DEPARTMENT OF MEDICINE

RESEARCH

& QI DAY

FRIDAY, MAY 21, 2021
08:00 AM - 12:30 PM

The Department of Medicine Research
&
Edmonton Zone Medicine Quality Council (EZMQC)
Strategic Clinical Quality Improvement Collaborative (SCIC) Day

MAY 21, 2021. 08:00 AM

NARMIN KASSAM

Department of Medicine Chair

Welcome to the first virtual Research and Strategic Clinical Quality Improvement (QI) Day hosted by the Department of Medicine and the Edmonton Zone Medicine Quality Council. I am honoured and proud to support and highlight the depth and breadth of the quality of scientific and QI research from our faculty members and trainees during my first year as Department Chair. We have had quite the year! However, despite the profound impacts of multiple lockdowns and the waves of CoVID-19 cases on clinical service, our faculty members and trainees have continued to work tirelessly and diligently on a broad range of quality improvement and scientific research projects. With ~460 trainees consisting of graduate students, postdoctoral fellows, core internal medicine residents, senior subspecialty residents and fellows, their research fosters collaborations across multiple disciplines within the Department, Faculty, University and Alberta Health Services. In fiscal year 2020-21, our researchers successfully secured in total over $8.4 million in newly awarded tri-council (CIHR, NSERC and SSHRC) research funding. In 2020 our members had over 900 publications, some of which are first authored by our trainees and published in prestigious high-impact journals (i.e. Circulation Research, JAMA Internal Medicine, etc.) leveraging local, national and international awareness for the department. We are looking forward to hearing what they have been working on for the past couple of years.

I am also proud to announce the renaming of the Department of Medicine's Translational Research Fellowship Award to the Ballermann Translational Research Fellowship Award in honour of her 10 years of service as Department Chair. During Dr. Ballermann's tenure, she made it a priority to secure funds for this prestigious award to be offered annually to a trainee whose work best demonstrates translational research (basic or clinical).

I would also like to welcome our two keynote speakers: Dr. Jayna Holroyd-Leduc, Professor and Head of the Department of Medicine at the University of Calgary and Dr. Jennifer Medves, Professor, from Queen's University.

Narmin Kassam
Professor and Chair, Department of Medicine

TABLE OF CONTENTS

JAYNA M. HOLROYD-LEDUC MD

Keynote Speaker

*Professor, Department of Medicine
University of Calgary*

Dr. Jayna Holroyd-Leduc is an academic geriatrician, Professor and Head of the Department of Medicine at the University of Calgary and Alberta Health Services (AHS) Calgary zone.

Her research utilizes knowledge translation (KT) science to improve care for older adults. She is the University of Calgary Brenda Strafford Foundation Chair in Geriatric Medicine.

She plays a leadership role within the Canadian Frailty Network, and was previously an Associate Editor for the Canadian Medical Association Journal (2010-2020).

She is also the past UofC Head of the Division of Geriatric Medicine (2016-2020), past Medical Director of AHS Calgary zone Specialized Geriatric Services (2016-2020) and previous Scientific Director of the AHS Seniors Health Strategic Clinical Network (2012-2015).

Dr. Jennifer Medves RN, Professor, School of Nursing, Queen's University has a broad interest in healthcare quality teaching, research and service as well as nursing.

Prior to emigrating from the UK to Canada, she qualified as a nurse, midwife, and neonatal intensive care nurse. In Canada, she had many different clinical positions including as an air evacuation and outpatient oncology nurse. A graduate of the U of A MN and PhD program led to an academic career and she held an Ontario funded Career Scientist position for five years.

Dr. Medves was the Vice-Dean (Health Sciences), Director of the School of Nursing for ten years and is on leave and has been more focused on research and supervision of graduate students in the PhD HQ program. Total funding in excess of 7 million dollars has allowed her to pursue her research program – Sustaining Rural Healthcare Practice.

Interdisciplinary research, teaching and service has provided multiple opportunities to study healthcare at the federal, provincial and local levels and advocate for upstream planning and delivery of healthcare. She has served on multiple committees at the provincial and federal level to determine best practice for maternity care and interprofessional education.

JENNIFER MEDVES PhD, RN

Keynote Speaker

Professor, School of Nursing
Queen's University

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.

JUNIOR FACULTY MEMBERS

ANITA AU
ASSOCIATE CLINICAL PROFESSOR
GENERAL INTERNAL MEDICINE

Dr. Anita Au is a general internal medicine specialist who obtained her medical degree from the U of A and did her residency at McGill University. She has a community practice in Wetaskiwin and also does inpatient medicine at the Grey Nuns Hospital. She is the director of the Wetaskiwin Cardiac Rehabilitation Program. She also has an interest in clinical research with a focus on quality improvement and is the Quality Improvement Lead for the Department of Medicine at the Grey Nuns Hospital.

FRANCES CARR
ASSISTANT CLINICAL PROFESSOR
GERIATRIC MEDICINE

I joined the Division of Geriatric Medicine in 2015, & I am currently an assistant clinical professor. My clinical practice includes inpatient work on the Acute Care of the Elderly unit & with the consulting service at the UofA Hospital, & outpatient clinics at the Westview Health Centre & Kaye Edmonton Clinic. My predominant research interest is in Quality Improvement, with a particular focus on medication (in particular, benzodiazepines) deprescribing, and I am regularly involved in both conducting & supervising QI projects. I also created & implemented a QI curriculum into the geriatric residency program.

DARREN LAU
ASSISTANT PROFESSOR
GENERAL INTERNAL MEDICINE

Dr. Darren Lau is a general internal medicine physician. He completed his PhD in clinical epidemiology at the School of Public Health in 2012, & his MD in 2014, both at the UofA. This is his second year of practice. In addition to attending inpatient teaching & non-teaching internal medicine wards, he runs a half-day teaching clinic on Monday afternoons for patients with complicated diabetes and internal medicine concerns. This presentation of two projects - one on-going, and one proposed - will illustrate his research interests and methods, which can be broadly summarized as "Outcomes of Medical Care in Adults with Type 2 Diabetes".

MOHAMMED OSMAN
ASSISTANT PROFESSOR
RHEUMATOLOGY

Dr. Mohammed (Mo) Osman is a clinician scientist & Assistant Professor in the Division of Rheumatology. Since his recruitment, he has established the first microvascular clinic in western Canada & acts as the director of the systemic sclerosis (SSc) clinic at the UofA. He is also a founding member of the western Canada autologous stem cell transplantation for SSc (ASCT SSc) research group. He has been involved in COVID-19-related research at the UofA.

Dr. Osman's laboratory research is focused on understanding the altered mechanisms present in fibroblasts & immune cells in different forms of early SSc. He has established one of the largest early SSc cohorts in Canada which is utilized in his research.

Meeting at a Glace

8:00 AM	Welcome Address
8:05 AM	Keynote Speaker *(Scientific)*
8:45 AM	Oral Presentations
9:45 AM	Break
10:00 AM	Keynote Speaker *(Quality Improvement)*
10:35 AM	Oral Presentations
11:20 AM	Ballermann Translational Research Fellowship Award
11:40 AM	Closing Address

ScientificResearch Awards

SCIENTIFIC ORAL PRESENTATIONS AWARD WINNERS
$300

RUNNER UP AWARD WINNERS
$100

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 3 highest scoring abstracts in research and top 3 highest abstracts in quality improvement were invited to present an oral presentation.

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

PAST RECIPIENTS

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

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

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

PAST RECIPIENTS

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: Eight 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 TM 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 Zoom. 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, 13 residents from core and 23 specialty residents. 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 MSc in Medicine with a specialization in 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 of Medicine

8:05 AM   **Keynote Speaker (Scientific Talk)**
Dr. Jayna Holroyd-Leduc, Professor, Department of Medicine Head at the
University of Calgary
A Career Well Spent: advice to help guide you along your Career Path

ORAL PRESENTATIONS

8:45 AM   Yongneng Zhang, Graduate Student, Division of Cardiology
Supervisor: Evangelos Michelakis
*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*

8:55 AM   David Li, Graduate Student, Division of Pulmonary Medicine
Supervisor: Kieran Halloran
*Prognostic implications of abnormal left-right lung perfusion differential on routine
post-transplant ventilation-perfusion scans*

9:05 AM   Dylan Johnson, PGY2, Division of Dermatology
Supervisor: Mohammed Osman
*Nailfold capillaroscopy abnormalities correlate with disease activity in adult
dermatomyositis*

FACULTY PRESENTATIONS

9:15 AM   Dr. Mohammed Osman, Assistant Professor, Division of Rheumatology,
Department of Medicine
*Not all "scleroderma" is the same: understanding the different forms of early systemic
sclerosis (SSc)*

9:30 AM   Dr. Darren Lau, Assistant Professor, Division of General Internal Medicine,
Department of Medicine
Outcomes of Medical Care in Adults with Type 2 Diabetes

9:45 AM   **BREAK**

ORAL QI PRESENTATIONS

10:00 AM   **Keynote Speaker (Quality Improvement Talk)**
Dr. Jennifer Medves, PhD, Professor, School of Nursing, Queen's University
Quality Improvement Capability and Capacity Development

Oral Presentations

10:35 AM   Nazia Sharfuddin, PGY5 Division of General Internal Medicine
Advancing Health Equity during the COVID-19 Pandemic through Digital Medical Interpretation Platforms

10:45 AM   Harry (Chaocheng) Liu, PGY2, Division of Dermatology
Beyond Skin Deep: Case-based Online Learning Modules to Improve the Understanding of Multidisciplinary Care in Dermatology among Students

Faculty Presentations

10:55 AM   Dr. Anita Au, Associate Clinical Professor, Division of General Internal Medicine
Reducing Laboratory Test Ordering Overuse in General Internal Medicine Units at the Grey Nuns Community Hospital – A Quality Improvement Initiative

11:05 AM   Dr. Frances Carr, Assistant Clinical Professor, Division of Geriatric Medicine, Department of Medicine
Benzodiazepine deprescribing in the hospital setting

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

11:20 AM   **Announcement**
the Ballermann Translational Research Fellowship Award Winner

11:25 AM   **Oral Presentation**
the Ballermann Translational Research Fellowship Award Winner

11:40 AM   **Closing Remarks**
Dr. Narmin Kassam, Chair, Department of Medicine

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

Aburhass, Salah (Graduate Student)
Hypoxia- induced TIMAP Upregulation Promotes Tumor Angiogenesis through Attenuation of ALK1-mediated TIMAP Inhibition
Supervisor: Barbara Ballermann (Nephrology)

Alam, Arafat UI (Graduate Student)
Increased prevalence of age-related comorbidities and health service utilization among adult men with hemophilia A in Alberta, Canada
Supervisor: Haowei (Linda) Sun (Hematology)

Alavi, Parnian (Graduate Student)
Aging causes alterations in level and expression pattern of von Willebrand Factor in an organ-specific manner
Supervisor: Nadia Jahroudi (Hematology)

Albino, Larissa (Resident)
DESMOID FIBROMATOSIS DIAGNOSED IN A 27-YEAR-OLD MALE AFTER BEING MISTAKEN FOR A GASTROINTESTINAL STROMAL TUMOUR
Supervisor: Levinus Dieleman (Gastroenterology)

Alrohimi, Anas (Clinical Research Fellow)
Early direct oral anticoagulation therapy after ischemic stroke in patients with atrial fibrillation: An individual patient data meta-analysis

Alrohimi, Anas (Clinical Research Fellow)
International survey of physicians on approach to the timing of direct oral anticoagulant initiation after atrial fibrillation related stroke
Supervisor: Kenneth Butcher (Neurology)

Assaedi, Ekhlas (Resident)
Hereditary Spastic Paraplegia: Clinicogenetic Lessons from a Well-Defined Cohort
Supervisor: Oksana Suchowersky (Neurology)

Baaklini, Charbel (Graduate Student)
Microglia and monocyte-derived macrophage contribution in myelin debris clearance during remyelination
Supervisor: Jason Plemel (Neurology)

SCIENTIFIC ABSTRACTS
FULL ABSTRACTS ENCLOSED

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)

Bihari, Allison (Graduate Student)
Defining Transition Success for Young Adults with Inflammatory Bowel Disease
Supervisor: Karen Kroeker (Gastroenterology)

Cromarty, Taylor (Graduate Student)
Social inequity, gender, and Helicobacter pylori infection in Arctic Canada
Supervisor: Karen Goodman (Gastroenterology)

Duchesne, Marc (Graduate Student)
Time-dependent increases in alarmin-type cytokines in airway epithelial cells following allergen stimulation
Supervisor: Paige Lacy (Pulmonary Medicine)

Gerla, Luke (Graduate Student)
SARS-CoV-2 infection induces increases in intracellular alarmin-type cytokines in airway epithelial cells
Supervisor: Paige Lacy (Pulmonary Medicine)

Guo, Yimeng (Jimmy) (Resident)
TARGETING METABOLISM AS AN EMERGING THERAPEUTIC OPTION FOR INFLAMMATORY BOWEL DISEASE
Supervisor: Levinus A. Dieleman (Gastroenterology)

Johnson, Dylan (Resident)
Nailfold capillaroscopy abnormalities correlate with disease activity in adult dermatomyositis
Supervisor: Mohammed Osman (Rheumatology)

Lai, Justine (Graduate Student)
The novel oncogenic role of NPM1 in FLT3-mutated Acute Myeloid Leukemia
Supervisor: Peng Wang (Hematology)

Li, David (Graduate Student)
Prognostic implications of abnormal left-right lung perfusion differential on routine post-transplant ventilation-perfusion scans
Supervisor: Kieran Halloran (Pulmonary Medicine)

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)
Cell-Specific Regulation of the GATA-4/6 Transcription Factors by the Metabolic Enzyme PKM2 Provides Insight into a Biologic Function Essential for Cardiac Health and Survival
Supervisor: Gopinath Sutendra (Cardiology)

Masoud, Andrew (Graduate Student)
Characterizing The Role of Phosphatidylinositol 3-kinase Beta Catalytic Subunit in Vascular Injury Repair of The Chronic Allograft Vasculopathy in Mice Heart Allografts
Supervisor: Allan Murray (Nephrology)

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

Puri, Alisha (Graduate Student)
The evaluation of frailty assessment tools and their measurement properties in Chronic Kidney Disease (CKD)
Supervisor: Stephanie Thompson (Nephrology)

Rahman, Md Mizanur (Graduate Student)
Mechanism of CLIC5A recruitment to, and Rac1 activation in the Plasma Membrane-associated Ezrin Complex
Supervisor: Barbara Ballermann (Nephrology)

Reyes-Serratos, Eduardo (Graduate Students)
Characterization of three monoclonal antibodies targeting the middle, amino- and carboxyl-terminus segments of Calcium-binding protein, spermatid-associated 1 (CABS1)
Supervisor: Marcelo Marcet-Palacios (Endocrinology & Metabolism)

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

Singh, Noreen (Resident)
Learning from a Rare Phenomenon: Spontaneous Clearance of Hepatitis C Virus Post-Liver Transplant
Supervisor: Rahima Bhanji (Gastroenterology)

Stanton, Amanda (Resident)
Internet search results correlate with seasonal variation of sarcoidosis
Supervisor: Steven J Katz (Rheumatology); and

Stanton, Amanda (Resident)
Pre-Transplant Medications and Primary Graft Dysfunction Risk in Lung Transplant Recipients
Supervisor: Kieran Halloran (Pulmonary Medicine)

Suliman, Muhammad Imran (Resident)
IGF-1: a new biomarker for muscle dysfunction associated with decompensation in patients with liver disease
Supervisor: Rahima A. Bhanji (Gastroenterology)

Sun, Ken (Senior Subspecialty Resident)
Diagnostic yield and impact of bronchoscopy in patients with a hematological malignancy or hematopoietic stem cell transplant presenting with pulmonary complications
Supervisor: Mohit Bhutani (Pulmonary Medicine)

Wang, Dennis (Resident)
Comparing EPA entrustability scores given by staff physicians vs senior trainees to PGY1 residents
Supervisor: Steven Katz (Rheumatology)

Watt, Makayla (Graduate Student)
Exploring Patient Perspectives on an Online, Stress Reduction Intervention in Inflammatory Bowel Disease
Supervisor: Puneeta Tandon (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

Atkins, Kerry (Resident)
Mask wearing and skin health during COVID19: a preventative approach for the general population
Supervisor: Marlene Dytoc (Dermatology)

Au, Anita (Faculty)
Reducing Laboratory Test Ordering Overuse in General Internal Medicine Units at the Grey Nuns Community Hospital – A Quality Improvement Initiative
(General Internal Medicine)

Barber, Paul (Resident)
Evaluation of a Summer Healthcare Improvement Program (SHIP) in Undergraduate Medicine
Supervisor: Narmin Kassam (General Internal Medicine)

Campbell, Carley (Graduate Student)
Exploring the Patient Perspective of In-hospital Blood Testing
Supervisor: Pam Mathura (General Internal Medicine)

Carr, Frances (Faculty)
Ending PJ Paralysis: A Quality Improvement Initiative
Supervisor: Darryl Rolfson (Geriatric Medicine)

DeVito, Victoria (Resident)
Heparin-Induced Thrombocytopenia Testing and 4Ts Score Utilization at the UAH
Supervisor: Cynthia Wu (Hematology)

Ghuman, Arjun (Resident)
Stopping Routine Admission Urine Tests for Stroke Rehabilitation Inpatients
Supervisor: Jaime Yu (Physical Medicine & Rehabilitation)

Johnson, Emily (Graduate Student)
Implementing a cirrhosis order set: a qualitative analysis of provider-identified barriers and facilitators
Supervisor: Puneeta Tandon (Gastroenterology)

Liu, Harry Chaocheng (Resident)
Beyond Skin Deep: Case-based Online Learning Modules to Improve the Understanding of Multidisciplinary Care in Dermatology among Students
Supervisor: Marlene Dytoc (Dermatology)

Luthra, Tania (Resident)
Reducing Length-of-Stay for Stable Antepartum Patients
Supervisor: Winne Sia (General Internal Medicine)

Nahirney, Marissa (Graduate Student)
Trialing a Psoriasis Education Tool for Patient-Physician Decision-Making about Biologics
Supervisor: Marlene Dytoc (Dermatology)

Oliver, Monika (Clinical Fellow)
A Retrospective Review of the Appropriateness of D-Dimer Ordering and Interpretation Using Wells' Clinical Probability Criteria
Supervisor: Cynthia Wu (Hematology)

Poonja, Sabrina (Resident)
Ethnic and Gender Disparities in Access to Deep Brain Stimulation Surgery for Movement Disorders in a Canadian Center
Supervisor: Fang Ba

Raffael, Kendra (Resident)
Improving the Use of Oxygen on General Internal Medicine (GIM) Units at the University of Alberta Hospital (UAH): A Quality Improvement Initiative
Supervisor: Narmin Kassam (General Internal Medicine)

Sharfuddin, Nazia (Resident)
Advancing Health Equity during the COVID-19 Pandemic through Digital Medical Interpretation Platforms
Supervisor: Narmin Kassam & Dr. Lindsay Bridgland (General Internal Medicine)

Soong, Laura (Resident)
Identifying quality improvement opportunities in a vulvar dermatology clinic
Supervisor: Marlene Dytoc (Geriatric Medicine)

Swaleh, Rukia (Senior Subspecialty Resident)
Building Clinically Actionable Information for Improving Diabetes Care: Starting from Electronic Medical Record and Administrative Health Data
Supervisor: Roseanne O Yeung (Endocrinology & Metabolism)

Truong, Leslie (Research Fellow)
Improving Timely Treatment of Adult Sickle Cell Anemia Patients Presenting with Vaso-Occlusive Pain Episodes at the University of Alberta Hospital Emergency Department
Supervisor: Linda Sun (Hematology)

Turk, Tarek (Graduate Student)
Improving Healthcare Delivery to Patients with Psychodermatological Conditions
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

Hypoxia- induced TIMAP Upregulation Promotes Tumor Angiogenesis through Attenuation of ALK1-mediated TIMAP Inhibition

Salah Aburahess, Aashiq Hussain, Parnian Alavi, Marya Obeidat, Laiji, Li, Nadia Jahroudi, and Barbara J Ballermann
Supervisor: Dr. Barbara Ballermann

INTRODUCTION

TIMAP (TGF-B1 inhibited membrane associated protein) is an endothelial cell (EC)-predominant inhibitor of myosin phosphatase, first discovered in our laboratory as a member of the myosin phosphatase targeting subunit (MYPT) family (Am J Physiol Cell Physiol 283: C327, 2002). TIMAP is proangiogenic, promoting EC proliferation, survival, and sprouting angiogenesis in vitro (Am J Physiol Renal Physiol 307: F623, 2014). Here we utilized the murine breast cancer model to investigate whether in vivo angiogenesis requires TIMAP. We also determined the mechanisms regulating TIMAP abundance in cultured EC.

METHODS

Mouse mammary adenocarcinoma cells (E0771) were injected into mammary glands of 5 pairs of female TIMAP+/+ and TIMAP-/- mice. Each pair was euthanized on the day the tumor diameter in one mouse of the pair exceeded 1.5 cm. Tumor weight, mean tumor diameter, and tumor vascular density were quantified. EC markers for immunofluorescence microscopy (IF) and western blot (WB) analysis were PECAM1 and Tie 2, respectively. Mice were exposed to chronic hypoxia and their lung tissue was then evaluated for TIMAP abundance and localization. TIMAP abundance was evaluated in human umbilical vein EC (HUVEC) cultured in 21% and 1% O2 with or without ALK1 pathway activation

RESULTS

At the time of euthanasia, tumor size (figure-1A), weight (figure-1B) and blood vessel density (figure-1C,D&E) were significantly lower in TIMAP-/- compared to TIMAP+/+ mice. Mouse lung tissues revealed that TIMAP was significantly higher in hypoxic compared to control mouse and is localized to the EC. In cultured EC, ALK1 activation reduced whereas ALK1 inhibition raised TIMAP abundance. Hypoxia reduced ALK1 activation significantly raised TIMAP levels (figure-1F&G).

CONCLUSIONS

The data show that TIMAP is pro-angiogenic protein and its expression is significantly upregulated by hypoxia. The data from cultured HUVEC furthermore imply that hypoxia induces TIMAP expression by repressing EC ALK1 pathway activation.

Supervisor: Dr. Barbara Ballermann
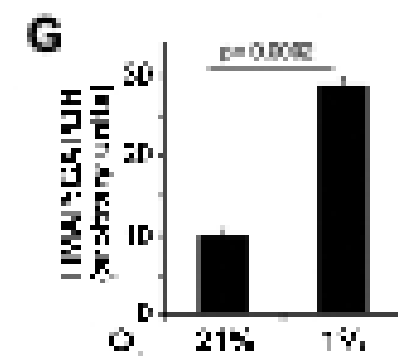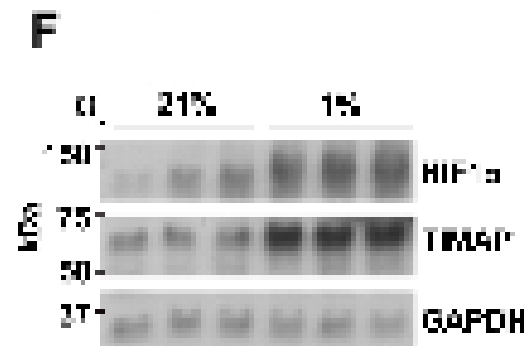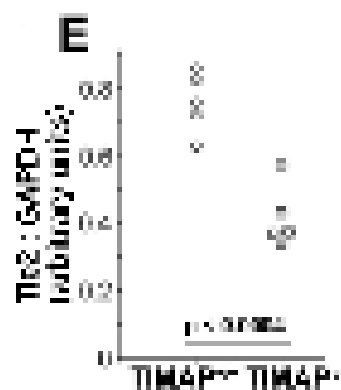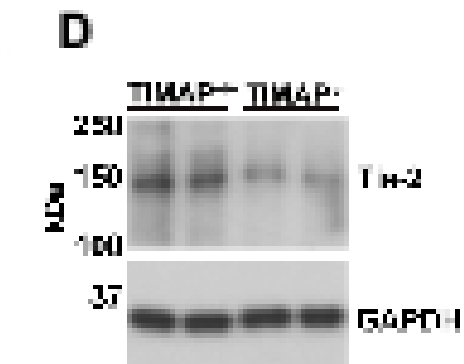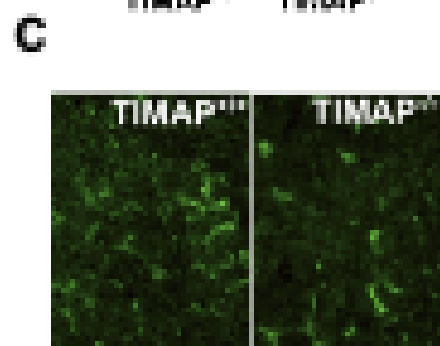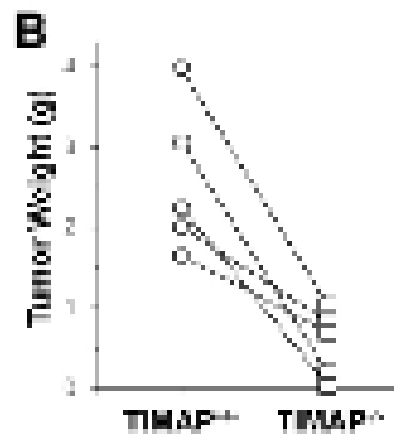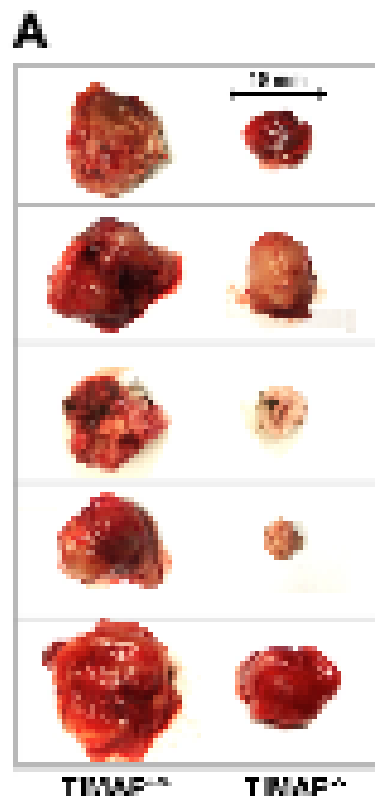
Increased prevalence of age-related comorbidities and health service utilization among adult men with hemophilia A in Alberta, Canada

Arafat Ul Alam, Cynthia Wu, Haowei (Linda) Sun
Supervisor: Dr. Haowei (Linda) Sun

INTRODUCTION
Improvements in treatment strategies over time have led to increased life expectancy of persons with hemophilia (PWH). Consequently, age-related comorbidities become increasingly relevant and pose challenges in management. We aimed to evaluate the prevalence of age-related comorbidities and health service utilization among adult men with hemophilia A compared to the general population.

METHODS
We conducted a retrospective cohort study using linked administrative data. Cases of hemophilia were identified in Alberta, Canada from 2012 to 2019 with a validated case definition and were age and sex-matched (1:3) with population controls. Comorbidities were identified by presence of at least 2 international classification of diseases (ICD) codes. Research ethics approval was obtained.

RESULTS
We identified 206 male adult patients with hemophilia A. Twenty-seven (13.2%) were over age 65. There was a significantly higher prevalence of hypertension (14.1% vs 6.6%), hyperlipidemia (2.4.% vs 0.3%), liver diseases (13.1% vs 0.8%) and malignancy (5.8% vs 2.3%) in hemophilia cases than controls (Table 1). However, prevalence of cardiovascular and other major organ diseases was not significantly different from the general population. Hemophilia was associated with significantly higher rates of hospitalization (53.4% vs 18.8%), intensive care unit admission (5.8% vs 1.8%), emergency department visit (83.5% vs 68.4%), and longer surgical admission length of stay (15.7 days vs 7.4 days) (Table 1).

CONCLUSIONS
Despite advanced care, hemophilia is associated with higher acute care utilization than the general population. PWH have higher prevalence of malignancies and cardiovascular risk factors without increased risk of vascular diseases. Future studies are needed to examine the reasons for increased health service utilization.

Supervisor: Dr. Haowei (Linda) Sun

Table1: Comorbidities and health service utilization among adult men with hemophilia A compared with age- and sex-matched control population

	Case N=206 (%)	Control N=618 (%)	P [a] value
Comorbidities			
Hypertension	29 (14.1)	41 (6.6)	0.001
Hyperlipidemia	5 (2.4)	2 (0.3)	0.01
Diabetes mellitus	24 (11.7)	48 (7.8)	0.09
Obesity	4 (1.9)	3 (0.5)	0.07
Renal disease	3 (1.5)	6 (1.0)	0.69
Coronary artery diseases	9 (4.4)	18 (2.9)	0.21
Cerebrovascular diseases	8 (3.9)	12 (1.9)	0.12
Peripheral vascular diseases	1 (0.5)	3 (0.5)	0.99
Atrial fibrillation	7 (3.4)	19 (3.1)	0.82
Congestive heart diseases	0 (0.0)	13 (2.1)	0.05
Venous thromboembolism	0 (0.0)	10 (1.6)	0.07
Malignancy	12 (5.8)	14 (2.3)	0.02
Chronic pulmonary disease	9 (4.4)	13 (2.1)	0.08
Liver disease	27 (13.1)	5 (0.8)	<0.001
Neurological disease	3 (1.5)	12 (1.9)	0.77
Health Service Utilization			
Hospital admission	110 (53.4)	116 (18.8)	<0.001
Intensive care admission	12 (5.8)	11 (1.8)	0.002
Emergency department visit	172 (83.5)	423 (68.4)	<0.001
Ambulatory orthopedic surgery visits	56 (27.2)	62 (10.0)	<0.001
Orthopedic surgery inpatient admission	22 (10.7)	10 (1.6)	<0.001
Hematology inpatient admissions	11 (5.3)	0 (0.0)	<0.001
Mean LoS[b] (±SD[c]) in Medicine departments	31.9 (±56.0)	25.5 (±42.6)	0.43
Mean LoS (±SD) in Surgery departments	15.7 (±31.6)	7.4 (±10.5)	0.04

a: Based on chi square or fisher's exact test (as appropriate) for categorical variable and t-test for continuous variable; b: length of stay; c: standard deviation

Aging causes alterations in level and expression pattern of von Willebrand Factor in an organ-specific manner

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

INTRODUCTION

Von Willebrand factor (VWF) is an endothelial specific pro-coagulant protein with a major role in hemostasis and thrombosis. Increased circulating levels of VWF have been associated with aging and unregulated elevated VWF levels present a risk factor for thrombus formation.

METHODS

Elisa, Western blot, and RT-PCR analyses were used to determine circulating plasma, cellular protein, and mRNA levels of VWF in young and aged mice. Immunofluorescent analyses of major organs were performed to establish the vascular pattern of VWF and the presence of platelet aggregates. Cultured endothelial cells were used as an in vitro model of aging to explore the mechanism of increased VWF levels.

RESULTS

Increased plasma levels of VWF were observed in aged mice. VWF mRNA and protein levels were increased in the endothelium of the brains, lungs and livers, but not kidneys and hearts of aged mice. The distribution of VWF expression in target organs was altered from primarily large vessels in young, to include small vessels in the aged mice. Increased platelet aggregates formation in vessels of aged organs were concomitant with increased VWF expression, consistent with increased thrombogenicity. Prolonged maintenance of endothelial cells in culture, resulting in cell senescence, correlated with increased VWF levels. Increased VWF expression was specifically detected in the senescent cell population. Aged mice treated with lipid nanoparticles (LPN) that target p53 expressing senescent cells for destruction, exhibited a significant reduction in platelet aggregates formation in the brain vasculatures compared to control.

CONCLUSIONS

VWF levels and expression patterns are significantly altered in response to aging in an organ-specific manner, and this is concomitant with increased platelet aggregates formation. A potential mechanism of age-associated increase in VWF expression maybe through cell senescence. These results provide insight for the future design of appropriate vascular bed specific targeted therapies to combat thrombogenic complications that occur with aging.

Supervisor: Dr. Nadia Jahroudi

DESMOID FIBROMATOSIS DIAGNOSED IN A 27-YEAR-OLD MALE AFTER BEING MISTAKEN FOR A GASTROINTESTINAL STROMAL TUMOUR

Larissa Albino (1), MD, Yimeng (Jimmy) Guo (1), MD MSc, and Levinus A. Dieleman (2), MD PhD.
(1)Department of Medicine and (2)Division of Gastroenterology, University of Alberta Hospital, Edmonton, AB
Supervisor: Dr. Levinus Dieleman

INTRODUCTION

The gastrointestinal tract can be affected by epithelial and non-epithelial tumours. When considering non-epithelial tumours, gastrointestinal stromal tumours (GISTs) are the most common, with an incidence of 7-15 cases/million/year. Desmoid fibromatoses, on the other hand, are rarer, with an incidence of 2-4 cases/million/year. Despite being distinct lesions, these tumours may appear similar on imaging when they involve the stomach wall or bowel. As a result, they may be confused with one another when initially diagnosed, potentially leading to inappropriate management or incorrect prognosis.

METHODS

Retrospective review of one patient.

RESULTS

A 27-year-old gentleman presented with a two-day history of left-sided abdominal pain and postprandial fullness. A CT-abdomen/pelvis demonstrated a large exophytic mass arising from the lesser sac of the stomach, in keeping with an aggressive GIST. He was further investigated with an endoscopic ultrasound, which demonstrated an exophytic mass arising from the muscularis propria of the gastric wall. Again, this was most consistent with a GIST and urgent surgical resection was recommended. On exploratory laparotomy, a soft tissue tumour was found tethered to the left mesentery of the transverse colon, despite previous imaging suggesting involvement of the stomach. This mass was resected, and a biopsy of the peritoneum was collected. Pathology identified a low-grade spindle cell tumour, CD117/CD34 negative with patchy cytoplasmic and nuclear beta-catenin staining, in keeping with desmoid fibromatosis.

CONCLUSIONS

This case illustrates how GISTs and desmoid tumours are often mistaken for one another when associated with the stomach wall or bowel, despite a vast amount of literature describing the differences between them. Pathology, with a focus on the immunohistochemistry profile, is necessary in majority of cases to distinguish the two. This distinction is paramount for proper prognostication and appropriate management, including timely investigation for associated diseases such as Familial Adenomatous Polyposis in patients with desmoid tumours.

Supervisor: Dr. Levinus Dieleman

Early direct oral anticoagulation therapy after ischemic stroke in patients with atrial fibrillation: An individual patient data meta-analysis

Alrohimi A, Gioia LC, Kate M, Ng K, Dowlatshahi D, Stotts G, Thirunavukkarasu S, Shamy M, Kalashyan H, Hussain D, Sivakumar L, Emery D, Bussiere M, Jeerakathil T, Jickling G, Shuaib A, Sharma M, Buck B, and Butcher KS
Supervisor: Ken Butcher

INTRODUCTION
The timing of anticoagulation after stroke in patients with atrial fibrillation (AF) is unknown. We aimed to objectively assess the rate of radiological hemorrhagic transformation (HT) associated with early anticoagulation and the rate of recurrent ischemic stroke.

METHODS
An individual patient data meta-analysis of three prospective, open label, single arm studies of direct oral anticoagulant (DOAC) initiation within 14 days of ischemic stroke onset was conducted. The primary endpoint was radiographic incident HT rates, which were assessed as Objective Performance Criteria. The results were reported as odds ratio (OR) with 95% confidence interval (CI). The heterogeneity among the studies was evaluated using the I2 statistics with fixed effect model.

RESULTS
A total of 261 patients, with mean age of 75±12 were enrolled. Median infarct volume was 2.7 (0-12.25) ml. Median time from onset to DOAC initiation was 2 (1-6) days, and median baseline National Institutes of Health Stroke Scale was 2 (0-4). Incident HT was seen on follow-up scan in 17 patients. Initiation of DOAC =< 2 days was not significantly associated with incident HT (pooled OR 0.33, 95% CL 0.11 – 1.03, Q=0.55, P for heterogeneity=0.76). No patients developed symptomatic HT. Conversely, 19 patients developed recurrent ischemic events, 73.7% of which occurred within 14 days. Initiation of DOAC =< 2 days did not significantly reduce the risk of recurrent ischemic events (pooled OR 0.65, 95% CL 0.25 – 1.69, Q=2.16, P for heterogeneity=0.34). Compared to incident HT, recurrent ischemic event was significantly associated with poor functional outcomes (OR=4.7, 95% CL 1.77 – 12.73, p=0.002).

CONCLUSIONS
Early DOAC after stroke did not precipitate incident or symptomatic HT. Recurrent ischemic events were common and associated with poor outcomes. These data may be used for calculating sample size and predicting major clinical outcomes for future trials of early versus late DOAC initiation after AF-related stroke.

Supervisor: Dr. Ken Butcher

Table 1. Baseline Patient Characteristics and outcomes

	Pooled data	CPASS	EASSE	RASS
Authors		Alrohimi A, et al. Can J Neurol Sci 2020	Alrohimi A, et al. J Neurol 2021	Gioia LC, et al. Stroke 2016
Sample size	261	101	100	60
NIHSS cutoff		=< 3	No cutoff	< 9
DOAC agent	-----------	Dabigatran	Apixaban	Rivaroxaban
Study duration	-----------	30 days	90 days	90 days
Type of imaging	-----------	CT	CT	MRI
Primary outcome		Symptomatic HT	Symptomatic HT	Symptomatic HT
Mean ± SD, age	75 ± 12	72.4 ± 11.5	79 ± 11	73.5 ± 13.2
Male	59%	65%	49%	67%
Full DOAC dose	70%	64%	79%	64%
Median (IQR) Infarct volume (ml)	2.7 (0-12.25)	0 (0-7.2)	4 (0.5 – 10.75)	7.9 (1.5 – 14.75)
Median (IQR) time from index event onset to DOAC initiation (days)	2 (1-6)	2 (1-5)	2 (1-6)	3 (1.5-6)
Median (IQR) Baseline NIHSS	2 (0-4)	1 (0-2)	4 (1 – 9)	2 (0-4)
Median (IQR) Pre-morbid mRS	0 (0-1)	0	0 (0 – 1)	0
Baseline HT	47 (18%)	7/101 (7%)	15/100 (15%)	25/60 (45%)
Primary outcome				
Incident radiological HT	17	6	3	8
Secondary outcomes				
Symptomatic HT (PH2)	0	0	0	0
New parenchymal hemorrhage (PH1 or asymptomatic PH2)	0	0	0	0
Systemic hemorrhagic complication(s)	0	0	0	0
Recurrent ischemic event(s)	19	4	13	2
Clinical outcomes				
Median (IQR) day 90 mRS	1 (0-2)	1 (0-2)	2 (0-3)	1 (0-2)
Median (IQR) day 90 NIHSS	0 (0-2)	0 (0-1)	1 (0-3)	0 (0-1)
Mortality	4.6%	1%	9%	3.3%

DOAC, direct oral anticoagulants; CT, computed tomography; MRI, magnetic resonance imaging; HT, hemorrhagic transformation; SD, standard deviation; IQR, Interquartile Range; NIHSS, National Institute of Health Stroke Scale; mRS, Modified Rankin Scale; PH, parenchymal hemorrhage.

International survey of physicians on approach to the timing of direct oral anticoagulant initiation after atrial fibrillation related stroke

Alrohimi A and Butcher KS
Supervisor: Ken Butcher

INTRODUCTION

The timing of anticoagulation after stroke in patients with atrial fibrillation (AF) is unknown. Most guidelines are inconsistent and based on expert opinion.

METHODS

To explore practice differences in deciding the timing of initiating direct oral anticoagulant (DOAC) after AF-related stroke, we used electronic survey with practice-related demographic and clinical questions of 10 cases with different stroke severities and sizes: TIA, small, medium, large, and strokes with hemorrhagic infarction (HI) and parenchymal hematoma (PH). Differences between groups were compared using Mann-Whitney-U tests.

RESULTS

A total of 268 respondents from 4 continents completed the survey; 74.3% identified as neurologist. Neurologists (aOR: 12.97, 95% CI 4.97 – 33.8, p < 0.0001) were more likely to make decision without radiology reports. Median days of DOAC initiation in two cases of small strokes were 3 (1-6) and 0.5 days, respectively, P < 0.0001. The significant difference was driven by high National Institutes of Health Stroke Scale (NIHSS) in one case. For moderate and large strokes, the median was 4 (2-6) and 10 (7-14) days, respectively. The size of stroke significantly influenced the timing of DOAC initiation in 3 patients with HI1, 10 (7-14), 7 (5-10), and 8.5 (7-14) days, p < 0.0001. In patients with PH, the grade impacted the timing decision, 7 (5-10) and 14 (7-14), p < 0.0001. With exception to the presence of PH2, most respondents feel comfortable not repeating imaging after DOAC initiation. Fifty – 60% and 10 – 30% of respondents think the timing of DOAC after AF- related stroke is not an equipoise in TIA and mild & small stroke, and other stroke sizes and severities, respectively.

CONCLUSIONS

Our results demonstrate heterogenous decisions related to the timing of DOAC after AF-related stroke. Stroke size, severity, and the grade of hemorrhage, if present, seem to influence the decision. Our results highlight the need for higher quality trials and evidence-based guidelines.
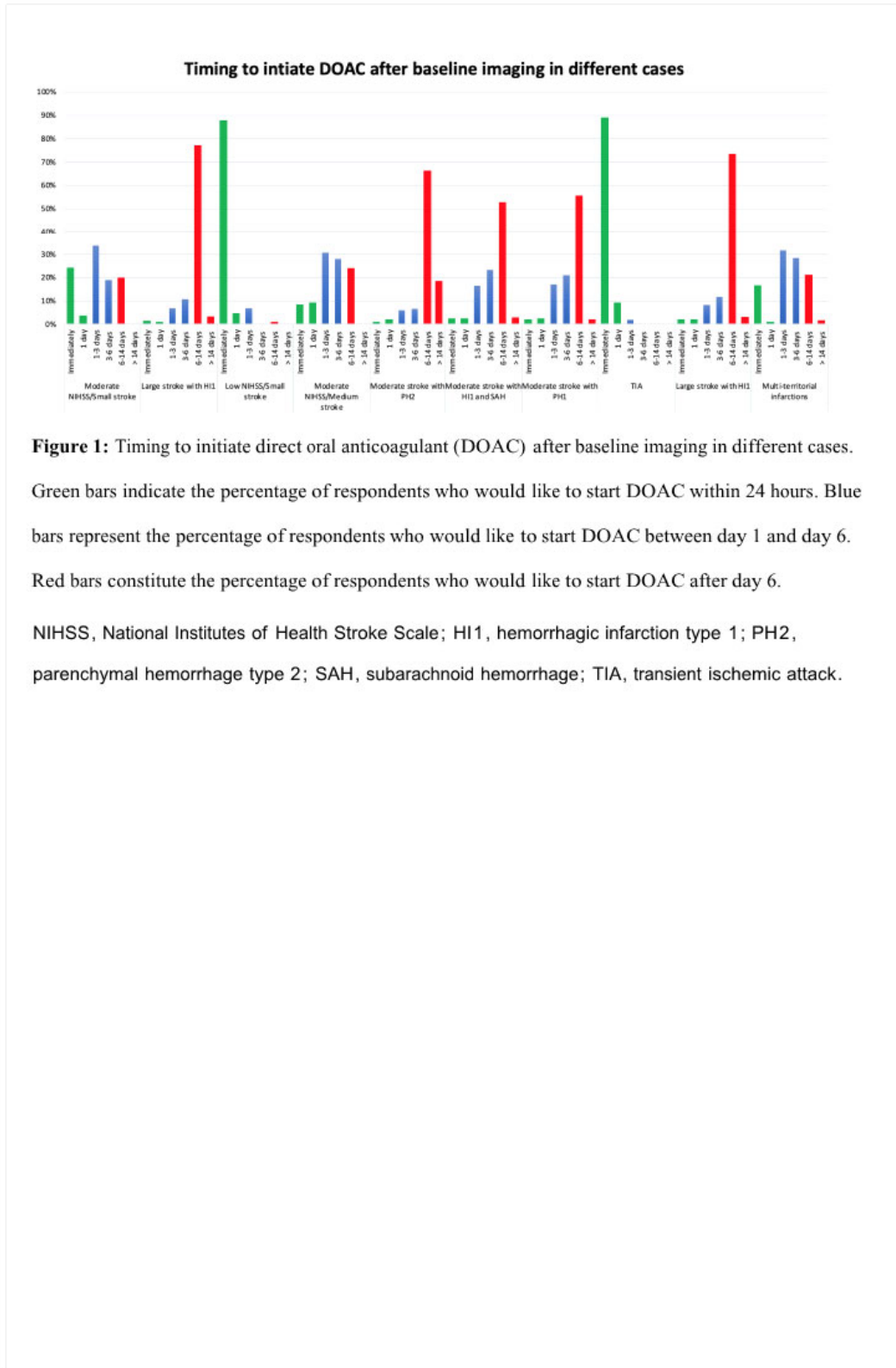
Supervisor: Dr. Ken Butcher

Figure 1: Timing to initiate direct oral anticoagulant (DOAC) after baseline imaging in different cases.

Green bars indicate the percentage of respondents who would like to start DOAC within 24 hours. Blue bars represent the percentage of respondents who would like to start DOAC between day 1 and day 6. Red bars constitute the percentage of respondents who would like to start DOAC after day 6.

NIHSS, National Institutes of Health Stroke Scale; HI1, hemorrhagic infarction type 1; PH2, parenchymal hemorrhage type 2; SAH, subarachnoid hemorrhage; TIA, transient ischemic attack.

Hereditary Spastic Paraplegia: Clinicogenetic Lessons from a Well-Defined Cohort

Ekhlas Assaedi, Setareh Ashtiani, Mehrdad A. Estiar, Ziv Gan-Or, Erica McKenzie, Guy Rouleau, Aakash Shetty, Oksana Suchowersky
Supervisor: Dr. Oksana Suchowersky

INTRODUCTION

HSP is a group of heterogeneous hereditary disorders that share the common core feature of leg spasticity leading to gait impairment with more than 60 identified genes. Previously, over 50% of HSP cases remained genetically unsolved. We aim to describe the clinical, radiological, and genetic features of a well-defined cohort of hereditary spastic paraplegia (HSP) patients in Alberta, Canada.

METHODS

Patients meeting the clinical criteria for HSP in Alberta were recruited through Neurogenetics clinics in Edmonton and Calgary between 2012 and 2019, and enrolled in an observational study. Clinical features were collected via a standardized inventory. Research whole exome sequencing was performed, and results confirmed in an accredited lab. For some patients, additional testing with commercial multi-gene panels was conducted. Disability was assessed using Spastic Paraplegia Rating Scale (SPRS).

RESULTS

A total of 105 HSP patients were enrolled and five patients were lost to follow up. Sixty-seven patients (67%) were found to have mutations in 21 genes. The majority of cases had complicated HSP (56%). Inheritance patterns were 32% autosomal dominant, 21% autosomal recessive, 4% X-linked, and 43% sporadic. Mutations were most frequent in SPAST (27%), SPG7 (22%), SACS (7%), SPG11 (6%), CAPN1 (4%), and SYNE1 (4%). Patients with SPG4 (SPAST) had an age of onset ranging from 1 to 38 years while SPG7 ranged from 13 to 55 years. Compared to SPG4, patients with SPG7 had a lower mean SPRS score (26.00 ± 12.2 vs.14.8 ± 5.9). Abnormalities of brain MRI were more frequently observed in patients SACS (80%, progressive cerebellar atrophy) and SPG11 (50%, thin corpus callosum). SPG7 was more associated with polyneuropathy.

CONCLUSIONS

This study provides large-scale data on patients with HSP in Alberta. Genetic results of well-phenotyped cohorts are of relevance to practicing neurologists and researchers studying the natural history of HSP with aim of therapeutic interventions.

Supervisor: Dr. Oksana Suchowersky

Microglia and monocyte-derived macrophage contribution in myelin debris clearance during remyelination

Charbel Baaklini, Kelly Lee, Daria Antoszko, Jeremies Ibanga, Mizuki Lopez, Jason Plemel
Supervisor: Jason Plemel

INTRODUCTION

Multiple sclerosis (MS) is a neurodegenerative demyelinating disease. Despite the successes in reducing disability, regenerative therapies are lacking. Remyelination is a regenerative process, associated with lower disability. Remyelination necessitates the clearance of inhibitory myelin debris, which is often impaired in MS. Myelin debris is phagocytosed by immune cells in the CNS, including microglia, the resident immune cell in the brain and spinal cord, and monocyte-derived macrophages (MDMs). However, it is unknown to what extent microglia and MDMs phagocytose myelin debris. I hypothesize therefore that microglia and MDMs phagocytose myelin debris to differing extents in an experimental model of MS.

METHODS

I induced focal demyelination by intraspinal injection of the demyelinating compound LPC. I injected LPC into transgenic mice (MicroTdTom) that fluorescently tag microglia, so that microglia could be differentiated from MDMs. To compare microglia and MDMs' phagocytic capacities, I euthanized MicroTdTom mice at 3 (peak of phagocytosis) and 7 (end of phagocytosis) days post-demyelination. Using volumetric assessment of microglial, MDM and the engulfed myelin debris, I measured the volume of phagocytosed myelin debris at these time points.

RESULTS

I found that microglia and MDMs have similar densities at 3 days, but microglia expanded to monopolize the LPC lesion by 7 days. Still, microglia and MDMs phagocytose myelin debris equally at 3 and 7 days. To understand how myelin debris clearance proceeds in the absence of microglia, I ablated microglia by genetically inserting the diphtheria toxin (DT) receptor into microglia and treating these mice and controls with DT. I found that MDMs compensate for microglial loss by phagocytosing more myelin debris, with no slowing of myelin debris clearance.

CONCLUSIONS

Microglia and MDMs jointly phagocytose myelin debris. Future work will characterize the transcriptomes of phagocytosing microglia and MDMs. Understanding phagocytic mechanisms will provide targets to ultimately boost remyelination.

Supervisor: Dr. Jason Plemel

The Association Between Access to Medical Care (physicians and nurse practitioners) and Impact on Resident Outcomes: A Retrospective Cohort Analysis

Krittika Bali
Supervisor: Dr. Andrea Gruneir

INTRODUCTION

Despite policy actions to reduce its provision, as Canada's population ages, there is an increasing need for nursing home care (NH). Ensuring quality of care remains paramount.

METHODS

The objective of this project is to use data collected in the Translating Research in Elder Care(TREC) longitudinal study to test the association between the availability of physicians and nurse practitioners (NP) in nursing homes and clinically-relevant resident outcomes. TREC has been collecting data on NH facilities, units, and care staff for nearly 15 years and then linking it to the routinely collected Resident Assessment Instrument – Minimum Data Set version 2.0 (RAI-MDS 2.0) in Western Canadian provinces. Recently, the TREC team undertook a priority setting exercise with their non-research partners, including people with lived experience and health system decision makers, to identify top research questions that could be addressed using TREC's available data.

RESULTS

Residents belonging to our cohort were mostly female (67.0%), 80 years of age or older (35.4%), and either had Alzheimer's disease or other dementia (62.5%). Almost 50% had mild/moderate impairment according to the Cognitive Performance Scale (CPS) and 83% were highly dependent in activities of daily living (ADL). Further analysis will explore the association between access to a physician or nurse practitioner and resident outcomes of physical restraint use, antipsychotic medication use with no indication of psychosis, hospitalization rates, and polypharmacy.

CONCLUSIONS

Data suggest that increased access to medical care is associated with less adverse resident outcomes. It is hypothesized that residents on units in nursing homes where physicians are actively involved in care planning are less likely to experience physical restraint use, less likely to be taking antipsychotic medication with no indication of psychosis, less hospitalizations, and experience less issues surrounding polypharmacy.

Supervisor: Dr. Andrea Gruneir

Defining Transition Success for Young Adults with Inflammatory Bowel Disease

Allison Bihari, Nima Hamidi, Cynthia Seow, Karen Goodman, Eytan Wine, Karen Kroeker
Supervisor: Karen Kroeker

INTRODUCTION
The incidence of childhood inflammatory bowel disease (IBD) is increasing in Canada; therefore, more patients will need to transition from pediatric into adult care. The literature on transition in IBD has focused mainly on preparation and while transition success is often referenced, it is not clearly defined. As transition is a process that relies on the collaboration of health care providers, parents, and patients, this study aims to define transition success by these stakeholders.

METHODS
A theoretical position of naturalistic inquiry was paired with qualitative description. Purposive sampling was used to recruit providers, parents, and patients from IBD clinics in Edmonton and Calgary. Virtual semi-structured interviews were conducted using interview guides. Interviews were transcribed and analyzed concurrently with data collection by latent content analysis. Participant recruitment and data analysis continued until no more themes emerged from the data – signalling thematic saturation.
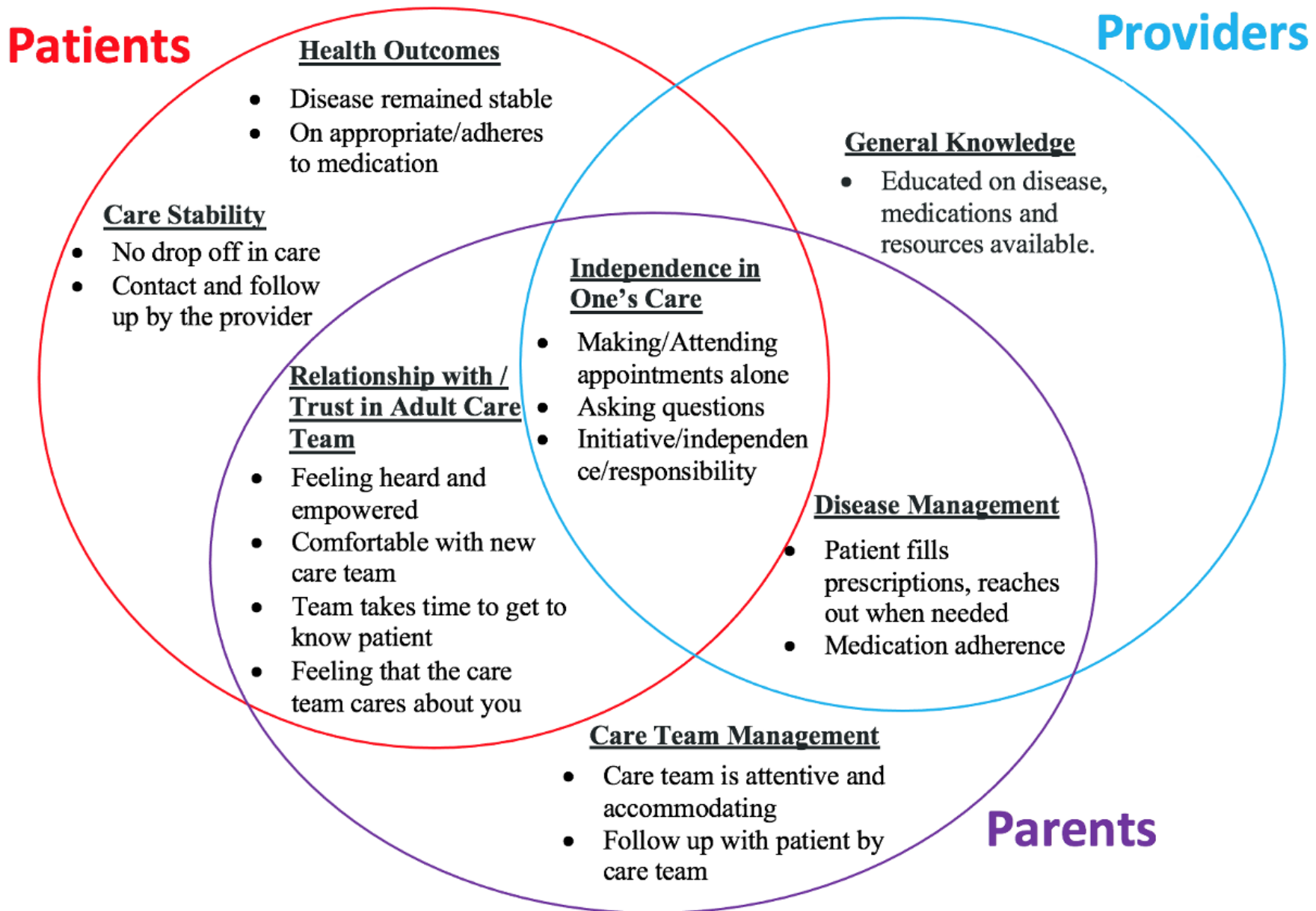
RESULTS
Thematic saturation was achieved within patient (n=17), healthcare provider (n=15), and parent (n=13) groups. The theme common among all groups was independence in care, characterized by the patient making and attending appointments, asking questions, while having an awareness about their health. The theme that emerged in both patient and parent groups was relationship with/trust in adult care team, characterized predominately as the patient being comfortable with their new team. The theme common to provider and parent groups was disease management, characterized by medication adherence and reaching out when needed. Additional themes that emerged within specific groups are outlined in Figure 1.

CONCLUSIONS
Healthcare providers, parents, and patients define pediatric transition success as independence in one's care. Themes specific to the stakeholder groups, include, relationship with/trust in adult care team, disease management, health outcomes, care stability, care team management, and general knowledge. Through creating a definition of transition success representative of all stakeholders, providers can help patients achieve success.

Supervisor: Dr. Karen Kroeker

Figure 1. Summary of themes emerging from interviews with patients, health care providers, and parents of young adults with inflammatory bowel disease.

Patients

Health Outcomes
- Disease remained stable
- On appropriate/adheres to medication

Care Stability
- No drop off in care
- Contact and follow up by the provider

Providers

General Knowledge
- Educated on disease, medications and resources available.

Relationship with / Trust in Adult Care Team
- Feeling heard and empowered
- Comfortable with new care team
- Team takes time to get to know patient
- Feeling that the care team cares about you

Independence in One's Care
- Making/Attending appointments alone
- Asking questions
- Initiative/independence/responsibility

Disease Management
- Patient fills prescriptions, reaches out when needed
- Medication adherence

Care Team Management
- Care team is attentive and accommodating
- Follow up with patient by care team

Parents

Social inequity, gender, and Helicobacter pylori infection in Arctic Canada

Cromarty T, Assi A, Geary J, Goodman KJ, Community Project Planning Committees, CANHelp
Working Group
Supervisor: Dr. Karen Goodman

INTRODUCTION

Helicobacter pylori (Hp) infection has an elevated prevalence in northern Indigenous communities in Canada. I investigated social inequities in the Hp-associated disease burden within Indigenous communities in the Northwest Territories and Yukon. I examined how deprivation indicators relate to this disease burden, with particular interest in differences in gender, and in households headed by unpartnered women relative to other households.

METHODS

I used data from projects conducted by the Canadian North Helicobacter pylori (CANHelp) Working Group to address community concerns about Hp-associated risks. I estimated the Canadian Deprivation Index (CDI), a validated predictor of health status, from its 3 components: home ownership; education; and food security. CANHelp Working Group researchers ascertained most variables by interviewing participants as they enrolled in community projects during 2007-2017; I ascertained food security in a subset of participants during 2017- 2018, using the Canadian Government Household Food Security Survey, adapted for Arctic communities. As a disease burden variable, I used the prevalence of Hp infection based on urea breath test, histopathology, and/or culture. I constructed a multivariable logistic regression model to estimate odds ratios for the effect of selected variables on Hp prevalence while controlling for the effects of other variables, with a random effects parameter for household to account for clustering of Hp infection in households.

RESULTS

Hp prevalence was higher among participants at higher deprivation levels, after adjustment for identified confounding variables. The estimated trend in Hp prevalence with increasing deprivation levels was more notable in members of households led by unpartnered women relative to members of other households, and in men relative to women, though there was insufficient statistical precision to conclude that observed differences in trend were beyond what would be expected from random variation.

CONCLUSIONS

The Hp-associated disease burden appears related to social and gender inequities within Indigenous communities in Arctic Canada.

Supervisor: Dr. Karen Goodman

Table 1: Adjusted odds ratios for the association of socioeconomic status, female head of household, children in household, and candidate adjustment variables with Hp prevalence; Western Arctic Communities, Canada, 2017- 2018.

		n	Hp+ (%)	Adjusted OR	95% CI
	Total	383	53	--	--
Sex					
	Male	147	60	Referent	--
	Female	236	50	0.80	[0.43, 1.50]
Ethnicity					
	Non-Indigenous	67	19	0.10	[0.02, 0.30]
	Indigenous	327	61	Referent	--
Children under 15 in Household					
	No	230	47	Referent	--
	Yes	165	63	1.9	[0.89, 3.9]
Household led by an Unpartnered Woman					
	No	288	56	Referent	--
	Yes	98	48	0.91	[0.46, 2.0]
Socioeconomic Status (Canadian Deprivation Index)					
	High	143	39	Referent	--
	Medium	111	58	2.0	[0.88, 4.6]
	Low	142	65	3.5	[1.4, 8.3]

Time-dependent increases in alarmin-type cytokines in airway epithelial cells following allergen stimulation

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

INTRODUCTION

The airway epithelium lining the lungs releases pro-inflammatory cytokines capable of inducing an immune response after sensing its environment through different receptor types. However, few studies have examined intracellular cytokine movement in allergen-stimulated airway epithelial cells. We hypothesize that airway epithelial cell activation by allergens induces intracellular production of pro-inflammatory cytokines through vesicular trafficking mechanisms. We also aim to study intracellular trafficking mechanisms utilized by airway epithelial cells to release cytokines after activation of their receptors.

METHODS

To serve as a model of airway epithelial cell activation and cytokine production, we established a cell culture of an airway epithelial cell line, BEAS-2B cells. BEAS-2B cells were grown in 24-well plates on glass coverslips until they reached 70-80% confluency. Cells were then stimulated with cockroach extract (CE) or house dust mite (HDM) extract (5 ?g/mL) over time (0 h, 4 h, 8 h, and 24 h). After stimulation, BEAS-2B cells were washed, fixed, and immunolabeled with primary antibodies to a panel of cytokines, which were detected by secondary antibodies conjugated to fluorescent dyes. Counterstaining of cells was carried out using rhodamine phalloidin to detect cytoskeleton and Hoechst to detect nuclei. Immunolabeled coverslips were imaged with an Olympus epifluorescence microscope, and image quantification analysis was performed using Volocity software, allowing analysis of arbitrary fluorescent intensities within cells delimited by cytoskeletal staining.

RESULTS

In unstimulated cells (0 h), baseline expression of intracellular IL-1?, IL-25, IL-33 and TSLP could be detected relative to isotype controls. After 8 h of CE stimulation, intracellular levels of IL-1? and IL-25 decreased (p < 0.01). Conversely, TSLP and IL-33 increased in a time-dependent manner levels following CE and HDM extract stimulation, with significant differences between 0 h, 8 h and 24 h (p < 0.01). These observations

CONCLUSIONS

Our findings show that BEAS-2B cells have detectable increases in intracellular TSLP and IL-33 levels, concurrently with decreased IL-1? and IL-25, in response to direct allergen stimulation. Such differential intracellular cytokine responses to allergen have not been reported in epithelial cells.

Supervisor: Dr. Paige Lacy

SARS-CoV-2 infection induces increases in intracellular alarmin-type cytokines in airway epithelial cells

Luke Gerla, Marc Duchesne, Eileen Reklow, Angie Hillaby, Tom Hobman, Irvin Mayers, Paige Lacy
Supervisor: Dr. Paige Lacy

INTRODUCTION

Infection of airway epithelial cells by SARS-CoV-2 has been shown to initiate a cytokine storm, in which a barrage of inflammatory cytokines is released that potentially overwhelm the immune system. However, there has been little evidence to show whether alarmin-type cytokines such as thymic stromal lymphopoietin (TSLP) are released in response to SARS-CoV-2. In this study, we analyze the cytokine response of lung epithelial cells in response to SARS-CoV-2.

METHODS

NHBE, AHBE, and patient bronchial brushings were grown in culture until they reached >80% confluency. Samples were then infected with SARS-CoV-2 at a multiplicity of infection of 1, for 24 hours. After infection, the cells were fixed and stained using a primary mouse anti-human TSLP antibody and a secondary antibody conjugated with Cy3. Images were collected using an Olympus IX81 fluorescent microscope and the mean intracellular fluorescence intensity was quantified using an automated algorithm on Volocity software.

RESULTS

A significant increase in TSLP immunofluorescence ($p<0.05$) was detected in NHBE and AHBE cells after 24 h infection with SARS-CoV-2 compared to isotype controls. At the time of writing, three bronchial brushings (AW01, AW02, AW03) were collected. Bronchial brushings AW01 and AW03 showed a significant increase in immunofluorescence after 24 h infection, while bronchial brushings from AW02 did not show a significant increase in fluorescence after 24 h infection.

CONCLUSIONS

Infection of lung epithelial cells with SARS-CoV-2 was associated with a significant increase in TSLP immunofluorescence in airway epithelial cells. Therefore, lung epithelial cells can potentially initiate immune signalling through the production and secretion of TSLP. Overexpression of pro-inflammatory cytokines during a SARS-CoV-2-induced cytokine storm may result in a disproportionate response to an infection, resulting in symptoms such as bronchoconstriction. This study provides the framework to analyse and identify potential therapeutic targets for TSLP during SARS-CoV-2 and other viral pulmonary infections.

Supervisor: Dr. Paige Lacy

TARGETING METABOLISM AS AN EMERGING THERAPEUTIC OPTION FOR INFLAMMATORY BOWEL DISEASE

Yimeng (Jimmy) Guo , Levinus A. Dieleman , Hitesh Dooky , Harshad Joshi , Eytan Wine , Shairaz Baksh
Supervisor: Dr. Levinus A. Dielema

INTRODUCTION
Persistent inflammation can trigger altered epigenetic, inflammatory and bioenergetic states. Inflammatory bowel disease (IBD) is a heterogeneous disease with an abnormal inflammatory state and subsequent metabolic syndrome disorder. Current IBD therapeutics only inhibit a small subset of inflammatory pathways. We hypothesize that in order to achieve mucosal healing and to keep patients in remission we must (i) inhibit inflammation and, importantly (ii) also resolve secondary effects of inflammation such a reset of metabolic dysfunction. The aims of this study are to explore correlations between inflammation/metabolic markers and the severity of the disease to uncover emerging new therapeutics.

METHODS
More than one hundred patients were recruited and underwent colonoscopy. In order to explore how biomarkers change with disease and time, all patients had longstanding IBD for more than 10 years versus those less than 5 years. Those diagnosed with non-colorectal cancer, celiac disease, or diabetes were excluded. Using intestinal biopsies from non-IBD, UC and CD patients, we explored immunohistochemistry and immunoblotting to assess expression/activation levels of markers of inflammation (such as the inflammatory kinase RIPK2) and metabolism (the kinase AMPK) in order to gain insight into correlations with clinical severity of the disease. In addition, the in vivo role for AMPK was explored using metformin- treated mice in a dextran sodium sulfate (DSS) model of IBD.

RESULTS
Patients with longstanding IBD exhibited elevation of RIPK2 kinase activity with a simultaneous loss in AMPK activity in colon biopsy sections. These characteristics together were robust factors in driving the inflammatory phenotype and metabolic dysfunction in the colon of patients with IBD. Interestingly, RIPK2 remains elevated even in patients that are currently on IBD therapeutics. Furthermore, using metformin in a mouse model of IBD, inflammation was inhibited when AMPK levels were elevated. Metformin allowed for metabolic reset to regain AMPK levels in the colon promoting mucosal healing and allowing > 80% survival of animals from DSS-induced inflammation injury.

CONCLUSIONS
Therapeutics inhibiting inflammation (RIPK2) and stimulating metabolic drivers of the disease (AMPK) should be explored to completely eliminate intestinal inflammation, reset abnormal metabolism and achieve deep remission in IBD patients with longstanding disease.

Supervisor: Dr. Levinus A. Dielema

Nailfold capillaroscopy abnormalities correlate with disease activity in adult dermatomyositis.

Dylan Johnson, Charmaine van Eeden, Naima Moazab, Desiree Redmond, Cecile Phan, Stephanie Keeling, Robert Gniadecki, Jan Willem Cohen Tervaert, and Mohammed Osman
Supervisor: Dr. Mohammed Osman

INTRODUCTION

Dermatomyositis (DM) is an idiopathic inflammatory myopathy characterized by proximal muscle weakness and characteristic cutaneous findings. The diagnosis of DM is based on clinical features, complemented by detection of myositis-specific antibodies (MSAs), elevation in muscle enzymes such as creatinine kinase (CK), or muscle biopsy. By contrast, monitoring response to treatment is largely clinical as the relationship between disease activity and biomarkers is not firmly established.

Nailfold video capillaroscopy (NVC) is a point-of-care tool for directly visualizing microvascular changes associated with different connective tissue diseases [2]. While microvascular changes are present in DM, the role of NVC in monitoring disease activity in adult DM has not yet been established. In this study, we performed a prospective analysis of NVC findings and disease activity in adult DM.

METHODS

We performed a prospective single center study of 15 adult patients with dermatomyositis. Study participants underwent two assessments at least nine months apart including clinical, laboratory and NVC evaluations. Disease activity was measured by the Myositis Intention to Treat Index (MITAX). NVC evaluation included assessment of capillary density, capillary apical diameter (?m), and the number of microhemorrhages per digit.

RESULTS

Microvascular abnormalities were present in most DM patients. Of these, capillary density (4.71 vs 6.84, p=0.006) and mean apical diameter (56.09 vs 27.79, p=0.003) significantly improved over the study period in concordance with improving disease control (MITAX 8.53 vs. 2.64, p=0.002). Longitudinal analysis demonstrated that capillary density was independently associated with MITAX (?= -1.49 [CI -2.49, -0.33], p=0.013), but not other parameters such as CRP and CK.

CONCLUSIONS

Nailfold capillary density is a dynamic marker of global disease activity in adult DM. NVC may be utilized as a non-invasive point-of-care tool to monitor disease activity and inform treatment decisions in patients with DM.
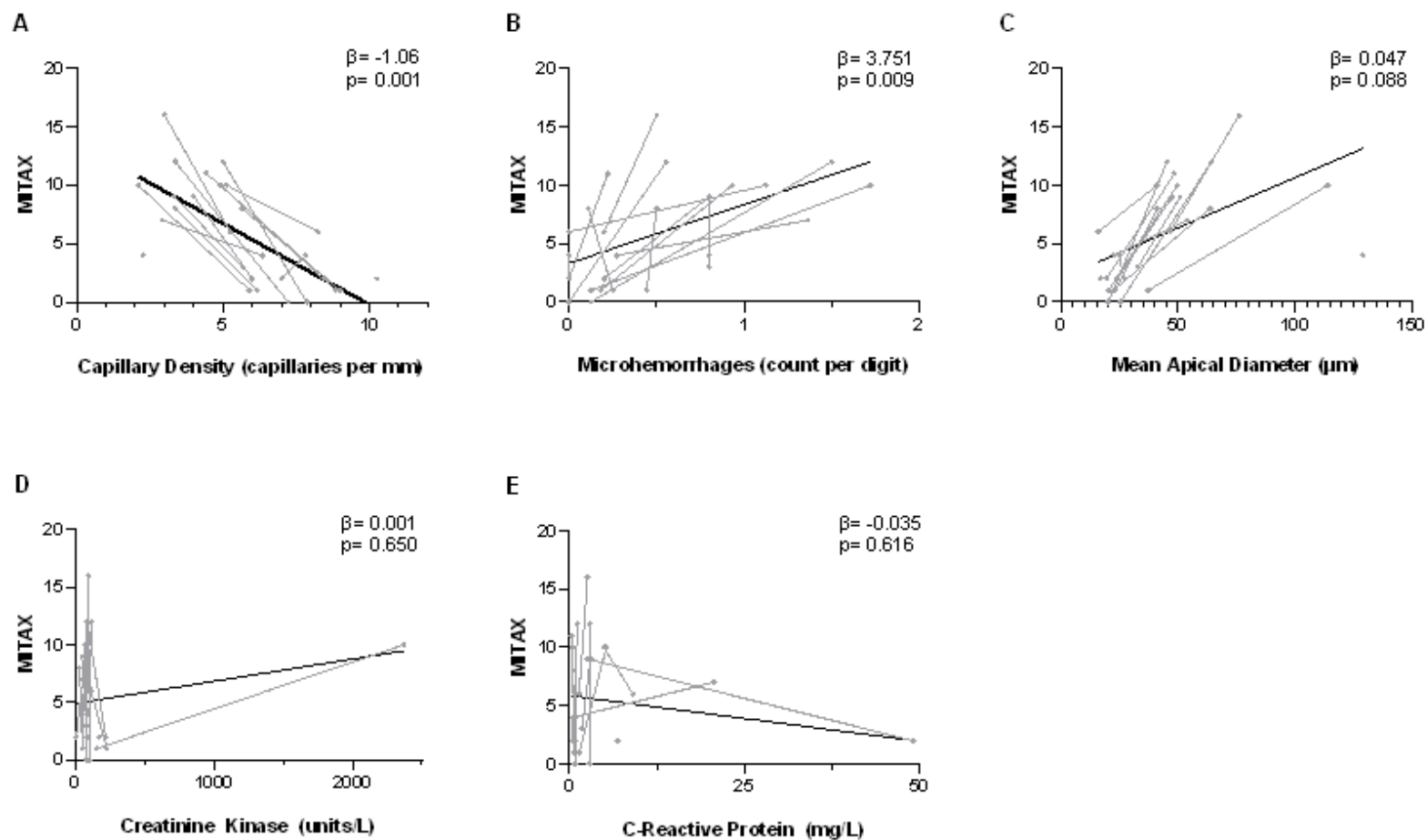
Supervisor: Dr. Mohammed Osman

Figure 1. Correlation between nailfold capillary measurements and MITAX. Disease activity is indicated on the y-axis as measured by MITAX. The NVC measurements capillary density (**A**), microhemorrhages (**B**), and apical diameter (**C**) as well as biochemical indices CK (**D**) and CRP (**E**) are indicated on the x-axes. Single assessments are indicated in grey, with lines connecting the longitudinal assessments for one individual patient. The overall fitted line is indicated in black. Fixed effect estimates (β) and significance (p) are the result of individual mixed-linear models with dependent variable MITAX and time as a random effect.

The novel oncogenic role of NPM1 in FLT3-mutated Acute Myeloid Leukemia

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

INTRODUCTION

FLT3-ITD mutations, which occur in 25% of acute myeloid leukemia (AML) cases, correlate with a poor outcome. Interestingly, the co-existence of NPM1 mutations in these cases significantly downgrades the clinical risk. This clinical observation is counter-intuitive, as NPM1 mutations are leukemogenic. We hypothesize that, under the influence of FLT3-ITD, NPM1 paradoxically acts as an oncoprotein by increasing the expression of Myc, a key oncoprotein promoting leukemia stemness and chemoresistance. Thus, mutations of NPM1 diminish the oncogenic effects of FLT3-ITD and improve clinical outcome.

METHODS

The NPM1-Myc relationship was examined in HEK293 cells (human embryonic kidney cells), since they are readily gene-transfectable. NPM1 expression was manipulated using shRNA knockdown or an expression vector. Myc expression was assessed using western blot. This NPM1-Myc relationship was compared to that in HEK293 cells co-transfected with FLT3-ITD, as well as AML cell lines expressing wild-type FLT3 or FLT3-ITD.

RESULTS

In HEK293 cells, NPM1 overexpression decreased Myc, whereas shRNA knockdown of NPM1 increased it. This inverse NPM1-Myc relationship was also identified in AML cells with wild-type FLT3. In contrast, the NPM1-Myc relationship was opposite in HEK293 cells co-transfected with FLT3-ITD as well as AML cells carrying FLT3-ITD mutations. Furthemore, gene transfection of mutated NPM1, which was expected to disrupt NPM1 functions, effectively attenuated the Myc-promoting effect of NPM1 in HEK293 cells transfected with FLT3-ITD. The NPM1-mediated regulation of Myc was highly dependent on the proteasomal degradation pathway, since its effects on Myc were not at the transcriptional level, but dramatically inhibited by MG132, a proteasome inhibitor.

CONCLUSIONS

Our findings support the model that FLT3-ITD can convert NPM1, which is normally a tumor suppressor, into an oncoprotein, by means of upregulating the expression of Myc. Our model may explain why NPM1 mutations, which disrupt NPM1 functions, attenuates the oncogenic effects of NPM1 in AML carrying FLT3-ITD and confers better prognosis.

Supervisor: Dr. Peng Wang

Prognostic implications of abnormal left-right lung perfusion differential on routine post-transplant ventilation-perfusion scans

David Li, Jonathan Abele, Parveen Sunner, Ali Kapasi, Alim Hirji, Justin Weinkauf, Dale Lien, Rhea Varughese, Jayan Nagendran, Kieran Halloran.
Supervisor: Dr. Kieran Halloran

INTRODUCTION

Lung ventilation-perfusion (VQ) scans can be used for diagnosing pulmonary embolism, surgical lung resection planning and monitoring after lung transplant. Long-term implications of abnormalities on routine post-transplant studies however are unknown. The relative lung perfusion distribution obtained from VQ scans provides an assessment of the pulmonary blood flow with a 55%-45% right-to-left differential typically considered the threshold of normal. We hypothesized that unbalanced relative lung perfusion on 3-months post-transplant VQ scan would be associated with poorer long-term survival and secondarily with increased frequency or severity of chronic lung allograft (CLAD) and baseline lung allograft dysfunction (BLAD).

METHODS

We studied all double lung transplant recipients at UAH between 2004-2016. The primary variable of interest was perfusion differential, with an abnormal threshold ?10% on 3-months VQ scan. We used Kaplan Meier estimates with log-rank tests to assess the association between lung perfusion differential and survival as well as CLAD development. Fisher's Exact and Cochran-Armitage tests were used to evaluate the relationship between perfusion differential and baseline lung allograft dysfunction (BLAD, defined as failure to achieve both FEV1 and FVC ?80% predicted on 2 consecutive tests ?3 weeks apart).

RESULTS

Of 340 patients who met inclusion criteria, 169 (49%) had a relative perfusion differential of at least 10% on their 3-months VQ scans. Patients with increased perfusion differential had longer hospital stays (24 days vs. 21 days; p=0.004), poorer overall survival (p=0.011) and increased CLAD onset (p=0.012). Increased perfusion differential was also associated with increased risk of BLAD (42% vs. 32%; p=0.043) and higher grade BLAD (p=0.006).

CONCLUSIONS

Abnormal relative lung perfusion differential is common after lung transplant and associated with increased risk of death, poor post-transplant baseline function and CLAD. We feel this measurement warrants further exploration as a potential predictor of future lung dysfunction and its related risk, particularly the mechanisms and risk factors.
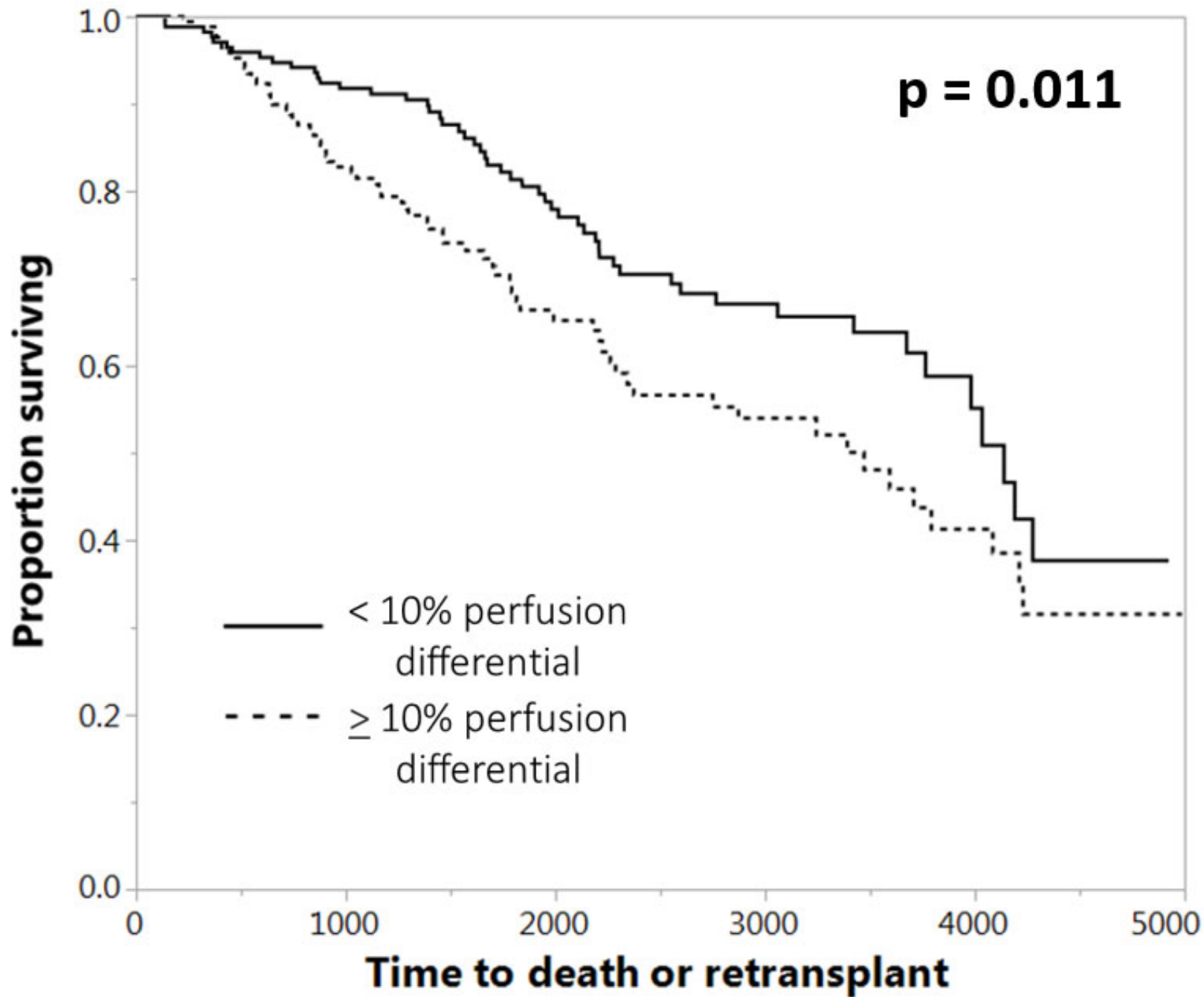
Supervisor: Dr. Kieran Halloran

Figure 1. *Kaplan-Meier estimation of overall survival.*

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

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

INTRODUCTION

Plakoglobin (PG) is a dual cell adhesion and signaling protein that generally acts as a tumor suppressor. We have shown that one mechanism by which PG 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. Notably, p53 is mutated in 50 % of all cancers and 90% of metastatic tumors. The majority of TP53 alterations are missense mutations in the DNA binding domain (DBD). The mutant p53 (mp53) may lose tumor suppressor properties and/or gain oncogenic function (GOF). GOF mutants are classified as conformational (change the DBD structure) and contact (maintain the DBD structure but decrease p53-DNA interaction). We previously showed that PG interacted with several mp53s, restoring their in vitro tumor/metastasis suppressor activities. Here, we have compared the effect of PG on conformational mp53R175H (arginine 175 to histidine) or contact mp53R273H (arginine 273 to histidine) relative to wild-type (WT) p53.

METHODS

PG and p53 deficient H1299 cells were transfected with p53 (WT, R175H, R273H) without or with PG and assessed for cell proliferation, anchorage-independent cell growth, migration, invasion and the expression of several adhesion proteins, signaling molecules and regulators of p53 stability.

RESULTS

The results showed that PG interacted with p53-WT, p53R175H and p53R273H similarly. However, the reduction in the in vitro tumorigenic/metastatic properties of H1299-p53-R273H-PG cells was not as drastic as those of p53-R175H-PG cells. Consistent with this observation, changes in the level of N-cadherin, b-catenin, AKT2 and NPM were more drastic in p53-R175H-PG cells relative to p53-R273H-PG, which was similar to that of p53-WT-PG cells.

CONCLUSIONS

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

Supervisor: Dr. Nadia Jahroudi

Cell-Specific Regulation of the GATA-4/6 Transcription Factors by the Metabolic Enzyme PKM2 Provides Insight into a Biologic Function Essential for Cardiac Health and Survival

Maria Areli Lorenzana Carrillo; Keshav Gopal; Nikole J. Byrne; Bruno Saleme; Subhash K. Das; Saymon Tejay; Yongneng Zhang; Alois Haromy; Farah Eaton; Jason R. B. Dyck; John R. Ussher; Evangelos D. Michelakis; Gopinath Sutendra.
Supervisor: Gopinath Sutendra

INTRODUCTION
Pyruvate Kinase M2 (PKM2) is a glycolytic enzyme that can translocate to the nucleus and regulate different transcription factors. Although its function has been studied extensively in cancer, its biologic role in the heart, and specifically terminally differentiated adult cardiomyocytes, remains elusive. Because PKM1 is the more abundant isoform in cardiomyocytes, we speculated that PKM2 would not have a genetically redundant role to PKM1, but instead may be critical in regulating cardiomyocyte-specific transcription factors.

METHODS
A transverse aortic constriction (TAC) banding model was used to assess the levels and modifications of PKM2 during heart failure. Constitutive cardiomyocyte-specific PKM2-deficient mice were generated to evaluate the biological role of PKM2 in adult cardiomyocytes. Unbiased RNA sequencing was utilized to assess novel PKM2-induced signaling pathways in adult cardiomyocytes. Induced pluripotent stem cells (iPSCs) were used to translate mechanistic findings to mature human cardiomyocytes.

RESULTS
PKM2 levels were lower (while PKM1 was higher), but serine-37 phosphorylated PKM2 (S37P-PKM2) was higher in terminally differentiated tissues, including the heart, brain, and skeletal muscle. Cell-specific analysis showed S37P-PKM2 was preferentially localized in the nucleus of cardiomyocytes, compared to cardiac fibroblasts (where PKM2 was mainly cytoplasmic). In a heart failure model, PKM2 levels increased in cardiac fibroblasts but correspondingly decreased in cardiomyocytes, in comparison to sham controls. Cardiomyocyte-specific PKM2-deficient mice developed age-dependent cardiac dysfunction with decreased survival, compared to their control littermates. Mechanistically, PKM2-deficient hearts had decreased levels of the cardiomyocyte-specific survival transcription factors GATA4 and GATA6, compared to control hearts. Finally, the E3 ubiquitin-ligase TRIM35, which was induced in heart failure, ubiquitinated and degraded PKM2, along with GATA4 and GATA6 in adult mouse or human iPSC-derived cardiomyocytes.

CONCLUSIONS
This study shows a new and previously unrecognized biologic role for PKM2 in the regulation of cardiomyocyte-specific transcription factors and identifies a novel therapeutic target (TRIM35) in heart failure.
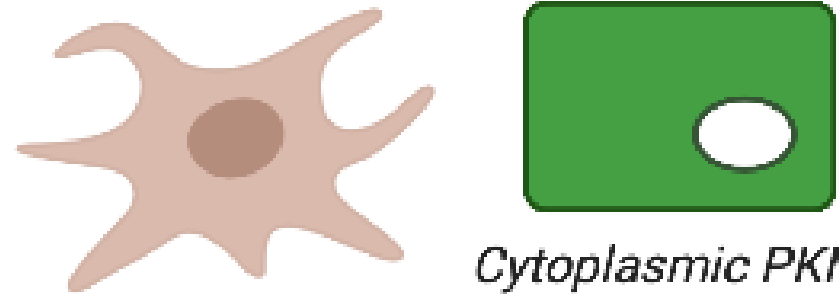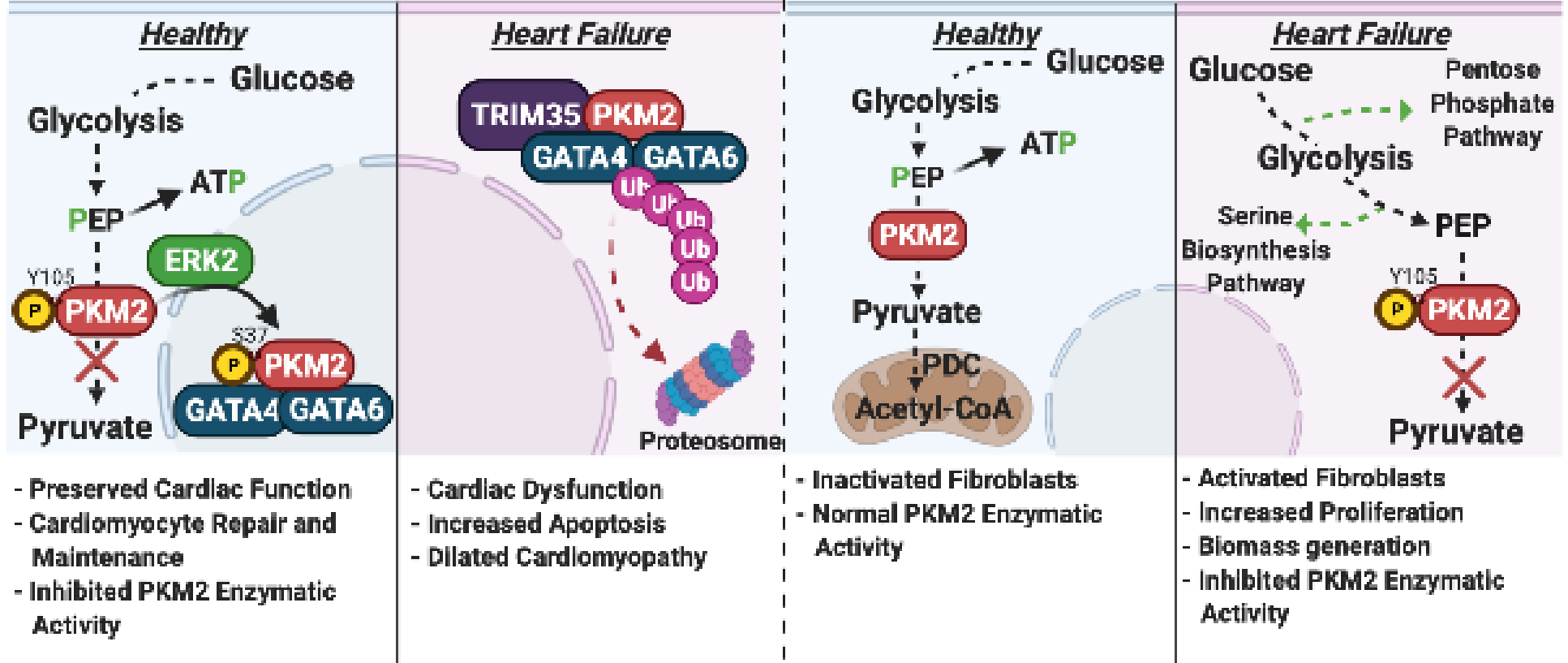
Supervisor: Dr. Gopinath Sutendra
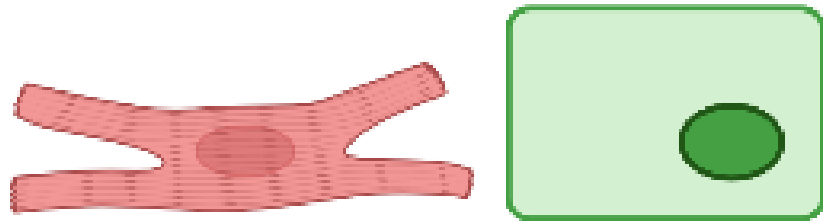
Characterizing The Role of Endothelial Phosphatidylinositol 3-kinase Beta Catalytic Subunit in Vascular Injury Repair of The Chronic Allograft Vasculopathy in Mice Heart Allografts

Andrew G. Masoud, Jiaxin Lin, Lin F. Zhu, Kesheng Tao, Zamaneh Kassiri, Colin C. Anderson, Gavin Y. Oudit, Lori J. West, and Allan G. Murray
Supervisor: Allan Murray

INTRODUCTION

Despite heart failure management progression, heart transplantation remains the definitive therapy for end-stage cardiac patients. Yet, donor hearts are scanty, transplant rates have remained stagnant, and many recipients die on the waiting list. Thus, to maximize heart allograft survival is quintessential.

Chronic allograft vasculopathy (CAV) of the transplant hearts is the leading cause of mortality beyond the first year of transplantation. It develops as a maladaptive repair to the injured endothelial cells (ECs) lining epicardial and branch arteries, developing obliterative fibro-intimal thickening, microvessel injury, diminshed blood supply and graft failure.

Phosphatidylinositol 3-kinase beta (PI3KB) is a class IA PI3 Kinase that is significantly involved in cellular proliferation, survival, migration, and angiogenesis. It was reported to mediate microvascular EC repair of thrombotic microangiopathy (TMA). Additionally, postnatal EC-specific PI3KB deletion led to acute kidney failure in TMA mouse models, indicative of its potential protective role.

We hypothesize that PI3KB loss worsens CAV injury and maladaptive repair.

METHODS

We induced CAV via transplanting HY-minor histocompatibility antigen-mismatched male EC-specific PI3KB knockout (P110bTie2Mer) or PI3KB littermate (P110bflx/flx) hearts into wild-type female mice, to be harvested at 2 or 6 weeks post-transplantation to characterize: intimal area, EC loss, microvessel density, inflammatory-cell infiltrate, tip-cell genes in coronaries and the myocardium, and the in vivo PI3KB pharmacological inhibitor (GSK2636771) effect on heart allografts.

RESULTS

Surprisingly, P110bTie2Mer donor hearts and GSK2636771-treated allograft-harboring mice showed: suppressed allograft vasculopathy, preserved microvessels, and less EC and smooth muscle cell injury/apoptosis without changes in tip-cell genes at 2 and 6 weeks post-transplantation nor the allogeneic immune response quality.

Furthermore, PI3KB inhibition alleviated in-vitro induced inflammaging in human umbilical vein ECs.

CONCLUSIONS

These protective effects of PI3KB inhibition could serve as pharmacotherapeutic targets to preserve allografts' function.

Further characterization of the PI3KB-inhibited EC response to the infiltrating immune cells and the other PI3K isoforms' activity is critical.

Supervisor: Dr. Allan Murray
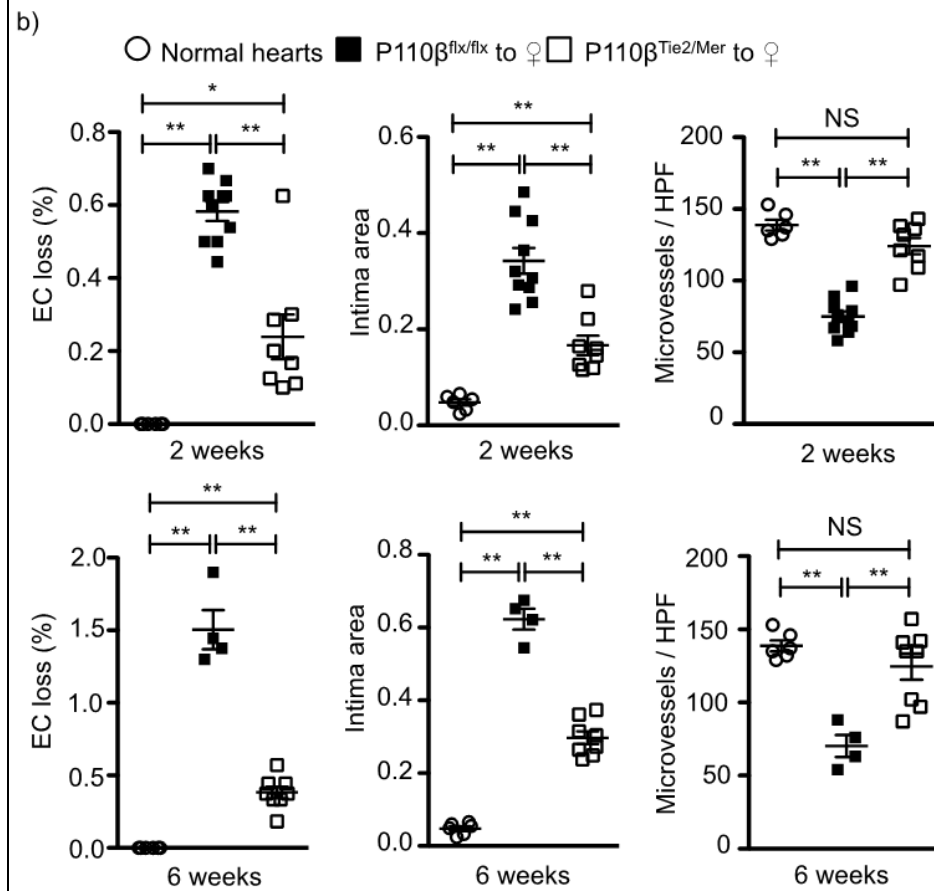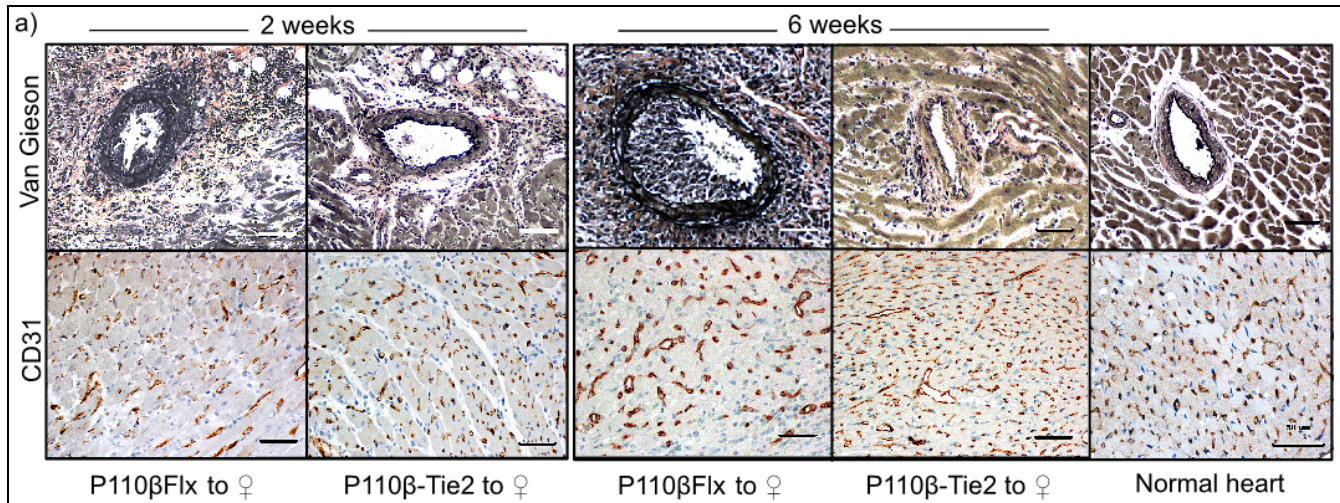
a) A depiction showing histological micrographs of the Van Gieson staining for intimal characterization and the endothelial PECAM-1 (CD31) staining for microvessels in both the P110b ^Flx/Flx (control) and the P110b ^Tie2Mer (endothelial specific KO) heart allograft harboring mice at 2 or 6 weeks post-transplantation (n=6-10).

b) Quantification of the endothelial gaps/loss %, intima area, and the microvessel density in mice groups of a) vs normal hearts (n=6-10).

c) Quantification of the endothelial gaps/loss %, intima area, and the microvessel density in the vehicle-gavaged or the PI3Kβ inhibitor daily oral gavaged female wild-type mice harboring male wild-type heart allografts from week 2 till week 6 post-transplantation vs normal hearts (n=6-9).

P *<0.05, **<0.01, NS= Non Significant via one-way ANOVA with Bonferroni's post-hoc test.

Scale bar = 50 uM
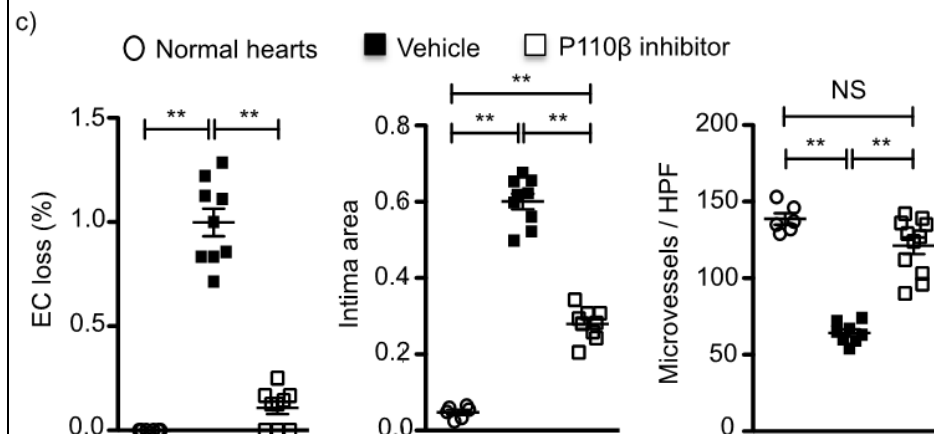
Proximal tubular reabsorption impacts on microvascular regulation via the TGF system

Shayan Poursharif, Will Cupples and Branko Braam
Supervisor: Dr. Branko Braam

INTRODUCTION

Nephrovascular units (NVUs) (nephrons with attached afferent and efferent arterioles) form a network in autoregulation of renal blood flow (RBF). This is mediated via the tubuloglomerular feedback (TGF) mechanism, which stabilizes macula densa solute delivery by controlling afferent arteriolar diameter. We reviewed how changes in proximal tubular sodium reabsorption lead to changes in TGF activity and affect microvascular regulation by NVUs.

Compounds decreasing proximal tubular sodium reabsorption increase the concentration of solutes reaching macula densa, activate TGF system and strengthen the network among NVUs. Moreover, some of these compounds affect tubular reabsorption and TGF responsiveness simultaneously, which could offset or amplify the effect of changes in distal solute delivery.

Important proximal tubular sodium transporters are sodium-hydrogen exchanger 3 (NHE3) and sodium-glucose co transporter 2 (SGLT2). Angiotensin II, endothelin, insulin and aldosterone increase NHE3 function, while glucagon, dopamine and serotonin decrease NHE3 function. SGLT2 is regulated at the transcriptional level by Angiotensin II, insulin and hepatocyte nuclear factor. Compounds inhibiting these transporters would decrease sodium reabsorption in the proximal tubule, which ultimately increase TGF activity and enhance coupling among NVUs.

SGLT2 inhibitors, angiotensin-converting enzyme inhibitors (ACEI) and furosemide decrease sodium reabsorption in the proximal tubule. Also, it has been demonstrated that TGF is capable of realigning to a new state during chronic activation by furosemide to accommodate long term alterations in macula densa solute delivery.

In some pathophysiological conditions such as diabetes mellitus there is an enhanced proximal tubular sodium reabsorption which can weaken network among NVUs. In such situations, compounds decreasing proximal tubular sodium reabsorption could strengthen network among NVUs. Consequently, as proximal tubular sodium reabsorption is decreased by SGLT2 inhibitors, we would like to investigate the effects of SGLT2 inhibitors on TGF activity and network function among NVUs in diabetic rats.

METHODS

RESULTS

CONCLUSIONS

Supervisor: Dr. Branko Braam

The evaluation of frailty assessment tools and their measurement properties in Chronic Kidney Disease (CKD)

Puri A, Lloyd A, Bello A, Tandon P, Campbell S, Thompson S
Supervisor: Dr. Stephanie Thompson

INTRODUCTION
The burden of frailty is high among people with Chronic Kidney Disease (CKD) ranging from 30-73%, which is three to seven times higher than the non-CKD population. This high prevalence is owing in part to shared pathophysiology, such as inflammation, cardiovascular disease and malnutrition. To address frailty in CKD, validated and reliable frailty screening tools are necessary to assess the condition and to predict the risk of hospital-related adverse outcomes. Our aim is to evaluate the measurement properties of frailty assessment tools used in CKD populations and to recommend the most appropriate tool(s) for application in research and clinical practice.

METHODS
This is a systematic review of original studies. We searched PROSPERO, OVID Medline, OVID EMBASE, OVID Health and Psychosocial Instruments, Cochrane Library (CDSR and Central), EBSCO CINAHL, Proquest Dissertations and Theses Global and SCOPUS for studies that were in English, included CKD populations at any stage or modality, and evaluated a frailty screening tool. Eligible articles were assessed by two independent reviewers. As per COSMIN guidelines, data on the validity and reliability of frailty tools was extracted. Methodological quality assessment and data synthesis will be performed.

RESULTS
The literature search yielded 647 articles, of which 61 studies (n =16026 participants) met the inclusion criteria. Thirty-six (59%) of the studies evaluated frailty tools in dialysis populations. Commonly used frailty assessment tools were: the Clinical Frailty Scale (CFS), Edmonton Frail Scale, Frailty Index, FRAIL Scale, Fried's Phenotype, G8 Questionnaire, Groningen Frailty Indicator (GFI), Strawbridge Frailty Questionnaire (SQ), and the Tilburg Frailty Indicator (TFI). Of the measurement properties defined by the COSMIN Taxonomy, 80% of the frailty assessment tools presented predictive validity for hospital-related outcomes.

CONCLUSIONS
With the high prevalence of frailty in people with CKD, identifying and measuring the response to frailty interventions is critical. This review will help identify the appropriate tool.

Supervisor: Dr. Stephanie Thompson

Mechanism of CLIC5A recruitment to, and Rac1 activation in the Plasma Membrane-associated Ezrin Complex

Md. Mizanur Rahman, Laiji Li, and Barbara J. Ballermann
Supervisor: Dr. Barbara Ballermann

INTRODUCTION

Despite their name, CLIC (Chloride Intracellular Channel) proteins have not been proven to be membrane-spanning channels in vivo. We reported that CLIC5A is a component of the Ezrin/Podocalyxin/Actin complex in kidney glomerular podocytes and endothelial cells, preventing hypertension-induced glomerular injury. ERM (ezrin, radixin, moesin) proteins help organize the actin cytoskeleton by linking membrane-spanning proteins to actin. CLIC5A stimulates Rac1-GTP-dependent phosphatidylinositol-4,5-bisphosphate [PI (4,5) P2] generation, causing Ezrin activation and phosphorylation, thus coupling Podocalyxin, via Ezrin, to the cytoskeleton. We hypothesized that CLIC5A may associate with the plasma membrane by binding Ezrin which, in turn, results in Rac1 activation.

METHODS

Fractionation of isolated glomeruli was used to define the CLIC5A sub-cellular localization. Direct protein-protein interactions were determined by Yeast two-hybrid (Y2H) assay. Human glomerular endothelial cells were transduced with adenoviral GFP/CLIC5A or GFP-vector and transfected with Ezrin-specific or control siRNA followed by quantification of CLIC5A-stimulated Rac1-GTP.

RESULTS

CLIC5A was found to be a largely cytosolic protein, though a portion also associated with the plasma membrane and cytoskeletal fractions. A Y2H screen revealed that CLIC5A interacts directly with the C-terminal domain of ERM proteins, domain mapping showed that it binds the Ezrin C-terminus (432-586) but not full-length (1-586) Ezrin. Phosphorylation of Ezrin 432-586 at T567 increased the CLIC5A binding affinity. Phosphomimic Ezrin (432-586; T567D) mutant competitively inhibited CLIC5A-stimulated phosphorylation of endogenous Ezrin. Finally, siRNA silencing of endogenous Ezrin significantly reduced CLIC5A stimulated-Rac1 activation (Fig. 1).

CONCLUSIONS

CLIC5A interacts directly with Ezrin, and Rac1 activation by CLIC5A is Ezrin-dependent. The finding that direct interaction of CLIC5A with full-length Ezrin was not detected suggests that only the active, open Ezrin conformation, freeing the C-terminus, has a high affinity for CLIC5A. We interpret the data to indicate that the direct CLIC5A/Ezrin interaction results in localized Rac1 activation and Ezrin phosphorylation in the CLIC5A/Ezrin/Actin complex.

Supervisor: Dr. Barbara Ballermann
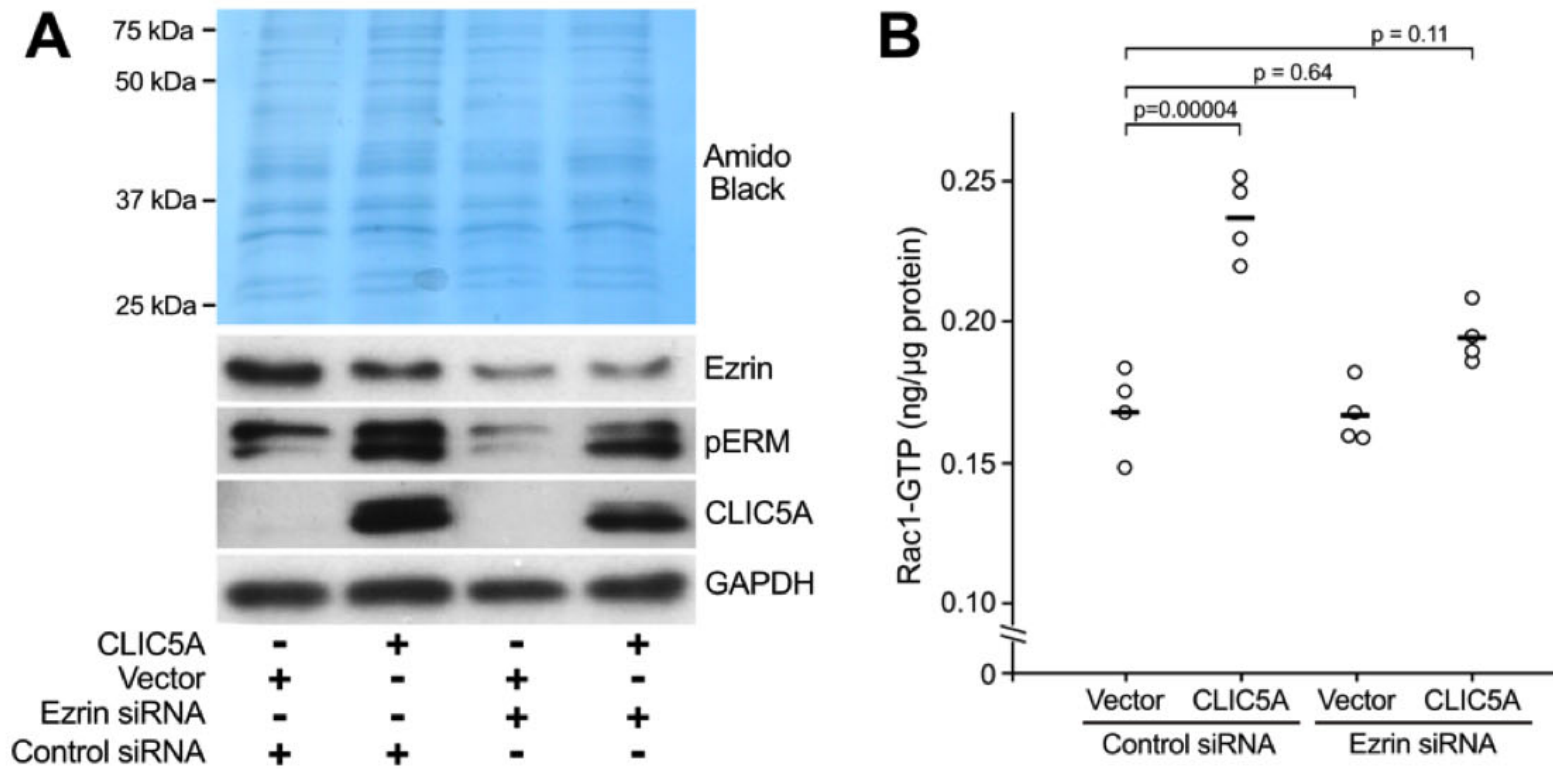
Figure 1. CLIC5A-dependent Rac1 activation requires Ezrin. (A) hGEN cells were transduced with adenoviral GFP/CLIC5A or GFP- vector and transfected with Ezrin-specific or control siRNA. Amido black: upper panel. (B) Effect of Ezrin siRNA on CLIC5A-stimulated Rac1-GTP (mean±SD, n=4 experiments, One-way ANOVA, and Dunnett's comparison to a common control ("vector/control siRNA").

Characterization of three monoclonal antibodies targeting the middle, amino- and carboxyl-terminus segments of Calcium-binding protein, spermatid-associated 1 (CABS1)

Reyes-Serratos E, Befus AD, Marcet-Palacios M
Supervisor: Dr. Marcelo Marcet-Palacios

INTRODUCTION
Previously, we identified a seven amino acid, C-terminal anti-inflammatory polypeptide in the rat protein Submandibular Rat 1 (SMR1). Computational analyses showed that although humans do not have the SMR1 gene, humans express a very similar amino acid sequence within another gene called Calcium-binding protein, spermatid-associated 1 (CABS1). We developed polyclonal antibodies (pAbs), named H2 and H1, targeting a middle section and the C-terminal anti-inflammatory peptide of CABS1, respectively. Using Western blot (WB), pAbs identified CABS1 in human submandibular gland, lung, testis, and saliva. These results suggested that CABS1 polypeptides that vary in molecular size are present in human-derived samples. Moreover, H2 identified CABS1-derived bands whose levels correlate to psychological distress and to resilience to stress. To further this research, we made monoclonal antibodies (mAbs) to CABS1. We hypothesize that novel mAbs raised to different CABS1 domains will recognize with higher specificity CABS1-derived polypeptides and have begun their characterization.

METHODS
We made 30 hybridomas to CABS1 and selected three for detailed characterization, namely, 15B11 (analog to H2), 13G3 (analog to H1) and 4D1 (targeting CABS1 N-terminus). We characterized CABS1 in an overexpression cell lysate (OEL) and a negative control cell lysate (NCL) using these mAbs in WB and compared the results with those using our pAbs.

RESULTS
All mAbs detected a band at ~80 kDa in OEL, just as H1 and H2. mAb 13G3 detected a faint band at ~65 kDa, just as H1. Initial characterization of our mAbs aligns well with the corresponding pAbs analyses of CABS1 in OEL. As expected, mAbs did not react with NCL, a disadvantage we had previously identified in pAb H2 (Figure 1).

CONCLUSIONS
Our data indicates that our mAbs bind to CABS1. We will use these mAbs to further characterize, immunoprecipitate, and sequence CABS1 in human-derived samples. Future studies will evaluate function and receptor targets of CABS1.

Supervisor: Dr. Marcelo Marcet-Palacios

Transient overexpression cell lysate controls

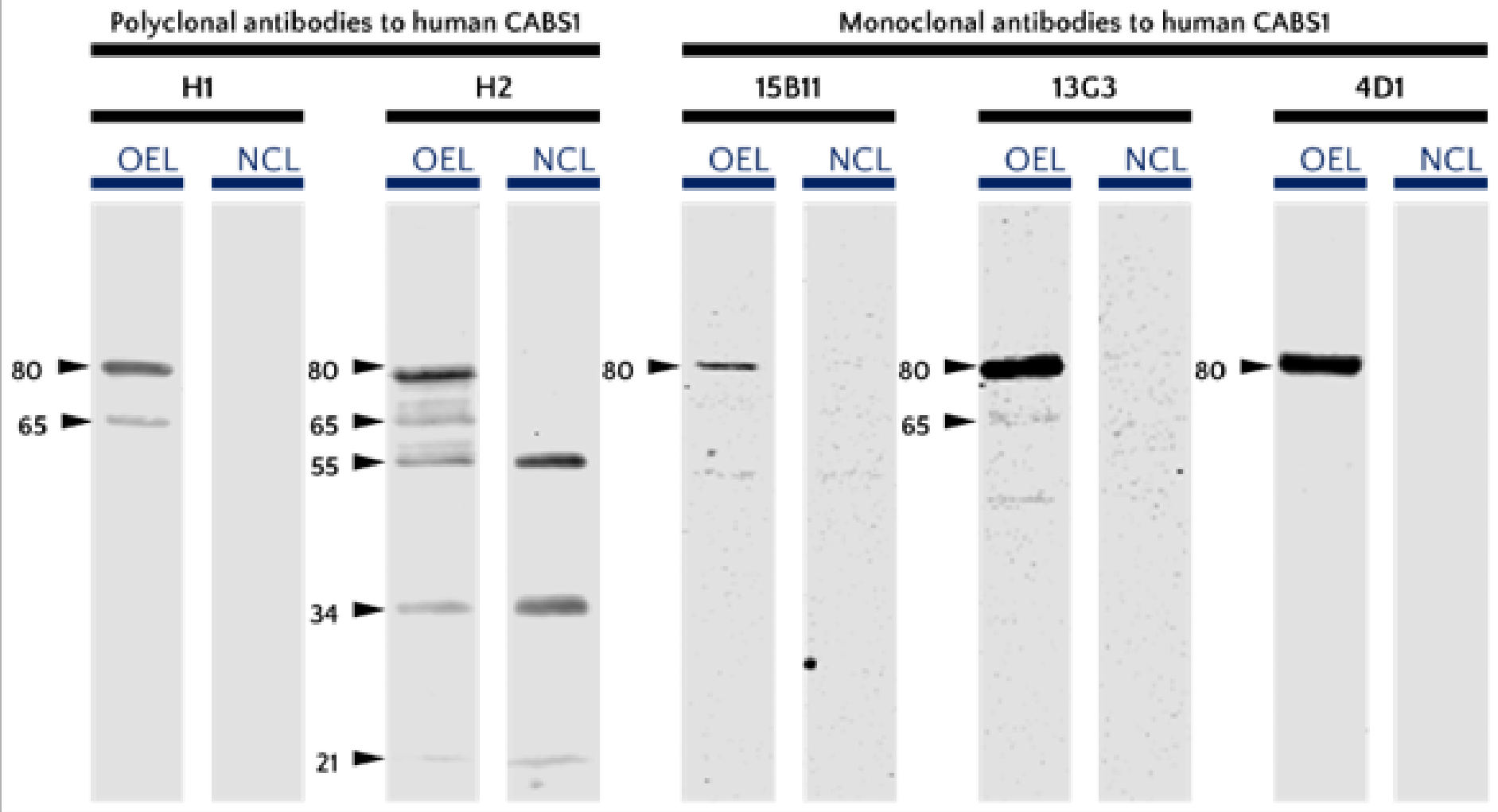**Figure 1. Western blots of CABS1 overexpression cell lysate (OEL) and its negative control cell lysate (NCL) immunoprobed using monoclonal and polyclonal antibodies targeting CABS1.** Molecular weight (kDa) is indicated next to arrows pointing to bands. All antibodies see a strong band at ~80 kDa. H1 and 13G3 detect a fainter band at ~65 kDa. H2 interacts with NCL at 55, 34, and 21 kDa, suggesting these bands may not be CABS1.

Learning from a Rare Phenomenon: Spontaneous Clearance of Hepatitis C Virus Post-Liver Transplant

Singh, Noreen, Mang, Ma, Montano-Loza, Aldo & Bhanji, Rahima
Supervisor: Dr. Rahima Bhanji

INTRODUCTION

Hepatitis C virus (HCV) can lead to chronic liver damage resulting in cirrhosis and hepatocellular carcinoma. Spontaneous clearance of HCV has been documented after an acute infection in 20-45% of individuals (1). However, spontaneously resolved chronic HCV following liver transplant is rare and has been documented only in a few case reports. The phenomenon of spontaneous clearance of chronic HCV occurs together with other meaningful events, which are typically associated with significant changes in the host immunity.

(1)Seeff LB. (2002). Natural history of chronic hepatitis C. Hepatology, 36(5 Suppl 1), S35-46

METHODS

We report three cases of spontaneous resolution of chronic HCV following liver transplantation (LT) and review of prior case reports. HCV treatment with direct-acting antivirals has an excellent cure rate but understanding the mechanisms behind this unusual event may provide clinicians with important insights with regards to timing and duration of treatment following transplant.

RESULTS

Though the small number of cases prevents the identification of predictors of clearance however some factors have emerged. For instance, viral load can be used to determine the duration of treatment; with shorter duration in those with low viral load. Median time to spontaneous HCV clearance was 11 months (IQR 3.6, 66 months); with almost half of the patients achieving spontaneous clearance within 6 months.

CONCLUSIONS

From our case report, we have concluded that treatment for HCV following LT could therefore be started after 6 months. This would provide an additional advantage of limiting drug-drug interactions early in the post-transplant setting. In conclusion, spontaneous resolution of chronic HCV following LT is a rare phenomenon and seems to be related to immunomodulatory effects. Learning from this rare event may be the first step to individualized medicine.

Supervisor: Dr. Rahima Bhanji

Table 1: Summary of Cases of Spontaneous Hepatitis C Clearance Post-Liver Transplant. Cases 1 – 15 adapted from Haque et al., (2010); Cases 16 – 20 adapted from Elsiesy et al., (2015); Cases 21 – 22 adapted from Urzúa et al., (2014), Case 23 adapted from Kogiso et al., (2015); Cases 24 – 27 adapted from Tamaki et al., (2015) and Cases 28-30 from our reported cases.

ID	Author (published year)	Age (years)	Sex	Preoperative HCV RNA (IU/ml)	HCV genotype	Rejection Episode	Concomitant Issues	Immunosuppression	HCV Clearance Time
1	Doughty et al., (2000)	49	M	+	N/A	3	---	MP, ZAA, CSA, CS	12 months
2	Casanovas-Taltavull et al., (2004)	46	M	+	1b	N/A	HBV infection	ATG, CSA, MMF, CS	66 months
3	Casanovas-Taltavull et al., (2004)	39	F	+	1b	N/A	Hydroxyurea	ATG, CSA, AZA, CS	96 months
4	Casanovas-Taltavull et al., (2004)	58	F	+	1b	N/A	CMV infection	ATG, CSA, MMF, CS	16 months
5	Casanovas-Taltavull et al., (2004)	60	M	+	1b	N/A	---	ATG, CSA, MMF, CS	N/A
6	Casanovas-Taltavull et al., (2004)	58	F	+	1b	N/A	---	ATG, CSA, AZA, CS	N/A
7	Neumann et al., (2004)	54	M	+	1b	1	HAT, retransplant	TAC, MMF, CS	3 months
8	Samonakis et al., (2005)	48	M	250,000	1a	3	Renal Failure	TAC, AZA, CS	75 months
9	Samonakis et al., (2005)	55	M	121,000	4	3	Renal Failure	TAC, AZA, CS	15 months
10	Bhagat et al., (2008)	43	M	564,000	N/A	3	HIV/HAART	MP, TAC, MMF	1 month
11	Bhagat et al., (2008)	44	M	450,000	N/A	3	HIV/HAART	MP, TAC	1 month
12	Suneetha et al., (2008)	69	F	+	3a	3	Renal Failure/Dialysis	MP, Il2a, CSA, CS	12 years
13	Weber et al., (2009)	53	M	2.5 million	1a	3	---	TAC, CSA, MMF →CSA	28 months
14	Dale et al., (2009)	32	F	3.2 million	N/A	1	Dialysis/Renal Tx	Basiliximuab, TAC, MMF, CS	5 months
15	Haque et al. (2010)	66	F	+	2a/2c	3	IVC thrombosis	TAC, MMF, CS	11 months
16	Seethararm et al., (2011)	48	M	675,000	1	0	---	MP, MMF, CS	2.25 months
17	Guiterrez-Morena et al., (2012)	38	M	2564	1	0	HIV	CSA, MMF, CS	5 months
18	Chin et al., (2012)	40	M	24	1a	1	Alcohol	Daclizumab, TAC, CS, MMF	34 months
19	Chin et al., (2012)	41	M	+	1	0	Alcohol	TAC, CS, AZA	9 years
20	Elsiesy et al., (2015)	32	F	65,553	4	0	AIH, DM	FK, CS, CSA, CS	1 months
21	Urzúa et al., (2014)	51	M	+	N/A	1	Colon Cancer	CSA, MMF, TAC	18 months
22	Urzúa et al., (2014)	48	M	280,998	3a	0	D2M, Alcohol	CSA, IL2a	56 months
23	Kogiso et al., (2015)	50	F	19,952	1	N/A	---	TAC, MMF, MP, CS	~3 month
24	Tamaki et al., (2015)	66	M	199,526	1b	0	Sepsis	Rituximab, TAC, MMF, MP, CS	5 months
25	Tamaki et al., (2015)	61	M	199	2	Yes	Sepsis	TAC, MMF, MP, CS	3.6 months
26	Tamaki et al., (2015)	55	M	125	1b	0	---	TAC, MMF, MP, CS	5.8 months
27	Tamaki et al., (2015)	55	M	316,227	1b	Yes		TAC, MMF, MP, CS	0.5 months
28	Our Case 1	57	M	+	1a	2	CMV infection	Sirolimus, MMF, CS	15 years
29	Our Case 2	64	M	+	1	0	Donor HBV core +	TAC, MMF	2 months
30	Our Case 3	57	M	+	1a	0	Renal tx	TAC, MMF	1 year

LT – liver transplant; N/A – not available/data not reported; HBV– Hepatitis B; CMV – cytomegalovirus; HAT – hepatic artery thrombosis; HAART – high activity anti-retroviral therapy; IVC – inferior vena cava; HIV – human immunodeficiency virus; AIH – autoimmune hepatitis; DM – diabetes melilites; MP – methyl prednisone; AZA, Azathioprine; CSA – cyclosporine; CS – corticosteroid ; ATG – anti thymocyte globulin; MMF – mycophenolate mofetil; Tac – tacrolimus; IL2a – interleukin 2 receptor antibody

Internet search results correlate with seasonal variation of sarcoidosis

Amanda Stanton, Steven J Katz
Supervisor: Dr. Steven J Katz

INTRODUCTION
The etiology and pathophysiology of sarcoidosis remains unclear, with epidemiologic studies limited by its relatively low prevalence. The internet has prompted patients to seek information about medical diagnoses online; Google Trends provides access to an anonymized version of this data, which has a new role in epidemiology. The purpose of this study was to determine if there is seasonal variation in the relative search interest of sarcoidosis, which would suggest seasonal variation in the incidence of sarcoidosis.

METHODS
Google Trends was used to assess the relative search volume from 2010 to 2020 for "sarcoidosis" and "sarcoid" in 7 countries. Analysis of variance with multiple comparisons was performed to compare the mean search volume by month and by season for each country, with a p-value of 0.05 indicating statistical significance.

RESULTS
Our analysis revealed a significant seasonal variation in search volume in 4 of the 7 countries and in the Northern Hemispheric countries combined. Direct comparison showed a higher search volume in spring, specifically March & April, than in the winter. Southern Hemisphere data was not statistically significant but showed a trend towards a nadir in December and a peak in September and October. The main limitations of this study included the absence of absolute data available from Google Trends and the assumption that search volume correlates with diagnosis of sarcoidosis.

CONCLUSIONS
Overall, these findings suggest seasonal variation with a possible peak in spring and trough in winter. This supports the hypothesis that sarcoidosis has seasonal variation and is more commonly diagnosed in spring, but more evidence is needed to support this, as well as investigation into the pathophysiology of sarcoidosis to explain this phenomenon.

Supervisor: Dr. Steven J Katz

Pre-Transplant Medications and Primary Graft Dysfunction Risk in Lung Transplant Recipients

Amanda Stanton MD, Rhea Varughese MD, Alim Hirji MD MSc, Justin Weinkauf MD, Ali Kapasi MD, Dale Lien MD, Kieran Halloran MD MSc
Supervisor: Dr. Kieran Halloran

INTRODUCTION
Primary graft dysfunction (PGD) is a serious complication which can occur immediately after lung transplantation marked by acute lung injury and reperfusion edema, but the effect of pre-transplant medication use on PGD risk is not known. We hypothesized that some pre-transplant medications could be associated with PGD risk, particularly anti-inflammatories activity like macrolide antibiotics and statins or vasoactives like anti-hypertensives and pulmonary vasodilators.

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

RESULTS
19% of 330 patients who underwent lung transplant during the study timeframe developed PGD3. Phosphodiesterase inhibitor (PDE5i), endothelin receptor antagonist, proton pump inhibitor, and beta blocker (BB) use were associated with PGD3 risk. After adjusting for known PGD risk factors [including indication for transplant], PDE5i and BB use remained associated with increased PGD risk, with odds ratios of 3.12 (p=0.0438) and 2.63 (p=0.0475) respectively. The association between BB use and PGD3 persisted despite further correction for left ventricular end diastolic pressure (LVEDP).

CONCLUSIONS
Our exploratory analysis identified pre-transplant PDE5i and BB use as two candidate medications which could modify PGD risk independent of indication, given adjustment for pulmonary diagnosis, mPAP, and LVEDP. We did not identify associations with use of macrolides or statins. These novel associations would benefit from further exploration in dedicated individual studies.

Supervisor: Dr. Kieran Halloran

IGF-1: a new biomarker for muscle dysfunction associated with decompensation in patients with liver disease

Muhammad Imran Suliman, Clara Zhou, Jessica Chow, Maryam Ebadi, Aldo J. Montano-Loza, Rahima A. Bhanji
Supervisor: Rahima A. Bhanji

INTRODUCTION

Skeletal muscle abnormalities like sarcopenia (loss of skeletal muscle mass and function), and myosteatosis (fatty infiltration of the muscle), are associated with adverse clinical outcomes in liver cirrhosis. Insulin-like growth factor 1 (IGF-1) is an important mediator of muscle growth and reduces muscle fiber degeneration. IGF-1 deficiency may contribute to decreased muscle mass or function. We hypothesized that IGF-1 could be used as a predictor of muscle abnormalities and determine its impact on patient and graft survival post-liver transplant.

METHODS

Adult patients (n=474) who underwent liver transplant between 2007 to 2020 were analyzed. Low IGF-1 was defined as <74 ng/ml. Sarcopenia was diagnosed based on skeletal muscle index (SMI) at L3 vertebra using CT scan (defined as SMI <50cm2/m2 in male and <39cm2/m2 in females). Myosteatosis was defined as <41 mean Hounsfield units in patients with a BMI up to 24.9, and <33 mean Hounsfield units in those with a BMI ?25. Six minute walk test (6MWT) was done to evaluate muscle function; poor performance was defined as ?250 m.

RESULTS

Patients with low IGF-1 [n=390(82.3%)] had more severe disease evidenced by higher MELD, decompensation, increased inflammation (higher CRP) and more likely to have ascites and hepatic encephalopathy. Sarcopenia was present in 50% (29) of patients with low IGF-1 and 64% (9) of patients with normal IGF-1 levels (p = 0.39). Myosteatosis was present in 45% (26) of patients with low IGF-1 and 57% (8) of patients with normal IGF-1 (p=0.55). Low IGF-1 was associated with a poor performance on the 6MWT. There was no association between low IGF-1 levels and either patient (p =1.0) or graft survival (p=1.0).

CONCLUSIONS

Pre-transplant low IGF-1 was associated with severe disease, decompensation and poor performance on 6MWT (suggesting an association with muscle function). There was no association with either graft or patient survival following transplant.

Supervisor: Dr. Rahima A. Bhanji

Table #1

Demographics	Normal IGF (n=84)	Low IGF (n=390)	p-value
Age in years	53 [41,61]	51 [43,59]	0.39
Sex -males	54 (64%)	268 (69%)	0.44
BMI (Kg/m^2)	25 [24,32]	27 [24,32]	0.89
Etiology	Normal IGF	Low IGF	p-value
HBV	8 (9.5%)	13 (3.3%)	0.02
HCV	19 (22.6%)	60 (15.4%)	0.11
ALD	9 (10.7%)	73 (18.7%)	0.08
NASH	8 (9.5%)	48 (12.3%)	0.58
AILD	24 (28.6%)	117 (30%)	0.89
HCC	32 (38.1%)	106 (27.2%)	0.05
Other	8 (9.5%)	45 (11.5%)	0.70
Severity of Liver Disease	Normal IGF	Low IGF	p-value
MELD-Na	15 [8-21]	16 [12,24]	0.01
Child Pugh Score Median	8 [6,11]	10 [8,12]	<0.001
Hepatorenal	12 (14.6%)	66 (17.4%)	0.63
Ascites	50 (59.5%)	299 (76.7%)	<0.01
Encephalopathy	34 (40.5%)	238 (61%)	0.001
Muscle Abnormalities	Normal IGF	Low IGF	p-value
Skeletal Muscle Index (cm^2/m^2)	44 [40,46]	47 [41,55]	0.29
Muscle radiodensity (HU)	35 [29,45]	40 [30,47]	0.73
6MWT (meters)	572[495,682]	528 [438,595]	0.01
Laboratory Findings	Normal IGF	Low IGF	p-value
C-reactive protein (mg/L)	4.7 [1.5,15]	8.8 [4,22]	0.001
Testosterone AM (nmol/L)	11 [1,20]	49 [1,19]	0.53
Vitamin D (nmol/L)	69 [47,95]	49 [29,71]	<0.001
Ammonia (µmol/L)	36 [31,51]	47 [29,69]	0.27

Table#2

	Patient Survival		Graft Survival	
	HR [95% CI]	P value	HR [95% CI]	P value
Age	1.06 [1.03,1.09]	<0.001	1.02 [0.99,1.06]	0.10
Sex	1.47 [0.9,2.5]	0.15	1.19 [0.64,2.23]	0.58
MELD	0.99 [0.98,1.03]	0.95	0.99 [0.97,1.02]	0.60
IGF-1	1.00 [0.99,1.00]	0.79	1.00 [0.99,1.00]	0.82

Diagnostic yield and impact of bronchoscopy in patients with a hematological malignancy or hematopoietic stem cell transplant presenting with pulmonary complications.

Sun, Ken, Hirji, Alim, Bhutani, Mohit
Supervisor: Mohit Bhutani

INTRODUCTION

Patients with hematological malignancies or hematopoietic stem cell transplant (HSCT) frequently develop pulmonary complications. Flexible video bronchoscopy is often performed to assist in the diagnosis of these complications. However, the impact of this intervention on treatment decisions is variable. In this study, we aim to assess the overall diagnostic yield and impact of bronchoscopy in this population and assess for predictors associated with improved diagnostic yield.

METHODS

We conducted a retrospective review of all adult patients admitted to our center with a hematological malignancy or HSCT who underwent flexible bronchoscopy between January 1, 2014 and June 30, 2019. Charts were reviewed to establish clinical course, radiographic findings, bronchoscopy results, and management change. Complication rates associated with bronchoscopy, including the use of blood products were assessed.

RESULTS

During the study period, 210 bronchoscopies were performed. Most patients had acute leukemia (70.0%), history of HSCT (16.7%), or lymphoma (5.7%). The diagnostic yield of bronchoscopies was 89/210 (42.4%), of which 51/89 (57%) led to a change in management. When a bronchoscopy was negative, 5/121 (4.1%) led to a de-escalation in therapy.

Univariate and multivariate analysis showed that HSCT, repeat bronchoscopy, previous pathogen identification, and transbronchial biopsies increase the yield of bronchoscopy. HSCT was strongly associated with a positive bronchoscopy (adjusted OR 2.45, 95% CI 1.06-5.69, p=0.036). The incidence of complications was 8.1%. 126/210 (60.0%) cases required pre-procedure blood products, on average, 1 unit of platelets.

CONCLUSIONS

This study of the impact of bronchoscopy in the management of patients with hematological malignancies or HSCT is the largest to date. Bronchoscopy in the evaluation of pulmonary complications in this population is a low risk, moderate-to-high yield intervention. Positive bronchoscopy led to a change in management in 57% of cases. Negative bronchoscopy did not lead to significant management changes, and this will require further study.

Supervisor: Dr. Mohit Bhutani

Comparing EPA entrustability scores given by staff physicians vs senior trainees to PGY1 residents

Dennis Wang, Steven Katz
Supervisor: Dr. Steven Katz

INTRODUCTION

Competency by Design (CBD) formally began July 1, 2019 for PGY1 Canadian Core Internal Medicine (CIM) residents. Many Entrustable Professional Activity (EPA) observations allow for documentation by either a staff physician, senior medicine resident (SMR), or subspecialty resident (SSR). This study aims to identify differences in EPA entrustability scores given to PGY1 residents by staff physicians vs senior trainees (SMRs and SSRs).

METHODS

Scores and comments of EPAs completed between July 1, 2019 and June 30, 2020 for all CIM PGY1 residents were extracted anonymously from the University of Alberta CBD platform. Scores given by staff physicians vs senior trainees were compared with the Mann-Whitney U test. Scores given by staff physicians vs SMRs vs SSRs were compared with the Kruskal-Wallis test. Word counts for positive and constructive comments written by staff physicians vs senior trainees were compared with the independent T test. Word counts for comments written by staff physicians vs SMRs vs SSRs were compared with one way ANOVA. The most common two-word phrases in comments were identified with QI Macros software.

RESULTS

2226 EPAs were observed (staff = 1174, senior trainees = 1052). EPA scores given by staff physicians (M = 4.56, SD = 0.639) were significantly lower (U = 501706, P <0.001) compared to senior trainees (M = 4.8, SD = 0.423). EPA scores given by SSRs (M = 4.73, SD = 0.48) were significantly lower (U = 93633.5, P <0.001) compared to SMRs (M = 4.85, SD = 0.38). Constructive comments written by staff physicians (M = 14.06, SD = 16.84) had significantly lower word counts compared to senior trainees (M = 15.85, SD = 16.43) for overall EPAs (t(2224) = -2.528, P = 0.012).

CONCLUSIONS

Staff physicians gave lower EPA scores and had lower word counts on constructive comments, compared to senior trainees.

Supervisor: Dr. Steven Katz

Exploring Patient Perspectives on an Online, Stress Reduction Intervention in Inflammatory Bowel Disease

Makayla Watt BSc1, Ashley Hyde PhD1, Farhad Peerani MD FRCPC1, Karen Madsen MSc PhD1, Puneeta Tandon MD MSc FRCPC1
Supervisor: Dr. Puneeta Tandon

INTRODUCTION

Despite strong connections between stress and inflammatory bowel disease (IBD) associated symptoms, there has been limited research on stress reduction interventions for patients with IBD. Moreover, the research that has been conducted on this topic has shown mixed results with very few studies having used qualitative methods to explore the patient experience. The objectives for this study were to explore: (i) the experience of having IBD, (ii) the influence of an online 12-week stress reduction program on participant's physical and emotional symptoms of IBD and (iii) the acceptability of the online program.

METHODS

A qualitative descriptive approach embedded within a larger randomized control trial (RCT) was used to explore the experiences of participants. Upon completion of the 12-week program, participants were invited to participate in semi-structured interviews. Interviews were analyzed through an inductive process whereby transcripts were coded, with codes grouped into larger categories and then themes.

RESULTS

A total of 55 interviews were analyzed with three main themes emerging from the data: (i) IBD as a source of stress and uncertainty, (ii) understanding the positive impacts of the stress reduction program, and (iii) enhancing program desirability. Participants reported a reduction in IBD symptom burden with improvements in their ability to manage everyday and disease-associated stressors, while building a positive mindset. Variation in program content and fostering connections with others in the IBD community were identified as potential program improvements.

CONCLUSIONS

The findings of this companion study highlight the debilitating nature of IBD, with participants reporting significant disruptions to daily activities, uncertainty, and stress which served to worsen symptoms. Stress reduction programs like the one explored in this study offer an accessible avenue for reducing perceived stress, enhancing resilience and improving the physical condition of individuals diagnosed with IBD.

Supervisor: Dr. Puneeta Tandon

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

Yongneng Zhang, Sotirios D. Zervopoulos, Aristeidis E. Boukouris, Gopinath Sutendra, Evangelos D. Michelakis
Supervisor: Dr. Evangelos Michelakis

INTRODUCTION
Loss-of function SNPs for SIRT3 (a mitochondrial deacetylase) and UCP2 (an atypical uncoupling protein enabling mitochondrial calcium entry) have been associated with both PAH and insulin resistance, however its characterization in patients and collective role in patients remains elusive.

METHODS
In a prospective cohort of PAH patients (n=60) we measured SNPs for SIRT3 and UCP2. In addition, we characterized PAH severity (molecular and pathologic features) in a double knockout model with mice lacking both genes.

RESULTS
We found SIRT3 and UCP2 SNPs often both in the same patient in a homozygous or heterozygous manner and their presence correlated positively with PAH severity upon referral, the presence of type II diabetes and 10-year outcomes (death, transplantation). To explore this mechanistically, we generated and studied double KO mice for Sirt3 and Ucp2 using closed-chest right heart catheterization and echocardiography. We found increasing severity of pulmonary hypertension (PHT) in Sirt3+/--Ucp2+/-, Sirt3-/--Ucp2+/-, Sirt3+/--Ucp2-/- and Sirt3-/--Ucp2-/- mice, associated with decreasing cardiac output and increasing right ventricular hypertrophy, dilatation and dysfunction (TAPSE), compared to wild-type (WT) mice. The LVEDP in all mice was normal. There was increasing severity of vascular remodeling with increasing levels of CD4+ cell infiltration, while Sirt3-/--Ucp2+/-, Sirt3+/--Ucp2-/- and Sirt3-/--Ucp2-/- mice also developed frequent plexogenic lesions. In vivo and in vitro pulmonary artery smooth muscle cells (PASMC) expressed higher levels of Ki67, compared to WT mice. In vitro, the Sirt3-/--Ucp2+/-, Sirt3+/--Ucp2-/- and Sirt3-/--Ucp2-/- PASMC exhibited more apoptosis-resistance, higher nuclear levels of proliferative transcription factors (HIF1, NFATc2), decreased respiration and higher levels of glycolysis, similarly to previous reports of animal and human PAH PASMC. Compared to WT, Sirt3-/--Ucp2-/- mice showed in vivo evidence of insulin resistance.

CONCLUSIONS
Our work supports the metabolic theory of PAH and shows that these mice exhibit spontaneous severe PAH (without environmental or chemical triggers) in a gene-dose dependent manner that mimics human PAH and may explain the findings in our patient cohort. Our study offers a new mouse model of PAH, with several features of human disease.

Supervisor: Dr. Evangelos Michelakis

Quality Improvement Abstracts

Mask wearing and skin health during COVID19: a preventative approach for the general population

Dr. Kerry Atkins MD, Dr. Navjeet Gill MD, Pamela Mathura Msc, and Dr. Marlene Dytoc MD PhD FRCPC
Supervisor: Dr. Marlene Dytoc

INTRODUCTION

The City of Edmonton mandated the wearing of face coverings in indoor public places and public vehicles on July 29, 2020. Prior to this, it had been well demonstrated among healthcare workers that continuous mask wearing poses multiple skin challenges including acne (colloquially referred to as "maskne"), perioral dermatitis, contact dermatitis, pressure injury, and exacerbations of pre-existing dermatologic conditions, such as eczema, rosacea, and seborrheic dermatitis. In anticipation of widespread continuous mask wearing in workplaces, schools, social gatherings, and recreation facilities, there was an opportunity to mitigate some of these issues in the general population by providing evidence-based, preventative skin care measures in a straightforward and easy-to-understand format. Our long-term goals are threefold: first, improve the experience of continuous mask wearing in an effort to increase compliance with public health measures and decrease the transmission of COVID19; two, decrease referrals to general practitioners and dermatologists for preventable dermatologic issues; and three, minimize absenteeism and lost working hours due to preventable dermatologic issues secondary to continuous mask wearing.

METHODS

The purpose of this study was to consolidate and simplify evidence-based skin care recommendations into an educational poster that could direct practices before, during, and after mask wearing. A literature search was conducted on August 10, 2020 to better understand what the most common skin issues were related to continuous mask wearing and what evidence-based preventative measures existed. The language was restricted to English.

RESULTS

The result of the project was a visual poster depicting ideal skin care practices before, during, and after mask wearing.

CONCLUSIONS

The final poster offers a wide variety of first line preventative measures one can take to promote skin health while mask wearing.

Supervisor: Dr. Marlene Dytoc

Mask and Skin Health

BEFORE

- **Clean mask**
- **Proper fit**
- **Cotton fabric**
- **Connectors for ear loops to alleviate pressure**

- ✗ **Soiled mask**
- ✗ **Loose/tight**
- ✗ **Synthetic fabric**

With clean hands, moisturize skin including behind ears to prevent rash

Moisturizer Petroleum Jelly

Avoid harsh products or fragrance

With clean hands/cotton swab, moisturize lips with petroleum jelly.

Avoid lip biting or licking

AFTER

Cleanse and moisturize face with gentle non-comedogenic products

Avoid irrirating, exfoliants, chemical peels, and scented products

WASH

Wash cloth masks daily with fragrance-free, hypoallergenic detergent

DURING

Makeup: avoid when possible and use non-comedogenic* products

Avoid oil-based and fragranced products

NON-COMEDOGENIC

Every few hours: take breaks from mask safely outside/social-distanced, moisturize face/lips, and drink water

*non-comedogenic: products that do not block pores.

Reducing Laboratory Test Ordering Overuse in General Internal Medicine Units at the Grey Nuns Community Hospital – A Quality Improvement Initiative

C. Phan, P. Mathura, A. Au, L. Chivers and N. Kassam
Supervisor: Dr Anita Au

INTRODUCTION
At the Grey Nuns Hospital (GNCH) on the General Internal Medicine (GIM) units, electrolytes, complete blood count (CBC)/complete blood count with differential (CBCD), urea, and creatinine make up 66% of all laboratory tests ordered. Upon admission, CBCD and basic chemistry are commonly ordered on a repeating daily basis. A standardized process for laboratory test ordering frequency currently does not exist. This lack of process may increase the number of inappropriate laboratory tests creating system-wide wastes, increasing operational costs and negatively impacting patient experience while often causing iatrogenic anemia. Therefore, we developed a multifaceted quality improvement (QI) initiative to reduce laboratory test ordering overuse with a focus on blood urea nitrogen testing.

METHODS
Our interventions were guided by information gathered via multiple QI tools and implemented in sequential plan-do-study-act (PDSA) cycles. Our first intervention was to provide ongoing resident education regarding appropriate ordering practices. Indications were provided for when to order urea, encouraged no 'daily' ordering, and assess ordering frequency and test results for timely adjustments. Our second intervention included Unit Clerks reviewing lab orders frequency and flagging charts with daily orders. Physicians were provided with copies of ongoing blood work form with highlighted daily orders for their patients. If orders were daily, they were auto-substituted to "daily x3". Our third intervention was to have patients that are deemed medically non-acute have an Alternate level of Care (ALC) sticker placed in their chart for reassessment of all blood work. Analysis was done on comprehensive lab data from units 44 and 54 (GIM units) for the 15 months preceding project initiation and during the project from December 2018 to December 2019. Baseline chart audits were performed on the units documenting appropriateness and frequency of ordering.

RESULTS
There was a 48% reduction in urea ordering from 2018 to 2019 at the completion of the study resulting in a cost avoidance of approximately $8615. There was a 16% increase in CBCD ordering from 2018 to 2019. The number of auto-substitution labels used on both intervention units varied weekly with a range of 3 to 16 labels used during September to December 2019, suggesting that further physician awareness regarding daily orders on admission may be required.

CONCLUSION
The multifaceted QI intervention resulted in a significant decrease in Urea blood testing, but did not result in a shift to ordering less CBCD tests.

Evaluation of a Summer Healthcare Improvement Program (SHIP) in Undergraduate Medicine

P. Barber, J. Halasz, L. Truong, K. Raffael, C. Phan, P. Mathura, J. Croden, Dr. T. Hillier MD and Dr. N. Kassam MD
Supervisor: Dr. Narmin Kassam

INTRODUCTION
Currently, across Canada there is minimal experiential education for undergraduate medical students regarding Quality Improvement (QI). In a response to this opportunity, the UofA DoM, AHS and UofA UME office developed the Summer Healthcare Improvement Program (SHIP). The aim of SHIP was to offer students with a large role in QI projects, providing QI education and application, where students gain experience co-leading projects.

METHODS
To provide students with hands-on QI experience, a 15-week program was launched in 2017 as a pilot project. Since then, 19 students have engaged with 22 projects. Students are hired during the semester and over the summer work closely with a Sr. Quality Consultant and a physician to gain on-the-ground experience running projects. Each student received Evidence-based Practice in Quality (EPIQ) certification, optional QI readings, and opportunities to attend quality council meetings and Edmonton Zone QI days. To assess the effectiveness of the SHIP program, a pre and post-survey was implemented to analyze participants' experiences and allow iterative improvements each year alongside a SWOT analysis.

RESULTS
90% of students who responded to the surveys thought their peers could benefit from participating in SHIP and 71% of the respondents thought their SHIP experiences would be useful in future practice. 72% of all students found the training they received, through the EPIQ as helpful. Students expressed a desire to learn more about QI and were engaged when given the opportunity to learn more.

CONCLUSIONS
The combination of QI consultant, faculty physician, and student involvement in the leadership of SHIP influenced a high satisfaction rate from the students. There is appetite for students to take leadership roles within clinical projects and this program offers students an opportunity to co-lead and participate which results in experience that can be applied to take on future QI efforts.

Supervisor: Dr. Narmin Kassam

Exploring the Patient Perspective of In-hospital Blood Testing

Pamela Mathura, Carley Campbell, Karen Binns, Christine Phan, Mae Deans, Kendra Raffael
Supervisor: Pam Mathura

INTRODUCTION
Within the Edmonton zone in Alberta, Canada, blood test ordering has increased by 1.5 million tests in the last 5 years. In response to this steady growth, quality improvement studies were undertaken to identify intervention components from hospital admission to discharge that reduce lab test ordering overuse (LTOO). Understanding the patient perspective on in-hospital blood testing was undertaken. The aim of this project was to determine patient's perspective on in-hospital blood testing to recommend an intervention that supports patient needs.

METHODS
A focus group session with Alberta Health Services Patient and Family Advisory Council was held in June 2019 that used a structured facilitation technique. The insights gained from the focus group supported the development of a brief survey questionnaire. This questionnaire was used to collect information from general internal medicine inpatients in the fall of 2019. A thematic analysis and descriptive statistics supported data analysis.

RESULTS
Identified themes from the focus group suggest patients trust that physicians order what is required, prefer comprehensive communication, and value shared decision-making. Questionnaire findings corroborated the themes and indicated that patient preferences vary. Joint findings propose that patient consultation preferences include a daily, physician-led, structured, beside blood test conversation, using non-clinical language to encourage shared decision-making. Furthermore, some patients are concerned about blood test over-ordering. The challenge observed was that most patients are not aware of LTOO and indicated minimal blood testing knowledge to begin a conversation or question test order decisions.

CONCLUSIONS
An intervention that provides a practical approach for clinicians to discuss blood testing is aligned with Choosing Wisely Canada and encourages shared decision-making, supporting patient involvement in their care. We propose a hospital-wide campaign using the TESTing acronym [T- Test name, E- Explain need and frequency, S- Support shared decision-making, T- Test results provided] for further study.

Supervisor: Dr. Pam Mathura

Ending PJ Paralysis: A Quality Improvement Initiative.

Frances Carr, Angela Morgan, Shehani Devapura, Christina Williams, Jennifer Symon, Carolyn Howe-Ridely, Angela Miller, Jennifer Boone, Kevin Ebbage, Shalmin Jadaviji, Pamela Mathura
Supervisor: Dr Darryl Rolfson

INTRODUCTION

PJ paralysis refers to the negative effects seen amongst hospitalized patients who remain inactive and within their pajamas in hospital. Despite the many complications associated with PJ paralysis, it is a common problem within acute care facilities, which needs addressing

METHODS

A 3 month quality improvement study was conducted at the University of Alberta Hospital. The aim was for 50% of patients on ward 5G2 to get dressed in their own clothing by midday, sat up for all meals, and mobilizing to activities. Our intervention involved providing education and assistance to get patients dressed in their own clothing by midday, up for meals and mobilizing to activities. Measures included: daily percentage of patients dressed in their own clothing and up for all meals, weekly mobilization rates, number of nursing staff required, nursing assessment time, and complication rates (e.g. falls).

RESULTS

70 patients were included in the study. 14.3% of patients were dressed in their own clothing daily, and 6.4% of patients were up for all three meals. The average number of patients mobilized weekly was 4.7. A trend was observed towards decreased falls, with little change observed in staff numbers, nursing assessment time or other complication rates. Patient feedback revealed improvement in their self-identity.

CONCLUSIONS

While our aim was not met, our intervention revealed improvement in patients' self-identity, consistent mobilization rates, a trend towards decreased falls, with little change observed in complications, number of staff or care assessment duration. Our simple intervention had a positive impact in several areas, with few complications. Post study, this intervention continued, providing evidence of its sustainability and ease of implementation by frontline staff. Future plans include repeating a second cycle next year to determine sustainability and impact.

Supervisor: Dr Darryl Rolfson

Heparin-Induced Thrombocytopenia Testing and 4Ts Score Utilization at the UAH

Dr. Victoria DeVito, Dr. Michelle Lamarche
Supervisor: Dr. Cynthia Wu

INTRODUCTION

Heparin-induced thrombocytopenia (HIT) is a hypercoagulable disorder that carries significant morbidity and mortality, requiring prompt recognition and treatment with non-heparin anticoagulants. Patients with a low 4Ts score (< 4) are unlikely to have HIT and do not require further biochemical testing. Despite this, HIT testing is over-used, and the 4Ts score is under-utilized.

METHODS

We conducted a retrospective chart review of unique adult patient admissions to the University of Alberta Hospital (UAH) between 2016-2019, identified and included if a HIT test was performed during that admission. Patients were excluded if they underwent cardio-pulmonary-bypass. In 14 HIT-positive patients and 159 randomly selected HIT-negative patients, we compared 4Ts score utilization, score components, appropriateness of HIT testing, and interim treatment.

RESULTS

Of 173 patients reviewed, 53.4% were male, with average age 60.7 years. There were 48%, 24% and 28% from medical, surgical and intensive care units respectively. The 4Ts score was rarely documented prior to HIT testing (5.0% vs 28.6% in HIT negative and positive patients, respectively [p=0.001]). In patients ultimately tested negative for HIT, 51.6% had a retrospectively calculated 4Ts score <4 compared to no patients ultimately HIT-positive (Figure 1). Comparing components of the 4Ts score, a platelet count drop >30% was present less frequently in HIT-negative patients (72.3% vs 100%). HIT-negative patients had a lesser absolute drop in platelet count (43.9% vs 63.8%). HIT-positive patients more frequently had heparin discontinued (50.3% vs 100%) and non-heparin anticoagulants started (23.4% vs 92.7%).

CONCLUSIONS

At the UAH, HIT tests are often sent inappropriately based on the 4Ts validated pre-test probability score, and interim treatment is unequally undertaken. 4Ts score is rarely documented prior to testing, which could be a future target for intervention and study, especially with the implementation of EMRs.
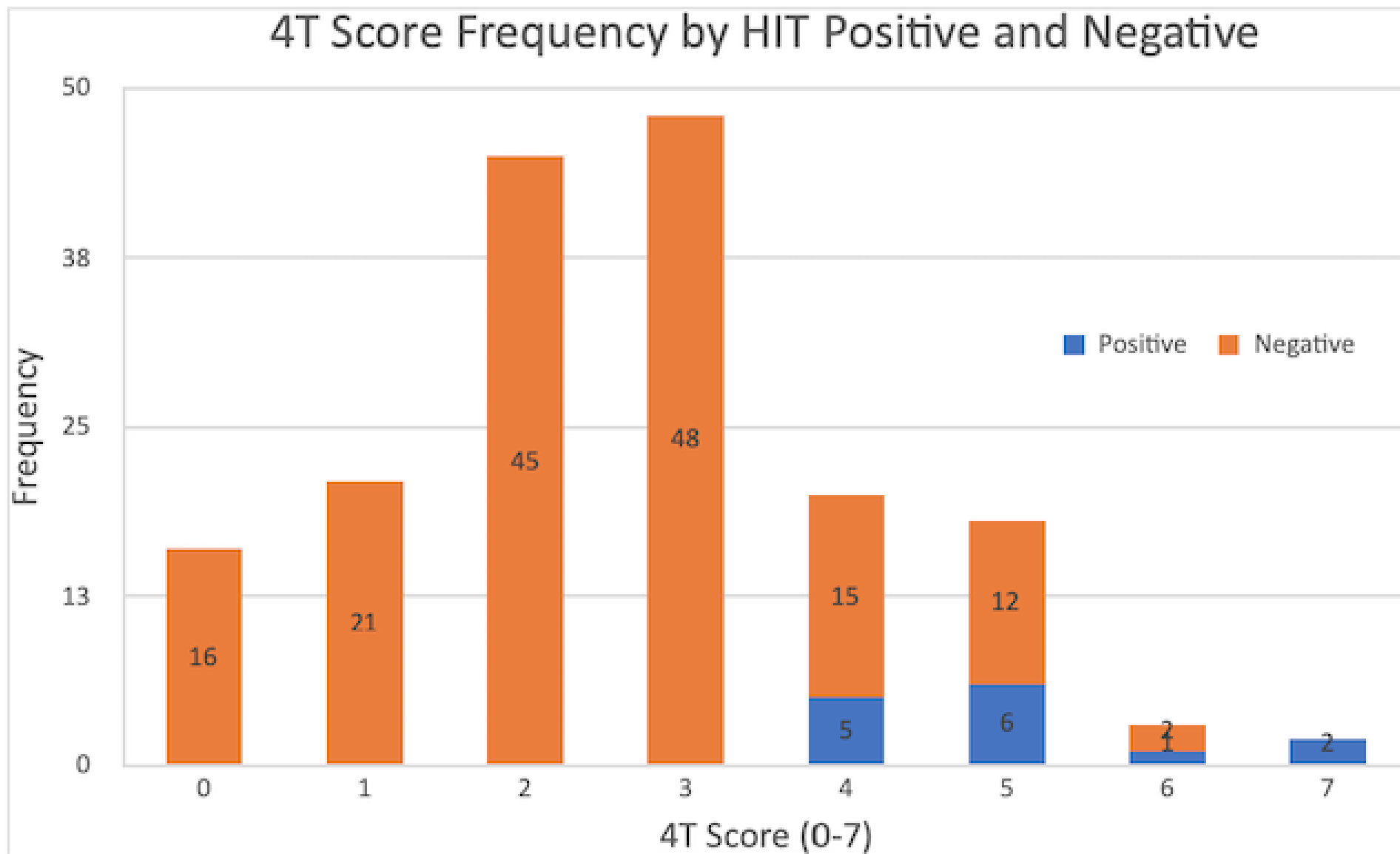
Supervisor: Dr. Cynthia Wu

Figure 1: Breakdown of retrospective 4Ts scores for 173 patients tested for Heparin-induced Thrombocytopenia at the UAH.

Stopping Routine Admission Urine Tests for Stroke Rehabilitation Inpatients

Arjun S Ghuman, MD; Pamela Mathura, MBA; Uma Chandran, MD, FRCPC; Jaime Yu, MD, MEd, FRCPC
Supervisor: Dr. Jaime Yu

INTRODUCTION

Urine testing (urinalysis and culture) on asymptomatic patients is not aligned with Choosing Wisely recommendations; however, stroke survivors may have trouble communicating symptoms, and urinary tract infections (UTI) are a recognized post-stroke complication. All stroke rehabilitation inpatients at the Glenrose Rehabilitation Hospital undergo routine urine testing on admission. We completed a QI project on one stroke rehabilitation unit with the aim to reduce the routine use of urine testing upon admission from 100% to 0%, unless clinically indicated.

METHODS

Baseline chart audit over two weeks identified 27 of 28 patients had urine tests completed, and no patient required UTI treatment despite 3 positive culture results. Estimated cost of urine testing was $675. Quality improvement tools identified that the standardized admission form facilitated automatic urine testing. Intervention consisted of education, clinicians crossing off urine orders, and flagging admission orders for prompt reassessment using a sticker over 4 weeks.

RESULTS

Post intervention, a chart audit (n=23) revealed 1 patient had negative urine tests completed on admission, 22 orders were crossed out, 1 sticker was applied, and the estimated cost of urine testing declined from $675 to $25. Balancing measures were 6 urine tests completed after admission, and 2 patients required antibiotic treatment for a UTI.

CONCLUSIONS

There is no clinical benefit in screening all stroke survivors transferred to a tertiary stroke rehabilitation unit or facility. Inappropriate and expensive ordering behaviour can be improved by engaging clinicians and updating standardized admission order forms to enhance resource stewardship.

Supervisor: Dr. Jaime Yu

Implementing a cirrhosis order set: a qualitative analysis of provider-identified barriers and facilitators

Emily Johnson, Michelle Carbonneau, Denise Campbell-Scherer, Puneeta Tandon*, Ashley Hyde* *co-senior and co-corresponding
Supervisor: Dr. Puneeta Tandon

INTRODUCTION
Cirrhosis is the leading cause of mortality and morbidity in individuals with gastrointestinal disease. Multiple care gaps exist for hospitalized patients with cirrhosis, resulting in high rates of re-hospitalization (e.g. 44% at 90 days in Alberta). The Cirrhosis Care Alberta (CCAB) is a 4-year multi-component pragmatic trial with an aim to reduce acute-care utilization by implementing an electronic order set and supporting education across eight hospital sites in Alberta. As part of the pre-implementation evaluation, this qualitative study analyzed data from provider focus groups to identify barriers and facilitators to implementation.

METHODS
We conducted focus groups at eight hospital sites with a total of 54 healthcare providers (3-12 per site). A semi-structured interview guide based upon constructs of the Consolidated Framework for Implementation Research (CFIR) and Normalization Process Theory (NPT) frameworks was used to guide the focus groups. Focus groups were recorded and transcribed verbatim. Data was analyzed thematically and inductively.

RESULTS
Five major themes emerged across all eight sites: (i) understanding past implementation experiences, (ii) resource challenges, (iii) competing priorities among healthcare providers, (iv) system challenges, and (v) urban versus rural differences. Site-specific barriers included perceived lack of patient flow, time restraints, and concerns about the quality and quantity of past implementation interventions. Facilitators included passionate project champions, and an ample feedback process.

CONCLUSIONS
Focus groups were useful for identifying pre-implementation barriers and facilitators of an electronic orders set. Findings from this study are being refined to address the influence of COVID-19, and the data will be used to inform the intervention roll-out at each of the sites.

Supervisor: Dr. Puneeta Tandon

Beyond Skin Deep: Case-based Online Learning Modules to Improve the Understanding of Multidisciplinary Care in Dermatology among Students

Harry (Chaocheng) Liu, Vivienne Beard, Megan Chan, Marlene Dytoc
Supervisor: Dr. Marlene Dytoc

INTRODUCTION
Canadian medical schools offer limited clinical dermatology training, and it is difficult for students to understand the strong relevance of dermatology to other areas of medicine. Only 29% of the undergraduate dermatology directors think the education provided at their school is adequate. The objective of this study is to create case-based online modules to fulfill the learning gap and evaluate their effectiveness in improving the understanding of multidisciplinary care in dermatology among medical students.

METHODS
Our team composed of an academic dermatologist, a dermatology resident, and medical students created 10 case-based modules on skin conditions that overlaps with 14 other disciplines. The modules are composed of multiple-choice questions with explanations, learning objectives, and take-home messages. Their content emphasizes multidisciplinary care in dermatology and centers around patients with different socioeconomic status and skin colors. 36 students were surveyed regarding perceptions of their dermatology curriculum. 21 of them with interests in 17 specialties completed the modules and a survey afterwards.

RESULTS
Only 14% of 36 students feel their dermatology education is sufficient, and 72% did not feel comfortable seeing patients with skin conditions in clinical settings. All 21 students who completed the modules found the format fits their learning style. Over 90% agree that the modules enhanced their knowledge and would help them manage skin conditions in clerkship. 86% agree that the modules enhanced their understanding of the multidisciplinary nature in the management of skin conditions in each case.

CONCLUSIONS
These findings indicate a need for additional dermatology education for students. Case-based online modules are effective tools to help students better understand the multidisciplinary care in dermatology and provided insight into ways of providing dermatology education for medical students when clinical teaching resource are limited.

Supervisor: Dr. Marlene Dytoc

Reducing Length-of-Stay for Stable Antepartum Patients

A. Rentz, B. Sullivan, P. Mathura, T. Luthra, A. Thiele, R. Rich and M. Gleddie
Supervisor: Dr. Winne Sia

INTRODUCTION

The Royal Alexandra Hospital (RAH) is the obstetrical tertiary referral centre for northern Alberta, northern British Columbia, and the Northwest Territories. Many out-of-town antenatal patients are transferred to the RAH to receive care for prematurity, such as premature rupture of membranes (PPROM). These patients often become candidates for outpatient management following inpatient stabilization. However, for out-of-town patients this poses significant geographic, social, and financial challenges and often results in prolonged hospital admissions.

Alberta Perinatal Health Program (APHP) data showed 1186 patients were admitted to the RAH with PPROM and cervical diagnoses, and 133 patients for >7 days (2823 bed-days). These admissions account for at least $1.8 million annually. Amongst this cohort 48% of patients reside in communities outside of Edmonton. This suggests the need for alternative housing accommodations for this patient demographic. Our quality improvement (QI) project aims to reduce the inpatient length-of-stay for stable antepartum patients at the RAH by developing an outpatient housing accommodation program.

METHODS

A brief literature review, the Model of Improvement and Donabedian conceptual evaluation frameworks were used to determine the areas for improvement and key performance measures to be collected. To determine intervention effect, we developed a formalized patient experience evaluation tool.

RESULTS

4 intervention domains were identified: infrastructure, care team, referral process, and a check in/out process. An accommodation facility was provided at the RAH - the Boarder Rooms - to conduct Plan Do Study Act (PDSA) cycles, where a multidisciplinary team will provide care on an outpatient basis starting in June, 2020.

CONCLUSIONS

Our objective is to optimize healthcare resources by reducing acute care bed utilization. We also hope to improve patient experience by offering independence and privacy, and by reducing unnecessary medical interventions.

Supervisor: Dr. Winne Sia

Trialing a Psoriasis Education Tool for Patient-Physician Decision-Making about Biologics

M Nahirney, M Hum, P Mathura, M Dytoc
Supervisor: Dr. Marlene Dytoc

INTRODUCTION

Biologics are a class of systemic immunomodulatory drugs used to treat moderate-to-severe psoriasis. With many new biologics being released, it is important that patients are informed about their treatment options and that physicians are knowledgeable about the unique features of each biologic. However, presenting large amounts of clinical information may be intimidating to patients. To help in patient education and shared decision making, we developed a quality improvement project centered on an educational visual aid which consolidated characteristics of 12 common biologics.

METHODS

We completed one Plan-Do-Study-Act (PDSA) cycle for 3 months to evaluate the visual aid's effect. The visual aid was developed using the most updated product monograph information, non-profit reports, and peer-reviewed literature in September 2019. We recruited dermatologists, senior dermatology residents and patients from a single dermatology clinic in Edmonton to participate. Physicians completed a pre-intervention questionnaire, and both patients and physicians completed post-intervention questionnaires 3 months following implementation. Descriptive statistics were calculated to assess baseline and post-implementation prescribing characteristics, and perceived utility of the visual aid.

RESULTS

Our project included 16 participants: 8 psoriatic patients who were being considered for treatment with biologics, and 8 dermatologists and residents. Pre-implementation, dermatologists and residents were mostly influenced by patient co-morbidities (n=8, 100%), efficacy (n=7, 87.5%), and contraindications (n=7, 87.5%). Physicians felt there was no significant impact of the visual aid on their biologic choice (n=3, 100%). However, patients indicated that the visual aid was either somewhat (n=4, 50%) or very useful (n=3, 37.5%) in explaining treatment options.

CONCLUSIONS

There was no observed effect on physicians' biologic choice using the visual aid, although patient responses suggest that it supports patient education. Thus, the visual aid may improve patient involvement in their treatment decisions. Additionally, this resource's consolidated format encourages dermatologists to conveniently compare biologics, thus identifying the best treatment for their patient.

Supervisor: Dr. Marlene Dytoc

Table 1: Visual aid describing characteristics of 12 biologics approved by Health Canada between 2000-2019

Biologic	PsO Treatment Indications	Other Compatible Conditions	Contraindications	Dosing	Annual Cost (First Year)	Common Adverse Reactions (>10%)	Efficacy – Primary Outcome and Effect Maintenance[a]	Market Date	PSP
Adalimumab (Humira) TNFi	Moderate-severe[1] Nail[2] Scalp[3] Hands/feet[4]	Pregnancy Breastfeeding PsA Crohn's/UC[10-16]	Active TB or other severe infections Malignancies Hepatitis B Demyelinating disease Heart Failure[b,1]	Every 2 wks (SC)[1]	$21,559[7]	Injection site rxn Headache Skin rash Antibody Development Upper respiratory infection Other infections[1]	**PASI 75 @ Week 16:** 71-79% **Loss of Adequate Response[d] @ Week 52:** 5%[1]	2004	AbbVie Care
Certolizumab pegol (Cimzia) TNFi	Moderate-severe[9]	Crohn's Disease PsA Pregnancy Breastfeeding[9]	Active TB or other severe infections Heart failure[9]	Every 2 wks (SC)[9]	$19,271[10]	Headache Nausea Antibody development Upper respiratory infection Other infections[9]	**PASI 75 @ Week 16:** 75-80% **% of PASI 75 responders maintained until Week 48:** 89-98%[9]	2009	Cimzia Solutions
Etanercept (Enbrel) TNFi	Moderate-severe[13] Nail[2] Scalp[3]	PsA Pregnancy Breastfeeding[5,6,13]	Hypersensitivity to etanercept Patients at risk of sepsis syndrome[13]	Twice weekly for 3 mo, then once weekly (SC)[13]	$25,983[7]	Injection site rxn Headache Skin rash Upper respiratory infection Other infections[13]	**PASI 75 @ Week 12:** 47-49% **PASI 75 @ Week 96:** 51%[13]	2000	Enliven
Infliximab (Remicade) TNFi	Chronic, severe[15] Nail[2] Scalp[3] Hands/feet[16]	Crohn's/UC PsA Pregnancy Breastfeeding[5,6,15]	Severe infections[c] Heart failure[15]	IV Infusion at 0, 2, and 6 wks, then every 8 wks after[15]	$39,080[7]	Infusion rxn Headache Antibody development Gastrointestinal symptoms Upper respiratory infection Other infections[15]	**PASI 75 @ Week 10:** 75-80% **PASI 75 @ Week 50:** 55-61%[15]	2001	BioAdvance
Biosimilar Infliximab (Inflectra) TNFi	Chronic, severe[18]	Crohn's/UC PsA/AS/RA[18]	Severe infections Heart failure Pregnancy Breastfeeding[18]	IV Infusion at 0, 2, and 6 wks, then every 8 wks after[18]	$21,000[19]	Infusion rxn Headache Antibody development Gastrointestinal symptoms Upper respiratory infection Other infections[18]	Not reported (refer to infliximab)[18]	2014	enCompass
Brodalumab (Siliq) IL-17i	Moderate-severe[20]	PsA Hepatitis B/C Pregnancy Breastfeeding[20]	Crohn Disease Hypersensitivity to brodalumab[20]	Weekly for 3 wks, then every two wks (SC)[20]	$18,060[19]	Upper respiratory infections Other infections[20]	**sPGA 0/1 @ Week 12:** 76-80% **% of sPGA responders maintained until Week 52:** 79-83%[20]	2017	Siliq Solutions
Ixekizumab (Taltz) IL-17i	Moderate-severe[23] Genital[24]	PsA Hepatitis B/C[23]	Hypersensitivity to ixekizumab Pregnancy[6]	Every two wks until week 12, then every 4 wks (SC)[23]	$25,823[19]	Upper respiratory infections Injection site rxn[23]	**sPGA 0/1 @ Week 12:** 73-83% **% of sPGA responders maintained until Week 60:** 75%[23]	2016	LillyPlus

A Retrospective Review of the Appropriateness of D-Dimer Ordering and Interpretation Using Wells' Clinical Probability Criteria

Oliver, M., Karkhaneh, M., Karathra, J., Goubran, M.,, Wu , C.
Supervisor: Dr. Cynthia Wu

INTRODUCTION

The D-dimer is validated for use in the diagnosis of venous thromboembolism (VTE). The Wells score for Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) are pre-test probability tools which help guide physicians on D-dimer ordering in patients with suspected VTE.

We suspect these scoring tools are underutilized by physicians leading to inappropriate D-dimer ordering.

METHODS

We conducted a retrospective chart review of 482 patients in whom a D-dimer had been ordered over a 3-month period at the University of Alberta Hospital. Charts were reviewed for patient demographics, ordering physician speciality, indication for ordering, risk factors for VTE and evidence of pre-test probability calculation.

 If no pre-test probability score was documented, we retrospectively calculated Wells DVT or PE scores. VTE was deemed likely with a Wells score for DVT ?2 or Wells score for PE ?4.5. We also reviewed subsequent investigations thought to be influenced by the D-dimer result including: ventilation/perfusion (V/Q) and pulmonary angiography (CTPA) scans, and doppler ultrasounds.

RESULTS

Seventy eight percent of D-dimers were ordered by emergency physicians while 15.3% were drawn on admitted patients. Of the D-dimers ordered, 45.7% were positive. Pre-test probability scores were documented in only 8 (1.6%) cases. All of those documented were the Wells PE score. When Wells DVT and PE scores were calculated retrospectively, 30.0% and 17.2% were deemed 'likely' for VTE, respectively. Imaging was performed in 172 cases (34.6%), including in 36 cases despite a negative D-dimer result.

CONCLUSIONS

Inappropriate ordering of D-dimers remains a problem despite pre-test probability algorithms, namely the Well's scores meant to guide physicians. This leads to unnecessary cost, radiation exposure, and prolonged contact with the health-care system for patients. This suggests the need for quality improvement initiatives which draw physician's attention to tools which can curb inappropriate ordering.

Supervisor: Dr. Cynthia Wu

Ethnic and Gender Disparities in Access to Deep Brain Stimulation Surgery for Movement Disorders in a Canadian Center

Sabrina Poonja, Kevin Yen, Janis Miyasaki, Aakash Shetty, Tejas Sankar, Fang Ba
Supervisor: Dr. Fang Ba

INTRODUCTION

Deep brain stimulation (DBS) is an important treatment for Parkinson's disease (PD), tremor, and dystonia in appropriate patients. DBS is efficacious, safe, and improves quality of life when medical treatment alone cannot manage symptoms. Nonetheless, DBS may be underused in certain patient populations.

Barriers to receiving DBS that could account for underuse amongst different gender and ethnicities are poorly investigated in Canada. Comparing gender and ethnicity of DBS patients to population demographics can help determine whether there is the expected uptake of DBS in various groups.

We aimed to study disparities in gender and ethnicity among DBS patients to reduce differences in access to care by implementing strategies to address patient-identified barriers and deliver information in a culturally sensitive manner.

METHODS

The study design was two pronged. In the first study, DBS patients at the University of Alberta selected the most applicable of the following ethnicities: European, Asian, East Indian, and Indigenous. Gender and self-reported ethnicity were retrospectively analyzed. In a future prospective study, in both implanted patients and suitable candidates, barriers to DBS access will be identified using surveys and strategies implemented in an effort to increase patient comfort.

RESULTS

Among 94 DBS patients followed between 2016 to 2019, there were 66 men and 28 women (M:F=2.36). Patients who received DBS surgery were European (85, 90.4%), Asian (4, 4.3%), East Indian (4, 4.3%), and Indigenous (1, 1.1%). Not a single African-Canadian was treated in our program. The gender and ethnicity of our cohort underrepresent population demographics.

CONCLUSIONS

This project increases awareness by uncovering gender and ethnicity disparities when providing DBS for movement disorders. In the future, we plan to identify the barriers to access to referral and explore patient understanding of the system and resources, informed (and non-informed) personal preferences, geographic variations, and provider biases.

Supervisor: Dr. Fang Ba

Improving the Use of Oxygen on General Internal Medicine (GIM) Units at the University of Alberta Hospital (UAH): A Quality Improvement Initiative

Dr Caitlyn Collins, Pamela Mathura, Kendra Raffael, Eddie Huang, Courtney Link, Matthew Ohrt, Dr Narmin Kassam, Yvonne Suranyi
Supervisor: Dr Narmin Kassam

INTRODUCTION
Clinical observations suggest oxygen is overused on GIM units. Liberal oxygen use can increase mortality, morbidity, length of hospital stays, and healthcare costs. Our objective was to increase oxygen weaning by 50% by October 2019.

METHODS
A literature search identified oxygen therapy best practices. The current processes at the UAH were assessed. A Gemba Walk and surveys identified the following gaps: (1) lack of standardized weaning orders, (2) lack of centralized documentation identifying patients on oxygen, triggering weaning, (3) outdated oxygen policy and (5) variability in provider comfort with oxygen therapy/weaning. Fifty GIM charts were sampled. Patients spent an average of 9.4 days on oxygen total, and 4.7 days at target saturations. 90% had no documentation to wean. In the 10% with weaning orders, 3.8 days elapsed at target saturations prior to orders being written. A Plan Do Study Act (PDSA) cycle was implemented for one month on unit 5D2, which included: (1) education sessions on ordering/weaning, (2) visual cues to promote weaning, (3) daily communication about patients on oxygen via the "Doctor's Board," and (4) a weaning flowchart. A second chart audit was then completed.

RESULTS
Thirteen 5D2 charts were sampled. 30% of patients had weaning orders compared to the initial 10%. Weaning orders were written within one day. Patients spent an average of 4 days total on oxygen compared to the previous average of 9.4 days. However, one emerging trend was inappropriate weaning, particularly in palliative patients and those on home oxygen.

CONCLUSIONS
Overall, oxygen weaning improved following PDSA cycle 1. Gaps remain in the system, and a second IT focused PDSA cycle is planned: (1) Add oxygen orders to Connect Care under "medications", (2) continue education on appropriate weaning, (3) create triggers in Connect Care oxygen graphs for weaning, and (4) adding a weaning algorithm into Connect Care.

Supervisor: Dr Narmin Kassam

Advancing Health Equity during the COVID-19 Pandemic through Digital Medical Interpretation Platforms

Nazia Sharfuddin, Pam Mathura, Emily Ling, Ellen Bruseker, Lindsay Bridgland, Narmin Kassam
Supervisor: Dr. Narmin Kassam & Dr. Lindsay Bridgland

INTRODUCTION

Medical Interpretation Services (MIS) is the gold-standard for communicating with patients who have limited English proficiency (LEP) or hearing loss, leading to improved patient care. Ad-hoc interpreters increase risk of adverse outcomes by failing to interpret accurately, violating patient confidentiality, and triggering trauma. MIS supports equitable care by reducing the outcomes of communication barriers between patient and clinician, particularly relevant during the COVID-19 pandemic. Cost of MIS is covered by Alberta Health Services; however, it is not consistently utilized across the province. Trained in-person interpreters are costly & pose availability concerns; however, remote MIS via digital platforms, such as video and phone, are available on-demand and more affordable. Our project's aim is to improve equitable delivery of care by increasing University of Alberta Hospital's Emergency Department & Medicine inpatient wards usage of digital MIS by 25%, within 18 months, for patients with LEP and hearing loss.

METHODS

Applying quality improvement methodology, a multi-phased intervention comprised of introducing digital MIS technology and education was launched. Phase 1 included the Emergency Department (ED) and Phase 2 included the inpatient Medicine wards. Number of MIS minutes and calls were measured monthly, and healthcare providers were surveyed on awareness, technology accessibility and perception of MIS integration into clinical workflow. Phase 1 results led to the development of a digital MIS toolkit and patient questionnaire for further adoption and assessment.

RESULTS

Digital MIS was utilized consistently in the ED from the beginning of the COVID-19 pandemic (March 2020). Using digital MIS in the ED realized an estimated cost avoidance of $53,524.96. ED healthcare providers indicated that digital MIS led to improved communication with patients and workflow. Phase 2 is currently in progress.

CONCLUSIONS

Providing digital MIS access, education and training is a means to advance health equity and patient-centered care, as well as improve healthcare cost savings.

Supervisor: Dr. Narmin Kassam & Dr. Lindsay Bridgland

Identifying quality improvement opportunities in a vulvar dermatology clinic.

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INTRODUCTION
Vulvar concerns are a common reason for women to visit a health care provider and for specialist care referral. Based on review of the literature, further research on how to optimize efficiency, patient centered care, and delivery of physician education in vulvar dermatology is needed. In this study, we performed a review our local vulvar dermatology clinic patient data to identify quality improvement opportunities to further meet the needs of our patients and referring physicians.

METHODS
A retrospective chart review of 187 new consultations in the vulvar dermatology clinic from May 2019 to May 2020 was completed. Demographic, referral, and clinic visit information was gathered and analyzed.

RESULTS
The gaps identified were that patients used self-remedies while awaiting appointment and could be treated by the referring physicians, considering wait time and travel distance to first appointment. Documentation of sexual function and quality of life was sparse. Further, referring physicians' clinical descriptions were often vague, which may impact referral triage.

CONCLUSIONS
We identified several quality improvement opportunities focusing on patient and physician education, use of telemedicine, and a focus on quality of life documentation. Next steps will involve further development, implementation, and evaluation of the identified interventions.

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Building Clinically Actionable Information for Improving Diabetes Care: Starting from Electronic Medical Record and Administrative Health Data

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INTRODUCTION

Quality improvement (QI) in diabetes care is urgently needed since diabetes remains the leading cause of blindness, non-traumatic limb amputations, and dialysis. 3.7 million Canadians have diabetes, expected to rise to 4.9 million by 2030. Electronic Medical Records (EMRs) and administrative databases are powerful tools for QI but have limitations. We explored the feasibility of using these data sources to establish baseline understanding of healthcare delivery across specialist diabetes clinics in partnership with Alberta Health Services Edmonton Zone Diabetes Quality Council and the Physician Learning Program.

METHODS

Retrospective cross-sectional analysis using EMR and administrative data for patients > 18 years at five Edmonton Zone diabetes clinics between March 2017-December 2018 was performed to obtain descriptive statistics including patient demographics, service use, diagnoses, and standard diabetes benchmarks. We describe the emergent processes and perform limitations analysis in obtaining results.

RESULTS

11714 unique patients (average age 41.2) were included. Proportion of diabetes diagnoses were 19.2% type 1; 27.6% type 2; 30.2% gestational; 23.0% unknown. 58.7% and 59.1% of visits respectively had blood pressure and body mass index recorded and extractable. 68.4% of patients had insulin prescribed, 5.7% had a clinical encounter for diabetic ketoacidosis within 1 year of the study period. The process of using EMR and administrative data for QI is non-linear and iterative, and involves co-creating clinical questions, obtaining resourcing for data access, analysis, and interpretation (Figure 1). Our limitation analysis grouped clinical questions into answerable (e.g demographics), answerable with limitations (e.g. types of diabetes), and non-answerable with available resources (e.g proportion with neuropathy).

CONCLUSIONS

Substantial gaps in key data elements were found that limit the ability of EMR and administrative data to simplify or automate QI. Assumptions must be tempered as limitations and human processes must be accounted for.

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Figure 1: The process of answering clinical questions for quality improvement using secondary analysis of administrative and EMR data
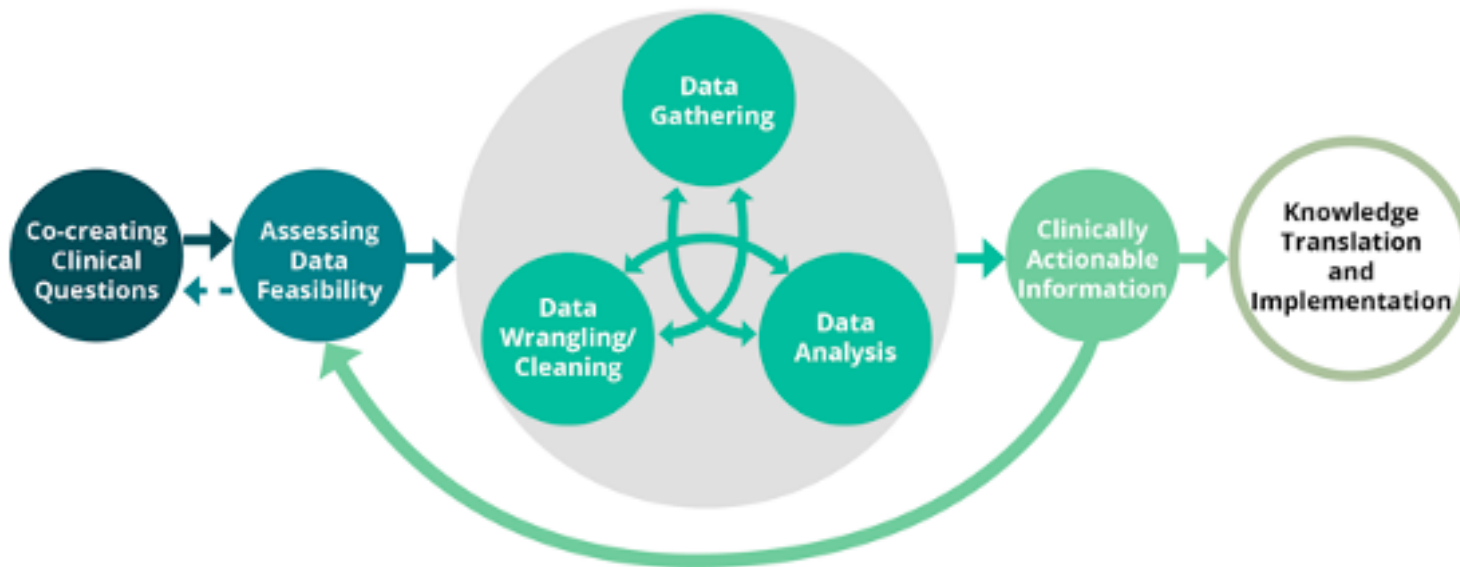
Improving Timely Treatment of Adult Sickle Cell Anemia Patients Presenting with Vaso-Occlusive Pain Episodes at the University of Alberta Hospital Emergency Department

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INTRODUCTION

Patients with sickle cell disease (SCD) experience recurrent vaso-occlusive episodes (VOE). Consensus guidelines recommend administration of the first dose of analgesia within 30-60 minutes of Emergency Department (ED) triage of VOEs. However, the University of Alberta Hospital (UAH) is not meeting these targets. In an audit of 26 patients presenting with 56 VOEs, the median time from ED triage to first dose of analgesia was 1.8 hours. In response, we developed a multifaceted QI initiative to improve timely treatment of adult SCD VOE at the UAH.

METHODS

Our initiative consisted of three interventions. First, we updated an individualized plan and wallet cards with patient-specific analgesia regimens. Second, we developed and implemented a standardized adult VOE order set. Third, we delivered educational sessions to clinical nurse educators, ED nurses and physicians, and disseminated educational posters in ED lounges focusing on unconscious bias in SCD. We presented our project at an ED physician departmental meeting, to advocate the use of standardized order set. Chart audits were performed in the 12-month period pre- and post-intervention.

RESULTS

In the pre-intervention period (July 2017-June 2018), 27 patients presented to UAH ED for a total of 68 VOEs. The median time from triage to physician assessment was 1.4 hours, with 26% experiencing a wait time ?2 hours. This corresponded to a triage level of 2 on the Canadian Triage and Acuity Scale (CTAS) in 68%. The median time from ED triage to the first dose of opioids was 2.2 hours. As the order set was not implemented in ConnectCare until mid-2020, we postponed the post-intervention audit (July 2020-June 2021).

CONCLUSIONS

Completion of the first Plan-Do-Study-Act (PDSA) cycle in fall 2021 will allow us to assess the impact of this QI intervention and identify areas for improvement. Findings will be shared with ED staff to maintain sustained engagement.

Supervisor: Dr. Linda Sun

Improving Healthcare Delivery to Patients with Psychodermatological Conditions

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INTRODUCTION

Psychodermatology encompasses the interaction between the cutaneous and neuropsychiatric systems. Psychodermatologic conditions are commonly encountered in medical practice. However, these are frequently underreported, misdiagnosed or undertreated. In Canada, there are few studies addressing these issues and limited services in this field.

METHODS

We have started a quality improvement project using different methodologies: 1) a review of Alberta Health Services (AHS) data to identify patients with potential psychodermatological conditions, estimate the burden of the issue and the expected demand on future services; 2) a national online survey to dermatologists in Canada to assess several areas in psychodermatology including their knowledge, practice patterns and challenges.

RESULTS

Of 243,963 dermatology patients identified through AHS data, 28.6% had received at least one psychotropic medication. Rates of concurrent psychotropic medications were highest for pruritus and related conditions. In the survey, of the 78 dermatologists, >75% reported treating patients with psychodermatologic conditions at least occasionally (1 patient/month). However, practitioners' confidence in their understanding of psychodermatology was intermediate (median = 4 on a 1-5 scale), and their level of comfort to approach these patients was lower (median=3). The confidence in prescribing psychotropic medication was markedly low (median=2), and 50% reported that a "multidisciplinary approach" would be the best approach. Poor access to psychiatry was the most reported (26.9%) challenge, but time constraints, lack of training, poor communication with patients, lack of patient insight and resources were also reported.

CONCLUSIONS

Several interventions were proposed to bridge the identified gaps. We have established a multidisciplinary psychodermatology clinic, which will increase accessibility to care, decrease referral system complications and potentially address patient-related concerns such as denied referral and compliance issues. Also, we have published our results to increase medical evidence on psychodermatology in Canada, collaborate with several partners to facilitate training sessions and create resources for patients.

Supervisor: Dr. Marlene Dytoc