (PSP) is to bring patients, caregivers, and clinicians together to identify and prioritize evidence uncertainties that could be addressed by future research and to ensure that research and funding align with the goals of these important stakeholders.

Methods:
This study uses the James Lind Alliance methodology (https://www.jla.nihr.ac.uk/), a validated process for identifying research priorities, which involves five steps: 1) partner identification and awareness-raising, 2) identifying research questions and uncertainties with an initial survey, 3) refining questions and uncertainties, 4) interim prioritization, and 5) a final priority-setting workshop. The output is a top-10 list of uncertainties for future research.

Results:
There were 76 respondents, of whom 25 (33%) were patients, 9 (12%) were caregivers, and 42 (55%) were clinicians (physicians n = 16, nurses n = 15, and allied health n = 11). 36 respondents (47%) were female, and 40 (53%) were male. 172 unique questions were submitted and grouped into topics (169 in scope and 3 out-of-scope): 53 (31%) from patients, 11 (6%) from caregivers, and 105 (61%) from clinicians. Topics proposed included prognosis (n = 30), education (n = 26), recipient evaluation and selection (n = 26), immunosuppression (n=19), patient and caregiver support (n=18), acute rejection (n=10), chronic lung allograft dysfunction (n=10), transplant team and care delivery (n=9), complications (n=7), infections (n=6), donor selection and management (n=4), extra-corporeal life support (n=3), and bioengineering artificial grafts (n=1).

Conclusions:
Stakeholders in lung transplant research in Alberta, Canada, identified unique questions for future research. The next steps include broadening the survey across Canada, verifying uncertainties against the existing literature, interim prioritization, and a final virtual workshop to establish the top 10 research uncertainties.

Abstracts - Poster Presentation

Neonatal Tolerance to Heart Transplants Induced with Neonatal Allogeneic Liver Cells: Trafficking, Interactions and Fates of Donor Cell Types

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Background:
A tolerizing inoculum of allogeneic newborn liver cells (allo-NLC) injected into newborn mice prolongs survival of donor-type hearts transplanted as adults. We now study the trafficking and fates of injected allo-NLC in an attempt to optimize the tolerance induction process toward an eventual clinical protocol for infants.

Methods:
C3H/He (C3H; H-2k) mice were injected within 24 hr of birth with newborn GFP+ B6 (H-2b) NLC ~15x106 cells/mouse. Trafficking and fates of injected cells were monitored by whole body/organ imaging and high resolution microscopy.

Results:
GFP+ B6 NLC were attacked and cleared by day (d) 6 post-injection in neonatal C3H mice. Injection of an anti-CD8a monoclonal antibody (mAb; clone 53.67) protected allo-NLC from attack. At d6 post-injection, strong donor chimerism was detected in spleen, lymph node, bone, and liver of mAb-injected mice. In spleen, donor cells were sparsely present in the sub-capsular and red pulp regions and more densely located in the white pulp. Stem cells (c-kit+) were observed in red pulp regions but few were GFP+. Large GFP+ donor cells in the red pulp immunostained for CD41+ suggesting them to be megakaryocytes. In white pulp, donor lymphocytes were mainly B cells (B220+), with few if any T cells (CD3+). Portions of d6 host liver appeared discolored with white fibrotic-like areas (H&E staining) suggesting infarcts and a need to use heparin.

Conclusions:
Allo-NLC chimerism in the presence of anti-CD8a mAab suggests tolerance induction. Absence of donor regulatory CD4+ T cells suggests a further need for optimization.

Abstracts - Poster Presentation

Neutrophil-targeting anti-Ly6G antibody preserve pancreatic islet graft function in subcutaneous space

Kateryna Polishevska[1,2], Nerea Cuesta Gomez[1,2], Purushothaman Kuppan[1,2], Mandy Rosko[1,2], Joy Paramor[1,2], Jessica Worton[1,2], Chelsea Castro[1,2], Gregory Korbutt[1,2], Andrew Pepper[1,2]

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Background:
Pancreatic islet transplantation represents a proven strategy to restore physiologic glycemic control in T1D patients who suffer from impaired hypoglycemia awareness. However, limiting factors prevent islet transplantation from replacing insulin therapy, including donor shortage, lifelong immunosuppression, and procedural risks. The prevascularization of the subcutaneous (SC) space preconditions this transplant site into a sustainable microenvironment for islet survival. However, immune modulation is still required. Previous studies have identified that neutrophil recruitment mediates islet transplant rejection. Therefore, we hypothesize that using a neutrophil-targeting anti-Ly6G antibody (Ab) for prevascularized SC islet transplantation will increase engraftment efficacy by minimizing inflammation associated with early graft failure.

Methods:
To validate the efficacy of anti-Ly6G antibody therapy which increases engraftment and function within a prevascularized SC space, 500 BALB/c syngeneic islets were transplanted into diabetic mice. Ly6G (40 mg/mouse) was administrated i.p. at days -3 to +1 peritransplant. Islet transplant groups included: 1) renal subcapsular (internal control), 2) anti-Ly6G SC, and 3) IgG2a SC (isotope control). Blood was collected for flow cytometry analysis to confirm neutrophil depletion.

Results:
Interim data demonstrates that anti-Ly6G Ab treatment effectively facilitates early islet engraftment. Flow cytometry confirmed the impact of the anti-Ly6G Ab, revealing a notable reduction in the number of circulating neutrophils compared to baseline levels.

Conclusions:
The present study demonstrates that anti-Ly6G Ab therapy is a promising modality to augment in vivo islet functional potency within SC space. This transplantation approach holds the potential to decrease post-transplant inflammatory responses, thereby improve islet survival and expediting graft function.

Abstracts - Poster Presentation

Evaluating the impact of the Transplant Wellness Program

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Background:
Nearly 500 solid organ transplants (SOTs) were conducted in Alberta in 2022. There is a need to support SOT candidates and recipients throughout the transplant journey. The Transplant Wellness Program (TWP) is a 12-week exercise behaviour change intervention that aims to improve the health of kidney, liver, and lung transplant patients both pre- and post-transplant. The proposed series of studies aims to evaluate the effectiveness and implementation of the TWP for future program scale-up and sustainability.

Methods:
A series of four studies is proposed to evaluate the impact of the TWP. Study one will examine if self-efficacy to engage in exercise differs between those who receive the TWP pre- versus post-transplant. Study 2 will investigate behaviour change technique (BCT) delivery. BCTs are the strategies enacted within an intervention to support behaviour change. This study will use fidelity checks to examine how planned BCTs are, or are not, delivered within TWP exercise sessions. Study 3 will examine system-level implementation of the TWP. A mixed-methods study with healthcare practitioners will occur to understand what factors influence successful program implementation. Study 4 will be a preliminary program evaluation of the first 80 participants of the TWP using the RE-AIM evaluation framework that includes both individual and system level factors.

Implications:
This evaluation of the TWP will advance the practice of exercise and wellness interventions for transplant populations. Overall, these studies will facilitate understanding how exercise and wellness programs can be used to support enhanced quality of life pre- and post-transplant.

Abstracts - Poster Presentation

Quantifying Ice Crystal Control and Toxicity of Novel Ice Control Agent in Rat Lung Perfusion Model

Ivan J. Ma [1], Sayed Himmat [1], Nishaka William [2], Larissa Lautner [1], Sanaz Hatami [1], Guilherme Mainardi [1], Xiuhua Wang [1], Darren H. Freed [3], Jayan Nagendran [4], Jason P. Acker [2]

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Background:
The limited storage time of donor lungs in static cold preservation (6 hours) contributes to non-optimal organ allocation. Cryopreservation offers an opportunity for indefinite storage which can improve donor lung availability. Ice control agents (ICAs) are small molecules that prevent existing ice crystals from growing in cryo-frozen organs. We investigated the potential toxic effect of the ICA to lungs and their ability to control ice growth.

Methods:
Lungs from Sprague Dawley rats (350-500g) underwent pulmonary artery perfusion and ventilation for 4-hours. The treatment group (n=4) received ICA (15mM) dissolved in the perfusate. Blood gas and lung physiology parameters were monitored during perfusion. Post-perfusion, core biopsies (0.8mm) were snap frozen and freeze substitution techniques allowed ice visualization on H&E slides.

Results:
No significant difference in edema (wet/dry ratio) or pulmonary vascular resistance (PVR). Lung compliance improved during perfusion for both groups (control: p<0.002; ICA: p<0.02). All lungs showed stable oxygenation, partial pressure of oxygen / fraction of oxygen in room air (PO2/FiO2) for control and ICA was 552 ± 13 and 541 ± 20, respectively. Ice grain area was significantly larger around vessels than bronchioles in both groups (p<0.0001), with no difference between control and ICA groups.

Conclusions:
ICA exhibited no lung toxicity during normothermic perfusion, with lungs displaying normal physiology and function compared to controls. Lung structure showed inherent heterogeneity affecting ice grain distribution and size. Future attempts to analyze the ice grains in alveolar spaces may show the benefit of ICA in controlling ice growth during lung cryopreservation.

Abstracts - Poster Presentation

Testing different temperatures and Oxygen supplementation during Hypothermic ex-situ heart perfusion

Guilherme Mainardi [1], Mitchell J. Wagner [1], Parham Hassanzadeh [1], Sanaz Hatami [1,2], Xiuhua Wang [1], Benjamin A. Adam [4], Jayan Nagendran [1], Darren H. Freed [1,3]

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4. Department of Laboratory Medicine and Pathology, University of Alberta

Background:
Hypothermic oxygenated perfusion (HOP) of the donor heart is a safer and simpler alternative to normothermic ex-situ heart perfusion for transport. However, in hypothermic oxygenated perfusion an optimal temperature has not been defined, nor much investigation on the absence of oxygen supplementation and how they affect heart function preservation. Therefore, we compared different temperatures and oxygen supplementation on heart function preservation during 12h-HOP using Belzer machine perfusion solution.

Methods:
Hearts were procured from 39-55 Kg pigs (n=35) randomized into 3 preservation therapies: 6h-static cold storage (SCS, n=5); 12h-HOP (n=15) and 12h hypothermic non-oxygenated perfusion (HNOP-without oxygen supplementation, n=15). Moreover, normal function was measured in additional animal hearts (n=3) in our normothermic device. We tested three temperatures in the HOP and HNOP hearts (5°C/10°C/15°C). After the preservation, all the hearts were transferred to a normothermic perfusion device for function assessment.

Results:
HOP hearts had the highest cardiac index (CI) and left ventricular stroke work (LVSW) when compared to other preservation method groups. The 5°C and 10°C HOP hearts presented two-fold CI values (5HOP: 20.95±1.66 mL/min/g_tissue and 10HOP: 20.92±2.73 mL/min/g_tissue; median±SEM) compared to SCS hearts (10.16±1.61 mL/min/g_tissue). HNOP had lower heart function results compared to HOP and SCS.

Conclusions:
HOP for 12 hours had better heart function preservation than SCS for 6h. HNOP hearts had the lowest results among the preservation methods. HOP can safely enhance heart function preservation compared to SCS.

Abstracts - Poster Presentation

Characterizing the left ventricular transcriptome of donation after circulatory death (DCD) porcine hearts undergoing prolonged ex situ heart perfusion (ESHP) in the presence and absence of a multi-drug postconditioning treatment

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Background:
We have previously shown that a multi-drug postconditioning treatment of Intralipid, sevoflurane and remifentanil improved the function and viability of extended criteria donation after circulatory death (DCD) porcine hearts undergoing prolonged ex situ heart perfusion (ESHP). However, the changes in the cardiac tissue transcriptome as a result of the prolonged ESHP and multi-drug postconditioning treatment have not been investigated.

Methods:
Porcine DCD hearts were mounted on a custom ESHP apparatus and perfused with or without multi-drug postconditioning treatment for 6 hours (n=5 per group). The treatment consisted of 1% Intralipid, 2% (v/v) sevoflurane and 3 nM remifentanil. Hearts not subjected to the ESHP process served as an unperfused control (n=8). Left ventricular tissue was collected and processed for next generation messenger RNA (mRNA) sequencing. Data was analyzed using SEQUIN (https://sequin.ncats.io/app/) and Gene Set Enrichment Analysis software.

Results:
Of the 21,849 genes identified, 5,344 genes were differentially expressed between perfused and unperfused hearts. Acute inflammatory response (TNFα, IL-1, IL-17) as well as hypoxia and oxidative stress pathways (HIF-1α) were enriched in the perfused group. The multi-drug postconditioning treatment resulted in a small, but significantly regulated group of 48 genes, including those involved in maintaining lipid homeostasis (SREBF1, SCD), DNA repair as well as cytokine (IL-2, IL-6) signaling pathways.

Conclusions:
Prolonged ESHP activated stress-induced genes and produced an inflammatory mRNA signature in the DCD heart. Multi-drug postconditioning treatment differentially regulated genes controlling metabolism and cytokine signaling in the myocardium, likely contributing to its cardioprotective effects and improved organ function.

Abstracts - Poster Presentation

Diaphragm function via ultrasonography and mean inspiratory pressure testing in lung transplant recipients: A pilot study

Alisha Rullay[1], Kieran Halloran[1], Jason Weatherald[1]

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

Background:
Lung transplant is a lifesaving therapy for patients with end stage chronic lung disease, but lung function may fail to reach normal values in up to 40% of patients, which we termed baseline lung allograft dysfunction (BLAD). The causes are unclear, but one potential contributor is reduced function of the diaphragm, the large muscles that help pump our lungs. This study will explore the association between BLAD and diaphragm function.

Methods:
We began measuring diaphragm function in consenting lung transplant recipients transplanted in June 2023 via standard diaphragm ultrasonography and mean inspiratory pressure (MIP) testing at 3-months post-transplant. We measured diaphragm excursion during normal breathing, deep breath, and sniff maneuver, and diaphragm thickening fraction. We compared these values to 3-month BLAD status. We depicted the results graphically but not statistically due to low numbers of patients in this pilot study.

Results:
We included 10 patients in this pilot study, with a median age of 58, a median BMI of 27, and mainly transplanted for interstitial lung disease. 60% of the cohort met criteria for BLAD. BLAD status was associated with lower MIP and mean expiratory percent predicted values, but not with lower diaphragm excursion or thickening fraction values.

Conclusions:
BLAD status is preliminarily associated with lower MIP and MEP values but not clearly with reduced diaphragm movement or thickening fraction in small pilot cohort. We plan to expand the dataset with greater patient numbers to assess the utility of these tests in explaining BLAD at 3-months and 1-year post-transplant.

Abstracts - Poster Presentation

Harnessing the Utility of High-Resolution HLA Typing by Applying Molecular Mismatch for Post-Transplant Risk Assessment

Ze Chen (Eric) Wang[1], Ahmed Mostafa[1,2], Fang Wu[1,2]

1. University of Saskatchewan
2. Saskatchewan Health Authority

Background:
In the ever-changing landscape of transplantation and post-transplant management, there remains a demand for precise risk stratification and personalized treatment to minimize the side effects of immunosuppression. High-resolution HLA typing can be applied to analyze and evaluate patient and donor compatibility through epitope mismatch. Epitope mismatch is more descriptive than antigen mismatch and has the potential to improve graft survival by improving matching and transplant management.

Methods:
To assess the relationship between epitope mismatch and graft survival, we used data collected from 626 patients monitored after renal transplantation in Saskatchewan and examined for the development of de novo DSA. Then, we used the Brazilian Eplet registry database to calculate eplet mismatches in HLA Matchmaker. High-resolution HLA data was obtained directly or predicted based on low-resolution typing through the HaploStats database.

Results:
A wide range of eplet mismatch loads existed within the study population at each HLA locus. We found a significant correlation between eplet mismatch cut-offs and DSA formation as well as risk thresholds in HLA-A, B, C, and DQ (15, 11, 9, 9, p<0.05). Subsequent Kaplan-Meier survival analysis confirmed these findings and revealed a significant difference in DSA-free survival between risk-stratified groups (5%, 3%, 10% at 10 years, p<0.05).

Conclusions:
Epitope mismatch is a novel application of high-resolution sequencing with significant advantages over antigen mismatch. It can guide clinicians in determining risk and offer patients accurate prognoses. Integrating clinical data and further exploring the significance of specific epitopes can improve post-transplant management and patient care.

Abstracts - Poster Presentation

ABO-incompatible transplantation following enzymatic A-antigen removal in a mouse model: A-antigen re-expression and prevention of early antibody-mediated rejection

Tate Erickson [1], Bruce Motyka [1], Kesheng Tao [1], Jean Pearcey [1], Peter Rahfeld[2], Jayachandran N. Kizhakkedathu[3], Marcelo Cypel[4], Peter J. Cowan[5], Stephen G. Withers[6], Lori J. West [1]

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2. Avivo Biomedical Inc., Vancouver, BC
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5. St Vincent's Hospital Melbourne, Melbourne, Australia
6. Dept of Chemistry, University of British Columbia, Vancouver, BC

Background:
The ABO histo-blood group barrier challenges equitable organ allocation due to high risk of rapid antibody-mediated rejection (AMR) of ABO-incompatible transplants (ABOi Tx). Enzymatic reduction of ABO-A-antigen using Azymes (FpGalNAc deacetylase and FpGalactosaminidase) has successfully converted human ABO-A lungs to ABO-O. A-transgenic (A-Tg) mice constitutively express A-antigen on vascular endothelium. We used this to model ABOi Tx: we evaluated A-antigen re-expression kinetics and determined if early AMR is prevented by pre-transplant donor organ Azyme treatment.

Methods:
After i.v. administration of Azyme (or control), hearts from A-Tg C57BL/6 mice (male/female, n=4/4; 15-19 weeks of age) were heterotopically Tx'd into sex-matched wild-type C57BL/6 recipients and harvested 1, 4, or 7 days later. To model AMR, wild-type recipients were Tx'd with an A-Tg heart (+/- Azyme treatment) then administered mouse anti-A antibody and rabbit complement intravenously. Graft function was assessed by palpation 1d post-Tx; A- and H-antigen expression and C4d deposition were assessed by immunohistochemistry.

Results:
Azyme-treated A-Tg heart grafts had minimal A-antigen staining and were H-antigen positive 1d post-Tx, showed weak A-antigen staining 4d post-Tx, and resembled untreated grafts 7d post-Tx. In the AMR model, untreated grafts showed reduced graft function, C4d deposition, and lymphocyte infiltration, whereas Azyme-treated grafts did not.

Conclusions:
Cardiac graft A-antigen re-expression following Azyme treatment occurred within 7 days post-Tx. Preliminary findings showed that A-antigen removal by Azyme treatment prevented early AMR. Clinical application of Azymes may permit additional ABOi Tx, offering lifesaving treatment to patients for whom compatible organs may not be found.

Abstracts - Poster Presentation

eMPower – Online mind-body wellness programming for adults living with chronic physical conditions - A three-armed randomized controlled trial to improve mental health outcomes

Emily Johnson[1], Puneeta Tandon[1]

1. Division of Gastroenterology (Liver Unit), Department of Medicine, University of Alberta, Edmonton

Background:
Adults living with chronic physical conditions experience high rates of mental health symptoms, including anxiety and depression, and reduced quality of life. Mind-body wellness programming, including yoga, tai chi, meditation, and psychology practices, offer potential solutions to manage this symptom burden. In this randomized controlled trial, we will assess the impact of a 12-week online wellness program (eMPOwer) for individuals 18+ living with various chronic physical conditions on the primary outcome of anxiety and depression symptoms.

Methods:
Participants must be 18+, have access to an internet-connected device, and not experiencing any uncontrolled psychiatric symptoms. Participants are randomly assigned to waitlist control or one of two treatment arms: (1) online program or (2) online program + weekly brief check-ins with members of the study team. Weekly, participants navigate through (a) a tip from a clinician, (b) guided mind-body routines at five levels (chair exercise, standing yoga, standing/floor yoga, and tai chi), and (c) psychology tips based on Acceptance and Commitment Therapy via an online web platform called eMPower. Participants will also complete self-efficacy surveys at week 4, week 8, and week 12, in addition to secondary and exploratory outcomes including sleep, quality of life, and frailty.

Results:
Six hundred and thirteen participants have been randomized across 10 chronic physical condition grouping: Primary Biliary Cholangitis, Primary Sclerosing Cholangitis, Cirrhosis, Digestive Disease, Post-transplant, Post-cancer treatment, Chronic Kidney Disease, Heart Failure, Women who've experienced cardiac events, and a general group. Partnerships with the Patient Partner Organizations and social media campaigns continue to recruit participants.

Conclusions:
There is a high prevalence of mental health symptoms in adults living with chronic physical conditions. The eMPOwer program offers a potential management strategy to begin addressing this burden.

Abstracts - Poster Presentation

Defining optimal cryopreservation conditions of regulatory T cells for tolerogenic cell therapy in transplantation

Sarjana Alam [1], Rebecca Mercier [2], Lavinia Ionescu [3,4], Lori West [1,3,4,5], Jason P. Acker [1,2,4], Esme Dijke [1,4,5,6]

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5. Canadian Donation and Transplantation Research Program
6. Alberta Precision Laboratories, Edmonton, AB, Canada

Background:
Regulatory T cell (Treg) tolerogenic therapy is a promising innovation to inhibit transplant rejection. Defining optimal Treg cryopreservation conditions would enhance successful clinical implementation. To develop an optimized protocol, we assessed toxicity and cryoprotection of various cryoprotectant agents (CPA).

Methods:
Tregs were isolated from peripheral blood of healthy volunteers (n=3) and expanded in culture. Cells were suspended in: 1) base solution, 2) 10% dimethyl sulfoxide (DMSO) (standard protocol), 3) 5% DMSO, 4) 5% DMSO with ice recrystallization inhibitor (IRI), and 5) 5% DMSO with 5% dextran for 0-4 hours at 4 °C, 22 °C and 37 °C. Cells were also cryopreserved, thawed, and cultured. Recovery and viability were assessed by an automated cell counter, and phenotype by flow cytometry.

Results:
Cells (88-91%) were CD4+CD25+FOXP3+; this Treg phenotype was maintained throughout expansion and after cryopreservation. Cells exposed to 10% DMSO had a median recovery of 30% and 4% after 2 and 4 hours at 37 °C, respectively, which was substantially lower compared to all other conditions (median: > 75% at 2 h and > 69% at 4 h). No clear viability differences were observed between 5% DMSO alone, with IRI, or with dextran (n=3). Immediately post-thaw, cells cryopreserved in 5% DMSO with 5% Dextran showed highest recovery compared to other conditions (n=2). After 48 hours in culture, no clear differences were observed between conditions.

Conclusions:
Decreased DMSO concentration may be key to improving Treg recovery after cryopreservation. Identifying the optimal CPA for Tregs will improve cryopreservation of therapeutic Tregs.

Abstracts - Poster Presentation

Rebranding Transplantation: Eliminating the Organ Shortage Through a Combination of Artificial Intelligence, Xenotransplantation, Tissue Engineering/Regenerative Medicine, and Bio-artificial Organs

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Background:
With the success of the first pig kidney to living human transplant on March 16th, 2024, we can be more confident about the future and rebrand transplantation around eliminating the organ shortage. The earlier Chinese decedent study of a pig liver transplant on March 10th is also important because the FDA was concerned that successes would begin to occur outside the US, so this will stimulate US clinical trial approvals. Initially xenotransplantation and artificial intelligence (AI) are the engines behind this ending of the organ shortage, but in the long run it will be regenerative medicine and AI. The increased pace of innovation brought about by AI will require new Banff classifications for xenotransplantation pathology, tissue engineering pathology, and bioartificial organ pathology.

Methods:
The impossibility of humans recreating the long loops of Henle and the medullary osmotic gradient in the kidney will be made possible by AI, and the challenge of getting the right cells in the right places is also possible with AI and bio-electricity organized reseeding and regeneration at a more macroscopic level, the collective intelligence of the body (Michael Levin 2023), rather than cell by cell.

Results:
We have identified 31 PubMed articles from 2023 and 2024 that support our idea of the positive outcome with AI and transplantation from 153 total search results with ChatGPT and other entities.

Conclusions:
It is the ultimate dream of transplantation to provide organs for everyone. This plan will accomplish that, and sooner than you think, at least by 2030!

Abstracts - Poster Presentation

Impact of age, thymus excision, organ type and immunosuppression on lymphocyte subpopulations in pediatric transplantation

Angela Hamie [1,2] , Lavinia Ionescu[1,2] , Maryna Yaskina [3], Seema Mital [2,4], Bethany J. Foster [2,5], Upton Allen [2,6], Robert Ingham [7,8] , Simon Urschel [2,9]

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8. Striving for Pandemic Preparedness — The Alberta Research Consortium, University of Alberta, Edmonton, AB, Canada
9. Division of Pediatric Cardiology, University of Alberta, Edmonton, AB, Canada

Background:
Younger solid organ transplant (Tx) recipients show lower rejection rates, however have increased risk of adverse effects on standard immunosuppression. We hypothesized that the adaptive immune system composition in childhood Tx is affected by age, organ type, thymus excision and immunosuppression.

Methods:
In a national collaboration (CNTRP-POSITIVE), peripheral blood mononuclear cells (PBMCs) from children listed for heart, lung, and kidney Tx were analyzed pre-Tx, 3-, and 12-month post-Tx (n=115, 89, 73). Immune system characterization utilized flow cytometric deep phenotyping, grouped by age (0-2, 2-<10, and 10-18 years).

Results:
Heart and liver recipients were younger than kidney recipients (median ages: 1.6/1.7/10.3 years). CD4 + T cell count decreased at 3 months post-Tx, particularly in < 2-year olds (p<0.001), whereas regulatory T cells proportion increased at 3 months post-Tx (p= 0.0126). CD4+ counts recovered by 12 months post kidney and liver Tx, but not in heart Tx (p<0.001). CD19 + B cell count decreased at 12 months post-Tx in the < 2 year olds (p < 0001). Transitional B cells decreased at 3 months post-Tx in kidney recipients but increased in heart recipients (p=0.0584). Thymoglobulin induction reduced CD4+ T cell and B cell counts, while basiliximab reduced B cells.

Conclusions:
Infants (< 2 years) show the strongest effect of Tx on CD4+ T and CD19+ B cells. The persistent inability of heart Tx recipients to recover CD4+ T counts post- Tx is likely related to thymus excision. Induction therapy persistently alters lymphocyte composition.

Abstracts - Poster Presentation

Drone-Assisted oRgan Transport - DART

Pierre Lardeux

Following a successful test flight by Sage et al. (2022), in September 2021 in Toronto, it appears that the transport of organs for transplantation via remotely piloted aircraft system (RPAS, UAV, generally called drone) is becoming a viable option, though still under active research.

In this poster, we will explore: 1) what are the constraints that currently exist in Alberta for organ transport between the location of the donor and the location of the recipient, 2) what are the most critical aspects of the transport (duration, smoothness, temperature and other environmental parameters), 3) is the Toronto experience reproducible in Edmonton, AB, given the wide differences in conditions (distance, weather, topography) and finally 4) what are the challenges arising from transitioning from a research flight to a fully operational program to transport organs from the Edmonton International Airport (YEG) to the University of Alberta Hospital and also between hospitals in the urban centre of Edmonton.

Much of the work for this research project is theoretical (literature review, specification definition and legislative investigation), but the main goal of this poster is to generate interest for a research project and gather information from the transplant scientific community and reactions to this novel way of organ transport that includes cutting-edge technology. Ideally, discussions at ATI Research Day will lead to a research collaboration with physicians/clinicians of the University of Alberta.

3:30 - 3:50 pm (Bernard Snell Hall & Zoom)
Closing Remarks: Dr. Lori West

Lori West, MD, PhD

Professor
Pediatric Transplant Cardiologist
ATI director

Change is in the Air:
Celebrating a successful year for the Alberta Transplant Institute, and
looking ahead to the next decade

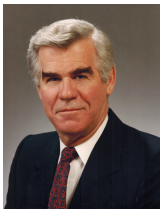
3:50 - 4:40 pm (Bernard Snell Hall & Zoom)
Keynote Speaker: Dr. Marie-Josée Hébert

Marie-Josée Hébert, MD

Professor
Transplant Nephrologist
University of Montreal

"Microvascular reserve in transplantation, the key to long-term allograft function?"

Dr. Marie-Josée Hébert earned a specialized degree in nephrology at the Université de Montréal, followed by postdoctoral studies at Brigham and Women's Hospital, Harvard. Since 1998, she is Professor of Medicine at Université de Montréal (UdeM), researcher and nephrologist–transplant physician at CHUM. She holds the Shire Chair in Nephrology, Renal Transplantation and Regeneration at UdeM. Her laboratory focuses on the role of programmed cell death as a major pathway contributing to immune dysregulation, rejection and abnormal vascular repair. Findings from her team have led to the characterization of new mediators of rejection and renal failure in humans. They also contributed to a better understanding of the mechanisms of fibrogenesis triggered by endothelial injury, autophagy and apoptosis. Dr. Hébert co-founded and co-directed the Canadian National Transplant Research Program (CNTRP, now CDTRP) from 2012 to 2022. Fellow in the Canadian Academy of Health Sciences, Marie-Josée Hébert received the Dr. John B. Dossetor Research Award (2015) and the Medal for Research Excellence (2016) from the Kidney Foundation of Canada. In May 2023, she received the City of Montreal's highest honor, Chevalière de l'Ordre de Montréal. She is also the Chair of the Governing Council of the Canadian Institutes of Health Research.



Supported by the William H. Lakey Transplantation Lectureship Fund

This visit has been funded in part by the Walter MacKenzie Visiting Speaker Fund, Faculty of Medicine and Dentistry

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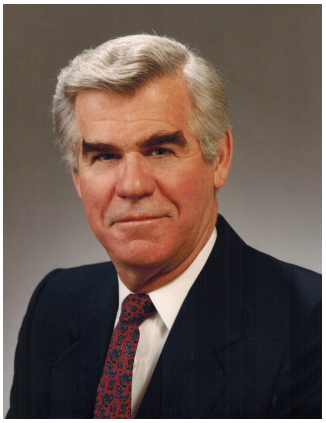

William H. Lakey

Transplantation Lectureship Fund

The Dr William H Lakey Transplantation Lectureship was created through the generosity of the Lakey family. Dr Bill Lakey performed the first kidney transplant at the University of Alberta Hospital in 1967 and would go on to perform nearly 800 more. Dr Lakey was a true transplantation pioneer who bettered the lives of countless Canadians through his passion and dedication.

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