2011-12

LEADERS IN MEDICINE
UNIVERSITY OF CALGARY

FACULTY OF MEDICINE | UNIVERSITY OF CALGARY

Prepared for the Dean of Medicine
Prepared by Michelle Selman and Dr. Paul Beck

Research Symposium Mosaic

Adam Thomas' photo of Northern Lights near Yellowknife, NWT
while completing Clerkship as member of the Rural Integrated Community Clerkship program

ANNUAL REPORT

Reporting another successful year for the University of Calgary's Leaders in Medicine (LIM) program from June 2011 to May 2012. The program began in 1996.

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INTRODUCTION

The Leaders in Medicine program's goal is to train and encourage students to pursue dual careers in medicine and research and to become leaders in the changing world of health care.

Starting with an enrolment of two students in 1996-97, the program's enrolment has consistently grown and is now at 54. New enrolment each year either matches the number or exceeds the number of students completing the program and the full program enrolment currently remains consistently between 50 and 60.

2011-12 was an exceptionally successful year. All students actively participate in seminars, symposiums and other events. The program has an energetic student executive and mentorship program which helps motive our students. Our goal, to encourage students to pursue varied paths that can involve dual careers, is succeeding.

This report will demonstrate accomplishments made by individual students and by the program as a whole.

OVERVIEW

In order to be part of the Leaders in Medicine's full program, a student must be accepted into a University of Calgary graduate program and also accepted in the University of Calgary medical school. The student applies separately to both programs. The typical student will be in first or second year of his/her graduate program when he/she receives acceptance into the Undergraduate Medical Education program. When that acceptance is received, the student can apply to LIM and once enrolled will make a decision whether to defer medical school in order to complete the graduate program or to enter medical school and complete the graduate program later. The majority of students choose to complete graduate school first, but they have the option to start medical school and complete graduate school later. After discussion with both the Leaders in Medicine program director, his/her graduate program supervisor and UME the student is asked to make a plan for completion and if acceptable can design an individual option.

The following is a chart of sample options of choices (not numbered in order of importance or program recommendation) to complete a joint degree within the Leaders in Medicine Program:

MD/PhD Option I

18 months	48 months		18 Months
MD	Graduate study and thesis defence		MD
MD Systems courses	Graduate courses, candidacy exams, research and writing of thesis	Thesis Defence	Clerkship and completion of MD curriculum

MD/PhD Option II

48 months		36 months
Graduate course, candidacy exam, research and writing of thesis	Thesis Defence	MD Curriculum including clerkship

MD/PhD Option III

24 months	18 months	24 months		18 months
Graduate courses, candidacy exam, research and thesis proposal	MD systems courses	Completion of research and writing of thesis	Thesis Defence	Clerkship and completion of MD program

MD/MSc Option I

18 months	24 months		18 Months
MD	Graduate study and thesis defence		MD
MD Systems courses	Graduate courses, research and writing of thesis	Thesis Defence	Clerkship and completion of MD curriculum

MD/MSc Option II

24 months		36 months
Graduate course, research and writing of thesis	Thesis Defence	MD curriculum including clerkship

All these options and others are available with permission from the program director and dean of medical school. Graduate Students who are accepted into medical school are encouraged to first complete their graduate degree before entering medical school.

PROGRAM ADMINISTRATION

Although the program administration is overseen by the Director, Dr. Paul Beck, the Co-Director, Dr. Morley Hollenberg and administration on a daily basis is done by the LIM Program Advisor, Michelle Selman, none of those positions are full-time within the program. The directors are volunteers and the Graduate Science Education department in the Faculty of Medicine supports the program advisor position with one-third of that position's responsibilities being LIM. Therefore in order to make the program work as well as it does, much of it is student led.

LIM is a Program for the Students by the Students!

Students are an important part of administration of the LIM program, especially the educational events. Many students are involved in the overall organization of the program with a dedicate group that organizes the Research Symposium, Research in Progress (RIP) meetings, Translational Journal Club and Visiting Speaker series *(more about these starting on page 5 of this report.)* Students are involved in every aspect of the program including presenting program details to incoming new graduate and medical students. Student administration is by Executive Committee.

2011-12 LIM Student Executive:

Chair — Andrea **Mosher** MD/PhD

Committees:

Communications	Lorie **Kwong** MD/MSc; Jason **Bau** MD/PhD and Hamza **Jalal** MD/MSc
Visiting Speaker Series	Kimchi **Nguyen** MD/MSc
LIM Research Seminar	Kyla **Huebner** MD/PhD and Braedon **McDonald** MD/PhD
Research in Progress	Chris **Sibley** MD/PhD and Dustin **Anderson** MD/PhD
Journal Club	Dustin **Anderson** MD/PhD
Social Committee	Kovid **Lee** MD/MSc; Taryn **Hill** MD/MSc and Ian **Hons** MD/PhD

This year the communications committee created a new brochure for the program. The executive also started a student survey which proved to be very helpful in planning the direction of the program.

MEMBERSHIP SURVEY

In June 2012 the Executive sent out a survey to the LIM membership in order to measure satisfaction on a number of levels, 46 students responded. Here are a few of the results and questions:

"How would you rate your satisfaction with the Leaders in Medicine Program at the University of Calgary?"

87.8% responded **Satisfied to Very Satisfied.**

Comments:

"I have appreciated the recent brainstorming and group consultations re: a specific topic. It has allowed people from various backgrounds to bring forth their area of expertise and perspective."

"I really enjoyed the Research in Progress format this year. I thought it was great to have a format that developed critical thinking, rather than just sitting through more lectures (like most RiPs)"

"The flexibility of the program is unprecedented. Excellent support from the program directors to do whatever we can envision."

Other positive comments were along the same line, noting the program's flexibility, administrative and director support, mentorship and educational programs.

"How would you rate the leadership of program Directors?"

89.8% responded **Good to Excellent.** Another 9% responded Average

Comments:

"They are very interested in making sure the students maintain a balance with life, school and extracurricular. I think it is important to hear from them that sometimes we have to say no, and prioritize a certain way, and they do a very good job of making sure we think about what is important to us and how we can succeed in those areas."

"Excellent support of LIM members throughout they're (sp) combined degree. They support new ideas that members have. They foster collaborations with other organizations and universities."

"How satisfied were you with the quality of the Research in Progress sessions this year?"

61.4% were **Satisfied to Very Satisfied.** About 10% were not satisfied.

Any suggestions for improvement are to be addressed for next year's program.

"How satisfied were you with the Journal Club sessions this year?"

84.6% were **Satisfied to Very Satisfied.** The rest were Neutral.

Comments:

"A good mix between epidemiology, basic science, translational science and research information sessions. Information sessions regarding pursuing research and medicine together."

"I think it is just important to balance the clinical and research, in order to keep people involved and discussion open."

"How satisfied were you with the format of the LIM Research Symposium?"

79.54% responded **Satisfied to Very Satisfied.** 17% were Neutral.

Comment:

"The symposium is well-run and wee-attended. Would it be possible to organise a Western-Canadian symposium for MD-plus students?"

All responses from the survey that included suggestions for improvement are passed on to be discussed by the directors and the new student executive committee for possible implementation in the upcoming year. Surveys are used as part of the ongoing goal of growth and program improvement.

Program Director's Report

Dr. Paul Beck Dr. Morley Hollenberg

This has been an exciting year for LIM students. With 54 full and 33 affiliate members we have a large, enthusiastic student body. Our attendance at all LIM activities (including Research in Progress, Visiting Speaker Series, Translational Journal Club and the LIM Research Symposium) is excellent. We had great success at the Winnipeg and CITAC National clinician-science in training conference with our students winning a number of the presentation awards! All the LIM students did extremely well on the residency match this year with all getting their first choice and one student getting their second choice. This success at the match is much above the general medical school student body. LIM students Published 59 papers (many in very high impact journals), 21 are submitted. They had 100 abstracts, 6 book chapters and did 118 presentations (69 local and 49 at National/International Meetings!) Our students won approximately 95 awards, many that were at the Provincial and National level and some at the International level! Overall it has been an outstanding year!

Mentorship

Mentorship is a critical aspect of the LIM program. The director (Dr. Beck) and co-director (Dr. Hollenberg) as well as our program administrator (Ms. Selman) frequently meet with students. We developed a program where clinical clerks from the LIM Program return and talk to the 1st and 2nd year medical students to give them advice on clerkship. This has been an outstanding success. We strive to set up "mentorship flow" where we help identify mentors for the students to help them through their graduate program, medical school, clerkship, residency and ideally to the point of their first faculty position. We identified ex-LIM students and/or others at all universities across Canada that can help mentor students when they start at a new medical facility. This has been critical to aid many students while settling in, to quickly get involved in research groups and other such programs as they pursue residency.

Dr. Beck was recognized for his mentorship work and Awarded the van de Sande Distinguished Achievement Award for Mentoring, Department of Medicine, University of Calgary, 2012, the International Research Mentor Award, American Gastroenterology Association Institute Council Immunology, Microbiology and Inflammatory Bowel Disease Section, 2012 as well he received the Watanabe Distinguished Achievement Award for overall excellence. This is one of the highest awards given out by the University of Calgary, Faculty of Medicine, 2011 and was Awarded the Outstanding Achievement Award for the individual that has contributed the most to the Division of Gastroenterology at the University of Calgary 2011. He was also recognized by his clinical peers and awarded the Outstanding Clinician Award at the Foothills Hospital, 2011. Both Drs. Beck and Hollenberg remain committed to mentoring LIM students so they can achieve success in research, medicine, teaching and mentorship.

LEADER IN MEDICINE – EDUCATIONAL EVENTS

In order to maintain active membership in the Leaders in Medicine program, students must attend a number of seminars, events, and when possible academic conferences. Students commit to between 2 to 4 hours per month in order to attend at least one of these events. Monthly there is a Research in Progress seminar and a Journal Club meeting where students either share their particular research interests or listen to presentations. Approximately every 3 months or more a visiting speaker is invited to present and students not only attend the seminar but often attend an informal lunch where they ask questions and share ideas with the speaker. Once a year there are two specific out-of- town conferences for which students are encouraged to submit abstracts and if possible attend – the Canadian National Medical Student Research Symposium (CNMSR) and the Clinician Investigator Trainee Association of Canada (CITAC). LIM student travel to these conferences is funded in part or in total by the program.

CNMSR is held in June and this year 4 Leaders in Medicine students submitted and presented at the symposium in Winnipeg, sponsored by the University of Manitoba. The CITAC symposium is held in Ottawa in September. This year 16 students attended and presented posters. Several won awards *(see full report under specific CITAC report on page 7.)*

The jewel in our Educational Events is the Annual Research Symposium, held in November. This year, a successful, former, Leaders in Medicine graduate, Dr. Douglas Hamilton was keynote speaker. More than 60 students participated: 55 presenting posters and 6 offering oral presentations.

ANNUAL LEADERS IN MEDICINE SYMPOSIUM

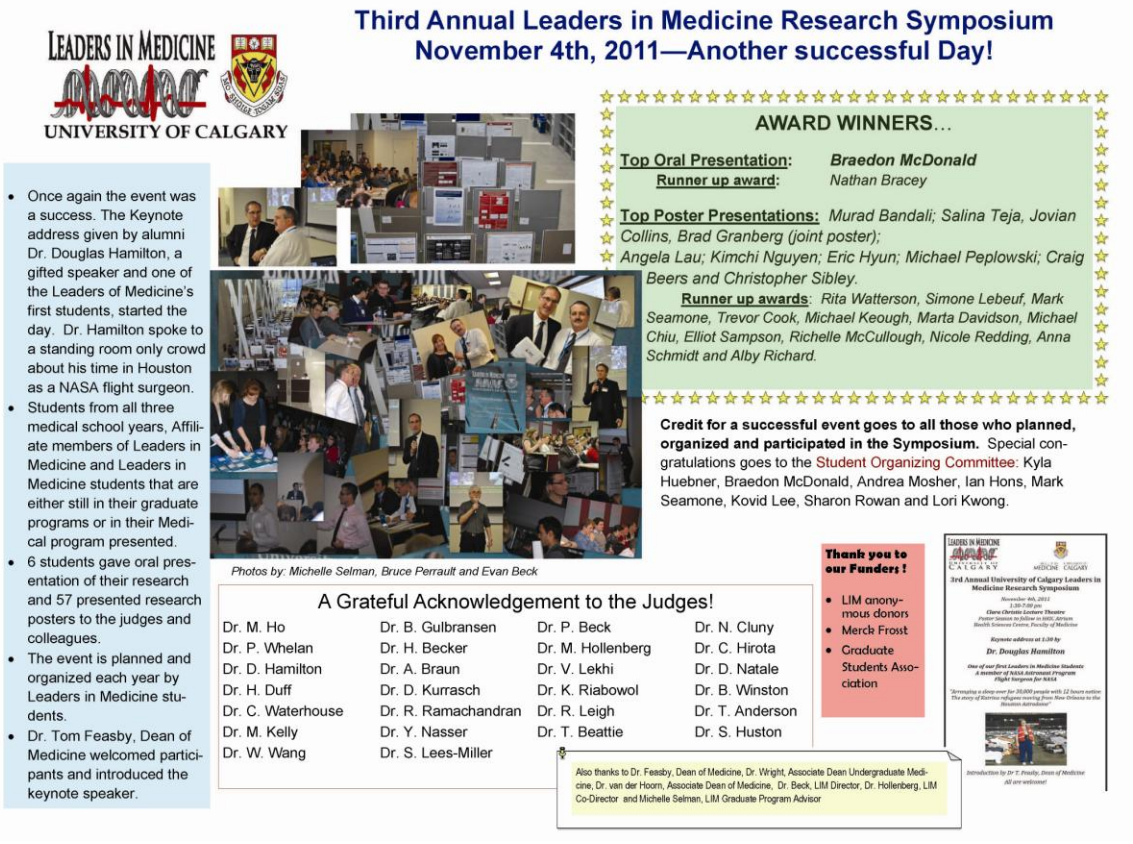
This event, which is student organized and run, continues to more successful each year. A call for abstracts brought a large response, 55 posters were accepted along with 6 oral presentations. Keynote speaker, Dr. Hamilton is a joint degree Alumni *(see page 10.)*

Dr. Hamilton's presentation

Collage of events

Dr. Beck and oral presentation winner Braedon McDonald

Summary Poster of the 3rd Annual Leaders in Medicine Research Symposium



See Appendix A for all details.

RESEARCH IN PROGRESS (RIP) – STUDENT SPEAKER SERIES

This monthly meeting allows students to share their specific research. Presentations are short and specific with much time given to questions and discussion. This program is student-run Dustin Anderson and Chris Sibley co-chairs this series.

Example of presentations:

Date	Speaker(s)	Title	# attending
June 7, 2011	Saara Rawn (1) Kevin Solverson (2)	Various	27
Aug 6, 2011	Groups	3 groups to discuss research interests	49
Dec 13, 2011	Guest speaker: Dr. John Lau		30
Feb 7, 2012	"patient"	Patient presentation – Obesity Study experiences	45
May 8, 2012	Miscellaneous	Various	32
Aug 1, 2012	Schmidt/MacEachern/Beck	Enteric glia medicate ion transport abnormalities in mouse coleon during colitis	45
Sep 4, 2012	Blades/Lewinson/Keough	Various	26
Oct 2, 2012	Bau/Sullivan/Tulk	Research updates and TED talks	41
Nov 6, 2012	Miscellaneous	Various	43
Dec 4, 2012	Wiber/Sampson/Eslinger	Various	39

JOURNAL CLUB – SEMINAR SERIES

Another monthly event, this is designed to provide opportunities to learn about research outside a student's field. These are moderated by invited experts from the Faculty of Medicine.

Date	Speaker(s)	Title	# attending
May 19, 2011	Saara Rawn		27
June 14, 2011	Rithesh Ram		33
Aug 29, 2011	Chris Sibley	Microbiology	31
Sep 30, 2011	Ian Hons	Brain-Gut Interactions	35
Oct 28, 2011	Sarah Tulk	The Inflammasome	40
Nov 25, 2011	Nathan Bracey	Neutrophil Chemotaxis	42
Jan 27, 2012	Craig Beers	Epilepsy and clinical functional magnetic resonance imaging	22
Feb 22, 2012	Christina Thornton	Gut Microbiome	18
Mar 30, 2012	Angie Karlos	Men are from Mars, Women are from Venus: Research Implications of Being from Different Planets	12
Apr 27, 2012	Amanda Eslinger	Obesity	23
May 25, 2012	Kim Williams	Changes in BMI over 6 years: The role of demographic and neighbourhood characteristics	27
Jun 29, 2012	Dustin Anderson	ION Channels	17
Aug 31, 2012	Dr. Paul Beck		37
Sep 28, 2012	Andrea Mosher	Progesterone & Labour	26
Nov 30, 2012	Miscellaneous	Various	43

VISITING SPEAKER SERIES

An important aspect of the LIM program is the active promotion of mentoring opportunities for its students. A constant challenge in training the next generation of clinician scientists is to allow connections with clinician scientist to develop and nurture over the course of the training program. The obvious time limitations (on both the part of the student and faculty) can limit these opportunities, a detriment for those interested in pursuing a clinical investigator career path. Therefore the program has made it is priority by incorporating a speaker series with local clinician scientists. Faculty members are asked to discuss training and career paths as well as their current research to a group of students and students are encouraged to ask questions that might not come up outside of this format. Questions have included, "what were your greatest challenges?" "What is the most rewarding part of your job or your most difficult career decision?" These sessions provide a unique opportunity for students to broaden their understanding of the career of a clinician scientist. A student committee coordinates the series each year with a goal of one every 3 months or more.

CANADIAN NATIONAL MEDICAL STUDENT RESEARCH SYMPOSIUM

This is a unique education opportunity for Leaders in Medicine students to meet with MD/PhD students, medical students and researchers from other parts of Canada. Four students received travel awards through Leaders in Medicine funding one of those was funded partially by her graduate program supervisor. Students attending: Kathleen Gibson (Affiliate); Mark Gillrie; Andrea Mosher and Judy Luu.

CITAC/CSCI Young Investigators Forum

Held in September, this was a particularly successful event for LIM students. Here's a copy of the notice of winners. One of our students is editor and designer of the CITAC Newsletter for January 2012 and the program's student executive chairperson, Andrea Moser was a key contributor, writing about the Annual meeting in Ottawa and reporting on our Annual Leaders in Medicine Research Symposium. Newsletter is attached as Appendix C.

Students attending are asked to apply for a graduate program or UME travel awards, and if available their CIHR or AI-HS research allowances however, no student is refused because of lack of funding. Any travel expenses not paid by other funders are reimbursed through the Leaders in Medicine funds from anonymous donors.

Three of our students received poster awards and one an oral presentation award.

Congratulations to the 2011 Young Investigators Forum Prize Winners!
Poster Prize Winners:

Braedon McDonald, University of Calgary
Christopher Sibley, University of Calgary
Alby Richard, McGill University/University of Calgary
Andrew Perrin, University of Toronto
Clara Westwell-Roper, University of British Columbia
Gareth Mercer, University of British Columbia

Oral Presentation Prize Winner:

Nathan Bracey, University of Calgary

Student accepted to attend 2011 CITAC/CSCI Forum

Thornton, Christina – Poster
Ludwig, Taryn – Poster
Kwong, Lorie – Poster
Schmidt, Anna – Poster
Nguyen, Kimchi – Poster
Reikie, Brian (Affiliate) – Poster
Ram, Rithesh – Poster
Richard, Alby (Affiliate) – Poster
Sibley, Chris – Poster
Rawn, Saara – Poster
Mosher, Andrea – Poster
Bracey, Nathan – Oral Presentation
Lawson, Keith – Poster
Roy, Amrita – Poster
Chiu, Michael – Poster
McDonald, Braedon – Poster

Current Leaders in Medicine Student Stats

This program year included 54 students from several graduate programs within the Faculty of Medicine:

MDBC	-	3 MSc	1 PhD
MDCH	-	6 MSc	3 PhD
MDCV	-	0 MSc	2 PhD
MDGI	-	0 MSc	1 PhD
MDIM	-	3 MSc	3 PhD
MDMI	-	1 MSc	2 PhD
MDNS	-	2 MSc	4 PhD
MDSC	-	7 MSc	6 PhD

There are 10 students in other Graduate programs:

BISI	-	1 MSc	1 PhD
Chem	-	1 MSc	0 PhD
KNES	-	4 MSc	1 PhD
M Eng	-	1 MSc	0 PhD
CPSC	-	1 MSc	0 PhD
Total:		30 MSc	24 PhD

STUDENT LIST 2011-12 (FULL LIM STUDENTS = 54)

Name	Degree/Program		Name	Degree/Program	
Anderson, Dustin	MD/PhD	MDNS	Moser, Joanna	MD/PhD	MDSC
Beers, Craig	MD/PhD	MDNS	Mosher, Andrea	MD/PhD	MDSC
Bracey, Nathan	MD/PhD	MDSC	Mummery, Ashley	MD/MSc	MDSC
Chiu, Michael	MD/MSc	BISI	Nguyen, Kimchi	MD/MSc	MDIM
Cook, Trevor	MD/MSc	MDCH	Nicholl, David	MD/MSc	MDSC
Damani, Zaheed	MD/PhD	MDCH	Nicholson, Cherie	MD/MSc	MDCH
Dunbar, Mary	MD/MSc	MDNS	O'Connor, Pamela	MD/PhD	BISI
Dykeman, Jonathan	MD/MSc	MDCH	Peplowski, Michael	MD/PhD	MDSC
Eslinger, Amanda	MD/MSc	MDBC	Ram, Rithesh	MD/PhD	MDCH
Esmail, Kaisra	MD/MSc	MDSC	Rawn, Saara	MD/PhD	MDBC
Gillrie, Mark	MD/PhD	MDIM	Redding, Nicole	MD/MSc	MDSC
Hons, Ian	MD/PhD	MDGI	Rowan, Sharon	MD/MSc	KNES
Huebner, Kyla	MD/PhD	MDSC	Roy, Amrita	MD/PhD	MDCH
Hyun, Eric	MD/PhD	MDSC	Sampson, Elliot	MD/MSc	MDSC
Jalal, Hamza	MD/MSc	MDNS	Sarna, Neha	MD/MSc	KNES
Kapur, Puneet	MD/MSc	CPSC	Schmidt, Anna	MD/PhD	MDCV
Karlos, Angela	MD/MSc	KNES	Seamone, Mark	MD/MSc	MDIM
Keough, Michael	MD/PhD	MDNS	Sibley, Christopher	MD/PhD	MDMI
Khambati, Husain	MD/MSc	MDMI	Solverson, Kevin	MD/MSc	MDMI
Kwong, Lorie	MD/MSc	MDIM	Thomas, Adam	MD/MSc	MDCH
Lail, Prabh	MD/MSc	MDCH	Thornton, Christina	MD/PhD	MDMI
Lee, Kovid	MD/MSc	CHEM	Tsang, Allison	MD/MSc	MDBC
Leung, Karen	MD/MSc	MDCH	Tulk, Sarah	MD/MSc	MDBC
Lorincz, Caeley	MD/PhD	KNES	Wadhwani, Aman	MD/MSc	MDSC
Ludwig, Taryn	MD/MSc	M ENG	Walsh, Sarah	MD/PhD	MDNS
Luu, Judy	MD/PhD	MDCV	Xiang, Richard	MD/PhD	MDIM
McDonald, Braedon	MD/PhD	MDIM	Yaraskavitch, Megan	MD/MSc	KNES

LEADERS IN MEDICINE AFFILIATE PROGRAM

The LIM Affiliate Program was started last year at the request of the medical school student body. A group of medical students approached the Directors, stating that they wanted to be involved in the program even though they were not currently pursuing a joint degree. Some of these students had completed graduates degrees before medical school (thus not eligible for the joint degree LIM program) others were finishing graduate programs at a different University (and again not eligible for standard LIM membership) and finally many students were interested in the program to further their education but did not have a graduate degree. Since furthering and enriching education in regard to basic science or other areas is our mandate we developed the LIM Affiliate Program. Medical students are allowed to participate in all activities (including Research in Progress, Visiting Speaker Series, translational Journal Club and the LIM Research Symposium). They are also eligible to present at the national meetings for clinician-scientists in training (CITAC) and they were eligible to apply for a LIM travel award in order to attend other conferences. This program is a success and has grown to enrolment of 33 students. Affiliates are actively involved in LIM activities and greatly enhance the LIM student body. Some of these students have decided to put medical school on hold and pursue a graduate program (thus becoming full LIM members).

STUDENT ACCOMPLISHMENTS

ALUMNI

Leaders in Medicine students go on to be successful doctors and clinicians. The following are highlights of two of joint degree students:

Douglas R. Hamilton, MD/PhD 1991
Associate professor, Faculty of Medicine and W21C member
former NASA Flight Surgeon

Article from Faculty of Medicine website -

Dr. Hamilton practicing CPR in zero gravity. Douglas Hamilton, former NASA Flight Surgeon and now associate professor and W21C member, University of Calgary, has been awarded the Exceptional Engineering Achievement Medal by NASA. This Agency Honor Award is given for accomplishments far above others in quality, scope, and impact which are explicit, significant, and demonstrate results.

Dr. Hamilton received this award for his work in identifying and clarifying the potential risk of electric shock that could happen to astronauts who were performing spacewalks (also referred to as extra-vehicular activities or EVAs) on the International Space Station.

From continued construction to daily maintenance, EVAs are a necessary component to day-to-day living for most astronauts on the station and eventually the moon. Through collaboration with the Naval Medical Research Unit Directed Energy Weapons Laboratory and NASA/Boeing Space Environments Division, Dr. Hamilton was instrumental in the development of super-computer models to predict where electric discharge may occur along the metal points in spacesuits during EVA. This work clearly modeled an electrical conductance pathway through the human body that could cause serious or fatal electric shock to astronauts. Dr. Hamilton's work has served to inform the design of new EVA suits, has reworked the space vehicle electrical human systems standards, and is being considered for use in the automotive, aerospace, and toy manufacture industries to increase public safety.

The medal was presented during the NASA Honor Awards Ceremony to Dr. Hamilton on September 6, 2012 at the Johnson Space Center in Houston, Texas.

Dr. Hamilton has previously been awarded a number of accolades including the University of Calgary's Distinguished Alumni Award.

Dr. Hamilton was this year's Leaders in Medicine Annual Research Symposium's Keynote Speaker. He has 41 publications. http://www.ncbi.nlm.nih.gov/pubmed/?term=Hamilton%2C+douglas+r

Slava Epelman, MD/PhD 2005
Instructor of Medicine, Center for Cardiovascular Research,
Cardiovascular Division, Washington University of Medicine
St. Louis, Missouri, USA

Here is a portion of his bio on the Washington University in St. Louis website –

B.Sc. Hon (Molecular Biology), University of Calgary. Calgary, Alberta, Canada (1993-1998); PhD. (Immunology) University of Calgary, Calgary, Alberta, Canada (1998-2005); M.D. University of Calgary, Calgary, Alberta, Canada (2002-2005); Resident, Internal Medicine, Cleveland Clinic, Cleveland, OH, (2005-2008); Clinical Cardiology Fellow, Baylor College of Medicine, Houston, TX. (2008-2010); Clinical Cardiology Fellow and Postdoctoral Research Fellow, Washington University (2010-2011); Instructor of Medicine, Center for Cardiovascular Research, Cardiovascular Division, Washington University (2012 - present)

My research interests are both basic science and translational in nature. My basic science research is focused on understanding the role monocytes play within the myocardium during health and disease. Monocytes are a heterogeneous population of cells with distinct phenotypes and functions, participating in the initial inflammatory and subsequent wound healing responses after myocardial tissue injury. Understanding how individual monocyte subsets are activated, what factors regulate their entry, persistence and fate after entry into the myocardium are the current focus of my work. In addition, I have ongoing integrated translational projects that focus on the corresponding human monocyte subsets, how they are activated and how their activation state relates to myocardial function and myocardial recovery in patients following myocardial infarction. Lastly, I am interested in biomarkers in the setting of myocardial dysfunction, in particular how angiotensin converting enzyme 2 (ACE2) - a novel member of the renin-angiotensin system, can be used to risk stratify patients with cardiovascular disease.

Dr. Epelman has won a number of Honors and Awards, and has 16 published papers, many in high impact journals.
http://cardiology.wustl.edu/faculty/15-faculty/research/148-slava-epelman-md-phd.html

CURRENT STUDENTS

2011-12 RESIDENCY RESULTS:

Another successful graduating group:

LIM Student Name		Degree	CARMS	Speciality	Location
Gillrie	Mark	MD/PhD	Internal Medicine, Calgary	1st	1st
Lail	Pragh	MD/MSc	Internal Medicine, Calgary	1st	1st
Khambati	Husain	MD/MSc	Vascular, Ottawa	1st	1st
Yaraskavitch	Megan	MD/MSc	Neurology, Calgary	1st	1st
Dunbar	Mary	MD/MSc	Pediatric Neurology, Vancouver	1st	1st
Hyun	Eric	MD/PhD	General Surgery, Halifax	1st	2nd
O'Connor	Pamela	MD/PhD	Dematology, Vancouver	1st	2nd
Lorincz	Caeley	MD/PhD	Family Medicine, Calgary	2nd	1st
Walsh	Sarah	MD/PhD	Neurology, Ottawa	1st	2nd
Esmail	Kaisra	MD/MSc	Radiology, Ottawa	1st	3rd

AFFILIATES

Chretien	Marc	MD/	Internal Medicine, Montreal	1st	2nd
Gibson	Katherine	MD/	Family Medicine, Toronto	1st	1st

AWARDS

More than ninety (90) awards were given to LIM students this year. Below is a highlight of some students who had an extremely successful year.

Neuroscience Grad Wins Governor General's Gold Medal Award *by Léora Rabatach*

Dustin Anderson is the winner of this year's Governor General's Gold Medal Award at the doctoral level. This is one of the most prestigious awards that a student in a Canadian educational institution can receive.

Along with supervisor Ray W. Turner and co-supervisor Gerald Zamponi, Anderson was central to the team discovering a link between two separate classes of ion channels that would normally be expected to work against one another, in terms of modifying electrical excitability. Instead, Anderson found that they actually work in tandem to affect nerve impulse generation in the brain - helping brain cells communicate with each other.

In addition to providing scientists with a more accurate picture of electrical regulation in neurons of the cerebellum, this groundbreaking research redefines how scientists view the control of neurons that express these ion channels throughout the brain. In the future, this could lead to advances in drug therapies for a number of neurological and movement disorders.

Anderson is part of the **Leaders in Medicine Program** at the Faculty of Medicine's Hotchkiss Brain Institute. He completed his PhD in June of 2011, and is now in his first year of medical school at the University of Calgary.

For more than 137 years, the Governor General's Academic Medals have recognized the outstanding scholastic achievements of students in Canada. Anderson will receive the award at a convocation ceremony at the University of Calgary on November 10, 2011.

Craig Beers, MD/PhD: First Place Poster, 3rd Annual Leaders in Medicine Symposium – Nov 2011; Best Overall Poster, Alberta Graduate Conference, Alberta Graduate Council – May 2011

Mark Gillrie, MD/PhD: Gold medal for top MD/PhD presentation at the CIHR National Medical School Student Research Symposium – Jun 2011; Excellence in Research Award for thesis defence, Immunology Department March 2012

Joanna Moser, MD/PhD: Medical Science Academic Productivity Scholarship, MDSC Graduate Program, University of Calgary, Faculty of Medicine, Oct 2011; Honorary Izaak Walton Killam Pre-Doctoral Scholarship, University of Calgary, Faculty of Medicine, Jul 2011; and Honorable Mention 2011 Dr. Lydia Sikora Memorial Award, Undergraduate Medical Education, University of Calgary, Faculty of Medicine, Jan 2012.

David Nicholl, MD/MSc: Medical Sciences Program Publication Award, Department of Medical Sciences, Faculty of Medicine, University of Calgary, December 2011, January 2012 and February 2012;

Rithesh Ram, MD/PhD: Dr. Gary McPherson Leadership Scholarship, 2012; Canadian Federation of Medical Students/Royal Bank of Canada Leadership Scholarship, 2011; Laurence Decore Award for Student Leadership, Government of Alberta, 2011; American College of Physicians: Internal Medicine 2011 Research Poster Competition Winner, 2011;

Christopher Sibley, MD/PhD: Winner, Canadian Investigator Trainee Association of Canada Young Investigators Forum, Ottawa, 2011; Best Poster Presentation and Poster of Distinction, Third Annual Leaders in Medicine Research Symposium, University of Calgary, 2011; Canadian Institutes of Health Research MD/PhD Award, 2011; Winner, Building Bridges Program Competition (MD/PhD University of Calgary – University of British Columbia Exchange Program), 2011; Runner-up, Lydia Sikora Award for Research Excellence, Faculty of Medicine, University of Calgary, 2011

Christina Thornton (nee Eshaghurshan) MD/PhD: Top Oral presentation, Alberta Graduate conference, May 11; Alberta Graduate Citizenship Award, Government of Alberta Jan 11; Alberta Graduate Award, Government of Alberta Jan 11.

TYPES OF AWARDS (listed by LIM Students' 2011-12 Annual Reports)

1. The Lung Association - Studentship, Alberta and NWT, May 11-Mar 12, $10,000
2. Persons Case Scholarship, Alberta Government, December 11, $1,000
3. Nat Christie Foundation Medical Entrance Award (Renewal), University of Calgary, Faculty of Medicine, 11-12, $5,000
4. Graduate Student's Heritage Scholarship, Government of Alberta, 2012, $3000
5. Faculty of Kinesiology MSc Travel Award, University of Calgary, Faculty of Kinesiology, Mar 12, $500
6. Faculty of Kinesiology Graduate Scholarship, University of Calgary, Faculty of Kinesiology, 11-12, $8000
7. Alberta Cancer Foundation Graduate Studentship, 11-12, $20,000
8. Poster prize runner-up, University of Calgary 3rd Annual Leaders in Medicine Research Symposium, 2011
9. Best Student Paper, 1st Annual University of Alberta Urology Research Day. Edmonton, Alberta, Oct 2011, $500.
10. 1st Place Kidney Session/Poster Presentation, 87th Western Section American Urological Association Annual Meeting; Vancouver, BC, Aug 2011.
11. Alberta Cancer Foundation Graduate Studentship Award, Alberta Cancer Foundation, Jul 2011. $40,000
12. 2011 American Association of Immunologists Trainee Achievement Award, $1000.
13. American Association of Immunologists Abstract Award, 2011, $500**.**
14. Immunology Program Research Excellence Award, University of Calgary, Faculty of Medicine. 2011, $1000
15. JB Hyne Research Innovation Award, University of Calgary, Faculty of Graduate Studies. 2011, $500
16. 2011 CSCI Young Investigators Forum (CSCI) Poster Presentation Award, CSCI. 2011, $75
17. AHFMR MD-PhD studentship award. AHFMR/AIHS. 2008-2012, $20,000 per year
18. Queen Elizabeth II Graduate Scholarship, University of Calgary, Faculty of Medicine, 2011 (discontinued upon start of CIHR funding), $10,500.00
19. Frederick Banting and Charles Best Canada Graduate Scholarships – Master's Award, CIHR, 11 – 12; $17, $500.00
20. LIM MD/PhD Scholarship, CIHR and University of Calgary, Faculty of Medicine, Sept - Aug, $21,000
21. Leaders in Medicine Tuition Award, University of Calgary, Faculty of Medicine, $14,000
22. Dr. Gerald Stewart Memorial Award, University of Calgary, Faculty of Medicine Dec, $750
23. Dr. Lydia Sikora Memorial Award, Runner-up, University of Calgary, Faculty of Medicine Dec, $1,500
24. Young Investigator Award, Runner-up, at American Society of Tropical Medicine and Hygiene (ASTMH) at the ASTMH 60th Annual Meeting Dec, $250
25. Gold medal for top MD/PhD presentation at the CIHR Canadian National Medical Student Research Symposium – 2011, $1,000
26. MD-PhD Studentship, AIHS Alberta Innovates-Health Solutions. Sep 2011 – Aug 2017 (Renewable Annually): $30,000.
27. Have-a-Heart Bursary, Canadian Cardiology Society. October 2011. Conference Award funding, no monetary value.
28. Gerry L. Weber Cosmopolitan Award for Research in Diabetes. September 2011. $20,000 (AI-HS MD-PhD studentship annulled eligibility).
29. Achievers in Medical Sciences Award, University of Calgary, Faculty of Medicine, Sept 2011 – Aug 2012, $25,000
30. MD / PhD Studentship, Alberta Innovates – Health Solutions, September 2012 – August 2018, $30,000/year
31. Leaders in Medicine Tuition Award, University of Calgary, Faculty of Medicine, $14,000
32. CIHR MD/PhD Top up award; Jan 12-Aug 10 $5,000
33. Alberta Innovates Health Solutions Award, Sept 2011-Sept 2012 $30,000
34. MS Society of Canada Award, Sept 2011-Sept 2012 $5,400
35. RBC Royal Bank Scholarships for Medical and Dental Students, External Award. Sept '11-Aug '12, $15,000
36. Investigator-Driven Small Grant from the Alberta Centre for Child, Family and Community Research. 2011-2012 $40,000
37. Frederick Banting and Charles Best Canada Graduate Scholarship – Doctoral Award, Canadian Institutes of Health Research (CIHR), Sept 2011-Aug 2012, $30,000 stipend + $5,000 research allowance
38. Achievers in Medical Science (AIMS) Research Excellence Award, University of Calgary. Sept 2011–Dec 2011, $3,500
39. Alberta Health Innovates Solutions, University of Calgary, Faculty of Medicine, Sept 11 $30,000/year
40. Leaders in Medicine Tuition Award with CIHR Stipend, University of Calgary, Faculty of Medicine, $21,000
41. Distinguished Poster Award, Leaders in Medicine Symposium, University of Calgary, Faculty of Medicine $50

42. Undergraduate Medicine Elective Travel Award, University of Calgary, Faculty of Medicine, 2011, $6,000
43. Girard, L., M. D. Parkins & **C. D. Sibley** (2011) Department of Medicine Research Development Fund $9,990
44. Winner, Canadian Investigator Trainee Association of Canada Young Investigators Forum, Ottawa, 2011
45. Best Poster Presentation and Poster of Distinction, Third Annual Leaders in Medicine Research Symposium, University of Calgary, 2011
46. Canadian Institutes of Health Research MD/PhD Award, 2011 $6,000 CAD
47. Winner, Building Bridges Program Competition (MD/PhD University of Calgary – University of British Columbia Exchange Program), 2011
48. Runner-up, Lydia Sikora Award for Research Excellence, Faculty of Medicine, University of Calgary, 2011 $2 000
49. Leaders in Medicine Tuition Award/CIHR top for MD/PhD $21,000
50. First Place Poster, Leaders in Medicine Symposium, University of Calgary, Faculty of Medicine, November 2011, $50
51. Neuroscience Program Award, University of Calgary, Department of Neuroscience, Fall 2012, $3,000.00
52. Best Overall Poster, Alberta Graduate Conference, Alberta Graduate Council, May 2011, $5,000.00
53. Queen Elizabeth II Scholarship (Doctoral), Department of Neuroscience, May 11-April 12, $15,000.00
54. Dr. Gary McPherson Leadership Scholarship, 2012, $2,000
55. 3M National Student Fellowship (shortlisted – awaiting result), 2012, $5,000
56. Canadian Federation of Medical Students/Royal Bank of Canada Leadership Scholarship, 2011, $2500
57. Laurence Decore Award for Student Leadership, Government of Alberta, 2011, $500
58. American College of Physicians: Internal Medicine 2011 Research Poster Competition Winner, 2011, $300
59. Canadian Medical Association Award for Young Leaders (shortlisted), 2011,
60. Canadian Institute of Health Research (CIHR) MD/PhD Studentship Award, Aug 2011-July 2012, $21000
61. Dean's Publication and Mentorship Prize, University of Calgary, Faculty of Medicine, May 2011, $10000
62. Leaders in Medicine Tuition Award and CIHR top up, University of Calgary, Faculty of Medicine, 2011, $21,000/annum
63. Governor General's Gold Medal Award, University of Calgary, Faculty of Medicine, October 2011
64. Cystic Fibrosis Canada Studentship. Cystic Fibrosis Canada. To Apr 12. $19,000/yr.
65. Canadian Institutes for Health Research Studentship. CIHR Canada. To Sept 11. $17,500/yr.
66. Alberta Innovates Health Research MD/PhD Studentship. To July 16. $30,000/yr.
67. Persons Case Scholarship. Government of Alberta. Nov 11. $2,500.
68. Angus & Mary McKinnon Scholarship for Community Service. First Calgary Financial. Nov 11. $1,000.
69. Top Oral Presentation, Alberta Graduate Conference. May 11. $5,000.
70. Microbiology & Infectious Diseases Travel Award, University of Calgary, Faculty of Medicine. Oct 10-Oct 11. $3,000.
71. Alberta Graduate Citizenship Award. Government of Alberta. Jan 11. $2,000.
72. Alberta Graduate Award. Government of Alberta. Jan 11. $3,000
73. Frederick Banting and Charles Best Canada Graduate Scholarship Doctoral Award, Canadian Institutes of Health Research, Jan 11 – Dec 13, $35,000
74. PhD Studentship, Alberta Heritage Foundation for Medical Research, June 08 – Dec 10, $21,500.
75. PhD Studentship (Incentive Award), Alberta Innovates – Health Solutions, Jan 11 – Sept 11, $8,500.
76. PhD Studentship (Incentive Award), Alberta Innovates – Health Solutions, Oct 11 – May 12, $13,500
77. Achievers in Medical Science Research Excellence Award, University of Calgary, Sept 08 – Aug 12, $3,500
78. Medical Science Conference Travel Award, University of Calgary, Faculty of Medicine, Jun 11, $1,000
79. Medical Science Conference Travel Award, University of Calgary, Faculty of Medicine, Feb 12, $500
80. Student Activities Fund Grant, University of Calgary, Feb 12, $650
81. Leaders in Medicine Symposium 1st Place Poster Presentation Award (Group G), Nov 11, $50
82. Achievers in Medical Science Award, University of Calgary, Faculty of Medicine 2012, $40,000
83. Leaders in Medicine Tuition Award, CIHR MD/PhD top up Award, 2011 $21,000
84. Best poster presentation award (Group F) at Leaders in Medicine Research Symposium
85. Poster of Distinction Award at Leaders in Medicine Research Symposium $50
86. Nat Christie Scholarship, University of Calgary Faculty of Medicine 2012 –2013 $500/year

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PUBLISHED - Total reported 59

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28. Picard M, Ritchie D, Wright KJ, Romestaing C, Thomas MM, **Rowan SL**, Taivassalo T, Hepple RT. Mitochondrial functional impairment with aging is exaggerated in isolated mitochondria compared to permeabilized myofibers. *Aging Cell* 2010; 9: 1032-46.

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ABSTRACTS

Total Reported 100

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9. **Beers C**, Pittman D, Goodyear B, Federico P. Simultaneous intracranial EEG- functional MRI in humans at 3.0 Tesla. Human Brain Mapping 2011; Quebec City, QC; June 26-30, 2011

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12. **Eshaghurshan CS,** Grinwis ME, Sibley CD, Rabin HR, Surette MG. Diversity within the viridans streptococcal antibiotic resistome of adult cystic fibrosis patients. North American Cystic Fibrosis Conference. Anaheim, USA; Nov 3-5th, 2011.

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22. **Eslinger AJ,** Reimer RA (2011) Comparison of Gut Microbiota in Rats Fed Pulse-Derived Ingredients Versus the Prebiotic Fiber Oligofructose. Leaders in Medicine Research Symposium, Calgary, AB; November 4, 2011.

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28. **Karlos AK,** Gnatiuk EA, Hittel DS. High LDL In A Young, Healthy, Canadian Population: A Valuable Target For Gene-stratified Interventions. Conference; American College of Sports Medicine 2012, Scientific Meeting, San Francisco, CA; 2012

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40. **McDonald B.** Intravascular immunity during sterile inflammation. American Transplant Congress. Boston, Massachusetts; June 2, 2012. ***(invited speaker).***

41. **McDonald B.** Intravascular immunity to infection and sterile inflammation. National Academy of Science of Germany (Leopoldina Symposium). Munster, Germany; Nov. 25, 2011. **(*invited speaker*).**

42. **McDonald B**., Urrutia R., Jenne C., Yipp B., Kubes P. Intravascular neutrophil extracellular traps (NETs) protect against bacterial dissemination in Gram-negative sepsis. Leaders in Medicine Research Symposium. Calgary, AB; Nov. 4, 2011. Oral platform.

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44. **McDonald B.** Lighting the way: Visualizing the inflammatory response to infection and sterile injury *in vivo*. Canadian National Medical Student Research Symposium. Winnipeg, Manitoba; June 7-9, 2011. (***invited speaker***)

45. **McDonald B**, Zhuo L, Kimata K, Kubes P. Activation of TLR4 on endothelium alone initiates neutrophil adhesion within the liver microcirulation during endotoxemia. American Association of Immunologists annual meeting. San Fransisco, CA; May 15, 2011. Oral platform.

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47. **Mosher AA**, Wood S, Slater DM. Distinct responses to prostaglandin E_2 in upper and lower segment human myometrial smooth muscle cells. *3rd Canadian National Medical Student Research Symposium*; Winnipeg, MB; June 7-9, 2011

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57. Zalucky AA, **Nicholl DDM**, Mann MC, Hemmelgarn BR, Sola DY, Ahmed SB. Fat Distribution and Regulation of the Renin Angiotensin System in Healthy Humans. *American Society of Nephrology Annual Meeting.* Philadelphia, PA, USA. November 8-13, 2011.

58. Abdi-Ali A, **Nicholl DDM**, Hemmelgarn BR, MacRae JM, Sola DY, and Ahmed SB. The Role of Vitamin D on Aortic Augmentation Index and Pulse Wave Velocity in Healthy Humans. *American Society of Nephrology Annual Meeting.* Philadelphia, PA, USA. November 8-13, 2011.

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72. Kwong LM, Zee JM, **O'Connor PM,** Mydlarski PR. The Role of MicroRNAs in Cutaneous Squamous Cell Carcinomas. Canadian Society of Investigative Dermatology. April 2011.

73. **Peplowski MA**, MacNaughton WK. Aquaporin 3 expression is downregulated in HT29 colonic epithelial cells exposed to tumour necrosis factor alpha and interferon gamma. *Canadian Journal of Gastroenterology* 2010:24: Supplement A, 246.

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78. **Rawn SM**. Feto-Placental Production of Placenta-Specific, Prolactin-Related Hormone Encoding Genes (PPRH) is Essential for Murine Pregnancy. Leaders in Medicine Symposium; Calgary, AB; November 4, 2011.

79. **Roy A**, Thurston WE, Patten SB, Tough S, Crowshoe L, Beran T. Methods for measuring oppression: A scoping literature review of Aboriginal population health research. *Clinical and Investigative Medicine.* 2011; 34 (6S): 1-40.

80. Yelland G, Kania A, **Roy A**, Patel A, Nguyen D, Verhoef M. Looking for a "complexity" perspective in health promotion evaluations. *Alberta Graduate Conference*, Calgary (AB), May 4-6, 2011.

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88. **Sarna N**, Hughey C, Shearer J, Hittel D. The effects of fatty-acid oversupply on skeletal muscle mitochondrial function in C57BL/6J mice. *CITAC-CSCI Annual Meeting*; Ottawa, ON, September 20-22, 2010

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91. **Sarna N**, Hughey C, Shearer J, Hittel D. Decreased muscle mitochondrial respiration observed in high-fat fed mice. *The U of C Graduate Multidisciplinary Conference*. Calgary, May 2009

92. **Seamone** A direct comparison of spectra domain optical coherence tomography (SD-OCT) and multifocal electroretinography (mfERG) findings in early-stage hydroxychloroquine retinopathy Mark E. **Seamone**[1], Katherine Milton[2], Micheline Deschênes[2], Mark Hanna[2], Amin Kherani[2,3], Michael Fielden[1] and R. Geoff Williams[2,3], [1]Department of Medicine, [2]Calgary Retina Consultants, [3]Department of Surgery, University of Calgary, Calgary AB. ASRS August 2012 Las Vegas NV

93. **Seamone** A direct comparison of spectra domain optical coherence tomography (SD-OCT) and multifocal electroretinography (mfERG) findings in early-stage hydroxychloroquine retinopathy Mark E. **Seamone**[1], Katherine Milton[2], Micheline Deschênes[2], Mark Hanna[2], Amin Kherani[2,3], Michael Fielden[1] and R. Geoff Williams[2,3], [1]Department of Medicine, [2]Calgary Retina Consultants, [3]Department of Surgery, University of Calgary, Calgary Alberta Canada. Ophthalmology research day Calgary Alberta Canada, April 2012.

94. **Schmidt A,** Lau D, Friedrich M. Diffuse Microvascular disease in asymptomatic patients with type 2 diabetes. *Canadian Cardiology Congress.* Vancouver, British Columbia; October 2011

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96. **Schmidt A,** Lau D, Friedrich M. Subclinical perfusion deficits in patients with type 2 diabetes detectable with CMR. Society of Cardiovascular Magnetic Resonance/Euro CMR Imaging conference. Nice, France. February 2011

97. **Tsang, AR**, Wyatt, HDM, Lobb, DA, Ting, NSY and Beattie, TL. Characterization of naturally occurring hTERT mutants. *Cold Spring Harbor Telomere & Telomerase Meeting*; Cold Spring Harbor, NY; May 3-7, 2011.

98. **Tulk SE**, Hirota SA, Beck PL, MacDonald JA. Vitamin D downregulates NLRP3 and protects against *Clostridium difficile* toxin-induced cell death. *CDDW*; Montreal, QB; February 24 – 27 2012

99. Aman **Wadhwani**, Wallace K. MacNaughton. Intracellular signaling pathways responsible for trypsin-induced change in transepithelial resistance across intestinal epithelial cells. Abstract published for poster presentation at "The World Congress on Inflammation 2011", 25th – 29th June 2011, Paris, France.

100. A.**Wadhwani**, M. Dicay, W.K. MacNaughton. MECHANISMS OF THE PROTEASE-INDUCED INCREASE IN TRANSEPITHELIAL RESISTANCE IN INTESTINAL EPITHELIAL CELLS. Abstract accepted for an oral talk at "The Annual Canadian Digestive Diseases Week 2012", Montreal, QC.

BOOKS/BOOK CHAPTERS

Total reported 6

1. McKay, B.E., Tadayonnejad, R., **Anderson, D.**, Engbers, J.D.T., Iftinca, M. and Turner, R.W. (2010) Establishing *in vivo* like activity in rat cerebellar cells maintained *in vitro.* Isolated Neural Circuits, in *Neuromethods* (Ballanyi, K., ed.), Springer, *In Press*.

2. Turner, R.W., **Anderson, D.** and Zamponi, G.W. (2011). Signaling complexes of voltage-gated calcium channels. *Channels* 5(5): 440-448.

3. **McDonald B.**, and Kubes P. Leukocyte trafficking. In: Horfman, Weyand, Langford, and Goronzy. Inflammatory Diseases of Blood Vessels. Ch. 7. Oxford: Wiley-Blackwell. (2012) In Press.

4. **Moser JJ** and Fritzler MJ. *Chapter 15: Relationship of other cytoplasmic ribonucleoprotein (RNP) bodies to GW/P Bodies* in Ten Year History of Progress in GW/P Body Research. (Submitted, expected publication date in 2012).

5. **Moser JJ**, Chan EKL, Fritzler MJ. *Chapter 16: An SNP in the trinucleotide repeat region of the TNRC6A gene maps to a major GW182 autoepitope in patients with autoantibodies to GW182* in Ten Year History of Progress in GW/P Body Research. (Submitted, expected publication date in 2012).

6. Noormohamed R, Ireland L, Goulet S, Cochrane T, Daniels C, Beatt L, Thurston WE, **Roy A**, Turner D, Morgan C. (2012). Intergenerational trauma and Aboriginal youth: A scoping review. Calgary, AB: City of Calgary, Family and Community Support Services. [Research Report].

PRESENTATIONS

Total reported 118

LOCAL - Number Reported 69

1. **Bau** JT. Untying the knot and preventing a bad break. What Dr. Phil can't tell you but topoisomerases can. *Work in Progress Presentation to SACRI;* Calgary, AB; November 10, 2011.

2. **Beers C**, Pittman D, Goodyear B, Federico P. Simultaneous Intracranial EEG-fMRI for Epilepsy Imaging. *Seaman Family MR Centre First Annual Public Outreach Lecture Series;* Peter Lougheed, Visitor Centre, Kanasksis Country, AB; Feb 2012 (Oral)

3. **Beers C**, Pittman D, Goodyear B, Federico P. Networks in Epilepsy Studied with Intracranial EEG-fMRI. *Advanced Imaging Series, Seaman Family MR Centre;* Calgary, AB; November 2011 (Oral)

4. **Beers C**, Pittman D, Goodyear B, Federico P. Epileptic Networks Studied with Intracranial EEG- fMRI at 3.0 Tesla. Leaders in Medicine Symposium; Calgary, AB; November 4, 2011 (Poster)

5. **Beers C**, Pittman D, Goodyear B, Federico P. Simultaneous intracranial EEG- functional MRI in humans at 3.0 Tesla. Exploring the Source – Seeing the Potential, Research Symposium; Calgary, AB; May 2011. (Poster)

6. **Beers C,** Pittman D, Goodyear B, Federico P (May 2011). Simultaneous intracranial EEG- functional MRI in humans at 3.0 Tesla. Alberta Graduate Conference; Calgary, AB; May 5-7, 2011. (Poster)

7. **Damani, Z**. Single-Entry Models: Value and Acceptability among Orthopaedic Surgeons in Canada. *Leaders in Medicine Research Symposium*; Calgary, AB: November 4, 2011

8. **Dunbar M**, Friesen A & Mercimek-Mahmutoglu S. (2011). Improvement of Autism in a Patient with GAMT Deficiency and Autism: a Case Report. In *Leaders in Medicine Research Symposium*. (Poster), Calgary, Alberta.

9. **Eshaghurshan CS,** Grinwis ME, Sibley CD, Rabin HR, Surette MG. Investigation into the viridans group streptococci isolated from adult cystic fibrosis patient sputum. Bacterial Pathogenesis Research Group. Calgary, AB, Canada. (Oral) 2012.

10. **Eshaghurshan CS,** Grinwis ME, Sibley CD, Rabin HR, Surette MG. Investigation into the viridans group streptococci isolated from adult cystic fibrosis patient sputum. Snyder Institute of Inflammation, Infection and Immunology Research Day. Calgary, AB, Canada. (Oral) 2011.

11. **Eshaghurshan CS,** Grinwis ME, Sibley CD, Rabin HR, Surette MG. Diversity within the viridans streptococcal antibiotic resistome of adult cystic fibrosis patients. Alberta Graduate Conference. Calgary, AB. (Poster) May 6th, 2011.

12. **Eshaghurshan CS,** Grinwis ME, Sibley CD, Rabin HR, Surette MG. Diversity within the viridans streptococcal antibiotic resistome of adult cystic fibrosis patients. Alberta Graduate Conference. Calgary, AB. (Oral) 2011.

13. **Eslinger AJ,** Reimer RA (2011) Comparison of Gut Microbiota in Rats Fed Pulse-Derived Ingredients Versus the Prebiotic Fiber Oligofructose. Leaders in Medicine Research Symposium, Calgary, AB; November 4, 2011.

14. **Eslinger AJ**, Duffy OA, Reid DT, Eller LK, Reimer RA (2011) Pulse-derived ingredients differentially modulate microbiota in diet-induced obese rats: a comparison to oligofructose. Alberta Children's Hospital Research Institute 2011 Research Symposium, Calgary, AB; April 18-19, 2011.

15. **Esmail K**, Crichton ACS. Removal of the Valve Mechanism in Failing Ahmed Implants. *Ophthalmology and Visual Sciences Research Day;* Calgary, AB; May 9, 2011.

16. **Esmail K**, Crichton ACS, Steinke R, Wyse P. Transillumination and Marfan Syndrome: A Case Study. *Ophthalmology and Visual Sciences Research Day;* Calgary, AB; May 9, 2011.

17. **Huebner KD**, O'Brien EJ, Heard BJ, Chung M, Achari Y, Shrive NG, Frank CB. Post-natal Molecular Adaptations in Anteromedial and Posterolateral Bundles of the Ovine Anterior Cruciate Ligament: One Structure with Two Parts or Two Distinct Ligaments? *Leaders in Medicine 3rd Annual Symposium*; Calgary, AB; November 4, 2011.

18. Icilin, an agonist of cold activated receptor potential (TRP) channels attenuates colonic inflammation in mice. Eric **Hyun,** Rithwik Ramachandran, Paul Beck, Nathalie Vergolle, and Morley Hollenberg. LIM Research Symposium – 2011

19. **Keough, MB.** Chondroitin sulphate proteoglycans: A candidate for remyelination failure. *Axon Biology and Regeneration Annual Research Day*; Kananaskis, AB, Oct 3, 2011

20. **Keough, MB.** Overcoming chondroitin sulphate proteoglycans: inhibitors of central nervous system remyelination. University of Calgary*Leaders in Medicine Research Symposium*

21. **Keough, MB**. Glial cell interactions in CNS remyelination. *Hotchkiss Brain Institute Glial Cell and Nerve Regeneration Workshop;* Calgary, AB; March 6, 2012

22. **Kwong LM**, Tran JM and Mydlarski PR. The role of microRNAs in cutaneous squamous cell carcinomas. *Alberta Graduate Conference*; Calgary, AB; May 7, 2011 (Poster).

23. **Kwong LM**, Tran JM and Mydlarski PR. The role of microRNAs in cutaneous squamous cell carcinomas. *Leaders in Medicine Research Symposium*; Calgary, AB; November 4, 2011 (Poster).

24. **Lawson** KA, Shi ZQ, Spurrell J, Kawakami J, Morris D. Suntinib augments reovirus tumour regression in an immunocompetent murine model of renal cell carcinoma. 1st Annual University of Alberta Urology Research Day. 2011 October 21. Edmonton, Alberta

25. **McDonald B**., Urrutia R., Jenne C., Yipp B., Kubes P. Intravascular neutrophil extracellular traps (NETs) protect against bacterial dissemination in Gram-negative sepsis. Leaders in Medicine Research Symposium. Calgary, AB 2011. (Oral)

26. **Moser JJ**. Reform Canada's Oral Health Program for Aboriginals: Help Stop Tooth Decay and Prevent Rheumatoid Arthritis, An Advocacy Memo to the Minister of Health, Government of Canada Responsible for the First Nations, Inuit & Aboriginal Health Branch of Health Canada. Healthy Populations Poster Presentation Day, Calgary, Alberta, Canada, March 07, 2011.

27. **Moser JJ**. Global Health Issue in Focus: Vitamin A deficiency, blindness and the political and regulatory barriers to implementation of Golden Rice in developing nations. Presentation at the Global Health Symposium, October 24, 2011.

28. **Moser JJ**. Pre-op Assessment for Anesthesiology: A quick guide for the medical student to evaluate airway and assess for potential problems. Presentation at the Calgary Anesthesia Interest Group Intubation Skills Night, October 24, 2011.

29. **Moser JJ**, Fritzler, MJ, Rattner JB. Repression of GW/P body components and the RNAi microprocessor impacts primary ciliogenesis in human astrocytes. 3rd Annual University of Calgary Leaders in Medicine Research Symposium, Calgary, Alberta, Canada, November 04, 2011.

30. **Mosher AA**. Distinct responses to prostaglandin E_2 in upper and lower segment human myometrial smooth muscle cells. *ACHRI Symposium*; Calgary, AB; April 18, 2011

31. **Mosher AA**. Distinct responses to prostaglandin E_2 in upper and lower segment myometrial smooth muscle cells. *Clara Christie Research Day*; Calgary, AB; May 13, 2011

32. **Mosher AA**. Secretory phospholipase A_2 group IID: a novel phospholipase contributing to the regulation of arachidonic acid output in human pregnancy? *Leaders in Medicine Symposium*; Calgary, AB; November 4, 2011

33. **Nguyen K**. Peripheral T_{reg}s Suppress Sickness Behaviour Development Associated with Inflammatory Liver Disease. *Leaders in Medicine Research Symposium*; Calgary, AB; November 4, 2011.

34. **Nicholl DDM.** CPAP for Metabolic Syndrome. *Vascular Biology Journal Club;* University of Calgary, Calgary, Alberta; (Talk)

35. **Nicholl DDM.** Obstructive Sleep Apnea, the Renin Angiotensin System, and Glycemic Control. *The Cosmopolitan International Club of Calgary;* Calgary, Alberta; March 14, 2012. (Talk)

36. **Nicholl DDM.** Obstructive Sleep Apnea and the Renin Angiotensin System: An Update. *Renal Research Rounds;* Foothills Medical Centre, University of Calgary, Calgary, Alberta; February 3, 2012. (Talk)

37. **Nicholl DDM**, Hemmelgarn BR, Turin TC, MacRae JM, Muruve DA, Sola DY, and Ahmed SB. Urinary Albumin and Protein Excretion are Associated with Increased Vascular Renin Angiotensin System Activity in Healthy Humans. *Leaders in Medicine Research Symposium.* Calgary, AB, Canada. November 4, 2011. (Poster)

38. **Nicholl DDM.** Volunteering Abroad - Peru. *Health and Medicine Club;* University of Calgary, Calgary, AB; Oct 3, 2011. (Talk)

39. **Peplowski MA**. Aquaporin 3 Expression and Localization is Altered Early in the Dextran Sodium Sulfate Model of Colonic Inflammation. *Leaders in Medicine Research Symposium;* Calgary, AB; November 4, 2011.

40. **Peplowski MA**. Aquaporin 3 Expression and Localization is Altered Early in the Dextran Sodium Sulfate Model of Intestinal Inflammation. *Inflammation Research Network Seminar Series*; Calgary, AB; December 14, 2011.

41. **Peplowski MA**. Aquaporin 3 Expression and Localization is Altered Early in the Dextran Sodium Sulfate Model of Intestinal Inflammation. *Kananaskis Inflammation Workshop;* Kananaskis, AB; January 21, 2012.

42. **Ram R.** From Doctors' Strike to Double Digit Compensation Increases: What are Physicians' Responsibilities to the "Sustainability" of the Canadian health care system. *Presentation to the Leaders' In Medicine Program*. June 2011, Calgary.

43. **Rawn SM.** Feto-Placental Production of Placenta-Specific, Prolactin-Related Hormone Encoding Genes (PPRH) is Essential for Murine Pregnancy. Leaders in Medicine Symposium; Calgary, AB; November 4, 2011.

44. **Rawn SM.** A cure for HIV? Leaders in Medicine Journal Club; Calgary, AB; May 18, 2011.

45. **Roy, A**. Determinants of prenatal depression in pregnant Aboriginal women. *Mind & Brain Workshop, Calgary Institute of Population and Public Health*, Calgary (AB), November 14, 2011. (Oral).

46. **Roy A**. Methods for measuring oppression: A scoping literature review of Aboriginal population health research. *Leaders in Medicine Research Symposium*, Faculty of Medicine, University of Calgary, November 4, 2011. (Poster).

47. **Sampson E,** M Opoku-Darko, K Gratton, OF Bathe. Examining the functional consequences of TEM8 in human breast cancer cells. University of Calgary 3rd Annual Leaders in Medicine Research Symposium; Calgary, AB; November 2011.

48. **Sampson E,** Understanding the Role of TEM8 in a Human Breast Cancer Cell Context. *Southern Alberta Cancer Research Institute Work in Progress*; Calgary, AB; October 20, 2011.

49. **Schmidt A.** Diffuse Microvascular disease in asymptomatic patients with type 2 diabetes. *Leaders in Medicine Symposium*. Calgary, Alberta. November 2011. *Award recipient*

50. **Schmidt A.** Novel Imaging Derived Biomarkers for the Early Detection of Diabetic Cardiomyopathy. *Calgary Advanced Imaging Seminar.* Calgary, Alberta; April 2011.

51. Mark E. **Seamone** A direct comparison of spectra domain optical coherence tomography (SD-OCT) and multifocal electroretinography (mfERG) findings in early-stage hydroxychloroquine retinopathy Mark E. **Seamone**[1], Katherine Milton[2], Micheline Deschênes[2], Mark Hanna[2], Amin Kherani[2,3], Michael Fielden[1] and R. Geoff Williams[2,3], [1]Department of Medicine, [2]Calgary Retina Consultants, [3]Department of Surgery, University of Calgary, Calgary Alberta Canada . Retina Rounds, Calgary Alberta Canada 2012 (Oral)

52. Mark E. **Seamone** Susac's Syndrome: A case study. Mark E. **Seamone**[1] and Michael Fielden[2] [1]Department of Medicine, [2]Calgary Retina Consultants. Interesting Case Rounds Ophthalmology Calgary Alberta Canada November 2012 (Oral)

53. Mark E. **Seamone** A direct comparison of spectra domain optical coherence tomography (SD-OCT) and multifocal electroretinography (mfERG) findings in early-stage hydroxychloroquine retinopathy Mark E**. Seamone[1]**, Katherine Milton[2], Micheline Deschênes[2], Mark Hanna[2], Amin Kherani[2,3], Michael Fielden[1] and R. Geoff Williams[2,3], [1]Department of Medicine, [2]Calgary Retina Consultants, [3]Department of Surgery, University of Calgary, Calgary Alberta Canada . LIM symposium September 2012 (Poster) (Runner-up)

54. **Sibley, C. D.**, (2012) Future directions in cystic fibrosis research. Summit Foundation Annual Meeting, Calgary, AB.

55. **Sibley, C. D.**, (2011) The polymicrobial nature of airway infections in cystic fibrosis. Clinician Investigator Trainee Association of Canada Annual General Meeting, Ottawa, ON.

56. **Sibley, C. D.**, (2011) The polymicrobial nature of airway infections in cystic fibrosis: clinical applications. Calgary Laboratory Services, Calgary, AB.

57. **Tsang, AR.** The role of naturally occurring telomerase mutations on enzyme function and cellular lifespan. *3rd Annual Leaders in Medicine Research Symposium*; Calgary, AB; November 4, 2011.

58. DeVetten, G., Watterson, R., **Thomas, A.D.**, Wiebe, A., Nicholson, C., Myhre, D., Hatfield, J. Training the Future Physician: Undergraduate Medical Education with a Concentration in Global Health; *Global Health Conference: Advancing Health Equity in the 21st Century*, Montreal, QC; November 12, 2011.

59. **Tulk SE**, Hirota SA, Beck PL, MacDonald JA. Vitamin D downregulates NLRP3 and protects against *Clostridium difficile* toxin-induced cell death. *GIRG Symposium*; Banff, AB; January 27 – 29 2012

60. **Tulk SE**, Hirota SA, Beck PL, MacDonald JA. Vitamin D downregulates NLRP3 and protects against *Clostridium difficile* toxin-induced cell death. *Kananaskis Inflammation Workshop*; Kananaskis, AB; January 21 – 22 2012

61. **Tulk SE**, Hirota SA, Beck PL, MacDonald JA. Vitamin D downregulates NLRP3 and protects against *Clostridium difficile* toxin-induced cell death. *Leaders in Medicine Research Symposium;* Calgary, AB; November 4 2011

62. **Tulk SE**, Hirota SA, Beck PL, MacDonald JA. Vitamin D downregulates NLRP3 and protects against *Clostridium difficile* toxin-induced cell death. *Synder Institute Research Day;* Calgary, AB; October 3 2011

63. **Tulk, S.E**., Ng, J., Hirota, S.A., Potentier, M.S., Beck, P.L., and MacDonald, J.A. Clostridium difficile toxin elicits differential cytokine responces in tissue isolated from Ulcerative Colitis and Crohn's Disease patients: Insight into the increased risk of CDAD in Inflammatory Bowel Disease. *Shaffer Awards*, June 2 2011, Calgary, AB, Canada

64. Aman **Wadhwani**, Wallace K. MacNaughton. Intracellular signaling pathways responsible for trypsin-induced change in transepithelial resistance across intestinal epithelial cells. Abstract accepted for *poster* at "The LIM Symposium 2011", 2nd November 2011, Calgary, AB.

65. Aman **Wadhwani**, Wallace K. MacNaughton. Intracellular signaling pathways responsible for trypsin-induced change in transepithelial resistance across intestinal epithelial cells. *Poster* at "III Research Day", October 2011, Calgary, AB.

66. **Xiang R.** SAP knockdown occurs after 72 hours. *Synder Institute Research Day*; University of Calgary; Octorber 3, 2011

67. **Xiang R.** SAP knockdown occurs after 72 hours. *Leader in Medicine Research Day*; University of Calgary; November 4, 2011

68. **Yaraskavitch** M. From Food Poisoning to Therapeutics: Botulinum toxin A (Botox) and its effect on muscle. *Leaders in Medicine Seminar Series;* Calgary AB, February 2011.

69. **Yaraskavitch** M. Altered Level of Consciousness in an Elderly Woman: Case Presentation. *Leçons du Mardi Neurology Rounds;* Calgary, AB; August 2011.

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1. **Anderson D.** The Cav3-Kv4 complex. Department of Neurobiology, Harvard Medical School; Boston MA; January 2011.

2. **Beers C**, Pittman D, Gaxiola I, Goodyear B, Federico P. The minimum number of discharges needed to detect BOLD signals using intracranial EEG-fMRI at 3 T. Human Brain Mapping 2012; Beijing, China; June 10-14, 2012.

3. **Beers C**, Pittman D, Goodyear B, Federico P. Epileptic Networks Studied with Intracranial EEG- fMRI at 3.0 Tesla. American Epilepsy Society 65th Annual Meeting; Baltimore, MD; December 2-6, 2011.

4. **Beers C**, Pittman D, Goodyear B, Federico P. Simultaneous intracranial EEG- functional MRI in humans at 3.0 Tesla. Human Brain Mapping 2011; Quebec City, QC; June 26-30, 2011

5. **Damani, Z**. Single-Entry Models: Value and Acceptability. *Western Canada Waiting List Investigators In-Person Meeting*; Toronto, ON: January 29/30, 2012

6. **Damani, Z**. Single-Entry Models: Value and Acceptability in Canada. *Taming of the Queue Pre-Conference Workshop*; Ottawa, ON: March 28, 2012

7. **Eshaghurshan CS,** Grinwis ME, Sibley CD, Rabin HR, Surette MG. Diversity within the viridans streptococcal antibiotic resistome of adult cystic fibrosis patients. North American Cystic Fibrosis Conference. Anaheim, USA. (Poster) Presentation. November 3-5th, 2011.

8. **Eshaghurshan CS,** Grinwis ME, Sibley CD, Rabin HR, Surette MG. Diversity within the viridans streptococcal antibiotic resistome of adult cystic fibrosis patients. Gram Positive Conference. Montecatini Terme, Italy. (Poster) 2011.

9. **Eshaghurshan CS,** Grinwis ME, Sibley CD, Rabin HR, Surette MG. Changes in the Streptococcal antibiotic resistome of adult cystic fibrosis patients results from mutation rather than horizontal gene transfer. CSCI/CITAC Young Investigators Forum. Ottawa, ON, Canada. (Poster) 2011.

10. **Eslinger AJ**, Reimer RA (2011) Comparison of Gut Microbiota in Rats Fed Pulse-Derived Ingredients Versus the Prebiotic Fiber Oligofructose. Obesity Society (NAASO) 29th Annual Scientific Meeting, Orlando, FL; October 1-5, 2011.

11. **Gillrie, MR**. Plasmodium falciparum histones induce endothelial proinflammatory response and barrier dysfunction. American Society of Tropical Medicine and Hygiene (ASTMH) Young Investigator Award at the ASTMH 60th Annual Meeting; Philadelphia, PA, December 6-8, 2011.

12. **Gillrie, MR**. Plasmodium falciparum histones induce endothelial proinflammatory response and barrier dysfunction. CIHR Canadian National Medical Student Research Symposium; Winnipeg, MB, June 7-9 2011.

13. Icilin, an agonist of cold activated receptor Potential (TRP) channels protect mice against colitis. Eric **Hyun**, Rithwik Ramachandran, and Morley Hollenberg. Digestive Disease week – DDW 2011

14. **Karlos AK,** Gnatiuk EA, Hittel DS. High LDL In A Young, Healthy, Canadian Population: A Valuable Target For Gene-stratified Interventions. Conference; American College of Sports Medicine 2012, Scientific Meeting, San Francisco, CA; 2012

15. **Khambati H.**, Choueiri T., Kollmannsberger C., North S., Bjarnason G., Vaishampayan U., Wood L., MacKenzie M., Rini B., and Heng D. for the International mRCC Database Consortium. Efficacy of targeted therapy for metastatic renal cell carcinoma in the elderly patient population. *Genitourinary Cancer Symposium;* Orlando, Florida; February 19, 2011.

16. **Lawson** KA, Shi ZQ, Spurrell J, Kawakami J, Morris D. Oncolytic virotherapy combined with targeted therapy for the treatment of renal cell carcinoma. 67th Canadian Urological Association Meeting. June 24-27 2012. Banff, Alberta

17. **Lawson** KA, Lockyer J, Vicas I, Hofmeister M, Carlson K. Antibiotic prophylaxis for trans-urethral resection of prostate (TURP): A need for Canadian guidelines? 67th Canadian Urological Association Meeting. June 24-27 2012. Banff, AB

18. **Lawson** KA, Spurrell J, Shi ZQ, Morris D. Preclinical development of reovirus as a novel therapeutic for renal cell carcinoma. Canadian Society for Clinical Investigation Annual Meeting. 2011 September 11-14. Ottawa, Ontario, Canada.

19. **Lawson** KA, Spurrell J, Shi ZQ, Kawamai J, Trpkov K, Morris D. Oncolytic reovirus therapy for renal cell carcinoma. 87th Western Section American Urological Association Annual Meeting. 2011 August 21-25. Vancouver, British Columbia

20. **Leung, K.K**., Vincent, N., Silvius, J., Pimlott, N., Dalziel, W., & Drummond, N. Health expectations, patient satisfaction with primary care medicine, and the relationship between them: A structured literature review. North American Primary Care Research Group (NAPCRG) Annual Meeting. Banff, AB. November 12, 2011

21. **Ludwig TE**. Osteoarthritic Synovial Fluid Deficient in Proteoglycan 4 Demonstrates Decreased Boundary Lubricating Ability. *CITAC/CSCI YIF;* Ottawa, ON; September 12-14, 2011 (Poster)

22. **Luu, Judy**. Functional significance of BOLD-CMR in patients suspected of coronary artery disease – a validation study using FFR. 3rd Canadian National Medical Student Research Symposium. Winnipeg, Manitoba; June 2011.

23. **McDonald B.** Intravascular immunity during sterile inflammation. American Transplant Congress. Boston, Massachusetts; June 2, 2012. *(invited speaker).*

24. **McDonald B.** Intravascular immunity to infection and sterile inflammation. National Academy of Science of Germany (Leopoldina Symposium). Munster, Germany; Nov. 25, 2011. (*invited speaker*).

25. **McDonald B**., Urrutia R., Jenne C., Yipp B., Kubes P. Intravascular neutrophil extracellular traps (NETs) protect against bacterial dissemination in Gram-negative sepsis. Canadian Society for Clinical Investigation annual conference. Ottawa, Ontario; Sept 12-14, 2011. Oral and poster.

26. **McDonald B.** Lighting the way: Visualizing the inflammatory response to infection and sterile injury *in vivo*. Canadian National Medical Student Research Symposium. Winnipeg, Manitoba; June 7-9, 2011. (*invited speaker*)

27. **McDonald B**, Zhuo L, Kimata K, Kubes P. Activation of TLR4 on endothelium alone initiates neutrophil adhesion within the liver microcirulation during endotoxemia. American Association of Immunologists annual meeting. San Fransisco, CA; May 15, 2011. (Oral)

28. **McDonald B.** Anatomy of Innate Immunity: Intravascular immunity to infection and sterile inflammation. Society for Toxicological Pathology annual meeting. Denver, CO; June 14, 2011. (*invited speaker*)

29. **Mosher AA**. Distinct responses to prostaglandin E_2 in upper and lower segment human myometrial smooth muscle cells. *3rd Canadian National Medical Student Research Symposium*; Winnipeg, MB; June 7, 2011

30. **Mosher AA**. Distinct responses to prostaglandin E_2 in upper and lower segment myometrial smooth muscle cells. *CSCI Young Investigators Forum*; Ottawa, ON; September 13, 2011

31. **Mosher AA**. Validation of upper and lower segment human myometrial smooth muscle cells in culture. *20th Annual Western Perinatal Research Meeting*; Banff, AB; February 16, 2012

32. **Nguyen K**. Peripheral T_{reg}s Suppress Sickness Behaviour Development Associated with Inflammatory Liver Disease. *Clinician Investigator and Trainee Association of Canada (CITAC) Annual Conference and Young Investigators' Forum*; Ottawa, ON; September 12-14, 2011.

33. **Nicholl DDM**, Hemmelgarn BR, Turin TC, MacRae JM, Muruve DA, Sola DY, and Ahmed SB. Urinary Albumin and Protein Excretion are Associated with Increased Vascular Renin Angiotensin System Activity in Healthy Humans. *American Society of Nephrology Annual Meeting.* Philadelphia, PA, USA. November 8-13, 2011. (Poster)

34. **Nicholl DDM**, Ahmed SB, Loewen AHS, Hemmelgarn BR, Sola DY, Beecroft JM, Turin TC, and Hanly PJ. Validity of the Berlin Questionnaire and Adjusted Neck Circumference in Identifying Sleep Apnea in Patients with Chronic Kidney Disease. *American Society of Nephrology Annual Meeting.* Philadelphia, PA, USA. November 8-13, 2011. (Poster)

35. **Nicholl DDM**, Ahmed SB, Loewen AHS, Hemmelgarn BR, Sola DY, Beecroft JM, Turin TC, and Hanly PJ. Clinical Presentation of Sleep Apnea in Patients with Chronic Kidney Disease. *American Society of Nephrology Annual Meeting.* Philadelphia, PA, USA. November 8-13, 2011. (Poster)

36. **Nicholl DDM.** Proteinuria and the Renin Angiotensin System. *6th Annual Western Canadian Kidney Day Research Symposium;* University of Calgary, Calgary, Alberta; October 13, 2011. (Talk)

37. DeVetten, G., Watterson, R., Thomas, A.D., Wiebe, A., **Nicholson, C**., Myhre, D., Hatfield, J. Training the Future Physician: Undergraduate Medical Education with a Concentration in Global Health; *Global Health Conference: Advancing Health Equity in the 21st Century*, Montreal, QC; November 12, 2011.

38. **Peplowski MA**. Aquaporin 3 Expression and Localization is Altered Early in the Dextran Sodium Sulfate Model of Colonic Inflammation. *10th World Congress on Inflammation;* Paris, France; June 26, 2011.

39. **Peplowski MA**. Aquaporin 3 Expression and Localization is Altered Early in the Dextran Sodium Sulfate Model of Intestinal Inflammation. *Canadian Digestive Diseases Week 2012;* Montreal, QC; February 25, 2012.

40. **Ram R**. Re-evaluation of dyslipidemia treatment for young adults with a low CVD risk score. *Young Investigators Forum for the Canadian Society of Clinical Investigation*. Ottawa. September 2011.

41. **Ram R**. Meeuwisse W. Wiley P. The efficacy of sclerotherapy with a solution of dextrose and Lidocaine to treat chronic Achilles tendinopathy: 1 year follow-up of a randomized controlled trial. *American College of Physicians: Internal Medicine 2011*. San Diego. April 2011.

42. **Rowan** SL, Solbak NM, Purves-Smith FM, Hepple RT. Denervation contributes to fiber atrophy and myosin heavy chain co-expression in senescent skeletal muscle. *American College of Sports Medicine Conference on Integrative Physiology of Exercise*; Miami, FL; September 22-25, 2010.

43. **Roy A**. A scoping review of the measurement of oppression in the literature on Aboriginal population health: review methodology. *Canadian Society of Epidemiology and Biostatistics* National Student Conference, Montreal (QC), 2011. (Poster).

44. **Roy A**. The measurement of oppression in Aboriginal population health research: methods and preliminary findings of a scoping literature review. *Native Health Research Conference*, Niagara Falls (NY), June 27-30, 2011. (Poster).

45. **Roy A**. Methods for measuring oppression: A scoping literature review of Aboriginal population health research. Joint Meeting and Young Investigators Forum, CSCI (*Canadian Society for Clinical Investigation*) and CITAC (*Clinician Investigator Trainee Association of Canada*), Ottawa (ON), September 12-14, 2011. (Poster).

46. **Sibley, C. D.,** (2011) The polymicrobial nature of airway infections in cystic fibrosis. MD/PhD Building Bridges Program: University of British Columbia, Vancouver, BC.

47. Aman **Wadhwani**, Wallace K. MacNaughton. Intracellular signaling pathways responsible for trypsin-induced change in transepithelial resistance across intestinal epithelial cells. Abstract published for poster presentation at “The World Congress on Inflammation 2011”, 25th – 29th June 2011, Paris, France.

48. A.**Wadhwani**, M. Dicay, W.K. MacNaughton. MECHANISMS OF THE PROTEASE-INDUCED INCREASE IN TRANSEPITHELIAL RESISTANCE IN INTESTINAL EPITHELIAL CELLS. Abstract accepted for an oral presentation at “The Annual Canadian Digestive Diseases Week 2012”, Montreal, QC.

49. **Yaraskavitch** M. HaNDL Syndrome: Case Presentation. *Neurology Rounds;* Toronto, ON; June 2011.

APPENDIX A: ANNUAL RESEARCH SYMPOSIUM

The following documents include the Agenda, Keynote Speaker information, Oral Presentation and Poster Presentation and list of abstracts submitted.

The 3rd Annual Leaders in Medicine Research Symposium was held November 4, 2011

3rd Annual

University of Calgary
Leaders in Medicine Research Symposium

November 4, 2011

Distinguished Guest and Speaker:

Dr. Douglas Hamilton MD, PhD
NASA Flight Surgeon

3rd Annual
University of Calgary
Leaders in Medicine Research Symposium

November 4, 2011
1:30-7:00 p.m.
Health Sciences Centre, Faculty of Medicine

Program

1:30 — 1:50 pm: **Welcome and Introduction of Keynote Speaker**
Dr. Tom Feasby, Dean of Medicine

1:50 — 2:50 pm: **Keynote Address**
Dr. Douglas Hamilton MD, PhD
"Arranging a sleepover for 30, 000 people with 12 hours notice: The story of Katrina refugees moving from New Orleans to the Houston Astrodome"

2:50 — 3:00 pm: Refreshments

3:00 — 4:30 pm: **Oral Presentations**

4:30 — 4:45 pm: Refreshments

4:45 — 6:15 pm: **Poster Presentations**

6:15 — 7:45pm: Reception**, Awards and Closing Remarks**

Keynote Speaker

Dr. Douglas Hamilton MD, PhD
NASA Flight Surgeon

We are very excited to have **Dr. Douglas Hamilton** (MD'91, PhD'91), a University of Calgary alumnus and NASA flight surgeon, as our keynote speaker this year. While completing his medical training at the University of Calgary, Dr. Hamilton also obtained his PhD in Cardiovascular Physiology, becoming the University's first joint MD/PhD graduate. Dr. Hamilton has had a life-long passion for space, and he is well recognized for his achievements as a NASA flight surgeon, working alongside astronaut Dr. Robert Thirsk (BSc'76). In addition to his accomplishments at NASA, Dr. Hamilton has pursued many research endeavors in space medicine and electrical engineering. He has published numerous papers and was involved in the design and construction of medical equipment for space missions. In 2000, the University of Calgary honoured Dr. Hamilton with a Distinguished Alumni Award. Presently, Dr. Hamilton is involved with establishing management systems to handle health issues that may arise during space missions. He is also the chair of the Space Life Sciences Department at the International Space University.

In addition to his academic and professional achievements, Dr. Hamilton has a record of humanitarian contributions. Notably, Dr. Hamilton has been highly lauded for his work during the Hurricane Katrina disaster. During the crisis, Dr. Hamilton served as the lead night physician at the Houston Astrodome, leading a medical team that organized the triage and emergency care of 30,000 evacuees from New Orleans in three days.

Dr. Hamilton is truly a leader in medicine and an inspiration to students and faculty alike. We are honoured to have Dr. Hamilton as our Distinguished Guest and Speaker for the 3rd Annual University of Calgary Leaders in Medicine Research Symposium.

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3:15 — 3:30	Nathan Bracey	Protein Kinase C Regulates the NLRP3 Inflammasome to Drive Cardiac Dysfunction in Heart Failure	2
3:30 — 3:45	Brian Reikie	HIV exposed uninfected (HEU) infants express a hyperinflammatory innate immune profile	3
3:45 — 4:00	Keith Lawson	A Novel Therapeutic Approach For The Treatment Of Renal Cell Carcinoma	4
4:00 — 4:15	Daniel Bai	Internal Cerebral Vein Sign as an Indicator of Ipsilateral Cerebral Hypo-perfusion on CT Angiography	5
4:15 — 4:30	Zaheed Zamani	Single-entry models to manage waiting times for hip and knee replacement: value and acceptability among orthopaedic surgeons in Canada	6

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Presentation Number: 1

Presenter's Name: Braedon McDonald

Program and Year: MD/PhD, Year 5

Category: Basic Science Project

Intravascular Neutrophil Extracellular Traps (NETs) protect against bacterial dissemination in Gram-negative sepsis

Braedon McDonald, Rossana Urrutia, Bryan Yipp, Craig Jenne, and Paul Kubes

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Background: A key feature of the systemic inflammatory response syndrome of severe bacterial sepsis is profound recruitment of neutrophils into the microcirculation of highly vascular organs such as the liver. The reasons for this sequestration of neutrophils within the liver remain unknown. We hypothesized that neutrophils are recruited to the liver as part of a coordinated host defense mechanism to protect against bacterial dissemination during septic infections. Specifically, we hypothesized that neutrophils release neutrophil extracellular traps (NETs, extracellular webs of decondensed chromatin covered in anti-microbial proteins) to ensnare bacteria from the bloodstream and prevent dissemination.

Methods: Dynamic *in vivo* imaging with spinning-disk confocal intravital microscopy was used to visualize the liver microvasculature of anesthetized experimental mice. Various labeled antibodies and selective dyes were used to visualize and quantify neutrophils, platelet-neutrophil interactions, NETs release, and bacterial trapping *in vivo*. Bacterial dissemination was investigated in a model of *E. coli* sepsis ($1x10^7$ *E. coli* Xen14, i.p.) by quantifying colony-forming units (CFU) of *E. coli* in various organs 24 hours post-infection.

Results: Intravascular *in vivo* imaging revealed NETs within liver sinusoids in response to endotoxemia or intraperitoneal *E. coli* infection. NETs production within liver sinusoids was dependent on platelet-neutrophil interactions, as depletion of platelets or neutrophils, or disruption of a key adhesion molecule mediating platelet-neutrophil interactions (LFA-1) significantly inhibited the generation of NETs. In Gram-negative sepsis, blocking intravascular NETs release (by platelet-depletion, LFA-1 deficiency, or administration of i.v. DNase to degrade intravascular NETs) resulted in significantly reduced trapping of bacteria in liver sinusoids, together with significantly increased dissemination of bacteria to distant organs.

Conclusions: We provide the first direct visual evidence that intravascular NETs ensnare bacteria from the circulation of septic mice, greatly improving trapping efficiency in blood and protecting against the spread of bacteria during Gram-negative sepsis.

Presentation Number: 2

Presenter's Name: Nathan Bracey

Program and Year: MD/PhD, Year 3

Category: Basic Science Project

Protein Kinase C Regulates the NLRP3 Inflammasome to Drive Cardiac Dysfunction in Heart Failure

Nathan A. Bracey, Paul L Beck, Jiqing Guo, Habib I Jabagi, Daniel A Muruve, Simon Hirota, James Wright, Justin MacDonald, James P. Lees-Miller, Daniel Roach, Lisa M Semeniuk, Henry J. Duff

Libin Cardiovascular Institute, University of Calgary, Alberta, Canada

Background: Chronic diseases of diverse etiology share a systemic, low-grade sterile inflammation that contributes to disease progression. For example, persistent cardiac inflammation post myocardial infarction results in heart failure and is associated with adverse clinical outcomes including arrhythmic deaths. IL-1β is a pro-inflammatory cytokine released in response to danger signals. On recognition of danger associated molecular patterns (DAMPs) a multiprotein complex termed the inflammasome is activated. This leads to activation of the cysteine protease caspase-1, which cleaves pro- IL-1β into its active form. Cardiac specific overexpression of the calcium dependent phosphatase calcineurin (CN/Tg) stimulates hypertrophic programs. CN/Tg mice develop cardiac hypertrophy followed by inflammation, dilatation and heart block. Given the role of inflammation in other chronic diseases, we hypothesized that the inflammasome is activated in the CN/Tg heart failure model and that IL-1β contributes to myocardial dysfunction and arrhythmias.

Methods and Results: Cardiac tissue from CN/Tg mice had elevated NLRP3 mRNA and increased conversion of pro-IL-1β, IL-18 and pro-caspase-1 to their active forms. *In vitro* IL-1β prolonged action potential duration and induced a slowly inactivating component of I_{Na} in WT myocytes, which was abolished on PKC inhibition with BIS. Blockade of PKC in CN/Tg ventricular myocytes resulted in restoration of I_{Na}. *In vivo*, CN/Tg mice treated with recombinant IL-1Ra had significantly improved systolic performance ($p<0.001$) and reduced episodes of heart block ($p<0.00001$). Lastly, inhibition of isozyme specific PKC-β2 in CN/Tg mice resulted in less activation of caspase-1 and IL-1β with reduced myocardial infiltrate.

Conclusions: Taken together, our results indicate that the inflammasome is active and contributes to myocardial dysfunction and arrhythmogenesis in CN/Tg mice through a PKC dependent pathway. Blockade of IL-1β reversed these phenotypes. These results identify the inflammasome as a potential novel target for subsequent therapeutic exploitation in the treatment of heart failure.

Presentation Number: 3

Presenter's Name: Brian Reikie

Program and Year: MD Year 2, PhD Year 5

Category: Translational Science Project

HIV exposed uninfected (HEU) infants express a hyperinflammatory innate immune profile

Brian Reikie[1,2], Aleksandra Leligdowicz[2], Rozanne Adams[3], David Speert[2], Corena De Beer[4], Mark Cotton[5], Monika Esser[3,5] & Tobias Kollmann[2,3,6]

University of Calgary Faculty of Medicine, Calgary, AB; Department of Paediatrics[2], Vaccine Evaluation Centre[6], Vancouver, BC; Department of Pathology[3], Division of Medical Virology[4], KID-CRU[5], University of Stellenbosch, Tygerberg, South Africa

Objectives/Introduction: 300,000 HEU infants born in South Africa every year are at a higher risk of morbidity and mortality, and aberrant immune responses likely contribute to increased susceptibility to infection. In order to investigate immunological correlates of increased morbidity, we conducted a prospective cohort study investigating innate immune function in South African HEU and HIV Unexposed (UE) infants.

Methods: Biological samples were collected at 2 and 6 weeks, 6, 12 and 18 months of age. HEU or UE blood was treated with multiple pathogen-associated stimuli and immune function was assessed. Flow cytometric data on markers of inflammation is presented for conventional dendritic cells (cDC), plasmacytoid dendritic cells (pDC) and monocytes (Mo).

Results: HEU (n=31) and UE (n=29) infants who participated in the study were from the same communities. Statistical differences were found over the first year of life for various combinations of mono and polyfunctional cytokine responses. The most substantial differences between HEU and UE groups were with HEU cDCs expressing higher levels of TNFα or TNFα & IL12p40 at 2 weeks of age and with pDCs producing more IFNα or IFNα & TNFα by 6wks. Of note, all statistical differences that were detected demonstrated a more pro-inflammatory profile in HEU infants.

Conclusion: South African HEU infant innate immune responses are hyperinflammatory. This striking finding provides the first evidence of aberrant innate immune responses in HIV exposed but uninfected infants. Delineating etiological factors underlying these immune abnormalities will be essential to curb high levels of morbidity and mortality seen in HEU infants.

Presentation Number: 4

Presenter's Name: Keith Lawson

Program and Year: MD/MSc, Year 3

Category: Translational Science Project

A Novel Therapeutic Approach For The Treatment Of Renal Cell Carcinoma

Keith A. Lawson, Zhong Qiao Shi, Jason Spurrell, Don G. Morris
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Purpose: In this study, we sought to characterize the response of RCC to reovirus as a monotherapy and in combination with sunitinib, a first line agent currently used to treat metastatic RCC.

Materials and Methods: A panel of RCC cell lines (786-O, A498, ACHN, Caki-1, Caki-2, RENCA) were treated with escalating doses of reovirus, sunitinib or a combination of these agents. Cytotoxcitiy and viral progeny release were assessed via the WST-1 assay and plaque titration assay, respectively. Additive effect, synergism and antagonism resulting from combination therapy was determined via the Chou and Talalay method. *In vivo*, 8-9 week BALB-c mice were implanted with s.c. RENCA tumours and treated with reovirus [2.0×10^8 pfu/ml q4d], sunitinib [20 mg/kg qd] or a combination of these agents. Body weight and tumour size were followed to assess toxicity and efficacy of these agents.

Results: All cell lines displayed greater than 50% cytotoxicity following 48hr treatment with reovirus at 40 MOI, suggesting that RCC is highly sensitive to reovirus oncolysis. The ability of reovirus to replicate in RCC was confirmed via viral progeny assays in the A498, RENCA and 786-O cell lines. Combination of reovirus with the multi-tyrosine kinase inhibitor, sunitinib, resulted in an antagonistic cytotoxic effect in A498, ACHN, RENCA and 786-O cells *in vitro*. *In vivo*, intravenous reovirus administration decreased tumour burden and this effect was augmented by sunitinib.

Conclusion: These preclinical results suggest that RCC is sensitive to reovirus oncolysis both *vitro* and *in vivo*. To our knowledge, this has not been previously reported. Our work has also demonstrated that combing reovirus with the first line RCC therapeutic, sunitinib, further decreases tumour burden. Thus, the use of reovirus as both a single agent and in combination with sunitinib warrants further investigation.

Presentation Number: 5

Presenter's Name: Daniel Bai

Program and Year: MD/MSc, Class of 2013

Category: Clinical Project

Internal Cerebral Vein Sign as an Indicator of Ipsilateral Cerebral Hypoperfusion on CT Angiography

Daniel Bai, Bijoy Menon, Jayesh Modi, Sung Sohn, Andrew Demchuck, Mark Hudon, Mayank Goyal, Tim Watson

Departments of Clinical Neuroscience and Neuroradiology, University of Calgary

Introduction: The use of computed tomography angiography (CTA) to assess cerebral arterial insufficiency in acute ischemic stroke via changes in venous perfusion has been previously documented. We hypothesize that a reduction in internal cerebral vein (ICV) perfusion on CTA may be a useful predictor of cerebral arterial occlusion. Here, we provide evidence for a relationship between decreases in contrast opacity of the internal cerebral vein (ICV sign) and internal carotid artery (ICA) occlusion with Willisian collateral insufficiency.

Methods: 239 patients with acute ICA occlusions diagnosed by CTA between 2002-08 were included in our study. Their CTA images were reconstructed using OsiriX to generate 2D images in 3 planes with slabs of 40 mm thick image slices. The degrees of ICV contrast opacity on the diseased cerebral hemispheres were compared to that of the normal sides.

Results: Of the 239 patients in our database, 153 were included in our study. Giving that the ICV drains proximal arteries, 57 out of 65 patients (87.7%) with both proximal and distal occlusions showed the ICV sign and 7/70 (10%) patients with isolated distal occlusion showed the ICV sign ($p<0.001$). Moreover, in the 8 patients without an ICV sign, all 8 were found to have prominent collateral arteries.

Conclusions: The ICV sign on CTA correlates well with the presence of ICA occlusions and reduced collateral arteries. In patients with isolated carotid occlusions, the sign correlates with reduced Willisian collaterals and is possibly a marker of ipsilateral cerebral hypoperfusion.

Presentation Number: 6

Presenter's Name: Zaheed Zamani

Program and Year: MD/PhD, Year 1

Category: Clinical Project

Single-entry models to manage waiting times for hip and knee replacement: value and acceptability among orthopaedic surgeons in Canada

Zaheed Damani, Barbara Conner-Spady, Tom Noseworthy

Western Canada Waiting List Investigators

Objectives / Introduction: Single-entry models (SEMs) have been shown to reduce waiting times, increase equity and general satisfaction by providing patients access to necessary services through a single point of entry. Questions remain about value and acceptability of SEMs by patients and their clinicians.

The objective is to understand surgeon acceptability (and under what conditions) of SEMs by Canadian surgeons receiving referrals for hip and knee replacement (H&KR).

Methods: Experienced surgeons were chosen from a larger study, came from 3 Provinces across Canada, and 68% accepted patients from a pooled list. Nineteen were interviewed regarding their views on SEMs as a means to access scheduled H&KRs. Academic/community-based, as well as urban/rural-based orthopaedic surgeons from Alberta, Manitoba and Nova Scotia were included. Data were collected through semi-structured telephone interviews. Thematic analysis was the primary methodology used to code, classify, interpret the findings.

Results: Eighty-four percent of surgeons interviewed rated SEMs as acceptable (47% very/37% somewhat). Both rural and urban surgeons were accepting of the basic tenets of SEMs, expressing an appreciation for the improved patient care, reduced waiting times afforded by SEMs. They disagreed and would oppose SEMs on the grounds of lack of continuity of care, surgeon autonomy/control, lack of patient choice, inappropriate patient referrals and lack of funding. Considerations needed for the implementation of SEMs and important incentives in making SEMs acceptable to surgeons and their patients include improving the appropriateness of referrals, trained staff, funding, standardised continuum of care, central intake, reduced waiting times and more surgeon control.

Interpretation: Though many surgeons appear to accept the value of SEMs and are in favour of implementing them, acceptability appears conditional, not uniform. There are particular critical success factors, which if considered, would increase surgeon acceptability and, accordingly, improve the opportunity for successful implementation, with generalizability to other scheduled services.

Poster Number: 1

Presenter's Name: Murad F. Bandali

Program and Year: MD, Year 3

Category: Clinical Project

False Positive Computed Tomographic Angiography for Stanford Type A Aortic Dissection

Murad F Bandali, Jehangir Appoo, Jason K Wong

Department of Radiology, Faculty of Medicine, University of Calgary

Background: Computed tomographic angiography (CTA) has emerged as the imaging modality of choice to rule out acute aortic dissection; however, it is not without flaws. We report a case of a false-positive CTA for Stanford Type A aortic dissection.

Case: A 52 year-old male presented with sudden onset shortness of breath but denied chest pain. Due to significantly elevated blood pressures and a bedside ultrasound suggesting an intimal flap in the aorta, CTA was preformed and revealed a Stanford Type A aortic dissection with thrombosis of the false lumen in the ascending aorta. However, intra-operatively, neither a dissection flap nor thrombus was found. The suspected aortic dissection and thrombosed false lumen were not visualized on repeat CTA two days later.

Discussion and Conclusion: Over-diagnosis of Stanford Type A aortic dissection on CTA can be the result of technical factors, streak artifacts, motion artifacts, and periaortic structures. While CTA remains the gold standard for diagnosis of acute thoracic aortic dissection, in the future if uncertainties on CTA arise, echocardiography or catheter angiography can be added to increase the accuracy of diagnosis.

Poster Number: 2

Presenter's Name: David Nicholl

Program and Year: MD/MSc 2011

Category: Clinical Project

Increased Urinary Protein Excretion in the 'Normal Range' is Associated with Increased Renin Angiotensin System Activity

Nicholl DDM[1,2], Hemmelgarn BR[1-3], Turin TC[1], MacRae JM[1-3], Muruve DA[1,3], Sola DY[1,2], Ahmed SB[1-3]

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Objectives/Introduction: Increased levels of albuminuria and proteinuria, both linked to augmented renin angiotensin system (RAS) activity, are associated with adverse kidney and cardiovascular events. However, the relationship between variations in urinary albumin excretion (UAE) and total protein excretion (UTPE) in the normal range and RAS activity is unclear. We examined the association between UAE and UTPE and hemodynamic response to angiotensin II (AngII) challenge, a well-accepted indirect measure of RAS activity, in healthy individuals with normal UAE and UTPE.

Methods: Forty subjects (15 men, 25 women; age, 38±2yrs; UAE, 3.32±0.55mg/day; UTPE, 56.8±3.6mg/day), were studied in high salt balance. Blood pressure (BP), arterial stiffness determined by applanation tonometry, and circulating RAS components were measured at baseline and in response to graded AngII infusion. The primary outcome was the BP response to AngII challenge at 30 and 60 minutes.

Results: UAE was associated with a blunted diastolic BP response to AngII infusion (30min, $p=0.005$; 60min, $p=0.17$), a relationship which remained even after adjustment (30min, $p<0.001$; 60min, $p=0.035$). Similar results were observed with UTPE (30min, $p=0.031$; 60min, $p=0.001$), even after multivariate analysis (30min, $p=0.008$; 60min, $p=0.001$). Neither UAE nor UTPE were associated with the systolic BP, circulating RAS component, or arterial stiffness responses to AngII challenge.

Conclusion: Among healthy individuals with UAE and UTPE in the normal range, increased levels of these measures were independently associated with a blunted diastolic BP response to AngII indicating increased vascular RAS activity, which is known to be deleterious to both renal and cardiac function. Larger, prospective studies are required to determine whether albuminuria and proteinuria have a causal role in the progression of kidney and cardiovascular disease.

Poster Number: 3

Presenter's Name: Ursula Madej

Program and Year: MD, Class of 2012

Category: Clinical Project

Practice Variation in Medical Therapy with Angiotensin Converting Enzyme (ACE) Inhibitors in Single Ventricle Patients Post-Fontan Procedure

U. Madej, K. Myers, D. Fruitman

Objectives/Introduction: ACE inhibitors have been shown to improve clinical outcome in adults and children with heart failure. The ability of ACE inhibitors to preserve ventricular function and improve outcomes in single ventricle patients post-Fontan procedure is unknown. The aim of this study is to gain an understanding of current management practices at a single institution post-Fontan.

Methods/Results: A retrospective chart review was performed of 36 patients followed at Alberta Children's Hospital, who underwent a Fontan procedure between January 1, 2000 and May 31, 2010. Data was obtained including diagnosis, surgical data, medications and clinical status pre- and post- Fontan. Median age at Fontan was 3.6 years (range 2.1-15 years). Twenty-one(64%) patients were on an ACE inhibitor prior to the Fontan. Early post-Fontan, 23(72%) patients were on ACE inhibitors. Of these, 16 remained on ACE inhibitors post-operatively, 7 patients were started on ACE inhibitors, and 3 patients were taken off ACE inhibitors. Follow-up data was obtained in 32 patients with a median of 3.4 years (range 0.3-8.2 years). Of 28 patients with echocardiographic data available, 4 had mildly reduced, 2 moderately reduced, and 1 severely reduced systolic function; 20 had mild and 2 had moderate atrioventricular valve regurgitation. At last follow-up, 18 (56%) patients were on ACE inhibitors, of which 15 continued use and 3 had an ACE inhibitor started for ventricular systolic dysfunction.

Conclusion: Despite limited data regarding the use of ACE inhibitors in children with single ventricle physiology post-Fontan procedure, greater than 50% of patients were on an ACE inhibitor on follow-up. This study illustrates the need to describe the practice variation on a larger scale across multiple centres, with the goal of defining a consistent treatment strategy for this patient population.

Poster Number: 4

Presenter's Name: Amrita Roy

Program and Year: MD/PhD, Year 4 of PhD

Category: Clinical Project

Methods for measuring oppression: A scoping literature review of Aboriginal population health research

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[1] Department of Community Health Sciences, Faculty of Medicine, University of Calgary; [2] Department of Ecosystem and Public Health, Faculty of Veterinary Medicine, University of Calgary; [3] Department of Psychiatry, Faculty of Medicine, University of Calgary; [4] Department of Pediatrics, Faculty of Medicine, University of Calgary; [5]Department of Family Medicine, Faculty of Medicine, University of Calgary

Background: An evidence-based approach to population health interventions requires scientifically rigorous evidence from context-relevant studies. The context of Aboriginal women's health includes intersecting sources of oppression from race, gender, social exclusion and the legacy of colonization. Oppression can impact health through pathways including disadvantage along social determinants of health, barriers to healthcare access and healthy living, unhealthy coping behaviours, and stress pathophysiology. Oppression is recognized theoretically as crucial for understanding Aboriginal women's health; however, relatively few quantitative studies assess it. Empirical methods of measurement are required.

Objective: To explore existing methods, we performed a scoping literature review to examine how concepts of oppression have been measured in Aboriginal population health studies. This review is the first step of a project aimed at developing an approach to comprehensively quantify oppression in epidemiological research in Aboriginal women's health.

Methods: Systematic searches of the peer-reviewed literature were conducted to identify eligible quantitative studies in Canada, USA, Australia and New Zealand. Information from each paper was abstracted and charted. The methods found were summarized and analyzed for strengths and weaknesses.

Findings: Perceived racism, racist attitudes, and domestic and sexual violence have been measured with various scales and indicator questions. Individual-level and area-level measures of social and economic disadvantage have been used to indicate social exclusion. The multigenerational impacts of colonization have been assessed with scales on historical loss trauma, and indicator questions on parental residential school attendance. Limited are measurements of gender oppression beyond domestic and sexual violence. Furthermore, little emphasis has been placed on measuring the intersections of sources of oppression.

Significance: Through mapping out existing methods, we have identified specific gaps that need to be addressed to allow for comprehensive and appropriate measurement. Improved measurement of oppression, and consequent understanding of how it can be addressed, will help in the design of effective interventions.

Poster Number: 5

Presenter's Name: Rita Watterson

Program and Year: MD, Class of 2013

Category: Clinical Project

A Gender-based Consideration of Diseases of Occupation: Narratives of Ultra-Poor Bangladeshi Women Heads of Household

Rita Watterson, Lynn McIntyre

University of Calgary Faculty of Medicine, Department of Community Health Sciences

Introduction: Although increased paid employment outside of the agricultural sector is one the three progress indicators for Millennium Development Goal 3, there are hazards to employment. The purpose of this study was to explore a broader definition of occupational health to shed light on the direct and indirect impact of work on the quality of life and health status of ultra-poor women and their children.

Methods: We conducted a a secondary analysis of in-depth ethnographic interviews collected on the daily life and food provisioning practices of 43 ultra-poor Bangladeshi women heads of household who worked in a variety of occupations: garment workers, petty traders, subsistence agriculturalists, and Garo workers. The original interviews were digitally recorded and translated by multiple skilled staff. NVivo coding was conducted on the original material. Analysis involved immersion and crystallization with three readers followed by recoding to assess saturation of themes.

Results: The health consequences of specific occupations paled in light of the general ill-health of the women. This observation notwithstanding, garment workers reported overuse injuries; day labourers reported spinal strain from such jobs as road digging; skin ailments were reported from rice paddy work; and severe chronic respiratory disease was reported among roadside street vendors. Beyond the ergonomics of work, though, women were harmed by working conditions that placed them outside of labour protection (e.g., unions, extended hours, inconsistent payment); in dangerous work situations (e.g., precarious travel, illegal border crossings); outside of the traditional market economy (no access to wholesale products); and in exploitative conditions (e.g., as sharecroppers absorbing all costs but reaping only half of the total profits).

Conclusion: A gendered examination of occupation beyond the physical hazards and exposures extends our understanding of what is required to achieve the MDG 3 and improve the lives of vulnerable women workers.

Poster Number: 6

Presenter's Name: Simone Lebeuf

Program and Year: MD, Class of 2014

Category: Clinical Project

The Map Task: Mapping the Development of Working Memory in the Preschool Years

Simone Lebeuf, Mahsa Khoei, Kelly West, Rebecca Visscher, & Sandra A. Wiebe

Department of Psychology, University of Alberta

Working memory (WM) is the ability to keep information in mind and manipulate it to guide current or later behaviour (Baddeley, 1992). It develops rapidly throughout the preschool years, that is, between 3 and 6 years (Gathercole, 1998). Numerous tasks are available to assess WM in adults, like the Backward Digit Span, but these may be too complex and unengaging for young children. More valid tasks are needed to test preschool WM. The Map Task, a modified version of the Nutley et al. (2010) visuospatial WM task, fills this gap. It uses a 3X3 grid with each square representing a playground activity. Children moved a toy to the same locations as the experimenter's toy in either forward or backwards order. We also administered two established WM tasks, Word Span (WS) and Delayed Alternation (DA), to examine convergent validity.

Participants included 46 2 ½- to 6-year-olds (M age = 4 years 6 months, SD = 10 months; 23 boys). Children were divided into two age groups: younger preschoolers (< 4.5 years; n = 21) and older preschoolers (> 4.5 years; n = 25).

Results showed older children performed better on all WM measures used. When age was statistically controlled, forward and backward Map Task performance significantly correlated with backward WS. This suggests that the Map Task measures the same construct as standard measures of WM currently in use. Anecdotally, experimenters reported that children found Map Task engaging and fun. Altogether, these findings indicate that Map Task is a promising test of WM for use in studies of preschool development.

Poster Number: 7

Presenter's Name: Brett Kilb

Program and Year: MD, Class of 2012

Category: Clinical Project

Defining the needs of Medically Complex Children and the development of a Transition Clinic model

Kilb B[a], Mainland S[b], Cooke S[b]

[a] *Faculty of Medicine, University of Calgary;* [b] *Department of Paediatrics, University of Calgary*

- **Introduction:** Medically Complex Children (MCC) are affected by a myriad of medical, social and economic issues requiring the coordination of multiple services. The proportion of in-patient MCC is increasing exponentially and conventional care models have proven inadequate in transitioning this population into the community, often resulting in avoidable re-admissions and unnecessary complications. Specialized care models for MCC have been shown to reduce the number of emergency department visits and the cost of care, however, literature is lacking with respect to the characteristics and requirements of MCC in the peri-discharge period.
- The objectives of this study were i) Characterize the MCC in-patient population and define their requirements in the peri-discharge period ii) Develop a contemporary model for a transition clinic for these patients.
-
- **Methods:** Chart review was performed on all MCC admitted to the Complex Care Team at a tertiary paediatric centre over a 17 month period. Based on the data collected and current literature, a proposal for a MCC *Transition Clinic* was developed.
-
- **Results:** Forty MCC were included in the analysis. Mean age was 3.6 years, 55% were males. The number of significant medical issues per child was 14.8, with 75% of the children affected by conditions of congenital aetiology. The use of mechanical devices was prominent (3.5 per child), and during a child's stay, he or she saw an average of 7.6 sub-specialists. In preparation for discharge, caregivers of MCC were taught an average of 5.4 outpatient therapies. In the first 6 months following discharge, outpatient procedures (4.6 per child) were frequent, as was follow-up with health professionals (7.3 contacts per child).
-
- **Conclusion:** The complexity of MCC requires novel approaches to provide appropriate transfer, bridging and peri-discharge management. We have developed a *Transition Clinic* model designed to promote the successful, sustained transition of these children into the community

Poster Number: 8

Presenter's Name: Nahbeel Premji

Program and Year: MD, Class of 2014

Category: Clinical Project

Comparing contrast sensitivity between accommodating and non-accommodating intra-ocular lenses post cataract surgery

Nahbeel Premji and Dr. Robert Mitchell

Objective: To compare the contrast sensitivity between the accommodating Crystalens and a standard monofocal intraocular lens (IOL) (Akreos) under mesopic conditions at 6 months post-cataract surgery.

Methods: 20 eyes that had undergone uncomplicated cataract surgery at least 6 months ago were selected, based on strict inclusion and exclusion criteria for each of the two IOL types. The distance contrast sensitivity under mesopic conditions with best-corrected visual acuity (BCVA) correction was measured. Statistical analyses were performed using the Mann-Whitney test.

Results: No statistically significant difference was found in the contrast sensitivity at each of the five spatial frequencies tested between the two types of IOL.

Conclusions: Multi-focal intraocular lenses cause a reduction in contrast sensitivity compared to monofocals. This study shows that the Crystalens does not reduce contrast sensitivity compared to a standard monofocal intraocular lens.

Poster Number: 9

Presenter's Name: Mark Seamone

Program and Year: MD/MSc, Year 2

Category: Clinical Project

A direct comparison of high-speed ultra-high-resolution optical coherence tomography (hsUHR-OCT) and multifocal electroretinography (mfERG) findings in early-stage hydroxychloroquine retinopathy

Mark E. Seamone[1], Micheline Deschênes[2], Mark Hanna[2], Amin Kherani[2, 3], Michael Fielden[1] and R. Geoff Williams[2, 3]

[1]Department of Medicine, [2]Calgary Retina Consultants, [3]Department of Surgery, University of Calgary, Calgary, Alberta, Canada

Hydroxychloroquine is a commonly used drug in the treatment of rheumatologic and dermatologic diseases. However, hydroxychloroquine can be the cause of ocular toxicity in the form of pigmentary retinopathy. The early detection of hydroxychloroquine retinopathy is essential to the visual prognosis of affected individuals. In spite of this, a definitive test for the assessment of hydroxychloroquine retinal toxicity prior to the identification funduscopic changes or visual field loss has not been described. Currently, multifocal electroretinogram (mfERG) is considered the gold standard for detecting early-stage hydroxychloroquine-induced retinal pathology. However, accessibility to mfERG is limited and discrepancies in mfERG recordings are often noted upon serial examination of individual patients. Spectral domain ocular coherence tomography (SD-OCT) is a newly described method of ocular imaging that allows for high-speed analysis of retinal pathology. It is the central hypothesis of this manuscript study that SD-OCT can be used to detect hydroxychloroquine-induced retinal pathology prior to the onset of clinically apparent disease. To address this hypothesis, twenty individuals who have been receiving hydroxychloroquine therapy (for a minimum of five years) will be selected retrospectively to compare mfERG and SD-OCT findings. This data will then be used to determine the sensitivity and specificity of SD-OCT for the diagnosis of early-stage hydroxychloroquine retinopathy. This analysis is of great clinical significance as detection of hydroxychloroqine retinopathy prior to the onset of clinically apparent disease may lead to alteration in treatment regimens that have a direct impact on the visual prognosis of affected individuals.

Poster Number: 10

Presenter's Name: Matt Henschke

Program and Year: MD, Class of 2013

Category: Clinical Project

Interdisciplinary Practices for Efficient Primary Care

Matt Henschke
University of Calgary Medicine

Introduction: Alberta is currently facing a shortage of family physicians. Fundamental economic principles dictate that such shortages can be overcome in three ways: increasing the supply, increasing efficiency and decreasing demand. Ontario has recently implemented interdisciplinary Family Health Team (FHT) models which have showed promising trends in all three areas.

Methods: A literature search was preformed in PubMed and the literature was then reviewed and selected based on relevance to Ontario's FHT model. Results were then analyzed and assessed and included based on level of evidence and methodology.

Results: Under the FHT model family physicians experienced higher job satisfaction and greater renumeration. Since the FHT model began medical students were 56% more likely to choose family medicine. The FHT model predicts that family physicians operating under the FHT model can provide primary care for 30% more patients. When pharmacists were incorporated into primary care practices chronic markers of disease, such as low density lipoprotein (LDL), glycated hemoglobin (HbA1c) and blood pressure (BP) were found to be under tighter control.

Conclusion: Interdisciplinary health teams, such as the FHT model have been shown to attract students to the field of family medicine. In addition, interdisciplinary health teams increase the efficiency of family practices, while providing enhanced patient care. Alberta should consider implementing a similar model in to facilitate effective and efficient primary care.

Poster Number: 11

Presenter's Name: Robbie Sidhu

Program and Year: MD, Year 3

Category: Clinical Project

Digoxin Toxicity and the use of Digibind: A Case Report & Review

Robbie Sidhu, Jack Cruikshank[1], Mark Yarema[2], P. Timothy Pollak[3]

1. Department of Medicine, University of Calgary; 2. Poison and Drug Information Service, Department of Emergency Medicine; 3. Departments of Cardiac Sciences, Physiology & Pharmacology

Digoxin has long been used in clinical cardiology for the treatment of systolic heart failure and supraventricular tachycardias, such as atrial fibrillation and atrial flutter. It's origin trace back to purified foxglove plant preparations.

Today, many physicians hesitate to use digoxin because of its narrow therapeutic index. The use of ACE inhibitors and beta-adrenergic antagonists have supplanted digoxin, leading to declining rates of its use. Although becoming rarer, digoxin toxicity remains important due to its serious consequences. High plasma concentrations can eventually result in confusion, delirium, and cardiac dysrhythmias including ventricular tachycardia/fibrillation, and complete heart block.

With the introduction of Digoxin Immune Fab (Digibind), the approach to digoxin toxicity has changed dramatically. Digibind works via Digoxin specific Fab antibody fragments that bind serum digoxin and prevent it from binding to its receptor. However, the indications of Digibind have not been studied extensively in the literature and its use is still controversial given its high price.

We present a case report of a 63 year old female who was transferred to Foothills hospital for Digoxin toxicity and given 14 vials of Digibind, at a cost of $500/vial. A complete literature review of digoxin toxicity and the use of digibind is also presented. Our goal is to develop an approach for the clinician in dealing with digoxin toxicity and the use of the antidote Digibind.

Poster Number: 12

Presenter's Name: Jill Stone

Program and Year: MD, Year 3

Category: Clinical Project

Incidence of Common Suture Placement Errors Made by Plastic Surgery Residents During Microsurgical Training: A Randomized Double-Blind Study

J Stone, C Doherty, C Schrag

University of Calgary: Department of Plastic Surgery

Although an integral part of training in many surgical specialties, microsurgical training is varied in its educational approach. Based on the observations of a senior microsurgeon at the University of Calgary, seven cardinal mistakes commonly committed by surgical residents have been identified. Identifying these common errors and the theoretical approach to prevent or repair them may provide benefit to trainees. We seek to investigate whether there is a difference in performance of residents if they receive a didactic teaching session with visual aids prior to their laboratory microsurgery course. Blinded evaluators assessed performance of the residents using a validated observational method. The study group outperformed the control group when comparing errors/day (P=0.04) and total number of errors made by the control and experimental group (P=0.02). The most common errors included creating loose anastomoses and backwalling the vessels. Given the differences in performance between the control group and experimental group, we can conclude that an introduction to these common errors and how to avoid them plays an important role in the laboratory setting. Originally designed as a trial survey, our intention is to expand on this study to encompass a larger study group drawing from other surgical specialties/centers. We hope to see this training platform incorporated as an integral part of microsurgical education in the future.

Poster Number: 13

Presenter's Name: Salina Teja, Jovian Collins and Brad Granberg

Program and Year: MD, Year 3

Category: Clinical Project

The Effect of Early Exposure to Patients with Chronic Disease on Students' Empathy: A Randomized Controlled Trial

Salina Teja, Jovian Collins, Brad Granberg, Dr. Heather Baxter, Dr. Kevin McLaughlin

Introduction/Objectives: Empathy is a key component of the physician-patient relationship, enabling patients to provide better historical data (10-17) and report enhanced satisfaction and psychosocial health (6-9 & 2-5). A relatively consistent finding from observational studies of medical students is that there is progressive erosion throughout training of both empathy and students' attitudes towards social issues affecting their patients. At the University of Calgary we introduced a pilot project entitled the Student Patient Collaboration Initiative (SPCI), the purpose of which was to encourage students to spend time (in a non-clinical role) with patients suffering from chronic illness, allowing a better understanding of the patient's experience and the impact of chronic disability. We predicted that exposure to the intervention should result in higher scores for empathy and attitudes towards social issues affecting patients.

Methods: 30 of 71 interested first year medical students were randomly allocated to the intervention group. These participants met with a patient five times between October 2010 and March 2011. Students met in a focus group three times to discuss their experience. We measured the impact of this program through the use of quantitative scales (ATSIM - Attitudes Towards Social Issues in Medicine and JSE - Jefferson Scale for Empathy) administered at the start and conclusion of the program, and qualitative data obtained from transcription of focus groups.

Results: At baseline and at the end of the intervention period, there was no significant difference between the intervention and non-intervention groups on either the JSE or ATSIM ratings.

Conclusion: In this study we failed to note a significant impact of our intervention on students' empathy and their attitudes towards social issues faced by their patients. These results should not, however, deter us from exploring ways to improve empathy and attitudes, as our qualitative data indicates a possible benefit to some form of this program.

Poster Number: 14

Presenter's Name: Trevor Cook

Program and Year: MD/MSc

Category: Clinical Project

Low Social Support as a Risk Factor for a Major Depressive Episode in Canadian Community Dwelling Seniors

Trevor Cook (1), Dr. JianLi Wang (2)

1. MD/MSc. Student, Department of Community Health Sciences, Faculty of Medicine, University of Calgary
2. Associate Professor, Departments of Community Health Sciences and Psychiatry, Faculty of Medicine, University of Calgary

Background: Major depression represents a great cause of disease burden worldwide. Further, the proportion of Canadian citizens aged 65 years of age and older is rapidly growing. Despite this, there is a lack of longitudinal data on risk factors for a major depressive episode in seniors, while comprehensive measures of social support are rarely employed in existing literature. A longitudinal approach to examining the relationship between depression and comprehensive social support tools has yet to be conducted in Canada.

Methods: This study will use 8-year population-based longitudinal data from the National Population Health Survey, collected by Statistics Canada. The survey will be restricted to individuals aged 65 years of age and older. Demographic and socioeconomic characteristics of the sample will be presented. The 2-year and 8-year incidence proportions of major depression in seniors will be estimated. The cross-sectional and longitudinal association between social support and a major depressive episode will be examined using multivariate logistic regression.

Results: The majority of participants were female, married and living with partner. Roughly 80% of participants reported a chronic condition, though only 25% reported a pain problem and a third restriction to activity. Chronic pain, chronic conditions, and restriction to activity were each associated with higher incidence of major depression. Only positive social interaction, affection and emotional social support were significant in incidence and modeling.

Conclusion: Some but not all types of social support are significant in the risk of a major depressive episode in longitudinal analysis. Chronic conditions, pain and activity limitations are important risk factors for depression.

Poster Number: 15

Presenter's Name: Aditi Amin

Program and Year: MD, Class of 2014

Category: Clinical Project

International Zinc Treatment of Childhood Diarrhea Scale-Up Projects (ZTCDSUPs): An Overview

Aditi Amin – BA, BSc(Hons)[1,2], MPH ; Dr. Charles Larson – MD, FRCP(C)[1,2,3,4]

[1]University of British Columbia; [2]Child & Family Research Institute; [3]Centre for International Child Health; [4]BC Children's Hospital

Introduction/Objectives: Diarrhea contributes to 19% of all under-five (U5) mortality globally. The micronutrient zinc has been found to be effective in preventing and treating diarrhea. Successfully scaling-up zinc treatment could save 400, 000 U5 lives annually. The objectives of this overview are threefold: 1) to identify ZTCDSUPs taking place internationally; 2) to collect baseline information on each ZTCDSUP; and 3) to identify and summarize best practices and recommendations for future ZTCDSUPs.

Methods: A mixed-method (qualitative/qualitative), semi-structured overview questionnaire was developed and e-mailed to potential participants who were provided the option of completing it electronically or by telephone interview. Quantitative data analysis consisted of generating descriptive statistics. Qualitative data analysis consisted of basic content analysis through reducing questionnaire responses into "patterns" and "themes".

Results: 12 questionnaires were completed. The majority of ZTCDSUPs were regional initiatives implemented in Asia. Some major challenges included: slow public sector action; unreliable zinc supply; product and packaging costs; dispelling inaccurate perceptions about zinc; and adherence to zinc treatment regimen. Some major accomplishments included: increasing awareness of zinc treatment; making progress in creating sustained behaviour change; and facilitating inter-sectoral partnerships.

Conclusions: As per the needs identified by the micronutrient scale-up community and the findings of this study, successful micronutrient scale-up requires: collaborative advocacy for and delivery of zinc treatment; ongoing communication amongst stakeholders; and enhanced knowledge translation and exchange surrounding scale-up best practices. Additionally, there should be an ongoing commitment to: engaging and linking the public and private sectors; using mass media; and monitoring and evaluation.

N.B. Previously presented at Canadian Public Health Association's 2011 Conference "Public Health in Canada: Innovative Partnerships for Action" in Montreal, Quebec (June 19-22, 2011).

Poster Number: 16

Presenter's Name: Luke Rannelli

Program and Year: MD/MSc, Year 2

Category: Clinical Project

Does physical attractiveness modify the effect of other non-cognitive attributes on teaching effectiveness ratings?

L.A Rannelli, K. McLaughlin, M. Paget & W. Woloschuk

Faculty of Medicine, University of Calgary

Objectives/Introduction: The crux of many successful medical education curriculums is inevitably tied to the "effectiveness" of it's educators. Less evident is the process by which education programs identify "effective" teaching traits. The definition of teaching "effectiveness" has been divided into two main attributes; cognitive (content knowledge) and non-cognitive characteristics (personality, speech). Research has demonstrated the importance of non-cognitive attributes in the perceived "effectiveness" of a teacher by students. However, complicating this theory is the influence of non-modifiable traits of a teacher such as physical attractiveness. The effect of non-cognitive characteristics verses physical attractiveness on perceived teacher "effectiveness" has not been established.

Methods: Fifty-one first year "naive" students from the University of Calgary Medicine, were asked to judge the effectiveness of a preceptor (not known to subjects) from a two-minute audio-clip (AC) on a Likert Global Rating Scale (GRS). Simultaneously, subjects were shown a photograph of the assumed teacher in the AC with variation in physical attractiveness and facial expressions (PA). The GRS ratings were compared to end-of-course evaluation (ECE) ratings for that preceptor.

Results: "Naive" student ratings of teacher's AC significantly correlated with ECE ($r=0.76$). However, PA did not have a significant affect on student ratings of teacher's AC when compared to ECE ($r=0.02$).

Conclusion: These results suggest "naive" students can accurately predict a teacher's ECE with only a brief exposure to a two minute AC. However, it does not seem that there was an effect of PA on student ratings of AC. In summary, this may suggest that modifying non-cognitive attributes of an educator may have an impact on their perceived "effectiveness" as a teacher.

Poster Number: 17

Presenter's Name: Mary Dunbar

Program and Year: MD/MSc, Year 4 (final year)

Category: Clinical Project

Improvement of Autism in a Patient with GAMT Deficiency and Autism: a Case Report

Mary Dunbar[1], Andrea Friesen[2], Saadet Mercimek-Mahmutoglu[3]

[1]Leaders in Medicine, University of Calgary, Department of Medicine, University of Calgary, [2]Department of Physiotherapy and Occupational Therapy, University of British Columbia, [3]Division of Biochemical Diseases, Department of Pediatrics, University of British Columbia

Objectives/Introduction: Guanidinoacetate methyltransferase (GAMT) deficiency is a creatine biosynthesis defect. Of the approximately sixty cases described in the literature, most experience developmental delay within the first year of life, accompanied by movement disorders, seizures, behavioral problems and autistic-like features later on. Here we describe a new patient with GAMT deficiency who presented with autistic features within the first two years of life and her successful outcome of her autistic features on treatment.

Methods: A creatine biosynthesis or transport defect was suspected when magnetic resonance spectroscopy (MRI) revealed an absent brain creatine peak, GAMT deficiency was confirmed by elevated guanidinoacetate (GAA) levels in body fluids and a known disease causing mutation in the GAMT gene. Autism was confirmed by various standard diagnostic tools. Creatine and ornithine supplementation and dietary restriction of arginine to increase creatine levels and decrease toxic GAA levels were started after diagnosis.

Results: At two years of therapy (45 months of age), she was able to interact with objects, respond to instructions, make eye contact and guide her family to communicate her interests nonverbally. Our patient showed improvements in her developmental milestones, sensorial-neural hearing loss and brain atrophy on cranial-MRI. Urinary GAA levels were normalized at 8 months of therapy. Serum GAA was decreased from 20.11 to 3.08µmol/L and cerebral spinal fluid GAA was decreased from 11.55 to 1.4 µmol/L (reference range 0.036-0.224) at two years of therapy.

Conclusions: We report the most favorable clinical and biochemical outcome of GAMT deficiency on treatment which may be explained by early diagnosis and initiation of therapy before two years of age. In only 5% of autistic cases a metabolic disorder can be identified; our patient highlights the importance of early recognition of developmental delay and thorough investigation with prompt initiation of treatment.

Poster Number: 18

Presenter's Name: Angela Lau

Program and Year: MD/MSc

Category: Clinical Project

The Public Health Consequence of Smear-positive Pulmonary Tuberculosis in Patients with Typical and Atypical Chest Radiographs

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Introduction: Using currently available digital technology, it should be possible to automate the detection of 'typical' post-primary tuberculosis (TB) on chest radiograph (CXR). Development of such a detection system is warranted if it can be demonstrated that patients with 'typical' (vs 'atypical') CXRs are responsible for most public health consequences (recently infected persons amongst close contacts; secondary cases amongst all cases).

Methods: Over 30 months beginning January 1, 2006, all adults (age >14 years) diagnosed with smear-positive pulmonary TB in Alberta, were identified in the TB Registry. Patient demographics and mycobacteriology were abstracted from public health records and the Provincial Laboratory for Public Health. Pre-treatment posterior-anterior and lateral CXRs were assembled and scored by 3 independent readers as 'typical' (having an upper lung zone infiltrate, with or without cavitation, but no discernable intrathoracic adenopathy) or 'atypical' (all others). The public health consequences, confirmed using molecular diagnostics, from each group were compared.

Results: There were 88 adults with smear-positive pulmonary TB, of whom 62 (70.5 %) had a 'typical' CXR. Patients with 'typical' CXRs had, on average, larger bacillary burdens and metabolically more active bacteria (larger semi-quantitative smears; shorter times-to-culture-positivity) than patients with 'atypical' CXRs. More importantly, they were responsible for most public health consequences: 0.39 vs 0.04 child-aged tuberculin skin test (TST) converter per source case, p=0.008; 0.83 vs 0 child-aged TST converter per Canadian-born source case, p=0.009; and 35 vs 4 secondary cases.

Conclusions: Adult smear-positive pulmonary TB patients with 'typical' CXRs are responsible for most public health consequences. Accordingly, the development of an automated TB detection system is warranted.

Poster Number: 19

Presenter's Name: Daniel Shafran

Program and Year: MD, Year 3

Category: Clinical Project

Assessment and Treatment of Thyroid Function in Calgary Heart Failure Clinics – incidence of abnormal thyroid function and impact on Heart Failure decompensation

Daniel Shafran BSc (Hons), Debra L. Isaac MD

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Objectives/Introduction: Abnormal thyroid function (TF) is associated with cardiac dysfunction and may result in decompensation in heart failure (HF) patients. International HF guidelines recommend routine assessment and treatment of TF. Two small, American studies demonstrated only 36-40% of HF patients had TF appropriately assessed. We sought to determine the extent to which TF is monitored in Canadian HF clinics, the incidence of abnormal TF in HF patients, and how TF abnormalities impact outcomes.

Methods: Retrospective chart review was performed for all patients managed at 3 HF clinics in Calgary from November 2010 to January 2011. The following was assessed: presence and timing of TF testing (TFT), use of thyroid-altering medication, and evidence of HF decompensation (IV diuretics; doubling oral diuretic dose; ER visits or hospitalizations for HF) in the previous 12 months.

Results: Charts of 773 patients were reviewed. 719 (93.0%) had documented TFT; 592 (76.6%) had TFT in the previous 12 months, and 54 (7.0%) had no record of TFT. Of 773 patients, 21.3% (165) had documented abnormal TF. Among these, 63% (104) had adequately treated thyroid dysfunction, 18.8% (31) were inadequately treated, and 18.2% (30) received no treatment. Of 658 patients with normal TFT, 30.2% (199) decompensated compared with 41.0% (25) of those with abnormal TFT (P=0.1109). Decompensation rates in patients with normal TFT versus patients whose TFT was abnormal or never measured were 30.2% (199) and 47.8% (55) respectively (P=0.0003).

Conclusions:

1) Calgary HF clinics performed TFT in greater proportions of patients than reported elsewhere.
2) Abnormal TF is common in Calgary HF clinics.
3) Rates of HF decompensation are significantly lower in patients with normal TFT than in those with unmeasured or abnormal TFTs. Further investigation is necessary to evaluate the role of assessment and treatment of TF in reducing HF decompensation.

Poster Number: 20

Presenter's Name: Jennifer Litzenberger

Program and Year: MD, Year 1

Category: Basic Science Project

Real-time imaging of *E. coli* model membrane architecture

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Introduction: EmrE is a membrane protein that exports toxic compounds from *E. coli*. Several EmrE monomers must come together in order to export the ligand from the cell. This oligomerization state is dependent on environmental conditions, suggesting that the enzyme surroundings - specifically the cell membrane - may influence its functional unit. My worked focused on the role of specific lipid classes relative to EmrE oligomerization.

Methods: The architecture of EmrE protein clusters in biomimetic lipid monolayers was investigated using Brewster angle microscopy, which allows membrane visualization in real-time. The influence of lipid polar headgroup, acyl chain length and degree of saturation on EmrE lipid-protein interactions could be determined through visual changes in lateral architecture during monolayer compression.

Results: We used model systems composed of the major *E. coli* lipids, phosphatidylethanolamine (PE) and phosphatidylglycerol (PG) at a ratio of 7:3 which reflects the natural membrane. Langmuir isotherms and imaging of 7 PE : 3 PG monolayers at increasing surface pressures revealed varying EmrE behavior depending on acyl chain composition. The data showed that some degree of acyl chain unsaturation was required. Moreover, binary systems were not sufficient to mimic extract data. Thus we screened the impact of saturated or unsaturared cardiolipin (the third most common lipid). The isotherms showed a strong interaction of unsaturated cardiolipin with EmrE.

Conclusions: The data clearly show that protein organization strongly depended on lipid structure and their physical characteristics, such as rigidity and negative surface charge. In order to determine the impact of lipid structures relative to *E. coli*, we compared the synthetic systems to complex biological membrane extracts. The cluster morphology in 7 POPE : 3 DPPG monolayer were most similar to that in *E. coli* polar extract. Moreover, unsaturated cardiolipin was important for the lateral organization of EmrE in the *E. coli* membrane.

Poster Number: 21

Presenter's Name: Joanna J. Moser

Program and Year: PhD/MD, Class of 2013

Category: Basic Science Project

Repression of GW/P body components and the RNAi microprocessor impacts primary ciliogenesis in human astrocytes

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Introduction: In most cells the centriolar component of the centrosome can function as a basal body supporting the formation of a primary cilium, a non-motile sensory organelle that monitors information from the extracellular matrix and relays stimuli into the cell via associated signaling pathways. Defects in the formation and function of primary cilia underlie multiple human diseases and are hallmarks of malignancy. The RNA silencing pathway is involved in the post-transcriptional silencing of >50% of mRNA that occurs within GW/P bodies. GW/P bodies are found throughout the cytoplasm and previously published live cell imaging data suggest that in a malignant cell type (U2OS), two GW/P bodies reside at the centrosome during interphase. This led us to investigate if a similar relationship exists in primary cells and if the inhibition of the miRNA pathway impairs primary cilium formation.

Methods and Results: Two GW/P bodies as marked by GW182 and hAgo2 colocalized to the basal body of primary human astrocytes (and human synoviocytes) during interphase using indirect immunofluorescence (IIF) analysis. Immunogold electron microscopy showed that GW/P bodies are located at the distal end of the basal body in the pericentriolar region. Since it is technically challenging to examine the two centrosomal GW/P bodies, we investigated the potential relationship between the global population of GW/P bodies and primary ciliogenesis. Astrocytes were transfected with siRNA directed to GW182 and hAgo2 and unlike control astrocytes, a primary cilium was no longer associated with the centrosome as detected in IIF assays. Ultrastructural analysis of siRNA transfected astrocytes revealed that knock down of GW182, hAgo2, Drosha and DGCR8 mRNA did not affect the appearance of the earliest stage of ciliogenesis but did prevent the formation and elongation of the ciliary axoneme. MicroRNA profiling of astrocyte GW/P bodies show differentially expressed miRNA that are predicted to regulate mRNA involved in primary ciliogenesis.

Conclusions: This study documents that GW/P bodies are resident at the centrosome in diverse non-malignant cells and demonstrates that repression of key effector proteins in the post-transcriptional miRNA pathway impairs primary cilium formation.

Poster Number: 22

Presenter's Name: Michael Keough

Program and Year: MD/PhD, Year 2

Category: Basic Science Project

Overcoming Chondroitin Sulfate Proteoglycans: Inhibitors of Central Nervous System Remyelination

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Objectives/Introduction: Following a demyelinating episode, such as occurs in multiple sclerosis (MS), humans exhibit a robust endogenous reparative response called remyelination. However, remyelination fails in chronic MS lesions, leaving central nervous system (CNS) axons devoid of myelin and susceptible to degeneration and death. It is therefore imperative to discern why remyelination fails and find novel strategies to overcome this problem. Oligodendrocyte precursor cells (OPCs) are the chief remyelinating cells of the CNS, and are found within chronic MS lesions in immature states. It is postulated that the lesion environment contains molecules that inhibit OPCs from maturing to remyelinating oligodendrocytes. We studied a family of extracellular matrix molecules known as chondroitin sulfate proteoglycans (CSPGs), which are over expressed in chronic MS lesions, on their ability to inhibit OPCs from maturation.

Methods: We used an *in vivo* model of spinal cord demyelination, which shows evidence of remyelination several weeks post injury. Various CSPG members were probed with immunohistochemistry in early and late stages of injury. Human OPCs were plated on CSPG substrates and assessed for markers of maturation. From preliminary findings that lesion CSPGs co-localize with infiltrating macrophages, we grew macrophages *in vitro* under proinflammatory conditions to test if they would express CSPGs. Finally, we designed and produced a CSPG synthesis inhibitor and tested its effects *in vitro*.

Results: Remyelination was incomplete at four weeks post injury, and the CSPG versican remained upregulated in the lesion core. Human OPCs showed reduced adherence and process outgrowth when plated on CSPG substrata. Macrophages expressed CSPGs under proinflammatory conditions, and this process was reduced when treated with our CSPG synthesis inhibitor.

Conclusions: CSPGs inhibit OPC maturation and may cause remyelination failure. Future *in vivo* experiments with our CSPG synthesis inhibitor will address if this strategy will be an effective intervention to treat demyelinating injury.

Poster Number: 23

Presenter's Name: Colin Franz

Program and Year: MD, Class of 2012

Category: Basic Science Project

The Effects of Trans-vertebral Electrical Stimulation on Peripheral Nerve Regeneration

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Objectives/Introduction: Peripheral nerve axons can regenerate, but complete recovery is seldom achieved after peripheral nerve injury (PNI) for multiple reasons including the misdirection of re-growing axons to inappropriate end organs. Therefore, strategies to increase the accuracy of reinnervation have the potential to improve PNI outcomes. Recently, brief electrical stimulation (ES) of axons has been shown to augment both the rate and accuracy of regeneration in rodents. Translation of ES has already begun in carpal tunnel patients with promising preliminary results, but was limited to patients receiving surgical intervention in order to place the stimulating electrodes. However, surgery is not always indicated in PNI thus less invasive approaches would be valuable. To this end trans-vertebral (Tv-) ES of the spinal cord is an alternative strategy for PNI.

Methods: Based on the protocol established by Gordon and colleagues (20Hz, 1hr), we studied the effects of Tv-ES delivered at the T1-3 level in mice following femoral nerve transection and repair. We assessed treatment effects on axon regeneration using retrograde tracing, immunohistochemistry and semi-thin nerve sections.

Results: At 2 weeks, we unexpectantly found fewer retrogradely labelled motorneurons (MNs; 57±11 vs 92±12, p=0.038, n=7/group) and DRG neurons (320±62 vs 534±61, p=0.037, n=5/group) in mice receiving the Tv-ES versus Sham treatments respectively. By 6 weeks, the total number of regenerated MNs was nearly identical between groups (143±12 vs 142±13, n=14/group), however MN regeneration was more accurate in the Tv-ES than Sham group (73±5% vs 60±4%, p=0.048, n=14/group). Semi-quantitative immunohistochemistry for Polysialic Acid (PSA), which has been previously been shown to be involved in femoral axon guidance, showed significantly augmented levels in Tv-ES versus Sham femoral nerves.

Conclusions: In summary, we've shown that Tv-ES initially delays axon regeneration, but ultimately promotes more accurate motor reinnervation and the expression of PSA, a known axon guidance molecule.

Poster Number: 24

Presenter's Name: Kimchi Nguyen

Program and Year: MD/MSc, Year 4

Category: Basic Science Project

Peripheral T_{reg}s regulate sickness behaviour development in inflammatory liver disease

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Introduction: Peripheral organ-centred inflammatory diseases are commonly accompanied by debilitating non-specific symptoms. These symptoms include fatigue, malaise and a loss of social interest, and have been collectively termed sickness behaviours. Regulatory T cells (T_{reg}s) have been broadly implicated in regulating inflammation; however, a role for peripheral T_{reg}s in modulating sickness behaviour development during peripheral organ-centred inflammatory diseases, such as hepatic inflammation, has not been evaluated.

Methods: A mouse model of inflammatory liver disease due to bile duct ligation (BDL) was used as the model of peripheral organ-centred inflammation. Flow cytometry of $CD4^+Foxp3^+$ T_{reg} cells was conducted in the peripheral blood and liver of BDR and sham mice. The effects of peripheral T_{reg} depletion (using an anti-CD25 antibody) and T_{reg} infusion upon sickness behaviours, circulating cytokine levels and hepatic mRNA levels were determined. Sickness behaviour was quantified in a social exploration study. Serum cytokine levels were measured using Luminex beads. Hepatic mRNA levels were determined via real-time PCR.

Results: BDL mice demonstrated a significant reduction in peripheral blood, and an increase in hepatic, T_{reg}s compared to sham mice. BDL mice developed sickness behaviours characterized by decreased social investigative behaviour and increased immobility. Elimination of functional peripheral T_{reg}s in BDL mice resulted in worsening of BDL-associated sickness behaviours, an effect that was reversed with T_{reg} cell infusion. Hepatic mRNA and plasma levels of IL-6, a cytokine implicated in inflammation-related sickness behaviours, were elevated in T_{reg}-depleted BDL mice. In contrast, infusion of T_{reg}s decreased circulating IL-6 protein and liver IL-6 mRNA levels. Sickness behaviour development in IL-6 knockout BDL mice was markedly reduced compared to wildtype BDL mice.

Conclusion: Peripheral T_{reg}s suppress sickness behaviour development in the setting of peripheral inflammation, an effect driven through T_{reg} inhibition of hepatic IL-6 production and, subsequently, reduced liver-to-brain signaling via IL-6 circulating in the peripheral blood.

Poster Number: 25

Presenter's Name: Saara Rawn

Program and Year: MD/PhD, Year 7

Category: Basic Science Project

Feto-placental production of placenta-specific, prolactin-related hormone encoding genes (PPRH) is essential for murine pregnancy

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Objectives/Introduction: A series of gene duplication events during evolution has produced a large family of prolactin (*Prl*)-related genes in some but not all mammals. In mice, there are 23 *Prl*-related genes all located in a locus on chromosome 13, whereas in humans there is a single *Prl* gene. Prl itself is produced by the pituitary and modulates many processes including reproduction. Interestingly, the other 22 placenta-specific, prl-related hormone encoding genes (PPRH) are expressed by the placenta but each has its own unique temporal and cell-type specific expression pattern. The potential for functional redundancy is also quite high, since this family has recently evolved and multiple hormones share the same receptor. As such, our aim is to determine the role of PPRH in pregnancy by generating a large-scale knock-out of all 22 PPRH.

Methods: A 1 Mb deletion on mouse chromosome 13 was made, using methods developed by Alan Bradley (Yu 2001), that deletes the 22 PPRH encoding genes. Two independent embryonic stem cell lines carrying the desired deletion have been created and have been bred for the past 11 months.

Results:
i) Homozygous mutants (PPRH-/-) mice from intercrosses of heterozygous (PPRH+/-) parents are viable
ii) PPRH-/- females were crossed with wild-type males; this results in a small reduction in litter size, but all pups were born healthy
iii) PPRH-/- females were crossed with PPRH-/- males; litters consisting of 100% mutants show dramatic abortions near term

Conclusions: Thus far, we have shown that i) PPRH do not have an essential paracrine role within the uterus since homozygous mutants are viable; ii) there is only a partial requirement for PPRH in the maternal decidua, since healthy pups can be born from placentas that lack maternal contribution of PPRH; and finally iii) feto-placental production of PPRH is essential for murine pregnancy.

Poster Number: 26

Presenter's Name: Amanda Eslinger

Program and Year: MD/MSc, Year 2 of MSc

Category: Basic Science Project

Comparison of Gut Microbiota in Rats Fed Pulse-Derived Ingredients Versus the Prebiotic Fiber Oligofructose

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Introduction: There is growing interest in dietary modification of gut microbiota to favor a lean phenotype. This study examined the effects of pulse derived ingredients on gut microbiota in diet-induced obese rats. A prebiotic fiber, oligofructose, was used as a comparison fiber.

Methods: Diet-induced obese Sprague-Dawley rats (n=50) were randomized to 1 of 5 diets for 6 wk: 1) control (C); 2) yellow pea flour (PFL, 33% wt/wt); 3) yellow pea starch (PS, 33% wt/wt); 4) yellow pea fiber (PF, 33% wt/wt w/ 12% fiber); 5) oligofructose (OFS, 12% wt/wt to match diet 4 fiber content). The primary outcome, gut microbiota, was measured in fecal matter using qPCR. Correlation analysis was performed between gut microbiota and gut satiety hormones.

Results: Rats fed OFS exhibited the greatest number of bifidobacteria ($p<0.001$) with PFL producing some bifidogenic effect. OFS rats also exhibited decreased Clostridium leptum ($p<0.05$) compared to all other groups. Bacteroides, typically decreased in obesity, were higher in OFS than PF, PFL and PS ($p<0.01$). Both Bacteroides ($r=0.292$, $p<0.05$) and Bifidobacteria ($r=0.599$, $p<0.01$) were positively correlated with peptide YY (PYY) secretion. Total gut bacteria ($r=-0.294$, $p<0.04$) was negatively correlated with glucagon-like peptide-1 (GLP-1) secretion.

Conclusion: Although there was some bifidogenic effect with PFL, OFS was the only diet enrichment to significantly modify gut microbiota, which may alter host metabolism. Our future work will promote growth of beneficial gut microbiota in dams prior to conception utilizing OFS. It is anticipated that detrimental programming in offspring will be reduced subsequent to this intervention.

Poster Number: 27

Presenter's Name: Sarah Tulk

Program and Year: MD/MSc, Year 2 of MSc

Category: Basic Science Project

Vitamin D downregulates NLRP3 and protects against *Clostridium difficile* toxin-induced cell death

Sarah E. Tulk[1,2] Justin A. MacDonald[1]; Paul L. Beck[2]

Depts. of Biochemistry and Molecular Biology[1] and Medicine[2], Faculty of Medicine

Objectives/Introduction: Infections and deaths caused by *Clostridium difficile* are rapidly increasing, giving rise to a demand for new therapeutic strategies. *C. difficile*-induced colonic damage by its toxins A and B (TcdA/B) is mediated by the NLRP3 inflammasome (Ng et al., 2010), the key producer of IL-1β. Vitamin D has been shown to induce production of proIL-1β and mature IL-1β in THP-1 cells (Lee et al, 2011), and it has been shown to upregulate NOD2 (Wang et al, 2010), an NLR protein in the same family as NLRP3. We hypothesize that the increased IL-1β seen following vitamin D treatment is a result of concurrent increases in NLRP3 expression, as has been shown for NOD2. This enhanced NLRP3 signalling by vitamin D contributes to damage by *C. difficile* TcdA/B.

Methods: PMA-differentiated THP-1 cells will be stimulated with vitamin D [100 nM] and assessed for inflammasome activation (NLRP3, ASC western blot and real-time qPCR; IL-1β ELISA and real-time qPCR). Further, cells will be stimulated with vitamin D and *C. difficile* toxins A and B (TcdA/B) [10 μg/μL] and assessed for cell death using an LDH assay. Significance will be assessed using one-way ANOVA and appropriate post-hoc test with significance at 0.05.

Results: Vitamin D upregulates gene expression of the IL-1β-converting-enzyme caspase-1 at 4 hours and of pro-IL-1β at 8 hours. IL-1β release is significantly increased by 24 hours, however, this is concurrent with decreased expression of NLRP3. This suggests that vitamin D induces NLRP3-independent production of IL-1β. Further, vitamin D is able to protect against TcdA/B-induced cell death.

Conclusions: Vitamin D downregulates expression of NLRP3 while simultaneously causing an increase in IL-1β release, suggesting that this IL-1β is NLRP3-independent. Further, vitamin D is able to protect macrophages against death induced by *C. difficile* TcdA/B. This suggests that vitamin D has potential use as a therapeutic against *C. difficile*, but further studies will be needed to completely characterize it's actions.

Poster Number: 28

Presenter's Name: Marta Davidson

Program and Year: MD, Class of 2014

Category: Basic Science Project

DNA replication stress results in expansion of dNTP pools and a mutator phenotype

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(1) The integrity of the genome depends on diverse pathways that regulate DNA metabolism. Defects in these pathways result in genome instability, a hallmark of cancer. (2) Deletion of *ELG1* in budding yeast, when combined with hypomorphic alleles of *PCNA* (3) results in a significant amount of spontaneous DNA damage during S phase that elicits upregulation of RNR activity. Increased RNR activity leads to a dramatic expansion of dNTP pools in G1 that allows cells to synthesize significant fractions of the genome in the presence of HU in the subsequent S-phase. Consistent with the recognized correlation between dNTP levels and spontaneous mutation, compromising *ELG1* and *PCNA* results in a significant increase in mutation rates. Of particular interest, deletion of distinct genome stability genes *RAD54*, *RAD55*, and *TSA1* also results in increased dNTP levels and mutagenesis. (4) Together, our data point to a vicious circle in which mutations in gatekeeper genes give rise to genomic instability during S phase, which in turn results in high levels of spontaneous mutagenesis.

Poster Number: 29

Presenter's Name: Jason Bau

Program and Year: MD/PhD, Year 4

Category: Basic Science Project

Modulation of drug-induced DNA damage signaling by sodium salicylate and non-steroidal anti-inflammatory drugs (NSAIDs) in human breast cancer cells.

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Salicylate-based drugs, including aspirin (acetylsalicylic acid), have long been used in the treatment of mild to moderate cancer pain and have been shown in population-based studies to have cancer chemopreventive properties. Several mechanisms have been hypothesized to underlie these effects, including the inhibition of cyclooxygenases and the inhibition of the transcription factor NF-κB. We have recently demonstrated, however, that salicylate, the primary metabolite of aspirin, is a novel catalytic inhibitor of DNA topoisomerase IIα (topo II), a nuclear enzyme essential for cell proliferation and division and the target of several widely used anti-cancer chemotherapeutics. As a consequence of this inhibition, and independent of its capacity to inhibit cyclooxygenases and NF-κB, we have demonstrated that a brief pretreatment of human breast cancer cells with salicylate attenuates the cytotoxicity of the topo II poisons, doxorubicin and etoposide. We have observed that salicylate prevents doxorubicin-induced DNA double-strand break generation, which is attributable to salicylate-mediated inhibition of doxorubicin-stabilized topo II-DNA cleavable complex formation *in vivo*. Together, these data suggest that co-administration of salicylates could negatively impact the efficacy of cancer treatment regimens incorporating topo II-targeting therapeutics.

We have now extended our investigation of salicylate to determine whether common salicylate- and non-salicylate-based non-steroidal anti-inflammatory drugs (NSAIDs) possess similar topo II inhibitory properties, initially by examining the effects of short-term exposure on doxorubicin-induced DNA damage signaling followed by a direct examination of their effects on topo II catalytic activity. Our experiments demonstrate that inhibition of topo II is readily observed with some, but not all, salicylate-based therapies at clinically achieved concentrations. In contrast, little to no inhibition of topo II is observed with non-salicylate-based NSAIDs. To expand our understanding of salicylate-based catalytic inhibition of topo II, we are also undertaking a systematic evaluation of structural derivatives of salicylate with an aim to identify critical substitutions modulating the observed effects.

Poster Number: 30

Presenter's Name: Michael Chiu

Program and Year: MD/MSc, Year 4, Class of 2013

Category: Basic Science Project

Biophysical Investigation of the Potential Antimicrobial Properties of ApoLp-III from Locust Migoratoria

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Recent studies with human, bovine and fish plasma have demonstrated bactericidal activity related to apoproteins, including ApoA-1 and ApoA-II. Apolipophorin III (apoLp-III) is an apolipoprotein involved in lipid transport in *Locust migoratoria*. Upon binding lipids, ApoLp-III adopts a helical shape displaying an amphipathic conformation. We propose that due to its cationic residues and amphipathic helical nature, it will preferentially interact with bacterial biomimetic membranes over mammalian models providing insight into its potential antimicrobial activity and as a template for future antimicrobial peptides.

ApoLp-III was recombinantly expressed in *E. coli*. Biomimetic large unilamellar vesicles (LUVs) representative of mammalian and bacterial membranes were composed of mixtures of different lipid species and extracts. Phosphatidylcholine and cholesterol were used to mimic the mammalian membrane and phosphatidylglycerol and phosphatidylethanolamine for the bacterial membranes. Erythrocyte ghost membranes and *E. coli* extract were used as a comparison to the mimetic systems. ApoLp-III-LUV interactions were monitored using calorimetry, fluorescence and circular dichroism.

Isothermal titration calorimetry (ITC) showed binding to both mammalian and bacterial model LUVs, however the interaction was considerably stronger with the bacterial models. Differential scanning calorimetry mirrored ITC results with large perturbations in the phase transitions for ApoLp-III with bacterial membranes. Dye leakage and circular dichroism data correlated well, indicating an increase in helicity with strong leakage from the bacterial membranes. Moreover monolayer surface pressure measurements showed an increase in surface pressure upon peptide association followed by a decrease in LUV size by dynamic light scattering.

These biophysical experiments demonstrate that ApoLp-III preferentially interacts with anionic PG lipids in the bacterial model membranes leading to bilayer disruption and leakage of intracellular contents upon adopting a helical profile. This suggests the potential for the involvement of ApoLp-III in the insect innate immune system and as an antimicrobial template for peptide and pharmaceutical development.

Poster Number: 31

Presenter's Name: Andrea Mosher

Program and Year: MD/PhD, Year 4

Category: Basic Science Project

Secretory phospholipase A_2 group IID: a novel phospholipase contributing to the regulation of arachidonic acid output in human pregnancy?

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[1]Physiology & Pharmacology, [2]Obstetrics & Gynaecology, Faculty of Medicine, University of Calgary

Introduction: Prostaglandins are strongly implicated in the process of labour; however, the precise role and regulation of the prostaglandin pathway in the human uterus is poorly defined. The first step in the prostaglandin pathway is the cleavage of membrane phospholipids by phospholipase A_2 (PLA_2) to generate arachidonic acid. We have previously demonstrated that secretory PLA_2-IIA is up-regulated in human myometrium with the onset of labour. It is known that there are numerous PLA_2 isozymes, each coded by a distinct gene. The aim of the present study is to investigate the presence of additional secretory PLA_2 ($sPLA_2$) isozymes contributing to prostaglandin production during pregnancy and labour.

Methods: Gestational tissues were obtained from pregnant women undergoing Caesarean section at term. Amnion, chorion, placenta, decidua and myometrium were collected. Patients were categorized as term non-labouring (TNL) or term labouring (TL). Conventional and real-time RT-PCR were used to determine $sPLA_2$-IID mRNA expression. Immunoblotting and immunohistochemistry were used to determine $sPLA_2$-IID protein expression and localization.

Results: Our results demonstrate that a novel $sPLA_2$ isozyme, $sPLA_2$-IID, is present in human gestational tissues. $sPLA_2$-IID mRNA expression is significantly higher in chorion compared to other gestational tissues. Interestingly, $sPLA_2$-IID mRNA expression is significantly decreased in decidua in TL patients compared to TNL patients, suggesting a labour-associated decrease in $sPLA_2$-IID expression. Moreover, $sPLA_2$-IID protein is localized abundantly throughout the decidua in TNL patients but decreases with labour. No significant labour-associated changes in $sPLA_2$-IID expression are observed in other gestational tissues.

Conclusion: Due to the decreased expression of $sPLA_2$-IID mRNA in decidua, coupled with an absence of change in other tissues, it is unlikely that $sPLA_2$-IID contributes to the increased prostaglandin production implicated in the transition from uterine quiescence to active contractions during labour. The precise function(s) of $sPLA_2$-IID in the human uterus remains to be determined.

Poster Number: 32

Presenter's Name: Kathleen E. Moncrieff

Program and Year: PhD (2011)/MD, Class of 2014

Category: Basic Science Project

Improving Our Understanding of Semi-Regular Type C Variable Stars

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Objectives: Semi-regular type C (SRC) variable stars are supergiant red stars that are nearing the end of their life cycles. They vary in brightness with semi-regular periods that range from several months to several years. Their brightness variations are caused by a combination of processes including pulsation and ejections of opaque dust. This the first comprehensive study of the variability of the stars both as individuals and as a group, which examines various properties using a baseline of at least several decades and, in some cases, more than a century.

Methods: We used data from a variety of sources to study 49 of the approximately 70 known SRC variable stars in our Galaxy, including new and archival spectroscopic data from the Dominion Astrophysical Observatory, archival spectroscopic data from the David Dunlap Observatory, archival photographic data from the Harvard College Observatory, archival visual brightness estimates from the American Association of Variable Star Observers, and temperature measurements made by Robert F. Wing et al. in the 1960s and 1970s.

Results: In individual stars, we examined several properties, including brightness variations, temperature variations, changes in mean brightness, and changes in the period of brightness variation. In the group, we examined relationships between period and brightness, period and radius, and temperature and brightness amplitude, and found them to be consistent with results for other pulsating variable stars. As an aid to future observers, we classified the stars into three categories based on the quality of the available data.

Conclusions: Stars with sufficient available data appear to reach their maximum temperature near their smallest dimensions, consistent with the behavior of other pulsating variable stars. We have found evidence of dust ejections occurring in several of the stars. Examination of properties of the stars as a group shows trends that are consistent with other pulsating variable stars.

Poster Number: 33

Presenter's Name: Daniel Soliman

Program and Year: MD, Year 2

Category: Basic Science Project

Inhibition of reverse-mode sodium-calcium exchange by the anti-anginal agent ranolazine

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Introduction: Reverse-mode activity of the cardiac sodium-calcium exchanger (NCX1.1) is a major contributor to the deleterious Ca^{2+} overload during ischemia-reperfusion injury, and is activated by intracellular sodium (Na^{+}_{i}) accumulation due to increased Na^{+} uptake by the sodium-hydrogen exchanger as well as augmentation of late sodium current (late I_{Na}). Inhibition of late I_{Na} by ranolazine attenuates Ca^{2+} overload, an effect that may underlie its anti-anginal effectiveness. As inhibition of reverse-mode NCX1.1 also attenuates Ca^{2+} overload, we assessed whether this mechanism also contributes to the pharmacological actions of ranolazine.

Methods: We measured the effects of ranolazine on 1) recombinant electrogenic forward and reverse-mode NCX1.1 currents using the inside-out excised patch-clamp technique 2) a cellular model of reverse-mode NCX1.1 mediated Ca^{2+}_{i} overload and 3) IR- and ouabain-induced intracellular Ca^{2+}_{i} overload in whole heart.

Results: Ranolazine inhibited reverse-mode NCX1.1 activity (IC_{50} = 89 nM), but had no effect on physiological forward-mode NCX1.1 activity. In intact neonatal rat ventricular myocytes in the presence of tetrodotoxin, ranolazine (10 µM) inhibited reverse-mode NCX1.1-mediated Ca^{2+}_{i} overload independent of late I_{Na} inhibition. Ranolazine (10 µM) reduced Ca^{2+}_{i} overload and improved left ventricular mechanical function of hearts reperfused following global no-flow ischemia (20 min) or exposure to ouabain (80 µM).

Conclusions: These results indicate that, at therapeutic concentrations (1 to 10 µM), a component of the cardioprotective action of ranolazine may be due to direct inhibition of reverse-mode NCX1.1 in addition to the previously documented inhibition of late I_{Na}.

Poster Number: 34

Presenter's Name: Aman Wadhwani

Program and Year: MD/MSc, Year 1 of MD

Category: Basic Science Project

Intracellular Pathways Responsible for Increase in Transepithelial Resistance in Intestinal Epithelial Cells

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Introduction: Patients with clinically active Crohn's Disease exhibit increased intestinal permeability. However, apical addition of serine proteases like trypsin to intestinal epithelial cell monolayers reduces permeability as shown by increased transepithelial resistance (RTE). This effect of trypsin is independent of activation of protease-activated receptors, but the underlying mechanism is unknown. Given the central role of epidermal growth factor receptor (EGFR) in epithelial cell biology and homeostasis, we hypothesized that trypsin increases RTE by activating EGFR.

Methods: RTE of confluent SCBN monolayers and mouse colonic tissue was measured in Ussing chambers. To determine a role for EGFR-associated signaling, cells were pretreated with inhibitors of EGFR (PD153035), ErBb2 (AG879),ERK-1/2 (PD98059), PI3K (LY294002) and MMPs (marimastat, MMT) and then stimulated apically by trypsin or EGF. Flux of FITC-dextran across the monolayer was measured following treatment with PD153035 or AG879 and trypsin.

Results: Apical trypsin increased RTE by 300% ($p<0.05$) within 60 min. PD153035 or AG879 caused a significant dose- dependent decrease in trypsin-induced ΔRTE, with IC50s of 0.38 and 2.73 μM, respectively. PD98059, LY294002 and MMT also reduced trypsin-induced ΔRTE by 66%, 63% and 25% respectively. Pretreatment of cells with PD153035 or AG879 prevented trypsin-induced reduction of dextran flux. Apical EGF increased RTE by 80%. PD153035 and AG879 reduced this increase by 99% and 84% respectively. Also, soybean trypsin inhibitor decreased RTE in mouse colon in vitro, suggesting that luminal serine proteases maintain barrier function.

Conclusions: Our data suggest that trypsin increases RTE via activation of EGFR and ErBb2 and partially via activation of ERK-1/2, PI3K and MMPs. Serine proteases may strengthen epithelial barrier to enhance the efficiency of electrolyte and nutrient transport, and may represent a method to counter barrier defects caused by intestinal inflammation.

Poster Number: 35

Presenter's Name: Eric Hyun

Program and Year: MD/PhD, Year 3 of MD

Category: Basic Science Project

Icilin, an agonist of cold activated Transient Receptor Potential (TRP) channels attenuates colonic inflammation in mice

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Objective/Introduction: Cold temperature is commonly used as a local anti-inflammatory treatment. Icilin is a known agonist for members of the transient receptor potential family of ion channels (TRPA1 and TRPM8), which are reported to play a role in various physiological events including detection of mild and noxious cold temperatures. We hypothesize that the supercooling agent icilin would diminish colonic inflammation by mimicking the anti-inflammatory effects of cold temperature.

Methods: Colonic inflammation in C57BL6 mice was induced by intracolonic injection of trinitrobenzene sulphonic acid (TNBS, 2mg in 100ul of 40% ethanol). Colitis was allowed to develop for 7 days and mice were injected daily with icilin (100µg in 3% DMSO/saline). Seven days after the induction of colitis, leukocyte trafficking (visualized by intravital microscopy), macroscopic damage scores and bowel thickness. Colonic tissues were harvested to measure myeloperoxidase (MPO) activity and inflammatory cytokines/chemokines.

Results: TNBS-induced increase in macroscopic damage scores and bowel thickness were significantly reduced in mice that received daily icilin treatment. Mice challenged with TNBS also showed reduced leukocyte adherence along the colonic vessels when treated with icilin. Lastly, icilin treatment significantly attenuated the levels of IL-1α, TNF-α, KC, monocyte chemoattractant protein-1, and macrophage inflammatory protein-1α/1β in the colonic tissues of TNBS treated mice.

Conclusions: Icilin confers protection against the development of colitis in mice, possibly *via* reducing leukocytes recruitment. Therefore, agents that can activate TRPA1 and/or TRPM8 may represent novel therapeutics for inflammatory bowel disease in the future.

Poster Number: 36

Presenter's Name: Richard Xiang

Program and Year: MD/PhD, Year 1

Category: Basic Science Project

SAP knockdown occurs 3 days post-transfection

Richard Xiang
Snyder Institute

Introduction: Patients with X-linked lymphoproliferative are immunocompromised due to a deficiency in the SLAM associated protein (SAP). SAP is a protein that is necessary for the signalling of various SLAM family receptors. Natural Killer (NK) cells have been shown to have a high levels of SLAM receptor expression, and these receptors have been shown in activate NK cell activity. In order to further elucidate the role of SLAM family receptors in NK cell function, a knockdown protocol needs to be developed. Since SAP is essential to multiple SLAM family receptors, knocking down SAP will allow screening of multiple receptors at once, making it the ideal target for siRNA knockdown.

Methods: YT cells were used as a human NK cell model. siRNA was transfected into the YT cells using the AMAXA nucleofector. YT cells were lysis at 24, 48, 72, 96, and 120 hours post-transfection. The cell lysates were analyzed by western blot for SAP.

Result: No noticeable drop in SAP expression was detected in the YT cell lysate for 24 and 48 hours post-transfection. After 72 hours a significant drop in SAP expression was detected, compared to mock transfected and non-targeting siRNA. This drop in SAP expression was maintained until the last time point tested (120h).

Conclusions: This project shows that SAP knockdown does not occur in YT cells until 72 hours post-transfection. Therefore, future experiments that want to test a loss of function of SAP in YT cells should perform the functional tests 72 hours post-transfection. Since the knockdown of SAP was maintained until 120 hours post-transfection, functional tests can be carried out until at least 5 days after transfection.

Poster Number: 37

Presenter's Name: Lorie Kwong

Program and Year: MD/MSc, Class of 2014

Category: Basic Science Project

The Role of MicroRNAs in Cutaneous Squamous Cell Carcinomas

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Introduction: Non-melanoma skin cancer (NMSC) is the most common form of cancer worldwide. While ultraviolet radiation, immunosuppression and chronic inflammation are established risk factors for developing NMSC, much remains unknown about the process of skin carcinogenesis. miRNAs are small, non-coding RNAs that regulate gene expression. Certain miRNAs function as oncogenes or tumour suppressors, yet their role in cancer development remains unclear. Herein, we investigate the role of miRNAs in cutaneous squamous cell carcinomas (SCC).

Methods: To compare the miRNA profile of normal human keratinocytes (NHK) and cutaneous SCC cells, total miRNA was extracted from commercially available cell lines. Using μParaflo® Microfluidic Biochip technology and probe content based on the Sanger miRBase Version 12.0, a genome-wide miRNA microarray analysis was performed.

Specific miRNAs were exogenously altered in SCC cells using miRNA mimics and inhibitors. The effects of miRNA deregulation on proliferation, differentiation, apoptosis and invasion were examined.

Results: Of 856 miRNAs studied, 27 miRNAs displayed high signal intensities and were significantly up- or down-regulated in the SCC cell lines. While the majority of miRNAs in the genome remain uncharacterized, several of the miRNAs altered in SCCs are implicated in carcinogenesis. Notably, miR-224 and miR-125b have functional relevance in tumour growth and invasion. For instance, miR-125b controls cell cycle progression and its inhibition is associated with increased proliferation, migration and invasion. Further, miR-224 over-expression, a marker of hepatocellular carcinoma, promotes proliferation and cellular invasion. Our data suggest that exogenous up-regulation of miR-125b in SCCs induces a loss of cellular differentiation that results in a more invasive phenotype.

Conclusions: The identification of unique miRNA profiles within NHKs and SCCs allows our dataset to serve as a roadmap for future studies of the microRNAome. By characterizing the specific miRNAs associated with SCCs, molecular insight will be gained into the process of skin cancer development.

Poster Number: 38

Presenter's Name: Allison Tsang

Program and Year: MD/MSc, Year 4

Category: Basic Science Project

The role of naturally occurring telomerase mutations on enzyme function and cellular lifespan

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Objectives/Introduction: Telomeres are protective nucleoprotein structures found at the ends of linear chromosomes and are crucial for maintaining genomic stability in cells. Telomeric DNA shortens after each round of cell division and critically short telomeres can lead to cellular senescence. However, telomeres can be synthesized by telomerase, a reverse transcriptase that minimally consists of a reverse transcriptase catalytic subunit (TERT) and an RNA molecule (TR). Short telomeres and abnormal telomerase activity have been associated with a variety of human diseases, including premature aging syndromes and many cancers. Recently, human TERT mutations have been identified in patients with idiopathic pulmonary fibrosis (IPF), a fatal lung disease characterized by alveolar damage and fibrosis. These patients exhibit shorter telomeres compared to age-matched controls; however, the underlying mechanism(s) behind this phenotype is still unclear. The objective of this study was to characterize the effects of IPF-associated hTERT mutations on telomerase function and cellular lifespan.

Methods: Telomerase mutations were reconstituted *in vitro* using the rabbit reticulocyte system. These mutants were assayed for telomerase activity and hTERT-DNA/RNA interactions. Subsequent studies in human cells were completed to examine the effects of these naturally occurring mutants on telomerase activity, hTERT-protein interactions, telomere length and cellular lifespan.

Results: Mutations to hTERT V144 and R865 led to defects in telomerase activity and telomere synthesis. These findings were possibly due to alterations in critical hTERT interactions with DNA, RNA and/or telomere-specific proteins. In cells, these defects ultimately led to altered cellular proliferation. As a result, hTERT V144 and R865 were identified as key amino acids involved in proper telomerase function and the determination of cellular lifespan.

Conclusion: We have identified two hTERT resides critical for telomerase function. In addition, this study has provided some insight into how these hTERT mutations may contribute to cellular aging and possible the development of IPF.

Poster Number: 39

Presenter's Name: Elliot Sampson

Program and Year: MD/MSc, Year 3 of MSc

Category: Basic Science Project

Examining the functional consequences of Tumor Endothelial Marker-8 (TEM8) expression in human breast cancer cells

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Background: Tumor Endothelial Marker 8 (TEM8) is a transmembrane protein overexpressed in tumor associated endothelial cells. We have found markedly elevated levels of TEM8 within invasive human breast cancer cell lines and reduced TEM8 expression in non-invasive breast cancer cells (MCF7, HTB20 , SKBR3). Previously we demonstrated that TEM8 overexpression is associated with enhanced tumor growth and metastasis in a mouse 4T1 breast cancer model. The functional significance of TEM8 expression in a human cancer context is unknown. The functional consequence of overexpression of TEM8 in non-invasive breast cancer cell lines was assessed from an *in vitro* and *in vivo* perspective.

Materials and Methods: MCF7, HTB20, and SKBR3 cells constitutively express low levels of TEM8. The cell lines were infected with lentivirus encoding pLentiTEM8 or control pLentiLacZ. Functional alterations in tumor cell behavior (i.e. viability, adhesion, migration, and invasion) were assayed. NOD-SCID mice were used to evaluate changes in tumor kinetics, and lung colonizing ability

Results: Viability on a panel of extracellular matrix (ECM) substrates indicate that TEM8 enhances viability of MCF7 and SKBR3 cell lines, but not HTB20. Similarly mild alterations in adhesion to ECM substrates were seen in MCF7pLentiTEM8 and SKBR3pLentiTEM8, but not in HTB20. Cell based assays for migration allegeTEM8 reduces migration on Collagen-I in MCF7 cells. No alterations in the invasive ability of the full complement of cell lines tested were seen. In vivo data indicate that TEM8 does not enhance tumor growth and lung colonizing ability *in vivo.*

Conclusions: TEM8 overexpression causes very little change in the biological behaviour of non invasive human breast cancer cells. TEM8 does not alter tumor growth and metastasis *in vivo*. These results, which are in contrast to our preliminary *in vivo* studies, advise TEM8 may be a functionally redundant protein. To confirm that TEM8 does not significantly alter tumor cell biology, TEM8 knockout mice are being constructed in both MMTV-neu (spontaneous breast cancer) and B6-RipTag-H2g7 (insulinoma) mouse lines.

Poster Number: 40

Presenter's Name: Richelle McCullough

Program and Year: MD, Year 1

Category: Translational Project

Hypercholesterolemia and Dietary Flaxseed Induce Changes in Adipokine Expression Independently of Caloric Intake

RS McCullough, AL Edel, RK LaVallee, CMC Bassett, E Dibrov, DP Blackwood, BP Ander, GN Pierce

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Objectives/Introduction: Dietary flaxseed has cardioprotective effects that may be achieved through its rich content of the omega-3 fatty acid, alpha linolenic acid (ALA). Because ALA can be stored in adipose tissue, it is possible that some of its beneficial actions may due to effects it has on the adipose tissue. We investigated the effects of dietary flaxseed both with and without an atherogenic cholesterol-enriched diet to determine the effects of dietary flaxseed on the expression of the adipose cytokines leptin and adiponectin.

Methods: Rabbits were fed one of four diets: a regular (RG) diet, or a regular diet with added 0.5% cholesterol (CH), or 10% ground flaxseed (FX), or both (CF) for 8 weeks. Levels of leptin and adiponectin expression were assessed by RT-PCR in visceral adipose tissue.

Results: Consumption of flaxseed significantly increased plasma and adipose levels of ALA. Leptin protein and mRNA expression were lower in CH animals and were elevated in CF animals. Changes in leptin expression were strongly and positively correlated with adipose ALA levels and inversely correlated with levels of en face atherosclerosis. Adiponectin expression was not significantly affected by any of the dietary interventions.

Conclusions: Our data demonstrate that the type of fat in the diet as well as its caloric content can specifically influence leptin expression. The findings support the hypothesis that the beneficial cardiovascular effects associated with flaxseed consumption may be related to a change in leptin expression.

Poster Number: 41

Presenter's Name: Kovid Lee

Program and Year: MD/MSc, Year 2

Category: Translational Project

Modeling, Control, and Performance Assessment of Blood Plasma Glucose Levels in Type I Diabetics

Kovid Lee, Mike Foley

Schulich School of Engineering, Faculty of Chemical Engineering and Faculty of Biomedical Engineering

Diabetes mellitus type I is a growing epidemic affecting millions of people worldwide, with the only current treatment being an intensified and invasive insulin therapy regimen. Consequently, the need to address the quality of life for patients suffering from type I diabetes has become a priority in the biomedical engineering field. With advances in continuous glucose sensing, fast-acting insulin analogs, and a mature technology in the construction of insulin pumps, there comes the commercial realization of a closed-loop pancreas. By removing the patient from the feedback loop and taking the role of a functioning pancreas, the artificial pancreas would be an invaluable solution. In designing such a biomedical device, one of the most vital components would be the development of a mathematical algorithm that models the body, capable of regulating an insulin infusion given a glucose sensor measurement.

The research conducted reviews the engineering and biomedical theory underpinning the artificial pancreas and simulates and compares the two most accepted diabetic models to date on MATLAB / Simulink: Bergman's minimal model (1981) and Parker's compartmental model (1999). Upon model selection, a novel and modified proportional-only controller was then fit to Parker's compartmental model and compared to other published controllers. Results show that the proportional-only controller proved superior in providing satisfactory glucose regulation in addition to being a more feasible solution as an artificial pancreas owing to its simplicity and universality.

In addition, the development of a performance assessment based on continuous blood glucose data is being proposed as to provide the type I diabetic and physician quantitative, standardized, and unbiased feedback for evaluating glycemic variability. This performance assessment is based on the works of Harris (1989) and Horch and Isaksson (1999), and is shown to be successful in discerning between adequate and poor blood glucose control, objectively confirmed with HbA1c results.

Poster Number: 42

Presenter's Name: David Cinats

Program and Year: MD, Year 2

Category: Translational Project

Facilitative Glucose Transporters: A New Generation of Physiological Markers for the Differentiation of Human Mesenchymal Stem Cells?

David Cinats[1], Andrei R. Manolescu[2], Charles Secretan[2], Deborah O'Neill[3], Chris Cheeseman[3], Keith Bagnall, and Nadr Jomha[2]

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Background: Hexose facilitative transporters (GLUTs) are proteins important for chondrocyte survival and may be utilized as markers of MSC differentiation. GLUT expression is influenced by oxygen tension and low oxygen tension is an important characteristic of the environment of both MSCs and articular chondrocytes.

Methods: Expression of GLUTs in MSCs and chondrocytes cultured under normoxic and hypoxic culture conditions were assayed using RT-PCR, qPCR, immunofluorescence, and fluxes.

Results: The GLUT expression profile in MSCs was significantly different from the GLUT expression profile in chondrocytes. qPCR and flux data suggested that hypoxic chondrocytes and MSCs utilize class II GLUTs for hexose uptake while normoxic cells rely on class III GLUTs for hexose uptake.

Conclusion: The difference in GLUT expression between MSCs and chondrocytes permits the use of GLUTs as novel markers for chondrogenesis of MSCs. The difference in expression between cells cultured in different conditions emphasizes the importance of hypoxia in MSC and chondrocyte cell culture.

Poster Number: 43

Presenter's Name: Kyla Huebner

Program and Year: MD/PhD, Year 4 of PhD, Class of 2014

Category: Translational Project

Post-natal molecular adaptations in anteromedial and posterolateral bundles of the ovine anterior cruciate ligament: One structure with two parts or two distinct ligaments?

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[1]McCaig institute for Bone and Joint Health, [2]Department of Medical Science, [3]Department of Surgery, [4]Department of Civil Engineering

Introduction/Objectives: The human anterior cruciate ligament (ACL) is a composite structure of two anatomically distinct bundles: an anteromedial (AM) and posterolateral (PL) bundle. Tendons are often used as autografts for surgical reconstruction of ACL following severe injury. However despite successful surgical reconstruction, some people experience re-rupture and development of osteoarthritis (OA) in later stages. Understanding the structure and molecular makeup of normal ACL is essential for its optimal replacement. Reportedly the two bundles display different tensions throughout joint motion and therefore may be fundamentally different. The present study assessed the similarities and differences in ultra-structure and molecular composition of AM and PL bundles to test the hypothesis that the two bundles of ACL develop unique characteristics with maturation.

Methods: ACLs from nine mature and six immature Suffolk cross sheep were compared. The bundles were examined for mRNA and protein levels of collagens types I, III, V, VI and two proteoglycans. Fibril diameter composition of the two bundles was examined with transmission electron microscopy.

Results: Maturation does alter the molecular and structural composition of the two bundles of ACL. Interestingly although PL band appears to mature slower than the AM band, no significant differences were detected between the bundles in the mature animals.

Conclusions: We thus reject our hypothesis that the two ACL bundles are distinct. The two anatomically distinct bundles of the sheep ACL can be considered as two parts of one structure at maturity and material that would ideally match these ligament properties can be used to replace each ACL bundle in the sheep.

Poster Number: 44

Presenter's Name: Taryn Ludwig

Program and Year: MD/PhD, Year 3

Category: Translational Project

Osteoarthritic synovial fluid deficient in proteoglycan 4 demonstrates decreased boundary lubricating ability

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Introduction: Proteoglycan 4 (PRG4) proteins in synovial fluid (SF) and at the surface of articular cartilage function as boundary lubricants; they reduce friction, preventing wear and degradation, when cartilage surfaces are in contact with each other. SF deficient in PRG4 lacks normal boundary lubricating ability. We hypothesised that PRG4 levels can be diminished during osteoarthritis (OA).

Objectives: (1) Quantify PRG4 and hyaluronan (HA) content in normal (NL) and chronic OA human synovial fluid (hSF). (2) Assess the normal human cartilage boundary lubricating ability of OA hSF with deficient and elevated PRG4 concentration compared to normal hSF, with and without supplementation of PRG4±HA.

Methods: OA hSF was aspirated from patients receiving therapeutic injection. Sandwich ELISA was used to measure PRG4 (custom assay) and HA (commercially available assay) concentration. Human cartilage boundary lubricating ability of OA hSF, supplemented hSF, and NL hSF was assessed using a previously characterized cartilage-on-cartilage friction test. Data presented as mean±SEM.

Results: OA hSF deficient in PRG4 ($N = 4$, 293.6 ± 70.8 μg/mL) compared to NL ($N = 12$, 508.5 ± 41.3 μg/mL, $p < 0.05$) failed to lubricate; lubricating ability was restored by supplementation with PRG4. OA hSF with elevated PRG4 ($N = 4$, 774.6 ± 69.2 μg/mL, $p < 0.05$ vs NL) lubricated as well as NL hSF and lubricating ability was not significantly altered by supplementation.

Conclusion: Normal PRG4 levels may not be present in all chronic OA hSF. Some post-injury and chronic OA patients may benefit from PRG4 supplementation as a biotherapeutic treatment.

Poster Number: 45

Presenter's Name: Michael Peplowski

Program and Year: MD/PhD, Year 5

Category: Translational Project

Aquaporin 3 Expression and Localization is Altered Early in the Dextran Sodium Sulfate Model of Intestinal Inflammation

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Introduction: Inflammatory bowel diseases (IBD) are characterized by altered water transport leading to the development of diarrhea. However, the status of Aquaporin (AQP) 3 expression, localization and its role in the barrier dysfunction that characterizes IBD remains unknown. *We hypothesized that AQP3 expression and localization were altered in IBD.*

Methods: C57Bl/6 mice were treated with 2.5% dextran sodium sulfate (DSS) in drinking water for up to 7 days to induce colonic inflammation. The establishment of colitis was verified morphologically and biochemically. AQP3 expression was assessed using real-time RT-PCR and localization was assessed by immunofluorescence of formalin-fixed paraffin-embedded colonic tissue. Furthermore, AQP3 expression was assessed both in human biopsy samples and in serum-starved HT29 colorectal adenocarcinoma cells exposed to human recombinant tumour necrosis factor (TNF) α and/or interferon (IFN) γ.

Results: DSS-treated mice had significantly increased granulocyte infiltration at 5, 7 and 14 days, but not at 3 days following commencement of DSS. AQP3 mRNA expression in mucosal scrapings was unaltered at both 3 and 7 days following the start of treatment. However, immunofluorescence studies revealed overall downregulated expression of AQP3 in 3 day DSS-treated tissues, with diminished basolateral staining in cells lining colonic crypts. Human biopsy sample analysis revealed no significant difference in AQP3 mRNA expression between healthy control, active and quiescent ulcerative colitis biopsy samples. Time-course experiments with a single treatment of TNFα (25ng/mL) or IFN γ (500U/mL) resulted in significantly reduced expression of AQP3 mRNA at 6 to 12 hr post-treatment, although total protein expression levels in these cells remained unaltered at 24 to 96 hr post-treatment.

Conclusions: Our data suggest that changes in AQP3 expression and localization represent early events that occur in colonic inflammation.

Poster Number: 46

Presenter's Name: Angie Karlos

Program and Year: MD/MSc, Year 2 of MSc

Category: Translational Project

AIMM Young: Assessing Inherited Markers of Metabolic Syndrome in the Young

Angie Karlos & Dr. Dustin Hittel
Faculty of Kinesiology, University of Calgary

Introduction: Approximately 34% of North American adults have metabolic syndrome. Metabolic syndrome is associated with an increased risk of type II diabetes (T2D) and cardiovascular disease (CVD). Twin and family studies have shown that the components of metabolic syndrome are highly heritable. Historically, genetic association studies on metabolic syndrome have examined older, symptomatic populations yielding small effect sizes. This has led to the hypothesis that a portion of this "missing heritability" may be due to gene-age interactions. Therefore, the purpose of this study is to explore genetic associations between candidate genes and cardiometabolic risk factors in a young, 18-35 year-old, healthy subjects. It is expected that using a young, healthy population will produce larger effect sizes due to the presence of fewer confounding variables.

Methods: This is a multi-centre international study with each site following a similar 3-visit, case-control study design. Subjects were recruited from undergraduate student populations at each university. Dependent variables include waist circumference, blood pressure, and body fat measured by a certified exercise physiologist, HDL, LDL, TG, glucose and insulin measured via fasting blood draw. The independent variable is genotype, measured by sequencing DNA extracted from whole blood.

Results: 200 subjects have been tested at UMass, 179 at Howard University, DC, and 90 at the University of Calgary (UCalgary). UCalgary has had 86 of 90 subjects complete all three visits. Subjects from UCalgary have been healthy with mean BMI, fasting glucose, TG, HDL and LDL values within normal ranges. Despite normal mean values, 42% of females and 30% of males had high total cholesterol values. Furthermore, 19% of females and 35% of males had a total cholesterol:HDL ratio >3.0.

Conclusion: Recruitment and adherence have been very successful at UCalgary in the first phase of the study. Future directions will focus on gene-stratified interventions based on altering blood lipid values based on preliminary data.

Poster Number: 47

Presenter's Name: Nicole Redding

Program and Year: MD/MSc, Class of 2014

Category: Translational Project

Differential sensitivity of high-risk neuroblastoma cells to myxoma and vesicular stomatitis virus

Nicole Redding[1,2], Karen Blote[1,2], Loen Hansford[3], XueQing Lun[1], Peter Forsyth[1], John Bell[4], Grant McFadden[5], David Kaplan[3], Donna Senger[1,2], Stephen Robbins[1,2], Paul Beaudry[1]

Hughes Children's Cancer Research Centre, Southern Alberta Cancer Research Institute and Department of Medical Science, University of Calgary[1], Department of Biochemistry and Molecular Biology, University of Calgary[2], Cell Biology Program, Hospital for Sick Children and Department of Molecular Genetics, University of Toronto[3], Department of Medicine, University of Ottawa[4], Department of Genetics, University of Florida[5]

Background: Neuroblastoma (NB) is a pediatric cancer common in children under one year of age. High-dose chemotherapy and radiation remain unsuccessful in high-risk patients, and over half of cured patients will have adverse effects from their therapy, including secondary cancers. Improved cure rates may be achieved with therapeutics targeted to these patients. Additionally, specific targeting may result in less toxicity. Naturally occurring and engineered oncolytic viruses have specifically targeted and destroyed various tumors in pre-clinical and clinical trials.

Hypothesis: Myxoma and vesicular Stomatitis Virus (VSV) are potential therapies for high-risk neuroblastoma.

Model: We are using a sub-population of primary cells isolated from bone marrow metastases of high-risk patients, termed NB tumour initiating cells (NB TICs), to evaluate the therapeutic value of oncolytic viruses. NB TICs, which have a number of properties of cancer stem cells, may drive metastasis and are much more tumourigenic in mouse models than established NB cell lines.

Results: We found that while myxoma and VSV infected and induced the death of NB cell lines *in vitro*, only myxoma induced substantial cell death in NB TICs. The differential sensitivity of NB TICs to VSV's oncolytic effects was maintained up to 120 hours post infection and was independent of passage number and growth conditions. While myxoma and VSV were able to replicate in NB cells *in vitro*, VSV protein levels were reduced in infected NB TICs when compared to NB cell lines. Further *in vitro* analysis demonstrated that the cells under investigation were infected with epstein-barr virus which may contribute to the lack of VSV cytotoxicity in NB TICs by triggering the endogenous expression of interferon stimulated genes. Using a subcutaneous xenograft model of NB cell lines in mice, we found that both myxoma and VSV were effective at limiting the growth and size of NB tumours *in vivo*. Similar to what was found *in vitro*, VSV was not effective at reducing the tumor burden of mice bearing NB TIC xenografts *in vivo*. The differential sensitivity of primary NB TICs to myxoma and VSV suggest that assessing the cytotoxicity of each patient's TICs *in vitro* to these viruses, prior to their clinical use, may be advisable.

Poster Number: 48

Presenter's Name: Aman Jivraj

Program and Year: MD, Year 3

Category: Translational Project

The Use of Computed Tomography in Assessing Atherosclerotic Plaque Vulnerability

Aman Jivraj, Dr. Naeem Merchant

Objectives/Introduction: Ischemic heart disease is one of the leading causes of death worldwide. Retrospective research has found ruptured coronary plaques to have the following characteristics; a fibrous cap, a large necrotic core, positive vascular remodeling, lack of calcification, increased inflammation, and vaso-vasorum neo-vascularization. Invasive imaging, such as intra-vascular ultra-sound (IVUS) is the current gold-standard for assessing some of these characteristics, however, a non-invasive screening tool has yet to be implemented. Computed Tomographic Angiography (CTA) has been used to visualize atherosclerotic plaques in great detail, and could be used as a viable screening tool.

Methods: Reports from previous studies were collaborated to determine whether CTA is able to identify the specific characteristics which put atherosclerotic plaques at risk of rupture. CTA is able to identify low attenuation (<30 HU); which corresponds to a lack of calcification, and positive remodeling. A total of 10 037 arterial segments, from 1059 patients were retrospectively characterized as having two feature positive (low attenuation and positive remodeling) plaques, one feature positive (low attenuation or positive remodeling) plaque, or no plaque.

Results: Of the 45 patients who exhibited both low attenuation and positive remodeling, acute coronary syndrome (ACS) developed in 10 (22.2%), while 1 (3.7%) of the 27 patients with plaques displaying either low attenuation or positive remodeling progressed to ACS. Conversely, only 4 (0.5%) of 820 patients who demonstrated neither of the features developed ACS.

Conclusion: Patients demonstrating positively remodeled plaques with low attenuation on CTA are at a higher risk of developing ACS than patients whose plaques do not. Therefore, CTA could one day be a valuable non-invasive screening tool to determine a patient's risk of ACS.

Poster Number: 49

Presenter's Name: Judy Luu

Program and Year: MD/PhD, Year 2

Category: Translational Project

Assessment of Significant Blood Oxygen Level Dependent (BOLD) Imaging in Patients with Coronary Artery Disease – A Validation Study Using Fractional Flow Reserve

Judy Luu, Jodi Harker, Dominik Guensch, James Hare, and Matthias Friedrich

University of Calgary

Background/Objectives: Blood oxygen level–dependent (BOLD) cardiac MRI (CMR) uses the signal generated by haemoglobin to directly measure tissue oxygenation and may represent a non-invasive method to assess myocardial ischemia in patients with coronary artery disease (CAD). The aim of this study was to validate whether BOLD CMR can detect and quantify alterations in myocardial oxygenation in CAD.

Methods: Oxygen-sensitive BOLD CMR scans were performed in patients who were scheduled for clinically-indicated coronary angiography. BOLD images were captured during rest and adenosine-induced coronary hyperemia. The mean BOLD signal intensity (SI) percent changes in segmental regions were calculated between rest and hyperemia and were compared to intracoronary fractional flow reserve (FFR) assessed on angiography. FFR is the current gold standard to assess the extent of coronary occlusion (FFR <0.80 indicates significant stenosis).

Results: Twenty-eight patients totaling 147 myocardial segments were available for analysis. 73 segments were excluded, with 66% of these being apical. The remaining 74 segments equated to 22 patients (60 +/- 9y, 19 males), eight of these had a normal FFR (≥ 0.80) and 14 had FFR values <0.80. Mean BOLD SI percent change was significantly less in patients with abnormal FFR values (-4.62 +/- 2.28% SEM), in comparison to patients with normal FFR values (8.54 +/- 3.08 % SEM); p=0.003. The Bland-Altman analysis indicated that the 95% limits of agreement between the two readers ranged from -23.6% to 27.8%, with a mean of 2.08%.

Conclusion: This pilot study found that BOLD-sensitive CMR can detect changes in oxygenation in patients with CAD. Our preliminary data suggests that BOLD-sensitive CMR may allow for a non-invasive approach to directly assess myocardial ischemia in patients with coronary artery disease.

Poster Number: 50

Presenter's Name: Craig Beers

Program and Year: MD/PhD, Year 3

Category: Translational Project

Epileptic networks studied with intracranial EEG-fMRI at 3.0T

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Introduction: Epilepsy is one of the most common serious neurological conditions, with seizures affecting 1% of the population. Focal epilepsy arises when seizures originate from a localized area in the brain. Finding that area can be difficult. Despite efforts at seizure localization and skilled neurosurgical technique, seizure cure is achieved in less than 50% of these patients. Scalp electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) have been successfully combined to help localize changes in brain activity associated with epilepsy, but has limited ability to detect discharges in small cortical areas or from deep structures. Intracranial EEG (ICE) uses electrodes placed directly on the surface of the brain, providing an opportunity to improve the power of EEG-fMRI. This is a novel technique that could improve treatment outcomes and further understanding of the neural networks involved in seizure generation. We are currently the only laboratory performing these studies at 3.0T field strength.

Methods: We recruited seven subjects undergoing intracranial EEG monitoring at the Foothills Medical Centre. Subjects underwent ICE-fMRI scans. Interictal discharges were identified on EEG and used to generate corresponding fMRI activation maps.

Results: Interpretable EEG data were obtained in four subjects, with three recordings lost due to artefact. Two subjects had malformations of cortical development (MCD), while the others had no obvious MCD lesion. Subjects with MCDs had more widespread fMRI activation than those without lesions. Specifically, activity was found in both ipsi- and contralateral hemispheres at locations distant from the suspected focus. Conversely, patients without lesion had maximal activity at the location where discharges were recorded.

Conclusions: We found intracranial EEG-fMRI to be a safe, effective tool for the assessment of patients with epilepsy. We have also shown that the networks underlying interictal discharges may be different between patients with no obvious lesion and those with MCDs.

Poster Number: 51

Presenter's Name: Francine van Rooyen

Program and Year: MD/MSc, Class of 2012

Category: Translational Project

Rehabilitative Therapy after Seizures Restores Typical Motor Map Size but not Typical Behaviour

Francine van Rooyen and G. Campbell Teskey

Dept. of Psychology and Dept of Cell Biology and Anatomy, University of Calgary, AB

Objectives/Introduction: We sought to determine whether rehabilitative behavioural therapy in the form of skilled reach training could reverse the seizure-induced expansion of neocortical movement representations (motor maps).

Methods: We electrically elicited seizures from the right ventral hippocampus of Long-Evans hooded rats, twice daily, until thirty afterdischarges had propagated to the frontal neocortex. Thereafter, rats were trained on the single-pellet reaching task for fifteen days to reach for a pellet with their right hand, and reaching behaviour (attempts, success and kinematics) was analyzed. Skilled unlearnt motor behaviour was also periodically assessed by the rung walking task. One to four days following the final reach training session, high resolution intracortical microstimulation was used to derive the forelimb movement representations in the left (un-implanted, contralateral to reaching hand) sensorimotor neocortex.

Results: Rats that had thirty cortical seizures and behavioural training demonstrated impairment in two skilled reaching subcomponents (Arpeggio and Grasp) compared to sham-stimulated controls. Rats that had seizures also showed deficits in skilled unlearnt motor behaviour, as demonstrated by their performance on the rung walking task. Neocortical forelimb motor maps in rats that had seizures and were then reach-trained were similar in size to those of sham-stimulated control rats and significantly smaller than seizure-expanded motor maps of rats that did not receive behavioural therapy.

Conclusions: Seizure-induced motor map expansion can be reversed by sensorimotor experience in the form of skilled reach training. Although the maps are restored the behaviours are atypical, indicating that it is not the size of the map but the history of experience that gives rise to behavioural expression.

Poster Number: 52

Presenter's Name: Aravind Ganesh and Matt Grossi

Program and Year: MD, Year 3 (AG) and Year 2 (MG)

Category: Translational Project

Identifying impairments in learning and decision-making pathways through functional MRI of pathological gamblers (*ongoing analysis*)

Dr. Bradley Goodyear (1), **Aravind Ganesh** (2), **Matt Grossi** (2), Dr. David Crockford (3), and Dr. Yuri Power (3)

(1) Hotchkiss Brain Institute, (2) University of Calgary MD Program, (3) Department of Psychiatry

Objectives: The Iowa Gambling Task (IGT) involves exploratory learning via rewards and penalties, with ideal performance requiring the sacrifice of shorter-term rewards for longer-term risk probabilistic rewards. Pathological gambling (PG) subjects perform worse on the IGT compared to controls owing to their discounting of delayed rewards, suggesting underlying differences in risk and reward-processing pathways.

Methods: 13 male PG subjects with no active comorbidities were compared to 13 demographically matched control subjects via functional magnetic resonance imaging (fMRI) while performing a computerized version of the IGT assessing behavioural performance and neural responses to high and low risk gambling decisions. The fMRI images were analyzed for connectivity patterns – similarities in activity – among various brain regions, with comparisons made between the PG and control subjects.

Results: A learning curve was observed for both PG and control subjects, on average over the first 20 trials, after which clear differences emerged in deck selection patterns. PG subjects performed worse on the IGT, accumulating greater losses overall and making more high risk choices compared to controls, particularly after experiencing losses, paralleling results from behavioural studies. Early analysis suggests decreased connectivity in the mesolimbic and mesocortical pathways in PG subjects compared to controls.

Conclusions: PG subjects perform worse on the IGT owing to their prediliction for high risk choices incumbent in delayed discounting. Preliminary observations of differences in connectivity of brain regions implicated in the extended reward and learning pathways between control and PG subjects suggests that pathological gambling and other addictions may develop and persist due to a combination of flawed decision-making and failed learning, resulting in the persistent favouring of higher risk, shorter-term rewards over lower risk, longer-term rewards.

Poster Number: 53

Presenter's Name: Rachel Lim

Program and Year: MD, Year 1

Category: Translational Project

NSAID Ulcer Prophylaxis in Patients Presenting with Nonvariceal Upper Gastrointestinal Bleeding

Rachel Lim, Duane Bates
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Background: In 2009 the American College of Gastroenterology and Canadian Association of Gastroenterology published guidelines for non-steroidal anti-inflammatory drug (NSAID) ulcer prophylaxis. The recommendations include both the gastrointestinal (GI) and cardiovascular risks of the patient. Previous studies have suggested poor compliance with NSAID ulcer prophylaxis.

Aim: To assess prevalence of gastroprotective strategies among patients admitted to hospital with nonvariceal upper gastrointestinal bleeding secondary to NSAID use.

Methods: Admissions from January 1 – June 30, 2009 at the three Calgary adult acute care sites were reviewed by Health Records using ICD-10 codes. Endoscopy reports were screened to identify potential patients. The design was a descriptive, retrospective cross-sectional study. NSAID users were stratified into low, moderate and high risk of GI events. Compliance with NSAID ulcer prophylaxis guidelines was assessed.

Results: There were 75 patients with ulcer complications attributable to NSAID use. Of the 43 patients at moderate risk and 13 at high risk, 3 (7%) and 3 (23%), respectively, were given ulcer prophylaxis. Half of all proton pump inhibitor prescriptions were double dose or used in conjunction with ranitidine or misoprostol.

Discussion: Seventy-five percent of our population had at least 1 to 2 risk factors for NSAID-induced upper GI complications. Despite the level of risk, the prevalence of gastroprotection was nominal.

Poster Number: 54

Presenter's Name: Tharindri Dissanayake

Program and Year: MD, Year 3

Category: Translational Project

Efficacy of methotrexate monotherapy compared to combination therapy with methotrexate and hydroxychloroquine in the treatment of early rheumatoid arthritis

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Medicine, University of Calgary

Introduction: Early treatment of rheumatoid arthritis (RA) with disease-modifying anti-rheumatic drug (DMARD) therapy leads to better clinical outcomes. Methotrexate (MTX) is the most commonly used DMARD in treating RA either as a monotherapy or in combination with other DMARDs. However data on the efficacy of MTX used at the current doses in treating early RA is lacking.

Objective: The purpose of this study is to compare the efficacy of high dose oral MTX (20–25 mg/ week) versus high dose oral MTX in combination with hydroxychloroquine (HCQ) 400 mg daily in DMARD-naïve patients with early RA, as determined by changes in Disease Activity Score 28 (DAS28) and Health Assessment Questionnaire (HAQ) scores.

Methods: Consecutive patients diagnosed with RA at our Early Inflammatory Arthritis Clinic (EIA) from 01/2008 to 09/2010 were included. Data collected prospectively on patients includes: age, gender, co-morbidities, medications, DAS28, HAQ, rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP). Patients were treated with MTX or MTX/HCQ based on participating physicians' practice. Patients in each group were offered a pulse of corticosteroids as acute treatment for their disease. Treatment responses were compared within and between groups after 3 months using pre- and post -treatment DAS 28 and HAQ scores.

Results: There were 35 (26F /9M) patients in the MTX and 39 (27F/12M) in the MTX/HCQ groups respectively. There were no statistical differences between the two groups for age, gender, medications, co morbidities or duration of symptoms. There was no statistical difference between the groups for RF status ($p= 0.61$), anti CCP ($p =0.26$), baseline DAS28 ($p=0.72$) or baseline HAQ scores ($p=0.95$). The number who received pulse steroid therapy at diagnosis ($p=0.19$) was similar. The DAS28 and HAQ scores improved in both groups. However, the mean change in DAS28 scores after 3 months was significantly greater in the MTX/HCQ group compared to the MTX group (-2.24 vs -1.31, $p= 0.003$). The improvement in HAQ scores was not significantly different between the two groups (-0.62 vs -0.46, $p=0.25$).

Conclusion: This study suggests study suggests that MTX/HCQ is more effective than MTX alone in the initial treatment of early RA using an objective measurement of disease activity (DAS28). Dual therapy should therefore be considered as the initial therapy in patients with early RA.

Poster Number: 55

Presenter's Name: Kimberly Williams

Program and Year: MD/MSc, Year 1 of MD

Category: Translational Project

The impact of combination Antiretroviral Therapy expansion on primary health care services in rural Southwest Uganda

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1. University of Calgary 2. University of Alberta 3. Kabarole District, Uganda

Introduction/Objectives: To achieve wide access to combination Antiretroviral Therapy (cART) in Africa, cART has been incorporated into primary health care (PHC) clinics, Little information exists on the impact of these additional program activities on already under-resourced PHC services. This study evaluated the impact of cART expansion on PHC programs delivered by clinics in Uganda.

Methods: This retrospective study collected qualitative and qualitative health service data before and after cART implementation. Data were obtained from clinic records, interviews with 210 randomly selected community members living in close proximity to three clinics, interviews with 15 Health Care Workers (HCWs) and six focus group discussions with community members.

Results: The number of deliveries per month increased significantly at the PHC clinics by a median of 19 ($p=0.01$) as did the number of new antenatal attendees by median of 18 ($p=0.01$). Most community participants (60.9%) felt health services had improved after cART expansion. Only 4.3% felt health services were worse and 34.8% felt no changes had occurred. HCWs were happy that they could provide cART, although this resulted in increased workloads. Laboratory testing increased by approximately 960% ($p<0.01$) after cART roll-out. The total number of immunizations decreased following cART expansion by approximately 4% ($p=0.01$). Both community members and HCWs reported an increase in waiting time for non-cART health services. A previously unreported observation by both staff and community was that staff prioritized cART patients. The study was limited by the before-and-after design and available data.

Conclusions: The findings point to increased human and material resources for cART programs are needed to mitigate negative consequences. cART program evaluation should routinely include outcome monitoring of basic PHC programs. Greater awareness of the prioritization of cART patients over others could prevent the emergence of diagnosis-based two-tier care, ensuring access to services for both cART and non-cART patients.

Poster Number: 56

Presenter's Name: Christopher Sibley

Program and Year: MD/PhD, Year 7

Category: Translational Project

Discovery of a Twenty-Five Year Outbreak of Clonal *Pseudomonas aeruginosa* Infecting Patients with Cystic Fibrosis

Christopher D. Sibley[1], Bryan A. Glezerson[1], Kristen A. Sibley[1], Michael D. Parkins[1,2,3]

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Objectives/Introduction: Individuals with cystic fibrosis (CF) can transmit common *Pseudomonas aeruginosa* strains between patients. Many studies have suggested that these strains are associated with a more aggressive disease course and potentially worse outcome. Recent reports from Ontario have confirmed the presence of transmissible strains in Canada. Therefore, we sought to determine if transmissible strains of *P. aeruginosa* existed in the Calgary Adult CF Clinic (CACFC).

Methods: We used pulse-field gel electrophoresis (PFGE) to compare the most recent *P. aeruginosa* isolate(s) available for each current CF patient to a comprehensive strain collection of previously described transmissible strains. To determine the durability of chronically infecting strains over time we compared the relatedness of a patient's isolate from their first clinic visit upon transferring to our clinic to their most recent clinical sample.

Results: Only one patient attending the CACFC was identified to have infection with a previously identified transmissible *P. aeruginosa* strain. Critically, a novel, not previously described, clonally related complex was identified within our clinic cohort. This clonal complex, termed the Prairie Epidemic Strain (PES) was present in 29% (31/108) of our cohort.

Conclusions: The epidemic spread of a novel trasmissible strain of *P. aeruignosa* has been occurring across the Canadian Prairies for at least twenty-five years. Studies are currently underway to determine the clinical impact of PES infection.

Poster Number: 57

Presenter's Name: Alby Richard

Program and Year: PhD (Completed)/ MD, Year 2

Category: Clinical Project

On the illusory perceptual compression of visual space during eye-head gaze saccades

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Background: In primates, inspection of a visual scene is typically interrupted by frequent gaze shifts, occurring at an average rate of three to five times per second. Perceptually these gaze shifts are accompanied by a *compression* of visual space towards the saccade target, which may be attributed to an oculomotor signal that transiently influences visual processing. While previous studies of compression have focused exclusively on saccadic eye movements made with the head artificially immobilized, many brain structures involved in saccade generation also encode combined eye-head gaze shifts, where gaze = eye-in-space = eye-in-head + head-in-space. In order to understand which brain areas are responsible for perisaccadic visual perception, is thus important to determine whether compression is towards the end-point of gaze saccades made head-unrestrained (HU).

Methods: Using a standard compression paradigm (Lappe M et al., *Nature*, 2000), we studied mislocalization in HU human subjects who made horizontal saccadic eye-head gaze shifts of 40 to 60 degrees. Subjects were instructed to report the perceived position a briefly (12ms) flashed vertical bar presented over a range of horizontal positions in a time-window ± 200 ms around gaze-shift onset.

Results: We found a powerful compression of visual space that depended on the time at which the vertical bar was presented relative to the onset and time-course of the gaze shift. Importantly, compression was toward the intended gaze target, rather than to the spatial location of the initial eye movement.

Conclusions: The spatial pattern of results could be captured by a model that involves interactions, on a logarithmic map of visual space, between two loci of neural activity that encode the gaze-shift vector and visual stimulus position relative to the fovea. In a broader sense, the present findings expand on what is known about the extra-retinal mechanisms that maintain perceptual constancy across gaze saccades.

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