UNIVERSITY OF ALBERTA

DEPARTMENT OF MEDICINE
FACULTY OF MEDICINE & DENTISTRY

ME2 MAJUMDAR RESEARCH & QUALITY IMPROVEMENT DAY

& QI DAY

MAY 18, 2023. 08:00 AM

NARMIN KASSAM

Chair, Department of Medicine

I am excited for another combined research and clinical quality improvement day (QI) day hosted by the Department of Medicine and the Edmonton Zone Medicine Quality Council, Strategic Clinical Improvement Committee. (SCIC). This year's event will be another hybrid event with in-person & virtual oral presentations and, I am happy to announce, the return of our poster presentations!

I am honored to welcome our keynote speakers: Professor Marc Humbert and Dr. Shobhan Thakore.

Dr. Humbert is the Dean of the Université Paris- Saclay Faculty of Medicine and the Director of the Inserm Research Unit 999 and of the Department of Respiratory and Intensive Care Medicine, French Pulmonary Hypertension Centre, Hôpital Bicêtre (Assistance Publique Hôpitaux de Paris).

Dr. Thakore is the Associate Medical Director for Quality Management and Clinical Lead for the Scottish Quality & Safety Fellowship programme which trains clinicians from Scotland, Northern Ireland, Denmark and Norway to become improvement experts.

Join me in listening to our trainees' accomplishments over the past year with research scientific presentations in the morning followed by quality improvement presentations in the afternoon.

This day is in honour of one of our greatest, and my friend, Sumit (Me2) Majumdar.

Narmin Kassam
Professor and Chair, Department of Medicine
Clinical Head, Medicine, Edmonton Zone

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

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PROFESSOR MARC HUMBERT

Keynote Speaker

Professor, Dean of the Université Paris- Saclay Faculty of Medicine.

This visit has been funded in part by the Walter Mackenzie Visiting Speaker Fund

Past President of the European Respiratory Society (ERS), Professor Marc Humbert is Dean of the Université Paris- Saclay Faculty of Medicine. He is the Director of the Inserm Research Unit 999 and of the Department of Respiratory and Intensive Care Medicine, French Pulmonary Hypertension Centre, Hôpital Bicêtre (Assistance Publique Hôpitaux de Paris). Marc Humbert was the Chief Editor of the European Respiratory Journal and he is currently Section Editor in charge of Pulmonary Vascular Medicine. He is a Foundation Fellow of the ERS.

He has received several distinctions including the Cournand Lecture Award (ERS), the Descartes-Huygens Award (Royal Netherlands Academy of Arts and Sciences), the Rare Disease Award (Fondation de France), the Award for Lifetime Achievement in Pulmonary Arterial Hypertension (ERS), the Excellence Award (Fondation du Souffle), and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation Distinguished Achievement Award (American Heart Association).

Since 2017, Marc Humbert is the coordinator and vice-coordinator of the French and European Reference Networks for rare and low prevalence respiratory diseases (RespiFIL and ERN-LUNG). Clarivate Analytics lists Marc Humbert as one of the world's highly cited researchers in the field of Clinical Medicine.

Dr. Shobhan Thakore has been an Emergency Medicine Consultant in NHS Tayside since 2003. He spent 8 years as Clinical Lead of the service and is now Associate Medical Director for Quality Management. In this role he helps to redesign and improve services by ensuring improvement science expertise supports operational teams. Part of this role includes leading Realistic Medicine in Tayside in collaboration with a multi-professional clinical team and innovative methods from the design community in Dundee.

He is also Clinical Lead for the Scottish Quality & Safety Fellowship programme which trains clinicians from Scotland, Northern Ireland, Denmark and Norway to become improvement experts. The programme delivers training in technical improvement skills but also leadership skills that help participants understand the importance of team engagement and the psychology of change.

Anyone wishing to contact Shobhan for further information can do so via email shobhan.thakore2@nhs.scot

DR. SHOBHAN THAKORE

Keynote Speaker

Associate Medical Director for Quality Management, NHS Tayside, Clinical Lead for the Scottish Quality and Safety Fellowship Programme, NHS for Education Scotland

ABOUT THE EZMQC - SCIC

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

ABOUT THE EZMQC - SCIC

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 an improvement leader/scientist and an assistant professor 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 includes leading quality improvement (QI) teams and providing foundational QI training. Pamela has published several articles in the area of improvement science and has a PhD in Healthcare Quality from Queens University.

Previous to this role Pamela has worked as a clinical quality improvement manager 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 30 years; her clinical background is in Laboratory Medicine where she held a leadership role in Anatomical Pathology at the University of Alberta Hospital.

FACULTY MEMBERS

JASON WEATHERALD
ASSOCIATE PROFESSOR
PULMONARY MEDICINE

Jason Weatherald is a pulmonologist and Associate Professor at the University of Alberta where he works in the Lung Transplant and Pulmonary Hypertension programs. He completed his undergraduate studies at McGill University, followed by an MD and Internal Medicine residency training at the University of Alberta. He completed his Respiratory Medicine fellowship training at the University of Calgary. He then received a European Respiratory Society long-term research fellowship to study pulmonary vascular diseases under the supervision of Prof. Marc Humbert and Prof Olivier Sitbon in Paris, France from 2016-2017. He completed a Masters of Science in Clinical Trials from the University of London - London School of Hygiene and Tropical Medicine in 2019.

MAHESH KATE
ASSOCIATE PROFESSOR
NEUROLOGY

Mahesh Kate is an Associate Professor with the division of Neurology. His research focuses on secondary stroke prevention with sustainable interventions and improving stroke patients' outcomes by understanding pathophysiological mechanisms. He co-designed the first study for the Indian Stroke Clinical Trial Network (INSTRuCT). SPRINT INDIA (Secondary Prevention by structured Semi-Interactive Stroke Prevention Package in India) study enrolled 4298 patients in 31 centres. This study was recently published in Lancet Global Health and highlighted the need for education to improve compliance. Currently, with help of the SMART network he is working on the precision and comfortable delivery of remote ischemic conditioning (RIC).

MARLENE DYTOC
CLINICAL PROFESSOR
DERMATOLOGY

Marlene Dytoc is a Clinical Professor of Medicine with the Division of Dermatology. She specializes in general dermatology as well as occupational and hand eczema, vulvar dermatology and psychodermatology, in collaborative or multidisciplinary clinics with the Departments of Preventive Medicine, Gynecology and Psychiatry. She serves as the deputy Edmonton Zone chief for Dermatology, undergraduate medical director for Dermatology, Dermatology lead for the Edmonton Zone Council for Quality Improvement and Dermatology lead for Connect Care for the province of Alberta. She obtained an MD and PhD in Microbiology from the University of Toronto. She completed residency training in Dermatology at the University of Alberta and specialty training in vulvar dermatology in the US and Canada. Dr. Dytoc has held a clinical appointment in the Department of Medicine's Division of Dermatology since 2002.

WINNIE SIA
PROFESSOR
GENERAL INTERNAL MEDICINE

Winnie Sia is a Professor in the Departments of Medicine and Obstetrics & Gynecology at the University of Alberta. She received her medical degree and residency training in Internal Medicine at University of Alberta. She then completed a 2-year fellowship in Obstetric Medicine, or Medical Complications in Pregnancy, at Brown University Rhode Island, USA. Currently, she is the Chief of department of Medicine at the Royal Alexandra Hospital and is the Director of Obstetric Medicine. Her clinical and research interests include preeclampsia, thromboembolism in pregnancy and longterm cardiovascular and vascular health in women with a history of hypertensive disorder of pregnancy

Meeting at a Glace

8:00 AM	Welcome Address
8:10 AM	Keynote Speaker *(Scientific)*
8:45 AM	Oral Presentations
10:15 AM	Break
10:30 AM	Ballerman Translational Research Fellowship Award
10:50 AM	Faculty Presentations
11:00 AM	Poster Presentations
1:00 PM	Keynote Speaker *(Quality Improvement)*
1:35 PM	Oral Presentations
2:35 PM	Faculty Presentations
3:00 PM	Closing Address

Scientific Research Awards

SCIENTIFIC ORAL PRESENTATIONS AWARD WINNER
$750

SCIENTIFIC POSTER ABSTRACT AWARD WINNER
$500

PAUL MAN AWARD WINNER
$500

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD WINNER
$24,500

Abstracts have been adjudicated in a blinded fashion by 3 reviewers. The top 6 highest scoring abstracts in research and top 4 highest abstracts in quality improvement were invited to present an oral presentation.

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

PAST RECIPIENTS

GINA SYKES (2022)
SUPERVISOR: GLEN JICKLING
The aging immune system in acute ischemic stroke: A transcriptomic analysis

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

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

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

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

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

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

PAST RECIPIENTS

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

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

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

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

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

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

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

MSC IN MEDICINE WITH SPECIALIZATION IN TRANSLATIONAL MEDICINE

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

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

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

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

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

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

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

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

ORAL SCIENTIFIC PRESENTATIONS

8:00 AM **Welcome Remarks**
Dr. Narmin Kassam, Associate Chair, Research, Department

8:10 AM **Keynote Speaker (Scientific Talk)**
Dr. Marc Humbert, Professor, Dean of the Université Paris- Saclay Faculty of Medicine

ORAL PRESENTATIONS

8:45 AM
Niall Pollock, Postdoctoral Fellow, Division of Neurology
Supervisor: Dr. Christopher Power
Gasdermin D activation in oligodendrocytes and microglia drives inflammatory demyelination in progressive multiple sclerosis

9:00 AM
Lamia Khan, Graduate Student, Division of Rheumatology
Supervisor: Mohammed Osman
Impaired DNA repair response activates a novel FOXO1-dependent metabolic remodeling in patients with progressive systemic sclerosis.

9:15 AM
Luke Gerla, Graduate Student, Division of Pulmonary
Supervisor: Dr. Paige Lacy
A prominent role for the lung epithelium in TSLP cytokine release in response to SARS-CoV-2

9:30 AM
Alexandra Saunders, Senior Subspecialty Resident, Division of Cardiology
Supervisor: Dr. Evangelos Michelakis
The invasive and noninvasive work up of patients with Pulmonary Hypertension: a critical appraisal of the U of A practice and opportunities for improvement.

9:45 AM
Lisa Van Lierop, Graduate Student, Division of Gastroenterology
Supervisor: Dr. Frank Hoentjen
Clonal patterns between pouch neoplasia and prior colorectal neoplasia in inflammatory bowel disease patients: an exploratory cohort study

10:00 AM
Areli Lorenzana-Carrillo, Graduate Student, Division of Cardiology
Supervisor: Dr. Gopinath Sutendra
TRIM35-Mediated Histone 2B Ubiquitination; An Epigenetic Modification that Reveals P53 Transcriptional Targets in Heart Failure

10:15 AM **Break**

ORAL SCIENTIFIC PRESENTATIONS

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

10:30 AM Ballermann Translational Research Fellowship Award Announcement

Oral Presentation

10:35 AM Ballermann Translational Research Fellowship Award Winner Presentation

FACULTY PRESENTATIONS

10:50 AM Dr. Jason Weatherald - Faculty Oral Presentation

11:02 AM Dr. Mahesh Kate - Faculty Oral Presentation (Scientific)

11:00 AM Poster Presentations

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

ORAL QI PRESENTATIONS

1:00 PM **Keynote Speaker (Quality Improvement Talk)**
Dr. Shobhan Thakore, Associate Medical Director for Quality Management, NHS Tayside; Clinical Lead for the Scottish Quality and Safety Fellowship Program, NHS for Education Scotland.
Realistic Medicine: A National Challenge to Think Differently

Oral Presentations

1:35 PM Shealynn Carpenter, Resident, Division of Infectious Diseases
Supervisor: Justin Chen
The period prevalence of a beta-lactam allergy label in patients prescribed carbapenems: A retrospective cohort study.

1:50 PM Amanda Brost, Resident, Division of General Internal Medicine
Supervisor: Dr. Anca Tapardel
Decreasing the Number of Patients Waiting to be Seen at the General Internal Medicine Kaye Edmonton Clinic.

2:05 PM Zainab Muhammad, Resident, Division of General Internal Medicine
Supervisor: Dr. Narmin Kassam
I*mproving Coding Practices for Alternative Level of Care (ALC) in Hospital Units.*

2:20 PM Crystal Liu, Resident, Division of Rheumatology
Supervisor: Steven Katz
A dive into paging frequency for internal medicine residents in a tertiary care hospital.

Faculty Presentations

2:35 PM Dr. Marlene Dytoc, Clinical Professor, Division of Dermatology, Department of Medicine

2:47 PM Dr. Winnie Sia, Professor, Division of General Internal Medicine, Department of Medicine

3:00 PM **Awards Ceremony & Closing Remarks**
Dr. Narmin Kassam, Chair, Department of Medicine

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

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

Alsaied, Mohammad (Resident)
Heterogeneity of treatment response to beta-blockers in the treatment of portal hypertension related to cirrhosis
Supervisor: Juan Abraldes (Gastroenterology)

Alzahrani, Khadija (Graduate Student)
Metabolic changes of the airway epithelium in asthma: role of insulin resistance
Supervisor: Harissios Vliagoftis (Pulmonary Medicine)

Basonbul, Asmaa (Graduate Student)
BCL-2 Inhibitor Venetoclax Enhances Temozolomide Sensitivity in AML
Supervisor: Joseph Brandwein (Hematology)

Bedard, Katherine (Graduate Student)
The Examination of Slice-Wise Hippocampal Subfield Volumes in Alzheimer's Disease: A Proof-of-Concept Study
Supervisor: Trevor Steve (Neurology)

Bihari, Allison (Graduate Student)
Patient Characteristics for Young Adults with IBD at the Time of Pediatric to Adult Transfer of Care: Impact of Distance to Clinic
Supervisor: Karen Kroeker (Gastroenterology)

Biswas, Sharmi (Graduate Student)
My eyes are burning: insights into the causes for dry eyes in other rheumatic diseases
Supervisor: Jan William Cohen Tervaert (Rheumatology)

Chappell, Kaitlyn (Graduate Student)
Virtual Mindfulness-Based Stress Reduction For Adults with Inflammatory Bowel Disease: A Feasibility Trial
Supervisor: Karen Kroeker (Gastroenterology)

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

Cooper, Matthew (Resident)
Trend in the burden of coronary artery disease in patients with chronic kidney disease in Alberta
Supervisor: Aminu Bello (Nephrology)

Duchesne, Marc (Graduate Student)
Trafficking of thymic stromal lymphopoietin in allergen-induced airway epithelial cells: colocalization with regulatory guanosine triphosphatase Rab11a
Supervisor: Paige Lacy (Pulmonary Medicine)

Fersovich, Jordana (Resident)
Rejection rates of lung transplant patients with reduced renal function on a sirolimus based immunosuppression regimen: A cohort characterization study
Supervisor: Dima Kabbani (Infectious Diseases)

Fujita, Kaden (Graduate Student)
SGLT-2 Inhibitors are Associated with Kidney Benefits at All Degrees of Albuminuria: A Retrospective Cohort Study of Adults with Diabetes
Supervisor: Darren Lau (General Internal Medicine)

Gouda, John (Resident)
Predicting Renal Function After Lung Transplantation
Supervisor: Kieran Halloran (Pulmonary Medicine)

Govindarajan, Karthivashan (Postdoctoral Fellow)
Diagnostic prospects of labelled native-PLGA nanoparticles in Alzheimer's Disease (AD) pathology
Supervisor: Satyabrata Kar (Neurology)

Kevin, Wang (Graduate Student)
Screening for mild cognitive impairment and dementia in kidney failure: a systematic review and meta-analysis
Supervisor: David Collister (Nephrology)

Khan, Lamia, (Graduate Student)
Impaired DNA repair response activates a novel FOXO1-dependent metabolic remodelling in patients with progressive systemic sclerosis
Supervisor: Mohammed Osman (Rheumatology)

Khan, Samina (Resident)
Factors influencing the quality of life in inflammatory bowel disease- A comprehensive review
Supervisor: Puneeta Tandon (Gastroenterology)

Krahn, Jessica (Resident)
Retrospective Cohort Study of Incentivised Testing and Treatment for Sexually Transmitted and Blood-Borne Infections in Outreach Populations
Supervisor: Ameeta Singh (Infectious Diseases)

Lai, Justine (Graduate Student)
ULK2 is a key pro-autophagy protein that contributes to the high chemoresistance and disease relapse in acute myeloid leukemia
Supervisor: Peng Wang (Hematology)

Liang, Xinyun (Christie) (Resident)
The association between maternal glucose levels in pregnancy and subsequent hypertension
Supervisor: Roseanne Yeung (Endocrinology & Metabolism)

Ma, Zechen (Resident)
Subcutaneous Immunoglobulin therapy as a maintenance agent for patients with idiopathic inflammatory arthritis: a real world single centre experience
Supervisor: Mohammed Osman (Rheumatology)

Mak, Kevin (Graduate Student)
Solution NMR studies reveal novel CLIC4 chaperone activity with respect to profilin-1
Supervisor: Peter M. Hwang (General Internal Medicine)

Mann, Darren (Graduate Student)
Engaging locomotor networks during paired non-invasive spinal cord neuromodulation after severe spinal cord injury: A case study
Supervisor: Vivian Mushahwar (Physical Medicine & Rehabilitation)

Mann-Nuttel, Ritu (Postdoctoral Fellow)
House dust mite allergen induces PAR-1 dependent CGRP release from cultured human pulmonary neuroendocrine cells
Supervisor: Paul Forsythe (Pulmonary Medicine)

Mast, Heather (Graduate Student)
Reduced mitochondrial complex I capacity early in life is associated with a longer lifespan in seed beetles
Supervisor: Hélène Lemieux (Cardiology)

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

Miranzadeh, Hajar (Postdoctoral Fellow)
Monkeypox infects primary human astrocytes and drives gasdermin B proteolytic cleavage to cause pyroptosis
Supervisor: Christopher Power (Neurology)

Motamedrad, Maryam (Graduate Student)
Biological Features of Muscle in Patients with Cirrhosis Receiving Liver Transplantation
Supervisors: Aldo Montano loza, Vera Mazurak (Gastroenterology)

Ogando, Natacha (Postdoctoral Fellow)
Discovering the molecular pathways associated with neurological post-acute sequelae of COVID-19
Supervisor: Christopher Power (Neurology)

Olagundoye, Olawunmi (Graduate Student)
A SCOPING REVIEW OF RISK FACTORS FOR URINARY INCONTINENCE IN OLDER MEN
Supervisor: Adrian Wagg (Geriatric Medicine)

Orenbuch-Harroch, Efrat (Clinical Fellow)
Breakthrough Invasive Fungal Infections in Lung Transplant Recipients Receiving Universal Prophylaxis: A Single Center Retrospective Study
Supervisor: Dima Kabbani (Infectious Diseases)

Paul, Pallabi Sil (Postdoctoral Fellow)
Inhibition of Amyloid β seed-induced tau aggregation by native PLGA nanoparticles and its significance in Alzheimer's disease
Supervisor: Satyabrata Kar (Neurology)

Pehar, Marcus (Graduate Student)
Proinflammatory responses of the HMC3 human microglial cell line are associated with changes in prion protein expression
Supervisor: Valerie Sim (Neurology)

Pollock, Niall (Postdoctoral Fellow)
Gasdermin D activation in oligodendrocytes and microglia drives inflammatory demyelination in progressive multiple sclerosis
Supervisor: Christopher Power (Neurology)

Rafid Feisal, Mohammad (Graduate Student)
Structure and activation mechanism of Staphylococcus aureus response regulator ArlR by solution NMR
Supervisor: Peter M. Hwang (General Internal Medicine)

Rafiee, Ata (Graduate Student)
Exploring Oxidative Stress andDNA Damage in Professional Welders Exposed to Welding Fumes
Supervisor: Bernadette Quémerais (Preventive Medicine)

Rajabali, Saima (Graduate Student)
Factors influencing the adoption and maintenance of healthy aging behaviours in community dwelling older adults – a Photovoice study
Supervisor: Adrian Wagg (Geriatric Medicine)

Rodrigues Meira, Sabrina (Graduate Student)
Exploring the heterogeneity of human mast cell-originated extracellular vesicles using proteomic profiling
Supervisor: Marcelo-Marcet Palacios (Endocrinology & Metabolism)

Rouhi, Azin (Senior Subspecialty Resident)
Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) after Immune Checkpoint Inhibition: a CanRIO Study
Supervisor: Carrie Ye (Rheumatology)

Santos, Joy Ramielle (Graduate Student)
Exploring Sequence Similarity in Upstream Regions of Genes: Implications for Co-Regulation of Genes and Chromatin Structure
Supervisor: Marcelo Marcet-Palacios (Endocrinology & Metabolism)

Sarmiento, Robert Joseph (Clinical Research Fellow)
Remote Ischemic Conditioning with Novel Optical Sensor Feedback Device in Acute Ischemic Stroke- a feasibility study
Supervisor: Mahesh Kate (Neurology)

Sarmiento, Robert Joseph (Clinical Research Fellow)
Short-term Outcomes in Ischemic Stroke patients with post-Endovascular thrombectomy Intracranial Hyperdensity
Supervisor: Mahesh Kate (Neurology)

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

Sedaghat, Navid (Graduate Student)
Wastewater Surveillance of Substance Use in Alberta, Canada
Supervisor: Sumantra Monty Ghosh (General Internal Medicine)

Seyyedi, Noorossadat (Graduate Student)
p53 associated de novo activation of VWF expression in tumor cells
Supervisor: Nadia Jahroudi (Hematology)

Siddique, Mujtaba (Graduate Student)
Hippocampal subfield thickness measurements evaluated using HippUnfold in patients with Mild Cognitive Impairment and Alzheimer's Disease
Supervisor: Trevor Steve (Neurology)

Skoreyko, Jessica, Sabrina (Graduate Student)
Quadruplex-binding ligands: the key to a cure for chronic Hepatitis B viral infections?
Supervisor: Vanessa Meier-Stephenson (Infectious Diseases)

Sohi, Nav (Resident)
L-type amino acid transporter 1 expression levels are associated with pituitary tumor behaviours
Supervisor: Toru Tateno (Endocrinology & Metabolism)

Soleas, John (Resident)
Effects of empagliflozin on T cells from ulcerative colitis patients
Supervisor: Karen Madsen (Gastroenterology)

Syed, Hussain (Graduate Student)
Lymphopenia in Primary Biliary Cholangitis
Supervisor: Andrew Mason (Gastroenterology)

Tejay, Saymon (Graduate Student)
Tumor-Secreted Nucleosides Can Promote RbFox1 Degradation and Signalling Pathways Relevant to Dedifferentiation in Cardiomyocytes; A Two-Hit Hypothesis with Implications for Cardiotoxicity
Supervisor: Gopinath Sutendra (Cardiology)

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

Umar, Narmeen (Graduate Student)
Liver stiffness measurement by vibration-controlled transient elastography predicts clinical outcomes in patients with autoimmune hepatitis
Supervisor: Aldo Montano-Loza (Gastroenterology)

van Lierop, Lisa (Graduate Student)
Long-term impact of the COVID-19 pandemic on inflammatory bowel disease healthcare: a two-year nationwide update
Supervisor: Frank Hoentjen (Gastroenterology)

van Lierop, Lisa (Graduate Student)
Clonal patterns between pouch neoplasia and prior colorectal neoplasia in inflammatory bowel disease patients: an exploratory cohort study
Supervisor: Frank Hoentjen (Gastroenterology)

Weyant, Benson (Resident)
Characterization of the urine microbiome-host interaction
Supervisor: Carlos Cervera (Infectious Diseases)

Yuan, Jack (Resident)
Burnout and fatigue amongst internal medicine residents: the impact of alternative scheduling models on resident wellness
Supervisor: Steven Katz (Rheumatology)

Zadunayski, Tanis (Graduate Student)
Determinants of Post-COVID ill-health in a cohort of Canadian health care workers
Supervisor: Nicola Cherry (Preventive Medicine)

Zanini, Umberto (Clinical Research Fellow)
The clinical impact of HFpEF on Interstitial Lung Diseases: clinical characteristics, comorbidities and outcomes
Supervisor: Jason Weatherald (Pulmonary Medicine)

QUALITY IMPROVMENT ABSTRACTS

FULL ABSTRACTS ENCLOSED

Alhaidari, Suliman (Senior Subspecialty Resident)
Biliary Stent use in ERCP: A Quality assurance study assessing adherence to clinical guidelines and cost outcomes
Supervisor: Gurpal Sandha (Gastroenterology)

Alhaidari, Suliman (Senior Subspecialty Resident)
Optimizing the indicators for biliary stent placement in patients with Choledocholithiasis: A Quality improvement initiative to enhance patient care and reduce healthcare resource utilization
Supervisor: Gurpal Sandha (Gastroenterology)

Brost, Amanda (Resident)
Decreasing the Number of Patients Waiting to be Seen at the General Internal Medicine Kaye Edmonton Clinic
Supervisor: Anca Tapardel (General Internal Medicine)

Carpenter, Shealynn (Resident)
The period prevalence of a beta-lactam allergy label in patients prescribed carbapenems: A retrospective cohort study
Supervisor: Justin Chen (Infectious Diseases)

Dar, Shamaila (Resident)
Exploring the Deprescribing Needs of Hospitalized Medicine Patients
Supervisor: Winnie Sia (General Internal Medicine)

Donnelly, Sarah (Resident)
Interhospital Variation in the Proportion of Admissions Managed with Critical Care Therapies or Invasive Hemodynamic Monitoring in Tertiary Cardiac Intensive Care Units: An Analysis from the Critical Care Cardiology Trials Network Registry
Supervisor: Sean van Diepen (Cardiology)

Liu, Crystal (Resident)
Timing of cholecystectomy after endoscopic retrograde cholangiopancreatography in a tertiary centre: Evaluation of outcomes
Supervisor: Sergio Zepeda-Gomez (Gastroenterology)

Liu, Crystal (Resident)
A dive into paging frequency for internal medicine residents in a tertiary care hospital
Supervisor: Steven Katz (Rheumatology)

QUALITY IMPROVMENT ABSTRACTS

FULL ABSTRACTS ENCLOSED

Muhammad, Zainab (Resident)
Improving Coding Practices for Alternative Level of Care (ALC) in Hospital Medicine Units
Supervisor: Narmin Kassam (General Internal Medicine)

Nanda, Kareena (Resident)
Social Determinants of Health as Barriers to Accessing Care for Vasculitis: A National Survey of Vasculitis Patients
Supervisor: Elaine Yacyshyn (Rheumatology)

Robin, Gabrielle (Resident)
Outcomes of first subsequent taxane (FST) therapy in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) who previously received docetaxel intensification (DI) for metastatic castration-sensitive prostate cancer (mCSPC).
Supervisor: Dr. Jason Weatherald

Turk, Tarek (Graduate Student)
Teledermatology in Atopic Dermatitis: A Systematic Review
Supervisor: Marlene Dytoc (Dermatology)

Turk, Tarek (Graduate Student)
Teledermatology versus in-person visits for the follow up of atopic dermatitis patients
Supervisor: Marlene Dytoc (Dermatology)

Turk, Tarek (Graduate Student)
Teledermatology: Canadian Dermatologists' Practice Patterns, Perceived Challenges and Future Recommendations
Supervisor: Marlene Dytoc (Dermatology)

Wagner, Amy (Amanda) (Clinical Research Fellow)
Workflow Metrics in Simultaneous Acute Code Stroke Activation and Stroke Reperfusion Therapies
Supervisor: Mahesh Kate (Neurology)

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Scientific Research Abstracts

Aging is associated with organ-specific alterations in level and expression pattern of von Willebrand factor

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

INTRODUCTION
Von Willebrand factor (VWF) is an endothelial specific pro-coagulant protein with a major role in thrombosis. Aging is associated with increased circulating levels of VWF, which presents a risk factor for thrombus formation.

METHODS
Circulating plasma, cellular protein, and mRNA levels of VWF were determined and compared in young and aged mice. Major organs were subjected to immunofluorescent analyses to determine the vascular pattern of VWF expression and presence of platelets aggregates. An in vitro model of aging, using extended culture time of endothelial cells, was used to explore the mechanism of age-associated increased VWF levels.

RESULTS
Increased circulating plasma levels of VWF were observed in aged rodents. VWF mRNA and protein levels were significantly increased in the brains, lungs, and livers, but not in kidneys and hearts of aged mice. Higher proportion of small vessels in brains, lungs and livers of aged mice exhibited VWF expression compared to young, and this was concomitant with increased platelets aggregate formation. Prolonged culture of endothelial cells resulted in increased cell senescence that correlated with increased VWF expression. VWF expression was specifically upregulated in senescent population of cultured endothelial cells and p53 knockdown prevented this upregulation. In vivo, a significantly higher proportion of VWF expressing endothelial cells exhibited senescent markers SA-β- Gal, and p53 in brain vasculature of aged mice compared to young.

CONCLUSIONS
Aging elicits a heterogenic response in endothelial cells with regard to VWF expression, leading to organ-specific increase in VWF levels, as well as alterations in its vascular tree pattern of expression. This is concomitant with increased platelets aggregate formation. The process of cell senescence and p53 transcription factor contribute to age-associated increase in VWF expression.

Heterogeneity of treatment response to beta-blockers in the treatment of portal hypertension related to cirrhosis

Alsaeid M, Sung S, Bai W, Cortes J, Cobo E, Gonzalez-Alastrue JA and Abraldes JG
Supervisor: Dr. Juan abraldes

INTRODUCTION

Non-selective beta-blockers (BB) improve clinical outcomes in patients with cirrhosis and portal hypertension. Indeed, patients who achieve a >20% reduction in Hepatic Venous Pressure Gradient (HVPG) with BB have an excellent prognosis, but only 30-50% achieve such response. This has been suggested as a reason for not using BB where no HVPG measurements are available. In this study we aimed to quantify how heterogeneous is the response to BB in patients with cirrhosis, by analyzing trials in which the effects of BB on HVPG were compared with those of placebo.

METHODS

We conducted a meta-analysis of differences in variance between trial arms. The degree of heterogeneity of HVPG response to BB was quantified with the pooled variability ratio (VR) (SD of the HVPG at the end of the trial in the BB group divided by that in the placebo group).

RESULTS

Our systematic search yielded 25 articles. Figure 1 shows a forest plot with the meta-analysis of the variability ratios (VR) in final HVPG. Pooled VR was 0.99 (95% CI 0.87-1.14). This indicates that there was no evidence for a higher average variability in the final HVPG in the beta-blocker treatment groups as compared to placebo groups, and hence there was no evidence to support that patients with cirrhosis exhibit a heterogeneous response to beta-blockers (i.e. there is no evidence to support that some patients responded to beta-blockers and others did not).

CONCLUSIONS

In conclusion, the analysis of RCTs comparing the HVPG response of beta-blockers with placebo in patients with cirrhosis does not suggest a heterogeneous hemodynamic response to beta-blockers. This, together with the fact that in most RCTs demonstrating the clinical benefits of beta-blockers treatment was not adjusted based on HVPG response, further supports the concept that there is no need to perform portal pressure measurements to guide treatment with beta- blockers.

Metabolic changes of the airway epithelium in asthma: role of insulin resistance

Alzahrani, Khadija and Vliagoftis, Harissios
Supervisor: Harissios Vliagoftis

INTRODUCTION

Airway epithelium has as essential role as a protective physical barrier against inhaled irritants that can activate and interact with epithelium directly. Airway epithelium dysfunction orchestrates airway inflammatory diseases such as asthma. Obesity and insulin resistance are associated with increased asthma and allergy symptoms. Lack of insulin in vitro exacerbated protease mediated inflammation in airway epithelial cells (AECs). We hypothesized that insulin resistance may initiate airway epithelial changes known in asthma. In other systems TNF, which is also increased in asthma, mediates insulin resistance through inhibitory phosphorylation of insulin receptor substrate -1 (IRS-1) Ser307 which impact insulin activation of PI3K/Akt pathway. In this project, we study the effects of inflammatory mediators and allergens on insulin-induced metabolic changes in AECs and the role of that in epithelium physiologic changes seen in asthma.

METHODS

Primary normal human bronchial epithelial (NHBE) cells were cultured in pre-coated tissue culture plates. More than 90% confluent cells were stimulated with TNF in the presence or absence of insulin. Western blot was used to detect pIRS-1 (Ser307) and pAkt (Ser473). Energetic phenotype alterations in TNF or house dust mite (HDM) stimulated cells in presence or absence of insulin was studied using real-time ATP production rate assay using Seahorse analyzer.

RESULTS

TNF increased p-IRS-1 (Ser307) and decreased insulin-induced pAkt (Ser473) in NHBE cells. TNF also decreased insulin-induced glycolytic ATP production and HDM altered AECs energetic phenotype.

CONCLUSIONS

We showed for the first time that TNF and HDM decreased insulin-induced effects and altered AECs energetic phenotype. These changes are related to metabolic changes in glycolysis and mitochondrial function which we are interested to further study. Furthermore, we will examine the role of insulin-related metabolic changes in AECs physiologic changes like growth and wound healing.

BCL-2 Inhibitor Venetoclax Enhances Temozolomide Sensitivity in AML

Asmaa Basonbul, MSc and Joseph Brandwein , MD, FRCPC
Supervisor: Dr. Joseph Brandwein

INTRODUCTION

Temozolomide (TMZ) is an alkylating agent, which adds a methyl group to O6 position of guanine, resulting in mismatch pairing with DNA strand breaks leading to apoptosis. The DNA repair enzyme O6-methylguanine methyltransferase
(MGMT) enhances tumor cell resistance to TMZ.

BCL-2 is an anti-apoptotic protein preventing cell to death. Venetoclax (Venet) is a small molecule promoting cell apoptosis through inhibition of BCL-2 protein. The objective of this study is to evaluate the ability of Venet to enhance TMZ sensitivity in acute myeloid leukemia (AML) cells with high and low MGMT expression.

METHODS

KG1, MV4-11 and MOLM13 AML cell lines were chosen. Western blot was used to measure MGMT, BCL-2 and C-PARP expression. Cells were incubated with TMZ alone and in combination with inhibitory concentration 50% (IC50) of Venet. Apoptosis was assessed by flow cytometry using Annexin V/ Propidium Iodide. Comet assay was used to assess the DNA damage. MOLM13 engrafted mice
treated with selected TMZ and Venet concentrations, alone and in combination, were evaluated for survival and by measuring bone marrow CD45+ and CD33+ expression.

RESULTS

In high (KG1) and low (MV4-11 and MOLM13) MGMT-expressing cells co-incubation of TMZ with Venet at IC50% resulted in a marked enhancement of TMZ sensitivity. Apoptosis was induced but C-PARP was only expressed in KG1 cells treated with Venet alone and combination. More severe DNA damage was observed in the combination-treated cells compared to TMZ alone in all cell lines. The combination- treated mice had the longest survival among the group; however, by the time of death, no difference was seen in CD45+ cells compared to the single drug or untreated groups.

CONCLUSIONS

Venetoclax enhances TMZ sensitivity and induces cytotoxicity and DNA damage, in high and low MGMT cells. The TMZ + Venet combination improved survival in mice, but did not prevent leukemia engraftment.

The Examination of Slice-Wise Hippocampal Subfield Volumes in Alzheimer's Disease: A Proof-of-Concept Study

Bedard, Katherine & Siddique, Mujtaba & Camicioli, Richard & Steve, Trevor
Supervisor: Dr. Trevor Steve

INTRODUCTION
Hippocampal atrophy is an early characteristic of Alzheimer's disease (AD) and is correlated with future neuropathological processes, such as cognitive decline. This is also observed in those with mild cognitive impairment (MCI), of which 10-15% go on to develop AD. The use of magnetic resonance imaging (MRI) for the estimation of hippocampal subfield volumes is a promising route that may help identify biomarkers towards diagnosing and monitoring AD. However, previous study results in this area vary greatly and thus a universal consensus on hippocampal subfield atrophy patterns has not yet been achieved. This study aims to close this knowledge gap by evaluating hippocampal subfields on a slice-by-slice basis.

METHODS
The T1- and T2-weighted MRI scans of 858 subjects (cognitive normal [CN], n=373; MCI, n=362; AD, n=123) were downloaded from the AD Neuroimaging Initiative database. These whole-brain images were processed by the HippUnfold
application, which generated bilateral subject-level segmented hippocampal renderings. ITK-SNAP was then used to re-label the subiculum, cornu Ammonis (CA) 1, CA2, CA3, CA4, dentate gyrus, and stratum lacunosum-moleculare (SLM) in each slice along the hippocampal long axis. All subfield-specific volumes were extracted, and mean slice-by-slice volumes for each subfield were then calculated.

RESULTS
The mean subiculum, CA1, and SLM slice-wise volumes are presented in Figure 1A, 1B and 1C respectively. Qualitative analysis of these mean volumes appears to demonstrate that the slice-wise subfield volumes of the MCI and AD cohorts are reduced relative to the corresponding CN volumes.

CONCLUSIONS
This study evaluated slice-by-slice hippocampal subfield volumes in CN, MCI, and AD patients. While qualitative analysis has shown a slice-wise volume reduction in MCI and AD cohorts, statistical analyses are currently underway to quantify the observed volume variances and determine significance. Subsequently, an analysis of the associations between slice-wise subfield volumes and existing disease- specific measures will be performed.

THE EXAMINATION OF SLICE-WISE HIPPOCAMPAL SUBFIELD VOLUMES IN ALZHEIMER'S DISEASE: A PROOF-OF-CONCEPT STUDY
(PAGE 2 OF 2)

Bedard, Katherine & Siddique, Mujtaba & Camicioli, Richard & Steve, Trevor
Supervisor: Dr. Trevor Steve

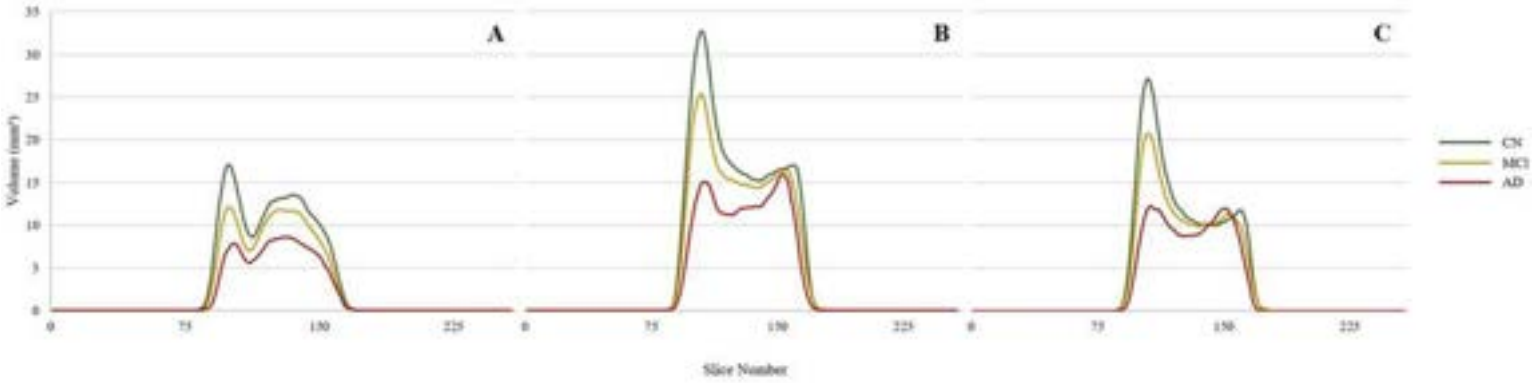


Figure 1. The mean slice-wise hippocampal volumes for the (A) subiculum, (B) CA1, and (C) SLM between cognitive normal, mild cognitive impairment, and Alzheimer's disease patient cohorts.

Patient Characteristics for Young Adults with IBD at the Time of Pediatric to Adult Transfer of Care: Impact of Distance to Clinic.

Bihari, Allison & Wine, Eytan & Kroeker, Karen
Supervisor: Karen Kroeker

INTRODUCTION
Patients diagnosed with inflammatory bowel disease (IBD) in childhood will transfer from pediatric to adult care when they turn 18. Travel distance has been cited as a barrier to accessing health care. We aim to assess the association of travel
distance to clinic with available factors extracted at transfer (first appointment in adult care).

METHODS
A retrospective medical chart review was done for patients with IBD who
transferred between 2014–2022 at an IBD clinic in Edmonton. Distance was categorized as <50km and >50km from patient's postal code to that of the
pediatric clinic. Binary outcome variables extracted included biologic use, recent biomarker (CRP, FCP) assessment (within 6 months of transfer), anxiety and depression, cigarette use, and history of surgery. Crude odds ratios measured the association between travel distance and outcomes.

RESULTS
Of 203 patients transferred, 51 patients lived >50km and 152 patients lived
<50km from clinic. Median time from referral to first appointment in adult care was similar between the two groups (156 days vs. 134 days, p-value=0.17). Mean age at diagnosis was also similar (14.0 vs. 13.8, p-value=0.52). Patients >50 km were more likely to report daily cigarette use [OR:4.4,CI:1.6-13] and less likely to have a recent biomarker assessment [(CRP OR:0.26,CI:0.098-0.68),(FCP OR:0.29,CI:0.15-0.58)] compared to those <50km. The odds of having anxiety and depression [OR:1.0,CI:0.45-2.4], on biologics [OR: 0.71,CI:0.37-1.4], and history of surgery [OR:2.6,CI:0.95-6.9] was not increased in patients >50km.

CONCLUSIONS
Compared to patients who lived <50 km from clinic, those >50 km away were 4.4 times more likely to use cigarettes daily and were less likely to have biomarker results within 6 months of first adult appointment. By understanding differences and similarities between pediatric transition patients characterized by distance to clinic, this research can inform personalized care plans.

My eyes are burning: insights into the causes for dry eyes in other rheumatic diseases

Biswas, S & Tervaert, JW & Redmond D, Osman M
Supervisors: Dr. Jan William Cohen Tervaert, MD, PhD

INTRODUCTION

Dry eye is a common condition in the general population and rheumatic patients. Dry eyes are due to impaired tear production or increased tear evaporation.
Patients with adjuvant induced autoimmunity syndrome (ASIA) have dry eyes. Providing a 5-item questionnaire for Sjogren Syndrome (SSSQ score) and Schirmer test measurement can detect the eye dryness level in ASIA patients. Many patients with ASIA due to implants complain about dry eyes and mouth. Whether they have dry eyes due to impaired tear production is not known. We are looking for Schirmer test measurement and SSSQ score between ASIA patients, healthy controls (HC) and Sjogren syndrome (SS) patients.

METHODS

38 consecutive ASIA patients with implants from the Rheumatology clinic were recruited. Exclusion criteria were >75 years, use of insulin, contact lenses. 9 HC
and 2 SS patients following the same exclusion criteria were also included. Participants needed to answer a 5-item questionnaire to get the SSSQ score (ref) in addition to a 5-minute Schirmer test to measure the level of eye dryness.

RESULTS

Among the 38 ASIA patients 10.5% (4/13) have severe dryness (0-1 mm) 26.3% (10/13) have moderate dryness (2-5 mm); 36.8% (14/38) have mild dryness (6-10mm);7.8% (3/38) have dry eyes (10-15mm) and 18.4% (7/38) have a normal measurement (25-30 mm). SSSQ scores of ≥7 was found in 15.8% (6/38) of our ASIA patients. The Schirmer test results in HC, 60% (6/10) are in normal range and 40% (4/10) have dry eyes. SSSQ scores in HC are all below 7. In 2 SS patients SSSQ scores are 6 and 9; one has severe dryness, and another has moderate dryness.

CONCLUSIONS

Schirmer test along with SSSQ questionnaire can be used in outpatient settings to detect impaired tear production in ASIA patients.

Virtual Mindfulness-Based Stress Reduction For Adults with Inflammatory Bowel Disease: A Feasibility Trial
Page 1 - 2

Chappell, Kaitlyn & Meakins, Diana & Marsh-Joyal, Melanie & Goodman, Karen J & Le Melledo, Jean-Michel & Lim, Allen & Peerani, Farhad & Kroeker, Karen I.
Supervisor: Karen Kroeker

INTRODUCTION
Patients with Inflammatory Bowel Disease (IBD) often suffer from high levels of stress, anxiety, and depression, which contributes to poorer health outcomes, but access to mental health care can be difficult due to increased cost and travel. Mindfulness-Based Stress Reduction (MBSR) can be delivered virtually and is covered by provincial health care plans making it an attractive option to meet gaps in care. It has been associated with reducing feelings of stress, anxiety, and depression in several high-quality trials. The feasibility of virtual delivery to IBD patients has not yet been investigated and is the aim of our study.

METHODS
Eligible participants aged 18-65 and attending gastroenterology clinics in Edmonton who self-identified as being stressed or were referred by their gastroenterologist could enroll after completing a symptom assessment and an interview with a psychiatrist. The MBSR protocol was an 8-week group-based intervention aimed at providing tools to effectively cope with stress and included 8 weekly sessions lasting 2.5 hours/week, a one-time weekend session lasting 5 hours, and 45-60 minutes of daily practice. Completion of the program required attendance of 6 of 8 weekly sessions and the weekend session.

RESULTS
Sixteen of 64 (25%) referred patients agreed to participate with the most common reason for decline being noted as a lack of time. The enrolled participants recorded a variety of age, gender, disease type and severity, and employment statuses. The 7 (43.8%) participants who completed the program saw encouraging effects including decreased stress and increased quality of life. Table 1 includes a summary of the feasibility and effectiveness of MBSR.

CONCLUSIONS
Only 25% of IBD patients with stress symptoms were willing to participate in an intensive 8-week virtual mindfulness virtual group. For those who completed the intervention, the effects were promising. Follow-up interviews are underway to identify the benefits and barriers to MBSR.

Virtual Mindfulness-Based Stress Reduction For Adults with Inflammatory Bowel Disease: A Feasibility Trial

Table 1: A Summary of Feasibility and Effectiveness Outcomes

Recruitment, n=64		n (%)
Enrolled		16 (25.0)
Declined		26 (40.6)
Lost to Follow-Up/Never Reached		21 (32.8)
Ineligible		1 (1.6)
Reasons for Declining (n=26)	*n (%)*	
Too Busy/Lack of Time	*21 (80.8)*	
Help Not Necessary	*3 (11.5)*	
Group Aspect Unappealing	*1 (3.8)*	
Not Enough Help	*1 (3.8)*	
Attrition and Attendance, n=16		n (%)
Completed		7 (43.8)
Finished, but Did Not Complete		2 (12.5)
Discontinued		7 (43.8)
Reasons for Discontinuing (n=7)		*n (%)*
Lack of Time		*2 (28.6)*
No Reason Noted		*5 (71.4)*
Adherence, n=7		minutes (*CI*)
Average Practice per Day		21.7 (*13.1-30.2*)
Measure of Effectiveness (Assessment Tool), n=7	Before MBSR (*CI*)	After MBSR (*CI*)
Stress, Anxiety, and Depression Score (*PHQ-SADS*)	11.86 (*7.45-16.26*)	7.78 (3.89-11.66)
Health Related Quality of Life Score (*SIBDQ*)	42 (*31.2-51.9*)	50 (*40.1-60.3*)
Self-Compassion Score (*SCS*)	2.37 (*1.62-2.79*)	3.01 (*2.42-3.60*)
Mindfulness Score (*MAAS*)	4.19 (*3.4-5.00*)	3.60 (*2.96-4.2*)

Trend in the burden of coronary artery disease in patients with chronic kidney disease in Alberta

Cooper, Matthew & Ye, Feng & Okpechi, Ikechi & Ghimire, Anukul & Oudit, Gavin & Bello, Aminu
Supervisor: Dr. Aminu Bello

INTRODUCTION
Care and outcomes of the general population with coronary artery disease (CAD) have improved over time, however it is unclear if this has occurred for patients with chronic kidney disease (CKD). We aimed to describe the temporal trend in the burden of CAD in patients with CKD in Alberta.

METHODS
This is a population-based retrospective cohort study using the Alberta Kidney Disease Network database. We included adult patients in Alberta with CKD, on dialysis or a kidney transplant diagnosed with CAD from 2003 and 2019. Patients with CAD were identified using the international classification of diseases (ICD) codes as well as procedural and physician billing codes. We calculated the annual incident rate of CAD and estimated the secular trend by CKD stage, dialysis and kidney transplant status.

RESULTS
100, 363 cases of CAD occurred in patients with CKD stage 3 to 5, on dialysis or with a kidney transplant between 2003 and 2019. The incidence of CAD decreased from 49.4, 58.9, 67.9, 48.8 and 31.9 per 100 person-years to 5.7, 6.1, 6.5, 5.0 and 10.9 per 100 person-years for patients with estimated glomerular filtration rates (eGFRs) of 45-59, 30-44, 15-29, <15 mL/min/1.73m2 and either on dialysis or with a transplant, respectively. There was no difference in the rate of change in annual CAD incidence between patients with eGFRs of 30-44, 15-29, <15 mL/min/1.73m2 and either on dialysis or with a transplant compared to patients with an eGFR of 45-59 mL/min/1.73m2.

CONCLUSIONS
Between 2003 to 2019, the annual incidence rate of CAD decreased for patients with CKD, on dialysis and those with a kidney transplant. Future analysis will compare trends in CAD in the general population and if differences in quality-of- care impacted cardiovascular related outcomes.

Trafficking of thymic stromal lymphopoietin in allergen- induced airway epithelial cells: colocalization with regulatory guanosine triphosphatase Rab11a

Marc Duchesne, Luke Gerla, Swai Khang, Paige Lacy
Supervisor: Paige Lacy

INTRODUCTION

Airway epithelial cells (AECs) are important cytokine-secreting cells for maintaining lung immunity. Alarmin cytokines, including thymic stromal lymphopoietin (TSLP) are a subclass of cytokines secreted by AECs with emerging roles as mediators of asthma. However, there is a fundamental lack of understanding of how TSLP is secreted by AECs. Previous research suggests that AECs may utilize recycling endosomes (REs) in the absence of detectable secretory granules. We hypothesize that allergen stimulation induces an increase in TSLP release through REs that can be tracked with the RE marker Rab11a.

METHODS

BEAS-2B, normal bronchial epithelial (NHBE), and asthmatic bronchial epithelial (AHBE) cells were used to examine AECs. AECs on glass coverslips were stimulated with cockroach extract (CE), house dust mites (HDM), or poly I:C for 0-24 h and fixed for immunofluorescence (IF). In total, 10 cytokines were screened following CE stimulation: IL-1β, -4, -6, -8, -13, -17, -25, -33, TNF-α and TSLP. Inhibitors of protein synthesis, verrucarin A, or transcription, actinomycin D, were applied. Coverslips were imaged using a high-resolution Zeiss Elyra microscope and analyzed with Volocity imaging analysis software. Supernatant cytokine levels were quantified with MSD kits. All experiments were n=3 with ANOVA used for statistical analysis.

RESULTS

Allergen-stimulated AECs showed quantifiable increases in TSLP, TNF-α, and IL-33, with TSLP having the highest levels ($p < 0.01$). The addition of verrucarin A or actinomycin D reversed increases in TSLP IF to basal levels in CE stimulation, suggesting TSLP de novo synthesis. Findings in BEAS-2Bs were confirmed in NHBEs and AHBEs. Co-labelling of Rab11a and TSLP showed colocalization.

CONCLUSIONS

Our results show for the time intracellular localization of TSLP and subsequent redistribution of TSLP during allergen stimulation. Colocalization of Rab11a and TSLP indicates that TSLP uses REs for its release following allergen stimulation. These findings are crucial for expanding our understanding of TSLP trafficking and release in AECs.

The Impact of Colonization by Multi Drug Resistant Bacteria on Graft Survival, Risk of Infection, and Mortality in Recipients of Solid Organ Transplant: Systematic Review and Meta-analysis

Abdulellah Almohaya MD, Jordana Fersovich MD, R Benson Weyant MD, Oscar A Fernandez Gracia, Sandra Campbell, Karen Doucette MD, MSc, Tamara Lotfi MD, MPH, Juan G. Abraldes MD, PHD, Carlos Cervera MD, PHD, Dima Kabbani MD, MSc
Supervisor: Dr Dima Kabbani

INTRODUCTION
Colonization with multi-drug resistant bacteria (MDR) in solid organ transplant (SOT) recipients increases the risk of post-transplant bacterial infection. The
impact of MDR colonization on graft survival and mortality is not well established.

METHODS
A search was executed by an expert librarian on PROSPERO, OVID Medline, Ovid EMBASE, Wiley Cochrane Library, ProQuest dissertations and Theses Global and SCOPUS, from inception until March 20,
2023, after PROSPERO registration. Adult SOT colonized with Methicillin resistant Staphylococcus aureus(MRSA), Vancomycin-resistant Enterococci (VRE), Extended- spectrum beta-lactamase (ESBL) or AmpC producing bacteria, carbapenem resistant Enterobacteriaceae (CRE), or MDR Pseudomonas were included and compared to non-colonized SOT. Pairs of reviewers screened abstracts and full studies for inclusion, and extracted data independently. We used RevMan to conduct a meta-analysis using the random effects models to calculate the pooled odds ratio (OR) with 95% confidence interval (CI) for the incidence of mortality, infection, or graft loss. Statistical heterogeneity was determined using the I2 statistic. The Newcastle-Ottawa Scale (NOS) was used for bias assessment.

RESULTS
Sixty four (abstracts and full manuscript) were included; of which 39 in the quantitative analysis. Liver tr (LT) (25 studies) and VRE (14 studies). 4077 SOT r with MDR colonization, Age: 29 to 60.9 and the % women (2.8-58.1%)
MDR colonized SOT had increased death and infection (Death: OR= 2.35 (95%CI 1.63-3.38; p<0.001 and I2= 49%; any infection: OR= 10.74 [95% CI 7.56, 15.26; p<0.001 and I2=58%]) but not increased graft loss (OR=1.17, 95%CI 0.81-1.69; p=0.41, I2=0%) In LT, CRE and MRSA colonization increased mortality (CRE: OR=6.98, 95%CI 1.27-38.43; p=0.03 and I2= 86%, MRSA: OR=2.25, 95%CI 1.25-4.05; p=0.007 and I2= 0%)but not VRE (VRE: OR= 1.63, 95%CI 0.57- 4.67; p=0.36 and I2= 62%).

CONCLUSIONS
MDR colonization in SOT increased infection and death but not graft loss. These data should be taken into account when stratifying the risk of transplant.

SGLT-2 Inhibitors are Associated with Kidney Benefits at All Degrees of Albuminuria: A Retrospective Cohort Study of Adults with Diabetes

Kaden K. FUJITA, Feng YE, David COLLISTER, Scott KLARENBACH, David CAMPBELL, Derek CHEW, Amity E. QUINN, Paul RONKSLEY, and Darren LAU
Supervisor: Dr. Darren Lau

INTRODUCTION
It is unclear if sodium-glucose cotransporter-2 inhibitors (SGLT2i) provide kidney benefits in adults with non-severe albuminuria, who are under-represented in kidney focused trials. However, clinical guidelines suggest SGLT2i for a broad
range of adults with diabetes and chronic kidney disease (CKD), most of whom have non-severe albuminuria.We performed a retrospective cohort study to examine the benefits of SGLT2i on eGFR decline and clinical kidney outcomes compared to dipeptidyl peptidase-4 inhibitors (DPP4i), among all adults, and those stratified by baseline albuminuria.

METHODS
Using Alberta administrative data, we created a cohort of adults with diabetes starting SGLT2i. Time conditional propensity score was used to match SGLT2i and DPP4i users (1:2). Spot urine albumin or equivalent was used to define albuminuria as mild (ACR < 3 mg/mmol), moderate (ACR 3-30 mg/mmol), or severe (ACR ≥ 31 mg/mmol). Linear regression was used to model eGFR, and Poisson regression for composite kidney outcomes (death from kidney causes, kidney replacement therapy, or > 40% loss of eGFR) and all-cause mortality.

RESULTS
SGLT2i users (n=19,238, median age 57.9, female 40.9%) had mostly mild albuminuria (70.7%). Acutely (≤ 60 days), SGLT2i was associated with 1.36 mL/min/1.73 m2 (95% CI 0.98-1.74, $p < 0.001$) decline in eGFR relative to DPP4i. After day 60, SGLT2i use resulted in 1.04 (0.93-1.15, $p < 0.001$) less annual eGFR loss. Reduction in adverse kidney outcomes (IRR 0.58 [0.47-0.71], $p < 0.001$) but not all-cause mortality (IRR 0.82 [0.66-1.01], $p = 0.06$) was observed in SGLT2i treated individuals. Findings were similar in sub-groups with mild (all outcomes), and moderate albuminuria (total eGFR).

CONCLUSIONS
SGLT2i use may prevent eGFR decline and reduce the risk of adverse kidney
events in adults with diabetes and varying albuminuria. Thus, the kidney benefits of SGLT2i likely apply to a broad range of adults with CKD.

Predicting Renal Function After Lung Transplantation

John Gouda MD, Karina Kaur, Alim Hirji MD MSc, Justin Weinkauf MD, Dale Lien MD, Rhea Varughese MD MSc, Jason Weatherald MD MSc, Kieran Halloran MD MSc
Supervisor: Dr. Kieran Halloran

INTRODUCTION

Lung transplant (LTx) is associated with high morbidity and mortality. Pre- transplant renal dysfunction has previously been shown to increase these risks further. We sought to evaluate the potential of pre- and peri-transplant factors for predicting post-transplant renal function with the eventual goal of aiding in candidate selection.

METHODS

We conducted a retrospective observational cohort study of patients who underwent LTx or heart-LTx in our program 2012 – 2020. We excluded patients < 18, immediate post-operative death, patients transferred out of province, and those without at least 3-month renal function assessment. Patients on renal replacement were coded as eGFR 15 mL/min/1.73m2. All variables were included in a screening multivariable linear model and ranked via their logworth association with the outcome, followed by backward elimination via p-value to develop the final model.

RESULTS

525 patients underwent transplant during this timeframe, of which 114 were excluded and 413 analyzed. The majority indication for LTx was interstitial lung disease (42%), with a mean age of 55 years and 33% female sex. Mean eGFR (with standard deviation) at the time of transplant, 3-months, 1-year, and 3-years' post- transplant were 96 (22), 81 (24), 57 (22), and 51 (24) [Figure 1]. The only variables associated with 1-year eGFR via logworth contribution with false discovery rate correction were sex, age, bridging extracorporeal membrane oxygenation (ECMO), and eGFR at transplant. The final model performance via R2 for 1-year eGFR was 0.225. The model predicted versus actual eGFR at 1-year were correlated.

CONCLUSIONS

Age, sex, eGFR at transplant, and use of ECMO as bridge to transplant were associated with post-transplant eGFR and used to produce a candidate model with predictive capacity for post-transplant renal function. We plan further analyses including confirmatory modelling, cross-validation, and validation in a second cohort. These findings may help the candidate selection process.

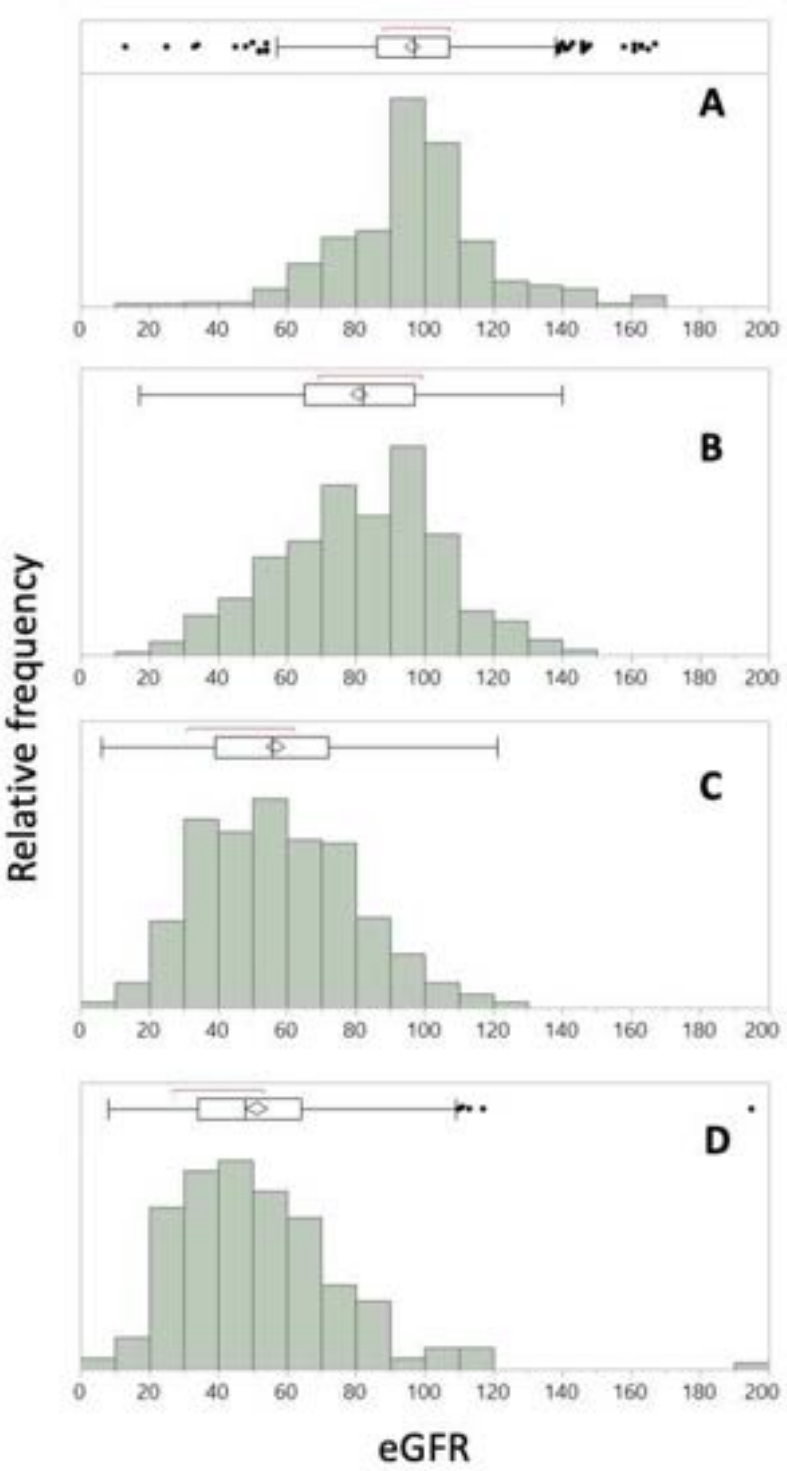


Figure 1. Renal function at transplant (A), 3 months (B), 1 year (C), and 3 years (D) post-transplant.

Diagnostic prospects of labelled native-PLGA nanoparticles in Alzheimer's Disease (AD) pathology

Govindarajan Karthivashan and Satyabrata Kar
Supervisor: Satyabrata Kar

INTRODUCTION

Alzheimer's disease (AD) is the most common cause of dementia among the elderly. Evidence suggests that elevated β-amyloid (Aβ) peptide levels/aggregation and increased phosphorylation of tau protein play crucial role in the development of AD. Presently, AD is clinically diagnosed using cognitive tests, neuroimaging, and detecting abnormal Aβ and tau levels/deposition. While measuring Aβ and tau levels can suggest disease state, neuroimaging of aggregated Aβ and tau protein in the brain using positron emission tomography (PET) allows for monitoring pathological changes in AD patients. We recently reported that FDA-approved native PLGA nanoparticles without conjugation with any drug/agent can interact with Aβ to reduce its aggregation/toxicity in cellular and animal models of AD. As a follow-up, we evaluated if labelled native PLGA can interact with Aβ-containing neuritic plaques in the 5xFAD mouse model of AD.

METHODS

5xFAD-Tg and wild-type (WT) mice were injected with a single intracerebral dose of labelled native-PLGA and then animals were fixed with Paraformaldehyde at 1h, 3h, 12h, 24h, 72h, and 1-week post-treatment. The brain tissues were then processed for Aβ-immunostaining or Congo red dye to evaluate their co-localization with labelled PLGA using the Pearson coefficient values from the merged-channel images.

RESULTS

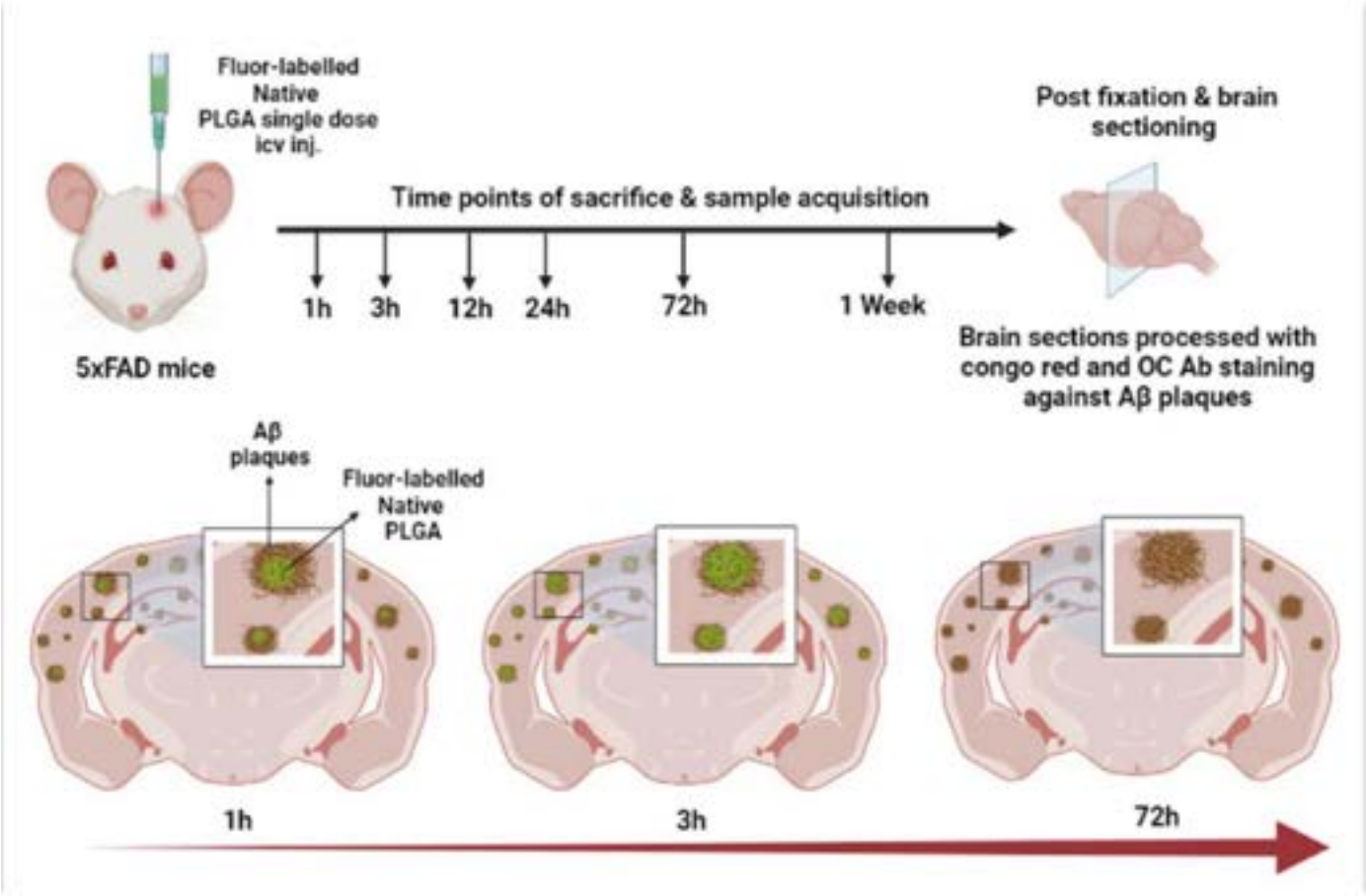
Our results revealed that fluorescence-labelled native PLGA following a single acute intracerebellar injection can identify the majority of the immunostained Aβ as well as Congo red labelled neuritic plaques in the cortical regions of 5xFAD mouse brains. PLGA-labelled plaques are apparent at 1hr, peak around 3hr, and then start declining by 24hr after injection. No fluorescent labelled PLGA was detected in the control cerebellum of 5xFAD mice or in any brain regions of wild- type control mice.

CONCLUSIONS

These results provide the very first evidence that native PLGA nanoparticles can be developed as a novel agent for the diagnosis and tracking pathological changes in AD.

Diagnostic prospects of labelled native-PLGA nanoparticles in Alzheimer's Disease (AD) pathology

Govindarajan Karthivashan and Satyabrata Kar
Supervisor: Satyabrata Kar



Screening for mild cognitive impairment and dementia in kidney failure: a systematic review and meta-analysis

Kevin Wang, David Collister
Supervisor: Dr. David Collister

INTRODUCTION
Cognitive impairment (CI) is common in chronic kidney disease (CKD) and kidney failure and is associated with adverse outcomes. Screening for CI has been studied in the general population, and optimal cut-offs for various instruments exist, but this has not been rigorously explored in the setting of kidney disease where cognition may differ due to comorbidities, uremic toxins and dialysis. In this systematic review, we sought to summarize the performance of screening tools for mild cognitive impairment (MCI) and dementia across the spectrum of kidney disease.

METHODS
A search strategy for PubMed, EMBASE, CINAHL, Psych Hub and the Cochrane Library, was developed with the assistance of a medical librarian. Studies that recruited adult patients with CKD or kidney failure (including dialysis and kidney transplantation) who were screened for MCI or dementia using an instrument that was compared to a diagnostic criteria for MCI or dementia, were included. Two reviewers independently identified studies meeting the inclusion criteria and a
third reviewer resolved conflicts. Studies that compared cognitive screening instruments to a gold standard and had outcomes such as sensitivity, specificity, PPV, NPV, AUROC were included.

RESULTS
Of 2511 eligible studies, we included 64 in full text review, and 10 unique studies for data abstraction. These studies evaluated the performance of the Mini-Mental Status Exam (MMSE) (6 studies), the Montreal Cognitive Assessment (MoCA) (7 studies), the Modified Mini-Mental State Exam (3MS) (1 study), Mini-Addenbrooke's Cognitive Evaluation (m-ACE) (1 study), and the Kidney Disease Quality of Life (KDQOL) scale (1 study). Optimal cut-offs and performance of screening
instruments varied among studies. Meta-analysis is ongoing.

CONCLUSIONS
Optimal cut-offs for CI screening in patients with kidney disease are different from those in the general population. Further research is needed to improve screening instruments for CI in the adult CKD and kidney failure populations.

Impaired DNA repair response activates a novel FOXO1-dependent metabolic remodelling in patients with progressive systemic sclerosis

Lamia Khan, Desiree Redmond, Robert Gniadecki, Jan Willem Cohen Tervaert and Mohammed Osman
Supervisor: Supervisor: Dr. Mohammed Osman

INTRODUCTION

Systemic sclerosis (SSc) is a deadly disease characterized by immune dysregulation, vasculopathy, and fibrosis. Disease-associated mortality primarily stems from fibrotic complications. Hence, a deeper understanding of its mechanisms is important. The cells promoting skin fibrosis in SSc are human dermal fibroblasts (HDFs) which develop a myofibroblast-phenotype, senescence- like-features, and resistance-to-apoptosis. We recently showed that increased genomic instability associated with double-stranded DNA breaks (DSBs) and senescence-like-features are present in dcSSc HDF. In cancer, dysregulated DSBs and senescence-like-features are associated with activation of the transcription factor forkhead box protein O (FOXO1) to promote metabolic remodeling. We hypothesized that DSBs promotes FOXO1 activation in dcSSc HDFs to promote fibrosis.

METHODS

Primary HDFs were generated from healthy volunteers (HC), less severe early limited (lcSSc), and severe diffuse (dcSSc) using 4 mm skin biopsies. DSBs were quantified by measuring γ-H2AX (DSB-marker) via immunoblot (IB) and immunofluorescence/confocal microscopy (IF). Nuclear FOXO1-translocation, myofibroblast-differentiation and fibrotic markers were measured using IF, IB and qRT-PCR; respectively in HC or dcSSc HDF. dcSSc HDF's were treated with FOXO1 inhibitor and pro-fibrotic signals were measured.

RESULTS

Severely fibrotic dcSSc patients had the highest levels of γ-H2AX compared to HC (*$p<0.05$) and lcSSc patients. They also had substantial nuclear accumulation of FOXO1 which was associated with increased mRNA expression of FOXO1 transcriptional target, pyruvate dehydrogenase kinase 4 (*$p<0.05$). FOXO1 inhibition resulted in decreased fibrotic-markers and PDK4-transcription (*$p<0.05$) in dcSSc HDF. Etoposide treatment promoted FOXO1- activation and myofibroblast differentiation in HC HDF.

CONCLUSIONS

DSBs are more commonly present in HDF from dcSSc patients, which may promote myofibroblast-differentiation, resistance-to-apoptosis and fibrosis. We propose that FOXO1 activation may promote a downstream metabolic remodelling and an associated senescence-like-signal. Together, our findings may provide a mechanistic model that may impart a deeper understanding for the role(s) of DSB- associated senescence in promoting fibrosis and/or immune dysfunction in SSc.

Factors influencing the quality of life in inflammatory bowel disease- A comprehensive review

Samina Khan, Sneha Annie Sebastian, Mihirkumar P. Parmar, Nitin Ghadge, Inderbir Padda, Ahmed S. Keshta, Naofel Minhaz, Apurva Patel
Supervisor: Dr. Puneeta Tandon

INTRODUCTION
Inflammatory bowel disease (IBD) is a group of chronic relapsing disorders, including Crohn's disease (CD) and ulcerative colitis (UC), which affects an increasing number of people worldwide. In the last few decades, the scientific world has witnessed many developments in IBD management by controlling debilitating symptoms and remaining in remission for more protracted periods. Even so, we still have a large population suffering from active IBD. An individual's quality of life (QoL) can be severely affected by IBD, like any other chronic illness.
In this article, we have reviewed factors influencing the QoL in IBD patients, including chronic pain, diet, physical activity, and psychological factors like depression, anxiety, and stress symptoms. We also discussed the mechanisms of diet-microbial-immune system interaction, currently available dietary therapies for active CD and UC, and early psycho-social interventions that can reduce the disease burden and improve QoL in IBD patients.

METHODS
Literature review

RESULTS
We will be working on a QI project based on this review article.

CONCLUSIONS
Patients must have access to a multidisciplinary team of physicians, dieticians, physical therapists, and mental health professionals to help maintain their healthy lifestyles. These components of care should be addressed in regular IBD follow-ups. Establishing clinics that specialize in IBD would improve patients' lives and reduce ER visits and hospital admissions. Small-scale quality improvement projects can provide more guidance about the practicability of such clinics or how to provide multidisciplinary services. A microsystem's refinement can then be propagated to a more extensive system. We also suggest further research providing more evidence on certain aspects, like the role of exercise and the involvement of a sexual health therapist in multidisciplinary teams in improving the QoL of IBD patients.

Retrospective Cohort Study of Incentivised Testing and Treatment for Sexually Transmitted and Blood-Borne Infections in Outreach Populations

Krahn J, Gratrix J, Khan M, Meyer G, Smyczek P, Singh AE
Supervisor: Dr. Ameeta Singh

INTRODUCTION
Rates of bacterial sexually transmitted infections have risen in Edmonton since 2014. This project examined the impact of incentives on testing and treatment for sexually transmitted and blood borne infections (STBBI) among outreach populations in Edmonton, Alberta. The primary outcomes were the case finding rates for tested STBBIs and the secondary outcome was the proportion of new
cases treated.

METHODS
We compared incentivized versus routine care for STBBI outreach test and treat services between October 2018-June 2019. Incentivized visits included a $10 gift card for testing and an additional $10 gift card for returning for results and/or treatment. Incentivized visits were offered to clients with a lack of housing/income, were difficult to locate, and had a history of being lost to follow-up to the program. All test and treat visits included chlamydia, gonorrhea, syphilis, and HIV testing and/or treatment as required and were completed by Registered Nurses from the Edmonton STI Clinic. Outreach visits were offered at subsidized housing locations, community-based organizations, and through street outreach.

RESULTS
From October 2018 to June 2019, 2384 outreach clients were reached; 453 (19.0%) received incentives and 1931 (81.0%) received routine care. 61.1% being male
with no gender differences between the two groups. There were no significant differences in case finding rates for chlamydia (4/8%), gonorrhea (2.9%), and HIV (0.1%); however, there was for syphilis (3.8% for incentivized visits vs. 1.9% for routine visits; p = 0.02). All newly diagnosed bacterial infections identified in the incentivised group received treatment as compared to routine visits (chlamydia 100% vs 79.1%, p=0.008, gonorrhea 100% vs 59.7%, p=0.002, and syphilis 100% vs 86.7%, p=0.08).

CONCLUSIONS
Incentivising STBBI testing and treatment increased case finding rates of syphilis and was associated with 100% treatment rates; this is a promising approach to decrease the burden of STBBI among outreach populations.

ULK2 is a key pro-autophagy protein that contributes to the high chemoresistance and disease relapse in acute myeloid leukemia

Justine Lai, Chuquan Shang, Claire Yang, Will Chen, Raymond Lai, Joseph Brandwein, Peng Wang
Supervisor: Dr. Peng Wang

INTRODUCTION

Most patients diagnosed with acute myeloid leukemia (AML) die from disease relapses, occurring shortly after the initial remission. We have recently developed an in-vitro model for AML relapse, where cell lines were treated with sufficient Ara- C to eliminate all detectable viable cells in culture, labelled as the 'in-vitro remission', followed by an 'in-vitro relapse' phase, marked by cell regeneration. Using this model, we found that cancer stem-like cells (CSLs) are major contributors to relapse. As a follow up study, we examined the key molecular events underlying relapse, with a focus on autophagy.

METHODS

We employed an autophagy oligonucleotide array comparing gene expression in untreated and Ara-C treated CSLs. CSLs were purified using the SORE6 reporter.
We tested if the identified gene targets play an important role in the in-vitro relapse model by manipulating the target through pharmacological inhibition.

RESULTS

Based on the autophagy array, ULK2, an autophagy initiating gene, was found to be the most differentially expressed gene between untreated and Ara-C treated CSLs, which was confirmed by quantitative RT-PCR and western blots. We then asked if ULK2 directly contributed to the chemoresistance property observed in CSLs. Treatment of CSLs with a ULK inhibitor, MRT68921, sensitized them to Ara-C, reducing the IC50 from 194.0 to 88.0 nM ($p<0.01$); no significant change was observed in bulk cells. Using our relapse model, the 'in-vitro relapse' cells showed a dramatic increase in the protein expression of ULK2. Importantly, MRT68921 treatment prevented 'in-vitro relapse'. To clinically validate the importance of ULK2 in relapse, we compared ULK2 expression in initial diagnostic and relapsed AML bone marrow clot sections. ULK2 expression was higher in relapsed samples.

CONCLUSIONS

Using our in-vitro relapse model, we are the first to implicate ULK2 in AML relapse. We believe this model is valuable in studying the biology of relapse and identifying potential therapeutic targets.

The association between maternal glucose levels in pregnancy and subsequent hypertension

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

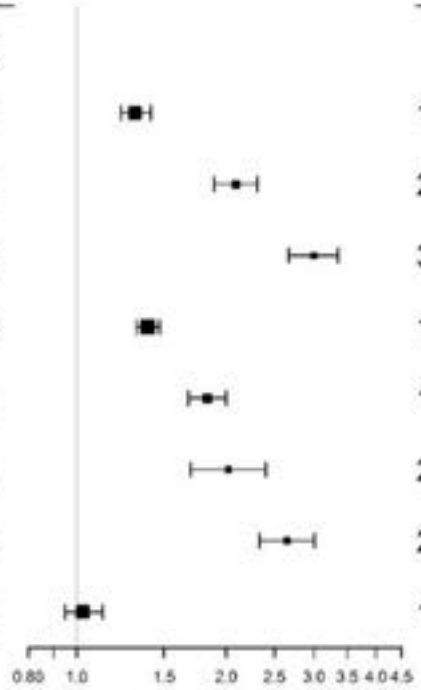
INTRODUCTION
There is little real-world data examining the association of maternal glucose levels in pregnancy and development of hypertension and cardiovascular disease (CVD).

METHODS
This population level, retrospective cohort study examined females aged 12-54 years with singleton pregnancies completed at ≥ 29 weeks of gestation from 1 Oct 2008 to 1 Dec 2018, followed until 31 Mar 2019 in Alberta, Canada (population ~4.2 million). Females were stratified by glucose levels in the 50-g glucose challenge test (GCT) as well as by 75-g oral glucose tolerance test (OGTT) subtypes (normal OGTT, elevated fasting plasma glucose only (EF), elevated post-load glucose only (EPL), or elevation in both fasting and post-load glucose (combined)). Primary outcome was development of hypertension >120 days postpartum, secondary outcome was development of CVD. Time to development of hypertension was modelled using Cox proportional hazard models.

RESULTS
Of 313,361 females, 231,008 (79.1%) underwent a GCT only while 60,909 (20.9%) underwent either OGTT only or both. 9,580 (3.1%) developed hypertension and 2,824 (0.9%) developed CVD over a median follow-up of 5.7 years. Every 1 mmol/L increase in glucose in the GCT increased risk of subsequent hypertension by 15% (adjusted hazard ratio (aHR) and 95% confidence interval(95% CI): 1.15 (1.14, 1.16)), respectively. Among those who underwent OGTT, combined group conferred the highest risk of subsequent hypertension, followed by the EF group, then the EPL group (reference: GCT≤ 7.1 mmol/L, aHR (95%CI): EPL 1.83 (1.68, 2.00); EF 2.02 (1.70, 2.40); Combined 2.65 (2.33, 3.01)) (Figure 1).

CONCLUSIONS
Increased maternal glucose levels in pregnancy are associated with increased risk of post-partum hypertension. CVD rates remained low, which was reassuring given the duration of follow up. These findings may help identify higher-risk females who should be targeted for earlier postpartum cardiovascular risk reduction.

	Female, N	HTN, n (%)	aHR (95% CI)
GCT <= 7.1 mmol/L	193347	4661 (2.4)	1
GCT 7.2-7.7 mmol/L	28635	986 (3.4)	1.31 (1.23 , 1.41)
GCT 7.8-11.0 mmol/L	5838	409 (7.0)	2.09 (1.89 , 2.31)
GCT >= 11.1 mmol/L	3188	318 (10.0)	3.00 (2.67 , 3.36)
Normal OGTT	44111	1632 (3.7)	1.39 (1.32 , 1.47)
EPL	11534	606 (5.3)	1.83 (1.68 , 2.00)
EF	2142	137 (6.4)	2.02 (1.70 , 2.40)
Combined	3122	254 (8.1)	2.65 (2.33 , 3.01)
No testing	21444	577 (2.7)	1.03 (0.95 , 1.13)



Subcutaneous Immunoglobulin therapy as a maintenance agent for patients with idiopathic inflammatory arthritis: a real world single centre experience

Zechen Ma; Dylan Johnson; Stephanie Keeling; Robert Gniadecki; Bruce Ritchie; Jan Willem Cohen Tervaert; Mohammed Osman
Supervisor: Mohammed Osman

INTRODUCTION
Idiopathic inflammatory myopathies (IIMs) are heterogenous diseases characterized by skeletal muscle inflammation associated with cutaneous, joint, gastrointestinal, pulmonary, and/or cardiac involvement. Intravenous immunoglobulin (IVIG) has been recommended as an adjunct therapy for IIM refractory to conventional corticosteroids and/or immunosuppression. However, IVIG therapy requires hospital resources, incurs high costs, has limited supply, and has increased risk of adverse reactions. Subcutaneous immunoglobulin (SCIG) therapy has been used as an alternative to IVIG in primary immunodeficiencies, and neuroinflammatory disorders. We assessed the effectiveness and patient satisfaction of SCIG as an adjunct maintenance therapy for IIM with stable disease activity.

METHODS
We retrospectively reviewed 21 patients with IIM on SCIG therapy for more than 12-months. Global disease activity was recorded using the Myositis Intention to Treat Index (MITAX), which accounts for seven disease domains 12-months prior to- and 12-months post-SCIG initiation. Disease flares, changes in immunosuppression, and cumulative prednisone doses were recorded. Patients' preference between IVIG vs. SCIG were surveyed using questionnaires utilized in studies with neuroinflammatory conditions.

RESULTS
15 patients were diagnosed with dermatomyositis, 2 with overlap myositis, 2 with immune-mediated necrotizing myositis, and 1 with unspecified IIM. 95.2% of patients initially required IVIG for their disease then were switched to SCIG. There was no significant difference in global disease activity pre-SCIG vs. post-SCIG initiation (MITAX 3.36 vs. 2.76). 3 patients experienced disease flares. 5 patients required escalation of therapy, while 4 patients de-escalated therapies. No statistical difference was detected in cumulative steroid doses prior to– or post- SCIG initiation. Most patients (78.9%) preferred SCIG over IVIG.

CONCLUSIONS
SCIG can be utilized as an adjunct maintenance immunomodulatory therapy for IIM. SCIG is preferred by patients over IVIG without increased disease activity nor escalation of immunosuppression. Future cost effectiveness studies may provide an additional rationale for utilizing SCIG over IVIG for maintenance therapy.

Funding: Nil.

Solution NMR studies reveal novel CLIC4 chaperone activity with respect to profilin-1

Kevin Y. Mak, M. Rafid Feisal, Zabed Mahmud, Philip B. Liu, Laiji Li, Shu Y. Luo, Olivier Julien, Richard Schulz, Barbara J. Ballermann, Peter M. Hwang
Supervisor: Dr. Peter M. Hwang

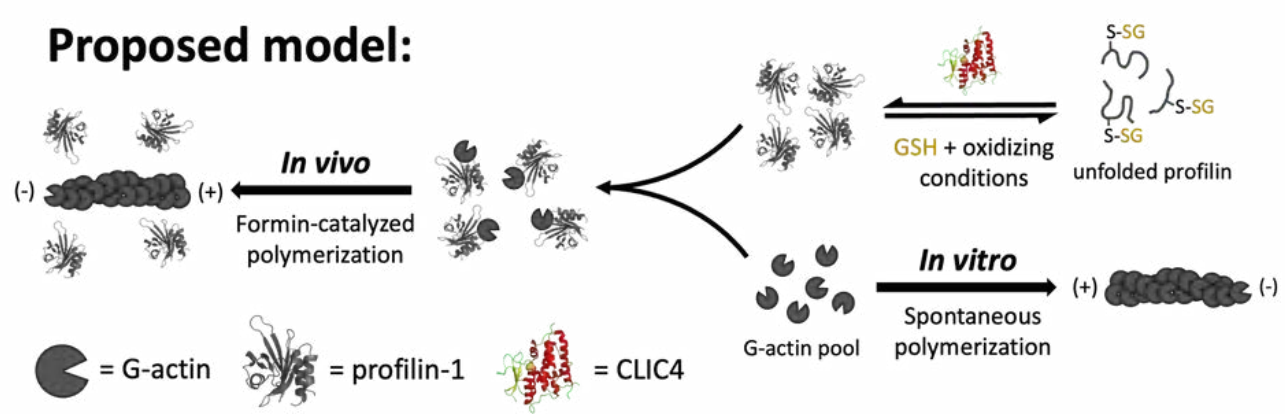
INTRODUCTION
Contrary to its name, chloride intracellular channel 4 (CLIC4) is a soluble enzyme that catalyzes glutathione-dependent thiol transfers. CLIC4 is implicated in numerous actin-dependent processes and directly binds with profilin-1, a critical regulator of the actin cytoskeleton. Profilin-1 is known to be glutathionylated in proteomic studies of cells exposed to oxidative stress which disrupts its structure and function. In this study, we aim to demonstrate that CLIC4 can reverse glutathionylation of profilin-1 and promote its refolding in cells and in vitro.

METHODS
The binding affinity between recombinant profilin-1 and CLIC4 was determined by microscale thermophoresis (MST). Backbone dynamics and amide hydrogen exchange studies of profilin-1 were performed using solution nuclear magnetic resonance (NMR) spectroscopy. Pyrene-labeled actin polymerization assays were used to track the effects of oxidative glutathionylation of profilin-1.

RESULTS
We confirmed a weak direct interaction between profilin-1 and CLIC4 by MST with a dissociation constant of 176 ± 20 uM. However, our amide hydrogen exchange studies demonstrate that CLIC4 has a higher affinity for profilin-1 when it is unfolded. The N- and C-terminal helices of profilin-1 readily unfold, whereas the central beta sheet core remains relatively intact. Interaction with CLIC4 increases amide exchange rates throughout profilin-1, indicating preferential stabilization of partially unfolded intermediates. Profilin-1 is unfolded by glutathionylation of
buried cysteine residues in its N- or C-terminal helices. This disrupts its ability to bind actin but CLIC4 helps to partially restore profilin function as measured by the pyrene-actin polymerization assay.

CONCLUSIONS
Our data suggests that oxidative glutathionylation of profilin-1 unfolds it and disrupts its function with respect to actin polymerization in vitro. CLIC4 can help to reverse this by preferentially binding to partially unfolded profilin-1, like a chaperone. Future studies will aim to establish the glutathionylation status of profilin-1 in the presence of CLIC4.

Solution NMR studies reveal novel CLIC4 chaperone activity with respect to profilin-1



Engaging locomotor networks during paired non-invasive spinal cord neuromodulation after severe spinal cord injury: A case study

Darren J. Mann, Jane A. Porter, Deborah O. Okusanya, Justin Lee, Zahra Karamzadeh, Monique Yuan, Trevor S. Barss, and Vivian K. Mushahwar
Supervisor: Dr. Vivian Mushahwar

INTRODUCTION
Functional electrical stimulation (FES)-assisted arm and leg (A&L) cycling is an effective rehabilitative intervention for improving walking following an incomplete spinal cord injury (SCI). This alternative to overground rehabilitative training is a more feasible, cost-effective, and accessible option that requires less personnel to operate. Subsequently, this exercise paradigm serves as an intervention with tremendous potential and generalizability to the community. The goal of this study was to assess the potential benefits of combining transcutaneous spinal cord stimulation (tSCS) with A&L cycling to potentially improve functional mobility for persons living with motor complete SCI.

METHODS
This is a case study of a participant with an AIS B SCI. The participant has been undergoing FES-assisted A&L cycling training combined with cervical and lumbar tSCS (1 hr/day, 5 days/week) for 37 weeks. Assessments were performed pre- training and every 6 weeks thereafter and include the International Standards for Neurological Classification of SCI (ISNCSCI), time able to stand while assisted, and training load of each exercise session.

RESULTS
Although there were no changes in the ISNCSCI scores, the duration of assisted standing increased from 10 s pre-training to 33.5 s at 36 weeks post-training. Interestingly, the addition of tSCS enhanced standing duration to 38.5 s. Moreover, the total power output exerted by the participant consistently increased over time.

CONCLUSIONS
This study provides, for the first time, evidence that FES-assisted A&L cycling paired with non-invasive tSCS can be safely completed after severe SCI and leads to improvements in training load and assisted standing. Additional assessments
will be incorporated to further identify improvements in function and quality of life. Furthermore, future work will assess the benefits of using epidural spinal cord stimulation combined with A&L cycling after a motor complete SCI.

House dust mite allergen induces PAR-1 dependent CGRP release from cultured human pulmonary neuroendocrine cells

Ritu Mann-Nuttel and Paul Forsythe
Supervisor: Dr. Paul Forsythe

INTRODUCTION

Pulmonary neuroendocrine cells (PNEC) have recently gained attention as rare airway epithelial cells that amplify allergic asthma responses. PNECs act through Calcitonin gene-related peptide (CGRP) to stimulate ILC2 cells in a murine asthma model. Studying PNEC function has been challenging due to a lack of suitable cell isolation methods. Here we established two in vitro human PNEC models and investigated the effect of environmental stimuli (house dust mite (HDM) extract, lipopolysaccharide (LPS) and a volatile chemical odorant (bergamot oil) on CGRP expression by these cells.

METHODS

PNECs were generated from human induced pluripotent stem cells (iPNEC) and from primary bronchial/tracheal epithelial cells (ePNEC) in transwells. Successful differentiation of neuroendocrine cells was evaluated with RT-PCR and immunohistochemistry. At day 60 of culture, cells were challenged with stimuli (HDM, LPS, bergamot oil) in the presence or absence of specific receptor inhibitors for up to 6h to assess CGRP expression.

RESULTS

Both naïve iPNEC and ePNEC do not express the CGRP encoding genes CALCA and CALCB. Stimulation with HDM, but not LPS or bergamot oil, lead to expression of CALCB in both cultures. The HDM induced expression of CALCB could be inhibited by the Protease activated receptor 1 (PAR1) antagonist Vorapaxar. ELISA
confirmed release of CGRP in the supernatant of HDM challenged iPNEC (81.4 4.3 pg/mL) and ePNEC (7.6 2.3pg/mL) but was not detectable in cells co-incubated with Vorapaxar. Immunofluorescent co-staining of the PAR1 receptor and the neuroendocrine marker, synaptophysin indicated that PAR1 is expressed by a subpopulation of both iPNECs and hPNECs.

CONCLUSIONS

Here we demonstrate, for the first time, that human PNEC express the immunomodulatory neuropeptide, CGRP in response to HDM, but not LPS or
volatile odorant stimuli, in a PAR1 dependent manner. In the future, PNEC and CGRP production by these cells may represent an entirely novel therapeutic target in allergic asthma.

Reduced mitochondrial complex I capacity early in life is associated with a longer lifespan in seed beetles

H. Mast, M. Đorđević, U. Savković, P.U. Blier, H. Lemieux
Supervisor: Dr. Hélène Lemieux

INTRODUCTION

Mitochondrial function is a suspected driver of aging that directly or indirectly affects practically all other hallmarks of aging. Though many studies show longer lifespan as the result of a reduction in mitochondrial complexes, few studies have actually measured integrated mitochondrial function. Even fewer have evaluated the connection between mitochondrial function and lifespan within the same animal species.

METHODS

Here, we measured integrated mitochondrial function in the seed beetle model, Acanthoscelides obtectus. Beetles were selected for early (E) and late (L) reproduction for over 37 years, leading to two lines with marked differences in lifespan (7 days in E line, 12-14 days in L line). At three timepoints (days 1, 5, and 8), we used high-resolution respirometry to measure the NADH, Succinate, Proline dehydrogenase, and Fatty acid oxidation pathways and complex IV activity in both sexes of each line of the same species. Using specific inhibitors, we also determined complexes I, II and IV's control strength over the maximal combined pathway flux.

RESULTS

Results showed that the NADH pathway's contribution to maximal flux was specifically lower in L line beetles compared to the E line at days 1 and 5, and the rotenone titration confirmed that this reduction was due to an increased control by complex I. In contrast, the Succinate pathway's contribution was higher in the L line compared to the E line at days 1 and 5, while the other pathways did not show differences between the lines.

CONCLUSIONS

Our data suggest that complex I's reduction early in life contributes to the lifespan extension seen in L line beetles. Our integrated mitochondrial function results reinforce the involvement of mitochondria in the control of lifespan, and suggest a functional link between evolutionary and mechanistic theories of aging, since selection for late reproduction decreased complex I's capacity, ultimately leading to an increased lifespan.

Monkeypox infects primary human astrocytes and drives gasdermin B proteolytic cleavage to cause pyroptosis

Hajar Miranzadeh, Y.C. Lin, N. Ogando, E. Moussa, O. Julien, R. Noyce, D.H. Evans, C. Power
Supervisor: Dr. Christopher Power

INTRODUCTION

Monkeypox virus (MPXV) is an orthopoxvirus zoonotic infection. Recently, MPXV infections have spread widely in Europe and North America. In addition to typical symptoms including fever, swollen lymph nodes, asthenia, and skin lesions,
infected persons also develop neurological manifestations such as headaches, myalgia, malaise, fatigue, altered consciousness, agitation, and encephalitis. Studies of MPXV-infected animals also suggest that the virus can also penetrate
the brain. The underlying pathophysiology resulting from direct viral neuroinvasion is currently unknown. Pyroptosis is an inflammatory type of regulated cell death that occurs downstream of inflammasome activation, resulting in plasma
membrane rupture (PMR). In the present study, we investigated the neural cell tropism of MPXV as well as its effects on neural cell inflammatory responses.

METHODS

MPXV-, vaccinia virus (VV)-, and mock-infected cultured human neural cells were investigated by immunolabeling, RT-PCR, western blotting, cell death assays and mass spectrometry.

RESULTS

Astrocytes were most permissive to MPXV (and VV) infections followed by
microglia, oligodendrocytes, with minimal infection of neurons. We observed morphological changes in astrocytes 48 hours post-infection that were associated with viral protein (I3) expression, evident by immunodetection. MPXV-infected astrocytes showed increased expression of cytokine transcripts (e.g., IL-12, IRF3, IFI-16, IL-6/8, IL-1β, TNFα) at 24 hr post-infection. MPXV infection induced
gasdermin B proteolytic cleavage with significant release of lactate dehydrogenase (LDH), indicative of PMR and associated pyroptosis, compared with the Vaccinia
and mock-infected groups, which was verified by SYTOX quantitation of PMR.

CONCLUSIONS

We show that human astrocytes are highly permissive to productive MPXV
infection compared to VV and caused inflammatory gene induction with accompanying pyroptosis. These findings could underpin the recently recognized neuropathgenic actions of MPXV infection in humans.

Biological Features of Muscle in Patients with Cirrhosis Receiving Liver Transplantation

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Supervisor: Dr.Aldo Montano loza, Dr. Vera Mazurakr

INTRODUCTION
Sarcopenia is a prevalent condition in patients with cirrhosis and increases risk of death. Whether sarcopenia is modifiable is not known and requires understanding of the underlying biology of muscle loss. This study aimed to further understand
the association between sarcopenia, muscle biological features, and impact on patients undergoing LT.

METHODS
Biopsies of the rectus abdominis muscle were taken from the surgical incision site at the time of LT from 48 patients with cirrhosis (29 males; 19 females). Muscle fiber types, size, and centralized nuclei (CN) were assessed by immunohistochemistry in serial sections of muscle. Triglyceride (TG) content of biopsies was quantified by gas chromatography. These biological features of
muscle were aligned with the quantity of muscle determined by cross-sectional CT or MRI images at the 3rd lumbar vertebra which were taken within 6 months before LT as part of standard clinical assessments. Sarcopenia was defined as L3 SMI <39 cm2/m2 for women and <50 cm2/m2 for men.

RESULTS
The prevalence of sarcopenia was 44% and 52% in males and females,
respectively. Males had significantly larger type I muscle fibers (Median; 3625.0 vs. 2354.9 μm2, p=0.007) and more CN compared to females (11.0 % vs. 6.0 %, p=0.007). Fiber type IIA were larger in non-sarcopenic patients compared to sarcopenic patients (Median; 4175.1 vs. 3418.2 μm2, p<0.053). TG content was higher in non-sarcopenic compared to sarcopenic females (39.8±20.9 vs. 21.4±8.2 μg/g, p=0.023) but was not significantly different in male groups.

CONCLUSIONS
Sarcopenia in cirrhosis is associated with differences in fiber size.

Discovering the molecular pathways associated with neurological post-acute sequelae of COVID-19

Natacha S. Ogando, Mohamed Elaish, Mahmoud Gheblawi, Hajar Miranzadeh, Gavin Oudit, Tom C Hobman, Christopher Power
Supervisor: Dr. Christopher Power

INTRODUCTION

Persistent neurocognitive and neuropsychiatric disorders have been reported in 10-30% of people infected with SARS-CoV-2. The neurological post-acute sequelae of COVID-19 (neuroPASC), also termed “Long COVID”, represents a spectrum of new, recurring, and/or ongoing clinical symptoms can be detected during acute illness or emerge weeks to months after recovery of infection. The risk of
developing neuroPASC remains increased up to 2 years after acute COVID-19, particularly in adults, and is independent of the virus variant, vaccination, and COVID-19 severity. In this study, we report an animal model that enables identification and understanding of the mechanism(s) underlying neuroPASC.

METHODS

To model sex and age-related neurological vulnerability, we infected C57BL6/J mice intranasally with mouse adapted SARS-CoV-2 and followed disease development
up to 21 days post infection(dpi). Viral RNA and host transcripts were measured by ddPCR and RT-qPCR, respectively. Animals were investigated for anxiety (Open
Field Test) and depression (Forced Swim Test) behaviors. Tissue and blood samples were collected for molecular analysis to detect viral load and immunological/ inflammatory responses. Additionally, pathological analyses were performed of brain and lung tissues.

RESULTS

Viral RNA was detected at 7-, 14- and 21-dpi in different regions of the brain (cerebrum, cerebellum and brainstem) in a few animals. At 7 dpi, increased interferon-beta and caspase-1 transcript levels were detected in different neuroanatomic sites. At 14 and 21 dpi, increased Monocyte chemoattractant
protein (MCP-1) and interferon-gamma were observed in the brainstem or cerebellum of infected animals. Behavioral testing revealed depressive behaviors
at 7 dpi with reduced movements and corner preference, while at 21 dpi anxiety manifestations were observed as increased time of movement and rotations.

CONCLUSIONS

The present results suggested an association between neuroinflammation and neurobehavioral deficit progression. These findings represent early stages in the identification of a translational model to advance diagnostic and potential therapeutic options for neuroPASC.

A SCOPING REVIEW OF RISK FACTORS FOR URINARY INCONTINENCE IN OLDER MEN

Olagundoye Olawunmi, Odusanya Benjamin, Kung Janice, Gibson William, Wagg Adrian
Supervisor: Dr. Adrian Wagg

INTRODUCTION
Most epidemiological studies have not systematically identified or categorized urinary incontinence risk factors in older men, despite a higher prevalence than in younger men. Considering the burden of UI, an understanding of risk factors can inform cost-effective prevention/treatment programs. This scoping review aimed to identify and categorize risk factors for UI in older men and identify gaps in the evidence for the first time.

METHODS
The Joanna Briggs Institute (JBI) method for scoping reviews guided the conduct and reporting of this review alongside the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping reviews (PRISMA-ScR) checklist. JBI's Population, Concept, and Context approach framed the inclusion criteria (all evidence sources on UI risk factors that included older men [65+]). We employed JBI's three-step search strategy, which included a limited initial search in Ovid MEDLINE, a detailed search in all included databases, and a search of reference lists of included studies, Google Scholar and grey literature. Study type or publication date was not restricted. Two independent reviewers screened,
selected, and extracted eligible studies. We analyzed data using descriptive statistics and qualitative content analysis.

RESULTS
Forty-seven articles that met the inclusion criteria identified 98 risk factors across six categories. Behavioral risk factors, reported by only two studies, were the least investigated of all the categories, whereas medical factors/diseases were the most investigated. No genetic factors were documented (Figure 1). The top five risk factors were increasing age/advanced age (n=12), Benign Prostatic Hyperplasia (n=11), Diabetes Mellitus (n=11), Detrusor overactivity (n=10), limitation in physical function/ADL disability (n=10), increased BMI/overweight/obesity (n=8), Dementia (n=8), and Parkinson's disease (n=7).

CONCLUSIONS
More primary research on behavioral risk factors for UI in older men is necessary due to the lack of evidence on the topic. These factors may play a role in health promotion and disease prevention in this area.

A SCOPING REVIEW OF RISK FACTORS FOR URINARY INCONTINENCE IN OLDER MEN (PAGE 2 OF 2)

Olagundoye Olawunmi, Odusanya Benjamin, Kung Janice, Gibson William, Wagg Adrian
Supervisor: Dr. Adrian Wagg

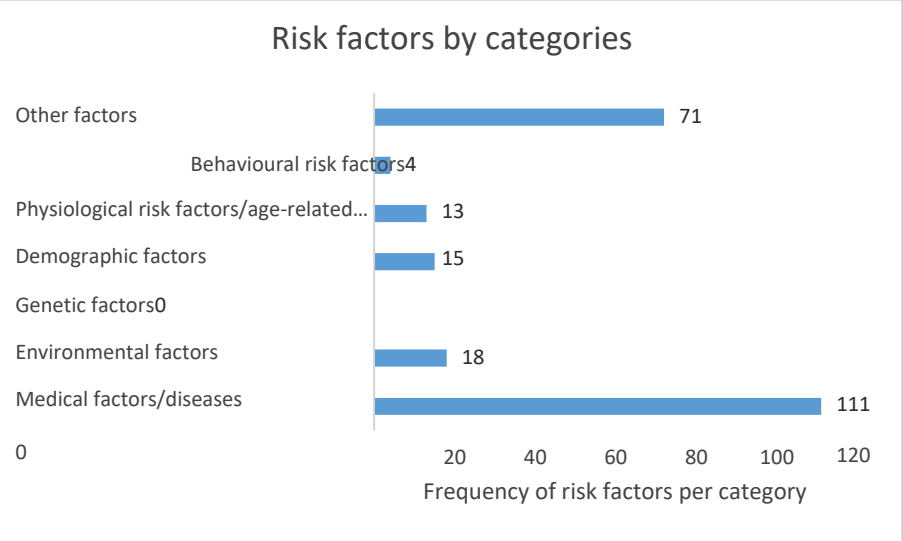

Figure 1: Frequency of risk factors by categories

Breakthrough Invasive Fungal Infections in Lung Transplant Recipients Receiving Universal Prophylaxis: A Single Center Retrospective Study

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Supervisor: Dr. Dima Kabbani

INTRODUCTION
Lung transplant patients are at high risk of early invasive fungal infections (IFI) and universal antifungal prophylaxis (AP) is the most used prevention strategy. Our objective was to assess the incidence and risk factors for breakthrough IFI (bIFI).

METHODS
Retrospective review of adult lung transplant recipients (LTR) between August 2019 and December 2021, receiving 3 months AP. IFI defined according to ISHLT consensus statement in the first 6 months post-transplant were included. Any IFI occurring from day 5 after initiation to 14 days after discontinuation of AP was considered bIFI.

RESULTS
147 thoracic (140 double LTR, 1 Single LTR, 6 Heart-LTR) transplants were included. Median age at transplant was 61 years (IQR 56-65), male sex (67.3%). Induction (basiliximab (96.6%), rATG (6.1%)). At transplant, mold colonization was present in 9 recipients (Aspergillus (7), Scedosporium (1), Paecilomyces (1)) and 3 donors (Aspergillus). AP regimen included: voriconazole + inhaled amphotericin B (51%), voriconazole (35%), posaconazole + inhaled amphotericin B (9.5%), and other combination (4.5%). BIFI was found in 17 LTR (11.5%): 5 invasive candidiasis, 6 invasive aspergillosis (IA), 4 mucormycosis, 1 scedosporiosis, and 1 invasive Exophiala spp. and Scedosporium spp. Four IFI occurred after AP discontinuation: 3 IA and 1 scedosporiosis. Median time from transplant to bIFI 32 days (IQR 10-76). Voriconazole trough levels were available in 7/17 patients during bIFI, of which 3/7 had levels <1. We did not find a difference between bIFI and no bIFI in age, lung reduction surgery for size mismatch, rATG or ECMO requirement. Although in 3 cases of bIFI patient's death was attributable to the infection, bIFI was not significantly associated with increased mortality at 1 year (23.5% bIFI vs 10.8% no bIFI, p=0.228).

CONCLUSIONS
bIFI in LTR is common despite universal AP. Multicenter studies are required to assess specific risk factors for its occurrence.

Inhibition of Amyloid β seed-induced tau aggregation by native PLGA nanoparticles and its significance in Alzheimer's disease

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Supervisor: Dr. Satyabrata Kar

INTRODUCTION

Increased levels and accretion of beta-amyloid (Aβ) peptide, together with enhanced phosphorylation/aggregation of tau protein, underlie the degeneration of neurons and subsequent development of Alzheimer's disease (AD), the most common cause of dementia affecting the elderly. While Aβ-induced tau hyperphosphorylation is necessary for neuron loss, misfolded tau protein facilitates spread of disease pathology, indicating a cooperative relationship between Aβ and tau in AD pathology. Our previous research showed that biodegradable native
PLGA nanoparticles can prevent Aβ aggregation, Aβ-induced tau phosphorylation and reduce AD pathology in cellular and animal models. However, it is unknown if native PLGA can influence tau aggregation induced by Aβ peptide. Thus, we investigated the effect of native PLGA on the aggregation of tau proteins induced by Aβ peptides.

METHODS

We used a variety of biophysical techniques including thioflavin-T fluorescence kinetic assay, circular dichroism, dynamic light scattering, fluorescence microscopy and transmission electron microscopy to examine the effects of native PLGA on Aβ seed-induced tau aggregation.

RESULTS

Our results showed that Aβ1-42 seed can induce tau aggregation and the effect is attenuated in a dose-dependent manner by native PLGA nanoparticles in the presence and absence of heparin as well as arachidonic acid. Remarkably, PLGA nanoparticles can inhibit the aggregation of different isoforms of tau (i.e., 4repeat and 3repeat) which are involved in the formation of neurofibrillary tangles in AD brains. Furthermore, native PLGA was found suppress tau aggregation observed in the presence of Aβ1-40, but not Aβ peptide containing the reverse sequence.

CONCLUSIONS

Our results suggest that PLGA nanoparticles, without conjugation with any drug/agent, can attenuate aggregation of tau protein which plays an important role in the development/spreading of tau pathology in AD pathology. These results, together with our previous results on Aβ-related peptides, highlights the
therapeutic potential of native PLGA in the treatment of AD pathology.

Proinflammatory responses of the HMC3 human microglial cell line are associated with changes in prion protein expression

Marcus Pehar, Ashley Wagner, Marianna Kulka, Valerie Sim
Supervisor: Dr. Valerie Sim

INTRODUCTION

Microglia are innate immune cells involved in modulating neuroinflammation in the central nervous system. These cells can be activated by the peripheral
inflammatory mediator histamine, which is physiologically released by brain mast cells. Histamine-induced stimulation of microglia has not been well-studied; however, recent research suggests that histamine induces the release of inflammatory mediators and alters protein expression in murine microglia. One
such protein of interest, the prion protein (PrPC), is thought to have a neuroprotective role in the central nervous system, and this protein is highly expressed in microglia. This study aimed to explore the neuroinflammatory aspects of the human microglial clone 3 (HMC3) cell line after stimulation with histamine and test the role of PrPC in neuroinflammation.

METHODS

qRT-PCR was used to measure the expression of histamine receptor mRNA. ELISA was used to measure the release of inflammatory mediators. Surface and total
PrPC protein expression were measured via flow cytometry and western blot.

RESULTS

Histamine treatment caused upregulation of HMC3 mRNA expression of histamine receptors (H1R, H3R, and H4R) by at least two-fold ($n=3$, $p<0.05$). 10 μM, 100 μM, and 1000 μM histamine treatments of HMC3 increased the production of pro- inflammatory mediators IL-6 by 1.58-fold, 1.59-fold, and 1.07-fold, respectively,
and IL-8 by 1.36-fold, 1.52-fold, and 1.18-fold, respectively ($n=3$, $p<0.05$). HMC3 expressed PrPC on their surface, and histamine treatment (10, 100, and 1000 μM) increased PrPC expression after 24 hours by 1.27-fold, 1.25-fold, and 1.46-fold, respectively ($n=3$, $p<0.05$). Notably, this effect appears to be time-dependent as 72-hour treatment of histamine decreased PrPC expression by 1.26-fold, 1.51-fold, and 1.58-fold, respectively ($n=5$, $p<0.05$).

CONCLUSIONS

We show, for the first time, that human microglia express histamine receptors, are stimulated by histamine, and that histamine alters expression of PrPC in a time- dependent, dynamic, and bimodal manner. Future experiments will determine whether changes in PrPC expression are transcription/translation-dependent.

Gasdermin D activation in oligodendrocytes and microglia drives inflammatory demyelination in progressive multiple sclerosis

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Supervisor: Dr. Christopher Power

INTRODUCTION

Central nervous system inflammatory demyelination and axonal injury are hallmarks of progressive multiple sclerosis (P-MS). Gasdermins are proteins involved in programmed inflammatory cell death, the best studied of which is gasdermin D (GSDMD). Proteolytic cleavage of GSDMD in oligodendrocytes and microglia causes inflammatory cell hyperactivation and death. Further understanding of the mechanisms behind GSDMD mediated demyelination will help in developing new effective treatments for P-MS.

METHODS

We used multiple different experimental models: in vitro cell culture studies, the cuprizone (CPZ) mouse model of P-MS demyelination and in vitro analysis on primary human cells. CPZ studies included RT-qPCR, proteomics, immunohistochemistry and immunofluorescent analysis, electron microscopy, PET imaging and behavioural studies. Human primary cells were used in immunofluorescent and RT-qPCR studies.

RESULTS

White matter from persons with P-MS showed significantly increased expression of GSDMD, NINJ1, IL-1β, and -18 within chronic active demyelinating lesions. Using the cuprizone (CPZ) model of P-MS in mice, the effects of knockout of Gsdmd were explored. Oligodendrocytes and microglia displayed increased Gsdmd immunoreactivity in the central corpus callosum (CCC) of CPZ-exposed Gsdmd+/+ mice, associated with significantly greater demyelination and reduced oligodendrocyte precursor cell proliferation compared to CPZ-exposed Gsdmd-/- animals. Electron microscopy showed the CCC of CPZ-exposed Gsdmd+/+ mice disclosed significantly increased G-ratios, accompanied by reduced axonal densities and total myelinated axons. Proteomic analyses revealed increased brain complement C1q proteins and hexokinases in CPZ-exposed Gsdmd-/- animals. [18F]FDG PET imaging showed increased glucose metabolism in the hippocampus and whole brain with preserved neurobehavioral performance in Gsdmd-/- animals after CPZ exposure.

CONCLUSIONS

Convergent GSDMD activation in both microglia and oligodendrocytes contribute to inflammatory demyelination and neuroaxonal injury, offering mechanistic insights into neuroinflammation in P-MS.

Structure and activation mechanism of Staphylococcus aureus response regulator ArlR by solution NMR

Mohammad Rafid Feisal, Philip B. Liu, Yurong Wen, Peter M. Hwang
Supervisor: Dr. Peter M. Hwang

INTRODUCTION
ArlRS is a member of the classic two-component regulatory system in Staphylococcus aureus, involved in biofilm formation and virulence. The response regulator ArlR is composed of a C-terminal DNA-binding effector domain linked to an N-terminal receiver domain that is activated upon phosphorylation by ArlS, the sensor histidine kinase.
Classically, phosphorylation of the receiver domain promotes dimerization, which perfectly positions two effector domains to bind DNA response elements. Unlike the canonical OmpR/PhoB DNA-binding domain, the ArlR effector domain crystallizes as a domain swapped dimer via N-terminal beta1-beta2 strands. However, this contradicts the canonical activation mechanism, and the swapped dimeric configuration is not optimized for DNA binding.

METHODS
Solution NMR was used to determine whether the ArlR effector domain folds as a monomer or domain-swapped homodimer. 15N NMR relaxation experiments were used to understand the relationship between the effector and receiver domains. A phosphomimic beryllium trifluoride reaction was used to determine the impact of receiver domain activation on the effector domain.

RESULTS
NMR structures demonstrate that the ArlR effector domain folds as a monomer in solution rather than a domain-swapped homodimer. Domain swapping of the effector domain does not occur upon activation and dimerization of the receiver domains using the phosphomimic beryllium trifluoride reaction. 15N NMR relaxation experiments indicate effector domains remain separate in the activated dimer but are rigidly positioned by inter-domain interactions. Solvent amide exchange rates for the effector domain reveal structural instability of the central beta-sheet that allows for the domain-swapping seen upon crystallization.

CONCLUSIONS
The ArlR effector domain folds as a monomer, and activation occurs via canonical mechanism described for bacterial response regulators: phosphorylation-driven dimerization of receiver domain, positioning two effector domains for DNA binding. Amide exchange studies reveal structural instability of the beta-strands involved in the X-ray crystal structure. Cross-talk between domains adds a potential environment-sensitive regulatory control.

Structure and activation mechanism of Staphylococcus aureus response regulator ArlR by solution NMR

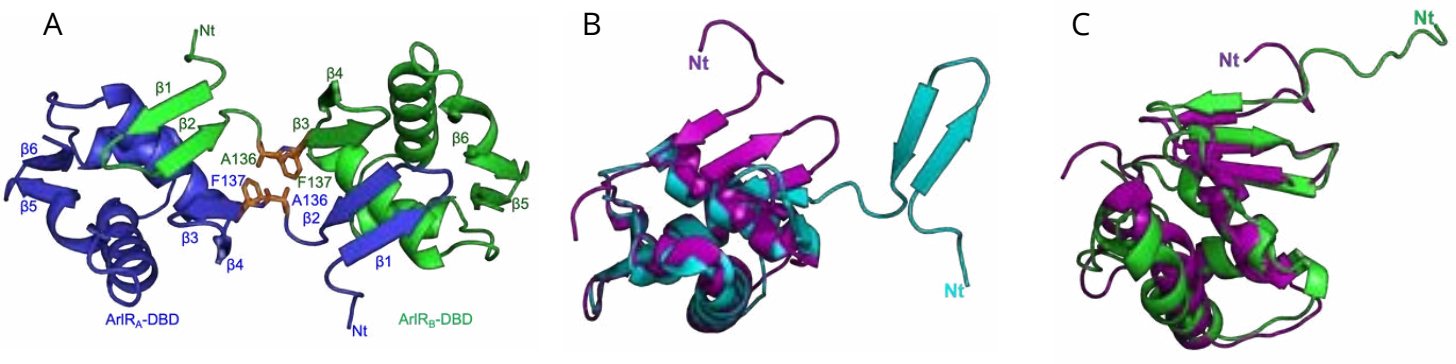


Figure 1: Comparison between the ArlR DNA-binding domain (DBD) crystal structure, solution NMR structure and PhoB crystal structure. A. Domain swapped homodimer DBD crystal structure. B. DBD monomer crystal structure (6IS4) superimposed with PhoB (1GXQ). C. Solution NMR DBD structure superimposed with PhoB. Figures rendered using Pymol.

Exploring Oxidative Stress andDNA Damage in Professional Welders Exposed to Welding Fumes

Ata Rafiee, Maria B. Ospina, Tona M. Pitt, Bernadette Quémerais
Supervisor: Dr. Bernadette Quémerais

INTRODUCTION
Given the importance of oxidative stress and DNA damage in the development of various diseases, this systematic review aimed to evaluate the associations between welding fumes exposure and changes in oxidative stress [superoxide dismutase (SOD) and malondialdehyde (MDA)] and DNA damage [8-hydroxy-2'-deoxyguanosine (8-OHdG) and DNA-protein crosslink (DPC)] markers in professional welders.

METHODS
This systematic review was conducted using the Cochrane guidelines, and the review protocol was registered on the PROSPERO database (CRD42022298115).
Six electronic bibliographic databases were searched to identify relevant studies. Two reviewers assessed the risk of bias and certainty of the evidence. The
Synthesis Without Meta-analysis (SWiM) method was used to perform narrative synthesis of results. Pooled mean differences with 95% confidence intervals were calculated in a random-effects meta-analysis for the outcomes of interest.

RESULTS
From 450 studies, 14 observational epidemiological studies met the inclusion criteria and were included in the review. Most studies reported significantly higher metal levels in welders than in controls. The narrative synthesis results of SOD showed a significant difference between welders and controls, while the meta- analysis results of MDA did not show a significant difference between the studied groups (MD = 0.26; 95% CI, -0.03, 0.55). The meta-analysis results of 8-OHdG (MD = 9.38; 95% CI, 0.55–18.21) and DPC (MD = 1.07; 95% CI, 0.14–2) revealed significant differences between the studied groups. The included studies were at high risk of exclusion and confounding bias. The certainty of the evidence for oxidative stress and DNA damage results were very low and moderate, respectively.

CONCLUSIONS
Exposure to welding fumes is associated with DNA damage in welders, and 8-OHdG and DPC might be considered reliable markers to assess DNA damage caused by welding fumes exposure. We recommend, however, that the assessment of oxidative stress attributable to welding fumes exposure not be solely based on
MDA and SOD.

Factors influencing the adoption and maintenance of healthy aging behaviours in community dwelling older adults – a Photovoice study

Saima Rajabali, Ali Ramji, Adrian Wagg
Supervisor: Dr. Adrian Wagg

INTRODUCTION

Population ageing has a major impact on healthcare, economics, employment and social engagement. There is an opportunity to educate and empower older adults in healthy ageing behaviours. There is evidence that even though behavioural interventions educate and encourage people to adopt healthy behaviours, the changes induced by such interventions are usually not maintained over time. There is a need to understand, from the perspective of older adults, factors helping or hindering them in maintaining healthy ageing behaviours after the completion of a health intervention. This study looked at the factors influencing the adoption and maintenance of healthy ageing behaviours by community dwelling older adults one year after receiving a peer delivered health education intervention.

METHODS

Data was collected from participants using a community based participatory research method called photovoice, which involved the older adult participants in all aspects of research. Participants took photos over two weeks of barriers and facilitators for maintaining healthy ageing behaviours, wrote journal reflections about each photo, and took part in individual interviews and group discussions about the photos. Data were analyzed using a content analysis approach. In order to ensure that the themes were an accurate representation of the participants' ideas, a focus group discussion was held. Based on the data from the focus group, an updated set of themes was created.

RESULTS

Fourteen participants took part in the study. Data analysis resulted in 12 categories and 5 themes. The themes representing barriers and facilitators to adopting healthy aging behaviours included: companionship, accessibility, exercise and recreation, health and sense of purpose.

CONCLUSIONS

The identified themes offer a unique perspective on the facilitators and barriers that older adults encounter in adopting and maintaining healthy aging behaviours. The findings from this study will help make health education interventions more effective and efficient.

Exploring the heterogeneity of human mast cell-originated extracellular vesicles using proteomic profiling

Sabrina Rodrigues Meira, Marcelo-Marcet Palacios, Marianna Kulka
Supervisor: Marcelo-Marcet Palacios

INTRODUCTION

Extracellular vesicles (EVs) are nanoscale lipid vesicles released by cells to facilitate intercellular communication by transporting proteins, lipids, and nucleic acids from one cell to another. Evidence suggests that EVs from human mast cells can deliver molecular cargo to distant tissues to induce metabolic changes. However, the size-dependent variation in their cargo is poorly understood and difficult to test.

METHODS

We activated transformed human mast cells (HMC-1.2) with ionophore A23187 and phorbol 12-myristate 13-acetate (PMA), and isolated EVs using magnetic EVtrap beads, ultracentrifugation, and tangential flow filtration (TFF). The size of the EV populations was analyzed by dynamic light scattering (DLS) and electron microscopy (EM). Proteomic profiling of EVtrap-isolated EVs was done using liquid chromatography-mass spectroscopy (LC-MS). NADH activity analysis was done to measure the metabolic activity and growth of HMC-1 cells treated with EVs obtained from activated cells.

RESULTS

Untreated HMC-1.2 produced three distinct populations of EVs: 100 nm, 1000 nm and 6000 nm. However, when HMC-1.2 were activated with A23187 (10 mM) and PMA (1 mM) for 6 hr, they produced EVs at 200 nm, 1000 nm and 6000 nm, indicating that activated HMC-1.2 produce larger EVs. The proteomic analysis showed that untreated EVs contained 3943 unique proteins. Comparison of resting versus activated EV proteomes showed that 25 proteins were significantly upregulated and 34 downregulated in the activated EVs. A SRING analysis of these proteins identified a strong correlation with mitochondria biology including enzymes that are directly involved in ATP production.

CONCLUSIONS

These results suggest that activated human mast cells alter their production of EV, both in terms of size and cargo. Activation with A23187 appears to stimulate secretion of EVs with cargo association influencing the metabolic process. We hypothesize that these EVs could alter the metabolic rate of target cells by delivering enzymes that could enhance energy production in target cells.

*undergraduate student

Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) after Immune Checkpoint Inhibition: a CanRIO Study

Azin Rouhi, Shahin Jamal, Marie Hudson, Janet Pope, Janet Roberts, Alexandra Ladouceur, Sara Hewitt, Carrie Ye
Supervisor: Dr. Carrie Ye

INTRODUCTION
Immune checkpoint inhibitors (ICI) have shown great promise in the treatment of different malignancies. The use of ICIs has been associated with toxicities known as immune related adverse events (irAE). Rheumatologic irAEs, such as inflammatory arthritis, have been described. Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) is a condition characterized by pitting edema in the distal extremities in addition to findings of synovitis on exam with negative serology for RF. RS3PE has been described as a paraneoplastic syndrome in association with different malignancies. To date, 9 case reports of RS3PE in association with ICI (ICI-RS3PE) have been reported in the literature. We present a series of 11 patients, who developed ICI-RS3PE after starting on ICI.

METHODS
The Canadian Research Group of Rheumatology in Immuno-Oncology (CanRIO) database, which includes a large prospective cohort of oncology patients on ICI therapy across Canada, was reviewed for all cases of ICI-RS3PE. Data including the type of malignancy, ICI therapy, clinical manifestations, time of onset and response to treatment were assessed.

RESULTS
We identified 11 patients, who received ICI therapy for malignancy and presented with ICI-RS3PE (Table 1).

The median time from start of ICI therapy to presentation with ICI-RS3PE was 26 weeks, while the median time from the diagnosis of malignancy to onset of ICI- RS3PE was 52 weeks. Seven out of 11 patients had stable cancer on imaging prior to onset of ICI-RS3PE, while 3 had partial response and 1 was in complete remission. Three patients had completed their course of ICI therapy prior to onset of ICI-RS3PE.

Ten out of 11 patients received prednisone as first line therapy (Table 2).
Additional immunosuppression with a conventional synthetic DMARD (cs-DMARD) was needed in 10 out of 11 patients.

CONCLUSIONS
ICI-RS3PE may be a new irAE, which can occur after ICI discontinuation. Current management varies widely and optimal treatment remains to be determined.

Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) after Immune Checkpoint Inhibition: a CanRIO Study

Table 1:

Patient	Age (years)	Gender	Stage and type of cancer	ICI treatment at time of ICI-RS3PE onset	Time (weeks) between ICI initiation and RS3PE-LS onset	Time (weeks) between cancer diagnosis and ICI-RS3PE onset	Tumor response before ICI-RS3PE onset*	Tumor response after ICI-RS3PE onset*
1	54	Female	Stage IV SCC	Darvalumab, Tremelimumab	48	92	Stable disease	Partial response
2	77	Female	Stage IV NSCLC	Pembrolizumab	28	34	Stable disease	Stable disease
3	80	Female	Stage IV SCLC	Nivolumab	12	22	Partial response	Stable disease
4	79	Female	Stage IIIC MM	Nivolumab	69	88	Stable disease	Stable disease
5	73	Male	Stage IV urothelial carcinoma	Pembrolizumab	126	287	Stable disease	Stable disease
6	76	Female	Stage IV NSCLC	Pembrolizumab	68	74	Stable disease	Stable disease
7	84	Male	Stage IV NSCLC	Pembrolizumab	4	8	Partial response	Partial response
8	62	Female	Stage IV SCC	Nivolumab	24	208	Stable disease	Stable disease
9	75	Male	Stage IV MM	Pembrolizumab	5	12	Complete response	Complete response
10	69	Male	Stage IV RCC	Ipilimumab, nivolumab	6	52	Stable disease	Stable disease
11	63	Male	Stage III NSCLC	Darvalumab	26	46	Partial response	Partial response

Abbreviations: ICI: immune checkpoint inhibitor, ICI-RS3PE: Remitting Seronegative Symmetrical Synovitis with Pitting Edema associated with ICI, SCC: Squamous cell carcinoma, NSCLC: Non-small cell lung cancer, SCLC: Small cell lung cancer, MM: Malignant melanoma, RCC: renal cell carcinoma.
*Based on Response Evaluation Criteria in Solid Tumors (RECIST)

Table 2:

Patient	Highest CTCAE grade	Serology	Glucocorticoids (dose/duration)	Additional immunosuppression	Response to additional immunosuppression
1	2	RF+ CCP -	DepoMedrol 40mg injection to both ankles.	MTX 20mg SC weekly	CR
2	2	RF - CCP -	Prednisone 20mg po daily tapered over 8 weeks.	MTX 20mg SC weekly	CR
3	2	RF - CCP not done	Prednisone 20mg po daily tapered over 4 weeks.	HCQ 200mg po daily	CR
4	2	RF - CCP -	Prednisone 10mg po daily for 3 weeks then prednisone 50mg daily tapered over 7 weeks	SSZ 500mg po BID Switched to MTX 25mg po weekly	CR
5	3	RF - CCP -	Prednisone 20mg daily then increased to 50mg daily tapered over 5 weeks.	HCQ 400mg po daily	CR
6	3	RF - CCP -	Prednisone 50mg po daily for 7 days then 20mg daily tapered over 8 weeks.	HCQ 200mg po daily PR switched to MTX 25mg SC weekly	CR
7	2	CR			
		RF - CCP -	1st episode of RS3PE-LS: Prednisone 30mg daily for 4 months. 2nd episode: prednisone 10mg daily for 3 months.		
8	3	RF - CCP -	Prednisone 5mg po daily for 10 months. Prednisone 20mg po daily for recurrence of synovitis with re-starting ICI tapered over 4 months	HCQ 300mg po daily. MTX 20mg po weekly	CR
9	3	RF - CCP -	Prednisone 20mg daily tapered within 10 months.	HCQ 300mg po daily	CR
10	3	RF - CCP -	Prednisone 10mg po daily tapered and stopped within 24 months	LEF 20mg po daily	CR
11	3	RF + CCP -	Prednisone 30mg po daily tapered over 12 weeks	SSZ 1000mg po BID	CR

Abbreviations: CR: complete response, HCQ: hydroxychloroquine, LEF: leflunomide, MTX: (methotrexate), PR: partial response, ICI-RS3PE: Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) associated with ICI, SC: subcutaneous, SSZ: (Sulfasalazine)

Exploring Sequence Similarity in Upstream Regions of Genes: Implications for Co-Regulation of Genes and Chromatin Structure (Page 1 of 2)

AuJoy Ramielle Santos, Marcelo Marcet-Palacios
Supervisor: Dr. Marcelo Marcet-Palacios

INTRODUCTION

The upstream regions of a gene (UGR) are rich in binding sites for key proteins such as RNA polymerase and transcription factors. These proteins play a critical role in the initiation of gene transcription and thus gene expression. It would therefore be reasonable to predict that these UGRs may exhibit sequence similarity and for that similarity to determine the co-regulation of certain genes.

METHODS

We developed an algorithm and scoring system to compare the 2000 nucleotides from all human UGRs. Our algorithm was validated against a known sequence comparison software, Clustal Omega. We used tools such as NCBI's Multiple Sequence Alignment Viewer to further visualize the matches. Additionally, we created heatmaps with genes arranged sequentially along both axes for each chromosome utilizing both Clustal Omega's comparisons and our derived similarities.

RESULTS

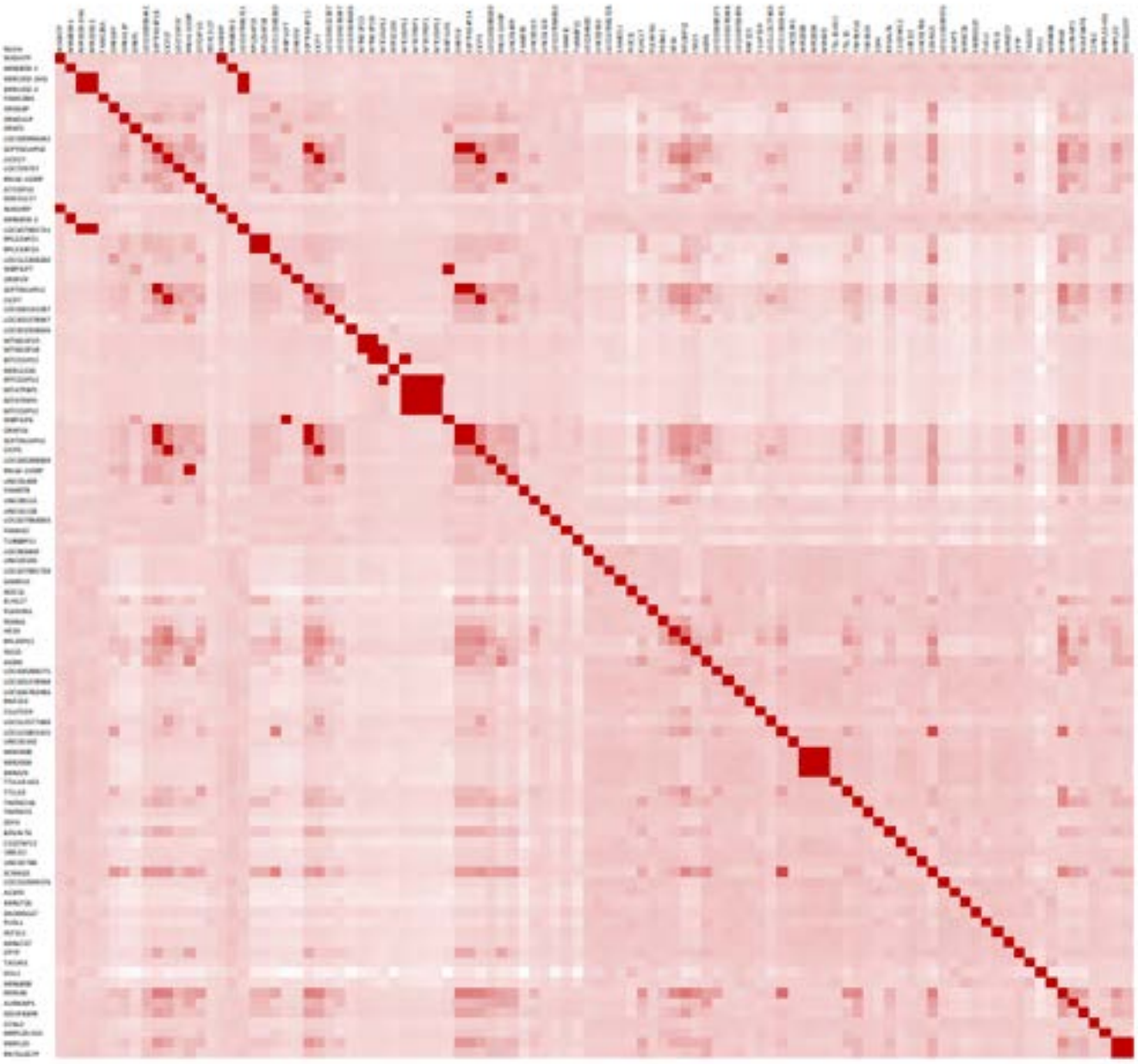
The algorithm resulted in a matrix 57064 by 57064 large that comprehensively compared every UGR in the Genome Reference Consortium Human Build 38 and showed percent similarity between each sequence. When visualized in a heat map, our algorithm similarities resulted in similar patterns to that of Clustal Omega. Analysis of the heat map for each chromosome elucidated unique patterns of similarity in adjacent genes. Patterns are highly suggestive of a 3D chromatin arrangement previously unidentified. We developed 3D models of the chromatin and plan to test these predictions using structural biology techniques.

CONCLUSIONS

The patterns that emerge from the similarity heatmaps of each chromosome may give some insight on the regulation of genes on the sequence level. We proposed that these patterns may also be related to the folding and overall structure of chromatin. Our findings suggest that the folding of chromatin may play a role in the spatial architecture of regulatory domains which has implications for our understanding of gene regulation.

Exploring Sequence Similarity in Upstream Regions of Genes: Implications for Co-Regulation of Genes and Chromatin Structure (Page 2 of 2)

AuJoy Ramielle Santos, Marcelo Marcet-Palacios
Supervisor: Dr. Marcelo Marcet-Palacios



Remote Ischemic Conditioning with Novel Optical Sensor Feedback Device in Acute Ischemic Stroke- a feasibility study

Robert Joseph Sarmiento1, Radhika Nair1, Ashfaq Shuaib1, Brian Buck1, Michel Gauthier1, Vivian Mushahwar1, Martin Ferguson-Pell1, Mahesh Kate
Supervisor: Dr. Mahesh Kate

INTRODUCTION
Objective: To check the feasibility of a novel Remote Ischemic Conditioning (RIC) device.

Background: RIC therapy is delivered by increasing the pressure in the arm cuff 50 mmHg above systolic BP to a maximum of 200 mmHg. This may be associated with discomfort and consequently reduced compliance with RIC therapy. Our group has developed a novel RIC device, with an optical skin perfusion sensor to assess distal limb ischemia during RIC therapy.

METHODS
This is a prospective, single-center, randomized control trial for the feasibility of the device. Patients of acute ischemic stroke with moderate to severe small vessel disease are randomized 2:1 to intervention vs sham control arms for a period of 7 days or until discharge. All patients randomized to the intervention arm will receive 5 cycles of ischemia/ reperfusion in a non-paralyzed arm. Patients in the sham control arm will receive pressure sensation by keeping the cuff pressure at 30 mmHg for 5 minutes for 5 cycles.

RESULTS
We have enrolled a total of 24 (14 Intervention arm and 7 Sham Control) patients to date at a median(IQR) 74.2 (38.9-115.525) hours after symptom onset, with mean±SD age of 71.74±10.29 years and median (IQR) NIHSS of 5(4-8.5). We found no differences in oxygenated hemoglobin and hemoglobin concentration with either 30 or 50 mmHg systolic BP increase in the arm cuff in the intervention group. The procedure-related comfort measured by the Likert scale showed a median(IQR) of 3.00(2-3, neither comfortable nor uncomfortable) in the intervention arm and 2(2-2, comfortable) in the sham control arm. No safety concerns were noted in the intervention or sham arm.

CONCLUSIONS
RIC with the skin perfusion sensor assessment is feasible. There were no safety concerns.

Clinical Trial Registration Number: clinicaltrials.gov NCT05408130

Short-term Outcomes in Ischemic Stroke patients with post- Endovascular thrombectomy Intracranial Hyperdensity

Robert Joseph Sarmiento, Brian Buck, Ashfaq Shuaib, Cian O'Kelly, Jeremy Rempel, Mahesh Pundlik Kate
Supervisor: Dr. Mahesh Kate

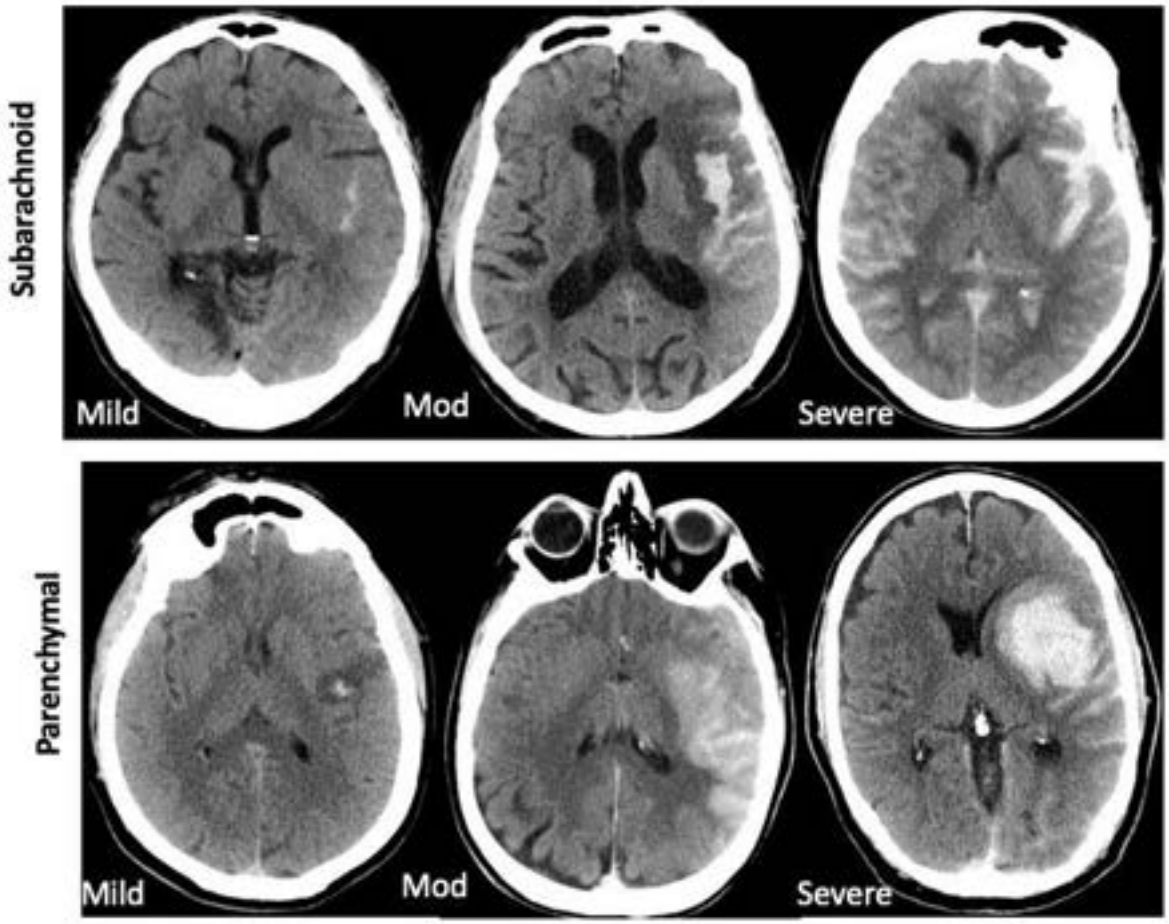
INTRODUCTION
Post-Endovascular thrombectomy intracranial hyperdensity (PEIH) (either contrast extravasation or intracranial hemorrhage or combination) is common. We aim to assess the short-term outcome in ischemic stroke patients with PEIH.

METHODS
All patients undergoing EVT with post EVT scans from March 2021 to October 2022 from the QuiCR (Quality Improvement and Clinical Research Alberta Stroke Program) Registry were included in the study. PEIH were assessed in the CT scan done within 24h after the procedure. PEIH were characterized based on severity (mild, moderate, severe) and location (subarachnoid, parenchymal, intraventricular, or combination). (Figure 1.0)

RESULTS
A total of 262 patients were included with a mean±SD age of 69.41±13.96 years, 45.8% (120) were female, with a median (IQR) NIHSS of 16 (11-19) during the study period. 93 (35.49%) received intravenous thrombolysis (IVT). 242 (92.37%) had anterior circulation strokes. 94 patients (35.8%) demonstrated PEIH, 35 (37.2%) were mild, 38(40.4%) moderate, and 21(22.3%) severe. PEIH was subarachnoid in 47 (50%), parenchymal in 25 (26.6%) and combination in 22 (23.4%). Presence of PEIH was associated with lower home time at 90 days (B 18.1 95% CI 9-27.2, $p<0.001$). Presence of PEIH was associated higher mortality (aOR 0.44 95% CI 0.24-0.81).

CONCLUSIONS
PEIH is common and more than half are moderate to severe grade. PEIH is associated with poor outcome and increased mortality. Novel treatment modalities are needed to improve outcome in these group of patients.

Figure 1.0



Wastewater Surveillance of Substance Use in Alberta, Canada

Navid Sedaghat, Monty Ghosh, Michael Parkins, Darina Kuzma
Supervisor: Dr. Sumantra Monty Ghosh

INTRODUCTION

Substance use has become a pressing public health issue worldwide, with Canada being no exception. Between 2020 to 2022, more than 3000 opioid overdose
deaths occurred in Alberta. A potential approach to understanding this issue in an inclusive, comprehensive, and cost-effective manner is wastewater-based surveillance (WBS). This study aimed to detect, quantify, and observe patterns regarding substances in wastewater collected from three municipalities and two facilities caring for high-risk individuals in Alberta. The results from one municipality and high-risk facility are included.

METHODS

Wastewater was collected three times a week using ISCO 5800 and CEC-A1 autosamplers at a municipal wastewater treatment plant (WWTP) and a high-risk facility, respectively. Samples were filtered using a 0.7 µm syringe glass fiber filter, stored at <6 ˚C, and analyzed within 3 days. Samples were analyzed following
direct injection using Agilent 1260 HPLC and Agilent 6460C Triple Quadrupole mass spectrometer (Agilent, Santa Clara, California) for 48 substances and their metabolites (4 amphetamines, 7 fentanyl, 8 other opiates, 2 cocaine, 15 benzodiazepines, 5 psychedelics, and 7 others). Data analysis was done through MassHunter Quantitative Analysis 10.0 using calibration curves and internal standards for the analytes of interest.

RESULTS

Most analytes were observed across locations. In particular, the abundance and variation of opiates and their metabolites were markedly increased in high-risk facilities relative to other communities. At WWTP, increased levels of several
targets of several classes of drugs (opiates, cocaine, and amphetamines) were consistently observed following weekends, coinciding with expected social
patterns. There were no clear patterns in the high-risk facility with highly variable concentrations over time.

CONCLUSIONS

WBS detects substance use trends. Future research will link wastewater analytes
to clinical outcomes including atypical drug reactions, and overdoses. WBS can aid public health officials and policymakers in addressing substance use issues and enable early harm reduction warnings to be issued to health providers and substance users.

p53 associated de novo activation of VWF expression in tumor cells

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

INTRODUCTION

The expression of the pro-coagulant protein von Willebrand Factor (VWF) under physiological condition is exclusively restricted to endothelial cells and megakaryocytes. However, its expression is also detected in cancer cells of non- endothelial/megakaryocytic origin and may promote their metastatic potential.

p53, a tumor suppressor and a transcription factor, is one of the most frequently mutated genes in cancers. Mutation in p53 leads to dysregulation of p53 target genes expression including NFIB, a transcriptional regulator of VWF. Previous studies have demonstrated that the dual adhesion and signalling protein

plakoglobin can interact with and restore tumor suppressor function of mutant p53. We hypothesized that p53 mutations may result in dysregulation of NFIB, a major transcriptional repressor of VWF, and consequently activate de novo expression of VWF, while plakoglobin interaction with mutant p53 reverts this effect.

METHODS

p53 null and plakoglobin deficient H1299 cells were transfected with wild-type
(WT) p53 and two types of oncogenic p53 mutants: a conformational (p53-R175H) and a contact (p53-R273H) mutant without or with plakoglobin and assessed for VWF and NFIB expression by qRT-PCR, western blot and immunofluorescence. To explore the scope of VWF-p53-NFIB association in various cancer cell lines, we surveyed the Human Protein Atlas and the TP53 database of target cancer cells.

RESULTS

We demonstrated that specifically conformational mutant p53-R175H expression in H1299 cells induced VWF and downregulated NFIB expression. Moreover, plakoglobin expression in H1299-p53-R175H transfectants reversed these effects. Our database search also demonstrated that amongst the VWF-positive cancer cell lines with no mutation in the NFIB gene, ~33% express p53 conformational mutation.

CONCLUSIONS

Our preliminary study revealed a novel mechanism of VWF expression associated with mutant p53. Altered level of NFIB in conformational mutant p53 expressing cells may potentially contribute to de novo activation of VWF expression, while plakoglobin reverts this effect in a p53-dependent manner.

Hippocampal subfield thickness measurements evaluated using HippUnfold in patients with Mild Cognitive Impairment and Alzheimer's Disease (Page 1 of 2)

Mujtaba Siddique, Mohamed Yousif, Richard Camicioli, Ali Khan, Trevor Steve, Alzheimer's Disease Neuroimaging Initiative (ADNI)
Supervisor: Dr. Trevor Steve

INTRODUCTION

Alzheimer's disease (AD) is the most common cause of dementia. Biomarkers are playing an emerging role in AD research - however, existing biomarkers have limitations. Magnetic Resonance Imaging (MRI) holds advantages over existing biomarkers as it is non-invasive and does not involve exposure to ionizing
radiation. This project aims to utilize MR images to measure subfield thickness throughout the hippocampal long axis using HippUnfold, a novel open-source automated hippocampal segmentation software, and compare it to Positron Emission Tomography (PET) phosphorylated tau as this is a prominent biomarker for the diagnosis of AD.

METHODS

High resolution (0.39x0.39x2mm) Hippocampal MR Images [control, (n= 278), mild cognitive impairment (MCI, n =205), and AD, (n = 41)] acquired by the Alzheimer's Disease Neuroimaging Initiative (ADNI) were analyzed with a segmentation software (HippUnfold) to compute thickness measurements throughout the entire hippocampal long axis. ADNI data such as Positron Emission Tomography (PET) for phosphorylated tau were acquired along with cognitive scores such as Mini-Mental State Exams and the Montreal Cognitive Assessments. Thickness measurements were correlated with the severity of phosphorylated tau deposition quantified with PET using linear regression models.

RESULTS

We found significant clusters correlation ($p < 0.05$) throughout the long axis when comparing reduced hippocampal subfield thickness to PET phosphorylated tau levels. More specifically as seen in Figure 1. we see two significant clusters when correlating reduced thickness to increased PET phosphorylated tau levels.

CONCLUSIONS

MRI is a promising non-invasive biomarker for AD. Existing automated
segmentation protocols enable measurement of only the body of the hippocampus due to the complex curved anatomy of the hippocampal head and tail. Hippunfold is a novel software that labels these subfields throughout the entire hippocampus. Here we have demonstrated correlations between MRI-measured hippocampal thickness to PET phosphorylated tau - suggesting its potential role as an emerging biomarker for dementia.

HIPPOCAMPAL SUBFIELD THICKNESS MEASUREMENTS EVALUATED USING HIPPUNFOLD IN PATIENTS WITH MILD COGNITIVE IMPAIRMENT AND ALZHEIMER'S DISEASE (PAGE 2 OF 2)

Mujtaba Siddique, Mohamed Yousif, Richard Camicioli, Ali Khan, Trevor Steve, Alzheimer's Disease Neuroimaging Initiative (ADNI)
Supervisor: Dr. Trevor Steve

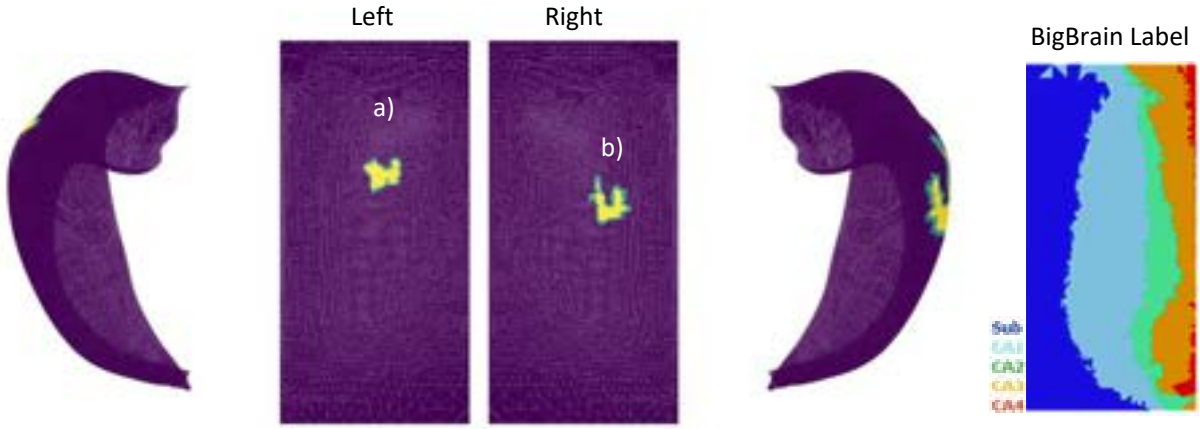


Figure 1. Linear regression models were performed by comparing hippocampal thickness to PET phosphorylated tau levels. Significant clusters were plotted on the flatmap of both the right and left hippocampus and then folded back into their 3D conformation. The figure shows two significant clusters, one in the left hippocampus and one in the right hippocampus. More specifically cluster a) contains 119 vertices and is located at the body of the Cornu Ammonis 1 and cluster b) contains 175 vertices and is located at the body of the Cornu Ammonis 1 and 2 regions of the hippocampus. The BigBrain subfield labels located on the right side of the figure were retrieved from Jordan DeKraker Roy AM Haast, Mohamed D Yousif, Bradley Karat, Jonathan C Lau, Stefan Köhler, Ali R Khan (2022) Automated hippocampal unfolding for morphometry and subfield segmentation with HippUnfold eLife 11:e77945.

Quadruplex-binding ligands: the key to a cure for chronic Hepatitis B viral infections?

Jessica Skoreyko1, Emma Kasinyabo2, Hoa Le2, Vanessa Meier-Stephenson1-3
Supervisor: Dr. Vanessa Meier-Stephenson

INTRODUCTION

Hepatitis B virus (HBV) chronically infects over 296 million people worldwide.
The virus remains chronic because of a form of the virus, the covalently closed circular DNA(cccDNA) that remains in the nucleus, untargeted by current therapies. A potential cure therefore lies within the capacity to target and eliminate the
virus's cccDNA. The recent discovery of a conserved G-quadruplex (GQ) structure
in the pre-core promoter region of HBV provides a unique target in cccDNA against which small molecule therapeutics can be designed. Currently, there are several GQ-binding ligands, originally developed as anti-cancer agents, available that can be used to target HBV. Our objective is to study the impact of these known GQ- binding ligands on HBV replication.

METHODS

Drug viability assays in HepG2-NTCP cells were performed using Alamar Blue.
Using a HepG2-NTCP infection model, cells were treated on the first day post infection (dpi) with 10μM TMPyP4, Braco-19 or tenofovir (TDF) and harvested at dpi 1, 4 and 7. Cells and supernatant were used to analyze viral markers including pgRNA, total HBV DNA, and HBsAg.
Data was corrected for beta-globin and baseline housekeeping genes were screened, including albumin, HPRT, and GAPDH. Further, as TMPyP4 can auto-fluoresce, imaging
studies were
performed to confirm cellular localization.

RESULTS

Viability assays show cellular viability at concentrations used. Cellular localization studies show that TMPyP4 can enter the HepG2-NTCP cell nucleus- the site of HBV cccDNA.
Preliminary data from the infection study show a decrease in viral RNA and DNA when treated with GQ-binding ligands. Confirmatory studies are ongoing with cellular
background impacts.

CONCLUSIONS

GQ-binding ligands appear to impact HBV replication. Through better
understanding of GQ-binding and off-target effects, we may be able to employ
these GQ-binders or variants thereof to target this conserved region more specifically, ultimately leading to a novel approach for targeting cccDNA.

L-type amino acid transporter 1 expression levels are associated with pituitary tumor behaviours

Navneet Sohi, Motoyasu Satou, Frank van Landeghem, Naoko Inoshita, Constance Chik, Toru Tateno
Supervisor: Dr. Toru Tateno

INTRODUCTION
Pituitary tumors (PTs) can cause significant mortality and morbidity due to limited biomarkers and therapeutic options. L-type amino acid transporter 1 (LAT1) expressed in a variety of tumor cells is reported to be a potential biomarker and a therapeutic target. Recently, we reported LAT1 is expressed in rat PT cells and LAT1 inhibition can reduce PT cell viability and hormone production. We hypothesized that LAT1 is expressed in human PT tissues and can be a biomarker for PTs, with higher expression associated with aggressive behaviours.

METHODS
We collected 34 null cell pituitary tumor tissue samples from the archives available at the University of Alberta and related clinical data with our research ethics approval. LAT1 expression in 34 null cell pituitary tumor tissue samples was detected using immunohistochemistry. LAT1 expression was considered positive only if distinct membrane staining was detected. Staining intensity, Endo-score was as follows: score 1: <10% of tumor area stained; score 2: 11 – 25% stained; score 3: 26 – 50% stained; score 4: 51% stained. Endo-score higher than 3 was evaluated as high expression and Endo-score lower than 2 as low expression. Chi- square analysis was performed to compare the clinical data between a high LAT1 expression group and a low LAT1 expression group.

RESULTS
There was no difference in tumor size nor Knops score ($p>0.05$). There is no clinically meaningful mean difference in the number of cases of invasion into the surrounding structures ($p=0.069$), but the relatively small number of cases would not lead to a statistically significant difference. The data showed pituitary tumors with higher LAT1 expression levels have a higher rate of optic chiasm compression ($p<0.05$).

CONCLUSIONS
Our data suggest involvement of LAT1 in the progression of pituitary tumors and its potential as a new biomarker for PTs. More cases are required to validate our findings.

Effects of empagliflozin on T cells from ulcerative colitis patients

John Soleas, Naomi Hotte, Karen Madsen
Supervisor: Dr. Karen Madsen

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic disease characterized by relapsing and remitting intestinal inflammation driven by dysregulated and pathological inflammatory immune response. Mainstays of current therapy are immunomodulators such as steroids and biologics which have a myriad of adverse side effects and can become ineffective over time. An exciting avenue for therapy arises from the emerging field of immunometabolism, wherein inflammatory immune cells are programed towards anti-inflammatory profiles through manipulation of their metabolic status. Empagliflozin (EMPA) is a highly selective sodium glucose cotransporter-2 inhibitor (SGLT2i) that has been shown to have anti-inflammatory effects in multiple disease states through immunometabolism. We hypothesized that EMPA would have direct effects on T-cells and reprogram inflammatory phenotypes towards anti-inflammatory phenotypes.

METHODS

Peripheral blood mononuclear cells (PBMCs) were obtained from patients with ulcerative colitis (UC) (n=4), and healthy controls (n=3). PBMCs were incubated with increasing doses of EMPA (1μM, 5μM, and 10μM). Changes in percentage of population of T regulatory (TREG) cells, pro-inflammatory CD161+T helper (Th)17 Cells, CCR6+Th17 Cells, and Th1+ T cells were assessed after 72 hours by flow cytometry.

RESULTS

Although results were not statistically significant likely due to small sample sizes, UC patients had higher percentages of Th1 (1.3±1.4 vs 0.4±0.3), CCR6+Th17 (9.2 ± 6.4 vs 6.2±3.5), and CD161+Th17 (1.8± 2.8 vs 0.4±0.3) cells compared with controls. An EMPA-induced dose-dependent decrease was seen in populations of Tregs, CD161+Th17, and CCR6+Th17 cells in PBMC from UC patients but not in controls.

CONCLUSIONS

Studies are ongoing to increase the number of patients and to examine effects of EMPA on other immune cell types. Further experiments are required to
conclusively determine if EMPA has direct effects on T cells. However, the concept of using SGLT2i to modulate metabolic pathways in immune cells towards anti- inflammatory phenotypes has tremendous potential to provide a new therapeutic option for IBD.

Lymphopenia in Primary Biliary Cholangitis

Hussain Syed, Greg Vallée, Bishoi Aziz, Andrew Mason
Supervisor: Dr. Andrew Mason

INTRODUCTION

PBC is an idiopathic liver disease characterized by destruction of small intrahepatic bile ducts. Patients have increased risk of infectious diseases and cancer
suggesting a potential link with immunodeficiency. Assessing neutrophil to lymphocyte ratios (NLR) as a prognostic marker for lymphopenia, we found that
NLR >2.7 after 12-month treatment had increased risk of liver failure. Our
objectives were to identify immune cell subsets linked with poor outcomes and analyze transcriptional differences in whole blood of PBC patients with and without lymphopenia.

METHODS

Prognoses of 140 PBC patients were assessed using Globe score and their
peripheral blood mononuclear cells were phenotyped for B-cells, T-cells, NK, and NK-like T-cells. An RNA-seq database of 88 PBC patients was analyzed to identify differential gene expression between high and low NLR using DESeq2 and gProfiler.

RESULTS

Reduced transplant free survival scores were associated with diminished CD4,
CD8, NK and NK-like T-cells. Effector memory CD4 T-cells and terminally differentiated CD4 T-cells were reduced, while all CD8 T-cell subsets (naïve,
central, effector memory, and terminally differentiated) were diminished. RNA-seq data showed increased CD4 and decreased overall CD8a gene expression in correlation with high NLR. Pathway enrichment linked high NLR with upregulation
of Interferon (IF) alpha, IF beta, Interleukin (IL)-1, IL-1 beta, IL-6, IL-8, and NF-κB signaling in addition to immune-senescence, increased glycolysis, hypoxia, and
CD4 T-cell activation. Low NLR demonstrated negative regulation of cytokine production and cellular senescence.

CONCLUSIONS

Loss of effector CD8 and NK cells in PBC patients suggests that a lack of interferon response may contribute to disease progression and lower transplant-free survival rates. Patients with high NLR demonstrated metabolic remodeling with increased transcription of proinflammatory responses alongside activation of MTORC1-mediated senescence, cellular glycolysis, and HIF1A pathways. Further evaluation of these mechanisms will help elucidate the mechanistic significance of these pathways in progressive liver disease.

Tumor-Secreted Nucleosides Can Promote RbFox1 Degradation and Signalling Pathways Relevant to Dedifferentiation in Cardiomyocytes; A Two-Hit Hypothesis with Implications for Cardiotoxicity

Saymon Tejay, Maria-Areli Lorenzana-Carillo, Joseph Nanoa, Yongsheng Liu, Alois Haromy, Ian Paterson, Edith Pituskin, John Ussher, Evangelos Michelakis, Gopinath Sutendra
Supervisor: Dr. Gopinath Sutendra

INTRODUCTION

It is well-documented that tumor cells can secrete numerous signalling factors that affect distant normal tissues. For example, tumor-secreted inflammatory factors can initiate muscle or fat tissue breakdown into protein or fatty acids, respectively, that can be used to feed the growing tumor, but consequently can severely decrease the weight of cancer patients. What remains incompletely understood is
if tumor-secreted factors (TSFs) can initiate a signalling cascade in the heart, rendering cardiomyocytes (the contractile cells of the heart) susceptible to cell death when treated with anti-cancer drugs.

METHODS

We utilized clinically relevant xenotransplant cancer mouse models to study the effect of secretions on the myocardium. We utilized serum and breast cancer samples from patients that did and did not develop cardiotoxicity. We isolated primary cardiomyocytes to elucidate our proposed signalling cascade. We generated transgenic cardiomyocyte specific RbFox1 KO mice and assessed heart function with echocardiography after anthracycline treatment.

RESULTS

We show that tumor secreted nucleosides (i.e. inosine), which are precursors for generating DNA in the cell, were significantly increased in the serum of mice with lung cancer and breast cancer patients that developed cardiotoxicity. Mechanistically, we found that tumor secreted inosine activates the A2A receptor on cardiomyocytes initiating a signaling cascade leading to degradation of the RNA splicing factor RbFox1. RbFox1 loss induces the formation of the mitochondrial permeability transition pore and release of cytochrome C (a precursor for cell death), while also promoting cardiomyocyte dedifferentiation and a more receptive chromatin for anti-cancer intercalating agents (which induce the pro apoptotic transcription factor p53). In keeping, RbFox1 deficient mice develop significant cardiotoxicity when treated with low dose intercalating agents, including the commonly used doxorubicin.

CONCLUSIONS

This work provides both a potential biomarker (i.e. inosine) and mechanism for susceptibility to our most cardiotoxic anti-cancer drugs including doxorubicin and cisplatin.

Liver stiffness measurement by vibration-controlled transient elastography predicts clinical outcomes in patients with autoimmune hepatitis

Narmeen Umar, Christina Plagiannakos, Gideon Hirschfield, Bettina Hansen, Ellina Lytvyak, Aldo Montano-Loza
Supervisor: Dr. Aldo Montano-Loza

INTRODUCTION
Autoimmune hepatitis (AIH) is a heterogenous liver disease that varies widely in clinical response and prognosis. The assessment of liver fibrosis in a non-invasive manner during follow-up seems fundamental to predicting disease prognosis and evaluating the effectiveness of therapies. We aimed to investigate the usefulness of vibration-controlled transient elastography (VCTE) in prognosis in a large cohort multicentric study of patients with AIH across Canada.

METHODS
We evaluated 761 patients with AIH who had a simplified international score ≥6 from the Canadian Network for Autoimmune Liver Diseases (CaNAL). All patients had at least one reliable liver stiffness measurement (LSM) taken by VCTE. The primary endpoint was the time to adverse outcomes defined as death or liver transplantation. Hazard ratios (HR) for adverse outcomes were determined using a Cox univariate and multivariate regression.

RESULTS
566 were female(74%) and median age at diagnosis was 45 years(IQR 28-58). 564 patients(76%) were Caucasians. The first VCTE was performed within a median of 35.7 months(IQR 2.9-111.6) after AIH diagnosis. The median LSM value was 8.80 kPa(IQR 5.8-17.3), and it was significantly associated with clinical adverse outcomes(HR 1.05, 95%CI 1.04-1.07; p<0.001). Considering the first VCTE as time zero, LSM was independently associated with adverse clinical outcomes(HR 1.03, 95% CI 1.02-1.04, P<0.001), after adjustment for age(HR 1.04, 95% CI 1.02-1.06, P<0.001), female sex(HR 0.83, 95% CI 0.57-2.00, P=0.8), cirrhosis at diagnosis(HR 0.87, 95% CI 0.56-1.98, P=0.8), and time from AIH diagnosis to first VCTE(HR 0.99, 95% CI 0.98-0.99, P<0.001) (Fig. 1a). Patients were classified into low, moderate, and high-risk groups for adverse outcomes based on VCTE cut-off values: <8 kPa, ≥8 and <14 kPa, and ≥14 kPa (Fig. 1b).

CONCLUSIONS
Liver stiffness measurement by VCTE is an important non-invasive tool to predict adverse outcomes in AIH. VCTE should be considered for stratification and
potential surrogate endpoints in clinical practice and controlled trials.

Liver stiffness measurement by vibration-controlled transient elastography predicts clinical outcomes in patients with autoimmune hepatitis

Figure 1a.

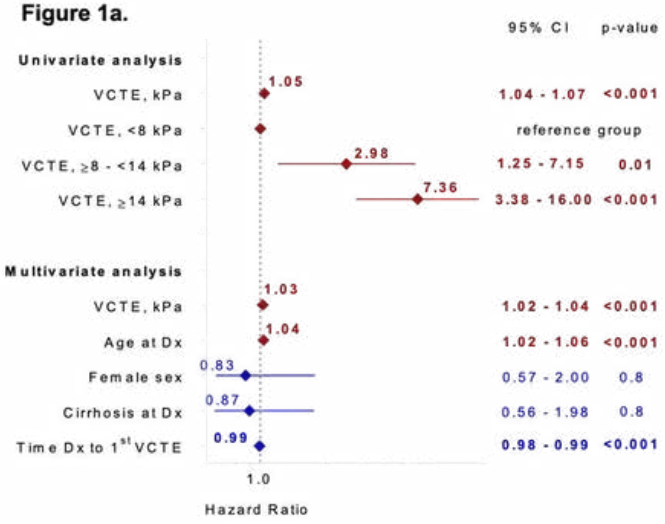
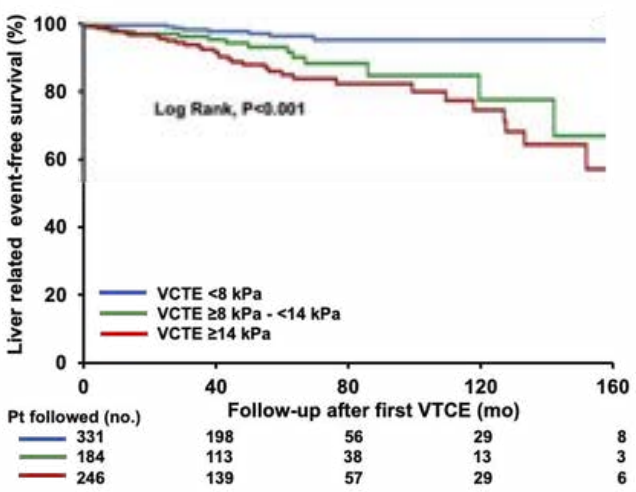


Figure 1b.



Long-term impact of the COVID-19 pandemic on inflammatory bowel disease healthcare: a two-year nationwide update

Lisa M.A. van Lierop, Monica E.W. Derks, Maarten te Groen, Chantal C.H.J. Kuijpers, Iris D. Nagtegaal, and Frank Hoentjen.
Supervisor: Dr. Frank Hoentjen

INTRODUCTION
The COVID-19 pandemic has caused a large reduction in inflammatory bowel disease (IBD)-related scheduled procedures in its early phases, as shown in our previous study. In this current nationwide study, we aimed to determine the impact of consecutive COVID-19 waves on IBD healthcare utilization including IBD-related diagnoses and procedures during the first two pandemic years.

METHODS
We conducted a search in PALGA to identify IBD patients who underwent an IBD- related procedure between March 1, 2018 and February 28, 2022. We determined the incidence of IBD-related endoscopic and surgical procedures, new IBD
diagnoses and neoplasia diagnoses (indefinite (IND), low-grade (LGD), high-grade dysplasia (HGD) and colorectal cancer (CRC)) during the first two years of the pandemic in the Netherlands (March 2020 – February 2022). The mean incidence
of the previous two years (March 2018 – February 2020) served as a comparator.

RESULTS
We calculated a net reduction of 2.9% (1,391 IBD procedures) compared to the two pre-pandemic years (endoscopic procedures: -3.1%, n=1,409; surgical procedures: +0.7%, n=18). For both endoscopic and surgical procedures, an initial net
decrease after the first year was followed by a net increase after the second year (-6.2% (n=1,413) versus +0.02% (n=4) and -1.3% (n=18) versus +2.7% (n=36), respectively). A net reduction of 0.9% (n=54) in new IBD diagnoses was observed (first year: -0.8%, n=24; second year: -1.0%, n=30). A net reduction of 1.9%
(n=74) in IND/LGD diagnoses was observed (first year: -10.9%, n=213: second
year: +7.1%, n=139).

CONCLUSIONS
We observed a mitigation of the initial reduction of IBD-related procedures after
the first COVID-19 wave. This finding illustrates the rapid adaptation of the national IBD healthcare system during the second year of the pandemic.

Clonal patterns between pouch neoplasia and prior colorectal neoplasia in inflammatory bowel disease patients: an exploratory cohort study

Lisa MA van Lierop, Maarten te Groen, Lauranne AAP Derikx, Bauke Ylstra, Frank Hoentjen, Iris D Nagtegaal, and Femke Simmer.
Supervisor: Dr. Frank Hoentjen

INTRODUCTION
Inflammatory bowel disease (IBD) patients with an ileo-anal pouch anastomosis (IPAA) bear an increased risk of pouch neoplasia, with prior colorectal neoplasia as the strongest predictor. It is unknown if pouch neoplasia develops independently or is derived from prior colorectal neoplasia. We aimed to assess potential clonality between prior colorectal neoplasia and pouch neoplasia in IPAA patients with IBD.

METHODS
In this explorative study we used the Dutch Nationwide Pathology Databank to identify IBD patients with both pouch neoplasia and colorectal neoplasia prior to colectomy. Clonality was assessed on colonic tissue of the lesion with shallow
whole genome sequencing based copy number aberration (CNA) analysis and validated with immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH).

RESULTS
We included 13 patients who fulfilled the inclusion criteria. Three patients showed matching clonality CNA profiles between prior colorectal neoplasia and pouch neoplasia, validated with matching IHC and FISH for p16 and HER2. Patients with matching clonal samples also showed on retrospective review concordant histology of the neoplastic lesion pre- and post IPAA, positive resection margins,
metastasized disease or a short interval (<2 years) between colorectal and pouch neoplasia diagnoses.

CONCLUSIONS
Three patients showed matching clonality patterns of neoplastic lesions, confirmed by clinical and histological data. Most pouch neoplasia in our cohort were molecularly different from their prior colorectal neoplasia. CNA provides a feasible method for clonality assessment in patients with colorectal neoplasia and subsequent pouch neoplasia.

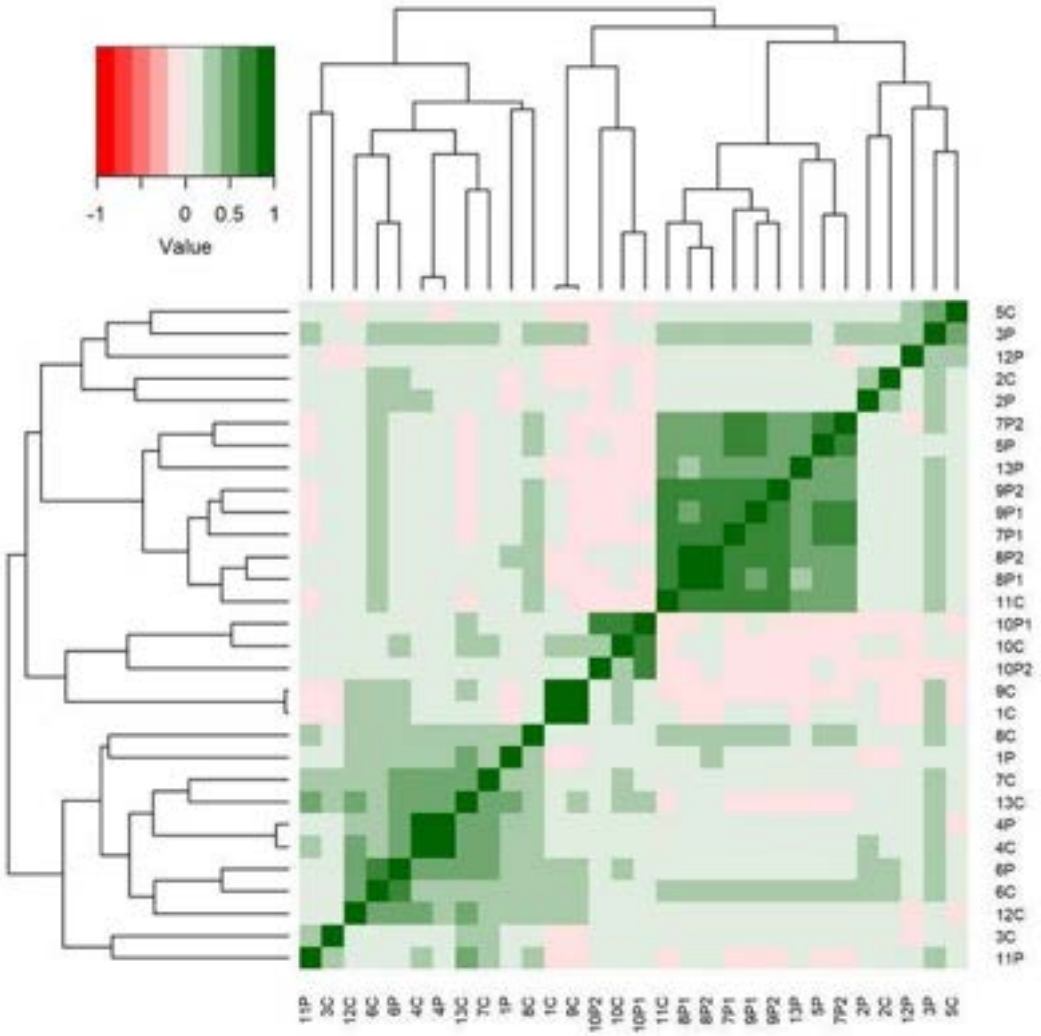


Figure 1. Hierarchically clustered correlation matrix of copy number data.

In the dendrogram the samples of patients 2, 4, 6, 10 cluster together. The color key displays the colors associated with each grade of correlation: dark green meaning high correlation (1), and dark read meaning no or negative correlation (-1). Numbering: patient number + C (colorectal sample) or P (pouch sample) + 1 / 2 in case of multiple samples.

Characterization of the urine microbiome-host interaction

Benson Weyant, Aja Rieger, Nimra Hooda, Cole White, Carlos Cervera
Supervisor: Dr. Carlos Cervera

INTRODUCTION
The human microbiome is highly researched, but its persistence, kinetics and host interactions are poorly understood. Using the urine microbiome as a model, this study aims to characterize the microbiome-host interaction. Our preliminary data shows the existence of biofilm-like bacterial aggregates surrounded by a thick capsule inside urothelial cells. We hypothesize that the main component of the urinary microbiome is intracellular.

METHODS
Urine samples were collected from 20 healthy volunteers. Samples were processed for scanning electron microscopy (SEM) imaging, volumetric flow cytometry and metagenomic sequencing. Microbiome analysis was done by amplifying the V4 region of the 16S rRNA on the urine pellet and cell-free supernatant in each participant.

RESULTS
The median age was 38 years (IQR 29-51) and 12 (60%) were women. We found intracellular bacteria in all participants and in a median of 13.9% (IQR 5.1-28.9) of urothelial cells. Significant correlation exists between the DNA concentration obtained from cell pellets and the number of urothelial cells containing bacteria ($p<0.0001$), but not with the cell-free sample ($p=0.78$). Using SEM, we visualized bacterial aggregates compatible with biofilms in 20/20 (100%) of participants. The urine microbiome was significantly less diverse in cell pellets and there were significant differences in taxonomy differential abundance between cell-free and cell pellet samples.

CONCLUSIONS
Our findings suggest that the urine microbiome is formed by highly organized intracellular structures, which explains its persistence in body cavities. The method for DNA extraction is key to properly characterize the composition of the microbiome. To the best of our knowledge, this is the first description of the complex intracellular microbiome in healthy individuals.

Table 1. Individual subject data. UTI = urinary tract infection, SEM = scanning electron microscopy.

Subject	Sex	Age	Race	Previous UTI	Urothelial cells/μL	Urothelial cells containing bacteria/μL	Percentage of cells containing bacteria	Biofilm-like structures by SEM
001	Male	52	White	No	5.45	2.33	42.86	Yes
005	Female	20	White	Yes	471.46	83.65	17.74	Yes
006	Female	41	White	No	364.12	35.52	9.76	Yes
007	Female	53	White	Yes	20.64	6.04	29.27	Yes
009	Male	28	Chinese	No	3.70	1.85	50.00	Yes
011	Female	30	White	Yes	28.41	2.94	10.34	Yes
012	Male	31	White	No	13.40	1.99	14.81	Yes
015	Male	28	Arabic	No	0.76	0.25	33.33	Yes
017	Male	27	White	No	5.64	0.94	16.67	Yes
018	Male	34	White	No	3.89	0.27	7.05	Yes
019	Female	60	White	No	2.00	0.26	12.96	Yes
020	Female	48	Black	Yes	268.17	76.62	28.57	Yes
021	Female	42	Filipino	No	66.01	40.86	61.90	Yes
023	Female	44	Filipino	Yes	2.80	0.42	15.00	Yes
026	Male	50	White	No	4.50	0.06	1.35	Yes
029	Female	27	White	No	644.20	20.74	3.22	Yes
031	Female	30	White	No	1.15	0.14	12.24	Yes
032	Female	35	Hispanic	Yes	54.95	1.22	2.22	Yes
033	Male	73	Hispanic	Yes	25.30	0.29	1.13	Yes
034	Female	71	Hispanic	No	20.20	0.23	1.13	Yes

Burnout and fatigue amongst internal medicine residents: the impact of alternative scheduling models on resident wellness

Jack H. Yuan MD, Yiming Huang MD, Brianna Rosgen M.Sc., Sarah Donnelly MD, Xiaoyang Lan MD Ph.D., Steven J. Katz MD
Supervisor: Dr. Steven Katz

INTRODUCTION
Fatigue and burnout are prevalent among resident physicians across Canada.
Shifts exceeding 24 hours are commonly purported as detrimental to resident health and performance. Residency training programs have employed strategies towards understanding and intervening upon the complex issue of resident fatigue, where alternative resident scheduling models have been an area of active investigation. This study sought to characterize drivers and outcomes of fatigue amongst internal medicine residents across different scheduling models.

METHODS
Cross-sectional surveys were conducted among internal medicine resident physicians at the University of Alberta. Anonymized socioeconomic demographics and medical education background were collected. Burnout and fatigue were assessed using the Maslach Burnout Inventory - Human Services Survey, and the Swedish Occupational Fatigue Inventory, respectively. Associations between demographic or work characteristics and fatigue and burnout outcomes were estimated.

RESULTS
Sixty-nine participants competed burnout questionnaires, and 165 fatigue questionnaires were completed. The overall prevalence of burnout was 58%. Lower burnout prevalence was noted among respondents with dependent(s) (p=0.048), who identified as a racial minority (p=0.018), or completed their medical degree internationally (p=0.006). The 1-in-4 model was associated with the highest levels of fatigue and reported increased risk towards personal health (OR 4.98, 95%CI 1.77-13.99) and occupational or household harm (OR 5.69, 95%CI 1.87-17.3). Alternative scheduling models were not associated with these hazards.

CONCLUSIONS
The 1-in-4 scheduling model was associated with high rates of resident physician fatigue and burnout. Alternative scheduling models appear protective for fatigue and burnout, and may be a viable method of reducing resident burnout and
fatigue. Protective factors against fatigue are best characterized as strong social supports outside the workplace. Further studies are needed to characterize the impacts of alternative scheduling models on resident education and patient safety.

Determinants of Post-COVID ill-health in a cohort of Canadian health care workers

Tanis Zadunayski
Supervisor: Dr. Nicola Cherry

INTRODUCTION
Post-COVID syndrome is a condition which occurs following the onset of COVID-19, is present after 3 months, and persists for at least 2 months. During the pandemic, health care workers (HCWs) were at risk of the SARS-CoV-2 virus infection and thus of developing a post-COVID condition. This study examined the rate of a post- COVID syndrome in HCW and attempted to identify risk factors for developing such a condition.

METHODS
We selected a study sample from a prospective cohort of Canadian HCWs. The study sub-cohort included all those with only one positive COVID-19 test who had completed a self-report questionnaire in the summer of 2022. In this sub-cohort, the rate of post-COVID syndrome was estimated for those with the case date at least 90 days before completion of the 2022 questionnaire. In the full cohort questionnaires were distributed four times from the start of the pandemic, collecting data on demographics, pre-pandemic medical history, COVID-19 infections, symptoms and severity, vaccination status, work-related factors, and mental health.

RESULTS
The full cohort comprised 4964 HCW. In our sub-cohort (N=1688), 1010 had a positive COVID-19 test at least 90 days before completing the 2022 questionnaire. Of these, 295 reported a post-COVID condition (29.2%; Table 1). Post-COVID syndrome was more likely among Licensed Practical Nurses (50.0%), females (30.7%), participants treated for anxiety or depression before the pandemic (38.3%), those who had not been vaccinated at the time they were infected (47.3%), were aged ≥55 years (36.4%), had a history of asthma or COPD (42.6%; 75.0%), and have ever smoked (39.5%).

CONCLUSIONS
The development of a post-COVID syndrome was systematically related to risk factors. It will be important to identify modifiable factors that reduce the risk of longer-term morbidity.

Determinants of Post-COVID ill-health in a cohort of Canadian health care workers

Table 1: Predictive factors examined in post-COVID rates among HCWs

	Reported post-Covid Condition				All		χ^2	p
	Yes		No					
Self-reported Gender	N	%	N	%	N	%		
Male	32	21.1	120	78.9	152	15.1	5.76	0.016
Female	263	30.7	595	69.3	858	85.0		
Job								
Physicians	47	18.8	203	81.2	250	27.8	23.8	<0.001
Registered Nurses	213	31.3	497	68.7	680	67.3		
Licensed Practical Nurses	11	50.0	11	50.0	22	2.2		
Personal Support Workers	18	43.9	23	56.1	41	4.1		
Health Care Aids	6	35.3	11	64.7	17	1.7		
Mental Health: treated Anxiety or Depression before the pandemic								
Yes	143	38.3	230	61.7	373	36.9	25.7	<0.001
No	128	25.1	382	74.9	510	50.5		
Unknown	24	18.9	103	81.1	127	12.6		
Days Between COVID-19 infection and Questionnaire								
>90 but <120	73	29.7	200	73.3	273	27.0	32.5	<0.001
>120 but <5 months	66	26.0	188	74.0	254	25.2		
>5 months but <1 year	83	24.9	250	75.1	333	33.0		
>1 year	73	48.7	77	51.3	150	14.9		
# of Vaccines at Infection Date								
0	69	47.3	77	52.7	146	14.5	29.5	<0.001
1	15	20.5	58	79.5	73	7.2		
2	84	27.9	217	72.1	301	29.8		
3	124	25.7	359	74.3	483	47.8		
4	3	42.9	4	57.1	7	0.7		
Age at March 2020								
<40	129	28.8	319	71.2	448	44.4	5.33	0.070
40 but <50	106	26.7	291	73.3	397	39.3		
55 or older	60	36.4	105	63.6	165	16.3		
Asthma before the pandemic								
Yes	86	42.6	116	57.4	202	20.0	25.2	<0.001
No	185	27.1	497	72.9	682	67.5		
Unknown	24	19.0	102	81.0	126	12.5		
Had chronic bronchitis, emphysema or COPD before the pandemic								
Yes	6	75.0	2	25.0	8	0.8	15.1	<0.001
No	265	30.3	610	69.7	875	86.6		
Unknown	24	18.9	103	81.1	127	12.6		
Ever Smoked Tobacco before the pandemic								
Yes	58	39.5	89	60.5	147	14.6	14.0	<0.001
No	213	28.9	523	71.1	736	72.9		
Unknown	24	18.9	103	81.1	127	12.6		
Total N	295	29.2	715	70.8	1010	100.0	–	–

The clinical impact of HFpEF on Interstitial Lung Diseases: clinical characteristics, comorbidities and outcomes.

Umberto Zanini, Giovanni Ferrara, Rhea Varughese, Meena Kalluri, Jason Weatherald.
Supervisor: Dr. Jason Weatherald

INTRODUCTION

Cardiovascular diseases such as coronary artery disease, pulmonary hypertension, and heart failure (HF) are among the most frequent comorbidities associated with interstitial lung disease (ILD). The overall prevalence of HF is estimated to be 1-2% in adults, rising to ≥10% among people older than 70. About 50% of patients with heart failure have preserved ejection fraction (HFpEF). Because many patients with ILD are elderly, HFpEF may affect many ILD patients. The prevalence, clinical features, and outcomes of patients with ILD and HFpEF are still unclear.

METHODS

This study is a retrospective cohort analysis of ILD patients who had an echocardiogram from Jan 2013 to Dec 2022 at the University of Alberta Hospital at their baseline visit. HFpEF was defined as a H2FPEF score >5 which reflects >95% probability of HFpEF. Clinical features and survival were compared between
patients with and without HFpEF.

RESULTS

Out of 137 ILD patients, 13 had HFpEF (9.49%). Patients with HFpEF were older (74.6±7.4 vs 65.1±14.8, $p<0.05$) and had higher body mass index (34.08±6.01 vs 29.2±6.8 kg/m2, $p<0.05$). Left atrial volume index was significantly greater in HFpEF patients (38.2±12.6 vs 24.1±8.5 mL/m2). There was no difference in baseline KB-ILD questionnaire and mMRC. Both groups had similar 6-minute walk distance (336.4±110.3 vs 391.5±113.8 m, $p=0.11$). Survival in patients with HFpEF was not different than patients without HFpEF ($p=0.47$).

CONCLUSIONS

In conclusion, the prevalence of HFpEF among ILD patients is similar to that of the general population (10%). Symptoms, clinical features, and survival were similar
for patients with HFpEF and without. Left atrial enlargement may be an additional clue to the presence of HFpEF.

Quality Improvement Abstracts

Biliary Stent Use In Ercp: A Quality Assurance Study Assessing Adherence To Clinical Guidelines And Cost Outcomes

Alan Decanini, MD, Suliman Alhaidari, MD, Ibrahim Alzahrani, MD, Manar Alhanaee, MD, Mahmod Mohamed, MD, Sergio Zepeda-Gomez, MD, Pam Mathura, PhD(c), Julie Zhang, and Gurpal Sandha, MBBS.
supervisor: Dr. Gurpal Sandha

INTRODUCTION
A perceived increase in the use of biliary stents during endoscopic retrograde cholangiopancreatography (ERCP) was observed by our nursing team leader and brought to the attention of the Director of Endoscopy.

METHODS
A chart review of all consecutive patients that underwent ERCP for one year (January 2020 to 2021) at the University of Alberta Hospital was performed. The need for biliary stent placement was assessed independently by two blinded reviewers and compared with published guidelines. Costs were calculated using AHS fee codes.

RESULTS
A total of 598 patients (316 F) with mean age of 60±19 years (range 3-99 years) underwent 842 ERCPs. Clinical indications for the initial ERCP were choledocholithiasis (376, 63%), malignant stricture (84, 14%), benign stricture (49, 8%), and others (89, 16%). Of the 244 patients that had a follow-up ERCP, the most common indications were stent removal (126, 52%), stent replacement (61, 25%), stent placement (28, 11%), and stone extraction (8, 3%). A total of 296 biliary stents were inserted, of which 223 stents (114 plastic, 109 metal) were inserted during initial ERCP (223/598, 37%) and 73 stents (43 plastic, 30 metal) during follow-up ERCP (73/244, 30%).
Of the 296 stents, 79 (27%) were inserted for indications not in accordance with published guidelines (63/223 initial ERCP, and 16/73 follow-up ERCP, kappa=0.62). Most of these were placed in choledocholithiasis cases (61/63 initial ERCP, 6/16 follow-up ERCP). In the subgroup of 376 patients with choledocholithiasis, 61 (16%) underwent stent placement not in accordance with published guidelines. The
added cost of such stent insertions and follow-up ERCPs for stent removal was $130,000.

CONCLUSIONS
Nonguideline-based stent insertion was identified in some patients with choledocholithiasis presenting for ERCP. To reduce avoidable follow-up procedures and healthcare resource utilization, ERCP stent insertion education based on published guidelines, as well as regular practice audit and feedback are required.

Optimizing The Indications For Biliary Stent Placement In Patients With Choledocholithiasis: A Quality Improvement Initiative To Enhance Patient Care And Reduce Healthcare Resource Utilization

Ibrahim Alzahrani, MD, Suliman Alhaidari, MD, Manar Alhanaee, MD, Alan Decanini, MD, Mahmod Mohamed, MD, Sergio Zepeda-Gomez, MD, Pam Mathura, PhD(c), Julie Zhang, and Gurpal Sandha, MBBS.
Supervisor: Dr. Gurpal Sandha

INTRODUCTION
A retrospective chart audit was performed to review biliary stent utilization from January 2020 to 2021 at the University of Alberta Hospital. Nonguideline-based stent insertion was identified in 16% of patients with choledocholithiasis presenting for endoscopic retrograde cholangiopancreatography (ERCP). To improve clinical practice, a quality improvement initiative was conducted.

METHODS
Results of the chart audit (pre-intervention) were shared with the ERCP group. The QI intervention was to align biliary stent insertion with published guidelines. A chart audit (post-intervention) was performed on all ERCPs from July, 2021 to June, 2022. Indications for stent insertion were assessed independently by two blinded reviewers.

RESULTS
A total of 661 patients (337 F) with mean age of 59±19 years underwent 885 ERCPs during post-intervention period. Of the 661 patients, 384 (58%) were referred for choledocholithiasis. A total of 192 biliary stents (105 plastic, 85 metal) were placed during initial ERCP (192/661, 29%), as compared to pre-intervention year (223/598, 37%, p=ns). However, only 13/192 stents (7%) were nonguideline- based (kappa=0.53), compared with 63/223 (28%) in pre-intervention year ($p<0.0001$). This accounts for a 75% reduction in overall avoidable stent placement, with 88% reduction seen in choledocholithiasis subgroup (8/384, 2% vs. 61/376, 16%, $p<0.0001$).

CONCLUSIONS
Education to align practice with published guidelines has demonstrated a significant improvement in biliary stent insertion during ERCP in patients with choledocholithiasis.

Decreasing the Number of Patients Waiting to be Seen at the General Internal Medicine Kaye Edmonton Clinic

Amanda Brost, Pamela Mathura
supervisor: Dr Anca Tapardel

INTRODUCTION

The General Internal Medicine (GIM) division at Kaye Edmonton Clinic (KEC) accepts referrals for individual physicians, Hypertension Clinic and a general GIM pool. In March 2022 there were 130 patients waiting to be scheduled for an initial appointment, anecdotally higher than prior years, many patients waiting more than 3 months to be seen. Our aim was to reduce the number of patients awaiting scheduling by 20%.

METHODS

To understand the current process, we reviewed 130 charts of patients awaiting scheduling, interviewed stakeholders, reviewed R4 Clinic capacity, and reviewed the ConnectMD process. We found many referrals (35%) were for Hypertension, heterogeneity in triaging practices, 33% of patients did not meet their schedule by date and ConnectMD was possibly underutilized. Immediate and longer-term interventions were implemented from July-Dec 2022 including standardizing triage definitions, encouraging fewer follow-ups in R4 Clinic, increasing awareness of ConnectMD, starting a Hypertension Rotation, and the opportunity for a GIM physician to see ~40 Hypertension referrals in a community clinic.

RESULTS

By December 31, 2022, the number of patients awaiting scheduling was reduced by 37%. Chart review in January 2023, indicated that 68% of referrals were triaged with the new definitions. The Hypertension Rotation has capacity for 12 new patients per week. Nineteen more new patients were seen in R4 clinic from July- December compared to the prior year. There was an upward trend of ConnectMD calls since August 2022.

CONCLUSIONS

Sustained decrease in the number of patients awaiting scheduling is likely due to immediate and longer-term interventions. We recommended continued use of triaging definitions, ongoing promotion of ConnectMD and continuation of the Hypertension Rotation. Areas of future study include development of thresholds to trigger bi-directional flow between KEC GIM clinics and other related clinics and gathering feedback from referring providers about ConnectMD.

The period prevalence of a beta-lactam allergy label in patients prescribed carbapenems: A retrospective cohort study

Shealynn Carpenter, Jackson Stewart, Cecilia Lau, Karen Fong, Dima Kabbani, Stephanie Smith, Karen Doucette, Justin Chen
supervisor: Justin Chen

INTRODUCTION
The rate of reported beta-lactam allergies is significantly higher than that of true hypersensitivity reactions. Inappropriate allergy labels are associated with adverse patient outcomes. Our primary objective was to evaluate the period prevalence of beta-lactam allergy labels in patients prescribed carbapenems at a major tertiary care centre. Secondary objectives included identifying the frequency of carbapenems prescribed explicitly because of an allergy label, stratifying allergy risk to determine opportunities for delabeling, and quantifying the potential days of carbapenem use that could be saved through allergy reconciliation.

METHODS
A retrospective chart review was performed on inpatients who were prescribed a carbapenem and prospectively audited by the antimicrobial stewardship program from July 2020 to July 2022. Subgroup analysis was completed regarding allergy reconciliation based on validated and previously published beta-lactam allergy delabeling algorithms.

RESULTS
Of 1815 carbapenem prescriptions audited, 360 were associated with a beta- lactam allergy label. Duplicate patients were removed resulting in a beta-lactam allergy period prevalence of 276/1399 (20%). Of all the carbapenem prescriptions
in those with listed beta-lactam allergies, 139/360 (39%) were directly related to the allergy label, representing 745 potential days of carbapenem use that could have been avoided through allergy reconciliation.

Amongst the total number of unique (non-cross-reactive) beta-lactam allergies, 273/312 (88%) were candidates for allergy delabeling through: immediate allergy removal 67/312 (21%), oral challenge 24/312 (8%), or skin test 18/312 (6%). Additionally, 96/312 (31%) were candidates for either an oral challenge or skin test but required additional allergy details to clarify. Finally, 68/312 (22%) of allergies could not be risk stratified due to insufficiently documented allergy history.

CONCLUSIONS
Beta-lactam allergies among patients prescribed carbapenems is overrepresented and is the primary reason for prescribing a carbapenem in over one third of cases. Allergy reconciliation represents an important intervention that could lead to a reduction in unnecessary carbapenem prescribing at our centre.

Exploring the Deprescribing Needs of Hospitalized Medicine Patients

Shamaila Dar, Rahul Mehta, Pamela Mathura, and Winnie Sia
supervisor: Winnie Sia

INTRODUCTION

Polypharmacy, defined as the use of five or more prescribed medications, occurs in approximately 66% of Canadian seniors, with 26% being prescribed ten or more. Deprescribing is the planned and supervised process of dose reduction or stopping of medication that might be causing harm or no longer be of benefit. We explored the need for deprescribing in medical inpatients and sought healthcare providers' perspectives about the barriers to deprescribing in the hospital.

METHODS

Aligning with deprescribing.org and Alberta Health Services (AHS) Deprescribing Resource guide, we reviewed 60 inpatient charts to identify the need for deprescribing medications. In addition, a voluntary online survey was sent to 100 Medicine inpatient physicians and pharmacists at Royal Alexandra Hospital to gather their perspectives about deprescribing medications in the hospital, upon discharge, the barriers, and suggestions for improvement. Further, quality improvement tools were completed to understand the process and to determine
the root causes.

RESULTS

From the chart review, 30% of hospitalized medical patients could benefit from deprescribing. For the survey, 14% of healthcare providers responded within one week, with 85% indicating that medications could be deprescribed before
discharge. Barriers cited were a lack of time and resources, patients' unwillingness to deprescribe, and limited interprofessional collaboration. Suggested interventions included the development of an electronic medical record 'smart phrases' to standardize and simplify describing discharge documentation, expanding the pharmacist role, establishing a deprescribing clinic, and physician education.

CONCLUSIONS

Deprescribing medications in a hospital setting is challenging and will require a multifaceted effort; thus, we are establishing a deprescribing outpatient clinic supported by General Internal Medicine physicians and developing physician education and smart phrases. To determine the initiative's impact, an evaluation plan is being established.

Interhospital Variation in the Proportion of Admissions Managed with Critical Care Therapies or Invasive Hemodynamic Monitoring in Tertiary Cardiac Intensive Care Units: An Analysis from the Critical Care Cardiology Trials Network Registry

Sarah Donnelly, MD, MSc1, Christopher F. Barnett, MD, MPH2; Erin A. Bohula, MD, DPhil3; Sunit-preet S. Chaudhry, MD4; Meshe D. Chonde, MD5; Howard A. Cooper, MD6; Lori B. Daniels, MD, MAS7; Mark W. Dodson, MD, PhD8; Daniel Gerber, MD9; Michael J. Goldfarb
supervisor: Dr Sean van Diepen

INTRODUCTION

In a large registry of tertiary and academic CICUs, we observed a more than four- fold interhospital variation in the provision of CCRx that were primarily driven by differences in patient acuity. The lack of difference in mortality between low, intermediate and high CCRx utilization sites suggest that the development of standardized CICU admission criteria that incorporate the need for CCRx could help reduce disparities in admission practices and improve health-resource allocation.

METHODS

The Critical Care Cardiology Trials Network (CCCTN) is a multicenter registry of tertiary and academic CICUs in the United States and Canada that captured consecutive admissions in 2-month periods between 2017 and 2022. This analysis included 17,843 admissions across 34 sites and compared the interhospital variability in CCRx and its association with in-hospital survival. The Pratt Index was used to quantify patient-related and institutional factors associated with CCRx variability.

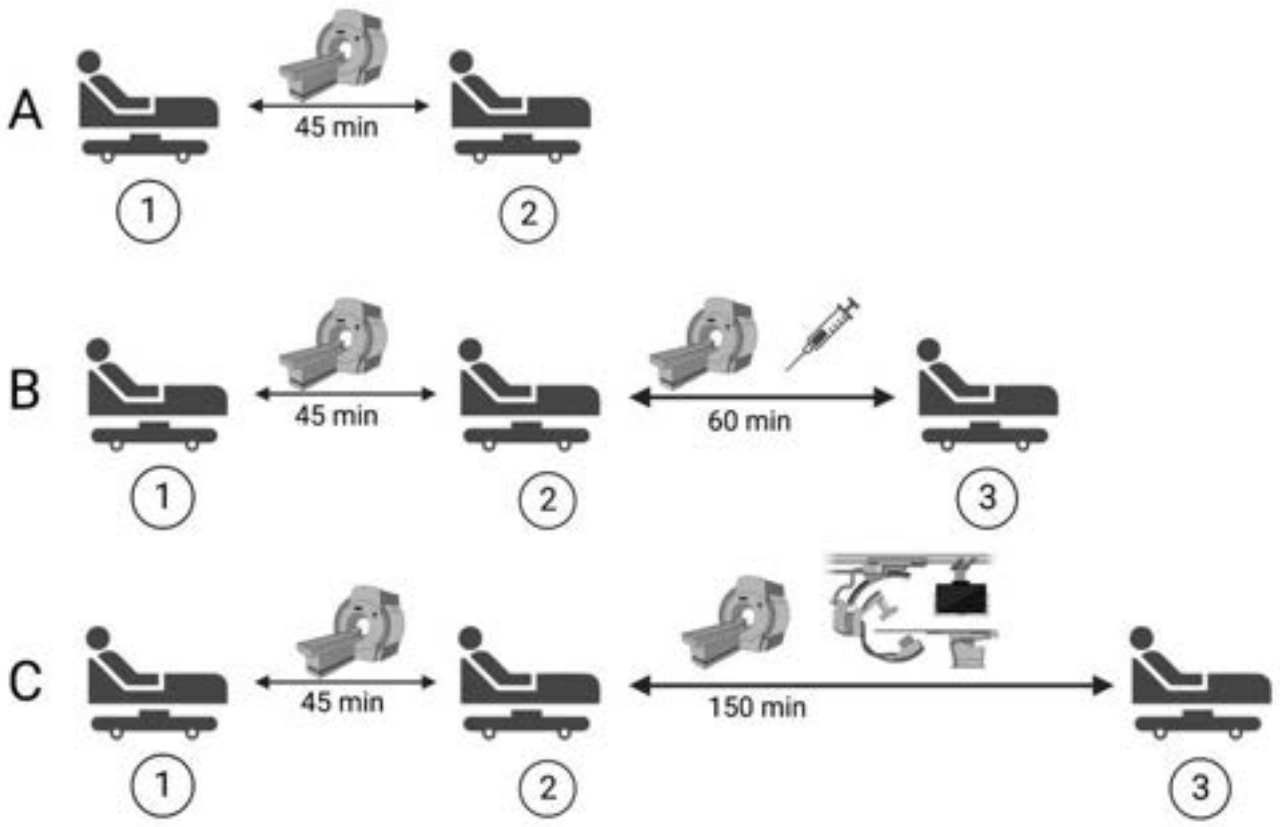
RESULTS

CCRx were provided to 61.4% (interhospital range of 21.3-87.1%) of CICU patients. Admissions to CICUs in the highest tertile of CCRx utilizers had a greater burden of comorbidities, more with STEMI, cardiac arrest, or cardiogenic shock, and higher SOFA scores. The unadjusted in-hospital mortality (median 12.7%) was 9.6%,
11.1% and 18.7% in low, intermediate, and high CCRx tertiles, respectively. No differences in adjusted mortality were observed when admissions were stratified
by the provision of CCRx across tertiles. Baseline patient-level variables and institutional differences accounted for 80.2% and 5.3% of the observed CCRx variability, respectively.

CONCLUSIONS

In a large registry of tertiary and academic CICUs, we observed a more than four- fold interhospital variation in the provision of CCRx that were primarily driven by differences in patient acuity. The lack of difference in mortality between low, intermediate and high CCRx utilization sites suggest that the development of standardized CICU admission criteria that incorporate the need for CCRx could help reduce disparities in admission practices and improve health-resource allocation.

Figure 1.0



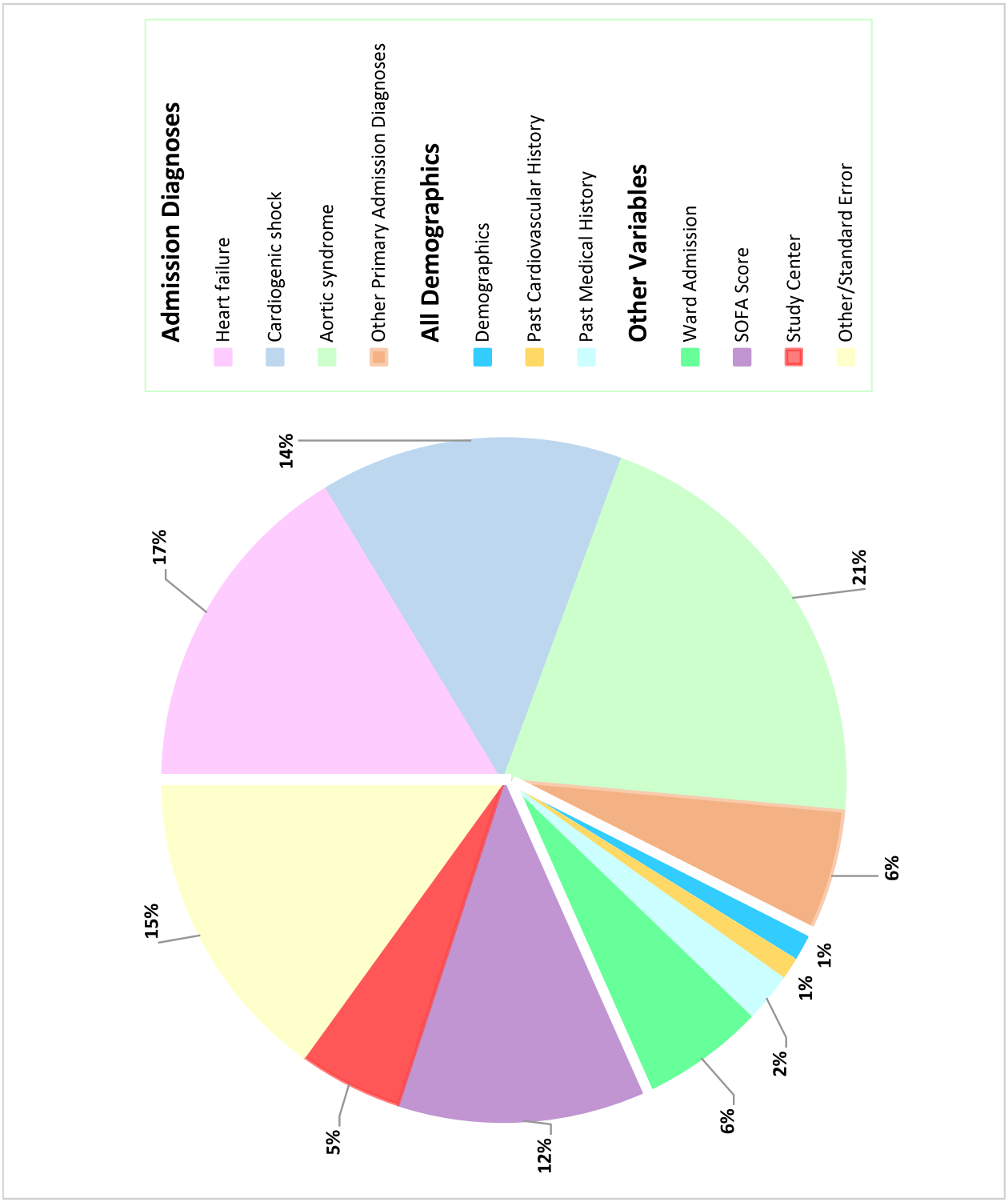


Figure 4: Pratt Index quantifying the proportion of critical care restricted therapy variability attributable to patient-level factors and CICU center

Timing of cholecystectomy after endoscopic retrograde cholangiopancreatography in a tertiary centre: Evaluation of outcomes

Crystal Liu, Dina Kao, Mahmod Mohamed, David Bigam, Sergio Zepeda-Gomez
supervisor: Dr. Sergio Zepeda-Gomez

INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is the treatment of choice for patients with choledocholithiasis. Early cholecystectomy (within 24 to 72 hours) is recommended after the initial ERCP to reduce the risk of subsequent biliary events.

METHODS

This is a retrospective analysis of adult patients who underwent cholecystectomy after ERCP from August 2021 to April 2022 at the UofA Hospital. Outcomes data were stratified according to the length of time between ERCP and cholecystectomy, within 72 hours (early) or after 72 hours (delayed).

RESULTS

In total, 30 (55%) subjects received cholecystectomy within 72 hours, while 25 (45%) subjects received cholecystectomy after 72 hours. The two groups were comparable in age, sex ratios, and comorbidities. Out of the patients who received cholecystectomy after 72 hours, 8 (32%) subjects received their cholecystectomy on a subsequent admission. Of these, 2 subjects developed recurrent biliary events before their cholecystectomy, and 1 subject required a conversion to open cholecystectomy. There were no recurrent biliary events amongst the individuals with early cholecystectomy.

Subjects who received early cholecystectomy had a shorter total hospital stay compared to those with delayed cholecystectomy (4.5 days vs 7.3 days, $p=0.0002$). There was no significant difference between early and late cholecystectomy in conversion rate (3% vs 8%, $p=0.58$), average operating time (86min vs 83min, $p=0.79$), intraoperative complications including adhesions (13% vs 12%, $p>0.05$) and empyema (27% vs 28%, $p>0.05$), as well as histological rate of chronic cholecystitis (88% vs 92%, $p=0.68$). Reasons associated with significantly delayed (>7 days) cholecystectomy after ERCP (n=12) include requiring coordination/consultation with other services prior to operation (3 subjects), prolonged course of gallstone pancreatitis (3 subjects), poor candidate for operation due to comorbidities (2 subjects), surgical cancellation/delays (2 subjects), post-ERCP pancreatitis (1 subject), and patient preference (1 subject).

CONCLUSIONS

Early cholecystectomy is associated with a shorter length of hospital stay and absence of recurrent biliary events.

A dive into paging frequency for internal medicine residents in a tertiary care hospital

Crystal Liu, Matthew Cooper, Steven Katz
supervisor: Steven Katz

INTRODUCTION

Paging is an important form of communication within the hospital, although it can interrupt patient care. The goal of this project is to better understand paging sources, relevance, and frequency.

METHODS

Internal medicine residents were recruited to document pages and secure messages they received while on call at the University of Alberta Hospital. Data
was obtained from call shifts in general internal medicine, critical care medicine, gastroenterology, cardiology, hematology, nephrology and respirology. Information regarding paging frequency was also obtained directly from the centralized paging platform, MediPage.

RESULTS

Data between July 2022 to February 2023 was obtained from 25 residents during
70 call shifts. Additional data from MediPage captured 53538 pages between February 2021 to February 2023, spanning 730 days, encompassing 10950 on-call hours.

On average, residents were paged 14.5 times per shift. 54.4% of pages were considered urgent and 38.2% non-urgent. 47.2% of pages changed patient care, 31.9% were clinically relevant but did not change patient care and 17.4% were clinically irrelevant.

The majority of pages were from nurses (75.5%) followed by staff consultants (12.1%), other residents (6.5%) and pharmacists (2.2%). Pages lead to
interruptions in patient care 58.8% of the time.

Residents experienced significantly greater paging volumes while on gastroenterology (15.5 pages/shift) and cardiology (14.1 pages/shift) compared to the other subspecialties studied ($F=24.3$, $p<0.00001$).

CONCLUSIONS

Paging is an important way to communicate urgent and clinically relevant information, however it interrupts patient care. More than a third of pages received by on-call internal medicine residents were non-urgent and almost half of those did not change patient care. Future initiatives looking at alternative forms of communication, such as encrypted electronic medical record messages, can be considered to reduce paging frequency, minimize distractions, and improve
resident wellness.

Improving Coding Practices for Alternative Level of Care (ALC) in Hospital Medicine Units

Zainab Muhammad and Banafsheh Manafian
supervisor: Narmin Kassam

INTRODUCTION

At the University of Alberta Hospital, many patients are classified as Alternate Level of Care (ALC), occupying an acute care bed when acute care services are no longer required. This classification establishes the hospital ALC timeframe, which is a component of a patient's average length of stay (ALOS) and identifies the barriers/reasons for discharge that could facilitate transition service planning. Additionally, measures the access gap between different healthcare settings and ensures that the hospital ALOS accurately reflects the intensity of care provided.

METHODS

A cross-sectional data review and quality improvement tools were completed, revealing that patients discharged from Family Medicine (FM) units had the highest non-specific ALC coding (ALC-TBD). A knowledge to practice gap was identified among physicians and nurses, a lack of understanding the ALC definition and completing associated electronic medical record workflows. A multicomponent intervention was developed that included: Medicine program 2-day coding expectation, ALC education, and audit and feedback. The intervention was trialed on two FM units for 3 months (Oct-Dec 2022).

RESULTS

ALC code specificity was improved by over 50%, and the time taken to update non- specific to specific codes decreased from 11 to 2 days. There was a decrease (over 75%) in the number of patients discharged with the ALC-TBD code. Patients whose ALC-TBD code was changed to a specific code had an increased average number of ALC days, this was supported by an increase in the initial ALC code assigned by physicians, suggesting earlier physician ALC designation. The ALOS for one FM unit decreased but increased for the other, suggesting that multiple factors impact this measure.

CONCLUSIONS

Reducing the ALC days and ALOS for hospitalized patients is a multipronged challenge that requires additional interventions beyond improved coding practices to target the specific discharge barriers/reasons identified.

Social Determinants of Health as Barriers to Accessing Care for Vasculitis: A National Survey of Vasculitis Patients

Kareena Nanda, Elaine Yacyshyn
Supervisor: Dr. Elaine Yacyshyn

INTRODUCTION
This study aimed to assess the unmet social needs of patients with vasculitis and its impact on accessing healthcare.

METHODS
An online survey was conducted on 100 participants recruited from the Vasculitis Foundation Canada and included a 20-question social needs assessment to evaluate various social determinants of health. Data was collected using REDCap and descriptive analysis was performed.

RESULTS
The mean age of participants was 59, 80% of participants were female, 88% were Caucasian, and 55% reside in urban areas. According to the social needs assessment, 56% of participants had at least one unmet need. Social and mental health (30%), financial security (18%), food security (17%), and health literacy (15%) were noted as common unmet needs. Furthermore, 29% of all participants noted social and emotional wellbeing as a barrier to accessing care for vasculitis. Financial insecurity (29%), poor health knowledge (25%), lack of transportation (13%) and discrimination or unfair treatment in the healthcare setting (14%) were also noted as barriers. Significantly, discrimination was noted as a major barrier to accessing care by 24% of participants who reported having faced discrimination. The study also revealed that participants viewed virtual visits, patient support groups, and increased access to educational materials on vasculitis as potential solutions to improve their care. Ninety-two percent of participants also suggested that rheumatologists should be involved in the management of social needs whether by screening for/counseling on SDOH or giving referrals to other resources. However, only 63% noted ever discussing social determinants of health with their rheumatologist.

CONCLUSIONS
The study highlights the need for increased awareness of and innovative solutions to unmet social needs by healthcare professionals at all levels of care. These findings emphasize the impact of social determinants of health on access to care and can be used to inform further quality improvement endeavors to improve patient outcomes.

Outcomes of first subsequent taxane (FST) therapy in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) who previously received docetaxel intensification (DI) for metastatic castration-sensitive prostate cancer (mCSPC).

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supervisor: Dr. Jason Weatherald

Introduction:
The management of advanced prostate cancer continues to rapidly evolve, particularly with earlier use of survival prolonging therapies in mCSPC. Though approved prior to the use of intensification therapy in mCSPC, taxane-based chemotherapies remain a relevant option for pts with mCRPC. However, there is little evidence determining outcomes of taxane chemotherapies as FST in mCRPC pts who received DI in mCSPC. The purpose of this study is to compare outcomes between the survival prolonging taxanes, docetaxel (D) and cabazitaxel (C), as FST after DI.

Methods:
New patient consults seen at the Cross Cancer Institute from 1 July 2014 to 31 Dec 2020 were reviewed. Pts were considered eligible if they received DI for mCSPC and then received either D or C in mCRPC. Variables of interest were collected from the electronic medical record. The primary endpoint was ≥50% PSA response at 12 weeks relative to baseline for FST. Secondary endpoints included OS from mCSPC diagnosis, as well as PFS and OS from FST start date. PSA responses were compared using chi-squared test and time-based endpoints were compared using the Kaplan-Meier method.

Results:
34 pts were identified: D=22, C=12 as FST. 91.2% of pts (D 95.5% vs C 83.3%) received FST in 2nd line mCRPC. Median age at diagnosis (63.1 vs 67.1 yrs, p=0.236) and median time to CRPC (18.6 vs 14.2 mos, p=0.079) were similar for D and C, respectively. Median time to FST (24.1 vs 34.6 mos, p=0.036) and OS from mCSPC diagnosis (30.9 vs 52.7 mos, p=0.002) were significantly shorter for pts receiving C vs D. PSA responses occurred in 40.9% of pts treated with D compared to 25.0% treated with C (p=0.645). There was no significant difference in median PFS (2.7 vs 3.5 mos, p=0.727) or median OS (11.4 vs 8.1 mos, p=0.132) from time of FST for pts treated with D vs C, respectively.

Conclusions:
Both D and C demonstrated activity as FST after DI in mCSPC. Pts who received C had shorter time to FST and OS from mCSPC. The reasons for this may reflect clinician preference for C in pts with aggressive or rapidly progressing disease. No difference was found in PSA response, PFS, or OS from FST with D compared to C. While limited by its retrospective nature and small sample size, this study suggests that D is active as FST despite treatment with DI in mCSPC.

Teledermatology in Atopic Dermatitis: A Systematic Review

Luvneet Verma, Tarek Turk, Liz Dennett, Marlene Dytoc
supervisor: Dr. Marlene Dytoc

INTRODUCTION
Telemedicine use has been increasing especially during the COVID-19 pandemic. Various studies have outlined benefits of telemedicine including improving health equity, reducing wait times, reducing risk of infection spread, and cost effectiveness. Skin diseases such as atopic dermatitis may potentially be managed via telemedicine. However, there are no evidence-based recommendations or a gold standard for best practices in telemedicine for supporting patients with atopic dermatitis.

METHODS
A review protocol was developed according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement. Two reviewers independently screened potential studies and extracted data. Studies were included if they evaluated any telemedicine assessment for primary atopic dermatitis.

RESULTS
Of 1196 identified studies, we identified five studies that met our inclusion criteria. Four of these were randomized controlled trials and one was a retrospective cohort study. Teledermatology models included web-based consultations and direct- access, online models. The studies evaluated outcomes such as disease severity, self-management behavior, health outcomes, health resource use, family costs, quality of life, and accuracy of diagnosis. Results indicated that teledermatology is as effective as in-person care in improving disease severity, self-management behavior, health outcomes, quality of life, and accuracy of diagnosis. Moreover, teledermatology may reduce costs and improve access to care for patients with mild-to-moderate AD.

CONCLUSIONS
Teledermatology may serve as an important tool for screening/triaging along with follow-up of patients suffering from atopic dermatitis. More randomized control trials are
needed to determine
which teledermatology models are most effective for virtual assessment of atopic dermatitis.

Teledermatology versus in-person visits for the follow up of atopic dermatitis patients

Tosin Odeshi, Tarek Turk, Loretta Fiorillo, Marlene Dytoc
Supervisor: Dr. Marlene Dytoc

INTRODUCTION
Access to dermatological care can be challenging, particularly in rural or remote areas. Teledermatology has emerged as a potential solution. We aim to compare teledermatology to in-person visits for the follow-up of mild-to-severe Atopic Dermatitis (AD).

METHODS
Patients of all ages with Ad were randomly recruited from two dermatology practices in Alberta, Canada. Patients were assessed at baseline, at 4-6 weeks, and at 8-12 weeks. Several validated dermatological outcome measures were used.
The frequency of complications and side effects during the treatment course were also evaluated.

RESULTS
Overall, 22 patients completed the study. The virtual and in-person groups were comparable in terms of sociodemographic factors. At baseline, there were no significant differences in dermatological outcome measures between the two groups. Longitudinal analyses revealed no significant differences in dermatological outcomes between the virtual and in-person groups over the course of follow-up. There were no significant differences in the frequency of complications and side effects during the treatment course between the two groups. Patient satisfaction ratings were high in both groups.

On average, patients who were on virtual visits had an 80% lower odds of moderate-to-severe uncontrolled disease (OR=0.20, 95%CI=0.08, 0.5) and an 82% lower odds of moderate-to-severe pruritus (OR=0.18, 95%CI=0.05, 0.6) over time, compared to those accessing care in persons. While the average odds of moderate- to-severe AD (as measured by IGA) was lower in the virtual group compared to the in-person group, this association was not statistically significant (OR=0.35, 95%CI=0.09, 1.3). Similarly, while average EASI, BSA, and LQI scores were lower for patients in the virtual group, these difference were not statistically significant.

CONCLUSIONS
This study provides evidence that virtual teledermatology visits might be equal or non-inferior compared to in-person visits for the follow up of mild-to-severe AD. Teledermatology may be a valuable tool to increase access to dermatological care.

Teledermatology: Canadian Dermatologists' Practice Patterns, Perceived Challenges and Future Recommendations

Sidra Safraz, Tarek Turk, Marlene Dytoc
Supervisor: Dr. Marlene Dytoc

INTRODUCTION
Teledermatology has become increasingly important during the COVID-19 pandemic. This study aimed to examine the practice patterns, advantages, and challenges of using teledermatology for the management of skin conditions in Canada.

METHODS
A cross-sectional survey was conducted among Canadian dermatologists. Participants were recruited through email lists and the Canadian Dermatology Association's media platforms. The survey included questions on participants' demographic characteristics, teledermatology practice patterns, advantages and disadvantages of using teledermatology, satisfaction with teledermatology platforms, and challenges of managing patients through teledermatology.

RESULTS
A total of 33 respondents completed the survey. Most participants (66.7%) started using teledermatology during the pandemic. Respondents reported that teledermatology constituted 0-25% of their practice, with store-and-forward being the most efficient interaction model (42.4%). Respondents were mainly neutral when asked about whether teledermatology lowers healthcare costs (30.3%) and enhances efficiency of care (30.3%). Approximately half of the participants stated they were in agreement with the statement "I plan to use or keep using teledermatology in the future". Respondents reported that the potential advantages of teledermatology were increasing healthcare access and health equity. The main challenges of managing patients through teledermatology were diagnostic accuracy and physical exams.

CONCLUSIONS
The study showed that most respondents started using teledermatology during the COVID-19 pandemic, and the majority of respondents used store-and-forward as the interaction model. Respondents were mainly neutral regarding whether teledermatology enhances efficiency of care and lowers healthcare costs. The potential advantages of teledermatology were found to be increasing healthcare access and health equity, while the main challenges were related to diagnostic accuracy and physical exams. These findings may inform future research and the implementation of teledermatology in clinical practice.

Workflow Metrics in Simultaneous Acute Code Stroke Activation and Stroke Reperfusion Therapies

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supervisor Dr. Mahesh Kate

INTRODUCTION

We aim to assess the effect of simultaneous acute code stroke activation (ACSA) in patients undergoing reperfusion therapies in the emergency department on workflow metrics and home time at 90 days

METHODS

We assessed ACSA over 20 months from the QuICR(Quality Improvement and Clinical Research Alberta Stroke Program) Registry. We defined Simultaneous ACSA, code activation within 60 min of the arrival of any patient receiving intravenous thrombolysis or code activation within 150 min of the arrival of any patient receiving endovascular thrombectomy or code activation within 45 min of the arrival of any patient receiving no reperfusion therapies (based on the Canadian Triage and Acuity Scale, average local door-to-needle and door-to- puncture times). (Figure 1.0)

RESULTS

A total of 2605 ACSA occurred at a mean±SD of 130.8±17.1 per month during the study period. 545 (20.9%) underwent acute reperfusion therapy with a mean age of 70.6±14.2 years, 45.9%(n=254) were female and a median (IQR) NIHSS of 13(8-18). Simultaneous reperfusion therapies occurred in 220 (40.4%). There was no difference in the median door-to-CT time between the simultaneous (16, 11-22 min) and non-simultaneous (15, 11-21 min, p=0.3) activations. There was no difference in the median home time at 90 days between the two groups.

CONCLUSIONS

Simultaneous ACSA is frequent in patients receiving acute reperfusion therapies. An optimal workflow may help mitigate the clinical and system burden associated with simultaneity.