NARMIN KASSAM

Department of Medicine Chair

I am proud to announce the renaming of this event to the Me2 Majumdar Research and Quality Improvement Day. Me2 was an outstanding academic clinician with more than $30 million in peer-review funding, over 300 peer-reviewed publications, and most significantly, he helped mentor more than 40 future clinicians, researchers and clinician-scientists formally and many more informally. His prodigious and influential research output is the essence of what we are here to celebrate today.

This is the second combined research and clinical quality improvement (QI) Day hosted by the Department of Medicine and the Edmonton Zone Medicine Quality Council. This year's event is a hybrid event with in-person & virtual oral presentations along with in-person & virtual attendees. These past couple of years have been arduous and I would like our clinicians, educators, researchers, and scientists to know we do not take for granted their continued efforts to secure funding in this highly competitive landscape and mentor the future generation. In 2021-22, our researchers secured over $12.8 million in newly awarded tri-council (CIHR, NSERC and SSHRC) research funding, have published in numerous high impact journals, and won a number of prestigious awards. Thank you to all who help support these significant achievements.

I would like to welcome our two keynote speakers: Dr. Paul Kubes, Professor, Department of Physiology and Pharmacology and Medicine, University of Calgary Cumming School of Medicine; and Dr. Francois P. Belanger, Vice President, Quality and Chief Medical Officer, Alberta Health Services.

Please join me in learning about what our vast number of trainees have been working on.

In honor of one of our greatest, Sumit (Me2) Majumdar.

Narmin Kassam
Professor and Chair, Department of Medicine

*Tri-council funding amounts obtained from the University of Alberta Tableau

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PAUL KUBES
PhD

Keynote Speaker

Professor, Department of Physiology & Pharmacology and Medicine, University of Calgary

Dr. Paul Kubes is a Professor at the University of Calgary Cumming School of Medicine and Founding Director of the Snyder Institute for Chronic Diseases. He also holds a Canada Research Chair in Leukocyte Recruitment in inflammatory disease.

Dr. Kubes has received numerous awards including the CIHR Investigator of the Year in 2011 for his basic science work on how the brain affects immunity. He has also received the Alberta Science and Technology Award and the Henry Friesen Award. Dr. Kubes has published basic science work in Cell, Science and the Nature journals and also has publications in both clinical journals including Lancet and more translational journals (JCI). His latest work has uncovered a key role for peritoneal cavity macrophage in healing visceral organs.

Dr. Kubes has extensive review experience with CIHR having been part of numerous committees including the Immunology panel, Cardiovascular A and B panel, the CIHR scholar panel and the Banting postdoctoral panel. He also served as a member of CIHR Governing Council and is chair of the college chairs. In addition, he has reviewed for NIH and he co-chairs the Gairdner Research Committee.

Dr. Belanger is the Vice President, Quality and Chief Medical Officer for Alberta Health Services(AHS) and member of the executive leadership team. His current role is to help oversee the integration and coordination of a complex health delivery model for the province through nine accountability functions: Office of the Chief Medical Officer and Medical Affairs, Quality & Healthcare Improvement, Clinical Informatics and Clinical Information Systems, Patient Relations, Health Information Management, Strategic Clinical Networks, Provincial Clinical Services, Alberta Surgical Initiative, Virtual Health and maintaining effective partnerships with academic institutions and other physician led organizations.

A key mandate of the Quality and CMO position is to maintain a strong emphasis on the importance of quality and patient safety, engagement, leadership development and relationships between the medical staff and the health care system.

Prior to assuming this role, Dr. Belanger was the Interim Vice President Quality and Chief Medical Officer AHS, Vice President and Medical Director Central and Southern Alberta AHS, and the Medical Director Calgary Zone AHS. He has also held several medical leadership positions in AHS and the former Calgary Health Region. These include Senior Vice-President and Zone Medical Director for the Calgary Zone (AHS); Acting Executive Vice-President and Chief Medical Officer of AHS; Zone Medical Director, Calgary Zone, (AHS); and the Calgary Health Region/University of Calgary interim and deputy department head of Pediatrics. He continues to practice as a Pediatric Emergency Physician at the Alberta Children's Hospital and South Health Campus in Calgary.

FRANCOIS P. BELANGER, MD

Keynote Speaker

Vice President, Quality & Chief Medical Officer, Alberta Health Services

**Edmonton Zone Medicine Quality Council –
Strategic Clinical Improvement Committee**

The University of Alberta Department of Medicine and Alberta Health Services Zone Medicine Program had overlapping strategic priorities to develop a strong clinical quality improvement agenda and improve outcomes for Medicine patients in the Edmonton Zone.

As a result, the Edmonton Zone Medicine Quality Council - Strategic Clinical Improvement Committee was formed in alignment with the DoM strategic plan and the AHS quality management framework supported by a DoM funded strategic clinical improvement consultant co-located with the AHS administrative lead for Edmonton Zone Medicine.

This council working closely with both academia and frontline care providers provides the platform for strategic quality improvement interventions to be developed, tested and shared with the Edmonton Zone Medicine divisions, hospital sites and community partners. Ensuring communication and collaboration as this pertains to the areas of clinical activity and clinical administration.

To serve as a resource for regular evaluation of clinical needs and priorities, initiatives and processes to build a dynamic cycle of continuous improvement in the in-patient and ambulatory patient experience.

Deputy Zone Clinical Department Head, Medicine

DR. ELAINE YACYSHYN

Yvonne Suranyi is Executive Director of University of Alberta/ Stollery Emergency and the University of Alberta Hospital/EZ Medicine Programs.

As part of one of Canada's clinical, research and teaching hospitals, her portfolio consists of approximately 244 medical beds, 8 Sleep Disorder beds, 74 Emergency beds (Adults and Pediatrics) with a range of Medical services including pulmonary, nephrology, Inpatient TB, Haematology, Geriatrics, Geriatrics Neurology, Family Medicine and General Internal medicine. She has strategic responsibility for medicine programs across the Edmonton zone.

The UAH/Stollery Emergency treats more than 140,000 patients annually. It is a quaternary, Level 1 trauma centre that serves as a major referral centre and hub for patients in the Edmonton Zone, northern Alberta (i.e., north of Red Deer), north-eastern British Columbia, north-western Saskatchewan, the Northwest Territories, and Nunavut.

Together we focus on patient flow, quality improvement and implementation of new evidenced based initiatives improving our patient, family and staff experience.

Previous to this role Yvonne has held several leadership roles in the Edmonton Zone during her 30 + years in health care delivery. Her administrative leadership contributions include quality improvement, and implementation of patient-centered care initiatives. In addition to her passion for health care, Yvonne enjoys time with her twin daughters and husband.

Pamela Mathura is a senior improvement leader and a clinical lecturer for the University of Alberta Department of Medicine and Alberta Health Services-Edmonton zone Medicine. Her role as a quality leader for the Edmonton zone medicine quality council-Strategic clinical improvement committee (SCIC) includes leading quality improvement (QI) teams and QI training. She is also the preceptor for a QI elective in the faculty of pharmacy. Pamela has published several articles in the area of improvement science and is currently pursuing a PhD in Healthcare Quality Philosophy from Queens University.

Previous to this role Pamela has worked as a clinical quality improvement consultant within Alberta Health Services. She has been involved in many large-multi-hospital QI projects which have been shared locally and provincially. Involved in healthcare delivery for the last 29 years; her clinical background is in Laboratory Medicine where she held a leadership role in Anatomical Pathology at the University of Alberta Hospital.

FACULTY MEMBERS

VANESSA MEIER-STEPHENSON
ASSISTANT PROFESSOR
INFECTIOUS DISEASES

Dr. Meier-Stephenson is an Assistant Professor with the Division of Infectious Diseases with an interest in chronic viral hepatitis and viral-host pathogenesis. She uses a combination of computational, biophysical and molecular virology methods to explore various viral DNA/RNA and host protein interactions to gain further understanding in viral pathogenesis and evaluate unique approaches to developing therapeutics.

GRACE LAM
ASSISTANT PROFESSOR
PULMONARY MEDICINE

Dr. Grace Lam is an adult respirologist and assistant professor who joined the Faculty of Medicine at the University of Alberta under the Division of Pulmonary Medicine in May 2020. She trained at the University of Toronto in the MD/PhD program where her PhD work focused on basic science research on autophagy and the intracellular immunity against Listeria monocytogenes, resulting in nearly 20 publications on this topic. She then completed her residency in core internal medicine and adult pulmonary at University of Alberta and went on to a post-graduate fellowship in adult cystic fibrosis (CF) in Vancouver.
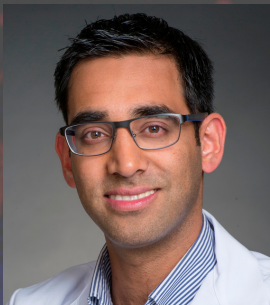
ALIM HIRJI
ASSOCIATE PROFESSOR
PULMONARY MEDICINE

Dr. Alim Hirji is an Associate Professor in the Department of Medicine at the University of Alberta. He received his Doctor of Medicine from McMaster University, completed his internal medicine training at the University of Toronto and his pulmonary medicine fellowship through the University of British Columbia. He completed a fellowship in lung transplantation in the Toronto Lung Transplant Program and has a Masters in Epidemiology through the London School of Hygiene and Tropical Medicine. His clinical practice includes lung transplantation, general pulmonary medicine, and interventional bronchoscopy. He is the current chair of the lung section for the Canadian Society of Transplantation

MONA GILL
ASSISTANT CLINICAL PROFESSOR
GENERAL INTERNAL MEDICINE

Dr. Gill is a General Internal Medicine specialist at the Misericordia and University Hospital, with interests in quality improvement, thrombosis, and obstetric medicine. She graduated from the University of Calgary Medical School and completed her postgraduate medical education at the University of Alberta

Meeting at a Glace

8:00 AM	Welcome Address
8:10 AM	Keynote Speaker *(Scientific)*
8:45 AM	Oral Presentations
10:30 AM	Break
10:45 AM	Ballerman Translational Research Fellowship Award
11:05 AM	Faculty Presentations
1:00 PM	Keynote Speaker *(Quality Improvement)*
1:30 PM	Oral Presentations
2:05 PM	Faculty Presentations
2:30 PM	Closing Address

ScientificResearch Awards

SCIENTIFIC ORAL PRESENTATIONS AWARD WINNER
$500

SCIENTIFIC POSTER ABSTRACT AWARD WINNER
$500

PAUL MAN AWARD WINNER
$500

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD WINNER
$24,500

Abstracts have been adjudicated in a blinded fashion by 3 reviewers. The top 7 highest scoring abstracts in research and top 2 highest abstracts in quality improvement were invited to present an oral presentation.

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

PAST RECIPIENTS

JOSEPH KAMTCHUM-TATUENE (2021)
SUPERVISOR: GLEN JICKLING
Prevalence of High-Risk Plaques and Risk of Stroke in Patients with Asympatomatic Carotid Stenosis: A Meta-analysis

ANDREW MASOUD (2020)
SUPERVISOR: ALLAN MURRAY
Apelin directs endothelial cell differentiation and vascular repair following immune-mediated injury

BRUNO SALEME (2019)
SUPERVISOR: GOPINATH SUTENDRA
Tissue-specific regulation of p53 by PKM2 is redox dependent and provides a therapeutic target for anthracycline-induced cardiotoxicity

MARYAM ABADI (2019)
SUPERVISOR: ALDO MONTANO-LOZA
Poor performance of psoas muscle index for identification of patients with higher waitlist mortality risk in cirrhosis

ABDUL KALAM AZAD (2018)
SUPERVISOR: ALLAN MURRAY
FGD5 Regulates VEGF Receptor-2 Coupling to PI3 Kinase and Receptor Recycling

RANIA SOUDY (2017)
SUPERVISOR: JACK JHAMANDAS
Cyclic AC253, a novel amylin receptor antagonist, improves cognitive deficits in a mouse model of Alzheimer's disease

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

PAST RECIPIENTS

BRANDON MILLAN & HEEKAK PARK (2016)
SUPERVISOR: KAREN MADSEN
Fecal Microbial Transplants Reduce Antibiotic-Resistant Genes in Patients with Recurrent Clostrdium Difficile Infection

ROXANNE PAULIN (2015)
SUPERVISOR: EVANGELOS MICHELAKIS
Sirtuin 3 Deficiency Is Associated with Inhibited Mitochondrial Function and Pulmonary Arterial Hypertension in Rodents and Humans

STACEY REINKE (2014)
SUPERVISOR: CHRIS POWER
Implementation of metabolomics strategies in multiple sclerosis

PETER DROMPARIS (2013)
SUPERVISOR: EVANGELOS MICHELAKIS
Pioglitazone reduces angiogenesis by altering mitochondrial function and reducing hypoxia inducible factor-1 activation

VAIBHAV PATEL (2012)
SUPERVISOR: GAVIN OUDIT
Loss of ACE2 Exacerbates Diabetic Cardiovascular Complications and Leads to Systolic and Vascular Dysfunction: A Critical Role of the Ang II/AT1 Receptor Axis

GOPINATH SUTENDRA (2011)
SUPERVISOR: EVANGELOS MICHELAKIS
Fatty Acid Oxidation and Malonyl-CoA Decarboxylase in the Vascular Remodeling of Pulmonary Hypertension

MSC IN MEDICINE WITH SPECIALIZATION IN TRANSLATIONAL MEDICINE

The Department of Medicine (DOM) has made **Translational Medicine (TM)** a top priority. TM facilitates the "translation" of molecular discoveries to actual patients and populations. It requires a different way of thinking at all stages of the journey from a discovery in an animal lab to the point that, following successful clinical trials, the government approves the discovered therapy for humans. TM is a critical component of **Precision Medicine**, a new discipline that aims for "custom-made" therapies for patients, as opposed to the traditional "one treatment fits all model". This is because in order to apply an optimal therapy to a patient, one needs to understand the molecular and genetic differences that distinguish all patients from one another. Precision Medicine is now a top priority for the FOMD.

The need: To optimize the development of new "precision" therapies and diagnostic tests, a researcher studying molecules and animals needs to learn how to think as a clinician; and a clinical researcher needs to understand the principles of molecular research. This is challenging because traditional teaching models focus on one or the other, with the learners following either an exclusive molecular or clinical research career track. Although all recognize the importance of TM, there are surprisingly few examples of training programs worldwide aiming to teach this new discipline to future medical researchers and leaders.

The action: Four years ago, the DOM launched and since then supports a novel training program, teaching the attitudes and skills required to excel in TM. This is the first training program of its kind in Canada and one of few in the world.

The innovations: The MSc in Medicine with specialization in translational medicine program attracts trainees from very diverse backgrounds and levels of training. Rather than teaching principles of basic or clinical research of specific diseases, the program teaches integrative and overarching concepts and skills to address the many challenges of bringing a molecular discovery to patients with diverse diseases. Since nothing needs to be "memorized", the final exams are "open book". Teaching objectives include, among others, new ways to design animal experiments or clinical trials compatible with PM, strategies to attract funding including grant writing skills, effective ways to communicate cross-disciplinary research findings, understanding of regulatory rules and "quality control" principles in preclinical and clinical research. Most of these principles are not taught in traditionally structured training programs. The trainees can either get credits towards their PhD or towards a novel Masters Program with "specialization in TM", the first of its kind in Canada.

The program uses eClass, the University of Alberta's centrally learning management system. eClass provides a digital platform in which the reading materials are archived as well as an out-of-class forum for ongoing discussions among trainees. All sessions are recorded through the eClass multimedia environment with Adobe Connect. This allows "live" streaming of sessions from other locations; thus the lectures can be attended interactively online by residents in a remote elective rotation or by trainees from other Universities. For example, in the last year 2 residents from UBC completed the program. The ability of residents to obtain a Masters degree during busy core Internal Medicine or specialty residency is a significant advantage to our clinical training programs.

The progress: A total of 109 learners have registered to the program so far. Of these, some took credits for their PhD and some participated as "open access" students. Of the 59 trainees that participated in the Masters track, there were 2 junior faculty members, 21 graduate students and 13 residents from core and 23 specialty residency programs. To complete the Masters requirements a submission of a thesis is required. So far 20 trainees have obtained their Master's with a specialization in TM degree.

The TM program is a major investment of the DOM, with many of its faculty contributing over the years. Currently, the program is directed by Evangelos Michelakis, MD, Gopinath Sutendra, PhD, Glen Jickling, MD, PhD and Eleni Karageorgos.

The MSc in Medicine with specialization in Translational Medicine class on April 19, 2018 (final exam day)

ORAL SCIENTIFIC PRESENTATIONS

8:00 AM   **Welcome Remarks**
Dr. Evangelos Michelakis, Associate Chair, Research, Department

8:10 AM   **Keynote Speaker (Scientific Talk)**
Dr. Paul Kubes, Professor, Department of Physiology & Pharmacology and
Medicine, University of Calgary
A Career Well Spent: advice to help guide you along your Career Path

ORAL PRESENTATIONS

8:45 AM   Luke Gerla, Graduate Student, Division of Pulmonary Medicine
Supervisor: Paige Lacy
*A potential role for TSLP from airway epithelial cells in driving the systemic immune
response to SARS-CoV-2*

9:00 AM   Rhys Beaudry, Postdoctoral Fellow, Division of Pulmonary Medicine
Supervisor: Michael Stickland
Persistent dyspnea after COVID-19 is not related to cardiopulmonary impairment

9:15 AM   Bruno Saleme, Graduate Student, Division of Cardiology
Supervisor: Evangelos Michelakis
*m6A bimodal peak signature mediates acute selective stress Translation specialized
cytoskeletal ribosomes via a MARK4-FTO-PKR axis*

9:30 AM   Amy Morrison, Graduate Student, Division of Endocrinology & Metabolism
Supervisor: Peter Senior
Improved Glycemia and Quality of Life Among Loop Users â€" Analysis of Real-
World Data from a Single Centre

9:45 AM   Karthivashan Govindarajan, Postdoctoral Fellow, Division of Neurology
Supervisor: Satyabrata Kar
A novel disease-modifying potential of native-PLGA nanoparticles in the treatment
of Alzheimer's Disease (AD) pathology

10:00 AM   Maria Areli Lorenzana-Carrillo, Graduate Student, Division of Cardiology
Supervisor: Gopinath Sutendra
Cardiomyocyte-Specific Nuclear PKM2 Provides a Molecular Platform to Stabilize
the Gata-4/6 Transcription Factors and Promote MDM2-Mediated p53
Degradation; Implications for Heart Failure

10:15 AM   Justin Lai, Graduate Student, Division of Hematology
Supervisor: Peng Wang
SORE6 reporter as a novel tool to decipher cancer stemness and disease relapses
in acute myeloid leukemia

ORAL SCIENTIFIC PRESENTATIONS

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

10:45 AM   Ballermann Translational Research Fellowship Award Announcement

Oral Presentation

10:50 AM   Ballermann Translational Research Fellowship Award Winner

FACULTY PRESENTATIONS

11:05 AM   Dr. Vanessa Meier-Stephenson, Assistant Professor, Division of Infectious Diseases
Anchoring on a knot of DNA - A unique approach to target chronic hepatitis B virus

11:17 AM   Dr. Grace Lam, Assistant Professor, Division of Pulmonary Medicine
Unraveling the causes of Long COVID symptoms

ORAL QI PRESENTATIONS

1:00 PM   **Keynote Speaker (Quality Improvement Talk)**
Dr. Francois P. Belanger, MD, FRCPC, Vice President - Quality and Chief Medical Office, Alberta Health Services

Oral Presentations

1:35 PM   Ruojin Bu, PGY2 Division of General Internal Medicine
A Quality Improvement Project to Enhance Adoption of the MyAHS Connect Patient Portal in Inpatient General Internal Medicine Settings

1:50 PM   Anastasia Howe, PGY3, Division of General Internal Medicine
Optimizing IV fluid therapy on medicine wards

Faculty Presentations

2:05 PM   Dr. Alim Hirji, Associate Professor, Division of Pulmonary Medicine
Telemonitoring to reduce adverse events for patients on high flow oxygen at the University of Alberta Hospital

2:17 PM   Dr. Mona Gill, Assistant Clinical Professor, Division of General Internal Medicine
Reduction of Urea test ordering in the Emergency Department

2:30 PM   **Closing Remarks**
Dr. Narmin Kassam, Chair, Department of Medicine

Alam, Arafat (Graduate Student)
Impact of Inherited Bleeding Disorders on Maternal Bleeding and Other Pregnancy Outcomes: A Population-based Cohort Study
Supervisor: Linda Sun; Cynthia Wu (Hematology)

Alavi, Parnian (Graduate Student)
Aging results in organ-specific alterations in the level and expression pattern of von Willebrand factor
Supervisor: Nadia Jahroudi (Hematology)

AlOhaly, Nasser (Clinical Fellow)
Feasibility of Remote Monitoring of Walking for People Living with Multiple Sclerosis Using a Wearable Device
Supervisor: Penny Smyth (Neurology)

Alzahrani, Khadija (Graduate Student)
Proinflammatory mediators-induced localized insulin resistance (IR) in airway epithelial cells
Supervisor: Harissios Vliagoftis (Pulmonary Medicine)

Bali, Krittika (Graduate Student)
The Association Between Access to Medical Care (physicians and nurse practitioners) and Impact on Resident Outcomes: A Retrospective Cohort Analysis
Supervisor: Dr. Andrea Gruneir (Geriatric Medicine)

Beaudry, Rhys (Postdoctoral Fellow)
Persistent dyspnea after COVID-19 is not related to cardiopulmonary impairment
Supervisor: Michael Stickland (Pulmonary Medicine)

Bihari, Allison (Graduate Student)
Letting Go of Control: Experience and Involvement of Parents of Young Adults with Inflammatory Bowel Disease Transitioning from Pediatric to Adult Care
Supervisor: Karen Kroeker (Gastroenterology)

Bu, Ruojin (Resident)
Inhalant use among pulmonary function testing (PFT) laboratory referrals
Supervisor: Dilini Vethanayagam (Pulmonary Medicine)

Bu, Ruojin (Resident)
Asbestosis requiring lung transplantation in a hairdresser: an occupational exposure to comb through
Supervisor: Alim Hirji (Pulmonary Medicine)

Chappell, Kaitlyn (Graduate Student)
Virtually-Delivered Mindfulness-Based Stress Reduction for Adults with IBD: A Feasibility Trial
Supervisor: Karen Kroeker (Gastroenterology)

Daniel, Nadia (Graduate Student)
FOXO1 transcription factors regulate Toll-like-receptor 3 in airway epithelial cells
Supervisor: Harissios Vliagoftis (Pulmonary Medicine)

Duchesne, Marc (Graduate Student)
Cytokine production in allergen-stimulated airway epithelial cells shows time-dependent de novo synthesis of thymic stromal lymphopoietin
Supervisor: Paige Lacy (Pulmonary Medicine)

Fung, David (Resident)
Rejection rates of lung transplant patients with reduced renal function on a sirolimus based immunosuppression regimen: A cohort characterization study
Supervisor: Alim Hirji (Pulmonary Medicine)

Gerla, Luke (Graduate Student)
A potential role for TSLP from airway epithelial cells in driving the systemic immune response to SARS-CoV-2
Supervisor: Paige Lacy (Pulmonary Medicine)

Govindarajan, Karthivashan (Postdoctoral Fellow)
A novel disease-modifying potential of native-PLGA nanoparticles in the treatment of Alzheimer's Disease (AD) pathology
Supervisor: Satyabrata Kar (Neurology)

Hammond, Keely (Resident)
Sepsis in the critically ill: An observational study of anatomic site of infection and microbiologic diagnosis
Supervisor: Justin Chen (Infectious Diseases)

Huang, Yiming (Resident)
Cultivating Wellness in Internal Medicine Residency Through Resident Led Seminars
Supervisor: Steven Katz (Rheumatology)

Imrran Suliman, Muhammad (Resident)
IMPACT OF DIABETES ON POST LIVER TRANSPLANT OUTCOMES
Supervisor: Rahima Bhanji (Gastroenterology)

SCIENTIFIC ABSTRACTS

Karimi-Dehkordi, Mehri (Postdoctoral Fellow)
Quality Indicators relevant to the care of older adults in various settings: A systematic review of reviews
Supervisor: Adrian Wagg (Geriatric Medicine)

Lai, Justine (Graduate Student)
SORE6 reporter as a novel tool to decipher cancer stemness and disease relapses in acute myeloid leukemia
Supervisor: Peng Wang (Hematology)

Liang, Xinyun (Christie) (Resident)
The association between maternal glucose levels on gestational diabetes screening tests and future cardiovascular outcomes
Supervisor: Roseanne Yeung (Endocrinology & Metabolism)

Lo, Tiffany (Graduate Student)
Differential Effects of Plakoglobin Expression on the Oncogenic Properties of p53 Conformational and Contact Mutants
Supervisor: Nadia Jahroudi (Hematology)

Lorenzana Carrillo, Maria Areli (Graduate Student)
Cardiomyocyte-Specific Nuclear PKM2 Provides a Molecular Platform to Stabilize the Gata-4/6 Transcription Factors and Promote MDM2-Mediated p53 Degradation; Implications for Heart Failure
Supervisor: Gopinath Sutendra (Cardiology)

Mast, Heather (Graduate Student)
The link between changes in mitochondrial function and divergent evolution of lifespan in the bean beetle (Acanthoscelides obtectus)
Supervisor: Helene Lemieux (Cardiology)

Moolla, Muhammad (Resident)
Outcomes of Pregnancy in Women with Hypertrophic Cardiomyopathy: A Systematic Review
Supervisor: Anoop Mathew (Cardiology)

Morrison, Amy (Graduate Student)
Improved Glycemia and Quality of Life Among Loop Users â€“ Analysis of Real-World Data from a Single Centre
Supervisor: Peter Senior (Endocrinology & Metabolism)

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

Mustapha, Jelili (Graduate Student)
Analyzing the Specificity protein 1 (Sp1) interaction with Hepatitis B Virus (HBV)'s G4-quadruplex: a novel approach to target chronic HBV
Supervisor: Vanessa Meier-Stephenson (Infectious Diseases)

Nezu, Masahiro (Postdoctoral Fellow)
IRE1a-XBP1s pathway in mouse ACTH-producing pituitary tumor cells
Supervisor: Toru Tateno (Endocrinology & Metabolism)

Poursharif, Shayan (Graduate Student)
Proximal tubular reabsorption impacts on microvascular regulation via the TGF system
Supervisor: Branko Braam (Nephrology)

Saleme, Bruno (Graduate Student)
m6A bimodal peak signature mediates acute selective stress Translation specialized cytoskeletal ribosomes via a MARK4-FTO-PKR axis
Supervisor: Evangelos Michelakis (Cardiology)

Siddique, Mujtaba (Graduate Student)
Novel automated hippocampal subfield volumetry throughout the entire long axis in patients with Alzheimer's Disease
Supervisor: Trevor Steve (Neurology)

Sparrow, Kaitlin (Resident)
Effect of Immunotherapy and Chemotherapy on Removal of Indwelling Pleural Catheters in Non-small Cell Lung Cancer Patients with Malignant Pleural Effusions
Supervisor: Pen Li (Pulmonary Medicine)

Sun, Ning (Graduate Student)
Metabolic remodeling and mitochondrial biogenesis in primary biliary cholangitis is linked with betaretrovirus infection
Supervisor: Andrew Mason (Gastroenterology)

Zhang, Yongneng (Graduate Student)
SNPs for genes encoding the mitochondrial proteins Sirt3 and Ucp2 are associated with disease severity, type 2 Diabetes and outcomes in Pulmonary Arterial Hypertension (PAH) patients and this is recapitulated in a new PAH mouse model lacking both genes
Supervisor: Evangelos Michelakis (Cardiology)

QUALITY IMPROVMENT ABSTRACTS

FULL ABSTRACTS ENCLOSED

Bu, Ruojin (Resident)
A Quality Improvement Project to Enhance Adoption of the MyAHS Connect Patient Portal in Inpatient General Internal Medicine Settings
Supervisor: Robert Hayward (General Internal Medicine)

Godfrey, Madison (Graduate Student)
Understanding Approaches to Empathy in Dermatologic Patient Care
Supervisor: Marlene Dytoc (Dermatology)

Howe, Anastasia (Resident)
Optimizing IV fluid therapy on medicine wards
Supervisor: Inka Toman (General Internal Medicine)

Jha, Divya (Graduate Student)
Evaluation of a patient-administered, physician supervised allergy patch test: A pilot study
Supervisor: John Elliott (Dermatology)

Li, Miriam (Resident)
Determining Areas for Improvement: Sun safety Knowledge and Practices in Elementary School Children
Supervisor: Marlene Dytoc (Dermatology)

Acknowledgements

DR. NARMIN KASSAM — Professor & Chair
Department of Medicine

DR. EVANGELOS MICHELAKIS — Associate Chair Research
Department of Medicine

DR. GOPINATH SUTENDRA — Associate Professor & Associate Chair, Graduate Programs
Department of Medicine

DR. AINSLIE HILDEBRAND — Assistant Professor
Chair - Core Internal Medicine
Resident Research Subcommittee

PAMELA MATHURA — Quality Improvement Specialist & Clinical Lecture, Department of Medicine

YVONNE SURANYI — Executive Director, UAH/EZ Medicine Program and UAH/Stollery Emergency

DR. ELAINE YACYSHYN — Deputy Zone Clinical Department Head, Medicine

DR. NADIA JAHROUDI — Associate Professor and Associate Chair, Graduate Programs
Department of Medicine

ELENI KARAGEORGOS — Team Lead - Research
Department of Medicine

ANDREA CLIFF — Strategic Communications & Events Team Lead
Department of Medicine

Scientific Research Abstracts

Impact of Inherited Bleeding Disorders on Maternal Bleeding and Other Pregnancy Outcomes: A Population-based Cohort Study

Arafat Ul Alam, Venu Jain, Padma Kaul, Cynthia Wu, Linda Sun
Supervisor: Dr. Linda Sun, Dr. Cynthia Wu,

INTRODUCTION

Increasing rate of postpartum hemorrhage (PPH) has been observed between 2003 and 2010 in Canada. Given that bleeding disorders contribute to the risk of PPH, it is important to identify the current trend in PPH in the last decade and assess the impact of inherited bleeding disorders on pregnancy outcomes.

METHODS

This is a retrospective population-based cohort study using the Alberta Pregnancy Birth Cohort. Number of deliveries per year in Alberta was determined by Vital Statistics birth registry from 2010 to 2018 and was linked with Discharge Abstract Database (DAD) to identify cases of PPH and other pregnancy outcomes. All diagnoses and procedures were identified by International Classification of Diseases (ICD)-10 codes and Canadian Classification of Interventions (CCI) codes, respectively. Inherited bleeding disorders including von Willebrand disease, hemophilia carriers, platelet function disorder, and hereditary deficiencies of other coagulation factors were identified by presence of at least two ICD codes. Univariate logistic regression analyses were used to compute odds of pregnancy outcomes.

RESULTS

311,330 women had a total of 454,400 pregnancies with live births. The rate of PPH did not have any significant change from 10.3 in 2010 (95% CI 10.0-10.6) to 10.9 (95% CI 10.6 -11.1) in 2018 (P for trend =0.28) . Women with bleeding disorders were more likely to experience PPH (OR 1.4; 95% CI 1.1-1.8), antepartum hemorrhage (OR 4.6; 95% CI 3.2-6.7), hysterectomy (OR 2.9; 95% CI 1.8-4.9) and transfusion of blood products (OR 2.5; 95% CI: 1.6-3.9) [Table 1]. However, there was no significant difference in prolonged labor, obstetric hematoma, low birth weight baby and neonatal death.

CONCLUSIONS

Despite a rise in the rate of PPH between 2003-2010, we observed no significant change in the rate of PPH in Alberta between 2010-2018. Women with inherited bleeding disorders are at an increased risk of bleeding events during pregnancy and childbirth.

Supervisor: Dr. Linda Sun, Dr. Cynthia Wu,

Table 1: Maternal and neonatal outcomes of pregnancies [a] with inherited bleeding disorders vs without inherited bleeding disorders during 2010-2018

	Pregnancies with Inherited bleeding disorders	Pregnancies without inherited bleeding disorders	OR [b] (95% CI [c])	P [d]
Total n (%)	522 (0.1)	453,878 (99.9)		
Post partum hemorrhage	73 (14.0)	47171 (10.4)	1.4 (1.1-1.8)	0.01
Ante partum hemorrhage	29 (5.6)	5687 (1.3)	4.6 (3.2-6.7)	<0.001
Mode of delivery				
Caesarean	171 (32.8)	131990 (29.1)	1.2 (0.9-1.4)	0.07
Vaginal	351 (67.2)	321888 (70.9)	0.8 (0.7-1.0)	0.07
Multiple pregnancy	6 (1.1)	8118 (1.8)	0.6 (0.3-1.4)	0.28
Hysterectomy (in the year of childbirth)	2 (0.4)	925 (0.2)	1.8 (0.5-7.6)	0.37
Hysterectomy (overall)	15 (2.9)	4477 (1.0)	2.9 (1.8-4.9)	<0.001
Prolonged labour	24 (4.6)	25949 (5.7)	0.8 (0.5-1.2)	0.27
Induced labour	180 (34.5)	137145 (30.2)	1.2 (1.02-1.5)	0.03
Uterine rupture	2 (0.4)	613 (0.1)	2.8 (0.7-11.4)	0.14
Obstetric hematoma	1 (0.2)	691 (0.2)	1.3 (0.2-8.9)	0.82
Blood transfusion	19 (3.6)	6770 (1.5)	2.5 (1.6-3.9)	<0.001
Gestational age (in weeks)				
<37	49 (9.4)	35312 (7.8)	1.2 (0.9-1.6)	0.17
37-42 (reference)	473 (90.6)	418485 (92.2)	1.0	
>42	0 (0)	81 (0.02)	N/A	N/A
Birth weight (in grams)				
<2500	32 (6.2)	24870 (5.5)	1.1 (0.8-1.6)	0.54
2500-3999 (reference)	441 (85.0)	383516 (85.1)	1.0	
>4000	46 (8.9)	42088 (9.3)	0.9 (0.7-1.3)	0.74
Neonatal death	2 (0.1)	520 (0.1)	1.2 (0.3-4.8)	0.80
ICH [e] (in neonatal period)	5 (0.3)	517 (0.1)	2.9 (1.2-7.2)	0.02

a: analysis restricted to all hospitalized deliveries with live births; b: odds ratio; c: confidence interval; d: from univariate logistic regression; e: intracranial hemorrhage

Aging results in organ-specific alterations in the level and expression pattern of von Willebrand factor

Parnian Alavi, Radya Yousef Abdualla, Douglas Brown, Jayan Nagendran, John Lewis, Stephane L. Bourque, Nadia Jahroudi
Supervisor: Dr. Nadia Jahroudi

INTRODUCTION

Von Willebrand factor (VWF) is an endothelial-specific pro-coagulant protein with a major role in thrombosis. Increased circulating levels of VWF have been associated with aging; however, the mechanism is unknown. Our objectives are 1) To explore the regulation of VWF expression during aging. 2) To determine the association of increased VWF expression with thrombogenicity during aging. 3) To determine the molecular mechanism of age-related upregulation of VWF.

METHODS

Circulating plasma, cellular protein, and mRNA levels of VWF in young and aged mice were determined. Immunofluorescent analyses of major organs were performed to establish the vascular pattern of VWF and the presence of platelets aggregates. An in vitro model of aging was used to explore the mechanism of increased VWF levels.

RESULTS

Increased plasma levels of VWF were observed in aged rodents. VWF mRNA and protein levels were significantly increased in the brains, lungs, and livers, but not in the kidneys and hearts of aged mice. In organs of aged mice that demonstrated increased VWF, it was detected in a significantly higher proportion of small vessels compared to young and was concomitant with increased platelets aggregate formation. The prolonged culture of endothelial cells exhibited cell senescence that correlated with a significant increase in VWF. Increased VWF expression was specifically detected in the senescent cell population. A significantly higher proportion of VWF expressing endothelial cells exhibited senescent markers in aged mice brains compared to young.

CONCLUSIONS

The aging process induces a heterogeneous response regarding VWF expression in endothelial cells, leading to an organ-specific increase in VWF levels. This is concomitant with increased platelets aggregate formation. The age-associated increase in VWF expression may be modulated through the process of cell senescence. This study will be a benefit to designing appropriate vascular bed-specific targeted therapies to combat thrombogenic complications that occur with aging.

Supervisor: Dr. Nadia Jahroudi

Feasibility of Remote Monitoring of Walking for People Living with Multiple Sclerosis Using a Wearable Device

Nasser AlOhaly, Vahid Abdollah, Hossein Rouhani, Chester Ho, Penny Smyth
Supervisor: Dr. Penny Smyth

INTRODUCTION

People living with Multiple Sclerosis (PwMS) require regular neurologist clinic visits to monitor disease progression. However, clinical evaluations may not identify walking difficulties that can fluctuate with anxiety, fatigue, and pain. In addition, remote evaluations of PwMS have increased due to the COVID pandemic; remote evaluations are limited by lack of objective measurements of MS disability, including walking.

Our study aims to assess the feasibility and validity of wearable technology for remote monitoring in PwMS. A secondary aim is to establish if wearable technologies identify the effects of MS symptom-related fluctuations upon daily activities and functioning.

METHODS

A goal sample size of 60 participants was planned. A chest-mounted sensor is delivered and worn 8 hours a day, for a total duration of 12 weeks. Feasibility was determined by confirmation of correct sensor application on the chest, transmission of data, and successful device shipping processes. Assessment of validity was analyzing collected data on continuous walking, and daily Timed Up and Go gait test and balance tests by participants at home, correlating with clinical standard of Expanded Disability Status Scale (EDSS) and functional sub scores done in clinic within three months of participation. Weekly MS-related symptoms questionnaires were completed for the secondary outcome.

RESULTS

The study was stopped after the initial 14 participants were recruited. By the end of week 2, all 14 patients had daily 8-hour data on walking. Only 4 patients completed daily gait and balance tests. There was adherence to weekly questionnaires by all 14 participants.

CONCLUSIONS

The study provided preliminary information that the process was logistically feasible, however the study protocol needed re-evaluation to increase participant adherence. Although continuous walking data were sufficient, lack of adherence to gait and balance testing prompted re-evaluation of the study protocol, and further planned analysis of clinical and functional scores was not done.

Supervisor: Dr. Penny Smyth

Proinflammatory mediators-induced localized insulin resistance (IR) in airway epithelial cells

Khadija Alzahrani and Harissios Vliagoftis
Supervisor: Harissios Vliagoftis

INTRODUCTION

Airway inflammatory diseases have been associated with hyperglycemia even in non-diabetic patients, and insulin resistance (IR) was previously hypothesized to play a role in the development of asthma and allergy. IR drive altered metabolism and mitochondrial functions. TNF and IL6 proinflammatory mediators cause impaired insulin signalling and IR in multiple cell types. TNF-induced insulin receptor substrate (IRS) phosphorylation at Ser307 and IL-6 induced SOCS3 both mechanisms blunt insulin signalling. We hypothesized that exposure of airway epithelium to TNF and/or IL6 results in localized insulin resistance and cause impaired mitochondrial metabolic changes.

METHODS

Primary normal human bronchial epithelial (NHBE) cells treated with TNF or IL6 for multiple time points. That was followed by insulin or no insulin for control conditions. Western blot used to detect Akt phosphorylation, TNF-induced pIRS Ser307, and IL6-induced SOCS3. IL6-induced SOCS3 mRNA was tested using quantitative real-time PCR.

RESULTS

NHBE treatment with TNF 10ng/ml for 30min or 1hr showed increase TNF-induced pIRS Ser307 the change was significant at 1hr. Using insulin 0.5 ug/ml for 30 min in 1hour TNF treated cells did not reduce Akt activity. However, stimulation with same dose of insulin for 5 minutes in 1hour TNF treated cells result in reduction of Akt activity in a pilot experiment. IL6 treated NHBE cells showed increased SOCS3 mRNA and protein release in a pilot experiment.

CONCLUSIONS

We showed significant increase in pIRS Ser307 which is well established as a leading cause of IR in TNF treated NHBE cells. Next, we are looking forward to translate the impaired insulin signalling in TNF treated airway epithelium to show insulin-related mitochondrial metabolic changes. This project will help build up the knowledge to look at airway allergic inflammation as disease of immunity and metabolism and understand the risk of metabolic disorders in asthmatics.

Supervisor: Dr. Harissios Vliagoftis

The association between access to medical care (physicians and nurse practitioners) and impact on resident outcomes: A retrospective cohort analysis

Krittika Bali, Adrian Wagg, Andrea Gruneir
Supervisor: Dr. Andrea Gruneir

INTRODUCTION
The nursing home population is comprised of a vulnerable, medically complex cohort, yet little is known about the kind of medical care they receive and the implications for quality outcomes. The goal of this thesis project is to understand those practice sensitive outcomes.

METHODS
This project used data from the Translating Research in Elder Care (TREC) longitudinal study and the routinely collected Resident Assessment Instrument – Minimum Data Set version 2.0 (RAI-MDS 2.0) to test the association between the availability of physicians (MD) and nurse practitioners in nursing homes (NHs) and clinically-relevant resident outcomes of antipsychotic medication (APM) use without indication of psychosis, physical restraint use, hospitalization and emergency department (ED) transfers, and polypharmacy issues. Eight models were created using a logistic regression model to show the association between access to a physician and nurse practitioner and resident outcomes.

RESULTS
The sample consisted of 10,888 residents across 92 facilities, 277 units reported a physician or NP visited daily and 318 units reported that the physician or NP could be reached when needed. Following adjustment for multiple confounding variables, there were no associations between either measure of access and any of the resident outcomes; however, wide confidence intervals on several estimates. For example, association between having NP visits and APM use (OR= 1.18, 95% CI: 0.56-2.53), NP visits and physical restraint use among residents (OR=2.08, 95% CI: 0.26-2.10) and MDs (OR=1.42, 95% CI: 0.54-3.75) should be noted. Associations between hospitalization and ED transfers and having visits with either an MD or NP at the unit level (OR=1.17, 95% CI: 0.46-3.10) and polypharmacy and visits by either NP or MD (OR=1.37, 95% CI: 0.64-2.93) should also be noted.

CONCLUSIONS
Limited research in this area renders investigating the provision of medical care in nursing homes and understanding relevant resident outcomes that shape the overall well-being of residents.

Supervisor: Dr. Andrea Gruneir

Persistent dyspnea after COVID-19 is not related to cardiopulmonary impairment

Rhys Beaudry, Andrew Brotto, Rhea Varughese1, Stephanie de Waal, Desi Fuhr, Ronald Damant, Giovanni Ferrara, Grace Lam, Maeve Smith, Michael Stickland
Supervisor: Dr. Michael Stickland

INTRODUCTION
Up to 53% of individuals who had mild COVID-19 experience symptoms for >3-months following infection (Long-CoV). Dyspnea is reported in 60% of Long-CoV cases and may be secondary to impaired exercise capacity (VO2peak) as a result of pulmonary, pulmonary vascular, or cardiac insult. This study examined whether cardiopulmonary mechanisms could explain exertional dyspnea in Long-CoV.

METHODS
A cross-sectional study of participants with Long-CoV (n=28, age 40±11 years, 214±85 days post-infection) and age- sex- and body mass index-matched COVID-19 naïve controls (Con, n=24, age 41±12 years) and participants fully recovered from COVID-19 (ns-CoV, n=14, age 37±9 years, 198±89 days post-infection) was conducted. Participants self-reported symptoms and baseline dyspnea (modified Medical Research Council, mMRC, dyspnea grade). Participants underwent a comprehensive pulmonary function test, cardiopulmonary exercise test, exercise diffusing capacity measurement, and rest and exercise echocardiography.

RESULTS
VO2peak, pulmonary function and cardiac/pulmonary vascular parameters were not impaired in Long- or ns-CoV compared to normative values (VO2peak: 106±25 and 107±25%predicted, respectively) and cardiopulmonary responses to exercise were otherwise normal. When Long-CoV were stratified by clinical dyspnea severity (mMRC=0 vs. mMRC?1), there were no between-group differences in VO2peak. During submaximal exercise, dyspnea and ventilation were increased in the mMRC?1 group, despite normal operating lung volumes, arterial saturation, diffusion capacity and indicators of pulmonary vascular pressures.

CONCLUSIONS
Persistent dyspnea after COVID-19 was not associated with overt cardiopulmonary impairment or exercise intolerance. Interventions focusing on dyspnea management may be appropriate for Long-CoV patients who report dyspnea without cardiopulmonary impairment.

Supervisor: Dr. Michael Stickland

Letting Go of Control: Experience and Involvement of Parents of Young Adults with Inflammatory Bowel Disease Transitioning from Pediatric to Adult Care

Allison Bihari, Dr. Cynthia Seow, Dr. Karen J Goodman, Dr. Eytan Wine, Dr. Karen Kroeker
Supervisor: Dr. Karen Kroeker

INTRODUCTION

Parents of patients with a pediatric diagnosis of inflammatory bowel disease (IBD)are typically active participants in their child's care by arranging appointments and medication pickups, while also managing financial and emotional challenges associated with chronic disease. As their child transitions from pediatric to adult care, parents need to step back and transfer disease management responsibility to their child. Within the literature, the difficulties that parents face during this period has not been adequately described; therefore, the study objective was to ascertain what parents of a child with IBD experience when their child transitions from pediatric to adult care.

METHODS

Participants from Edmonton and Calgary, Alberta were recruited for semi-structured interviews using purposive sampling. Inclusion criteria were having a child with IBD who: transitioned to adult care during 2018-2020; was diagnosed for at least a year prior to transitioning and participated in the patient arm of this study. We further excluded parents if they had another child with a chronic disease other than IBD. Interviews were transcribed verbatim and analyzed concurrently with data collection by latent context analysis.

RESULTS

We conducted 13 semi-structured interviews. Table 1 summarizes characteristics of participating parents. Main themes related to feelings about transition were sadness (n=5) and fear (n=7), though two parents mentioned neutral feelings. Parents were involved in their child's adult care through disease management (n=11), logistics of care (n=6), and indirect involvement (n=7). Themes related to parents' reasons for involvement included parents' feelings (n=5) and children's circumstances (n=4).

CONCLUSIONS

The results suggest that parents of children with IBD typically experience negative feelings about their child's transition. Reasons for parental involvement included parents' feelings and their perceptions of their child's circumstances. By consulting parents on their experience, interventions can be designed to counsel and support parents during the transition of responsibility for disease management to their child.

Supervisor: Dr. Karen Kroeker

Table 1. Demographics of parents who participated in semi-structured interviews

Demographics	Total N	n (%)
Parents	13	
Relationship to Child		
Mother		13 (100)
Father		0 (0)
Child's Living Situation		
Lives with parent		5 (38.5)
Does not live with parent		8 (61.5)
Highest Education Level Attained		
High school		5 (38.5)
Certificate		2 (15.4)
Diploma or undergraduate degree		5 (38.5)
Master's degree		1 (7.7)
Child's Sex		
Female		8 (61.5)
Male		5 (38.5)
Number of Other Children		
1		3 (23.1)
2		7 (53.8)
3		3 (23.1)
Occupation Field		
Administrative, business, finance, and management		6 (46.2)
Entertainment		1 (7.7)
Health		2 (15.4)
Other:		
IT service dispatcher		1 (7.7)
Stay at home mom		1 (7.7)
Long term disability		1 (7.7)
Day home provider		1 (7.7)

Inhalant use among pulmonary function testing (PFT) laboratory referrals

Ruojin Bu, Anne Hicks, Les Hagen, Yazid Al Hamarneh, Bo Pan, Ben Vandermeer, David Pawluski, Dilini Vethanayagam
Supervisor: Dr. Dilini Vethanayagam

INTRODUCTION

While the rates of cigarette smoking have declined in Canada, inhaled cannabis (IC) and vaping are on the rise, particularly among adolescents and young adults. Exposures to these inhalants can increase the risk of developing impaired lung function over time. PFT laboratories provide assessments for determining the presence and severity of impairment. Data from the PFT reference laboratory for Northern Alberta within Alberta Health Services was used to assess the prevalence and factors associated with different types of inhalant use.

METHODS

Referrals to the PFT laboratory affiliated with University of Alberta/Stollery Hospital over a 24-month period spanning January 2020 to December 2021 in individuals 5 years of age and older were included. Descriptive statistics were used to summarize demographic and clinical characteristics. Logistic regression models were used to identify factors that are associated with inhalant use at univariate and multivariate levels.

RESULTS

Total of 5281 individuals were captured, mean age 45.5 ± 22.8 years, 50.1% male, 82.7% Caucasian. One third or 33.7% reported current or prior use of inhalants; of these, 82.6% reported cigarettes, 9.3% reported IC, and 4.5% reported vaping; 88.8% used only one type of inhalant, and 75.5% endorsed quitting. In both univariate and multivariate analyses, cigarette had statistically significant association, with respectively, increased age, increased body mass index, male, chronic obstructive pulmonary disease, and preoperative assessment as indications for testing. A significant relationship was observed between reduced IC use and respectively, cystic fibrosis and post-lung transplantation as reasons for referral. The association between vaping and younger age was of statistical significance.

CONCLUSIONS

Identification of the prevalence and factors associated with specific inhalant can help direct further targeted interventions from healthcare providers, public health, and regulatory bodies in reducing long-term adverse health consequences implicated in cigarettes, IC use and vaping.

Supervisor: Dr. Dilini Vethanayagam

Asbestosis requiring lung transplantation in a hairdresser: an occupational exposure to comb through

Ruojin Bu, MD, Lakshmi Puttagunta, MD, Bryce Laing, MD, Mitesh Thakrar, MD, Alim Hirji, MD, MSc
Supervisor: Dr. Alim Hirji

INTRODUCTION
Asbestos is a group of fibrous mineral silicates known for tensile strength, chemical and thermal stability. At the height of its use, asbestos was found in over 3,000 applications worldwide. It is not widely known that asbestos was used in hair dryers as insulation and had been found in several types of talcum powder. Canada banned asbestos-containing products in 2018 given the health hazards associated with asbestos use. Asbestosis is a form of pulmonary fibrosis caused by an inflammatory response to the inhalation of excessive asbestos fibers. We present a case of asbestosis requiring lung transplantation in a hairdresser whose only significant asbestos exposure was asbestos-containing hair dryers and talcum powder.

CASE SUMMARY
A previously healthy 60-year-old male presented with progressive exertional dyspnea and an abnormal chest radiograph. He worked as a hairdresser from the 1980s to 2000s. High-resolution chest computed tomography demonstrated a probable usual interstitial pneumonia pattern and calcified pleural plaques. He had an exposure history to moldy hay and was empirically treated for chronic hypersensitivity pneumonitis with glucocorticoids but with no improvement. As his disease progressed, he was evaluated and subsequently underwent successful double lung transplantation. Pathology of his explant revealed asbestosis.

DISCUSSION
Most cases of asbestos-related diseases occurring in the developed world today stem from the historical use of asbestos. While modern hair dryers and talcum powder are prohibited from containing asbestos, asbestos-related lung disease continues to occur due to prolonged latency periods from initial exposure until diagnosis. Our patient's diagnosis of asbestosis was felt unlikely during pre-transplant evaluations because of the largely unrecognized occupational exposures for hairdressers prior to asbestos bans.

CONCLUSION
It is important to recognize hairdressers as an at-risk occupation for asbestos-related lung disease, so that proper identification and surveillance can be performed, as well as to ensure appropriate reporting and compensation.

Supervisor: Dr. Alim Hirji

Virtually-Delivered Mindfulness-Based Stress Reduction for Adults with IBD: A Feasibility Trial

Kaitlyn Chappell, Diana Meakins, Melanie Marsh-Joyal, Karen J Goodman, Jean-Michel Le Mélledo, Karen Kroeker
Supervisor: Dr. Karen Kroeker

INTRODUCTION

Patients with inflammatory bowel disease (IBD) are more likely to have mental health comorbidity such as anxiety and depression. Healthcare professionals are using mindfulness-based interventions, such as Mindfulness-Based Stress Reduction (MBSR), more frequently to reduce stress and improve the quality of life of people with chronic disease. Because it can be delivered virtually by a psychiatrist to a group, MBSR could be an efficient use of physician time and healthcare resources in Alberta.

METHODS

The study is designed as a single-arm pilot feasibility trial. The treatment will be delivered virtually via Zoom by MBSR-qualified psychiatrists to participant groups of 8-16 over the course of 8 weeks. Participants will be expected to attend one 2.5-hour group session each week, complete 30-45 minutes of daily practice, and attend one full-day session between week 6 and 7. Before beginning MBSR, participants will complete an initial screening to establish the presence of stress indicators as well as to ensure there is no need for further psychiatric intervention. The primary study outcome is feasibility. Secondary outcomes include stress indicators at baseline, when treatment ends, and 6-months post-treatment. These will be compared across the 3 time points. Participants will also complete the Adverse Childhood Experience (ACE) questionnaire so the study can assess whether childhood adversity modifies the effect of treatment on stress indicator levels.

RESULTS

One group of 7 participants has started MBSR. The median age of participants is 35 (IQR: 28.5-41.5). Of the 7 participants, 6 are female (85.7%) and 1 is male (14.3%). 4 participants (57.1%) have a diagnosis of Ulcerative Colitis and 3 (42.9%) have a diagnosis of Crohn's Disease. Median PHQ-SADS score before treatment is 12.3 (IQR: 6.3-18.3). Recruitment is ongoing.

CONCLUSIONS

Supervisor: Dr. Karen Kroeker

Table 1: Outcome Measures and How They Will Be Evaluated

Outcome measure	Primary or secondary outcome	Evaluation
Recruitment	Primary	Number of participants referred will be compared to the number of participants enrolled. Reason for declining to participate will be noted.
Attendance	Primary	Number of weekly MBSR sessions attended will be recorded.
Compliance	Primary	Average number of home practice minutes completed per day will be recorded.
Attrition	Primary	Number of participants who do not complete the program will be recorded. MBSR considered not completed if more than 2 sessions are missed or the weekend session is not attended.
Adverse childhood experience	Secondary	Adverse Childhood Experience questionnaire. Addresses abuse, neglect, and household dysfunction.
Change in IBD Clinical Indices	Secondary	Harvey Bradshaw Index or Partial Mayo Score
Mindfulness	Secondary	Mindful Attention Awareness Scale
Anxiety and Depressive symptoms	Secondary	Patient Health Questionnaire Somatic, Anxiety, and Depression Symptoms (PHQ-SADS)
Quality of Life	Secondary	Short Inflammatory Bowel Disease Quality of Life
Self-compassion	Secondary	Self-Compassion Scale-Short Form

FOXO1 transcription factors regulate Toll-like-receptor 3 in airway epithelial cells.

Nadia. M. Daniel & Harissios Vliagoftis
Supervisor: Dr. Vliagoftis

INTRODUCTION

Airway epithelium is the first defense mechanism of the respiratory system against microbial and other environmental insults that enter the body through inhaled air. In patients with asthma, bacterial or viral infections are the main causes for exacerbations and contributors to disease progression. Airway epithelial cells (AECs) can exacerbate airway inflammation in asthmatics though many mechanisms including through activation of Toll- like-receptors 3 (TLR3) during viral infections.

One transcription factor that has been associated with regulation of inflammation is the Forkhead Box protein O1 (FOXO1). Furthermore, FOXO polymorphisms are associated with asthma and COPD. AECs express FOXO1, but little is known about the functional significance of this expression. Our overarching objective is to study the role of FOXO1 in the airways. We hypothesized that FOXO1 regulates airway inflammation in the airways through TLR3 signaling.

METHODS

The biological effects of FOXO1 were studied in airway epithelial cell line BEAS-2B and human bronchial epithelial cells (NHBE). FOXO1 mRNA expression was silenced in BEAS-2B cells using shRNA lentivirus. FOXO1 was overexpressed by transfecting BEAS-2B with a plasmid expressing constitutively active FOXO1. BEAS-2B and NHBE were stimulated with TLR3 ligand PolyIC and FOXO1 inhibitor AS1842856.

RESULTS

FOXO1 knockdown was confirmed with qPCR, Western Blot and Immunofluorescence. Silencing FOXO1 expression in BEAS-2B reduced TLR3 gene expression. Inhibition of FOXO1 activity showed a decrease in TLR3 expression in BEAS-2B and NHBE. Whereas overexpressing FOXO1 in BEAS-2B increased TLR3 mRNA and protein expression. Stimulation with PolyIC increased mRNA expression of TLR3 targets IL8 and IL6, but this increase was reduced when FOXO1 was knocked down.

CONCLUSIONS

FOXO1 regulates TLR3 expression and downstream targets IL6 and IL8. Further research is needed to determine the mechanism of how FOXO1 regulates TLR3. Understanding the mechanisms of FOXO1 regulation in the airways may provide us with new therapeutic strategies to inhibit TLR3-mediated airway inflammation.

Supervisor: Dr. Vliagoftis

Cytokine production in allergen-stimulated airway epithelial cells shows time-dependent de novo synthesis of thymic stromal lymphopoietin

Marc Duchesne, Luke Gerla, Paige Lacy
Supervisor: Dr. Paige Lacy

INTRODUCTION

Asthma is a chronic inflammatory disease of the airways characterized by airway hyperresponsiveness and bronchoconstriction in response to allergens in atopic individuals. Few studies have examined cytokine expression in allergen-stimulated airway epithelial cells. We aim to study cytokine production from airway epithelial cells. We hypothesize that airway epithelial cell activation by allergens induces the production of newly synthesized cytokines.

METHODS

Airway epithelial cell cultures of BEAS-2B and NHBE were grown in 24-well plates on glass coverslips until they reached 70-80% confluency, then stimulated with cockroach extract (CE) or house dust mite (HDM) extract (5 ?g/mL) over time (0, 4, 8, and 24h). Cells were inhibited by protein synthesis inhibitors actinomycin D or verrucarin (10 ?g/mL). Stimulated cells were then fixed and immunolabeled with antibodies to their respective cytokines and imaged with an Olympus epifluorescence microscope.

RESULTS

In unstimulated cells (0h), baseline expression of intracellular IL-1?, IL-25 and TSLP was detected relative to isotype controls. After 8h of CE stimulation, intracellular levels of IL-1? and IL-25 decreased ($p < 0.01$). Conversely, TSLP increased in a time-dependent manner levels following CE or HDM stimulation, with significant differences over 0, 8 and 24h ($p < 0.01$). Actinomycin D and verrucarin A blocked increased intracellular TSLP stimulation ($p < 0.01$).

CONCLUSIONS

Our findings show that BEAS-2B and NHBE cells have detectable increases in intracellular TSLP levels following CE or HDM stimulation, concurrently with decreased IL-1? and IL-25. TSLP increases were inhibited by protein synthesis inhibitors, suggesting de novo synthesis of TSLP following CE and HDM stimulation. Such differential intracellular cytokine responses to allergens have not been reported in epithelial cells. These observations will contribute to our understanding of intracellular cytokine production in airway epithelial cells, and provide mechanistic insights into their trafficking and release.

Supervisor: Dr. Paige Lacy

Rejection rates of lung transplant patients with reduced renal function on a sirolimus based immunosuppression regimen: A cohort characterization study

David Fung, MD, Kieran Halloran, MD MSc, Rhea Varughese MD MSc, Jason Weatherald, MD MSc, Justin Weinkauf, MD, Dale Lien MD, Alim Hirji, MD MSc
Supervisor: Dr. Alim Hirji

INTRODUCTION
Lifelong immunosuppression is required in all lung transplant patients to prevent graft rejection. Tacrolimus, a calcineurin inhibitor (CNI), is commonly used for maintenance immunosuppression, but is associated with several side effects including nephrotoxicity. Sirolimus (SRL) is used as a renal-sparing agent but there is little literature examining adverse event rates of tacrolimus versus SRL in the context of a triple therapy regimen that includes mycophenolate mofetil and prednisone. This study aims to characterize the outcomes of patients who are switched to a SRL based regimen.

METHODS
A retrospective chart review of patients who underwent lung transplantation at the University of Alberta between August 2011 to August 2021 and were placed on a SRL regimen was performed. Primary outcome was acute cellular rejection rate, with secondary outcomes of survival, chronic lung allograft dysfunction (CLAD), proteinuria, trajectory of renal function, and triglycerides.

RESULTS
Eleven patients were placed on a SRL regimen while 16 patients on a tacrolimus/SRL combination. The median creatinine at time of transplant was 80 umol/L (eGFR 85 mL/min/1.73m2) and median creatinine at SRL initiation was 215 umol/L (eGFR 25 mL/min/1.73m2). Mean follow up was 5.95 years, during which time 22% had an episode of treated acute cellular rejection and 30% developed chronic lung allograft dysfunction. Improvement in creatinine at 6 months was seen in 28% of patients and persistent long-term Cr improvement was seen in 31% of patients. However, 15% of the cohort went on to require dialysis, while worsening proteinuria occurred in 47% of patients and worsening triglycerides in 56% of patients.

CONCLUSIONS
SRL can be considered for patients with CNI nephrotoxicity, as improvement in kidney function occurred in 30% of patients after switching to SRL, however rates of rejection, worsening proteinuria and triglyceridemia remain substantial and highlight the need for close monitoring of these patients.

Supervisor: Dr. Alim Hirji

A potential role for TSLP from airway epithelial cells in driving the systemic immune response to SARS-CoV-2

Luke Gerla, Subhabrata Moitra, Desmond Pink, Marc Duchesne, Eileen Reklow, Angela Hillaby, Tom Hobman, Irvin Mayers, Paige Lacy
Supervisor: Dr. Paige Lacy

INTRODUCTION

The epithelial-derived alarmin cytokine called thymic stromal lymphopoietin (TSLP) has been found to play a role in propagating proinflammatory responses during several viral respiratory infections such as respiratory syncytial virus, rhinoviruses, and influenza. Severe SARS-CoV-2 infections have been shown to be capable of initiating cytokines storms, potentially causing significant damage to the body. Little evidence has shown if TSLP is elevated during SARS-CoV-2 infection. In this study, we hypothesize that TSLP production in COVID-19 patients derives from SARS-CoV-2 infection of bronchial epithelial cells.

METHODS

Plasma samples were collected from healthy controls and SARS-CoV-2 positive patients (n=21) on the first date of hospitalization. Plasma TSLP levels were measured using an ultra-sensitive S-Plex human TSLP kit (LLOD=9.1 fg/ml).

Primary bronchial epithelial cells (NHBE) and patient bronchial brushings from patients undergoing elective bronchoscopy were infected with SARS-CoV-2 at multiplicity of infection (MOI) of 1, for 24h. After infection, cells were fixed and labeled using primary anti-TSLP and anti-SARS-CoV-2 spike protein. Images were collected using fluorescence microscopy. Mean intracellular fluorescence intensity was quantified using Volocity software.

RESULTS

Plasma TSLP levels in hospitalized COVID-19 patients were not significantly higher than uninfected controls (p=0.25). However, higher TSLP levels at the initial time of hospitalization were associated with increased period of hospitalization (p=0.03).

Increased TSLP immunofluorescence (p<0.001) was detected in NHBE cells (n=3) and three of seven patient bronchial brushings after 24h infection with SARS-CoV-2 compared to mock-infected samples.

CONCLUSIONS

Infection of primary airway epithelial cells with SARS-CoV-2 was associated with a significant increase in TSLP immunofluorescence. Therefore, lung epithelial cells may initiate immune signalling through the production and secretion of TSLP and suggests that this is an important mechanism that is amenable to therapeutic intervention in patients hospitalized with COVID-19.

Supervisor: Dr. Paige Lacy

A novel disease-modifying potential of native-PLGA nanoparticles in the treatment of Alzheimer's Disease (AD) pathology

Govindarajan Karthivashan, Qi Wu, Shuai Wang, Abhishek Dahal, Xiuju Li, Maryam Nakhaei-Nejad, Fabrizio Giuliani, Gopal Thinakaran and Satyabrata Kar.
Supervisor: Satyabrata Kar

INTRODUCTION
At present, there is no effective treatment for Alzheimer's disease (AD), the most prevalent cause of dementia affecting the elderly. Evidence suggests that enhanced levels and aggregation of beta-amyloid (Abeta) peptide contributes to neurotoxicity and progression of AD. Thus, preventing Abeta aggregation/toxicity may delay the onset/progression of AD. Recently, acidic poly(D, L-lactide-co-glycolide) (PLGA) nanoparticles, a class of FDA-approved biodegradable polymers, have been studied in delivering drugs/agents to the target areas in various diseases. The beneficial effects were attributed to conjugated drugs rather than PLGA nanoparticles. We recently reported that PLGA nanoparticles without any drug (native-PLGA) can suppress Abeta aggregation/toxicity. Thus, we evaluated the therapeutic potential of native-PLGA in the 5xFAD-Tg mouse model of AD and iPSC-derived AD neurons.

METHODS
In this study, 5xFAD-Tg and wild-type (WT) mice were administered intracerebroventricularly with native-PLGA or cerebrospinal fluid (CSF) for 28 days using mini-osmotic pumps. After treatment, animals (CSF-WT; PLGA-WT; CSF-5xFAD-Tg; PLGA-5xFAD-Tg mice) were subjected to cognitive tests, and their brains were processed for various anatomical, biochemical, and molecular analyses. In parallel, the effects of native-PLGA on Abeta -toxicity and its associated signaling were evaluated using iPSC-derived neurons from controls and AD patients.

RESULTS
Our results revealed that native-PLGA-treatment markedly attenuated cognitive deficits (spatial and recognition memory) and reduced various AD-related pathology including increased Abeta levels/deposits, oxidative-stress, and microglia activation in 5xFAD-Tg mice. Our RNA-seq data from the affected region showed that >2907 genes have been differentially altered in native-PLGA vs CSF-treated 5xFAD mice, some of which are related to the alleviation of the microglia-neuronal response. Furthermore, native-PLGA protects cultured iPSC-derived neurons of control and AD patients against Abeta mediated toxicity by attenuating signaling mechanisms including phosphorylation of tau-kinases and tau protein.

CONCLUSIONS
Collectively, these results provide unambiguous evidence that native-PLGA, by targeting different facets of the Abeta axis, can have unique therapeutic potential in the treatment of AD pathology.

Supervisor: Dr. Satyabrata Kar

Bio-physical studies

Native PLGA - inhibits spontaneous Aβ aggregation and triggers disassembly of aggregated Aβ$_{1-42}$ fibers

primary cultured neurons

Native-PLGA - protected mouse cultured neurons against Aβ-mediated toxicity by reducing tau-associated signaling mechanisms

←-Data under review-→

Native PLGA

Current data

iPSc-derived AD and control neurons

Native-PLGA protected iPSC-derived neurons from control and AD patients against Aβ-mediated toxicity by reducing tau-associated signaling mechanisms

5xFAD-Tg mouse model of AD

Native-PLGA treatment attenuated cognitive memory deficits; reduced - Aβ levels/deposition, plaque associated-microglia and oxidative stress in affected brain regions

Sepsis in the critically ill: An observational study of anatomic site of infection and microbiologic diagnosis

Keely M. Hammond, Wendy I. Sligl, Dawn Opgenorth, Tanis C. Dingle, John Conly, Sean M. Bagshaw, Justin Z. Chen
Supervisor: Dr. Justin Chen

INTRODUCTION

Sepsis affects many patients requiring the intensive care unit (ICU) and imposes a large mortality and cost burden on the health care system. Despite this, we do not fully understand the microbial ecology or prevalence of specific infection sites. Our primary objective is to describe the site of infection and microbiologic diagnosis in a cohort of patients admitted to the ICU with sepsis.

METHODS

We performed a secondary analysis of a cohort of adult patients admitted to a Canadian general systems ICU with sepsis. Patients were originally enrolled in a prospective, adaptive time series evaluating antimicrobial stewardship, procalcitonin, and rapid blood culture identification. From this cohort, anatomic site of infection and microbiologic diagnosis were ascertained. Sepsis was defined by the third international consensus definition; site of infection was defined by adapted CDC/NHSN surveillance definitions. A descriptive analysis was performed.

RESULTS

442 patients were included in this analysis. The median patient age was 60 years (IQR 50-69); 43% were female. Median Sequential Organ Failure Assessment score on ICU admission was 9 (IQR 6-12). 15% of the cohort did not have infection as the underlying diagnosis despite meeting sepsis criteria upon ICU admission. For those deemed to have an infection (n=372), pulmonary infections were most common (55%), followed by intra-abdominal (20%), skin/soft tissue (9%), genitourinary (8%), bloodstream (3%), bone and joint (2%), cardiovascular (2%), and central nervous system (1%). A microbiologic diagnosis was found in 74% of patients: 39% polymicrobial, 11% Escherichia coli, 10% Staphylococcus aureus, 8% respiratory viruses, 4% Streptococcus pneumoniae, and 28% other organisms.

CONCLUSIONS

In our cohort, most ICU patients admitted with sepsis had pulmonary infection. Intra-abdominal, skin/soft tissue, and genitourinary infections were also common. 74% of our patients had one or more causative organisms identified on microbiologic testing, higher than generally found in prior literature.

Supervisor: Dr. Justin Chen

Cultivating Wellness in Internal Medicine Residency Through Resident Led Seminars

Yiming Huang, Amanda Stanton, Kevin Lee, Dominic Mudiayi, Steven Katz
Supervisor: Dr. Steven Katz

INTRODUCTION

Burnout is a state of exhaustion related to chronic workplace demands. Without appropriate management, burnout is associated with poor health outcomes for physicians and their patients. Among Internal Medicine residents, previous literature reports 75% have experienced burnout. With increasing recognition towards the importance of preventing burnout, residency programs are instituting initiatives to improve wellness. Within the University of Alberta Internal Medicine residency program, we implemented "Wellness Rounds". Our study serves as a pilot proof-of-concept for this initiative towards improving resident wellness.

METHODS

On a quarterly basis, Wellness Rounds were held as seminars by and for Internal Medicine residents, with no staff physicians present. The organizers chose wellness related topics, created short presentations, then facilitated small-group discussions. Standardized surveys were distributed to attendees before and after each seminar. Likert scales quantified each participant's agreement to factors related to burnout and wellness.

RESULTS

The study period occurred from March 1, 2019 to December 1, 2021. Six Wellness Rounds were held. Each seminar had 20-40 residents in attendance. Mann-Whitney U test was used to compare pre- and post-seminar responses. Wellbeing was measured as a score out of 10 and demonstrated significant improvement post-session; mean 6.19 before vs. 6.72 after ($p=0.039$). Factors that did not demonstrate significant change after sessions included mood, demeanor, stress coping, clinical performance, energy, and social engagement. 71% of residents indicated improvement or significant improvement to their global wellness afterwards.

CONCLUSIONS

Wellness Rounds were well received by Internal Medicine Residents at the University of Alberta. Our pilot study serves as a proof-of-concept for our initiative that offers private spaces to discuss topics related to wellness and burnout. Further studies will expand the analysis to include a control group of residents who have never attended. We will also improve on the format of existing sessions by identifying the best topics and frequency of sessions.

Supervisor: Dr. Steven Katz

IMPACT OF DIABETES ON POST LIVER TRANSPLANT OUTCOMES

Muhammad Imran Suliman, Juan G. Abraldes, Rahima A. Bhanji.
Supervisor: Rahima Bhanji

INTRODUCTION

Metabolic Syndrome (MS) in Liver transplant (LT) candidates has an impact on long-term outcomes including post-LT morbidities {cardiovascular (CVD) and renovascular complications} and poor graft and patient survival. There is a paucity of studies assessing the impact of Diabetes Mellitus (DM) post-LT on graft or patient survival.

METHODS

Adults who underwent their first LT between 2016 to 2020, at the University of Alberta, were analyzed. Data for pre-LT DM (DM type, glycated hemoglobin levels (HBA1c), and pharmacotherapy), CVD, and chronic renal disease were reviewed.

RESULTS

A total of 338 patients were analyzed; those with pre-LT DM (23%) and without it (77%) were similar in terms of sex and race. Patients with pre-LT DM were more likely to have NASH cirrhosis (35% vs. 10%; $p < 0.001$) and HCC (52% vs. 24%; $p < 0.001$). Pre-LT median HBA1c was available for 77% of the patients and was 5.8 [5.1, 7.1]. More than half (54%) were on insulin and 60% were on metformin.

Pre-LT DM patients were more often diagnosed with hypertension, dyslipidemia, MS and pre-LT CVD. Following LT, HBA1c was available for 72% at 1 year (median 7.0 [6.1, 7.7]). De novo DM occurred in 10 (3.9% of the) patients. There was a trend to increased CVD in patients with DM (15% vs. 8%; $p = 0.08$). Patients with pre-LT DM were more likely to have CKD at 6 and 36 months (Table #1).

Having pre-LT DM did not have a significant impact on rejection, graft or patient survival. However, patients with pre-LT DM were more likely to die from renal complications (2.5% vs 0 %; $p = 0.05$).

CONCLUSIONS

Pre-LT DM was present in 23% of the patients and de novo DM only occurred in 3.9% of patients. Presence of pre-LT DM was associated with presence of CKD, but did not impact graft or patient survival.

Supervisor: Rahima Bhanji

Appendix #1
Table #1

Demographics	No pre-transplant Diabetes (n=259)	Pre-Transplant Diabetes (n=79)	p-value
Sex -males	164 (64%)	57 (72%)	0.18
Caucasian	196 (75%)	56 (71%)	0.69
Etiology	No Pre-LTx DM	Pre-LTx DM	p-value
Hepatitis B (HBV)	9 (3%)	3 (4%)	1.00
Hepatitis C (HCV)	50 (19%)	20 (25%)	0.27
Alcohol Liver Disease (ALD)	50 (19%)	11 (14%)	0.32
Non-Alcoholic Steatohepatitis (NASH)	25 (10%)	28 (35%)	<0.001
Autoimmune Liver Disease (AILD)	67 (26%)	10 (13%)	0.01
Hepatocellular Carcinoma (HCC)	62 (24%)	41 (52%)	<0.001
Acute Liver Failure (ALF)	39 (15%)	4 (5%)	0.02
Other	19 (7%)	3 (4%)	0.43
Complications	No Pre-LTx DM	Pre-LTx DM	p-value
Hepatorenal Syndrome (HRS)	44 (17%)	6 (8%)	0.05
Immunosuppression	No Pre-LTx DM	Pre-LTx DM	p-value
Corticosteroids	57 (26%)	19 (25%)	1.00
Tacrolimus	210 (95%)	68 (91%)	0.15
Sirolimus	82 (37%)	23 (31%)	0.33
Cyclosporine (CsA)	3 (1%)	2 (3%)	0.60
Mycophenolate Mofetil (MMF)	219 (99%)	74 (99%)	0.44
Cause of Death (COD)	No Pre-LTx DM	Pre-LTx DM	p-value
Renal	0 (0%)	2 (1%)	0.05
Graft Reject/Disease Recurrence	3 (1%)	2 (2%)	0.33

Malignancy	5 (2%)	0 (0%)	0.59
Infection	6 (2%)	2 (2%)	1.00
Cardiovascular Disease (CVD)	1 (0%)	1 (1%)	0.41
Other	4 (1%)	0 (0%)	0.58
Unknown	1 (0%)	1 (1%)	0.41
Pre-LT Comorbidities	No Pre-LTx DM	Pre-LTx DM	p-value
Hypertension	36 (14%)	28 (35%)	<0.001
Dyslipidemia	5 (2%)	13 (16%)	<0.001
Metabolic Syndrome (MS)	1 (0%)	18 (23%)	<0.001
Cardiovascular Disease (CVD)	36 (14%)	28 (35%)	<0.001
Post LT Comorbidities	No Pre-LTx DM	Pre-LTx DM	p-value
De Novo Hypertension	10 (4%)	5 (6%)	0.35
De Novo Dyslipidemia	3 (1%)	3 (4%)	0.14
De Novo Diabetes Mellitus	10 (4%)	Not applicable	
Cardiovascular Disease	21 (8%)	12 (15%)	0.08
Chronic Kidney Disease CKD (at 6 months)	72(32%)	35 (45%)	0.04
Chronic Kidney Disease CKD (at 12 months)	101 (45%)	43 (56%)	0.11
Chronic Kidney Disease CKD (at 36 months)	34 (30%)	20 (51%)	0.02
Peripheral Vascular Disease (PVD)	4 (1%)	1 (1%)	0.08
Outcomes	No Pre-LTx DM	Pre-LTx DM	p-value
Rejection	37 (14%)	11 (14%)	1.00
Mean Patient Survival Time in Years	4.8 ±0.09	4.5 ± 0.16	0.61
Mean Graft Survival in Years	4.9 ± 0.09	4.6 ± 0.13	0.79

Quality Indicators relevant to the care of older adults in various settings: A systematic review of reviews

Karimi-Dehkordi, Mehri; Hanson, Heather; Wagg, Adrian
Supervisor: Dr. Adrian Wagg

INTRODUCTION

Healthcare systems need to ensure the effectiveness, equity, and efficiency of services to ensure that older adults' regarding standard of care can be met and areas requiring further improvement can be identified.

Objectives: To identify a comprehensive set of quality indicators (QIs) to measure the quality of care for older adults in the community-care, continuing-care, and acute-care settings.

METHODS

A systematic search was conducted in October 2020 to identify any type of review studies published between 2010 and 2020, using six electronic databases and Google Scholars. The CADIT and TRIP Pro databases were used to identify the grey literature, and the Google search engine was utilized to identify the official websites of governments, healthcare organizations, and agencies that compiled or generated reports and guidelines about QIs related to the quality of older adults' care in various settings. The Joanna Briggs Institute critical appraisal checklist and the CRAAP test were used to appraise the methodological quality of peer-reviewed studies and the grey literature, respectively.

RESULTS

Of 4530 peer-reviewed articles identified through the systematic databases search and the literature identified via other methods, 13 peer-reviewed review studies and 44 grey literature were included in the analysis. A total of 4052 QIs were identified. The majority (40.13%) of the indicators were relevant to seniors & continuing care; The percentage of QIs pertinent to acute-care and community settings were 31.43% and 25.56%, respectively. Half of the QIs (51%) were related to the process domain. In total, 39 focus areas were identified. The three most frequent focus areas were the end of life/palliative care, neurocognitive conditions, and appropriate prescribing.

CONCLUSIONS

A comprehensive list of QIs classified based on their focus areas and either as a structure, process, or outcome domain measure serves as a resource for assessment of the quality of care for older adults within various settings.

Supervisor: Dr. Adrian Wagg

SORE6 reporter as a novel tool to decipher cancer stemness and disease relapses in acute myeloid leukemia

Justine Lai, Chuquan Shang, Raymond Lai, Joseph Brandwein, Peng Wang
Supervisor: Dr. Peng Wang

INTRODUCTION
Despite the recent therapeutic advances for acute myeloid leukemia (AML), most patients die from disease relapse which occurs shortly after the initial remission. Clearly, the biology underlying AML relapses needs to be better understood. The concept of cancer stem cells has been applied to explain AML relapses, but research has been hindered by the lack of experimental models.

METHODS
SORE6, an engineered reporter that emits green fluorescence when embryonic stem cell proteins are expressed and active, was successfully used to detect and isolate cancer stem-like cells (CSL's) in several cancers. Following lentiviral transduction of SORE6 into two AML cell lines, we purified SORE6+/SORE6- subsets using flow cytometry. These two cell subsets were subjected to biological/biochemical assays to assess their relative tumorigenicity, chemosensitivity and autophagic flux. The relative contribution of SORE6+/SORE6- cells in the regeneration of cytarabine (AraC)-treated cells was assessed using barcode labeling.

RESULTS
Compared to SORE6- cells, SORE6+ cells resembled CSL's, being more tumorigenic (hanging drop assay, 35 versus 75%, p=0.006) and resistant to AraC (19 versus 63 nM at 50% inhibition, p=0.0005) and Venetoclax (18.8 versus 39.6 nM at 50% inhibition, p=0.005). Large-scale oligonucleotide array studies showed that SORE6+ cells expressed significantly higher levels of key pro-autophagic markers (such as ULK2) than SORE6- cells. Preliminary results from experiments using barcoded SORE6+/SORE6- cells suggest that the SORE6+ subset is the major contributor to the regeneration of AraC-treated cells. Based on the differential protein expressions between SORE6+/SORE6- cells identified in our study, immunohistochemistry comparing the initial and post-treatment patient bone marrow samples is underway to clinically validate our model.

CONCLUSIONS
Our data supports that the dichotomy of SORE6+/SORE6- is a useful experimental model in delineating the contribution of CSL's to disease relapses in AML patients. Future studies using this novel model may yield promising therapeutic targets.

Supervisor: Dr. Peng Wang

The association between maternal glucose levels on gestational diabetes screening tests and future cardiovascular outcomes

Authors: Xinyun (Christie) Liang, Deliwe Ngwezi, Anamaria Savu, Padma Kaul, Roseanne O. Yeung
Supervisor: Dr. Roseanne Yeung

INTRODUCTION
There is little real-world data examining the association of maternal glucose levels in pregnancy and development of hypertension and cardiovascular disease.

METHODS
Retrospective cohort study of females aged 12-54y with singleton pregnancies, completed at ≥ 29 weeks of gestation from 1 Oct/2008 to 1 Dec/2018, followed until 31 Mar/2019. Females were stratified by glucose levels in the 50-g glucose challenge test (GCT) as well as by 75-g oral glucose tolerance test (OGTT) subtypes (normal OGTT, elevated fasting plasma glucose only (EF), elevated post-load glucose only (EPL), or elevation in both fasting and post-load glucose (Combined)). Primary outcome was development of hypertension >120 days postpartum, secondary outcome was development of cardiovascular disease. Time to development of hypertension was modelled using Cox proportional hazard models
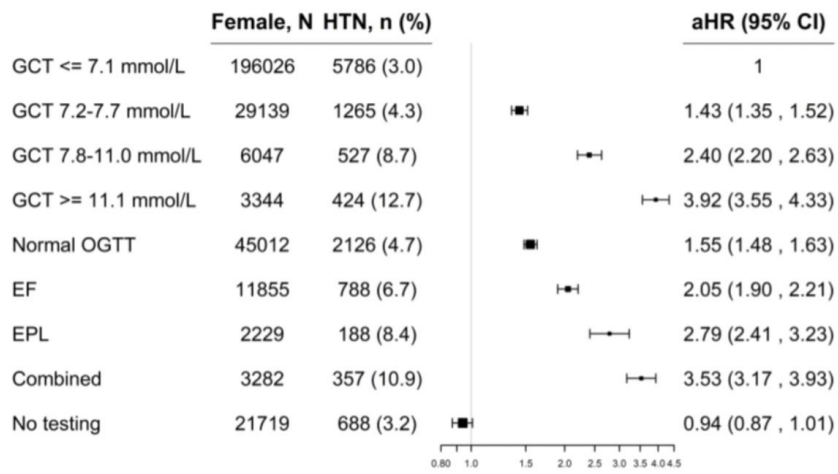
RESULTS
Of 318 653 females, 92.1% had a GCT, 18.5% had GCT+OGTT, and 1.1% had OGTT only. Mean follow up time was 5.6 years, 12 149 (3.8%) developed hypertension, and 2978 (0.9%) developed cardiovascular disease. Every 1 mmol/L increase in glucose in the GCT increased risk of subsequent hypertension (aHR (95% CI): 1.19 (1.18, 1.20)). Among those who underwent OGTT, combined group conferred highest risk (reference: GCT≤ 7.1 mmol/L, aHR (95%CI): EPL 2.05(1.90, 2.21); EF 2.79(2.41, 3.23); Combined 3.53(3.17, 3.93)).

CONCLUSIONS
Gestational GCT and OGTT associate with subsequent development of hypertension. Cardiovascular disease rates remained low, which was reassuring given the duration of follow up. These findings may help identify higher-risk females who should be targeted for postpartum cardiovascular risk development and earlier intervention.

Supervisor: Dr. Roseanne Yeung

Figure 1

	Female, N	HTN, n (%)		aHR (95% CI)
GCT <= 7.1 mmol/L	196026	5786 (3.0)		1
GCT 7.2-7.7 mmol/L	29139	1265 (4.3)		1.43 (1.35 , 1.52)
GCT 7.8-11.0 mmol/L	6047	527 (8.7)		2.40 (2.20 , 2.63)
GCT >= 11.1 mmol/L	3344	424 (12.7)		3.92 (3.55 , 4.33)
Normal OGTT	45012	2126 (4.7)		1.55 (1.48 , 1.63)
EF	11855	788 (6.7)		2.05 (1.90 , 2.21)
EPL	2229	188 (8.4)		2.79 (2.41 , 3.23)
Combined	3282	357 (10.9)		3.53 (3.17 , 3.93)
No testing	21719	688 (3.2)		0.94 (0.87 , 1.01)

0.80 1.0   1.5   2.0   2.5 3.0 3.5 4.0 4.5

Differential Effects of Plakoglobin Expression on the Oncogenic Properties of p53 Conformational and Contact Mutants

Tiffany Lo, Parnian Alavi, Nadia Jahroudi, Manijeh Pasdar
Supervisor: Nadia Jahroudi

INTRODUCTION

Plakoglobin is a dual cell adhesion and signaling protein that generally acts as a tumor suppressor. We have shown that one mechanism by which plakoglobin acts as a tumor suppressor is via its interaction with the tumor suppressor and transcription factor p53. p53 plays major roles in the maintenance of genome stability and in signaling networks that regulate tumor development and metastasis. p53 is mutated in 50 % of all cancers and 90% of metastatic tumors. The majority of *TP53* mutations are missense and in the DNA binding domain (DBD). The mutant p53 (mp53) may lose tumor suppressor properties and/or gain oncogenic function (GOF). GOF mutants interfere with p53-DNA interaction and are classified into conformational (change wild-type p53 conformation) or contact (affect amino acid residues that are directly involved with DNA interaction). We showed that plakoglobin interacted with several mp53s, restoring their *in vitro* tumor/metastasis suppressor activities. Here, we compared the effect of plakoglobin on restoration of tumor suppressor activity of conformational p53R175H (arginine 175 to histidine) and contact p53R273H mutants.

METHODS

Plakoglobin and p53 deficient H1299 cells were transfected with p53 (wild-type, R175H, R273H) without or with plakoglobin and assessed for their *in vitro* tumorigenic properties and expression of several p53 target genes.

RESULTS

The results showed that plakoglobin interacted with all three forms of p53 similarly. However, it was significantly more effective in reducing the *in vitro* tumorigenic properties of p53-R175H conformational mutant. Consistent with this observation, changes in the levels of target gene involved in cell growth, migration, and invasion were more drastic in p53-R175H- plakoglobin cells relative to that of p53-R273H- plakoglobin transfectants.

CONCLUSION

These results suggest that plakoglobin binding to p53R175H may restore the WT-conformation in this mutant and induce phenotypic changes that are more reflective of p53-wild-type properties.

Supervisor: Nadia Jahroudi

Cardiomyocyte-Specific Nuclear PKM2 Provides a Molecular Platform to Stabilize the Gata-4/6 Transcription Factors and Promote MDM2-Mediated p53 Degradation; Implications for Heart Failure

Maria Areli Lorenzana-Carrillo, Keshav Gopal, Nicole Byrne, Bruno Saleme, Saymon Tejay, Subhash Das, Yongneng Zhang, Alois Haromy, Farah Eaton, Michelle Mendiola Pla, Dawn Bowles, Jason Dyck, John Ussher, Evangelos Michelakis, Gopinath Sutendra
Supervisor: Dr. Gopinath Sutendra

INTRODUCTION
Pyruvate Kinase M2 (PKM2) is a glycolytic enzyme that can translocate to the nucleus and regulate different transcription factors (TF). Although its function has been studied extensively in cancer, its biological role in the heart and specifically terminally differentiated adult cardiomyocytes remains unresolved.

METHODS
Transverse aortic constriction (TAC) banding model was used to assess the levels and modifications of PKM2 during heart failure (HF). CM-specific PKM2-deficient and CM-specific Trim35 overexpressing mice were generated to evaluate the biological role of PKM2/Trim35 in adult CM. Human Dilated Left Ventricle biopsies were used to translate mechanistic findings to a clinical setting.

RESULTS
Here we show that nuclear PKM2 (S37P-PKM2) in cardiomyocytes interacts with several pro-survival or pro-apoptotic transcription factors, including Gata-4, Gata-6, and p53. Cardiomyocyte-specific PKM2-deficient mice developed age-dependent dilated cardiac dysfunction and had decreased levels of Gata-4/6, but increased levels of p53, compared to control Cre (+) hearts. Mechanistically, we found that nuclear PKM2 can prevent caspase-1 dependent cleavage Gata-4/Gata-6, while also providing a platform for Mdm2-mediated ubiquitination of p53. In a preclinical heart failure model, nuclear PKM2, along with Gata-4/6 levels decreased, but p53 levels increased (compared to sham controls). Loss of nuclear PKM2 was ubiquitination-dependent and associated with the induction of the E3 ubiquitin-ligase TRIM35. Cardiomyocyte-specific Trim35 overexpression mice had decreased S37P-PKM2 and GATA-4/6, along with increased p53 levels (compared to littermate controls) and had similar cardiac dysfunction to cardiomyocyte-specific PKM2-deficient mice. In a small but well-characterized cohort of patients with dilated left ventricles, we found a significant increase in TRIM35 levels, and this was associated with a decrease in S37P-PKM2, Gata-4/6 levels, but an increase in p53 levels, compared to non-failing control ventricles.

CONCLUSIONS
This study provides insight into a previously unrecognized biologic role for PKM2 in providing a molecular platform for transcription factors essential for preserving cardiac survival.

Supervisor: Dr. Gopinath Sutendra

The link between changes in mitochondrial function and divergent evolution of lifespan in the bean beetle (Acanthoscelides obtectus)

Mast, H. E., Holody, C. D., ?or?evi?, M., Savkovi?, U., Blier, P. U., Lemieux, H. L.
Supervisor: Dr. Hélène Lemieux

INTRODUCTION

Mitochondria produce the energy necessary for cell life, but changes in mitochondrial function can cause varied production of reactive oxygen species, oxidative damage to macromolecules, and altered longevity. As a result, it is important to understand how specific differences in mitochondrial oxidative phosphorylation (OXPHOS) pathways and control vary with age, and how these traits adjust when selecting for different longevities.

METHODS

Here we measured OXPHOS capacity and mitochondrial content (citrate synthase (CS) activity) at three time points (1, 5 and 8 days old) in males and females of two bean beetle (Acanthoscelides obtectus) lines selected for short (E, average life of 9 days in mated beetles) and long (L, average life of 13 days in mated beetles) life for over 250 generations. OXPHOS capacity was evaluated for the NADH (through complex I), the succinate (through complex II), and the proline (directly through the Q junction) pathways, as well as complex IV. Threshold plots with azide were also performed to measure the excess capacity of complex IV.

RESULTS

The flux control ratio, normalizing a specific pathway to the maximal OXPHOS capacity through all pathways, was increased for the succinate pathway in the L line compared to the E line, and the reverse was observed for the NADH pathway. The effect was more pronounced in males compared to females. In males, the complex IV excess capacity was also higher in the L line compared to the E line at day 1 (p=0.018), but not at day 5 (p=0.655). Furthermore, the L line seemed to have lower mitochondrial content than the E line in both sexes, as shown by CS activity (p<0.001 for both sexes).

CONCLUSIONS

These results suggest the presence of mitochondrial adaptation between populations with differing longevity and will lead to a better understanding of how selection of mitochondrial phenotype may favor increased lifespan.

Supervisor: Dr. Hélène Lemieux

Outcomes of Pregnancy in Women with Hypertrophic Cardiomyopathy: A Systematic Review

Muhammad Moolla, Anoop Mathew, Kevin John, Haran Yogasundaram, Waleed Alhumaid, Sandra Campbell, Jonathan Windram
Supervisor: Dr. Anoop Mathew

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is a genetic disorder that can be complicated by heart failure and sudden cardiac death. Pregnancy causes hemodynamic changes, which may be deleterious in patients with HCM. Existing cohort studies, analyzing maternal and fetal outcomes of pregnant HCM patients, are limited by small sample sizes. We performed a systematic review of maternal and fetal outcomes of pregnancy in patients with HCM.

METHODS

We performed a literature search for studies reporting maternal or fetal outcomes in pregnant women with HCM. Primary outcomes included maternal death, stillbirth, and fetal death. Secondary maternal outcomes included both sustained and non-sustained ventricular tachycardia (VT), atrial fibrillation, heart failure (HF), syncope, cesarean delivery, and preeclampsia/eclampsia. The secondary fetal outcome was preterm birth. We used a random-effects model to determine pooled incidences of outcomes.

RESULTS

We identified a total of 18 studies with 1624 pregnancies. The incidence of maternal death was 0.2%. The rates of sustained VT, any VT (including non-sustained), AF, HF, and syncope were 1% (0-1%), 6% (4-8%), 4% (2-6%), 5% (3-8%), and 9% (3-14%), respectively. Postpartum hemorrhage, preeclampsia/eclampsia, and caesarean section complicated 2% (1-4%), 4% (2-6%), and 43% (32-54%) of pregnancies, respectively. Neonatal death occurred in 0.2% of pregnancies. Stillbirth complicated 1% (95% CI, 0-3%) of pregnancies, whereas the incidence of preterm birth was 22% (95% CI, 18-25%).

CONCLUSIONS

Women with HCM considering pregnancy can be reassured that the risk of maternal, fetal, or neonatal death is low. However, they are at risk of several non-fatal cardiac and pregnancy-related complications.

Supervisor: Dr. Anoop Mathew

Improved Glycemia and Quality of Life Among Loop Users – Analysis of Real-World Data from a Single Centre

Amy Morrison, Kimberley Chong, Valerie Lai, Peter Senior and Anna Lam
Supervisor: Dr Peter Senior

INTRODUCTION

Despite being an unapproved method of insulin delivery, increasing numbers of people with type 1 diabetes (T1D) worldwide are choosing to use Loop, a form of Do-It-Yourself Automated Insulin Delivery system. We aimed to assess glycemic outcomes, safety and the perceived impact on quality of life (QOL), in a local Edmonton cohort of known Loop users.

METHODS

A cross-sectional study of adults with T1D using Loop was performed. Assessment of glycemic; HbA1c and time in range (TIR), and safety outcomes; hospital admissions and time below range (TBR), compared six months of Loop with the user's prior regulatory approved insulin delivery method. QOL outcomes were assessed using two validated instruments (INSPIRE, Diabetes Impact and Device Satisfaction (DIDS)) and semi-structured interviews.

RESULTS

24 adults with T1D, 67% female, median (IQR) age 33 (27.5-44.8), duration of diabetes 21.5 (17.3-32.0) years, with duration of Loop 18 (12-25) months. With Loop, median (IQR) HbA1c 7.1% (6.5-7.5) and TIR 76.5% (64.6-81.9); a significant improvement from prior therapy; 7.9% (7.6-8.3) and 58.0% (52.3-64.0), $p=0.001$ and $p=0.005$. With a non-significant reduction in TBR demonstrated; 3.0-3.9mmol/L 1.3% (0.6-2.4) vs 1.5% (1.0-2.8), $p=0.17$, and <3mmol/L 0.5% (0.5-0.5) vs 0.5% (0.5-0.8), $p=0.53$. Two episodes of DKA requiring hospital admission and no severe hypoglycaemia episodes occurred in a total of 470 patient-months of Loop use. Positive QOL impact, notably psychological impact of living with diabetes and greater flexibility in lifestyle, were explored in qualitative analysis and additionally demonstrated through median (IQR) INSPIRE 86.0 (79.5-94.6) out of 100, DI 2.8 (2.1-3.9) and DS 9 (8.16-9.43) out of 10.

CONCLUSIONS

In this first Canadian cohort of Loop users, through mixed-methods approach we demonstrate a beneficial impact of Loop use on both glycemic outcomes and QOL, with no safety concerns. A greater understanding of the lived experience of Loop use has been explored.

Supervisor: Dr Peter Senior

Figure 1. Glycemic outcomes; HbA1c and Time In Range (TIR) Pre-Loop and during Loop Use
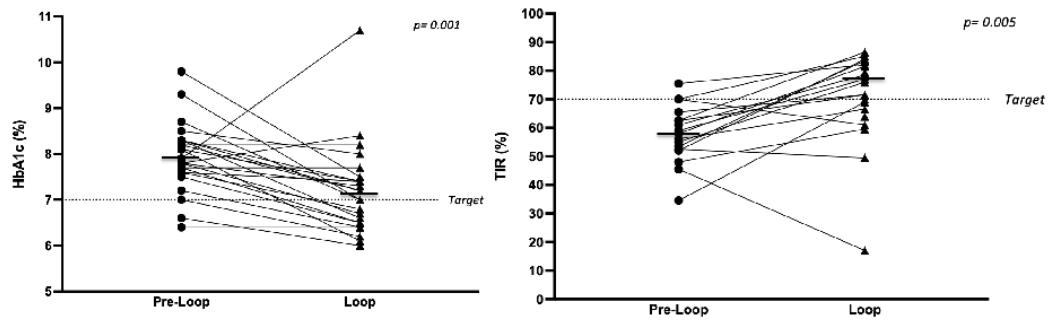
HbA1c and TIR Pre-Loop and with Loop use, median score line and individual values plotted. Demonstrating the number of individuals achieving a clinical target HbA1c <7% and TIR >70% at each timepoint. Wilcoxon signed rank test used to compare glycemic outcomes pre-Loop and with Loop use.

Analyzing the Specificity protein 1 (Sp1) interaction with Hepatitis B Virus (HBV)'s G4-quadruplex: a novel approach to target chronic HBV

Jelili Mustapha, Dr. Vanessa Meier-Stephenson
Supervisor: Dr. Vanessa Meier-Stephenson

INTRODUCTION

Globally, over 250 million people are chronically infected with Hepatitis B virus (HBV). Current therapeutic interventions only suppress HBV replication, thereby maintaining the chronic state of HBV. Covalently closed circular DNA (cccDNA) is responsible for HBV chronicity and persistence in the nucleus of infected cells; and current therapies cannot eliminate cccDNA.

Sp1 is a ubiquitous transcription factor that plays a crucial role in many cellular functions, including binding to GC-rich elements. Sp1 regulates the expression of HBV genes during viral infection. In HBV cccDNA, it binds in the pre-core promoter region where it interacts with the G4-quadruplexes. However, the nature of the interaction has never been elucidated.

METHODS

Using bacterial expression method, Sp1 will be produced as a recombinant glutathione-S-transferase protein and purified. The purified products will undergo binding studies with the folded purified HBV G4Q oligomers, using gel shift assays and microscale thermophoresis. Wild type and mutant G4Q oligomers will be trialled to assess the key nucleic acids involved in the interaction.

RESULTS

The Sp1 full length protein has been expressed and undergoing binding studies with the oligomers. Results of the binding studies will provide an insight into the interaction of G4Q and Sp1.

CONCLUSIONS

Information from these studies will be used to create a computational model that can be used to create a small molecule mimetic of Sp1 with the goal of selectively targeting the chronic form of HBV, the cccDNA.

Supervisor: Dr. Vanessa Meier-Stephenson

IRE1a-XBP1s pathway in mouse ACTH-producing pituitary tumor cells

Masahiro Nezu, Motoyasu Satou, Tae Nakano-Tateno, Constance Chik, Toru Tateno
Supervisor: Dr. Toru Tateno

INTRODUCTION
Cushing's disease is caused by adrenocorticotropic hormone (ACTH)-over producing pituitary adenoma that leads to manifestations of cortisol excess. If untreated, the five-year survival rate is 50%. Since surgery is curative in about 70% of patients, additional therapy is required to manage persistent or recurrent disease. As all current medical treatments have limited success in achieving disease control, there is an urgent need for novel effective therapies. The inositol requiring enzyme 1a (IRE1a)-X-box binding protein 1s (XBP1s) pathway is an important component of the endoplasmic reticulum (ER) stress response. This pathway is activated by the overload of immature protein in the ER and its elimination or repair can reduce ER stress. In this study, we aimed to clarify the association between Cushing's disease and the IRE1a-XBP1 pathway.

METHODS
We conducted in vitro experiments using AtT-20 cells derived from a mouse ACTH-producing pituitary tumor. To modify the IRE1a-XBP1s pathway, thapsigargin (ER stress inducer), STF08310 (IRE1a inhibitor), IRE1a siRNA and XBP1s expression vector were used. To cause ER stress by immature proopiomelanocortin (POMC), a precursor of ACTH, we used a mutant POMC (C28F) expression vector.

RESULTS
In AtT-20 cells, thapsigargin (2μM) promoted XBP1 activation whereas STF08310 (40μM) inhibited XBP1s activation, POMC production and cell proliferation. Similarly, XBP1s over-expression and IRE1a siRNA promoted and inhibited POMC production, respectively. In contrast, POMC siRNA suppressed IRE1a phosphorylation and cell proliferation. The mutant POMC (C28F) vector enhanced IRE1a phosphorylation and POMC production; in contrast, treatment with POMC (1-16 nM) had no effects.

CONCLUSIONS
In AtT-20 cells, our data indicate that immature POMC overproduction can cause ER stress response via the IRE1a-XBP1s pathway and stimulates cellular growth and POMC production, resulting in further activation of the IRE1a-XBP1s. Therefore, inhibition the IRE1a-XBP1s could represent a novel therapeutic target by correcting this vicious cycle in refractory Cushing's disease.

Supervisor: Dr. Toru Tateno

Effects of the loop diuretics furosemide on renal hemodynamics and synchronization among nephrons.

Shayan Poursharif, Shereen Hamza, Will Cupples, Branko Braam
Supervisor: Dr. Branko Braam

INTRODUCTION

Autoregulation of renal blood flow (RBF) among nephrons is synchronized via the tubuloglomerular feedback (TGF) mechanism. TGF mechanism controls macula densa solute delivery by adjusting afferent arteriolar diameter and GFR. Furosemide reduces loop of Henle sodium reabsorption, which increases macula densa sodium delivery and enhances TGF. Furosemide also inhibits macula densa sodium sensing by inhibiting NKCC2 transporters and inhibits TGF. We hypothesized that deactivating the TGF response by furosemide would impair synchronization among nephrons.

METHODS

Mean arterial pressure, RBF, heart rate, urine flow and GFR were measured in male Lewis rats (300-400 gr). Left kidney cortical perfusion was recorded using laser spackle imaging (LSI) and TGF synchronization assessed after frequency analysis. Following baseline, high dose furosemide was infused (10-30 mg/kg: n=8). Fluid loss was replenished by infusion of 0.9% NaCl matching urine loss. Mean phase coherence (PC), the magnitude of decay of PC and length constant associated with initial decay of TGF were used to assess synchronization.

RESULTS

Furosemide did not change MAP (101+10 to 105+39 mmHg, NS) or RBF (7.1+2.3 to 6.9+2.5 ml/min, NS). Right kidney GFR (1.10+0.22 to 1.27+0.27 ml/min, $P<0.05$) increased after furosemide, while left kidney GFR (1.06+0.22 to 0.92+0.16 ml/min, $P<0.05$) decreased. Furosemide strongly increased right (8+5 to 134+18 uL/min, $P<0.001$) and left (10+3 to 124+16 uL/min, $P<0.001$) kidney urine flow. Furosemide decreased the decay of PC (0.46+0.06 to 0.42+0.06, $P<0.05$) and length constant associated with initial decay of PC (-0.28+0.11 to 0.53+0.06, $P<0.001$). Furosemide did not affect average PC or the number of edges. No significant correlation was found between urine flow, RVR and GFR with parameters assessing synchronization.

CONCLUSIONS

High dose furosemide weakened synchronization among nephrons within lobules. However, it is likely that other mechanisms besides blocking the sensing step of the TGF system in the macula densa differentially affect synchronization among nephrons.

Supervisor: Dr. Branko Braam

m6A bimodal peak signature mediates acute selective stress Translation by specialized cytoskeletal ribosomes via a MARK4-FTO-PKR axis

Bruno Saleme, Saymon Tijay, Maria Areli Loranzana Carrillo, Aristeidis Boukouris, Sotirios Zervopoulos, Adam Kinnaird, Gopinath Sutendra, and Evangelos Michelakis
Supervisor: Dr. Evangelos Michelakis

INTRODUCTION

Stress responses are temporal pathways that prioritize resources to ensure survival. A global shut down of protein translation, an early universal stress response, conserves energy but poses a challenge to selectively translate required stress response proteins (SRP). This suggests that specialized cellular machinery selectively translates SRP mRNAs bypassing the global suppression. While unique mechanisms, such as IRES and uORFs provide selective translation of proteins like c-Myc or ATF4, it remains unknown whether there is a global translation machinery relevant to SRPs regardless of the type of stress. Here we hypothesized that a novel translation machinery translates SRPs acutely after stress, and facilitates transport of translated proteins throughout the cell, perhaps linked to the cytoskeleton.

METHODS

Stable-Isotope Labeling of Amino acids in Cell-culture (SILAC), mass spectrometry, methylated RNA immunoprecipitation sequencing (meRIP-seq), immunoblots and qRTs in control versus stressed A549 cancer cells (UV, 2DG, Methionine deprivation).

RESULTS

We found that dynamic epi-transcriptomic n6-methyladenosine (m6A) mRNA modification is used as an SRP mRNA marker, allowing for their selective translation in microdomains attached on the cytoskeleton (? tubulin), consisting of specialized ribosomes as well as the m6A demethylase FTO and MARK4 and PKR. SRP mRNAs are characterized by a dual peak methylation pattern, downstream of their 3UTR start site, at a site that hosts the eIF2a kinase PKR that inhibits their translation prior to stress. FTO, which also binds at the same site, is activated via a T6 phosphorylation by MARK4 and removes this dual peak methylation signature, releasing PKR, removing its inhibitory effects, allowing the translation of SRPs.

CONCLUSIONS

A previously unrecognized, SRP mRNA recognition and translation system enables the translation of SRP mRNAs while non-SRP mRNA translation is inhibited, during the critical early stages of acute stress, when swift, energetically efficient and selective adaptive mechanisms are mostly needed, via MARK4-FTO-PKR axis on CS-linked ribosomes.
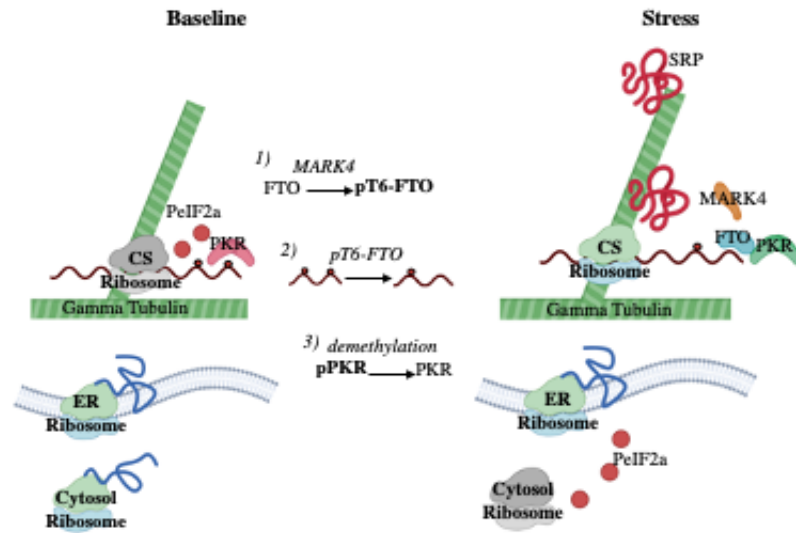
Supervisor: Dr. Evangelos Michelakis

Figure 1. Visual representation of CS-mediated SRP translation mechanism proposed. At baseline, cytosolic and ER ribosomes are actively translating transcripts while local PKR-mediated eIF2a phosphorylation along m6A peaks of SRPs maintains SRP translation suppressed in the CS ribosomal pool. After stress, eIF2a phosphorylation in the cytosolic ribosomal pool decreased translation in the cytosolic pool while MARK4-mediated phosphorylation of FTO on T6 activates the m6A peak demethylation along SRP mRNAs in the CS ribosomal pool, resulting in PKR inhibition and decreased eIF2a phosphorylation allowing for SRP translation to proceed on CS ribosomes. Gamma tubulin provides the platform for the localized binding and translation along the CS-ribosomes.

Novel automated hippocampal subfield volumetry throughout the entire long axis in patients with Alzheimer's Disease

Mujtaba Siddique and Trevor Steve
Supervisor: Dr. Trevor Steve

INTRODUCTION

Alzheimer's disease (AD) is the most common cause of dementia and is an emerging public health crisis with 150 million cases projected globally by 2050. Biomarkers are playing an emerging role in AD research - however, existing biomarkers have substantial limitations. Magnetic Resonance Imaging (MRI) holds advantages over existing biomarkers as it is non-invasive and does not involve exposure to ionizing radiation. In this project, we aimed to study a new automated method for hippocampal segmentation of MR images and compare the volume outputs to existing biomarkers and cognitive function.

METHODS

High resolution hippocampal MR Images (control (n= 351), mild cognitive impairment (MCI, n =238), and AD (n = 46)) acquired by the Alzheimer's Disease Neuroimaging Initiative (ADNI) were analyzed with an automated segmentation software (HippUnfold) to determine volumes for hippocampal subfields throughout the entire hippocampal long axis (Figure 1). Volumetric data were correlated with cognitive testing scores, cerebrospinal fluid, and positron emission tomography levels of amyloid and tau.

RESULTS

We found that novel automated long axis hippocampus segmentation with HippUnfold was feasible in subjects with MCI and AD. Furthermore, long axis-hippocampal subfield volumes were correlated with the severity of cognitive decline on neuropsychological test scores, as well as the severity of amyloid and tau deposition quantified with existing biomarkers.

CONCLUSIONS

MRI is a promising non-invasive biomarker for AD. The majority of existing automated segmentation protocols enable measurements of only the body of the hippocampus due to the complex curved anatomy of the hippocampal head and tail. Hippunfold is a novel automated software that labels these subfields throughout the entire hippocampus. Here we have demonstrated promising preliminary correlation between MRI-measured hippocampal volumes, existing biomarkers, and neuropsychological test scores. Automated MRI-based measurements of hippocampal subfields throughout the hippocampal long axis represents a promising and emerging biomarker for dementia research.
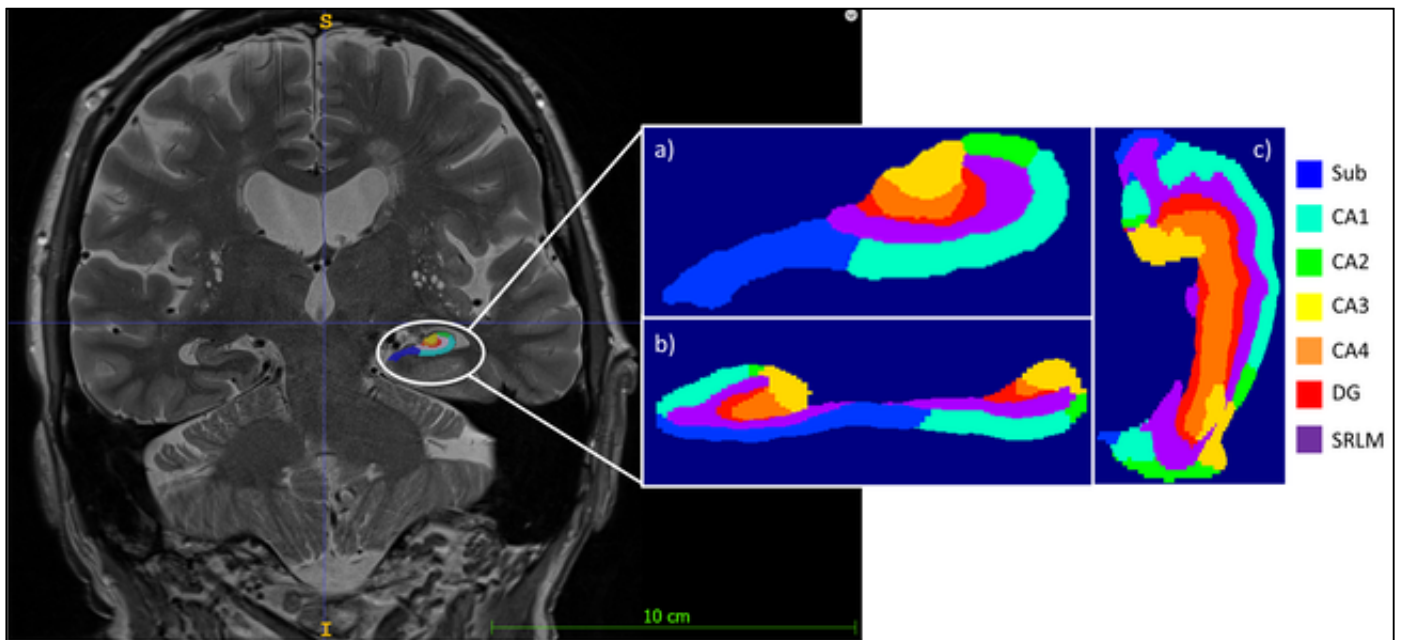
Supervisor: Dr. Trevor Steve

Figure 1. High resolution T2-weighted MR Images were processed with a novel automated segmentation software [Hippunfold] to measure hippocampal subfield volumes throughout the entire hippocampal long axis. Volumes were then compared with neuropsychological test scores, as well as CSF and PET biomarkers. Subfield labels are shown in the a) coronal plane, b) sagittal plane, and the c) axial plane. Sub= Subiculum, CA = Cornu Ammonis, DG = Dentate gyrus and SRLM=stratum radiatum, Lacunosum, and moleculare.

Effect of Immunotherapy and Chemotherapy on Removal of Indwelling Pleural Catheters in Non-small Cell Lung Cancer Patients with Malignant Pleural Effusions

Kaitlin Sparrow, Melissa Wang, and Pen Li
Supervisor: Dr. Pen Li

INTRODUCTION

Indwelling pleural catheters (IPCs) are a mainstay therapy for malignant pleural effusions (MPEs). Many patients treated with IPCs may eventually achieve pleurodesis and the IPC can be removed. It is important to patients how long they need to keep their IPC. We aimed to identify the effect that chemotherapy and immunotherapy have on IPC removal in patients with non-small cell lung cancer (NSCLC) associated MPEs.

METHODS

We reviewed adult IPC recipients with metastatic NSCLC at the Pleural effusion clinic at the Royal Alexandra Hospital from 2009-2020. Clinical data and treatment regimen when the IPC was in situ were recorded. We used logistic regression to assess the rates of IPC removal and Cox regression to assess the time to IPC removal.

RESULTS

232 patients met inclusion criteria with 248 IPCs reviewed. The overall pleurodesis rate was 42.7% with a median time to pleurodesis of 68 (IQR 38-140) days. Median time to death was 59 (IQR 28-125) days in patients who did not have IPC removed. In univariate analysis, when compared to patients who did not receive any treatment, immunotherapy (OR 3.30, CI 1.92-5.69), chemotherapy (OR 1.98, CI 1.04-3.79), and patients who received both immunotherapy and chemotherapy (OR 4.08, CI 1.47-11.31) were associated with higher rates of pleurodesis. In multivariate analysis, increased rates of pleurodesis were associated with an Eastern Cooperative Oncology Group performance status score of ?2 (OR 4.39, CI 2.03-9.47), the absence of distant metastasis (OR 1.91, CI 1.09-3.33), and immunotherapy (OR 2.34, CI 1.31-4.17). No variables were associated with earlier pleurodesis in univariate or multivariate analysis.

CONCLUSIONS

Treatment with immunotherapy is associated with increased rates of IPC removal in patients with NSCLC. Neither immunotherapy nor chemotherapy seem to be associated with shortened time to IPC removal in multivariate analysis.

Supervisor: Dr. Pen Li

Metabolic remodeling and mitochondrial biogenesis in primary biliary cholangitis is linked with betaretrovirus infection

Ning Sun, Steven Willows, Hussain Syed, Andrew Mason
Supervisor: Dr. Andrew Mason

INTRODUCTION

We have characterized a human betaretrovirus (HBRV) in patients with primary biliary cholangitis (PBC). PBC patients develop serum anti-mitochondrial antibodies (AMA) targeting pyruvate dehydrogenase complex-E2 (PDC-E2), which is aberrantly expressed in damaged cholangiocytes. We have demonstrated Koch's postulates in vitro by isolating HBRV and showing that viral infection leads to increased expression of PDC-E2 in healthy cholangiocytes. Preliminary proteomic, metabolomic and functional mitochondrial studies of PBC cholangiocytes reveals metabolic remodeling with evidence of glycolysis, inhibition of oxidative phosphorylation with compensatory mitochondrial biogenesis. Aims: We addressed the hypothesis that betaretrovirus infection mediates the metabolic remodeling observed in PBC cholangiocytes.

METHODS

RNAseq transcriptional and bioinformatic analyses were performed using (i) PBC whole blood vs healthy controls, (ii) PBC cholangiocytes vs other liver disorders, and (iii) cholangiocytes infected with purified betaretrovirus particles vs cholangiocytes controls.

RESULTS

By comparing all 3 datasets, we found evidence of hypoxia inducible factor 1 alpha (HIF-1) pathway activation, with increased transcription glycolytic enzymes, pyruvate dehydrogenase kinase (PDK), which inhibits PDC and oxidative phosphorylation. In PBC whole blood, patients had increased expression of all mitochondrial encoded genes with decreased nuclear encoded mitochondrial genes suggestive of mitochondrial inhibition, with increased mt-DNA and compensatory mitochondrial biogenesis, similar to PBC cholangiocytes. Following betaretrovirus infection of cholangiocytes, increased mitochondrial encoded genes transcription was observed at day 9, with a reduction in nuclear encoded mitochondrial genes by day 16, especially complex IV, with increased transcription of PDK1 and PDK3.

CONCLUSIONS

Metabolic remodeling triggered by betaretrovirus infection in cholangiocytes mimics the metabolic changes observed in PBC with HIF-1 pathway activation and mitochondrial biogenesis.

Supervisor: Dr. Andrew Mason
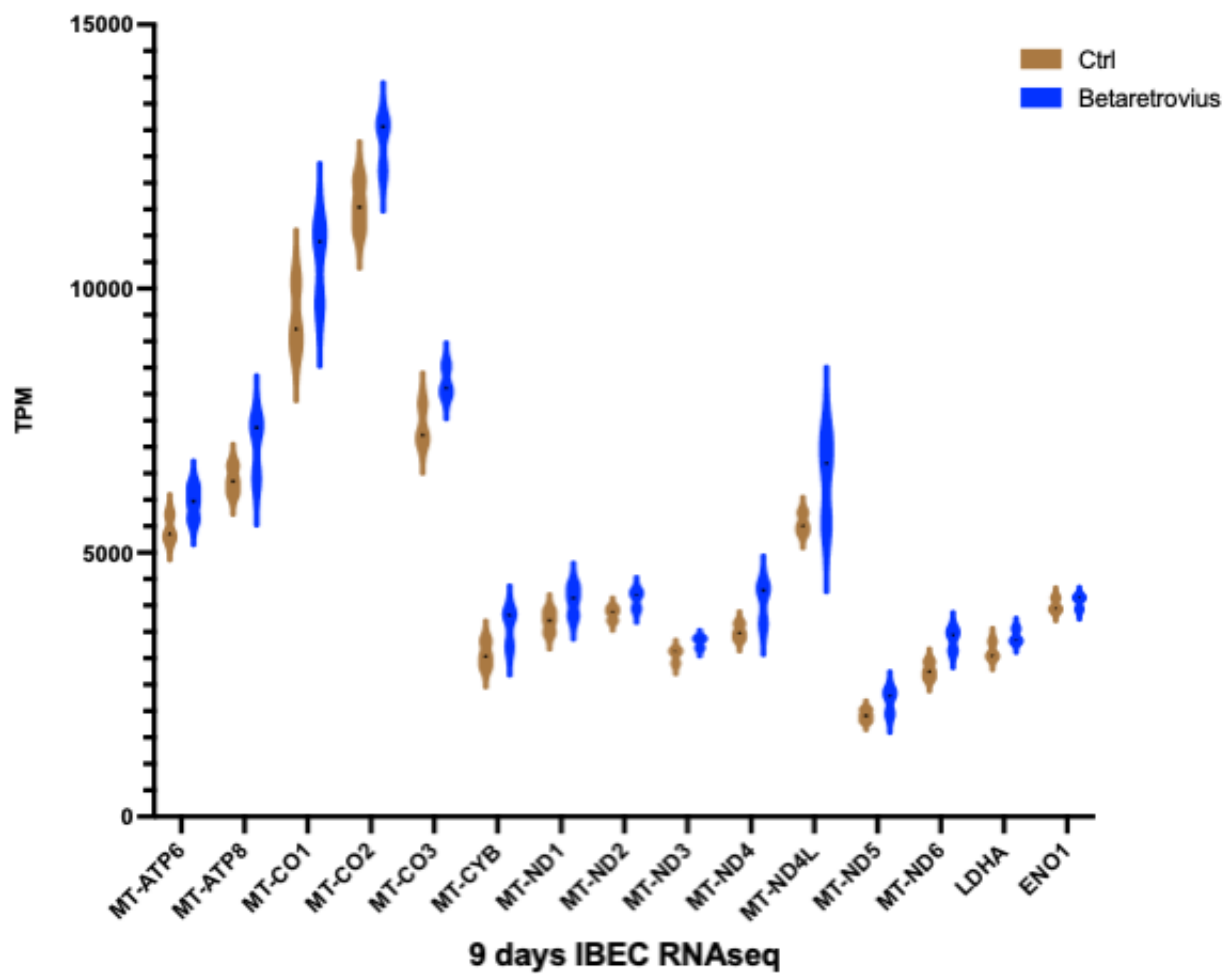
Figure 1 IBEC RNAseq following 9 days of betaretrovirus infection vs controls.
All transcriptions of mitochondrial encoded genes and glycolytic enzymes such as
LDHA and ENO1 were increased in IBEC after 9 days of betaretrovirus infection.

A critical contribution of cardiac myofibroblasts in RV failure and the role of UCP2 SNPs in the predisposition to RV decompensation in PAH

Yongneng Zhang, Maria Areli Lorenzana-Carrillo, Saymon Tejay, Yongsheng Liu, Alois Haromy, Gopinath Sutendra, Evangelos D. Michelakis
Supervisor: Dr. Evangelos D. Michelakis

INTRODUCTION

The compensatory stage in right ventricle hypertrophy (RVH) in pulmonary arterial hypertension (PAH) is much shorter than in left ventricle hypertrophy (LVH) in hypertension. Between 2 patients with the same degree of PAH one may have a much shorter compensated RVH (cRVH) stage than the other. We hypothesized that RV cardiac myofibroblasts (CMF) may contribute to these differences. Their ability to contract (stiffening), produce collagen and promote inflammation contributes to heart failure. Decreased mitochondrial calcium (mCa++) promotes CMF differentiation (from cardiac fibroblasts). Methylation of the mCa++ Uptake 1 (MICU1) and lack of UCP2 (a component of the mCa++ uniporter complex) activate CMF in the LV.

METHODS

In a rat PAH model (Monocrotaline-PAH), we measured the RV pressure from isolated perfused hearts and sarcomere shortening from isolated RV cardiomyocytes. In a cohort (n=25) of patients with pulmonary hypertension that had been treated with the same protocol for years and controlled for age/sex/duration of disease, the correlation between UCP2 loss-of-function SNPs and RV function was measured.

RESULTS

In isolated hearts, RV pressure is lower in decompensated RVH (dRVH) compared to normal RV, but in vitro there is no difference in cardiomyocyte sarcomere shortening between the two groups, pointing to potential detrimental role of RV CMF rather than contractile failure of RV cardiomyocytes. dRVH has much more CMF compared to normal RV. CMF from dRVH have increased MICU1 methylation and decreased UCP2 levels compared to normal RV fibroblasts. PAH patients with homozygotes for UCP2 SNPs have worse RV function compared to heterozygote or wild-type, despite similar PA pressures.

CONCLUSIONS

Our preliminary work suggests that RV CMF rather than RV cardiomyocytes may drive RV decompensation independent of RV afterload in PAH patients and this may be predicted by UCP2 SNPs that are relatively frequent in the population and have been shown to be associated with PAH outcomes (10-year survival, time to transplantation).

Supervisor: Dr. Evangelos D. Michelakis

A. Ex-vivo (Isolated perfused hearts)

Normal RV · dRVH

Basal RV pressure in two groups

B. In-vitro (Isolated cardiomyocytes)

Normal RV · dRVH

Basal sarcomere shortening in two groups

C

Normal RV · dRVH

Low Mag / High Mag — Vimentin, SMA, DAPI

50μm · 5μm

D

▼ sPHT n=7
□ PAH-UCP2-WT n=7
● (gray) PAH-UCP2 SNP-het n=6
● (red) PAH-UCP2 SNP-hom n=5

TAPSE (cm) vs mPAP (mmHg)

Figure 1. The differences between the normal RV and decompensated RV, and the role of UCP2 SNPs on RV function.

A. In isolated perfused hearts, decompensated RV has decreased RV pressure compared with normal RV. dRVH: decompensated right ventricle hypertrophy. RV: right ventricle. **, $p<0.01$ v.s. Normal RV.

B. In-vitro, No difference is shown in sarcomere shortening between cardiomyocytes from normal RV and decompensated RV.

C. Decompensated RV shows increased vimentin and smooth muscle actin (SMA) co-positive cells (*i.e.* cardiac myofibroblasts) compared to normal RV.

D. PAH patients with homozygotes for UCP2 SNPs (red dots) have worse RV function compared to heterozygote (gray dots) or wild-type (white squares), despite similar PA pressures. PAH: pulmonary arterial hypertension. TAPSE: tricuspid annular plane systolic excursion.

Quality Improvement Abstracts

A Quality Improvement Project to Enhance Adoption of the MyAHS Connect Patient Portal in Inpatient General Internal Medicine Settings

Dr. Ruojin Bu, Jesse Lafontaine, Chris Mayhew, Pamela Mathura, Dr. Robert Hayward
Supervisor: Dr. Robert Hayward

INTRODUCTION

A patient portal is a digital information service that can improve patient engagement and treatment adherence by providing individuals with secure access to their health record together with information about their care team, health services and communications. MyAHS Connect is a patient portal that launched with the Connect Care (CC) clinical information system at the University of Alberta Hospital in 2019. Use among hospitalized patients has been limited. We aimed to increase the percentage of active portal users on 5 General Internal Medicine (GIM) units by 10% over a 6 month period in conjunction with release of an inpatient-specific "day-at-a-glance" portal service.

METHODS

A multi-component intervention included four components: (1) Portal activation emails sent upon hospital registration from admitting, emergency department and GIM clinic settings; (2) Resident educational sessions and resources; (3) GIM-unit staff training and resources; (4) Development and socialization of CC clinical documentation templates exposing patients' portal use with embedded activation links. We evaluated the intervention using a CC dashboard tracking portal activation by location, as well as GIM-unit chart audits pre and post intervention.

RESULTS

The CC dashboard indicated an increase in active portal status across all sampled GIM units and the largest increase on a single unit was 6%. Comparison of pre to post intervention chart audits for the 5 GIM units revealed an increase in active portal status of 8%.

CONCLUSIONS

This is the first quality improvement project examining use of the MyAHS Connect patient portal by hospitalized patients. We identified a number of factors that promoted the use of patient portal as well as barriers to portal uptake. We found that staff education, patient education and public awareness are foundational elements that need to be further addressed. This information will help Alberta Health Services as it expands MyAHS Connect access in health care facilities.

Supervisor: Dr. Robert Hayward

Understanding Approaches to Empathy in Dermatologic Patient Care

Pamela V. Mathura MBA PhD(c) Madison R. Godfrey BSc, Kendra R. Martel MD, Zaheed Damani MD PhD, Marlene Dytoc MD PhD FRCPC
Supervisor: Dr. Marlene Dytoc

INTRODUCTION

Practice of empathy in medicine is advantageous to both patients and physicians, yet many physicians lack the tools to effectively convey and demonstrate empathy during patient interactions. The study objective is to determine physicians' perceptions of empathetic practices in a dermatology clinic and use these perceptions to identify actionable strategies for empathetic and efficient patient care.

METHODS

Using a qualitative design, a 2-hour virtual empathy educational program was utilized to provide awareness of empathetic actions. Focus group discussions and individually completed surveys were utilized to collect physicians' viewpoints.
Thematic analysis was used to identify themes inductively which supported the identification of empathetic interventions.

RESULTS

Twenty-one physicians (16 residents and 5 dermatologists) participated in the educational session. Four overarching themes were identified: (1) patient-centered communication techniques; (2) maintaining patient dignity, respect and comfort; (3) engaging in shared decision-making and (4) improving the patient waiting room experience. The intervention actions identified to encourage empathy were the following: (1) annual education regarding empathetic practices, (2) empathetic scripts and tip sheets for healthcare staff, (3) a patient welcome/orientation poster for waiting areas, (4) patient waiting time tracking labels, (5) provision of relevant informational resources pertaining to patient diagnoses and appropriate therapies, and (6) patient surveys assessing patient experience of empathy during the clinic visit to support continual improvement.

CONCLUSIONS

Providing empathetic education to physicians supported the identification of practical empathetic actions at various stages of the patient dermatology clinic visit.

Supervisor: Dr. Marlene Dytoc

Optimizing IV fluid therapy on medicine wards

Anastasia Howe, Vaishvi Patel
Supervisor: Dr Inka Toman

INTRODUCTION

Patients on medicine wards are frequently prescribed IV fluid therapy (IVFT), which can lead to complications, therefore, frequent reassessment is needed. Using diuretics and IV fluids at the same time is not considered optimal therapy in most cases.

Baseline chart audit in July 2021 (25 patients on 3 medicine units in the Sturgeon Community Hospital) indicated that a documented "stop time" in the electronic medical record (EMR) was rarely used (5% of patient orders) and 38.8% of patients receiving IVFT had unchanged order beyond 48-hours. Diuretic use at the same time as IVFT was noted in 22% of patients

METHODS

Multicomponent intervention was developed and implemented on 3 medicine wards. The intervention components included: (1) Staff surveys to raise awareness of the issue; (2) Educational presentation to all prescribers; (3) In person visit and discussion with prescribers onsite and electronic reminders placed by the nursing team ("sticky notes" in the EMR for cases with unchanged IVFT orders past 48 hours). To determine interventions effect chart audits were completed pre-intervention and post-intervention (tracking the number of un-reassessed orders, stop times on IVFT, simultaneous diuretic use and adverse events) and results were shared with the team for continuous encouragement in February 2022.

RESULTS

Number of unchanged IVF orders past 48 h decreased from initial 38.8% in July to 23% in Dec (post in person visit and "sticky note" implementation) and 17% in Feb (post feedback). Concurrent use of diuretics and IVT decreased from 22% in July to 12% in Dec and to 5% in Feb. Number of registered adverse events declined from 27.7% in July to 19% in December and to 16% in Feb. (Figure 1)

CONCLUSIONS

To promote sustainable IVFT optimization multimodal interventions were required such as standardized electronic communication, education, repeated encouragement, and feedback to staff
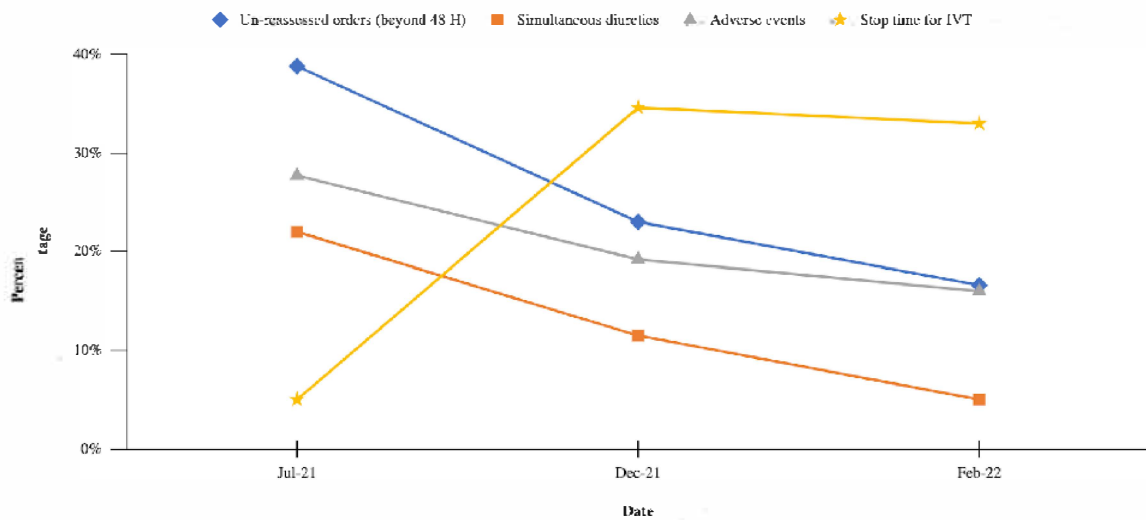
Supervisor: Dr Inka Toman

Figure 1: Changes in frequency of un-reassessed orders, stop time on IVFT orders, simultaneous diuretics use and adverse events over the course of the study. Timepoints and their corresponding activity:
July 2021- initial chart audit and prescriber and nursing staff surveys completed
August 2021- virtual education session on IVFT delivered to nursing staff and clinical assistants and mandatory stop time on IVF
October 2021- in-person visit to the site
December 2021- implementation of "sticky notes" and chart audit repeated
February 2022 - feedback shared with the staff and final chart audit completed

Evaluation of a patient-administered, physician supervised allergy patch test: A pilot study

Dr. John F Elliott, Divya Jha
Supervisor: Dr. John Elliott

INTRODUCTION

Allergic contact dermatitis is a frequent cause of itchy, painful rashes that can significantly impact a person's quality of life and ability to work. The COVID-19 pandemic has disrupted traditional physician-administered patch testing, which requires that each patient attend 3 clinic appointments. Patient-administered patch testing may reduce the financial and time burden of traditional patch testing, while still providing the necessary information for the identification of sensitizing allergens in 1 clinic appointment. Over 5 days, skin data is shared by the patient via standardized scoring forms and photographs, thus allowing the physician to identify in parallel the culprit allergen(s) before a final clinical assessment.

Our aims are to determine if patient-administered patch testing is comparable to physician-administered patch testing, and to identify improvements that will facilitate patient-administered patch testing in the home.

METHODS

This pilot study uses weekly test of change cycles to assess patient-administered patch testing. Our measures of interest include the proportion of patients who completed and were satisfied with patch testing, the rate of diagnostic concordance between physician and patient and the length of the final clinical assessment.

RESULTS

15 patients participated in this study. 14/15 patients successfully completed patch testing. At least 1 positive allergen was identified in 13/15 patients, and 75% of those allergens were identified by both physician and patient prior to the clinic assessment. Patients view patch testing as highly convenient and were satisfied with the degree of collaboration with the physician in diagnosing their skin problem. The length of the final clinical assessment remained 30 minutes long.

CONCLUSIONS

Patient-administered patch testing is readily completed by a subset of patients, and with a high degree of satisfaction. Preliminary data shows that patients tend to over-identify allergens. Further analysis will reveal if physician-supervised, patient-administered patch testing can be reliably incorporated into practice.

Supervisor: Dr. John Elliott

Determining Areas for Improvement: Sun safety Knowledge and Practices in Elementary School Children

Miriam Li, Navjeet Gill, Pamela Mathura, Marlene Dytoc
Supervisor: Dr. Marlene Dytoc

INTRODUCTION
Despite strong clinical evidence for the benefits of sun protection, less than 30% of young Canadians currently practice sun safety behaviors. Lack of early age sun protection is associated with an increased risk of melanoma and other skin cancers. Early interventions, by way of education and increased access, could increase adherence to sun safety practices in school children.

METHODS
The first Plan-Do-Study-Act (PDSA) included a single sixth grade class (n = 24). Baseline sun safety knowledge and habits were assessed with a combined knowledge & behavioural multiple choice questionnaire. Students then received a 30-minute presentation on sun safety. A repeat questionnaire was administered one week after the presentation. Gaps in knowledge and barriers to sun safety practices were assessed.

RESULTS
Students showed an 18.5% improvement in sun safety knowledge following administration of the presentation. We also identified a lack of access to sun-safety equipment during peak UV hours for most students, which played a large role in non-compliance. Almost all students were receptive to improving their sun-safety habits with increased access to sun-safety equipment.

CONCLUSIONS
These findings suggest that educational sessions help to improve sun safety knowledge, but do little for sustained behavioral change due to lack of access to sun safety equipment. These barriers to sun safety are targets for PDSA cycle #2: a school-wide sun safety campaign focused on improving access to sun safety equipment.
Dermatologist partnership in community education and continued community based interventions may support public behavior changes towards sun safety.

Supervisor: Dr. Marlene Dytoc