2013-14

CITAC Conference – Ottawa, September 2013

This is a report of accomplishments and highlights of the University of Calgary's Leaders in Medicine (LIM) program for the period of **May 2013 to April 2014**

Prepared for the Dean of Medicine, Faculty of Medicine
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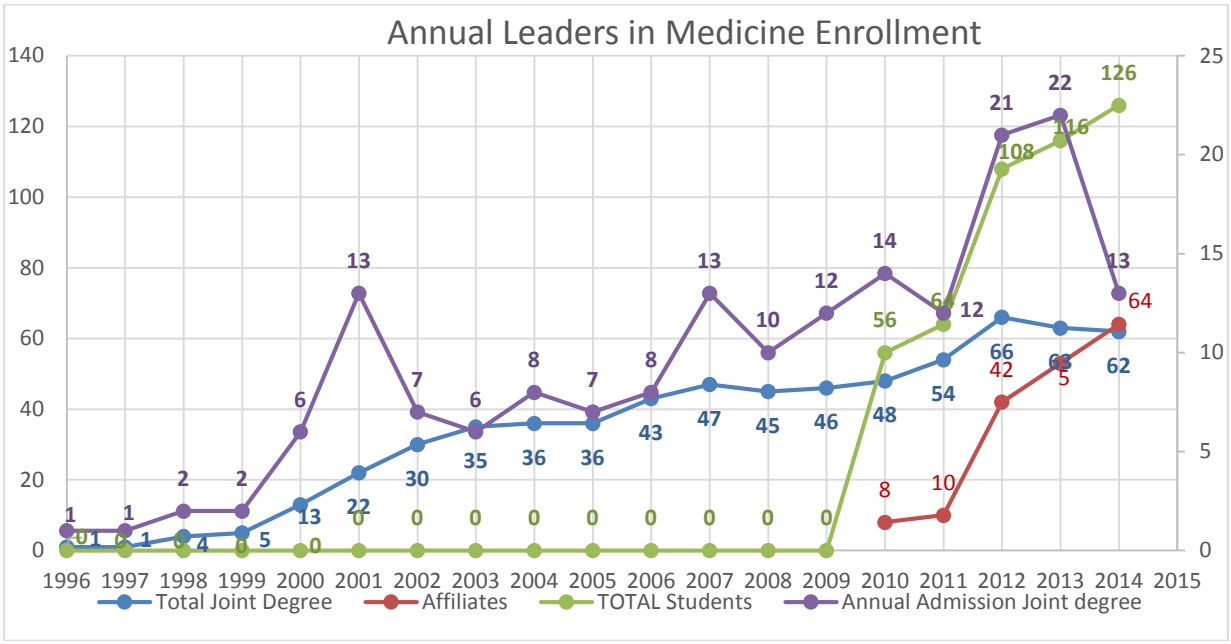
INTRODUCTION

Although the vision, when the first student joined the Leaders in Medicine program in 1996, was to create a successful integrated program to encourage clinical-research as a career, there was no way to know that the program would become the success it has. Growing from one to an average enrolment of 66 joint degree students and a growing Affiliate program that currently has 68 students.

The LIM joint degree program continues to be unique in Canada. Not only does it include students pursing their PhD or MSc and their medical degree, we have students working on an MA, a MBA, a MEng, as well as other graduate degrees. The program's intention, to train individuals in many disciplines related to medicine, is creating leaders and pioneers in a variety of facets for our future health care system. Award winning students continue to graduate from this innovative program.

Without the funding received from our anonymous donors, Canadian Institute of Health Research (CIHR) program grants, the program could not have grown successfully. Since the first CIHR program award, to fund one student in 2001, has allowed monthly stipends for many MD/PhD students. The generous anonymous donor funding that began in early 2000s, allows the program to offer travel awards, fund the annual research symposium and other events. Through that funding we also award MD/PhD students medical school tuition funding for students with no other funding. The Alberta Innovative Health Solutions (AIHS formerly AHFMR) has been generously funding joint degree MD/PhD students with an award which follows them through medical school.

Currently there is no limit to the number of students admitted into the joint program, however it is done only one per year. Our average has increased from 1 to 6 students to 6 to 10, this year we admitted 13 to the joint degree program. Affiliate members come on at various times through the year and increased by 14 this year.



OVERVIEW

The Leaders in Medicine joint degree program remains unique because of its flexibility. Enrollment requirements, however have not changed. A student must be accepted into both the University of Calgary's medical school and be active in or accepted into one of the university's graduate programs. The improvements in the application process implemented last year based on input from the graduate program supervisors and the Associate Dean of Graduate Science Education, Dr. van der Hoorn with the agreement of the Associate Dean of Undergraduate Medical Education (UME) and the LIM program directors has proven helpful. The medical school application supplemental form *"UME Applicants Currently Enrolled in a Graduate Degree Program"* that asks when the student plans to complete his/her graduate degree and if he/she plan to defer medical school or the graduate program, or withdraw from the graduate program. It helps UME count the number of openings to hold and, since it is given to the graduate student's supervisor, it is an alert regarding a student's plans should they be accepted into medical school. It gives a heads up to the student's supervisory committee so they can work with the student to complete in order to enter medical school, or decide the best plan for deferral until completion.

Last year the application process added a meeting between all new students and the LIM program administrator. The meeting occurs when applications are submitted and it is designed to discuss expectations, commitments and funding. It gives the applicant an opportunity to ask questions about the program and become familiar with processes.

PROGRAM ADMINISTRATION

The Cumming School of Medicine's, Graduate Science Education office continues to supports the program in many ways. The program has three award winning faculty members as Directors: Dr. Paul L. Beck, director, Dr. Morley Hollenberg, co-director and Dr. Bryan Yipp, associate director. The program's administrator is part of the GSE and provides one-third to one-half of her time for administration of LIM. This includes processing all enrolment and award applications, budgeting and many other daily duties. Administration of the program requires, working closely with program directors, the LIM student committee, Undergraduate Medical Education, the Faculty of Graduate Studies and of course with individual students as they work through their studies.

The student executive committee, chosen each year by the LIM membership, and student volunteers who help at events, run other aspects of the program. (See Executive Committee Chair's report below)

LEADERS IN MEDICINE STUDENT COMMITTEE

2013-2014 LIM EXECUTIVE:

Chair	Christina **Thornton** MD/PhD
Committees:	
Communications	Andrea **Mosher** and Amanda **Eslinger** MD/MSc
Visiting Speaker Series	Jason **Bau** MD/PhD and Michael **Peplowski** MD/PhD
LIM Research Seminar	Nathan **Bracey** MD/PhD and Jodie **Huebner** MD/PhD
Research in Progress	Michael **Keough** MD/PhD and Jodie **Roberts** MD/MSc
Journal Club	Megan **Blades** MD/MSc and Monica **Faria-Crowder** MD/PhD
Social Committee	Veronica **Ram** MD/PhD and Kristine **Woodward** MD/MSc

EXECUTIVE COMMITTEE CHAIR REPORT

The 2013/2014 academic year was another busy and successful time in the Leaders in Medicine (LIM) program. We saw our program continue its growth with increasing enrollment of both full and affiliate members. This year was one of expansion where continued academic events were maintained such as our popular visiting speaker series that occurs monthly with both local and international speakers. TED-talk style research in progress sessions also continued with such interest by students that sign up's at the first meeting filled up the entirety of the academic year.

One of the objectives this year was to form a sub-committee to start an alumni project. The student executive felt it is important to not only track where the alumni from the program go onwards in the future but to maintain those connections to facilitate future networking, such as inviting alumni as guest speakers and as judges for the annual symposium. Thus far, we built a database of alumni and are working expand, in order be able to report the success of the program as alumni move from residency forward.

This year the committee also focused on transparent communication and feedback from the LIM students to the faculty. The executive conducted a survey among attendee's to assess the strengths and weaknesses of the annual research symposium. As a result of this, the future symposiums will stratify abstracts and projects based on research experience (MD, MD/MSc, MD/PhD, MD/Post-doc) in order to freely facilitate engagement of all students.

Based upon feedback from students, we sought to modify our journal club this year and added several "quick fire" and "debate" sessions where several research papers were presented with differing hypothesis and students could provide evidence-based ideas behind different scientific and clinical theories. This has been a great success so far and will continue on into the future.

The LIM program provides a unique environment whereby clinical knowledge, potential to continue research, networking and strong mentorship exist for students. I can safely speak for other students when I say we are grateful for the opportunities provided by LIM to allow the harmony of clinical research to continue from the basic science bench to the bedside in a cohesive and effective manner and look forward to its continued growth in the upcoming academic years.

PROGRAM DIRECTORS' REPORT

Dr. Paul L. Beck, Director, Leaders in Medicine Program, recipient of numerous teaching, mentorship and research awards included the 2013 Division of Gastroenterology Research Mentor Award, the Alberta Society of Gastroenterology Distinguished Research Award and the Canadian Gastroenterology Visiting Research Professor Award.

The LIM Program at University of Calgary has continued to grow! This year we was the largest group of students in the history of the program with 126 students actively involved in the program with about half full members (currently enrolled in joint degrees) and the others being affiliates (previous graduate degrees and/or simply interested in the goals and aims of the LIM program). Under the guidance of Dr Bryan Yipp our Research in Progress Meetings, Translational Journal Clubs and Visiting Speaker Series have been a tremendous success with incredible attendance, great presentation and student/staff interaction. On November 8, 2013, the Leaders in Medicine (LIM) program hosted the 5th Annual Research Symposium. Dr. Jerrold Ellner, Chief of the Infectious Diseases section at Boston Medical Centre and Professor of Medicine at Boston University School of Medicine, was the keynote speaker and presented his lecture entitled "Tuberculosis – Past, Present and Future." The LIM symposium gives a forum for LIM as well as non-LIM medical students to present their research work in either as an oral or poster presentation. There were a total of 53 abstracts presented and 5 oral presentations. The symposium was attended by over 100 students and more than 30 staff members. Dr Ellner is a pioneer in TB and HIV research grave an incredible presentation followed by one on one interaction with our students and a small group luncheon session and interactions during the poster and oral presentations. Students both from the LIM program and medical school program presented their work to over 30 faculty and more than 70 students.

The proceedings and abstracts of LIM Research Symposium was published in the CIM Journal (see Appendix A1) with and accompanying article on our unique program entitled ***"A Prescription that Addresses the Decline of Basic Science Education in Medical School"*** (Appendix A2).

Not only was the LIM Program extremely successful but most importantly our students excelled with several receiving the coveted MD-PhD Studentships from Alberta Innovates Health Solutions. Our students received 42 other awards or scholarships during the year! They published 44 papers with another 26 submitted and/or in press. They published four book chapters and over 100 abstracts. LIM student also excelled in residency matching (see below) with the vast majority of student getting their first choice of specialty and location.

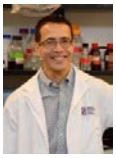
We have continued to grow our mentorship network and have been accumulating further willing mentors and reaching out to LIM alumni in this regard. We are in the stages of planning a student based additional mentorship program for new LIM members.

Our students were actively involved in numerous meetings locally, nationally and internationally. Again we had the largest group of student from across Canada to attend the excellent CITAC (Clinicians in Training Association of Canada) meeting where our student presented their work, attended career development sessions and research presentations as well getting to meet and interact with like-minded students and staff from across the county.

We receive feedback from our student body on a yearly basis and the report was again excellent with student stating they were excited about the enhanced programs and designs or the Research in Progress and translational Journal Clubs and their ability to request outside and local visiting speakers. We will continue to enhance our program with the help of our students that are involved in the executive and with our dedicated staff.

Program Director, Dr. Paul Beck

Dr. Morley Hollenberg, co-director, Leaders in Medicine program made the global most-cited list. Hollenberg is among the world's most often cited researchers. The Highly Cited Researchers list, which contains about 3,200 people represents the top one percent of the most numerous citations from 2002-2012. Hollenberg, 2013 recipient of the E.K. Frey – E Werle Commemorative Gold Medal



Dr. Bryan Yipp MD/MSc, Leader in Medicine alumni, Associate Director for Leaders in Medicine Program. As Associate Director, Dr. Yipp is on the program administrative committee with Drs. Beck and Hollenberg, the program administrator and a student representative, student committee chair, Christina Thornton. Dr. Yipp was named as a CIHR Canada Research Chair, 2013

During 2013-2014, the LIM journal club evolved into an innovative and interactive forum to discuss cutting-edge biomedical research. IN addition to enhancing the journal club format, we provided a longitudinal seminar series to supplement the trainees understanding of translational medicine. This included an introduction to Translational Medicine by Dr. Bryan Yipp. External experts provided specific education on multiple aspects of translational medicine. Dr. Matt Coffey (Chief Operating Officer of Oncolytics Biotech Inc) described how he took a bench research discovery and built a viable biotech company and novel pharmaceutical, while Dr. Don Morris (Director/Senior Scientist Translational Cancer Laboratories) educated us on how to conduct human trials using novel biological agents. Additionally, we hosted a discussion on biomedical intellectual property led by two external experts, Dr. David Wood (IP Lawyer and PhD in biochemistry) from Borden Ladner Gervais Law firm and Dr. Jaswinder Kubes PhD (director of IP management for Innovates Calgary).

During the translational journal club, trainees present a biomedical publication and were responsible for leading a 30 minute discussion about the translational aspects of the articles findings. Internal scientists with content expertise attended the journal clubs to guide us through the discussions, including Dr. Glenda MacQueen, Dr. Dan Muruve, Dr. Jaideep Bains and Dr. Ray Turner.

Dr. Slava Epelman MD/PhD, an accomplished LIM alumni, who is a cardiologist clinician scientist at the University of Toronto was invited to share his experiences and his research. He presented a lecture on cardiac macrophages and was a guest at a small lunch hosted by the LIM trainees to discuss career development.

Associate Program Director, Dr. Bryan Yipp

MENTORSHIP

Mentorship continues to be a key part of the Leadership in Medicine program structure. The director (Dr. Beck), co-director (Dr. Hollenberg) and acting assistant director (Dr. Yipp) believe that mentorship is critical to a successful program and along with being mentors to students, work to set up mentorships. Students in the graduate part of the program are encouraged to have a clinician on their thesis committee. The LIM program works to maintain a "mentorship flow" where mentorship is available while a student transitions from non-clinical activities to clinical activities which a critical to best support and guide the student. Ideally we provide mentorship during non-clinical training, clinical/medical training, into residency, fellowship and to further research training and a junior faculty position

LIM GRADUATE MENTORS

As part of our ongoing effort to provide a continuum of mentorship, as students begin to transition through graduate research, undergraduate medical education, and beyond, the program began a new initiative designed to connect current students with LIM program graduates nationwide. The expanding size of the program and increased number of graduates enrolled in a variety of residency and fellowship programs across the country provides an important resource for current LIM students. Recent LIM graduates provide a unique perspective and first-hand insight about information that is important to LIM students. Over the past year, a number of our students have been informally in touch with LIM graduates across the country in order to facilitate discussions about the transition from medical school into residency, get information about residency programs, the CaRMs application process, and opportunities for research. For example, students interested in doing electives or residency at the University of Toronto have been given the contact information of a 2010 LIM graduate who is currently an R1 in neurology at that institution.

We have received positive feedback from students as well as LIM graduates who are enthusiastic about keeping these lines of communication open. Undoubtedly, these relationships will serve our goal of "mentorship flow", as students are able to form mentorship bonds with graduates who may become their senior residents and can provide guidance into residency. Over the next year, we hope to formalize this mentorship initiative by creating a comprehensive database on our website of participating LIM graduates and their residency training program information. In this way, current students will have access to the experience and insight from those who have recently navigated the transition from research and medical education to residency training programs and beyond.

EDUCATIONAL EVENTS

Program Educational Events are intended to enrich the student research experience. LIM students and Affiliates are expected to commit to a minimum of 2 to 4 hours per month to the program and to attend up to an average of 60% of the monthly seminars. There are many opportunities to present research through seminars, the journal club, national conferences and the yearly LIM Research Symposium.

The program sponsors attendance at two main national symposiums. An average of 16 LIM students present research abstracts to the Clinician Investigator Trainee Association of Canada (CITAC), held in Ottawa each year in September. Five to 8 students are accepted to present at the annual Canadian National Medical Student Research Symposium (CNMSRS) held in Winnipeg in June.

Our students consistently win poster and/or oral research presentation awards at these events (see more information on specific events below). Students use their Leaders in Medicine CIHR or AI-HS MD/PhD research allowances and the program uses our anonymous donor funds to reimburse student expenses for these trips.

ANNUAL LEADERS IN MEDICINE SYMPOSIUM

Held in early November, the 5th Annual Symposiums had another successful year. Graduate and medical students presented through a talk or a poster and were judged by Faculty, Alumni and other students. See below and **Appendix A** for details on each year.

Summary Poster of the 2012 LIM Research Symposium

RESEARCH IN PROGRESS (RIP) – STUDENT SPEAKER SERIES

This speaker's series gives students the opportunity to share research and interests. The following is a list of presentations for this year.

Date	Name	Presentation
7-5-13	Andrea Mosher	Music & the brain
7-5-13	Robert Kosior	Quantitated T1 and T2 MR imaging for better determination of tissue fate in acute ischemic stroke
7-5-13	Michael Keough	My personal experience with publication bias
4-6-13	Angela Karlos	Men are from Mars, women are from Venus: research implications of being from different planets
4-6-13	Waleed Rahmani	In vivo genetic lineage tracing of dermal stem cells during hair follicle regeneration and wound healing
4-6-13	David Nicholl	Careers in medicine: what am I doing with my life?
6-8-13	Amanda Eslinger	What do you think?
6-8-13	Collin Luk	Terminator: The bionic hybrid lives: a story of bench side to media
6-8-13	Laura Ansell	Why do we go to grad school?
3-9-13	Monica Faria-Crowder	Are we over or under estimating sepsis infections?
3-9-13	Mehrnoosh Aghaei	What is the best mouse model?
1-10-13	Ann Zalucky	The doctorpreneur: bridging medicine and business to solve big world problems
1-10-13	Sarah Tulk	Interesting case: abdominal pain
1-10-13	Jodie Roberts	Can blinding reduce bias in surgical trials?
5-11-13	Jessica Ruzicki	Spontaneously resolving diplopia: to image or not to image
5-11-13	Jason Bau	Salicylate-mediated bypass of radiation-induced checkpoints
5-11-13	Menglin Yang	Characterization of pitcher fluid from Nepenthes plants as an oral therapeutic for the treatment of celiac disease
7-1-14	Veronique Ram	Caught Depression: alleviating fears of contraction in children's literature
7-1-14	Kristine Woodward	The effects of mass media on clinical research
7-1-14	Helena Zakrzewski	Measuring the quality of care of elderly patients
4-2-14	Joan Stilling/Collin Luk	When disciplines collide…Oh the places one may go
4-2-14	Prima Moinul	Comparison of Biometric Measurements Using IOL Master and LenStar Optical Biometry Systems
4-3-14	CJ MacMillan	Angiogenesis as a novel therapeutic target in Multiple Sclerosis
4-3-14	Connie Liao	Pressure and flow
4-3-14	Alex Frolkis	The problematic p-value
8-4-14	Sarah MacEachern	Adapted physical activity and early childhood development
8-4-14	Misha Bawa	Targeting MDSC *in vivo* reduces cancer incidence in the IL-10$^{-/-}$ mouse
8-4-14	Brandon Hisey	Behavior of skeletal muscle at long lengths

JOURNAL CLUB – SEMINAR SERIES

The LIM Journal Club is designed to provide opportunities to learn about important research that may be outside the student's field of study. Journal Club presentation are from 45 to-55 minutes and delve fairly deep into the subject matter. Presenters are welcome to talk about whatever is of interest to them, so long as the topic is translational. Average attendance this year was 35 per meeting. A survey of students indicated that the format was not optimal so it was modified in January 2014 to include the presentation then a breakout into 2 discussion groups. One to focus on critiquing the science and mechanisms in the paper and the other to discuss the implications in a broader context.

Date	Name	Presentation	Faculty
May 31	Nathan Bracey	The role of c-Myc in lymphocytes and embryonic stem cells.	Dr. Randy Johnston for discussion
Aug 27	Dr. Bryan Yipp	Translational research	n/a
Sep 28	Monica Faria and Megan Blades	Discussion of Manuscript: Regeneration and experimental orthotropic transplantation of a bioengineered kidney	n/a
Oct 24	David Wood from Borden Ladner Gervais and Jaswinder Kubes from Innovates Calgary	Discussion of patenting.	n/a
Nov 26	Amanda Eslinger	Discussion on paper: Conserved Shifts in the Gut Microbiota to Gastric Bypass Reduce Host Weight and Adiposity	n/a
Jan 28 *	Taryn Ludwig	Discussing Proteoglycan 4 Expression Protects Against the Development of Osteoarthritis	Dr. Dan Muruve attending as expert in adeno viral vectors
8-4-14	Brandon Hisey	Behavior of skeletal muscle at long lengths	n/a

*based on student survey, format was modified to include the presentation then a breakout into 2 groups, one focused on critiquing the science and mechanisms in the paper, the other to discuss the implications of the therapy in a broader context.

VISITING SPEAKER SERIES

A variety of visiting medical researcher, educators and clinicians, some jointly sponsored and others fully sponsored by LIM funding, are invited to visit and present to LIM students. This student organized program is set up in order to bring educators here to give a formal presentation and to meet students for an informal question and answer period, usually over lunch. This year was a particularly well planned and successful year, with a speaker attending almost monthly.

LIM Students were invited to attend the **2013 Canada Gairdner Lectures** and meet Investigators included a Nobel Laureate. Includes Sir Gregory Winter, Adrian P. Bird and Thomas A. Steitz.

List of Speakers 2013-14

Date	Speaker Name and Institution
June 17, 2013	Dr. Jennifer Chan, University of Calgary
September 24,	Dr. Richard Leigh, University of Calgary
October 23, 2013	Dr. Aru Narendran, University of Calgary
November 7, 2013	Dr. Jerrold Ellner, Boston University
January 17, 2014	Dr. Derrick MacFabe, McMaster University
February 14, 2014	Clerkship Panel (Dustin Anderson, Judy Luu, Aman Wadhwani, Ian Hons)
March 12, 2014	Dr. Harvey Fineberg, Institute of Medicine USA
March 24, 2014	Dr. Slava Epelman, Washington University
April 29, 2014	Dr. Matt Coffey & Dr. Don Morris (Translational Journal Club /Visiting Speaker Joint Seminar)
May	Dr. Jenny Souster, University of Alberta
May 15, 2014	Dr. Stefan Lohmander, University of Lund
June	Alumni Panel (Speakers TBD)

Canadian National Medical Student Research Symposium

An annual conference hosted by the University of Manitoba's Faculty of Medicine, the CNMSRS invites MD and MD joint degree students from other Canadian universities to present research. Held in conjunction with the CIHR Canadian Student Health Research Forum, students are invited to attend a number of presentations and symposia. This is a unique educational opportunity or trainees. Leaders in Medicine sends between 2 and 6 students each year. This year, Dr. Morley Hollenberg attended as faculty. (see photo on cover page)

CITAC/CSCI Young Investigators Forum

Each year, in conjunction with the annual general meeting, the Canadian Society for Clinical Investigators (CSCI) and Clinician-Investigator Trainee Association of Canada (CITAC, national MD-Plus student organization) host a young investigator forum. The meeting, this year in Ottawa, includes presentation of oral and poster presentations from 17 LIM students.

LIM STUDENTS AT CITAC DINNER 2013

Leaders in Medicine Social Events

To allow a more balanced work-life experience our students attend a number of social events each year. A welcome (to new and returning students) is held each autumn, for example. A graduation dinner and end of year dinner is held in spring and there are occasional luncheons sponsored during the year.

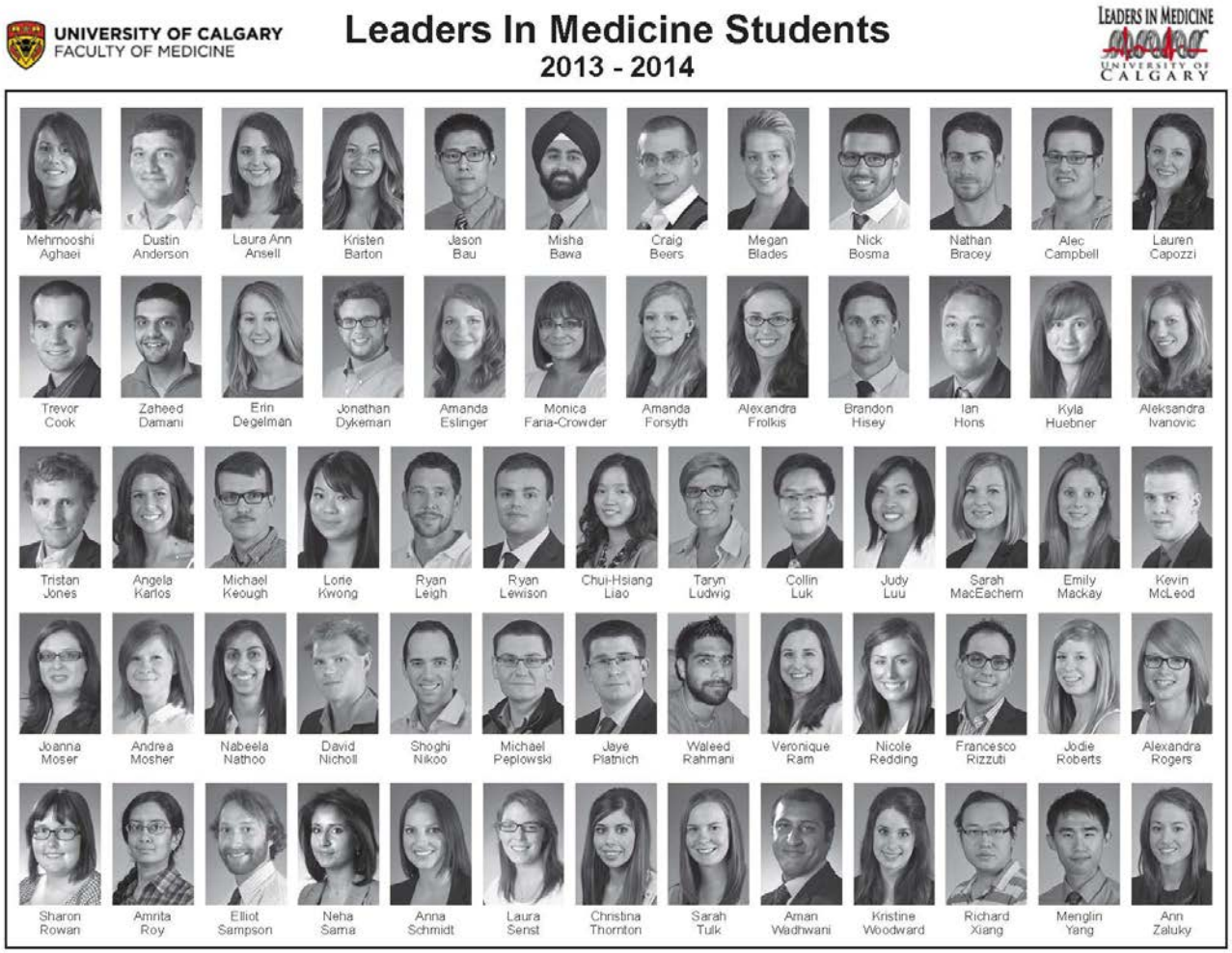
Leaders in Medicine Students

Current Joint Degree Students

Students in the LIM program are from the following graduate programs:

MDBC – Biochemistry & Molecular Biology
MDCH – Community Health Sciences
MDIM – Immunology
MDMI – Microbiology & Infectious Diseases
MDBT – Biomedical Technology
BMEN – Biomedical Engineering
ENG – English
MDCV – Cardiovascular/Respiratory Sciences
MDGI – Gastrointestinal Science
MDSC – Medical Sciences
MDNS – Neuroscience
KNES – Kinesiology
BISI – Biological Sciences
SOC – Sociology

This year enrolment totals 63.



AFFILIATE STUDENTS

The program created the Affiliate Program to allow medical students interested in research to participate in Journal Club, RIP and other events open to joint degree students. They are also supported to attend CITAC and CMNMRS events to present research. This year there are over 60 Affiliate members.

Student's comment regarding Affiliate program:

"I can't tell you how pleased I am to say I matched to Radiology in Vancouver (my first choice!) this year! I have been an Affiliate Member of the LIM program for the past couple of years, and I can't tell you how much it has enriched my education. My research has been in image-guided technology, mostly in Neurosurgery, while in the MD program. Completed a few peer-review papers, textbook chapters, posters and a presentation this past year, which for sure helped my CaRMS application immensely. I spent significant time in each of my interviews discussing research interests and past projects.

Thank you so much for all that you each do to make research in our tight 3-year MD program possible for the Affiliate Members! The LIM program is one of the best in the country (I know you know this, but I can now say it having visited most of the schools on my interviews!) and is one of the highlights of completing an MD in Calgary."

Jason Motkoski, MD

STUDENT ACCOMPLISHMENTS

2013-14 ACCOMPLISHMENTS:

Leaders in Medicine Students are high achievers. Following is a list of some general accomplishments and some specific accomplishments.

Taryn **Ludwig**, MD/PhD candidate received one of the inaugural Biomedical Engineering Graduate Program Director's award for Leadership. Given for extraordinary accomplishments and outstanding contributions in their program. http://www.ucalgary.ca/news/utoday/april5-2013/accolades-for-top-biomedical-students

Experimental Physiology 2013 Early Career Author Prize, Nathan **Bracy**

http://ep.physoc.org/site/misc/EarlyAuthorWinner/ep_early_investigator_winners_2013.xhtml

Alberta Innovates - Health Solutions researcher, and Leaders in Medicine student, Alexandra **Frolkis**, MD/PhD was published in the latest edition of the prestigious journal *Gastroenterology.* Alexandra, along with her mentor, Dr. Gilaad Kaplan, has shown that management of IBD has evolved over the past 50 years such that those diagnosed with IBD today will have a dramatically different future than those who were diagnosed as little as twenty years ago. http://cumming.ucalgary.ca/Gastroenterology-IBD-Frolis-Novebmer-26-2013 https://www.youtube.com/watch?v=cD_Kq6QmvZY

Ryan **Lewinson**, MD/PhD candidate awarded the J.B. Hyne Research Innovation Award for his PhD project studying how footwear influences mechanical loading in the knee. Ryan also received much attention for his research on design study of snow shovels http://www.ucalgary.ca/utoday/issue/2013-12-11/picking-right-snow-shovel-job

This study was followed in the Wall Street Journal.

Amrita **Roy** awarded the inaugural PHIRC Trainee Publication Prize in Population Health & Inequities (Population Health and Inequities Research Centre, Institute of Public Health, University of Calgary.

Rithesh **Ram** selected by the Canadian Medical Association (CMA) to receive the 2013 CMA Award for Young Leaders in the student category. The award is intended to celebrate the efforts of young physician leaders of tomorrow for their efforts.

Zaheed **Damani**, involved in organization of Campus Alberta Conference in Health (CASCH). The group put their heads together last year and started brainstorming an opportunity for new graduate students to meet, network with faculty members, plan out their research paths and see how those paths might fit together to solve real world problems.

http://www.ucalgary.ca/utoday/issue/2013-11-06/graduate-students-initiate-provincial-conference-health

2014 President's Award of Excellence in Student Leadership

Leader in Medicine joint degree student, Nabeela **Nathoo** and Affiliate student, Emily **Macphail** are among five (5) awardees:

http://www.ucalgary.ca/utoday/issue/2015-02-09/nominate-outstanding-graduating-student-presidents-award

Winners of the 2014 President's Award for Excellence in Student Leadership, from left: Amar Deshwar, Nabeela Nathoo, Emily Macphail, Elizabeth Romo Rábago and Yuan Jian (Jay) Wang.

Nabeela Nathoo, Leaders in Medicine joint degree MD/PhD student

Nabeela represented the Graduate Students' Association on various university research policy committees, contributed to the university's 2012 Strategic Research Plan, and received the Alberta Graduate Citizenship Award twice. She was also the recipient of a Lifetime Achievement Award from the GSA in 2013 for her significant contributions throughout her graduate studies. Nabeela started medical school this year.

Emily Macphail, Leaders in Medicine Affiliate student BHSc

With extraordinary dedication and commitment to the campus and local community. She spearheaded the Because You Matter initiative, a campus-wide effort to promote a culture of support, and has worked on mental health awareness efforts on and off campus. She was VP Academic for the Student' Union 2014. Emily was accepted into medical school at University of Calgary this year and became a LIM Affiliate.

LIM Students Awarded MD-PhD Studentship from Alberta Innovates Health Solutions

Beers, Craig	Hisley, Brandon		Roberts, Jodi
Bracy, Nathan	Keough, Michael	McDonald, Braedon	Roy, Amrita
Capozzi, Lauren	Leigh, Ryan	Mosher, Andrea	Schmidt, Anna
Cotton, James	Lewison, Ryan	Nathoo, Nabella	Spring, Aaron
Frolkis, Alexandra	Ludwig, Taryn	Rahmani, Waleed	Thornton, Christina

2013-14 Residency Results

Leaders in Medicine students continue to match well in Residency. This is a critical point in all medical students' career and it is an indication of the quality of our students and shows the usefulness of the program when so many of our students receive either first or second choice, in their desired Institution and Speciality. Matching their choice allows a student to follow his/her interest and for many passion.

Matches reported by joint degree and Affiliate LIM students**:**

Last Name	Given Names	Degree	MATCH	Place/program
Chiu	**Michael Hubert**	**MD/MSC**	**Calgary /Internal Medicine.**	**1st**
Jalal	Hamza	MD/MSC	Toronto/ Neurology	1st
Kapur	Puneet	MD/MSC	Saskatoon/Emergency	unknown
Lawson	Keith	MD/MSC	Toronto/ Urology	1st
Lee	Kovid Ka-Wai	MD/MSC	Calgary/O&G	1st
Leung	Karen Ka-Ka	MD/MSC	Edmonton/Family Medicine	unknown
McDonald	Braedon Alexander	MD/PHD	Vancouver/ Internal Medicine	1st
Nguyen	Kimchi	MD/MSC	Vancouver/ Family Medicine	2nd/1st
Ram	Rithesh	MD/PHD	Calgary/ Family Medicine	2nd/1st
Rawn	Saara Mirjam	MD/PHD	Northern Ontario/ Internal Medicine	1st
Seamone	Mark Edwin	MD/MSC	Dalhouse/Opthalmology	1st
Sibley	Christopher Daniel	MD/PHD	Ottawa/Dermatology	1st
Solverson	Kevin John	MD/MSC	Calgary Internal Medicine	1st
Tsang	Allison Ruo-Qi	MD/MSC	Kingston/Family Medicine	3rd
AFFLIATES				
Motkoski	Jason	MD	Vancouver/Radiology in Vancouver	1st
Nicholson	Cherie	MD	Toronto/O&G	2nd
Richard	Alby	MD	Montreal/Neurology	1st
Ng	Jeff	MD	St. John's NFL/Anesthesia	1st
Nohr	Erik	MD	Calgary/Anatomical Pathology	1st
Pabari	Reena	MD	Toronto/Paediatrics	1st

ALUMNI

The Leaders in Medicine program is set up to help train successful clinicians, medical practitioners and researchers. The program boasts of several highly successful alumni. This year an alumni, Dr. Bryan Yipp, a LIM graduate, joined the program as acting Associate Director. There are more plans being discussed to involve alumni in the program. A committee has been set up to identify and discuss.

Class of 2014, Drs Christopher Sibly, Braedon McDonald, and Rithesh Ram with Dr. Hollenberg

ALUMNI ACCOMPLISHMENTS:

Medical residents join PARAdime campaign to support the homeless. Alberta medical residents, one of which is LiM Alumni, Rithesh **Ram**, are involved in health care outside hospitals in February 2014. They organized the fifth annual PARAdime campaign. Medical residents – doctors who graduated and are now completing between two and five years of on-the-job-training are involved in this campaign.

AWARDS/SCHOLARSHIPS

TYPES OF AWARDS (as listed in Student's 2013-14 Annual Reports)

1. Vanier Canada Graduate Scholarship $150,000 over 3 yrs
2. Dr. T Chen Fong Doctoral Scholarship in Neuroscience $30,000
3. Achievers in Medical Science Research Excellence Award $3500
4. Achievers in Medical Science Award, LIM $40,000
5. Alberta Innovates Health Solutions Studentship $30,000
6. Dr. Gary MacPherson Leadership Scholarship $2000
7. Queen Elizabeth II Graduate Award MSc $10,800
8. Queen Elizabeth II Graduate Award PhD $15,000
9. J.B. Hyne Research Innovation Award
10. Leaders in Medicine Outstanding Achievement Award $1000
11. Medical Science Academic Productivity Scholarship $500
12. Leaders in Medicine's CIHR Stipend Scholarship $21,000
13. Lydia Sikora Award for Research Excellence $10,000
14. University of Calgary Eyes High Doctoral Research Excellence Award $5000
15. The Lung Association Alberta and NWT $10,000
16. 15th Anniversary Prize, Department of Biomedical Engineering $3000
17. The Dr. Benno Nigg Distinguished Faculty Graduate Achievement Award $1000
18. Graduate Award, Association of Professional Engineers & Geoscientists of Alberta $5000
19. NSERC CREATE Doctoral Award $21,000
20. Canadian Graduate Students Masters Scholarship $17,500
21. Alberta Graduate Student FGS Fee Scholarship $3000
22. University of Calgary Faculty of Medicine International Elective Studentship $1500
23. GRS Graduate Student Scholarship $2000

24. Frederick Banteng and Charles Best Canada Graduate Scholarship Doctoral Award $35,000
25. Dr. Gary McPherson Leadership Scholarship $2000
26. Nat Christie Foundation medical Entrance Award $5,000
27. BME Graduate Program Director's Prize for Leadership $2500
28. AITF PhD Scholarship $26,000
29. Alberta Cancer Foundation Graduate Studentship Award $40,000
30. Dawson Jarock Research Award in Pediatric Nephrology and Rheumatology $2500
31. Louise McKinney Award $2500
32. Professional Development Grant, University of Calgary $470
33. Biochemistry & Molecular Biology publication award $100
34. Cystic Fibrosis Canada Studentship $19,000
35. Persons Case Scholarship, Government of Alberta $2000
36. Gerald Weber Cosmopolitan International Club of Calgary Graduate Scholarship $21,000
37. American Society of Nephrology Student Scholar Grant $7000
38. Alberta Heritage Graduate Student Scholarship Award $3000
39. Scobey Hartley Doctoral Award, Alberta Centre for Child, Family and Community research $32,000
40. Izaak Walton Killam memorial Scholarship $36,000
41. IODE Canada War memorial Scholarship $15,000
42. Medical Science Academic Productivity Scholarship $500

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APPENDIX A:

5TH ANNUAL LEADERS IN MEDICINE RESEARCH SYMPOSIUM

Abstract Booklet for Symposium

APPENDIX A1: PROCEEDINGS FROM 5TH ANNUAL LEADERS IN MEDICINE RESEARCH SYMPOSIUM

APPENDIX A2: A PRESCRIPTION THAT ADDRESSES CIM

FACULTY OF MEDICINE | UNIVERSITY OF CALGARY

5th Annual
University of Calgary
Leaders in Medicine Research Symposium
November 8th, 2013

Distinguished Guest and Speaker:

Dr. Jerrold Ellner, MD
Chief of Infectious Diseases
Boston Medical Center

LEADERS IN MEDICINE
UNIVERSITY OF CALGARY

5th Annual
University of Calgary
Leaders in Medicine Research Symposium

November 8th, 2013
12:00-5:30 pm
Health Sciences Centre, Faculty of Medicine

Program

12:00 – 1:00 pm:	**Registration & Poster Set-Up – HRIC Atrium**
1:00 – 1:15 pm:	**Welcome and Introduction of Keynote Speaker – Theatre One**
1:15 – 2:15 pm:	**Keynote Address – Dr. Jerrold Ellner, MD – Theatre One**
2:30 – 3:30 pm:	**Oral Presentations – Theatre One**
3:45 – 5:00 pm:	**Reception & Poster Presentations – HRIC Atrium**
5:00 – 5:30 pm:	**Awards & Closing Remarks – HRIC Atrium**

Symposia Past

1st Leaders in Medicine Symposium | 6 November 2009

Dr. Lorne Tyrrell, MD, PhD

University of Alberta

2nd Leaders in Medicine Symposium | 5 November 2010

Dr. Ramnik Xavier, MD

Harvard Medical School

Massachusetts General Hospital

3rd Leaders in Medicine Symposium | 4 November 2011

Dr. Douglas Hamilton, MD, PhD

NASA Flight Surgeon

4th Leaders in Medicine Symposium | 2 November 2012

Dr. Hugh Scully, MD

Professor of Surgery and Health Policy

University of Toronto

Toronto General Hospital

5th Leaders in Medicine Symposium | 8 November 2013

Dr. Jerrold Ellner, MD

Chief of Infectious Disease

Boston Medical Center

The Leaders in Medicine Symposium Organizing Committee would like to thank:

Keynote Speaker: Dr. Jerrold Ellner

Oral and Poster Competition Judges:

Dr. Bryan Yipp
Dr. Daniel Yavin
Dr. Dave Hart
Dr. Gary Martin
Dr. Jennifer Chan
Dr. Jerrold Ellner
Dr. Kara Murias
Dr. Morley Hollenberg
Dr. Munier Nour
Dr. Nathalie Jette
Dr. Naweed Syed
Dr. Norman Schachar
Dr. Paul Beck
Dr. Petra Grendarova
Dr. Randal Johnston
Dr. Rebekah DeVinney
Dr. Samuel Wiebe
Dr. Sarah Lai
Dr. Scott Patten
Dr. Shawn Lewenza
Dr. Steven Drews
Mr. Patrick Schenk

LIM Program Directors: Dr. Paul Beck and Dr. Morley Hollenberg

LIM Program Associate Director: Dr. Bryan Yipp

LIM Program Advisor: Michelle Selman

LIM Symposium Chairs: Nathan Bracey, Jodie Roberts, Andrea Mosher, Amanda Eslinger, Christina Thornton, Jason Bau, Michael Peplowski, Kristen Barton, Ann Zalucky, Taryn Ludwig, Stuart Wiber

Funding provided by:

Department of Microbiology, Immunology, & Infectious Disease

Calvin, Phoebe and Joan Snyder Institute for Chronic Diseases

LEADERS IN MEDICINE
UNIVERSITY OF CALGARY

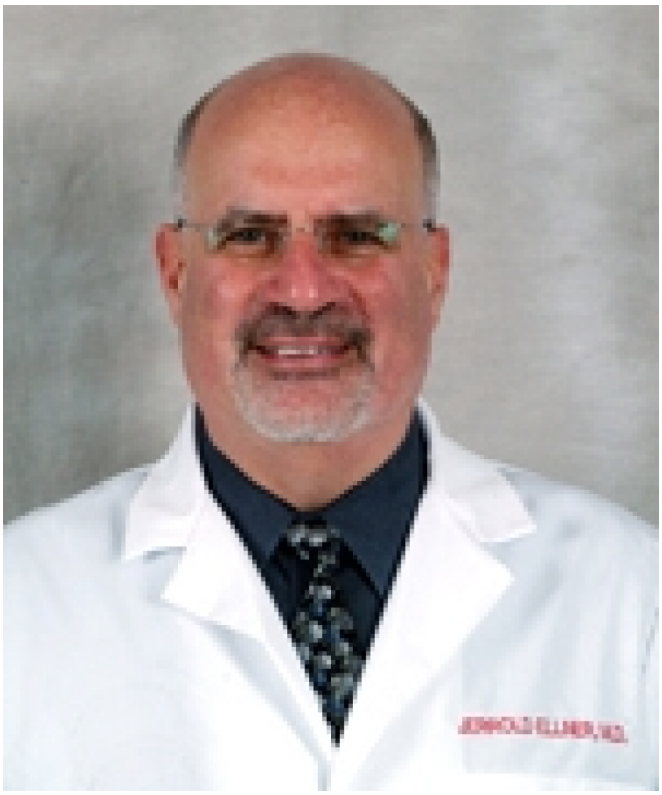
MERCK FROSST

Keynote Speaker

Dr. Jerrold Ellner, MD

Chief of Infectious Disease
Boston Medical Center

On November 8, 2013, the Leaders in Medicine (LIM) program will be hosting its 5th Annual Research Symposium from 12:00 – 5:30PM in Theatre One. This year, we are pleased to announce Dr. Jerrold Ellner, Chief of the Infectious Diseases section at Boston Medical Centre and Professor of Medicine at Boston University School of Medicine, as the keynote speaker presenting his lecture entitled "Tuberculosis – Past, Present and Future."



Dr. Jerrold Ellner, having published more than 250 original peer-reviewed articles, is an internationally known clinician-scientist whose work focuses on tuberculosis and its interaction with HIV infection. As former director of the Tuberculosis Research Unit at Case Western Reserve University in Ohio, Dr. Ellner was one of the principal architects involved in the development of the Uganda-Case Western Reserve University Research Collaboration, an international, multidisciplinary research initiative to study tuberculosis. Dr. Ellner is the principal investigator of an NIH-funded Clinical Diagnostics Research Consortium to evaluate investigation tuberculosis diagnostics in endemic areas. Dr. Ellner is former co-editor-in-chief of *Tuberculosis* and current executive editor of *Clinical and Translational Science*. In addition, he has and continues to serve on numerous government and non-governmental advisory panels related to his work on tuberculosis and HIV. Dr. Ellner's work has led him from the laboratory bench to global health campaigns in Africa, making him a true translational scientist and leader in his field.

Oral Presentations

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2:50 — 3:00	James Cotton	An assemblage A *Giardia* cathepsin B protease degrades interleukin-8 and attenuates neutrophil chemotaxis	4
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ORAL PRESENTATIONS

Presenter's Name: Amrita Roy

Program and Year: MD/PhD

Category: Clinical Project

Aboriginal identity, ethnic minority status, and prenatal depressive symptoms in a longitudinal pregnancy cohort study in Alberta

Amrita Roy[1], Wilfreda E. Thurston[1,2], Scott B. Patten[1,3], Tanya Beran[1], Lynden (Lindsay) Crowshoe[4], Suzanne Tough[1,5]

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

Introduction: Prenatal depression is a serious maternal-child health concern; risk factors and health consequences appear more prevalent in Aboriginal communities and ethnic minorities. However, research on these populations is limited. Research Questions:A) How do pregnant Aboriginal women, ethnic minority women and White/Caucasian women compare on levels of depressive symptoms, and on major risk and protective factors? B) Is non-dominant race associated with higher depressive symptoms? C) Through what pathways does race operate to contribute to depressive symptoms?

Methods: Data stem from the *All Our Babies* study (n=3354 pregnant women from Alberta recruited between 2008-2011, of whom 2636 are White/Caucasian, 32 are Aboriginal, and 686 represent minority groups). Depressive symptoms were measured with the Edinburgh Postnatal Depression Scale (EPDS). Descriptive statistics and ANOVA were used for Question A. Multivariable regression methods were used for Questions B and C.

Hypotheses: It is hypothesized that health inequities between White/Caucasian women and other women are driven by social inequities (notably the intersections of race and gender). Thus, in the analyses, Aboriginal and ethnic minority women are hypothesized to have significantly higher mean EPDS score estimates relative to White/Caucasian women. The association between race and EPDS score is hypothesized to be partially mediated by risk factors such as social and economic factors, health background, negative life experiences including discrimination and domestic violence, and chronic stress. Potential confounders are age, marital status, and parity. Protective factors (diet, social support, optimism) are hypothesized as buffers between stress and depressive symptoms.

Preliminary Results: Aboriginal and ethnic minority women have significantly higher mean EPDS score estimates relative to White/Caucasian women; the association persists across strata of major risk and protective factors. Other analyses are in progress.

Significance: A better understanding of the determinants of prenatal depression in specific populations may facilitate more effective public health and clinical interventions.

Presenter's Name: David Nicholl

Program and Year: MD/MSc, Class of 2015

Category: Basic/Translational Science Project

Obstructive sleep apnea treatment with continuous positive airway pressure decreases intraglomerular pressure and alters renal sensitivity to angiotensin II

Nicholl DDM[1,2], Hanly PJ[1,3,4], Handley GB[3], Hemmelgarn BR[1,2,5], Poulin MJ[4,6], Sola DY[1,2], and Ahmed SB[1,2,5]

1Department of Medicine, University of Calgary, Calgary, AB; 2Libin Cardiovascular Institute, University of Calgary, Calgary, AB; 3Sleep Centre, Foothills Medical Centre, Calgary, AB; 4Hotchkiss Brain Institute, University of Calgary, Calgary, AB; 5Alberta Kidney Disease Network; 6Department of Physiology and Pharmacology, University of Calgary, Calgary, AB

Introduction: Obstructive sleep apnea (OSA) has been associated with the progression of chronic kidney disease. The underlying mechanism may be related to changes in the renin angiotensin system (RAS). We sought to determine the effect of continuous positive airway pressure (CPAP) on renal hemodynamics at baseline and in response to Angiotensin II (AngII) infusion in OSA patients.

Methods: Twenty normotensive, non-diabetic, newly diagnosed OSA subjects (15 men, 5 women; 50±2y; respiratory disturbance index [RDI]>15hr^{-1}) with nocturnal hypoxia (oxyhemoglobin saturation [SaO_2] <90% for >12% of night) were studied in high-salt balance pre- and post-CPAP therapy (>4h CPAP use/night for 1 month). Glomerular filtration rate (GFR), renal plasma flow (RPF), and filtration fraction (FF), a surrogate for intraglomerular pressure, were measured pre- and post-CPAP therapy using inulin and para-aminohippurate clearance technique at baseline and in response to graded AngII infusion (3ng/kg/min·30min, 6ng/kg/min·30min).

Results: CPAP corrected OSA and nocturnal hypoxia (RDI: 42±4 vs 4±1hr^{-1}, p<0.001; duration SaO_2<90%: 36±5 vs 6±2%, p<0.001; all values pre- vs post-CPAP). Post-CPAP treatment, there was a reduction in baseline GFR (124±8 vs 110±6mL/min, p=0.014) and an increase in baseline RPF (692±36 vs 749±40mL/min, p=0.059), which resulted in reduced baseline FF (18.9±1.6 vs 15.3±1.0%, p=0.004). Post-CPAP therapy there was a blunted GFR response (-9±3 vs -2±2mL/min, p=0.033) to the low dose of AngII, while there was an augmented RPF response (-182±22 vs -219±25mL/min, p=0.024) to the high dose of AngII. The FF response to AngII was maintained (p=0.4). CPAP therapy also reduced baseline mean arterial pressure (94±2 vs 89±2mmHg, p=0.002), urinary protein excretion (61[39, 341] vs 56[22, 204]mg/day, p=0.003), and plasma aldosterone (149±18 vs 109±10 pmol/L, p=0.003).

Conclusions: CPAP treatment decreased intraglomerular pressure and improved renal hemodynamic sensitivity to AngII in OSA patients, supporting a role for the RAS in mediating OSA-associated hypertension and kidney disease.

Presenter's Name: James Cotton

Program and Year: MD/PhD, Year 4

Category: Basic/Translational Science Project

An assemblage A *Giardia* cathepsin B protease degrades interleukin-8 and attenuates neutrophil chemotaxis

James A. Cotton , Amol Bhargava, Jose G. Ferraz, Robin M. Yates, Paul L. Beck and Andre G. Buret

Biological Sciences, Inflammation Research Network, Host-Parasite Interactions

Introduction. Neutrophil (PMN) recruitment is a hallmark of acute intestinal inflammatory responses. Intestinal epithelial secretion of interleukin-8 (CXCL8) promotes PMN chemotaxis to the basolateral membrane of the intestinal epithelium. *Giardia duodenalis* is a protozoan parasite of the upper small intestine of animals, including humans, that is divided into eight genetic assemblages with assemblage A and B isolates infective to humans. *Giardia* infections are associated with attenuated inflammatory responses via unknown mechanisms. The *Giardia* genome contains 9 cathepsin B (catB) protease genes, most with unknown function. This study sought to determine if assemblage A and B *Giardia* catB proteases attenuate CXCL8 secretion.

Methods. *Giardia* trophozoites were co-incubated *ex vivo* with small intestinal mucosal biopsy tissues or *in vitro* Caco-2 colonic monolayers and administered pro-inflammatory interleukin-1β, *Salmonella typhimurium*, or recombinant CXCL8.

Results: Co-incubation of assemblage A trophozoites with small intestinal mucosal biopsy tissues or Caco-2 monolayers resulted in attenuation of IL-1β or *Salmonella*-induced CXCL8 secretion. Assemblage A trophozoites reduced CXCL8 supernatants levels in the presence or absence of Caco-2 monolayers and attenuated PMN chemotaxis. Assemblage B trophozoites did not attenuate CXCL8 secretion, reduce supernatant CXCL8, or attenuate PMN chemotaxis. Cathepsin activity was detected in assemblage A and B *Giardia* supernatants incubated in the presence or absence of Caco-2 monolayers. *Giardia* catB phylogenetic trees demonstrated assemblage A and B trophozoites contain a unique catB protease. In-gel cathepsin protease digestion assays indicated assemblage A and B trophozoites display distinct banding patterns. Inhibition of assemblage A *Giardia* cysteine proteases using a broad-spectrum cysteine protease inhibitor or a cathepsin-B specific inhibitor prevented *Giardia*-mediated degradation of CXCL8 and attenuation of CXCL8-induced PMN chemotaxis.

Conclusions: Assemblage A *Giardia* catB proteases degrade CXCL8 and attenuate CXCL8-induced PMN chemotaxis. This protease may explain how this parasite attenuates intestinal inflammation.

Presenter's Name: Krystyna Ediger, Alexander Arnold, Emily Shelton

Program and Year: MD, Class of 2015

Category: Clinical Project

Rebuilding the Calgary Student Run Clinic: A Model for Sustainability

Krystyna Ediger[1, 2], Alexander Arnold[1, 2], Emily Shelton[1, 2], Dr. Janette Hurley[1, 3]

University of Calgary Student Run Clinic[1], University of Calgary - Undergraduate Medical Education[2], University of Calgary - Department of Family Medicine[3]

Introduction: Since May 2012, The University of Calgary Student Run Clinic (SRC) has been rebuilding and restructuring its programs in order to create a sustainable and diverse clinic model. The goal of the clinic is to provide high quality, accessible health care to low income, marginalized, and/or homeless clients, as well as educational opportunities and clinical exposure to medical students.

Methods: Through an "umbrella" model, the SRC aims to act as a platform organization facilitating student involvement at multiple clinic sites. Each site offers services to a specific marginalized population, including children at a family emergency shelter, new Canadians at a refugee clinic, and older male patients experiencing addictions and homelessness on board a mobile clinic. Methods for sustainability include securing multiple sites, preceptors and funding sources.

Results: Today's SRC utilizes a two-pronged approach to delivery, focusing on inter-professional collaboration to provide primary care to its patients in various clinic settings, as well as engaging in health promotion initiatives in the community. With respect to health promotion, the SRC has developed a literacy program, a child care program at the family shelter site, a health education series, a community services night for low income women, and is an active participant in a health and community fair for Calgary's homeless population.

Conclusions: The SRC umbrella model has provided a framework for sustainability, both for its target population, but also as a professional, engaging clinical experience for medical students and health professionals. As a result, there has been a marked increase in capacity, with student participants growing from twelve to thirty. The number of permanent preceptors has increased from one to four, and the number of clinic sites has increased from one to three. This model has strengthened partnerships with the community and has lead to increased opportunities for funding and expansion.

Presenter's Name: Sarah MacEachern

Program and Year: MD/PhD, Class of 2016

Category: Basic/Translational Project

Inhibiting inducible nitric oxide synthase restores electrogenic ion transport in experimental IBD: a novel role for enteric glia

SJ MacEachern[1], BA Patel[2], DM McCafferty[1], WK MacNaughton[1], and KA Sharkey[1]

Hotchkiss Brain Institute and Snyder Institute of Chronic Disease, Department of Physiology and Pharmacology, University of Calgary, Calgary AB, [2]Centre for Biomedical and Health Sciences Research, University of Brighton, Brighton UK

Introduction: Over 200,000 Canadians have inflammatory bowel disease (IBD), which are serious inflammatory conditions of the gastrointestinal tract that place a large burden on our health care system. The etiology of IBD is unclear, but it is known that disturbances in the control of ion transport lead to epithelial barrier dysfunction in IBD. Enteric glia have recently been shown to regulate aspects of barrier function and, under physiological conditions, colonic ion transport through nitric oxide (NO). The role of enteric glia in the control of ion transport in IBD has yet to be elucidated. We investigated enteric glial regulation of ion transport in chemical and genetic mouse models of IBD in vitro and in vivo.

Methods: Electrically-evoked ion transport was measured as a change in short-circuit current using full-thickness segments of mouse colon in Ussing chambers. The production of nitric oxide (NO) was assessed using amperometry. Bacterial translocation was investigated in the liver, spleen and blood.

Results: Electrical stimulation of the mouse colon evoked a tetrodotoxin-sensitive secretory ion transport. In colitis, ion transport was almost completely abolished. Inhibiting inducible nitric oxide synthase (NOS II) or blocking glial function with fluoroacetate restored ion transport. In control colon, NO production was almost completely due to neuronal NOS I. In colitis, the production of NO was enhanced with a substantial NOS II component. Fluoroacetate treatment blocked the sensitive component of NO production in colitis. Bacterial translocation was increased during TNBS colitis and this was prevented by inhibiting enteric glial function in vivo.

Conclusions: Increased expression of NOS II in enteric glia contributes to the dysregulation of intestinal ion transport in mouse models of IBD. Blocking enteric glial function in colitis restores epithelial barrier function and reduces bacterial translocation. This could reveal a potential therapeutic target in the treatment of IBD.

POSTER PRESENTATIONS

Presenter's Name: Alec Campbell

Program and Year: MD/MSc, Year 2

Category: Basic Science/Translational Science Project

Exploiting the Immunomodulatory Capacity of the Rat Tapeworm *Hymenolepis diminuta* to Treat Colitis

Campbell, A.J.[1]; Wang, A[1].; MacDonald, J.A.[2]; McKay, D.M.[1]

1University of Calgary, Department of Physiology and Pharmacology; 2University of Calgary, Department of Biophysics and Biochemistry

Introduction: Epidemiological and proof-of-principle data support the concept of helminth therapy for several autoimmune disorders prevalent in Westernized societies. One goal is to isolate and characterize immunomodulatory molecules from parasitic helminths for drug development. We utilize the *H. diminuta*-mouse model system to explore novel anti-inflammatory possibilities. We hypothesize that one or more anticolitic molecules can be isolated from *H. diminuta.* To test this, mice are infected with *H. diminuta,* or injected with a crude extract thereof (HdAg), and the impact on dinitrobenzene sulphonic acid (DNBS)-induced colitis assessed.

Methods: Male Balb/C mice (n=7-8/group) were: (1) infected with 1, 3 or 5 cysticercoids of *H. diminuta* and colitis induced 8 days later with DNBS (3 mg in 100 μL 50% etoh., ir.); (2) given one injection (ip., sc. or im.) of 1 mg of PBS-soluble HdAg 6h after DNBS; or, (3) given 10 mg, 100 mg or 1 mg of HdAg ip. 6h after DNBS. Mice were monitored daily for 3 days, necropsied, and colitis assessed.

Results: We found that infection with even one *H. diminuta* protected mice from DNBS-induced colitis. This anticolitic effect was accompanied by increased IL-4, IL-5 and IL-10, typical of the mammalian helminth infection response. Moreover, a single ip. or sc. (but not im.) injection of HdAg was as effective as a prophylactic, viable 5 cysticercoid infection of *H. diminuta* at inhibiting DNBS-induced colitis. A threshold dose of 100 mg HdAg was needed for significant colitis inhibition.

Conclusions: The rat tapeworm, *Hymenolepis diminuta*, is identified as a remarkably potent anticolitic stimulus of DNBS colitis. We conclude that (a) infection with viable *H. diminuta* could be developed as a therapy for IBD, and (b) that *H. diminuta* has at least one effective anti-colitic molecule, the isolation and purification of which could result in a novel therapeutic immunomodulator.

Presenter's Name: Alex Frolkis

Program and Year: MD/PhD, Year 4

Category: Clinical Project

Short-term readmission and postoperative complications in Crohn's disease and ulcerative colitis patients – a province-wide cohort study

Alexandra Frolkis[1], Gilaad G Kaplan MD[1,2], Alka Patel[1], Peter Faris[1], Hude Quan[1], Nathalie Jette[1,2], Jennifer deBruyn[3]

Departments of Community Health Sciences[1], Department of Medicine[2], Department of Pediatrics[3], University of Calgary, Calgary, Alberta, Canada.

Introduction: Postoperative complications after surgical visits in Crohn's disease (CD) and ulcerative colitis (UC) have been commonly reported. However, short-term readmission has not been characterized in population-based studies. We therefore assessed the occurrence and risk factors of postoperative complications and short-term readmission following discharge from an intestinal resection.

Methods: We used Alberta-wide inpatient administrative data from 2002 to 2011, to identify 3197 hospitalizations with a diagnosis code for CD (International Classification of Disease, 10th version, Canadian edition [ICD-10-CA]: K50.X) or UC (ICD-10-CA: K51.X) and a procedure code for intestinal resection (Canadian Classification of Health Intervention: 1.NK.87.X, 1.NM.87.X, 1.NM.89.X, or 1.NM.91.X). Postoperative complications were identified from pre-defined ICD-9 codes converted to ICD-10-CA codes, and from ICD-10-CA codes identified by experienced clinicians. Short-term readmission was defined as an emergent readmission within 30 days of discharge from the surgical visit; age, admission type, surgery technique, and Charlson comorbidity index were independently evaluated as predictors using a Poisson regression fit to a binomial model.

Results: Among 2638 and 559 hospitalizations with intestinal resection for CD and UC, respectively, postoperative complications occurred in 34% and 36%, respectively. Gastrointestinal, wound, and infection were the most common systems involved, affecting 23%, 9%, and 9% of CD, and 23%, 9%, and 12% of UC, surgeries respectively. Short-term readmission occurred in 8.6% of CD, and 7.2% of UC surgeries. The presence of a postoperative complication at surgery *vs.* no complication (RR: 1.62; 95% CI 1.26-2.08), and emergent *vs.* elective admission at surgery (RR: 1.58; 95% CI 1.22-2.05) were significant risk factors for 30-day readmission in CD.

Conclusions: Postoperative complications occur commonly following intestinal resection for CD and UC. Patients with CD who develop postoperative complications in hospital, or who are emergently admitted to hospital require close monitoring by clinicians to anticipate need for readmission or interventions to prevent readmission.

Presenter's Name: Alexandra Rogers

Program and Year: MD/MSc, Year 3

Category: Basic Science/Translational Project

The Role of CIC in Neurodevelopment and Oligodendrogliomagenesis

Alexandra D. Rogers[1], Rajiv Dixit[2], Samuel O. Lawn[2], Saiqun Li[3], Carol J. Schuurmans[3], J. Gregory Cairncross[1], Jennifer A. Chan[2].

Departments of Clinical Neuroscience[1], Pathology & Laboratory Medicine[2], Biochemistry & Molecular Biology[3], University of Calgary.

Introduction: Oligodendrogliomas (ODG) are distinctive brain tumours composed of cells resembling oligodendrocyte precursors cells (OPCs). Recently, the gene encoding the transcriptional repressor Capicua (CIC) was identified as mutated in most ODGs with concurrent 1p/19q loss and IDH1/2 mutation – a genetic signature rare in other cancers. Mutation of the retained 19q CIC allele is likely functionally important, but how it contributes to ODG biology is unknown. We hypothesize that Cic, through its transcriptional repressor function, may restrict OPC proliferation, migration, or differentiation to the correct time and place in neurodevelopment. The aims of this study are to characterize the temporal and spatial expression of Cic in the normal cerebrum, and to determine if CIC loss affects proliferation or differentiation of neural progenitors to form abnormal OPCs.

Methods: To examine CIC expression, we performed immunofluorescence staining on mouse forebrain tissue over a time course from embryonic to adult stages. Double labeling was performed to determine which cells express CIC. To determine CIC biologic functions, we introduced CIC shRNA or control shRNA (co-electroporated with GFP) into neural progenitors using in utero electroporation. Brains were harvested at 2 and 4 days post-electroporation. GFP+ cells were examined for location, for proliferation by BrdU incorporation, and for cell identity using a panel of markers.

Results: Cic is present in immature and mature brain, but its expression increases and the localization of CIC increasingly shifts from cytoplasmic to nuclear in early postnatal stages. Nuclear Cic co-labels cells with markers of neuronal and astrocytic differentiation, but not with markers of oligodendrocyte lineage. Cic knockdown in vivo results in a change in location of cells, with more cells spread throughout the cortical layers and increases proliferation. Determination of cell types is in progress to assess differentiation.

Conclusions: Our data supports a role for Cic in regulating several processes in neural progenitors that are relevant to cancer – proliferation, migration and, possibly, differentiation toward OPCs. CIC loss due to mutational inactivation may thus deregulate these processes leading to an increase in proliferative, migratory OPC-like cells.

Presenter's Name: Amanda Eslinger

Program and Year: MD/MSc, Class of 2015

Category: Clinical Project

Treating donor site pain in burn victims that have undergone autologous split-thickness skin grafting: A review of the literature

Amanda Eslinger[1], Duncan Nickerson MD, FRCSC, FACS[1]

[1]Division of Plastic Surgery, Department of Surgery, University of Calgary

Introduction: Current standard of treatment for deep burn injuries is split-thickness skin grafting(STSG). STSGs are harvested from a remote area of healthy skin creating a new wound referred to as the donor site. Pain, caused by harvest, is reported to be one of the most distressing symptoms following STSG. Resultant pain can affect early mobilization, sleep and the need for analgesics post-operatively. Although donor site pain presents a significant problem, there are no evidence-based guidelines concerning its treatment. The purpose of this literature review was to synthesize information on current practices for managing donor site pain and to determine whether further investigation of donor site pain management is warranted.

Methods: Ovid MEDLINE was searched using the terms 'burn', 'donor site', 'pain', and 'split-thickness skin graft' from 2003–2013. Only human studies were included in the review. Non-English language articles were excluded from the review.

Results: The literature review identified five techniques used in minimizing donor site pain. One technique initiated treatment prior to STSG harvest by infiltrating the pre-harvest site with a combined anesthetic/tumescent solution. Four techniques initiated treatment immediately following STSG harvest: 1) continuous subcutaneous local anesthetic infusion (CSLA); 2) subcutaneous injection of anesthetic; 3) application of topical anesthetic gels; and 4) the use of ice packs. All studies measured pain using a visual analog scale(VAS). In a majority of studies subjects gave anecdotal reports of decreased pain at the donor site regardless of the technique used to treat pain. Few studies showed that a particular technique significantly decreased VAS scores.

Conclusions: Although donor site pain is of chief concern for both the patient and the physician its treatment is scantily addressed. This review highlights the need to design and carry out more rigorous and effective studies in order to work towards standardizing care and improving the patients' pain experience following STSG harvest.

Presenter's Name: Amanda Forsyth

Program and Year: MD/MSc, Class of 2016

Category: Basic Science/Translational Project

Breast cancer mediated osteoclastogenesis

Amanda Forsyth, Ashley Sutherland, Alexander Klimowycz, Jing Hui Hu, Florence Boutillon, Vincent Goffin, Patricia Tang, Don Morris, Anthony Magliocco, Carrie Shemanko

Introduction: Hormones such as prolactin (PRL) have long been studied for their role in the primary breast tumor, but not yet in modulating the secondary tumor microenvironment of the bone. Metastasis to the bone is a deleterious and debilitating aspect of many cancers, including breast cancer, where it is a preferred site of metastasis that results in bone loss. Tumor cells create a vicious cycle of bone loss at the bone metastatic microenvironment by inducing osteolytic osteoclast differentiation via osteoblasts or osteoclasts directly. Bone metastasis is incurable and has limited treatment options. Delineating the factors involved in how breast cancer cells direct bone cells to breakdown the bone (osteolysis) will identify new targets for treatment.

Methods/Results: Using quantitative immunohistochemistry, we determined that high PRL-receptor (PRLR) expression in the primary tumor was associated with a shorter time to bone metastasis. In an analysis of advanced breast cancer patients, we also detected the PRLR in circulating tumor cells of the blood. We hypothesized that PRL would stimulate PRL responsive breast cancer cells and/or osteoblasts to contribute to the vicious cycle. We identified a novel PRL-based mechanism by which PRL and the PRLR induce breast cancer cells in vitro to promote the differentiation of osteoclasts capable of bone resorption. This is in contrast to non-PRL treated breast cancer cells that can only induce morphological differentiation but not bone resorption. The pure PRLR antagonist, delta1-9G129R-hPRL, confirmed the requirement for the PRLR. The PRLR is not expressed in osteoclasts, suggesting that PRL is acting through breast cancer cells to stimulate osteoclast differentiation. To help elucidate the mechanism behind PRL induction of functional osteoclasts, a genome-wide gene array and large cytokine array have been conducted to identify potential PRL-regulated osteoclastogenic factors. Both arrays have identified novel PRL-regulated candidates and known osteoclastogenic factors. We have also created a bioluminescent PRL-responsive breast cancer cell line with bone homing properties as a tool.

Conclusions: We are part of a multidisciplinary research team that is establishing a large breast cancer patient cohort that will be followed prospectively for metastasis with a focus on bone metastasis. This research identifies PRL and its targets as possible points of therapeutic intervention to stop or ameliorate the vicious cycle of breast to bone metastasis.

Presenter's Name: Ann Zalucky

Program and Year: MD/MSc, Year 2

Category: Basic/Translational Science

The effect of nocturnal hypoxia on the vascular response to angiotensin II infusion in patients with obstructive sleep apnea

Ann A. Zalucky[1], David D.M. Nicholl[1], Patrick J. Hanly[1], Marc J. Poulin[1], Darlene Y. Sola[1] and Sofia B. Ahmed[1].

[1]Faculty of Medicine

Introduction: Obstructive sleep apnea (OSA) is a risk factor for hypertension though the mechanisms responsible are unclear. Emerging evidence suggests nocturnal hypoxia plays a role in up-regulating the renin angiotensin system (RAS), activation of which is deleterious to vascular outcomes. Our objective was to determine the relationship between nocturnal oxygen saturation and the vascular response to angiotensin II (AngII) challenge in OSA patients.

Methods: We conducted an observational human physiology study at a university-affiliated sleep clinic. Nocturnal oxygen saturation (SaO_2) was measured in adult, non-diabetic patients with untreated OSA (respiratory disturbance index (RDI) >15). The primary outcome measure was the association between nocturnal SaO_2 and the hemodynamic response to graded AngII infusion (3ng/kg/minx30min, 6ng/kg/minx30min.), a marker of vascular RAS activity, at 30 and 60 minutes.

Results: Twenty-eight OSA subjects (71% male, mean age 52±11years, mean RDI 41, mean duration of nocturnal oximetry 7.2 hours) demonstrated a median mean nocturnal SaO_2 of 90% (range 85-93%) and a median minimum SaO_2 of 73% (range 52-81%). Univariate analysis showed no association between measures of nocturnal hypoxia and the hemodynamic response to AngII challenge. However, after adjustment for covariates, lower mean nocturnal SaO_2 was associated with a blunted vasoconstrictor diastolic blood pressure response to AngII infusion ($p=0.03$ at 30min, $p=0.04$ at 60min). No association was observed between minimum nocturnal SaO_2 and the hemodynamic response to AngII challenge.

Conclusion: Nocturnal hypoxia due to untreated OSA is associated with augmented vasoconstrictor sensitivity to AngII, suggesting a pathophysiological mechanism for OSA-mediated hypertension.

Presenter's Name: Arjun Gupta

Program and Year: MD, Class of 2015

Category: Basic/Translational Science Project

Microwave-Assisted Radiosynthesis of 18F-FAZA, a Clinically Used Pet Tracer for Diagnosing Tumor Hypoxia

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Introduction: Positron-emission tomography (PET) is a specialized Nuclear Medicine technique that is extensively used in the diagnosis, staging and restaging, and the progression of several diseases including the cancer. Appropriate therapy plans for the patients are then defined. Fast-decaying radiopharmaceuticals (PERs) that can clear out quickly from the body are the best for such diagnoses. Clinical manufacturing of most of the clinical PERs utilizes conventional thermal labeling procedures (CTLPs), consumes large amounts of the precursors (5-20 mg), and leads to secondary reaction products necessitating extensive time consuming HPLC procedures. As a result, lower radiochemical yields (RCYs) are a norm. The current work is part of a project that aims at overcoming the deficiencies of CTLPs by developing microwave (MW)-based automated radiofluorination as an alternate synthesis method for short-lived PERs. 18FAZA, a hypoxia marker invented and developed at the CCI, was chosen as a representative for this development. 18FAZA is a short-lived PER that demonstrates hypoxia-specific accumulation in tumors, offers precise information about the stage and extent of hypoxia, and is currently part of several cancer clinical trials around the world. The clinical manufacture of 18FAZA is based on CTLP and, although automated, affords only 4-8% RCY in nearly 1h. Several side products generating during the labeling process force extensive HPLC purification.

Methods: To meet this challenge, we integrated an automated synthesis unit (ASU, Advanced Cyclotron Systems Inc.) for time-controlled automated delivery of the reagents and the precursor to the MW synthesis unit, and varied the MW reaction parameters sequentially to optimize and improve the RCY of 18FAZA.

Results: Our data using the 'MW-ASU-integrated set up' demonstrated that 18FAZA is consistently produced in almost 70% RCY in a shorter reaction time (22 min) and the reaction mixture also does not contain any major secondary product. These findings are far superior to the current clinical manufacture process (CTLP) for 18FAZA.

Conclusions: A completely automated MW-assisted synthesis development of 18FAZA is now warranted to exploit the superior features of this process and establish MW-assisted automated clinical manufacturing of 18FAZA and other short-lived PERs.

Presenter's Name: Carl Severson

Program and Year: MD, Class of 2016

Category: Clinical Project

Identification of Obstructive Sleep Apnea Syndrome Using Electronic Health Data
Antoine Seguin and **Justin Wong**

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[1]Faculty of Medicine, University of Calgary; [2] Department of Community Health Sciences, University of Calgary; [3] Division of Respirology, Department of Medicine, University of Calgary

Introduction: Diagnostic algorithms using a combination of administrative data and self-reported data can provide an accurate estimate of disease for a number of conditions. However, preliminary work by our group suggests that obstructive sleep apnea is not accurately identified using administrative data. The purpose of this study was to determine if diagnostic algorithms using electronic health data from an on-line questionnaire, could be used to accurately identify patients with obstructive sleep apnea syndrome (OSAS).

Methods: We identified all patients who underwent sleep diagnostic testing and/or clinical assessment at a tertiary sleep center in Calgary, Alberta, Canada. As part of the triage process, all patients were required to submit an online questionnaire outlining the nature of sleep complaints, medical history and medications. Two sleep physicians independently reviewed each patient chart and assigned a primary and secondary sleep diagnosis based on the International Classification of Sleep Disorders – Second Edition. A prediction equation was derived from multivariate predictors of OSAS identified by logistic regression. Measures of diagnostic accuracy for the identification of OSAS were also calculated against the reference standard physician diagnosis.

Results: A total of 1223 eligible charts were reviewed, of which 581 (47.5%) had a primary diagnosis of OSAS. Multiple logistic regression revealed that a history of snoring (odds ratio (OR) 5.13, $p<0.001$), witnessed apnea (OR 2.85, $p<0.001$), nocturnal choking sensation (OR 1.53, $p=0.004$), number of hours of sleep (OR 1.18/hr, $p<0.001$) and body mass index (OR 1.07/kg/m2, $p<0.001$) were predictive of a diagnosis of OSAS. The use of a sleep aid (OR 0.65, $p=0.007$), sleep latency (OR 0.99/hr, $p=0.002$) and Patient Health Questionnaire-9 score (OR 0.96/point, $p<0.001$) supported a diagnosis other than OSAS. Using a respiratory disturbance index (RDI) cut-off of > 15 hr^{-1} to define OSA, sleep diagnostic testing used in isolation had a sensitivity and specificity of 64% and 74%, respectively, for OSAS. A diagnostic algorithm derived from multivariate predictors had a sensitivity of 60%, specificity of 76%, positive predictive value of 68% and negative predictive value of 70%.

Conclusions: These results suggest that diagnostic algorithms derived from online questionnaires, sleep diagnostic testing data or a combination of both have limited utility in the identification of patients with OSAS. The diagnosis of OSAS thus relies on clinical assessment by a sleep practitioner in conjunction with sleep diagnostic testing.

Presenter's Name: Christina Thornton

Program and Year: MD/PhD, Class of 2016

Category: Basic Science/Translational Project

Harmless Commensal Microbial Neighbors Synergistically Trigger *Pseudomonas aeruginosa* Virulence Genes in Cystic Fibrosis

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Introduction: Cystic fibrosis (CF) is the most common lethal genetic disease among Caucasians. 90% of CF patients succumb to pulmonary failure from chronic respiratory infections. Traditionally, research has focused on a narrow spectrum of microorganisms as principal pathogens such as *Pseudomonas aeruginosa* (PA). The oropharyngeal flora (OF) have been implicated in enhancing pathogenesis of PA while acting as benign commensals, otherwise known as "synergens". These interactions may skew the balance between clinical stability and acute pulmonary exacerbation, leading to hospitalization. The objectives here were to evaluate these interactions and construct synergen mutants to identify the pathway(s) involved.

Methods: Seven oropharyngeal-derived microbes were isolated from sputum of adult CF patients (*Streptococcus*. sp, *Rothia*. sp and *Actinomyces*. sp) and screened *in vitro* for affecting PA virulence gene expression in co-cultures. The ability of these 'benign' microbe 'synergens' to stimulate PA virulence genes was evaluated using transformed PA reporters harboring luciferase constructs for known virulence gene promoters. The luciferase light production caused by the co-culture vs. monoculture of PA was monitored to quantify 'synergen' activity by measuring changes in light production. Transposon libraries in the synergens were constructed with 8000 mutants screened.

Results: Up-regulation of PA virulence gene expression was seen for all 7 synergens tested. The virulence pathways affected were for quorum sensing or bacterial communication. The highest up-regulation was by *Streptococcus*. sp, with 1800-fold increased virulence gene expression in co-culture as compared to PA alone. From 8000 synergen mutants, 526 were isolated as hits involved in co-culture. 61 of these mutants were conserved in all PA reporters, suggesting common interaction pathway(s) triggered by the synergens. 35 mutants displayed 10-fold or greater activation in co-culture as compared to the wild-type, demonstrating a gain-of-function mutation.

Conclusions: We have found that seemingly harmless non-pathogenic oropharyngeal 'synergen' microbes can trigger virulence genes in PA found in CF patients. The production of secondary signaling molecules have been shown to influence pathogen virulence profiles by modulating bacterial cell-cell communication pathways. Understanding the way in which commensal microbes synergistically trigger virulence will lead to better treatment and management of CF.

Presenter's Name: Christopher Skappak

Program and Year: MD/PhD, Class of 2015

Category: Basic/Translational Project

Virus induced airway hyperreactivity in allergen-sensitized animals is mediated by immunological memory and is ablated by dexamethasone

C. Skappak[1, 2], R. Ilarraza[2], Y Wu[2], and D Adamko[2, 3]

The Department of Medicine, University of Calgary[1], The Department of Pediatrics, University of Alberta[2], and the Department of Pediatrics, University of Saskatoon[3].

Introduction: Common cold viruses are the leading cause of asthma exacerbations. Why people with asthma develop such severe reactions is unclear. We hypothesize that it is not the severity of virus infection but the activation of memory T-cells and eosinophils, which cause the airway hyperreactivity (AHR). We have a model with virus memory T cells in allergen-sensitized guinea pigs (GP).

Methods: GP are sensitized (i.p.) to ovalbumin (OVA) or not. All receive an inhaled OVA challenge. Some of each group are exposed once to parainfluenza virus (PIV) then, 6 weeks later, re-exposed to either live virus or UV-inactivated virus. Measurements of AHR (histamine i.v.), inflammation (BAL/histology), and T cell memory (BrdU incorporation *ex vivo*) are measured. Additionally some animals from each group were pre-treated with dexamethasone (i.p.) before re-exposure to PIV.

Results: Both non-sensitized and OVA-sensitized GPs develop T cell memory to virus based on BrdU incorporation data from lymph node T cells. Unlike non-sensitized GP, OVA-sensitized GP show elevated numbers of eosinophils in the airways, except those pre-treated with dexamethasone. Unlike non-sensitized GP, OVA-sensitized GP develop airway hyperreactivity upon re-exposure to UV-inactivated virus, which is prevented by dexamethasone.

Conclusion: GP can develop T cell memory to PIV. Upon re-exposure to PIV antigens, this T cell memory can cause AHR but only sensitized animals, which we believe is mediated by eosinophils. Dexamethasone prevents AHR in sensitized animals re-exposed to viral antigens.

Presenter's Name: Collin Luk

Program and Year: MD/PhD, Class of 2015

Category: Basic/Translational Project

Miniature Contact Imaging System for Monitoring Calcium Changes in Fura-2 Fluorescently Loaded Live Neurons

Anil Kumar Mudraboyina[1], Lior Blockstein[1], **Collin C. Luk[2],** Naweed I. Syed[2], Orly Yadid-Pecht[1]

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Introduction: Non-invasive imaging of neuronal activity in a large network is pivotal to understanding brain function and development. Currently, this is achieved through conventional microscopy, which requires cumbersome optical components such as lenses, prisms, filters and a high precision microscope body. Due to these components, such systems are generally large, expensive and immobile. These characteristics limit the use of microscopy to laboratory environment and make it difficult to use in the clinical setting or as a diagnostic tool in live organisms. Therefore, we sought to create a contact imaging platform whereby the system was simplified to the level of cells being cultured directly onto a 4x4 centimeter image sensor.

Methods: We designed, fabricated and verified a novel CMOS image sensor based contact imaging system. Specimens were directly cultured onto our image sensor coated with our absorptive filter.

Results: Fluorescent images were acquired from live neurons by monitoring calcium changes with Fura-2 dye. Our current device consists of a removable absorption filter interfaced with a CMOS image sensor and an external DG-4 lamp for excitation. Fura-2 loaded *Lymnaea stagnalis* neurons were stimulated with dual excitation wavelengths of 340nm and 380nm and the sensor detected 510nm emission.

Conclusions: We show that our system is capable of detecting intracellular calcium changes in Fura-2 loaded neurons. This platform is not only a reduction in size and cost from traditional imaging setups, but also allows for longer term imaging of low fluorescent signals due to the close proximity of the sensor to the specimen. Further, this sensor also enables multiple neurons over a large surface area to be imaged simultaneously, an option that is not readily available in conventional light microscopy. This ability to interrogate calcium activity over extended periods of time on a mobile device opens up a new realm of biomedical research.

Presenter's Name: Connie Liao

Program and Year: MD/PhD, Class of 2016

Category: Basic/Translational Science Project

The role of NCX in the regulation of endothelial-dependent dilatin

Connie Liao[1], Emma Walsh[1], Serena Hou[1], Andrew Braun[1], William Cole[1]

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Introduction: Appropriate release of nitric oxide (NO) is critical for normal physiological functioning of the cardiovascular system. Although changes in intracellular Ca2+ concentration ($[Ca^{2+}]_i$) in endothelial cells (ECs) is thought to play an important role in the coordination of NO release, the molecular mechanism underlying this influx is poorly understood. It was not until the identification of transient receptor potential (TRP) channel proteins in the phototransduction pathway of *Drosophila* that TRP channels became widely viewed as molecular candidates for facilitating Ca^{2+} entry in ECs. However the non-selective nature of TRP channels lead to the suggestion that TRP channels can act as a Na+ entry pathway, which in turn drives the sodium-calcium exchanger (NCX) in its Ca^{2+} entry mode. The work presented here outlines the molecular mechanisms responsible for regulating endothelial $[Ca^{2+}]_i$ and its implication to NO production and release, and involved two major areas of study.

Results: Our data suggests that TRPV4/C1 co-localized with NCX1 in intact rat cerebral arteries (RCA) endothelium provides a physical basis for the involvement of NCX in flow-mediated dilation (FMD). The eNOS inhibitor, L-NAME, significantly reduced the magnitude of FMD, providing evidence for the involvement of NO in FMD. Inhibition of endothelial NCX by intraluminal perfusion of KBR or 6H2 NCX antibody also significantly reduced FMD. Moreover, FMD was associated with S1177-eNOS phosphorylation, which was inhibited in the presence of NCX blockers. Thus, Na^+ entry through TRPV4/C1-containing channels was likely involved to drive reverse-mode NCX, resulting in elevation of $[Ca^{2+}]_i$ and eNOS S1177 phosphorylation, and thereby NO synthesis and vasorelaxation.

Conclusions: These findings are significant because the potential involvement of a TRP-NCX signaling complex in ECs has been an unresolved issue for some time. Therefore the work presented here provides unique insight into the molecular mechanisms that contribute to the regulation of endothelial $[Ca^{2+}]_i$.

Presenter's Name: Craig Beers

Program and Year: MD/PhD, Year 5

Category: Clinical Project

Simultaneous intracranial EEG-fMRI for the presurgical assessment of patients with epilepsy

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1 – University of Calgary, Calgary, AB., 2 – Hotchkiss Brain Institute, Calgary, AB.

Introduction: Electroencephalography (EEG) is currently the primary tool used by epileptologists to localize seizure foci prior to epilepsy surgery. However, seizure cure is achieved in less than 50% of these patients, often due to challenging localization. Advances in functional neuroimaging provide the opportunity to improve the localization of epileptogenic tissue. Functional Magnetic Resonance Imaging (fMRI), which measures changes in neuronal blood flow, has been successfully combined with EEG to localize changes in brain activity associated with epileptiform discharges. Despite the success of scalp EEG-fMRI, it has limited ability to detect discharges in small cortical areas or from deep structures. Intracranial EEG (iEEG) can accurately record activity too small or too deep to be seen on scalp EEG. This project was designed to assess the Blood Oxygen Level Dependent (BOLD) response to focal iEEG discharges.

Methods: We recruited 10 patients undergoing intracranial video-EEG monitoring for seizure focus localization as pre-surgical assessment. Subjects were connected to an MR-compatible EEG system and studied with simultaneous fMRI. Epileptiform discharges were identified and marked by two electroencephalographers and used to generate parametric maps of active brain regions.

Results: Ten patients completed the iEEG-fMRI studies without adverse event. Three studies were excluded due to excessive artefacts leading to poor quality EEG. Spike locations included the mesial temporal (4 patients), necortical temporal (2), frontal (1), and parietal lobes (1). The locations of BOLD responses matched with spike location in 6 analyses (75%). In the remaining cases, the maximum BOLD response was seen in distant areas.

Conclusions: This study demonstrated that iEEG-fMRI could be safely performed in our 3.0T MR scanner with high (75%) concordance between the locations of epileptic spikes and BOLD responses. This opens a new avenue for better understanding of the hemodynamics of epileptogenic activity, and may provide a technique for improved seizure focus localization.

Presenter's Name: Dilip Koshy

Program and Year: MD, Class of 2015

Category: Clinical Project

An Outcome-based Approach to Assessing and Treating Patients with iNPH

Dilip Koshy, Geberth Urbaneja, Mark G Hamilton

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Introduction: The Calgary Adult Hydrocephalus Clinic (CAHC) manages patients by employing an outcome-based assessment and treatment model. As a quality assurance project, we review outcomes associated with this clinical care model for patients with potential idiopathic normal pressure hydrocephalus (iNPH).

Methods: We report data for patients enrolled in the CAHC from January 2009 to December 2012. A database and registry were used.

Results: For patients with a potential diagnosis of iNPH, initial assessment and post-treatment outcomes were assessed primarily using gait and cognitive measures following LP (lumbar puncture) and/or ELD (external lumbar drainage). In 2009, 8 of 100 such patients were managed with an outcome-based assessment. In 2012, this number increased to 37 of 127. 16 of these patients had LP assessments in 2012, 4 of which were positive and therefore treated with ventriculoperitoneal (VP) shunting thereafter. In the same year, 28 patients with a potential diagnosis of iNPH were evaluated by ELD, 22 of which were positive and subsequently underwent VP shunt insertion. Of these 26 patients who were treated with VP shunt, a positive outcome was achieved in 24 (92%).

Conclusions: Our experience in the CAHC illustrates how an outcome-based assessment and treatment model can be utilized in managing adult hydrocephalus patients, particularly those with a potential diagnosis of iNPH. This quality assurance data indicates that excellent success rates are possible in patients well selected for intervention following outcome-based assessment.

Presenter's Name: Elbert Manalo & Farah Ladak

Program and Year: MD, Class of 2015; MD, Class of 2016

Category: Clinical Project

Examining the Role of Pre-departure Training across Canadian Medical Schools for International Medical Electives

Elbert Jeffrey Manalo, Farah Ladak, Mary Halpine, Neil Arya, Kristin Neudorf, & Bill Cherniak

Canadian Federation of Medical Students

Introduction: The rising interest from Canadian medical students to participate in international medical electives demands an emphasis on structured Pre-departure Training (PDT) to prepare and optimize the student learning experience. At the core of PDT are five competencies: personal health, travel safety, cultural competence, language competence, and ethics. This study examines the completeness and effectiveness of PDT among Canadian medical schools.

Methods: A survey examining various components of PDT – core competencies, assessment of students' preparedness, length of PDT training, post-return debrief – was sent to one faculty member and one student representative at every Canadian medical school. The survey is an extension of similar surveys conducted in 2008 and 2010.

Results: Of the five core competencies of PDT, four (personal health, travel safety, cultural competence, and ethics) were covered by 100% of medical schools. Language competence was addressed by 93% of schools, which is a major improvement from 63% in 2010. Assessment of students' preparedness in the form of interviews, tests/assignments, and modules was assessed in 36% of medical schools.
In addition to PDT, 70% of schools reported that students received supplemental training and orientation at the site of their electives. Upon return from international electives, 93% of medical schools provided post-return debriefing activities.

Conclusions: While it is not possible to predict and prepare for every potential scenario that students might face, effective PDT enhances the international learning experience and equips students with tools to become responsible global citizens and professional representatives of the Canadian medical education system.

Presenter's Name: Elizabeth de Klerk

Program and Year: MD, Class 2014

Category: Clinical Project

Kawasaki disease disguised as retropharyngeal abscess

Elizabeth de Klerk BSc, Michelle Jackman MSc, MD, FRCP(C)

Section of Hospital Pediatrics, Department of Pediatrics, Alberta Children's Hospital

Introduction: Kawasaki disease is an acute and self-limited inflammatory vascular condition of undetermined etiology that primarily affects young children and infants. Cardiac complications of the disease can be severe and life threatening. However, the risk of the most severe cardiac complication, coronary artery aneurysm, can be significantly reduced by treatment with intravenous immunoglobulin (IVIG) within a 10-day window of fever onset. A prompt diagnosis is essential in ensuring good outcomes. In order to diagnose Kawasaki disease, clinicians rely on a classic pattern of symptoms. However, many children may present with non-specific findings or symptoms that mimic disease processes. In these cases, erroneous diagnoses may lead to delay in treatment of Kawasaki disease.

Case Description: This case describes a 3-year-old unimmunized boy who presented with four days of fever, irritability, neck pain, and headache. On clinical exam, the patient was febrile and had bilateral non-purulent conjunctivitis. Laboratory and radiological findings were consistent with retropharyngeal abscess and the patient was started on intravenous antibiotic therapy. Despite 48 hours of intravenous antibiotics, the patient remained febrile. Symptoms slowly began to evolve in sequence - he developed prominent right anterior cervical chain lymphadenopathy, bilateral edema of the hands, and a polymorphous rash. A diagnosis of Kawasaki disease was made. While the patient had a normal echocardiogram and a positive treatment outcome, appropriate high-dose aspirin and IVIG therapy was delayed by four days because of the atypical presentation.

Conclusion: Unusual clinical symptoms and radiographic findings in Kawasaki disease can be misleading and may contribute to delayed diagnosis and treatment. By recognizing that Kawasaki disease can initially present with specific head and neck manifestations such as retropharyngeal abscess, physicians may consider the diagnosis sooner, ultimately reducing the risk of cardiac sequelae in affected children.

Presenter's Name: Elizabeth Hodges & Veronica Tomcej

Program and Year: DVM, Class of 2016; MD, Class of 2015

Category: Basic Science/Translational Project

Should pollution be considered when identifying human and animal populations at high risk for emerging infectious disease?

Elizabeth Hodges, Veronica Tomcej, Craig Stephen DVM PhD

Introduction: Emerging infectious diseases (EID) have important impacts on human health, animal conservation, and animal productivity. Additionally, most recent human EIDs are of animal origin. Organizations worldwide are focussed on predicting high risk areas of disease emergence to enable preparedness for EIDs before clinical and population impacts. Despite it being known that exposure to chemical pollutants can immunomodulate humans and animals, little effort has been focussed on determining if pollution is a shared environmental exposure for EID risk.

Methods: We undertook a scoping literature review to determine whether data and experiences in human and veterinary medicine supported the hypothesis that variation in environmental contaminants could affect vulnerability to EIDs. We also took a more in-depth look at the body of knowledge surrounding four cases.

Results: We found (1) synergies and/or associations between rates of infectious diseases and levels of patient contamination could be found in both the veterinary and medical literature; (2) these trends could be found for multiple different species, exposure routes, diseases, and pollutants; (3) some associations could be found for the same contaminant in both people and animals; (4) biologically plausible and demonstrable mechanisms for these associations were present in the literature; (5) pollution patterns are not homogenous globally and some of the more highly polluted regions correspond to areas that have experienced EID events.

Conclusions: The literature supported our hypothesis and suggested that pollution tracking and control should be managed in concert with medical and veterinary programs intended to predict EID risk globally and reduce the impacts of infectious diseases.

Presenter's Name: Heena Singh

Program and Year: MD, Class of 2015

Category: Basic Science/Translational Project

Role of Serine Protease Inhibitor (SERPINB3) in radiation resistant invasive Squamous Cell Carcinoma of the cervix

Heena Singh, Dr. JB McIntyre, Dr. Tony Magliocco & Dr. Corrine Doll

Tom Baker Cancer Center, University of Calgary

Introduction: Cervical cancer is the second leading cause of death in women and accounts for 12% of all female cancers. The current screening test available for this cancer has not changed since the last 60 years. There are new demands for accurate diagnosis through prognostic and predictive factors for better selection of patients in treatment with chemoradiation. Currently, a majority of cancer patients receive radiotherapy at some point in their treatment, however only a subset are sensitive to radiation treatment. The aim of this project is to identify and validate a candidate radiation response biomarker SERPINB3 (serine protease inhibitor found to protect tumors from apoptosis) and its role in clinical radiation treatment.

Methods: Samples that passed GeneChip and Data QC were used in which eleven non-responder (NR) samples (patients with tumors that were radiation resistant) were used as control for the comparison with twelve responder samples (R) (patients with tumors who responded to radiation). These raw scores were analyzed with SERPINB3 probe sets in SPSS statistical software. Parametric and non-parametric analyses of these scores were correlated with histological, overall suvival (OS) and progression free survival (PFS). Next, real time PCR analysis on ten samples and normal cervix (control) were used to verify microarray dataset.

Results: Our microarray dataset demonstrates SERPINB3 levels were upregulated in responders and down-regulated in non-responders. This data was further supported by statistical analysis in which higher levels of SERPINB3 was correlated significantly ($p=0.033$) with responders. Furthermore, patients with higher levels of SERPINB3 (6.77-362.43) demonstrated significantly better overall ($p=0.000$) and progression free survival ($p=0.001$). Real-time PCR results on ten blind samples demonstrate similar results when compared with normal cervix data.

Conclusions: In our data, we found that SERPINB3 was upregulated in responders, however SERPINB3 should protect against radiation. Although these findings are interesting, further research is needed.

Presenter's Name: Helena Zakrzewski

Program and Year: MD, Class of 2016

Category: Basic/Translational Project

Identification of poor quality of surgical care of elderly patients in the emergent setting: a pilot study

Helena Zakrzewski[1], Mo Yu Li[1], Nadia Sourial[2], Michèle Monette[2], Dr. Fadi Hamadani[1], Debby Teasdale[2], Dr. Simon Bergman[1,2], Dr. Shannon Fraser[1,2]

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Introduction: The provision of effective surgical care to elderly patients who undergo emergent surgical interventions is challenging. This pilot study aimed to determine the feasibility of assessing quality of surgical care in the emergent setting and to compare the quality of surgical care received by elderly and non-elderly patients.

Methods: A retrospective cohort study of 148 (39 elderly (age ≥ 65) and 109 non-elderly) adult patients who underwent emergent major abdominal surgery at a single, university-affiliated institution was conducted. Patient characteristics were recorded. The main outcome was quality of surgical care, which was assessed by measuring adherence to 10 perioperative surgical quality indicators and quantified by calculating a patient quality score (#quality indicators passed/# quality indicators eligible x 100%). Secondary outcomes evaluated were length of stay, occurrence of complications, and discharge destination. Non-parametric bivariate analyses were performed.

Results: The mean age of the elderly cohort was 76.2 +/- 9.0 years and that of the non-elderly cohort was 42.0 +/- 13.2 years. The median (interquartile range) patient quality score of the elderly cohort was significantly lower than that of the non-elderly cohort (55.6 per cent (19.6 per cent) *versus* 57.1 per cent (21.4 per cent); $P = 0.031$). Elderly patients also had significantly longer lengths of stay, greater occurrence of complications, and were less likely to be discharged home.

Conclusion: This study describes a feasible approach to assessing quality of surgical care in the emergent setting. Elderly patients received poorer quality of surgical care than non-elderly patients in the emergent setting.

Presenter's Name: Jacqueline Williamson

Program and Year: MD, Class of 2016

Category: Basic/Translational Science Project

Promoting Child-Targeted Health Foods: An Analysis of Nutritional Content and Product Packages

Jacqueline Williamson[1], Charlene Elliott[2]

[1]Bachelor of Health Sciences, Faculty of Medicine, University of Calgary; [2]Department of Communication Studies, Faculty of Arts, University of Calgary

Introduction: Childhood obesity is a growing problem on the global stage, and is understood to be linked not only to adult obesity, but many other ailments such as cardiovascular disease, sleep apnea, dyslipidemia, and Type 2 diabetes. Organic and natural foods are perceived by many consumers as being 'healthier' than conventional foods, and have caused this area of the food market to grow in recent years.

Methods: All child-directed products were purchased from eight 'Organic' and/or 'Natural' oriented stores in Calgary, Canada, and packages were coded for food categories, package semiotics, verbal claims, and nutritional details. Univariate and bivariate analyses were conducted to assess associations between package and product characteristics and nutritional profiles.

Results: Eighty-four products from 32 unique brands were identified and analyzed, with all products coming from dry or frozen goods categories. Only half self-identified as organic products, and a mere 12 (14.3%) products were of good nutrition, with high sugar levels being the most prominent concern amongst products. Parent and environmental package claims were common, but most were still associated with poor nutrition.

Conclusions: Child-oriented food products from 'organic' and 'natural' food stores collectively had a poor nutritional profile. The 'halo effect' associated with such foods is misplaced and misleading for the average consumer. Nutrition education should include the understanding of package claims as a marketing tool, and should encourage consumers to critique products based on information provided in the Nutrition Facts table and ingredients list.

Presenter's Name: Jaclyn Strauss

Program and Year: MD, Class of 2015

Category: Basic/Translational Science Project

Determining the Biological Relevance of a Novel STAT3 Mutation Identified in a Pediatric Patient with Hyper IgE Syndrome

Jaclyn Strauss[1], Eadric Cai[1], Ian Hons[1] and Dr. Christopher Waterhouse[1,2]

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Introduction: Hyper IgE Syndrome, (HIES), is a primary immunodeficiency characterized by elevated levels of IgE, eosinophilia, eczema and recurrent bacterial infections of the skin and lungs. Autosomal dominant HIES results from mutations in STAT3, (Signal Transducer and Activator of Transcription), a component of the JAK-STAT signaling pathway. Sequencing of the STAT3 gene from a 6 year-old boy diagnosed with HIES at the Alberta Children's Hospital revealed a novel point mutation in the "linker region" of STAT3 and an autosomal dominant pattern of inheritance. Previously described STAT3 mutations in HIES have been localized to the DNA-binding and SH2 domains. Given that the function of the linker region has yet to be elucidated, we sought to determine the biological relevance of the mutation in this patient with HIES. The objectives of this study are to examine the effects of this STAT3 mutation on the JAK-STAT signaling pathway, specifically 1) phosphorylation and 2) nuclear translocation of STAT3.

Methods: HEK 293 cells transfected with mutant and wild-type GFP-tagged STAT3 clones were previously generated in the lab. The transfected cell lines were stimulated with human IL-6 to induce activation of the JAK-STAT pathway and immunofluorescence (IF) microscopy and an immune-precipitation (IP) assay with Western blotting were used to examine the effects of the mutant STAT3 allele on phosphorylation and nuclear translocation.

Results: IF microscopy and IP Western blots demonstrated that phosphorylation was unaltered in the mutant STAT3 allele isolated from the index patient. Preliminary evidence seen on IF microscopy appears to suggest that nuclear translocation may be similarly unaltered.

Conclusions: Evidence to date indicates that the novel STAT3 mutation identified in our index patient does not affect phosphorylation in the JAK-STAT pathway *in vitro*. Work is currently underway to determine if the mutant allele is able to successfully translocate to the cell nucleus.

Presenter's Name: Jan Rudzinski

Program and Year: MD, Class of 2014

Category: Clinical Project

Increasing Rate Of Fluoroquinolone Resistant Escherichia Coli And Incidence Of Infectious Complications Following TRUS Guided Prostate Needle Biopsy In Calgary, Alberta, Canada – A Retrospective Population Based Analysis

Jan K. Rudzinski, Dr. Jun Kawakami MD FRCSC

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Introduction: Increasing risk of infectious complications associated with colonic Escherichia coli (E.coli) following trans-rectal ultrasound guided prostate biopsy (TRUS-PB) has been observed across North America and Europe. Fluoroquinolone (FQ) antibiotics are used as the first line prophylaxis prior to TRUS-PB. We sought to evaluate whether increasing E.coli resistance correlates with increased incidence in infectious complications following TRUS-PB at our institution.

Methods: Retrospective chart and electronic health record review was conducted on 927 patients who underwent TRUS-PB between January and July 2012 in Calgary, Alberta, Canada. The variables collected prospectively included - age, pre-biopsy prostate specific antigen (PSA), and date of biopsy. We documented presentation to an emergency department (ED) within 30 days of TRUS-PB for infectious and non-infectious complications.

Results: Overall, 58 patients (6.3%) were admitted to the ED due to post TRUS-PB complications within 30 days post-biopsy. The most common infectious complication observed were sepsis in 21 patients (2.2%), followed by urinary tract infection (UTI) in 9 (0.9%), and prostatitis in 4 (0.4%) – 83% of the septic episodes and 66.6% of the UTIs were attributed to ciprofloxacin resistant *Escherichia coli* (E.coli). The incidence of non-infectious complications was as follows – urinary retention in 12 (1.2%), hematuria in 9 (0.9%), and rectal bleeding in 8 (0.8%).

Conclusion: Our results suggest increased incidence of infectious complications caused by FQ resistant organisms following TRUS-PB. This finding could be attributed to increasing community resistance to ciprofloxacin. The current antimicrobial prophylactic regimen needs to be re-evaluated, and a novel approaches will be considered at our institution.

Presenter's Name: Jason Bau

Program and Year: MD/PhD, Year 6

Category: Basic/Translational Project

Selective inhibition of topo IIα by salicylate occurs through a non-competitive mechanism by blocking DNA cleavage.

Jason T. Bau, Zhili Kang, Ebba U. Kurz

Southern Alberta Cancer Research Institute and Department of Physiology & Pharmacology

Introduction: Topoisomerase II (topo II) is a ubiquitous enzyme that is essential for cell survival through its role in regulating DNA topology and chromatid separation. Topo II is also the intracellular target of several common chemotherapeutics (topo II poisons), treatment with which results in the accumulation of cytotoxic enzyme-linked DNA double-stranded breaks. In contrast, non-break inducing topo II catalytic inhibitors have also been described and have more limited use in clinical chemotherapy. These agents, however, may alter the efficacy of regimens incorporating topo II poisons. We previously identified salicylate, the primary metabolite of aspirin, as a novel catalytic inhibitor of topo II (1). As catalytic inhibitors can function at various points within the catalytic cycle, we decided to examine the biochemical mechanism behind salicylate action. Furthermore, as mammalian cells express two isoforms of topo II (α and β), we examined if salicylate could selectively target one or both isoforms.

Methods: Using multiple independent, biochemical approaches, we interrogated each stage of the topo II catalytic cycle to examine the mechanism of salicylate-mediated inhibition.

Results: Our results demonstrate that salicylate is unable to intercalate DNA, does not prevent enzyme-DNA binding nor promote stabilization of topo IIα-DNA closed clamps. Interestingly, salicylate decreased topo IIα ATPase activity in a dose-dependent non-competitive manner. Salicylate was able to inhibit topo IIα activity after DNA binding but prior to strand cleavage. We also demonstrated that salicylate could preferentially inhibit topo IIα over topo IIβ at the concentrations tested.

Conclusions: Our work demonstrates that salicylate, a common and widely used anti-inflammatory agen, inhibits topo II activity by blocking the enzyme prior to strand cleavage, and furthermore suggests that the compound is selective for the topo IIα isoform over its topo IIβ counterpart. These findings provide a definitive mechanism for salicylate-mediated inhibition of topo IIα and provide support for further studies determining the basis for its isoform selectivity.

Presenter's Name: Jennifer Beatty

Program and Year: MD/PhD, Year 5

Category: Basic/Translational Science Project

A Model for Chronic Consequences of Acute Enteric Infection: The role of pathogen-mediated disruptions in the intestinal microbiota

J.K. Beatty[1,2], J. Smith[1,2], K. Rioux[3,4], P. Beck[2,3,4], A. Buret[1,2]

[1]Department of Biological Science, University of Calgary, [2]Inflammation Research Network, University of Calgary, [3] Department of Medicine, University of Calgary, [4] Gastrointestinal Research Group, University of Calgary

Introduction: *Giardia duodenalis* is a leading causes of water-borne infectious dysentery encountered worldwide. Following a number of recent outbreaks, the symptomology profile of giardiasis has been extended to include the development of long-term, and chronic gastrointestinal complications characteristic of post-infectious irritable bowel syndrome (PI-IBS). Despite its occurrence in upwards of 40% of individuals who have experienced previous enteric infection, the mechanisms underlying the generation of PI- IBS remain obscure. Disruptions in the normal species distribution of the intestinal microbiota in IBS patients have been observed, but remain incompletely characterized. Moreover, novel insights into the ability of enteropathogens to modify the phenotype of the mucosa-associated microflora, normally existing as a series of biofilm communities, must be expanded in order to fulfill an all-encompassing view of the poly-microbial interplay that can elicit gastrointestinal disease. This study uses *G. duodenalis* as a model to examine the impact of an acute enteropathogen on the structure, species composition, and resulting pathogenic profile of human mucosal biofilm communities.

Methods: Representative intestinal mucosal biofilms were cultivated from human colonic mucosal biopsy samples collected during routine colonoscopy procedures.

Results: *Giardia*-exposure results in a loss in diversity in the species composition of microflora biofilms, when compared to control-communities. Additionally, *Giardia* promotes a phenotypic switch from the normal biofilm mode of bacterial growth, to planktonic growth in microflora biofilms via a disruption in normal extracellular matrix production, characteristic of biofilm communities. Finally, *Giardia*-exposed biofilm communities induce higher levels of enterocyte apoptosis, and promote changes in Caco2 monolayer permeability.

Conclusion Human mucosal biofilm communities exposed to *Giardia* exhibit an alteration in the normal biofilm phenotype, as well as species composition. Furthermore, the detrimental effects of *Giardia*-exposed mucosal biofilms on enterocyte homeostasis outlines the potential consequences that complex poly-microbial interplay may have in initiating functional gastrointestinal disorders, such as PI-IBS.

Presenter's Name: Joan Stilling

Program and Year: MD, Class of 2015

Category: Basic/Translational Project

Nano-structured Neural Stimulating Electrodes: The Future Of Neural Prosthetics?

Joan Stilling, Nehar Ullah, Sasha Omanovic

Department of Chemical Engineering, McGill University

Introduction: The exceptionally promising field of neural interfaces and neural prosthetics relies on the successful electrical stimulation of nervous tissue through the use of electrodes. Current electrical stimulation therapies for various neurological disorders (i.e. Deep brain stimulation for Parkinson's disease, cochlear implants for hearing loss) utilize these neural interfacing devices. A principal problem with current neural electrodes is their lack of stimulus selectivity due to large electrode size relative to the targeted neuronal population. However, as bulk electrode size is reduced, charge density increases, which may cause irreversible damage to both the electrode and stimulated tissue. In an effort to find a balance between electrode size and charge density, our objective was to develop a novel iridium-nickel oxide bimetallic coating that could *intrinsically* offer high charge injection. Secondly, we attempted to nanostructure the surface of these coatings to create a higher surface/volume ratio which would result in a higher *extrinsic* charge storage capacity than currently used stimulating electrodes.

Methods: Thermal decomposition was used to fabricate iridium oxide, nickel oxide, titanium oxide and bimetallic iridium-nickel oxide coatings on titanium electrode substrates. Each sample was investigated using cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS), and scanning electron microscopy (SEM).

Results: Experiments showed that specific Ir/Ni-oxide coatings offered a significantly higher true, electrochemically-active surface area (i.e. higher roughness) than the currently used state-of-the art, Ir-oxide coatings. These bimetallic coatings were also capable of delivering significantly more charge than the control, both from the intrinsic and extrinsic point of view.

Conclusion: This work will assist in both the miniaturization of neural electrodes improving charge injection specificity and narrow the cyclization potential limits, thus decreasing the negative inflammatory effect of the electrodes on the surrounding tissue.

Presenter's Name: Joanna Moser

Program and Year: MD/PhD, Class of 2014

Category: Clinical Project

Systematic review and meta-analysis: impact of 4 childhood illnesses on I.Q.

Joanna J. Moser[1], Pamela M. Veale[2], Debbie L. McAllister[3], David P. Archer[4]

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Introduction: Concern has been expressed that children exposed to uneventful surgery and anesthesia may incur neurological injury that becomes manifest in poor scholastic performance or future learning difficulties. The purpose of our study is to provide context to the pediatric anesthesia neurotoxicity question by reviewing the evidence linking four childhood illness with neurocognitive development. In the present review we have sought to quantify the magnitude of the impact of chronic illness on neurocognitive development through a systematic review of publications that report the developmental trajectory of patients with 4 childhood diseases: cystic fibrosis (CF), hemophilia A, end stage renal disease (ESRD) and end stage liver disease (ESLD).

Methods: Studies were identified by searching the electronic databases OVID MEDLINE and Pubmed and scanning reference lists of articles. We used the following search terms: CF, HA, ESRD, ESLD in combination with academic performance, educational status, educational measurement, learning, achievement, developmental delay, learning disabilities, intellectual disabilities, behavioural disorders, I.Q. (intelligence quotient), cognition, school problems, absenteeism, school attendance, anxiety, learning regression or developmental regression. Reported data was analyzed with the Mantel-Haenszel method and using Review Manager.

Results: Children with CF and HA did not appear disadvantaged by their disease as general intelligence levels were comparable to the general population norms. In children with ESRD, mean I.Q. reported during dialysis improved after transplantation. Although they improved relative to their pre-transplantation cognitive functioning, children with ESLD who received transplants are approximately 8 I.Q. points below the population norm.

Conclusions: Overall, the results suggest that the burden of chronic childhood illness, by itself, does not impair cognitive development in children with HA and CF. Children with ESRD and ESLD, despite optimal management, show a mild cognitive deficit compared to the population norm. Given the impact of these four specific chronic illnesses on neurocognitive outcome in children and the improvement in I.Q. post-transplant in both ESRD and ESLD, the results suggest that the effect of an uncontrolled confounding illness on neurocognitive development is small.

Presenter's Name: Kristen Barton

Program and Year: MD/PhD, Year 1

Category: Basic/Translational Project

Motor, Behavioural and Pathological Deficits in a Rat Model of Cerebral Palsy

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Introduction: Severe injury to the knee joint, such as anterior cruciate ligament (ACL) tears and/or menisci damage often results in accelerated development of osteoarthritis (OA)1-3. It is thought that there may be an injury-induced, mechanical abnormality of the injured joint and subsequent interplay between altered mechanics and/or biological changes, such as inflammation, which may lead to cartilage damage. Dexamethasone (DEX) is a synthetic steroid with anti-inflammatory properties4, which could possibly be a treatment strategy5 for controlling inflammation. The purpose of this study is to characterize inflammation and joint mechanics following idealized ACL reconstruction (ACL-R) surgery after DEX injection.

Methods: A small pilot study was conducted in untrained sheep (n=2 ACL-R, n=2 controls). Surgeries involved an arthrotomy to the right stifle joint, with the left joint serving as the control. DEX was given immediately after ACL-R by an intra-articular injection (0.5 mg/kg body weight). Animals were sacrificed 2 weeks after surgery and tissues, synovial fluid, and blood were collected. Gross morphological grading was conducted for gross cartilage defects, osteophyte formation, and meniscal damage6. Histology of synovium was evaluated for microscopic changes with Hematoxylin and Eosin staining. This pilot study is the start of a large-scale project: 20 sheep allocated into 3 groups: ACL-R+DEX (n=8), ACL-R (n=8), and controls (n=8). Furthermore, an in vivo motion analysis system (instrumented spatial linkage) will measure kinematics. mRNA expression of inflammatory cytokines will be measured by real-time polymerase chain reaction.

Results: Combined gross morphological score in the ACL-R+DEX group was lower than that of the control for cartilage damage/defects, osteophyte formation, and meniscal damage. Mean aggregate synovitis score consisting of sub-intimal fibrosis, intimal hyperplasia, and cell infiltration in the ACL-R+DEX group was similar to that of the control group.

Conclusion: Preliminary results demonstrate that even one injection of DEX immediately after ACL-R surgery is sufficient to completely block induction of cartilage damage and synovitis.

Presenter's Name: Kristine Woodward

Program and Year: MD/MSc, Class of 2016

Category: Clinical Project

Resting-State Motor Networks in Frontal Lobe Epilepsy

KE Woodward, I Gaxiola, B Goodyear, P Federico

Introduction: Patients with frontal lobe epilepsy (FLE) often experience motor deficits. Previous studies have associated impairments in patients with epilepsy with changes in resting-state connectivity; a technique that examines temporally correlated brain regions at rest using modalities such as functional magnetic resonance imaging (fMRI). However, it is not known whether patients with FLE have altered motor networks, and if such alterations could contribute to functional motor deficits. Therefore, resting-state motor networks were examined in participants with FLE using fMRI.

Methods: Thirteen patients (seven right FLE, six left FLE) and ten control participants were examined. While in the MR scanner participants concentrated on a fixation cross for five minutes. fMRI data was analyzed using FSL. First, the left and right sensorimotor cortices were identified as regions of interest (ROI). The average BOLD signal from voxels in the ROI was compared to every voxel in the brain to determine the temporal correlation between BOLD signals. Mean maps were generated for each group and compared to determine voxels exhibiting a significant difference ($Z>2.3$, corrected cluster significance $p=0.05$). Laterality indices from resting-state maps were calculated for each patient and correlated with years since diagnosis, lifetime seizures, seizures in past year, and months since last seizure to determine significant relationships.

Results: Patients with FLE had significantly decreased connectivity between the left and right sensorimotor cortices compared to controls ($Z>2.3$). Laterality indices were significantly correlated to total lifetime seizures (left FLE: $r_s=0.89$, right FLE: $r_s=1.00$). As patients experienced more seizures, the healthy hemisphere sensorimotor cortex became less connected to the epileptic hemisphere sensorimotor cortex.

Conclusions: Resting-state motor networks are altered in patients with FLE compared to controls, and differences become more pronounced when patients experience more lifetime seizures. These results have important implications for understanding the mechanisms behind daily motor deficits experienced by patients with FLE.

Presenter's Name: Lauren Capozzi

Program and Year: MD/PhD, Year 3

Category: Clinical Project

Evaluating the ENHANCE Exercise Program: A supportive exercise program for head/neck cancer patients

Lauren Capozzi, Dr. Harold Lau, Dr. Barry Bultz, Dr. Nicole Culos-Reed

Faculty of Kinesiology, University of Calgary; Psychosocial Resources, Tom Baker Cancer Centre, Alberta Health Services.

Introduction: Physical activity (PA) interventions as a method to positively impact symptom management, treatment-related recovery and quality of life (QoL) have largely excluded head/neck cancer (HNC) populations. HNC patients deal with severe weight loss, with upwards of 70% attributed to muscle wasting, leading to extended recovery times, decreased QoL, and impaired physical functioning. There is a lack of treatment options to help sustain or rebuild this wasted muscle and manage treatment related side effects, but strength training and PA hold great potential.

Methods: The pilot ENHANCE Program was a structured 12-week group-based exercise program delivered with a collaborative clinical focus. Patients on or completed treatment were referred to the program and following assessment and education, engaged in once weekly group exercise classes and 2-3 days of home-based activity each week. Assessments pre- and post-intervention included physical fitness and functional testing as well as symptom management. This program evaluation included 17 head/neck cancer patients both on (n=5) and completed (n=12) treatment.

Results: Patients attended an average of 77% (9.24/12) of the weekly group exercise sessions and a total of 65% of the patients completed the program, with the main reason for dropout being return to work. Overall, patients on treatment experienced no change in fitness, whereas patients who had completed treatment experienced improved upper body strength ($p=0.012$), lower body muscular endurance ($p=0.003$) and increased bicep circumference ($p=0.001$). Patients reported a significant decrease in overall tiredness, depression, and drowsiness, and improvements in overall well-being (all $p's<.05$).

Conclusions: This program facilitated advancements in patient wellness, survivorship, and autonomy, and provided feasibility data for a current randomized controlled trial. This current study is examining the impact of timing of a 12-week PA and nutrition intervention (during or following treatment) for HNC patients on body composition, recovery, inflammatory response, QOL and PA adherence.

Presenter's Name: Liz Jack

Program and Year: MD, Year 1

Category: Basic/Translational Science Project

Associations between the built environment, perceived walkability, residential self-selection and nieghbourhood-based walking in adults.

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Introduction: Physical environmental and intrapersonal factors may jointly influence walking behaviour and, by extension, the downstream health outcomes associated with physical activity. This study examined the extent to which objectively-assessed and self-reported urban form characteristics were associated with neighbourhood-based walking.

Methods: A random cross-section of 1875 adults completed a telephone-interview and postal questionnaire capturing neighbourhood walkability, neighbourhood-based walking, socio-demographic characteristics, walking attitudes, and residential self-selection. Objective neighbourhood types (low [LW], medium [MW], and high walkable [HW]) were determined from cluster-analysis of Geographical Information System (GIS) data. Covariate-adjusted regression models estimated independent associations and interactions between weekly participation and duration in transportation and recreational walking, self-reported and objectively-assessed walkability, and reasons for neighbourhood self-selection.

Results: Compared with residents of objectively-assessed LW neighborhoods, residents of HW neighborhoods were more likely to participate in (odds ratio[OR]=3.06), and spend more time per week (193 min/wk) transportation walking ($p<.05$). Recreational walking was not associated with neighbourhood type ($p>.05$). Compared to LW neighbourhoods, respondents in HW neighborhoods positively perceived access to services, street connectivity, pedestrian infrastructure, and destination mix, but negatively perceived motor vehicle traffic and crime safety. HW neighbourhood residents also rated access to services as important to their choice of neighbourhood, whereas LW neighbourhood residents rated sense of community and ease of driving of higher importance. With regard to interactions, HW x utilitarian destination mix was positively associated with participation, HW x physical barriers and MW x pedestrian infrastructure were positively associated with minutes, and HW x safety from crime was negatively associated with minutes of transportation walking.

Conclusions: Objectively-assessed and self-reported built characteristics are associated with neighborhood-based transportation walking. Perceived walkability and self-selection may also moderate the relationship between the built environment and transportation walking. Interventions that target perceptions in addition to urban modifications could result in increases in physical activity among adults.

Presenter's Name: Marcia Abott

Program and Year: MD, Class of 2014

Category: Basic/Translational ScienceProject

Infection site evolution in the Trichomonads.

Marcia Abbott, Christopher Naugler

Introduction: Trichomonads are an important group of anaerobic protists to both the human and animal medical world. The Parabaslia Phylum is a diverse group that encompass pathogens and commensals in numerous hosts that include mammals, birds, reptiles, amphibians and many others. There is sparse research in the area of comparative site specificity for this group. The focus of this paper is to examine host site evolution in this group.

Methods: A GenBank search was used to locate all trichomonad species with archived rRNA sequences for the gene ITS-1/5.8S/ITS-2. Data was collected on the infection host and site through the original or additional articles. A phylogenic tree with 48 final data points on infection sites was constructed using the Mega5 computer program and host site evolution patterns were inferred through ancestral character state reconstruction using Mesquite V.2.75.

Results: Among the taxons included in this study, use of a genitourinary infection site is inferred to have evolved independently five times, lung infection site twice, and a free-living state twice.

Conclusions: As a group, trichomonads appeared to have evolved from infecting the gastrointestinal tract to other anatomic sites in a series of independent evolutionary events.

Presenter's Name: Mat Palakkamanil

Program and Year: MD, Class of 2015

Category: Clinical Project

Effects of Ocular Laser Exposure in a Population of Commercial Airline Pilots: A Retrospective Chart Review

Mathew Palakkamanil, Michael Fielden MD FRCSC ABO

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Introduction: Laser strikes on commercial pilots are occurring more regularly by pranksters who attempt to beam the laser into airplane cockpits during takeoff and landing. Despite stiff penalties and extended imprisonment, the reports of aircraft struck by lasers have steadily increased in the past years. Shining lasers at aircraft is extremely dangerous as it can cause momentary blindness in pilots attempting to land or take off as well permanent damage to the pilots' eyes. As laser induced injury to commercial pilots is a relatively new but growing occurrence, there is no data available to determine the effects of lasers on the eyes of pilots.

Methods: A chart review was conducted on 37 commercial airline pilots who have reported laser exposure while flying. Pilots visited the same ophthalmologist as soon as possible after the occurrence of the laser strike incident and a complete ophthalmic evaluation was conducted including visual acuity, colour vision, refraction, visual field, intraocular pressures, and a dilated fundus exam.

Results: Of the 37 patients evaluated, the average length of laser exposure was 12.3 seconds, the laser was most often of green light (63.2% of exposures), and the majority of incidents occurred at Toronto Pearson International Airport (29.6% of incidents). 62.5% of incidents occurred during plane landing; 38.4% were straight strikes whereas 61.6% were peripheral strikes. In regards to immediate symptoms, 35.1% of pilots experienced flash-blindness, 10.1% had facial burns; other ocular damages included retinal scars, corneal scars and prolonged photophobia.

Conclusions: Laser strikes on commercial aircraft can result in significant ocular damage to pilots as well as compromise the safety of airline passengers. Further studies must be conducted to learn more about the visual findings of laser exposure to the eyes in airline pilots and assist law enforcement to mitigate laser attacks in the future.

Presenter's Name: Menglin Yeng

Program and Year: MD/MSc, Year 2

Category: Basic/Translational Science Project

Characterization of the aspartic protease, nepenthesin, as a therapeutic for the treatment of celiac disease

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Introduction: Celiac disease (CD) is a highly prevalent autoimmune disorder that is triggered by the incomplete digestion of immune stimulatory peptides in the gliadin fraction of dietary gluten. The basis for gliadin resistance to digestion is due to the abundance of P (~15%) and Q (~30%) residues in its protein sequence. Currently, no therapeutic for CD exists but oral proteases aimed at efficiently digesting gliadin throughout the gastrointestinal tract have shown promise in clinical trials. In this study, we evaluate the potential of a novel aspartic protease from *Nepenthes* plant extracts, nepenthesin, whose properties appear suited for an oral protease therapeutic for CD.

Methods: Both isoforms of nepenthesin (I and II) were recombinantly expressed in *E. coli* and purified from inclusion bodies. Cleavage specificities of recombinant nepenthesins to native plant extracts were compared for functionality. Gliadin was digested *in vitro* with various concentrations of recombinant nepenthesins under simulated gastic conditions and analyzed by LC-MS/MS. Digestion of a immunodominant 33-mer peptide was quantified by indirect ELISA.

Results: The cleavage specificities of native plant extracts vs. recombinant nepenthesins showed that cleavage N-/C-terminal to all residues are retained except cleavage C-terminal to proline. *In vitro* digestions of gliadin showed that the average length of peptides, including all immunogenic epitopes, decreased in a dose-dependent manner at clinically relevant nepenthesin doses as compared to leading clinical candidates. Quantification by indirect ELISA showed that the immunodominant 33-mer peptide within gliadin extracts was digested by nepenthesin in a dose-dependent manner. In addition, digestion maps show cleavage within all known immunogenic epitopes, including the 33-mer peptide.

Conclusions: Preliminary results from the identification and initial characterization of the first aspartic protease that appears to efficiently process gliadin in all known immunogenic regions and act optimally in the stomach supports nepenthesins potential as an effective oral therapeutic candidate for CD.

Presenter's Name: Michael Greene

Program and Year: MD, Class of 2015

Category: Clinical Project

Evaluation of haptic controller dexterity with regards to driving surgical performance in teleoperated robotic- assisted surgery

Michael R. Greene, Tomas Hirmer, Kourosh Zareinia, Garnette Sutherland

Project neuroArm, University of Calgary

The field of haptic interface development is rapidly advancing, however there is currently no commercially available haptic hand controller designed specifically to enable robotic-assisted surgery. Surgeons require precision hand controllers that provide kinesthetic and in some cases tactile feedback, which also feature a wide range of motion and ergonomic considerations, for the duration of surgery. The lack of haptic interaction has been identified as a major drawback of most current robotic-assisted surgical systems, and a satisfactory solution has yet to be developed. The neuroArm Surgical Performance and Advanced Haptics Laboratory is investigating design considerations of a haptic hand controller optimized for use in multiple surgical disciplines, combining research on current commercially available hand controllers with input from experienced surgeons and engineers.

Seven commercially available haptic hand controllers have been procured for this study. Previous literature and experience within the neuroArm team has identified dexterity as a key metric of haptic controller performance. Results include dexterity quantification in the form of isodexterity mapping and global conditioning indices. Haptic controller performance metrics and study design are also outlined for a future trial involving surgeons from numerous surgical disciplines immersed in simulation-based (virtual reality) surgical skill-testing scenarios. Ultimately, conclusions from this study will contribute to the generation of requirement specifications for a surgeon's user-interface in the form of a haptic hand-controller designed specifically for teleoperated robotic- assisted surgical applications.

Presenter's Name: Michael Peplowski

Program and Year: MD/PhD, Year 6

Category: Basic/Translational Science Project

Distinct Cell Signaling Mechanisms Drive the TNFα and IFNγ-Induced Transcriptional Downregulation of Aquaporin 3 RNA Expression.

Michael A. Peplowski, Andrew J. Vegso & Wallace K. MacNaughton

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Introduction: Inflammatory bowel diseases (IBD) are characterized by altered water transport leading to the development of diarrhea, although the status of Aquaporin (AQP) 3 expression, localization and its role in the barrier dysfunction that characterizes IBD remains unknown. *We hypothesized that AQP3 transcription was inhibited in intestinal inflammation by the cytokines tumour necrosis factor (TNF) α and interferon (IFN) γ.*

Methods: 1. C57Bl/6 mice were administered 2.5% dextran sodium sulfate (DSS) in drinking water for up to 7 days to induce colonic inflammation. AQP3 protein expression was assessed using immunofluorescence of fixed tissue. **2.** The human adenocarcinoma cell line HT29 was used for treatments with either human recombinant TNFα (25 ng/mL) or human recombinant IFNγ (500 U/mL). AQP3 mRNA expression were assessed by real-time RT-PCR. Inhibitor studies to reverse the cytokine-induced downregulation of AQP3 were performed using a 1 hr inhibitor pre-treatment prior to the addition of cytokine.

Results: 1. AQP3 protein expression was downregulated early in colonic inflammation at 3 days post-commencement of DSS with diminished basolateral membrane staining in epithelial cells lining colonic crypts. **2.** Similarly, HT29 cells treated with TNFα or IFNγ resulted in an early decrease in AQP3 pre-mRNA expression at 2 hr, which was followed by decreased mRNA expression at 6-12 hr, suggesting transcriptional repression of AQP3 expression. The IFNγ-induced decrease in AQP3 mRNA expression at 12 hr was reversed using a broad-spectrum JAK inhibitor (JAK Inhibitor I, 10 μM), but not a JAK2 specific inhibitor (JAK2 Inhibitor II, 10 μM). In contrast, the TNFα-induced decrease in AQP3 mRNA expression at 12 hr was not reversed by inhibitors of the PI3K, AKT, NF-κB, ERK/MAPK and p38 MAPK pathways (LY294002, 10 μM; Triciribine, 1 μM; BAY11-7082, 30 μM; U0126, 10 μM and SB203580, 10 μM respectively), even though all of the above pathways were activated by TNFα and significantly inhibited by their respective inhibitors.

Conclusions: The data suggest that alterations in AQP3 expression represent early events that occur in colonic inflammation. *In vitro*, both TNFα and IFNγ are independently capable of decreasing AQP3 mRNA transcription through distinct mechanisms.

Presenter's Name: Murtaza Amirali

Program and Year: MD, Class of 2014

Category: Clinical Project

Duplex Ultrasonography, An Alternative to Temporal Artery Biopsy? A Decision Analysis Model

Murtaza Amirali, Dr. Duncan Nickerson

Faculty of Medicine

Introduction: Temporal arteritis (TA) is an inflammatory disease affecting medium to large blood vessels of body. Prompt identification through biopsy of the temporal artery (TAB) and urgent treatment by high dose corticosteroids, is the gold standard, and is necessary as the one of the sinister complications of this disease is blindness.

Methods: Temporal arteritis presents a complex clinical scenario and clinical uncertainty with regards to a definitive diagnosis through invasive biopsy or non-invasive ultrasound. To assist in the practice of evidence based clinical practice, a Markov model and clinical algorithm are proposed based on a literature review of the best evidence for the diagnosis of GCA. This will assist in providing the best evidence to determine how duplex ultrasonography can be used as a first-line investigation to temporal artery biopsy in the diagnosis of GCA.

Results: Duplex ultrasonography should become the first-line investigation and an alternative diagnostic test to TAB in the diagnosis of temporal arteritis. TAB should be reserved for patients with a intermediate risk score and negative scan.

Conclusions: Future studies need to include a sensitivity and cost-effective analysis on the utility of ultrasound in the diagnostic algorithm of TA so that health resources can be used effectively and efficiently.

Presenter's Name: Nabeela Nathoo

Program and Year: MD/PhD, Year 4

Category: Basic/Translational Science Project

Characterizing hypoxic vascular lesions using susceptibility weighted MRI in a model of multiple sclerosis

Nabeela Nathoo[1,2], James A. Rogers[2,3], V. Wee Yong[2,3], Jeff F. Dunn[1,2,3,4]

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Introduction: Multiple sclerosis (MS) is an inflammatory and demyelinating neurological condition. Susceptibility weighted imaging (SWI) is a magnetic resonance imaging (MRI) method sensitive to iron in hemosiderin, ferritin and deoxyhemoglobin (dHb) which has detected lesions not seen with conventional MRI in MS patients. Previously, we used SWI in the experimental autoimmune encephalomyelitis (EAE) mouse model of MS where two types of lesions were detected: 1) vascular lesions (or hypointensities), due to dHB, and 2) parenchymal white matter lesions, due to iron deposition/demyelination. Here, we aimed to determine if vascular and parenchymal lesions could be differentiated using SWI by increasing the inspired oxygen to reduce dHb in the blood. Vascular lesions would alter in appearance with high oxygen, whereas parenchymal lesions would not.

Methods: Control and EAE mice were imaged at 9.4T using 3D gradient echo with flow compensation (for SWI) with 30% O_2/70% N_2 then 100% O_2. A subset of mice were imaged with these gases and then after perfusion (to remove blood). Lesions were counted and compared between control and EAE mice, and the number of lesions seen with 30% O_2 was compared with the number that remained unchanged with 100% O_2. Iron deposition was assessed using DAB-enhanced Perl's staining.

Results: Most lesions (hypointensities) seen with 30% O2 altered in appearance with 100% O_2 in control ($p<0.001$) and EAE mice ($p<0.01$). Hypointensities that changed in appearance with 100% O_2 also disappeared after perfusion, supporting that they are due to dHb. Parenchymal white matter lesions appeared dark in MRI and did not change in appearance with high oxygen.

Conclusions: Changing the inspired oxygen concentration differentiates between vascular and parenchymal lesions in the EAE model *in vivo*. This method can be applied in MS patients, paving the way to investigate the pathophysiology of venous hypoxia and iron deposition in MS.

Presenter's Name: Prasan Patel

Program and Year: MD, Class of 2015

Category: Clinical Project

Does abdominal ultrasound show equivalence to Computed Tomography and Magnetic Resonance Enterography in predicting active Crohn disease and its complications?

S Batool, MBBS, A Wadhwani, BSc, **Prasan Patel, BSc**, K Novak, MD, SR Wilson, MD,

Introduction: Crohn disease (CD) is an inflammatory disease of the bowel that requires imaging for diagnosis and surveillance. Ultrasound (US) is a radiation free, cost-effective, and readily available modality that provides real-time assessment of the bowel in routine and emergent cases. Given the accuracy and safety of US, our objective is to demonstrate equivalence of US with computed tomography (CT) and magnetic resonance enterography(MRE) in detecting disease activity and complications in patients with established and suspected CD. We hypothesize that US can be used as a first-line investigative tool for routine diagnosis, surveillance and detection of complications in those with acute symptoms.

Methods: We analyzed 308 patients with known or suspected CD who had a positive bowel US exam with CT, CTE and/or MRE scans from May 2010-June 2013. Two reviewers, blinded to the pathology, evaluated the US images for active disease/complications. Disease was assessed with color Doppler or contrast-enhanced US (CEUS). Concordance was determined by the percentage of patients that showed agreement on US and the gold standard modality.

Results: US and gold standard concordance for disease activity were as follows: wall thickness-98.05%, blood flow-96.69%, and inflammatory fat-87.13%. US correctly ruled in 84/86(97.67%) strictures, 53/54(98.14%) fistulae, 28/29(96.5%) perforations, 43/44(97.7%) phlegmon, and 18/20(90%) abscesses. Real time US scanning identified dysfunctional peristalsis, fixed luminal apposition and bowel angulation strictures and partial bowel obstructions. Spatial resolution of US was superior in identifying perforations with phlegmon. MR was superior in predicting bowel wall edema and mucosal ulceration; insignificant difference between MR and US noted when determining active disease. Inflamed or perforated appendices were better visualized with US and but had 100% concordance to other modalities.

Conclusion: In patients with CD, our study shows equal and occasional superiority of US to CT/CTE/MRE in predicting disease activity and intestinal complications for routine evaluation, monitoring or acute presentations.

Presenter's Name: Prima Moinul

Program and Year: MD, Class of 2015

Category: Basic/Translational Science Project

Dopamine Prevents Form-Deprivation Myopia via Nitric Oxide Relay

Prima Moinul, Edwin Cheng, William Stell, MD, PhD.

University of Calgary

Introduction: Myopia (nearsightedness) is caused by excessive elongation of the growing eye in which images of distant objects appear out-of-focus without optical correction. Form-deprivation myopia (FDM) was induced in young chickens with translucent diffusers. Dopamine (DA) and nitric oxide (NO) prevent FDM by acting in series since antagonist to either one alone stops the prevention of FDM by brief goggle-removal. Here we tested the hypothesis that NO prevents FDM in chickens through a DA-D2-receptor relay.

Methods: One eye of chickens, 1-10 day-old, was goggled with a diffuser. Every 2nd day, (total 3x) drug was injected into the vitreous of the goggled eye and 1x PBS vehicle into the unoggled, fellow eye under O2-N2O-Isoflurane anesthesia. First, optimal doses of NO-donor (SNAP, to prevent FDM) and DA-D2R-antagonist (Spiperone, to prevent the effect of 2hr goggle-removal) were determined. Next, we gave optimal doses of SNAP and Spiperone simultaneously, leaving the diffuser on; control animals (without drug) had their goggles on or off permanently. After the third treatment, refractive error, eye size and weight were measured. Moreover, optimal doses of DA-agonist, ADTN, and NOS-inhibitor L-NIO, were determined similarly to test the alternate hypothesis that activation of DA-D2R prevents FDM via a NO-releasing relay.

Results: SNAP and ADTN prevented FDM, while Spiperone and L-NIO blocked myopia-prevention by 2hr diffuser-removal in chickens. The optimal doses were: Spiperone, 5nmol; SNAP, 500nmol; ADTN, 3mM; L-NIO, 20uM. At these doses, Spiperone did not block myopia-prevention by SNAP.

Conclusions: Since Spiperone did not block myopia-prevention by SNAP, NO does not prevent FDM via a DA-D2R relay. We are now determining whether a blocker of NO synthesis will block myopia-prevention by DA agonist, to reinforce the alternative hypothesis. These findings will lead to better understanding of the mechanisms underlying emmetropia and myopia, and may lead to novel therapies to prevent myopia.

Presenter's Name: Robert Kosior

Program and Year: MD/PhD, Year 2

Category: Clinical Project

Multimodal Quantitative MR Imaging in Acute Ischemic Stroke: Mapping Tissue Fate

Robert K Kosior[1,2], Ajay Mahajan[3], Sachin Mishra[1], Vivek Nambiar[1], Simer Bal[4], Richard Frayne[2], M. Louis Lauzon[2], Ursula Tuor[2], Philip A. Barber[1]

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Introduction: Stroke therapies are available within a "time window" (4.5 hours) of stroke onset with concerns about hemorrhagic transformation. We hypothesize that quantitative (q) implementations of conventional T1- and T2-relaxation magnetic resonance (MR) imaging will provide a more accurate depiction of tissue at risk of dying. Prediction of tissue fate is a step towards a "tissue window" paradigm of therapy where response to treatment is stratified by the "tissue properties" of ischemic brain.

Methods: Acute ischemic stroke patients were imaged within 6 hours of symptom onset and at 24 hours (3T MR scanner). T1 mapping was performed with a 3D-GRE-LL sequence (22 phases) or a DESPOT1 sequence (two spoiled-gradient acquisitions). T2 mapping was performed using a CPMG sequence with 8 echoes (30 ms intervals) or 16 echoes (15 ms intervals). Typical diffusion-weighted imaging was also performed to provide apparent-diffusion coefficient (ADC) maps. Volumetric and absolute value analysis of the infarct core was conducted on the ADC, T1 and T2 maps.

Results: Fourteen patients were included with a median time from onset to first MR exam of 228 min. Eleven had detectable ADC lesions; median infarct volume on ADC increased from 13 ml at baseline to 29 ml at 24 hours. Nine patients had visible qT2 changes. Eight patients showed early qT1 changes. Distinct differences in ADC, qT1 and qT2 evolution were observed: qT1 reversal occurred in 3 patients; qT2 changes increased in all patients by 24 hours; qT1 and qT2 depicted changes in different areas of the suspected ischemia compared to ADC.

Conclusion: Distinct qT1 and qT2 changes occur in acute ischemic stroke. The presence of qT2 concurrent with reduced ADC suggests a more complicated process than cytotoxic edema, with the influence of blood-brain barrier compromise. These findings suggest qMR can define ischemic tissue properties, and may help in determining tissue fate.

Presenter's Name: Ryan Leigh

Program and Year: MD/PhD, Year 4

Category: Clinical Project

The Effect of Land-Based Exercise on Pain and Function in Individuals with Hip Osteoarthritis – A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Introduction: To determine whether land-based exercise is an effective intervention for decreasing pain and improving function in individuals with hip osteoarthritis (OA) and to determine whether patient tailored exercise programs are more efficacious than generic exercise interventions.

Methods: Systematic review with meta-analysis of randomized controlled trials (RCTs) comparing land-based exercise to a control intervention in people with hip OA not awaiting surgery. Standardized mean differences (SMD) and 95% confidence intervals (95% CI) were calculated for pain and physical function (self-reported and performance-based). The PEDro quality index scale was used to determine the quality of the evidence.

Results: Eight RCTs involving 570 participants with hip OA were identified and included in the review. The eight identified RCTs scored an average of 7.5/10 on the PEDro quality index score indicating sound methodological quality. Meta-analysis of the included RCTs using a random effects model demonstrated exercise had a small treatment effect for pain (SMD (95% CI) = -0.40[-0.73, -0.06]), and no treatment effect on self-reported function (SMD (95% CI) = -0.41[-0.83, 0.01]) or performance-based physical function (SMD (95% CI) = -0.10[-0.35, 0.16]). When only those studies that provided a tailored exercise program were pooled, exercise was found to have a moderate treatment effect on pain (SMD (95% CI) = -0.65[-0.98, -0.31]) with no effect on self-reported or performance-based physical function outcome measures.

Conclusions: High quality evidence from eight RCTs demonstrated that land-based exercise has a small beneficial effect on pain but no effect on function outcomes in hip OA patients not awaiting surgery. Tailoring the exercise intervention to a hip OA patient's personal assessment findings appears to result in further reductions in pain and emphasizes the importance of a personalized and tailored approach in the management of OA.

Presenter's Name: Ryan Lewinson

Program and Year: MD/PhD, Year 4

Category: Basic/Translational Science Project

Influence of opening the joint capsule and inserting pressure film on knee abduction moments

[1,2,3]**Ryan T. Lewinson**, [2]Andrew Sawatsky, [2]Tim R. Leonard, [2,4]Jay T. Worobets, [1,2,3]Walter Herzog, [1,2]Darren J. Stefanyshyn

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Introduction: Both increases and decreases to knee abduction moments-of-force (KAMs) during running result in reduced knee pain for runners with patellofemoral pain – a precursor to patellofemoral osteoarthritis. We aim to study why both increases and decreases to joint loading are beneficial using a rabbit model where altered KAM magnitudes are electrically induced and patellofemoral pressures are measured, but before this can be done, the procedure must be validated. Specifically, the objective of this study was to ensure that opening the joint capsule and/or insertion of pressure film into the joint do not alter KAMs.

Methods: One rabbit was studied. A nerve cuff was surgically inserted at the femoral nerve and the rabbit was placed in a stereotaxic frame with bone pins inserted into the pelvis and femoral condyles to maintain the thigh in a fixed position. The knee angle was set at 60^{o}. Quadriceps muscles were isometrically activated maximally and a load cell at the distal tibia measured three-dimensional forces which were used to calculate the KAM. This was done with the knee joint capsule intact (Intact), the joint capsule opened (Open), and with pressure film inserted under the patella (Open-Film). KAMs were analytically compared between the three conditions.

Results: The knee extension moment across the three conditions differed by only ±4% suggesting muscular forces were well matched across conditions. Relative to the Intact condition, the peak KAM increased in the Open and Open-Film conditions by 70% and 120%, respectively.

Conclusions: Opening the joint capsule and inserting pressure film beneath the patella alters KAM magnitudes when extension moment magnitudes were held constant. This needs to be taken into account in future studies aimed at identifying the influences of altered knee moment magnitudes on patellofemoral pressures.

Presenter's Name: Ryan McGinn

Program and Year: MD, Class of 2016

Category: Basic/Translational Science Project

Dynamic Link Between Communication and Computation in an in vitro model of the human temporal neocortex.

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Introduction: We wished to better understand the role of interlaminar oscillations of the human neocortex and their role in the coordination of communication and computation. We hypothesized that the requisite circuitry for both local computation and long-range communication should overlap and be related in a dynamic and functional way.

Methods: We investigated electrical activity measured from dual electrophysiological recordings from the deep and superficial lamina of human temporal neocortical slices resected during surgery for epilepsy. We first used a measure known as cross frequency coupling (CFC) which is thought to represent a neural code implicated in local neuronal computation and a variety of behavioural and cognitive correlates such as spatial awareness, sensation and memory. Furthermore, inter-regional oscillatory coherence is thought to be marker for long-range communication, and is encapsulated in what is known as the communication through coherence (CTC) hypothesis. We use a measure known as phase-dependent power correlations (PDPC) which was generated from the CTC hypothesis.

Results: Here, we show that there is a strong correlation between the strength of CFC and CTC between trials of oscillatory activity at theta (4-15 Hz) frequency. This correlation was particularly marked between CFC in the deep cortical layers and CTC between layers, indicating that deep layers may play a preferential role in driving inter-laminar communication.

Conclusions: For the first time to our knowledge, we have demonstrated a quantitative correlation between local computation and long-range communication. This result supports further research into an integrative approach to studying brain activity, whether *in vivo*, *in vitro* or *in silico.*

Presenter's Name: Sandra Cortina

Program and Year: MD/MPH, Class of 2015

Category: Clinical Project

Is Housing First an appropriate model for community-based solutions that encourage connection with the homeless? A preliminary analysis of Calgary's Project Homeless Connect

Sandra C. Cortina, RN, MPH, MD candidate; Lorraine Lau, PhD, MD candidate; Janette Hurley MD, Student Run Clinic, University of Calgary

Student Run Clinic, University of Calgary

Introduction: Project Homeless Connect (PHC) is a one-day event where homeless can connect to community services at one location with reduced barriers (e.g. multiple travel, stigmatization). While non-housing services (e.g. hair cuts, medical) are offered, PHC's primary goal is to connect people to housing services. Guided by a Housing First model, the Calgary Homeless Foundation (CHF) has decided to discontinue PHC after finding most clients were drawn to the event for basic needs rather than housing support. This study aimed to gain a preliminary understanding of PHC's impact on housing service connection and personal empowerment among participants who sought medical care.

Methods: This cross-sectional study design asked participants receiving medical care to complete a post-appointment survey adapted from Denver's Guest Evaluation Survey PHC-7. Tool pre-testing was limited by short notice of PHC's discontinuation. SPSS was used for data analysis.

Results: Of 50 medical clinic participants, 20 completed the survey. 15 did not indicate "housing" as their primary purpose of attending PHC. Alternatively, reported purposes were: "personal needs" (60%), "food" (20%), and "employment assistance" (20%). However, 13.3% had used or planned to use housing services that day, and benefits on empowerment were also reported: improved feelings of isolation from the community (33%), improved confidence to take control over homeless situation (20%), and gained knowledge to change homeless situation (46.7%).

Conclusions: While the primary purpose of PHC attendance may not be "housing", the event may still offer other benefits such as service connection and self-empowerment. By focusing PHC on a Housing First model, we may be overlooking an important barrier: community disconnect. Rather than removing basic services for un-conforming behaviour, perhaps a harm reduction model, where the community can meet people where they're at would be more appropriate. Further research is warranted due to the methods and sample size of this study.

Presenter's Name: Sarah Sloan

Program and Year: MD, Class of 2014

Category: Clinical Project

Support for Early Treatment of Major Depressive Disorder in Recovering Alcohol Dependency: Improved Mood and Prolonged Abstinence

Sarah Sloan, Dr. Emad Hanna, MD

Introduction: This presentation seeks to demonstrate evidence to support early treatment of Major Depressive Disorder (MDD) in the newly abstinent patient with alcohol dependency to improve mood, prolong abstinence and lessen the psychiatric burden of these comorbid diseases. Alcohol dependency and MDD are prevalent and highly comorbid presentations in the community. Each condition worsens the course of the other creating greater impairment than either condition alone. This is true even when the patient is newly abstinent from alcohol; the presence of untreated MDD can hinder recovery efforts reducing the time to relapse. Traditionally, MDD was not treated in alcohol dependent patients until 4-12 weeks of abstinence had passed however recent data supports that the early treatment of MDD in patients with substance dependency offers subjective and clinical improvements in mood that can enhance recovery efforts. Further, when antidepressants are combined with an opioid-antagonist medication, the benefit of prolonged abstinence and reduced relapse are noted in addition to improved mood.

Methods: A literature review and analysis was undertaken to assess the clinical evidence for treatment of MDD in patients with alcohol dependency with consideration to the primary outcomes of improved mood and prolonged abstinence from alcohol.

Results: Three studies assessing the clinical effect of antidepressants on MDD in patients with substance use disorders were reviewed. The studies included one meta-analysis and two randomized control trials and each demonstrated improved mood in patients with comorbid MDD and alcohol dependency (NNT=9, $p=0.021$). The combination of an SSRI and an opioid-antagonist medication demonstrated greater abstinence and prolonged time to relapse than either medication achieved alone ($p=0.001$ and $p=0.003$, respectively).

Conclusions: Antidepressants are effective in the early treatment of MDD in newly abstinent patients with alcohol dependency. The addition of an opioid-antagonist to an antidepressant prolongs abstinence when compared to either monotherapy alone.

Presenter's Name: Shevaun Davis

Program and Year: MD, Class of 2016

Category: Basic/Translational Science Project

CD36 Recruitment and Actin Cytoskeletal Rearrangement via p130CAS Enhances Avidity of *P. falciparum* Adhesion on Human Microvascular Endothelium

Shevaun P. Davis, Matthias Amrein, Mark R. Gillrie, Kristine Lee, Daniel A. Muruve, Kamala D. Patel and May Ho

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Introduction: The adhesion of P. *falciparum*-infected erythrocytes (IRBC) to microvascular endothelium is critical in the pathogenesis of severe malaria. In this study, we used atomic force microscopy to analyze the adhesive force between IRBC and human dermal microvascular endothelial cells (HDMEC).

Methods: A single live IRBC, attached to the end of the cantilever, served as a functionalized probe that monitored the IRBC-endothelial cell interaction in real time.

Results: Our results show that the initial IRBC-HDMEC interaction generated a mean adhesion force of 166.7 ± 4.2 pN pN from the formation of either single or multiple bonds. The adhesion force was reduced by an anti-CD36 but not an anti-ICAM-1 antibody. Interestingly, the adhesion force increased with time as the IRBC was left in contact with the endothelium, so that by 300 seconds the force of adhesion had increased to 559.3 ± 45.5 pN. The time-dependent increase in the strength of adhesion was mediated by CD36, Src family kinases, the adaptor protein p130CAS, and actin cytoskeletal rearrangement in a calcium-dependent manner. The end result was both an increase in the affinity of binding between IRBC and HDMEC that was alkaline phosphatase dependent, and an increase in the number of ligand-receptor pairs through cytoskeletal rearrangement. These findings were supported by fluorescence microscopy imaging that showed recruitment of CD36 and actin in response to ligation of CD36 by IRBC, anti-CD36 or parasite peptide coated beads. Functionally, the increase in adhesion force enabled IRBC to remain adherent in shear stresses of up to 15 dynes/cm^2 in a flow chamber assay, an ability that was significantly reduced on HDMEC in which p130CAS expression was knocked down by siRNA.

Conclusion: Collectively, the data suggest a novel mechanism by which IRBC adhesion to CD36 activates a signaling pathway that leads to changes in the membrane localization of CD36, actin recruitment and increased binding avidity between IRBC and HDMEC.

Presenter's Name: Shoghi Nikoo

Program and Year: MD/MA, Year 2

Category: Basic/Translational Science Project

The grey matter of ethics in surgical innovation

Shoghi Nikoo, Ariel Ducey

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Introduction: Innovation in surgical medicine is an ethically grey area. Randomized control trials (RCTs) are demonstrably difficult to employ with surgical procedures, and some authors have questioned whether the knowledge produced by RCTs of surgical techniques can be effectively deployed to guide surgical practice. Further, development of new surgical treatments often occurs outside the context of RCTs and follows a trajectory that highlights ethical issues that concern medical innovation more broadly. This paper asks what ethical considerations arise in the context of surgical innovation, and what are the implications of those considerations for innovators and for practicing surgeons?

Methods: A case study of the development of the intravaginal slingplasty (IVS) procedure, precursor to the highly successful tension-free vaginal tape (TVT) surgery for female stress urinary incontinence, was used to demonstrate the ethical issues that arise from surgical innovation. Historical documents – particularly, a close reading of two monographs – constituted the data of this paper.

Results: The IVS was developed largely through a process of trial-and-error. Petros and Ulmsten, the developers of the IVS, learned from the mistakes they made on their early patients. These mistakes are inevitable and necessary for surgical innovation; however, they provoke questions around patient safety and how to balance innovation with protecting patients from harm. Furthermore, as Health Canada warnings about the use of such mesh implants as the TVT show, these studies do not produce sufficient information about low incidence but high impact risks.

Conclusions: Innovation is central to advancing medicine and improving patient care. There are, however, key ethical issues to consider when engaging in innovative medicine. Appropriate oversight and reporting, for example, are critical for patient welfare. As important is the need for a research paradigm that produces evidence surgeons can use to guide their practice.

Presenter's Name: Simran Shergill

Program and Year: MD, Class of 2015

Category: Clinical Project

A Systematic Literature Review of the Trail-Making Test and its Effectiveness in Identifying Cognitively Impaired Drivers

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Introduction: The medical community is well-placed to identify cognitively impaired drivers who may no longer be safe to drive. However, the validity of commonly used screening tools for identification of cognitive impairment for *decisions about driving* is not well established. The primary objective of this research was to examine the accuracy of the Trail Making Test (Parts A and B) [TMT] for determination of driving competency.

Methods: Using established systematic review methodology, a search of six electronic databases was conducted, with studies from database inception to June 2011 included. Key terms to identify studies using the TMT as a predictor variable for driving performance were used, with pre-defined inclusionary/exclusionary criteria used for study selection. Rigorous full-text review with data extraction was conducted by both investigators blinded to each other's results.

Results: From an initial sample of 4,441 studies, 30 articles met the inclusionary/exclusionary criteria and were included in the systematic review. The results from the 30 empirical studies yielded 46 unique data points. The majority (n = 36) of data points had on-road evaluation as the outcome measure, with 10 data points having crashes (n = 5) or simulator results (n = 5) as the outcome measure. The vast majority of studies relied on correlational analyses, with only 4 studies using cutpoints. Only one of the 4 studies using cutpoints examined sensitivity and specificity, with a reported sensitivity of 45% and a specificity of 86%.

Conclusion: The results from the 30 empirical studies reveal that TMT-A and -B scores are *associated* with driving outcomes. However, knowledge of that association provides little in the way of information for decision making on driving competency in the clinical setting. Without the aid of empirically determined cut points, the use of the TMT for decision making on medical fitness to drive is questionable.

Presenter's Name: Taryn Ludwig

Program and Year: MD/PhD, Year 5

Category: Basic/Translational Science Project

Viscosity of Lubricin: Effects of Concentration, Structure, and Interaction with Hyaluronan

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Introduction: The viscosity (resistance to flow) of synovial fluid (SF) is essential for its ability to provide lubrication and cushioning to articular joints. Hyaluronan (HA) is a large glycosaminoglycan that contributes significantly to the viscosity of SF. HA also works synergistically with lubricin (a mucin-like glycoprotein) to provide SFs lubricating ability. HA is currently used as an intra-articular treatment for pain relief of osteoarthritis (OA), a painful and debilitating disease affecting 13% of Canadians. Lubricin has demonstrated ability to slow cartilage degradation in animal injury models of OA, however the viscosity of lubricin alone and lubricin+HA solutions are unknown. The objective of this study was to measure the viscosity of 1) lubricin alone, 2) lubricin with naturally occurring disulfide bonded multimers broken by reduction and alkylation (R/A), and 3) lubricin+HA solutions.

Methods: Viscosity analysis of lubricin±R/A, HA, and lubricin+HA solutions was performed with high molecular weight HA and lubricin purified from media conditioned by bovine cartilage explants.

Results: Lubricin alone at physiologically normal concentrations demonstrated concentration- and multimer-dependent shear thinning behaviour (decreasing viscosity with increasing rate of deformation, like paint). However, lubricin viscosity at low concentration and when R/A was similar to that of water. When lubricin was added to low concentrations of HA, viscosity increased in a manner independent of lubricin concentration but dependent on multimeric structure. Viscosities for R/A lubricin+HA were similar to those of HA alone.

Conclusion: These results demonstrate that the disulfide bonded structure of lubricin is essential in the unknown mechanism of lubricin+HA interaction. They suggest that intra-articular treatment with lubricin might increase the viscosity of diseased SF; this is the objective of current HA treatments. Characterization of the viscosity of lubricin+HA solutions will contribute to the understanding of SF function in health and disease, and will be necessary for new lubricin±HA biotherapeutic treatments.

Presenter's Name: Tristan Jones

Program and Year: MD/MSc, Class of 2014

Category: Basic/Translational Science Project

Novel Glucose Biosensor and Sampling Platform Allowing Pseudo-continuous, Minimally-invasive Monitoring – The Electronic Mosquito

Jones, Tristan D[1]; Mintchev, Martin[1]; Kaler, Karan[1]; Birss, Viola[2]

University of Calgary; [1]Faculty of Engineering; [2]Faculty of Science;

Introduction: Diabetes is one of the most pressing issues in the modern world. With prevalence rates soaring above 8% in some countries, the number of individuals affected is staggering. Modern management of diabetes has advanced to the point where the once-fatal disease is now a chronic condition. Monitoring practices are, however, invasive, painful, and provide only 3-4 data points per day – potentially missing important high and low blood glucose levels. While some continuous glucose monitors have been developed, they are invasive, require periodic calibration with finger-prick tests, and must be exchanged frequently. The Electronic Mosquito [e-Mosquito] is a device designed to correct these shortcomings to increase monitoring accuracy and compliance.

Methods: A novel glucose sensor using iridium oxide nanoparticles [IrOx NPs] coupled to glucose oxidase [GOx] enzyme was miniaturized and tested *in-vitro* to characterize its response to glucose. This sensor was then integrated with the existing e-Mosquito prototype via a custom-designed potentiostat. Finally, the complete system was tested in an *in-vitro* setup using phosphate-buffered saline.

Results: The sensor was successfully integrated into the existing prototype and was shown to obey Michaelis-Menten kinetics. While manufacturing limitations meant that reproducibility of the electrodes was a big issue, the Michaelis-Menten parameters of the electrodes were determined. I_{max} was in the range of 60 – 100 μA and *Km* was in the range of 15 – 20 mmol. The potentiostat was also proven to work correctly and maintain electrical potential between the sensor electrodes while supplying sufficient current to perform the measurement.

Conclusion: This research has demonstrated the feasibility of using IrOx NPs in combination with GOx enzyme for glucose detection. While more reproducible manufacturing is required, the prototype functions as a proof-of-concept for minimally-invasive glucose biosensors. These devices have the potential to not only increase compliance, but to permit development of a fully artificial pancreas.

Presenter's Name: Veronique Ram

Program and Year: MD/PhD, Class of 2016

Category: Clinical Project

Every Body is a Story: Introducing Narrative Medicine

Véronique Dorais Ram

Introduction: Current international literature demonstrates that physicians and with exposure to the humanities improve their critical thinking skills and bring enhanced sensitivity and analysis to diagnostic reasoning. Medical programs, particularly in the United States, incorporate "narrative medicine" into the curriculum to enhanced training in communication skills, stronger knowledge translation aptitudes, more creative thinking tools, and lastly, to alter public perception of physician practices. Existing studies illustrate that this thriving area of research can highlight the importance of biomedical narrative forms and promote the balance of treatment options between belief systems, patient history, and the technological possibilities offered by medical science. Research Question: What are Canadian programs doing to keep up with this trend? Which studies clarify the principles of "narrative medicine" and how can we expand on the benefits that narrative medicine holds for clinical practice?

Methods: A review (as of June 2012) of Canadian and American medical program curriculums, and a literature search (Medline, UptoDate, MLA Bibliography, ERIC) was performed.

Results: The programming survey shows a substantial support for narrative medicine in the United States, and a growing interest at Canadian institutions (Alberta, Toronto, Dalhousie, Calgary, and McGill). There is a wealth of research on the defining characteristics of narrative medicine and the benefits of integrating the study of narratives into medical schools; however, there is a lack of research on physician "stories" (for example, the clinical chart) as narrative medicine.

Conclusion: The current trend of narrative medicine offers a theoretically complex and intellectual new avenue to examine physician practices. More clinically focused projects, however, are needed to research the benefits of narrative medicine beyond medical education and physician health to consider clinical charts and physician documents as narratives themselves. Only through the analysis and data collection of both sides of the story can narrative medicine actually prove beneficial to the patient-physician relationship.

Presenter's Name: Xiao-Ru Yang

Program and Year: MD, Class of 2016

Category: Clinical Project

Neurochemical alterations associated with repetitive transcranial magnetic stimulation intervention in adolescent major depressive disorder

Yang X, Kirton A, Wilkes C, MacQueen G, Liu I, Jaworska N, Damji O, Roe J, Rajapakse T, Lebel M, Fife M, MacMaster F

Departments of Psychiatry and Paediatrics, University of Calgary

Introduction: Repetitive transcranial magnetic stimulation (rTMS) is emerging as a possible treatment option for adolescents with treatment-resistant major depressive disorder (MDD). This study aimed to investigate the mechanisms of action of rTMS in treating MDD. The dorsolateral prefrontal cortex (DLPFC) and hippocampus were specifically investigated, as they are implicated in the pathophysiology of MDD. We hypothesized that an increase in DLPFC glutamate levels would occur after three weeks of rTMS treatment, in accordance with extant adult studies. Furthermore, we expected that changes in glutamate concentration would correlate with changes in MDD symptoms relative to baseline.

Methods: Proton magnetic resonance spectroscopy (1H-MRS) was used to detect changes in glutamate levels that occur following rTMS treatment of adolescents with treatment-resistant MDD (N=5). Voxels were placed in two brain regions implicated in MDD: the left DLPFC and the hippocampus bilaterally.

Results: Following rTMS, treatment responders (defined as a 50% reduction in depressive symptoms; N=3) showed an increase in left DLPFC glutamate levels (11%), which corresponded to an improvement in depressive symptom severity (67% reduction). Treatment non-responders (N=2) had elevated baseline glutamate levels compared to responders in that same region, which decreased slightly with rTMS (-9%).

Conclusions: In responders, rTMS may act by elevating (normalizing) glutamate levels in the left DLPFC, thereby leading to symptom improvement. Having elevated baseline glutamate levels may be predictive of poorer outcomes with rTMS treatment.

Presenter's Name: Zaheed Damani

Program and Year: MD/PhD, Year 3

Category: Clinical Project

A comprehensive case study of an orthopaedic surgery referral service in the Winnipeg Regional Health Authority: A single-entry model to manage waiting times for total joint replacement surgery of the hip and knee.

Zaheed Damani (MD-PhD Student)[1], Eric Bohm[2], Gail MacKean[1], Hude Quan[1], Tom Noseworthy[1], Deborah Marshall[1]

Department of Community Health Sciences, University of Calgary[1]; Concordia Hip and Knee Institute[2]

Introduction: Single-entry is a wait time management strategy that allows for multiple queues to be consolidated into a single queue, where patients can see the next-available surgeon. Increasingly being used across Canada, they have been shown to reduce wait times and improve patient experience but studies have not shown if or how this model affects quality of care. Objective: To comprehensively evaluate a single-entry model (SEM), with emphasis on the measurement of stakeholder experiences and changes in/implications for quality of care.

Methods: We will evaluate the Winnipeg Central Intake Service (a SEM for hip and knee replacement surgery) using a mixed-methods, case study approach. We will conduct semi-structured telephone interviews with patients, family physicians, surgeons, surgical office assistants, and those who designed it. Administrative data analysis will be performed with data from before and after the implementation of the WCIS to measure changes in quality of care. This will be based on 6 dimensions of quality and 20 corresponding quality of care indicators.

Results: Approximately 70 interviews have been completed, with all stakeholder groups ("Round 1"). Experiences have been mixed; preliminary results indicate divergent expectations and conditional acceptance of SEMs. Policy-makers and patients are proponents; family physicians and surgeons are skeptical about potential to improve and surgical office assistants, although initially opposed, are cautiously optimistic. Administrative data analysis will commence Fall 2013; Round 2 interviews in January 2014, with data analysis and final recommendations to be presented by 2015.

Conclusion: This will be the first study to assess a SEM's implications for health and health services. Evidence-informed policy options will be developed to enable health authorities to better respond to patient and system needs with the aim of improving patient care on all quality dimensions. Other clinical areas and jurisdictions will benefit, especially regions where single-entry is currently being used.

Christina S. Thornton, BSc,
Michael B. Keough, BSc
Jodie I. Roberts, BSc
Bryan Yipp, MD
Morley Hollenberg, Phd, MD
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Paul L. Beck, PhD, MD.

Proceedings from the 5th Annual University of Calgary Leaders in Medicine Research Symposium

On November 8, 2013, the Leaders in Medicine (LIM) program hosted the 5th Annual Research Symposium. Dr. Jerrold Ellner, Chief of the Infectious Diseases section at Boston Medical Centre and Professor of Medicine at Boston University School of Medicine, was the keynote speaker and presented his lecture entitled "Tuberculosis – Past, Present and Future". The LIM symposium gives a forum for LIM as well as non-LIM medical students to present their research work as either an oral or poster presentation. There were a total of 53 abstracts presented and five oral presentations. The symposium was attended by over 100 students and more than 30 staff members.

The oral presentations included

- Amrita Roy, Aboriginal identity, ethnic minority status, and prenatal depressive symptoms in a longitudinal pregnancy cohort study in Alberta.
- David Nicholl, Obstructive sleep apnea treatment with continuous positive airway pressure decreases intraglomerular pressure and alters renal sensitivity to angiotensin.
- James Cotton, An assemblage A *Giardia* cathepsin B protease degrades interleukin-8 and attenuates neutrophil chemotaxis.
- Krystyna Ediger, Alexander Arnold and Emily Shelton, Rebuilding the Calgary Student Run Clinic: A Model for Sustainability.
- Sarah MacEachern, Inhibiting inducible nitric oxide synthase restores electrogenic ion transport in experimental IBD: a novel role for enteric glia.

See the article on the University of Calgary Leaders in Medicine Program, "*A Prescription that Addresses the Decline of Basic Science Education in Medical School*" in this same issue of CIM for more details on the program. In short, the LIM Research Symposium has the following objectives: (1) to showcase the impressive variety of projects undertaken by students in the LIM Program as well as U of C medical students; (2) to encourage medical student participation in research and special projects; and, (3) to inform students and faculty about the diversity of opportunities available for research and special projects during medical school and beyond.

The following abstracts are those that were put forward for publication.

Clin Invest Med 2014; 37 (5): E292-E310.

Every Body is a Story: Introducing Narrative Medicine

Véronique D. Ram, MD/PhD Candidate, Class of 2016

Faculty of Medicine/Faculty of Arts, University of Calgary

Background/Purpose: Current international literature demonstrates that physicians and with exposure to the humanities improve their critical thinking skills and bring enhanced sensitivity and analysis to diagnostic reasoning. Medical programs, particularly in the United States, incorporate "narrative medicine" into the curriculum to enhance training in communication skills, strengthen knowledge translation aptitudes, provide more creative thinking tools and to alter public perception of physician practices. Existing studies illustrate that this thriving area of research can highlight the importance of biomedical narrative forms and promote the balance of treatment options between belief systems, patient history, and the technological possibilities offered by medical science.
Research Questions: What are Canadian programs doing to keep up with this trend? Which studies clarify the principles of "narrative medicine" and how can we expand on the benefits that narrative medicine holds for clinical practice?
Methods: A review (as of June 2012) of Canadian and American medical program curriculums and a literature search (Medline, UptoDate, MLA Bibliography, ERIC) were performed.
Results: The programming survey shows substantial support for narrative medicine in the United States, and a growing interest at Canadian institutions (Alberta, Toronto, Dalhousie, Calgary and McGill). There is a wealth of research on the defining characteristics of narrative medicine and the benefits of integrating the study of narratives into medical schools; however, there is a lack of research on physician "stories" (for example, the clinical chart) as narrative medicine.
Conclusion: The current trend of narrative medicine offers a theoretically complex and intellectual new avenue to examine physician practices. More clinically focused projects, however, are needed to research the benefits of narrative medicine beyond medical education and physician health to consider clinical charts and physician documents as narratives themselves. Only through the analysis and data collection of both sides of the story can narrative medicine actually prove beneficial to the patient-physician relationship.

Examining the Role of Pre-departure Training across Canadian Medical Schools for Global Health Electives

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Background: The rising interest from Canadian medical students in participating in international medical electives demands an emphasis on structured Pre-departure Training (PDT) to prepare and optimize the student learning experience. At the core of PDT are five competencies: personal health, travel safety, cultural competence, language competence and ethics. This study examines the completeness and effectiveness of PDT among Canadian medical schools.
Methods: A survey examining various components of PDT – core competencies, assessment of students' preparedness, length of PDT training, post-return debrief – was sent to one faculty member and one student representative at every Canadian medical school. The survey is an extension of similar surveys conducted in 2008 and 2010.
Results: Of the five core competencies of PDT, four (personal health, travel safety, cultural competence and ethics) were covered by 100% of medical schools. Language competence was addressed by 93% of schools, which is a major improvement from 63% in 2010. Students' preparedness was assessed in the form of interviews, tests/assignments and modules in 36% of medical schools.

In addition to PDT, 70% of schools reported that students received supplemental training and orientation at the site of their electives. Upon return from international electives, 93% of medical schools provided post-return debriefing activities.
Conclusion: While it is not possible to predict and prepare for every potential scenario that students might face, effective PDT enhances the international learning experience and equips students with tools to become responsible global citizens and professional representatives of the Canadian medical education system.

Support for Early Treatment of Major Depressive Disorder in Recovering Alcohol Dependency: Improved Mood and Prolonged Abstinence

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Objectives/Introduction: Alcohol dependency and Major Depressive Disorder (MDD) are prevalent and highly comorbid presentations in the community. Each condition worsens the course of the other creating greater impairment than either condition alone. This is true even when the patient is newly abstinent from alcohol; the presence of untreated MDD can hinder recovery efforts reducing the time to relapse. Traditionally, MDD was not treated in alcohol-dependent patients until 4-12 weeks of abstinence had passed; however, recent data supports the conclusion that the early treatment of MDD in patients with substance dependency offers subjective and clinical improvements in mood that can enhance recovery efforts. Further, when antidepressants are combined with an opioid-antagonist medication, the benefit of prolonged abstinence and reduced relapse are noted in addition to improved mood.
Methods: A literature review and analysis were undertaken to assess the clinical evidence for treatment of MDD in patients with alcohol dependency with consideration to the primary outcomes of improved mood and prolonged abstinence from alcohol.
Results: Three studies assessing the clinical effect of antidepressants on MDD in patients with substance use disorders were reviewed. The studies included one meta-analysis and two randomized control trials and each demonstrated improved mood in patients with comorbid MDD and alcohol dependency (NNT=9, p=0.021). The combination of an SSRI and an opioid-antagonist medication demonstrated greater abstinence and prolonged time to relapse than either medication achieved alone (p=0.001 and p=0.003, respectively).
Conclusion: Antidepressants are effective in the early treatment of MDD in newly abstinent patients with alcohol dependency. The addition of an opioid-antagonist to an antidepressant prolongs abstinence when compared to either monotherapy alone.

Is Housing First an appropriate model for community-based solutions that encourage connection with the homeless? A preliminary analysis of Calgary's Project Homeless Connect

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Objective: Project Homeless Connect (PHC) is a one-day event where homeless can connect with community services at one location with reduced barriers (e.g., multiple travel or stigmatization). While non-housing services (e.g., hair cuts and medical appointments) are offered, PHC's primary goal is to connect people with housing services. Guided by a Housing First model, the Calgary Homeless Foundation (CHF) has decided to discontinue PHC after finding most clients were drawn to the event for basic needs rather than housing support. This study aimed to gain a preliminary understanding of PHC's impact on housing service connection and personal empowerment among participants who sought medical care.
Methods: This cross-sectional study design asked participants receiving medical care to complete a post-appointment survey adapted from Denver's Guest Evaluation Survey PHC-7. Tool pre-testing was limited by short notice of PHC's discontinuation. SPSS was used for data analysis.
Results: Of 50 medical clinic participants, 20 completed the survey. Fifteen did not indicate "housing" as their primary purpose of attending PHC. Instead, reported purposes were: "personal needs" (60%), "food" (20%) and "employment assistance" (20%); however, 13.3% had used or planned to use housing services that day. Benefits on empowerment were also reported: decreased feelings of isolation from the rest of the community (33%), improved confidence in ability to take control over homeless situation (20%) and knowledge gained on how to change their homeless situation (46.7%).**Conclusion:** While the primary purpose of PHC attendance may not be "housing", the event may still offer other benefits such as service connection and self-empowerment. By focusing PHC on a Housing First model, we may be overlooking an important barrier: community disconnect. Rather than removing basic services for un-conforming behaviour, perhaps a harm reduction model, where the community can meet homeless people where they are would be more appropriate. Further research is warranted due to the limited methods and small sample size of this study.

Increasing Rate Of Fluoroquinolone-Resistant Escherichia coli And Incidence of Infectious Complications Following TRUS-Guided Prostate Needle Biopsy in Calgary, Alberta, Canada – A Retrospective Population-Based Analysis

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Introduction: Increasing risk of infectious complications associated with colonic *Escherichia coli* (*E.coli*) following transrectal ultrasound guided prostate biopsy (TRUS-PB) has been observed across North America and Europe. Fluoroquinolone (FQ) antibiotics are used as the first line prophylaxis prior to TRUS-PB. We sought to evaluate whether the increased *E.coli* antibiotic resistance correlates with increased incidence of infectious complications following TRUS-PB at our institution.
Methods: Retrospective chart and electronic health record reviews were conducted on 927 patients who underwent TRUS-PB between January and July 2012 in Calgary, Alberta, Canada. The variables collected prospectively included age, pre-biopsy prostate specific antigen (PSA) and date of biopsy. Presentations to an emergency department (ED) within 30 days of TRUS-PB for infectious and non-infectious complications were documented.
Results: Overall, 58 patients (6.3%) were admitted to the ED due to post TRUS-PB complications within 30 days post-biopsy. The most common infectious complications observed were sepsis in 21 (2.2%), followed by urinary tract infection (UTI) in nine (0.9%) and prostatitis in four patients (0.4%) – 83% of the septic episodes and 66.6% of the UTIs were attributed to ciprofloxacin-resistant *E.coli*. The incidence of non-infectious complications was as follows: urinary retention in 12 (1.2%); hematuria in nine (0.9%); and, rectal bleeding in eight patients (0.8%).
Conclusion: Our results suggest increased incidence of infectious complications caused by FQ-resistant organisms following TRUS-PB. This finding could be attributed to increasing community resistance to ciprofloxacin. The current antimicrobial prophylactic regimen needs to be re-evaluated, and novel alternative approaches will be considered at our institution.

Obstructive sleep apnea treatment with continuous positive airway pressure decreases intraglomerular pressure and alters renal sensitivity to angiotensin II

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Background: Obstructive sleep apnea (OSA) has been associated with the progression of chronic kidney disease. The underlying mechanism may be related to changes in the renin angiotensin system (RAS). The effect of continuous positive airway pressure (CPAP) on renal hemodynamics was investigated at baseline and in response to Angiotensin II (AngII) infusion in OSA patients.
Methods: Twenty normotensive, non-diabetic, newly diagnosed OSA subjects (15 men, five women; age 50±2 years; respiratory disturbance index [RDI]>15 hr^{-1}) with nocturnal hypoxia (oxyhemoglobin saturation [SaO_2] <90% for >12% of night) were studied in high-salt balance pre- and post-CPAP therapy (>4 hr CPAP use/night for one month). Glomerular filtration rate (GFR), renal plasma flow (RPF) and filtration fraction (FF), a surrogate for intraglomerular pressure, were measured pre- and post-CPAP therapy using inulin and para-aminohippurate clearance technique at baseline and in response to graded AngII infusion (3 ng/kg/min·30 min, 6 ng/kg/min·30 min).
Results: CPAP-corrected OSA and nocturnal hypoxia (RDI: 42±4 *vs.* 4±1 hr^{-1}, p<0.001; duration SaO_2<90%: 36±5 *vs.* 6±2%, p<0.001; all values pre- *vs.* post-CPAP). Post-CPAP treatment, there was a reduction in baseline GFR (124±8 *vs.* 110±6 mL/min, p=0.014) and an increase in baseline RPF (692±36 *vs*. 749±40 mL/min, p=0.059), which resulted in reduced baseline FF (18.9±1.6 *vs.* 15.3±1.0%, p=0.004).

Post-CPAP therapy there was a blunted GFR response (-9±3 *vs.* -2±2 mL/min, p=0.033) to the low dose of AngII, while there was an augmented RPF response (-182±22 *vs.* -219±25mL/min, p=0.024) to the high dose of AngII. The FF response to AngII was maintained (p=0.4). CPAP therapy also reduced baseline mean arterial pressure (94±2 *vs.* 89±2 mmHg, p=0.002), urinary protein excretion (61[39, 341] *vs.* 56[22, 204] mg/day, p=0.003), and plasma aldosterone (149±18 *vs.* 109±10 pmol/L, p=0.003).
Conclusions: CPAP treatment decreased intraglomerular pressure and improved renal hemodynamic sensitivity to AngII in OSA patients, supporting a role for the RAS in mediating OSA-associated hypertension and kidney disease.

Ethics in surgical innovation: Lessons of the intravaginal slingplasty

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Background*:* Innovation in surgical medicine provokes important ethical questions. Development of new surgical treatments often occurs outside the context of RCTs and follows a trajectory that highlights ethical issues concerning medical innovation. This paper asks what ethical considerations arise in the context of surgical innovation, and what the implications of those considerations are for innovators and for practicing surgeons. **Methods*:*** A case study of the development of the intravaginal slingplasty (IVS) procedure, the precursor to the highly successful tension-free vaginal tape surgery for female stress urinary incontinence, was used to demonstrate ethical issues that can arise in response to surgical innovation. Historical documents constituted the data of this paper.
Results*:* The IVS was developed largely through a process of trial-and-error. The developers of the IVS learned from the mistakes they made on their early patients; these mistakes iteratively contributed to the shape of subsequent versions of the IVS. These mistakes are inevitable and necessary for surgical innovation; however, they provoke questions regarding patient safety and how to balance the need for innovation with the need to protect patients from harm. Additionally, some choices in the series of studies leading up to the IVS and vagaries in published material conflict with standard norms of scientific rigour, calling into question whether the burden of risk carried by patients was justified.
Conclusions*:* Innovation is central to advancing medicine and improving patient care. There are, however, key ethical issues to consider when engaging in innovative medicine. The trial and error process through which medical devices develop necessitate errors that can cause negative outcomes for whole cohorts of patients, causing us question how to control harm to patients while encouraging surgical innovation. The IVS case also shows how choices about study design are ethical choices – in order to justify the risk inherent in experimental studies, high quality study design and communication is paramount.

Dopamine Prevents Form-Deprivation Myopia via Nitric Oxide Relay

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Purpose: Myopia (nearsightedness) is due to excessive elongation of the growing eye, which causes images of distant objects to be out of focus without optical correction. Form-deprivation myopia (FDM), an established experimental model for human myopia, was induced in young chickens with translucent diffusers. It is known that dopamine (DA) and nitric oxide (NO) prevent FDM by acting in series, because an antagonist to either agent alone blocks FDM rescue by brief goggle-removal. In this study, the hypothesis that NO prevents FDM in chickens through a DA-D2-receptor pathway was tested.
Methods: A series of dose response experiments was performed to determine the optimal doses of a
NO-donor, SNAP to prevent FDM, and a DA-D2R-antagonist, spiperone, to block the effect of 2-hr goggle-removal. Male chickens (1-10 day old) were maintained on a 12:12 hour light:dark cycle. One eye was goggled with a diffuser, while the fellow eye remained ungoggled as an internal control. Predetermined doses of SNAP (dissolved in 1% DMSO) and spiperone were administered separately and together in goggled eyes; control animals (injected with vehicle) had goggles on or off permanently. The drug was injected into the vitreous cavity of the goggled eye and 1x PBS vehicle into the ungoggled fellow eye, every second day for one week, under O_2-N_2O-isoflurane anesthesia. The day after the third treat-

ment, refractive error and eye size and weight were measured. Optimal doses of a DA-agonist, ADTN, and a NOS-inhibitor, LNIO, were also determined, and the reverse hypothesis that the DA-D2-receptor acts via NOS to prevent FDM was tested similarly. The protocol was approved by the University of Calgary Animal Care Committee, and the study was supported by an NSERC Discovery Grant (W.K.S.) and O'Brien Centre Summer Studentships (P.M., E.C.)

Results: The optimal doses (weight/injection) were: spiperone, 5 nmol; SNAP, 500 nmol; ADTN,
3 mM; L-NIO, 20 μM. SNAP or ADTN inhibited FDM, and spiperone or L-NIO alone blocked myopia-prevention by diffuser-removal. The inhibition of FDM by SNAP was not diminished by spiperone, but preliminary results indicated that the effect of ADTN was diminished by L-NIO.

Conclusions: Spiperone did not block the effect of SNAP, indicating that the inhibition of FDM by NO does not require downstream activation of DA-D2. L-NIO, however, did block the effect of ADTN, indicating that the inhibition of FDM by dopamine may require downstream activation of NOS. These findings enhance our understanding of the mechanisms underlying emmetropia and myopia and may lead to novel anti-myopia drug therapies.

Infection site evolution in Trichomonads

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Introduction: Trichomonads are an important group of anaerobic protists in both human and animal medicine. The Parabaslia phylum is a diverse group that encompass pathogens and commensals in numerous hosts that include mammals, birds, reptiles, amphibians and many others. There is sparse research in the area of comparative infection site specificity for this group. The focus of this paper is to examine host site evolution in this group.

Methods: A GenBank search was used to locate all trichomonad species with archived rRNA sequences for the gene ITS-1/5.8S/ITS-2. Data was collected on the infection host and site through the original or additional articles. A phylogenic tree with 48 final data points on infection sites was constructed using the MEGA5 computer program and host site evolution patterns were inferred through ancestral character state reconstruction using Mesquite V.2.75.

Results: Among the taxons included in this study, use of a genitourinary infection site appears to have evolved independently five times, lung infection site twice and a free-living state twice.

Conclusions: As a group, trichomonads appear to have evolved from infecting only the gastrointestinal tract to other anatomic sites via a series of independent evolutionary events. The limitations of this study include 1) using only a single gene to derive the phylogeny and 2) not all species were included due to missing information. As recent studies have suggested that the ITS gene used may not be the most suitable one to use for the study of this phylum so future studies could investigate a multigene phylogenic tree. Additional species, pathogenicity, protein evolution and function and host evolution could also be examined.

Nano-structured Brain Stimulating Electrodes: The Future of Neural Prosthetics?

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Introduction: The exceptionally promising field of neural interfaces and neural prosthetics relies on the successful electrical stimulation of nervous tissue through the use of electrodes. Current electrical stimulation therapies for various neurological disorders (i.e., deep brain stimulation for Parkinson's disease and cochlear implants for hearing loss) utilize these neural interfacing devices. A principal problem with current neural electrodes is their lack of stimulus selectivity due to large electrode size relative to the targeted neuronal population; however, as bulk electrode size is reduced, charge density increases, which may cause irreversible damage to both the electrode and the stimulated tissue. In an effort to find a balance between electrode size and charge density, our objective was to develop a novel iridium-nickel oxide bimetallic coating that could intrinsically offer high charge injection. Secondly, we attempted to nanostructure the surface of these coatings to create a higher surface/volume ratio, which would result in a higher extrinsic charge storage capacity than currently used stimulating electrodes.

Methods: Thermal decomposition was used to fabricate iridium oxide, nickel oxide, titanium oxide and bimetallic iridium-nickel oxide coatings on titanium substrate electrodes. Each

sample was investigated using cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS) and scanning electron microscopy (SEM).
Results: Experiments showed that specific iridium-nickel oxide coatings offered a significantly higher true, electrochemically-active surface area (i.e., higher roughness) than the currently used state-of-the art, iridium oxide coatings. These iridium-nickel oxide bimetallic coatings were also capable of delivering significantly more charge than the iridium oxide control, both from the intrinsic and extrinsic point of view.
Conclusion: Nano-structuring the surface of stimulating electrodes with a high surface area coating will assist in the miniaturization of neural electrodes. This will ultimately improve charge injection specificity and narrow the cyclization potential limits, decreasing the negative effect of the electrodes on surrounding tissue.

Does abdominal ultrasound show equivalence to Computed Tomography and Magnetic Resonance Enterography in predicting active Crohn disease and its complications?

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Background/Purpose: Crohn disease (CD) is an inflammatory disease of the bowel that requires imaging for diagnosis and surveillance. Ultrasound (US) is a radiation-free, cost-effective, and readily available modality that provides realtime assessment of the bowel in routine and emergent cases. Given the accuracy and safety of US, our objective was to demonstrate equivalence of US with computed tomography (CT) and magnetic resonance enterography (MRE) in detecting disease activity and complications in patients with established and suspected CD. We hypothesize that US can be used as a first-line investigative tool for routine diagnosis, surveillance and detection of complications in those with acute symptoms.
Methods: We analyzed 308 patients with known or suspected CD who had a positive bowel US exam with CT, CTE and/or MRE scans from May 2010-June 2013. Two reviewers, blinded to the pathology, evaluated the US images for active disease/complications. Disease was assessed with color Doppler or contrast-enhanced US (CEUS). Concordance was determined by the percentage of cases that showed agreement on US and the gold standard modality.
Results: US and gold standard concordance for disease activity were as follows: wall thickness-98.05%, blood flow-96.69% and inflammatory fat-87.13%. US correctly ruled in 84/86(97.67%) strictures, 53/54(98.14%) fistulae, 28/29(96.5%) perforations, 43/44(97.7%) phlegmon and 18/20(90%) abscesses. Real time US scanning identified dysfunctional peristalsis, fixed luminal apposition and bowel angulation strictures and partial bowel obstructions. Spatial resolution of US was superior in identifying perforations with phlegmon. MR was superior in predicting bowel wall edema and mucosal ulceration; insignificant difference between MR and US noted when determining active disease. Inflamed or perforated appendices were better visualized with US and but had 100% concordance to other modalities.
Conclusion: In patients with CD, our study shows that US is equal and occasionally superior to CT/CTE/MRE in its ability to predict disease activity and intestinal complications for routine evaluation, monitoring or acute presentations.

Treating donor site pain in burn victims that have undergone autologous split-thickness skin grafting: A review of the literature

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Introduction: Current standard of treatment for deep burn injuries is split-thickness skin grafting (STSG). STSGs are harvested from a remote area of healthy skin creating a new wound, which is referred to as the donor site. Pain, caused by harvest, is reported to be one of the most distressing symptoms following STSG. Resultant pain can affect early mobilization, sleep and the need for analgesics post-operatively. Although donor site pain presents a significant problem, there are no evidence-based guidelines concerning its treatment. The purpose of this literature review was to gather information on current practices for managing donor site pain and to determine whether further investigation of donor site pain management is warranted.

Methods: Ovid MEDLINE was searched using the terms 'burn', 'donor site', 'pain' and 'split-thickness skin graft' from 2003–2013. Only human studies were included in the review. Non-English language articles were excluded from the review.
Results: The literature review identified five techniques used in minimizing donor site pain. One technique initiated treatment prior to STSG harvest by infiltrating the pre-harvest site with a combined anesthetic/tumescent solution. Four techniques initiated treatment immediately following STSG harvest: 1) continuous subcutaneous local anesthetic infusion (CSLA); 2) subcutaneous injection of anesthetic; 3) application of topical anesthetic gels; and, 4) the use of ice packs. All studies measured pain using a visual analog scale (VAS). In a majority of these studies, subjects gave anecdotal reports of decreased pain at the donor site regardless of the technique used to treat pain. Few studies showed that the use of a particular technique significantly decreased VAS scores.
Conclusion: Although donor site pain is of chief concern for both the patient and the physician, its treatment is scantily addressed. This review highlights the need to design and carry out more rigorous and effective studies in order to work towards standardizing care and improving the patients' pain experience following STSG harvest.

Controlling inflammation to prevent the development of osteoarthritis following reconstruction anterior cruciate ligament and drill hole surgery

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Introduction: Severe injury to the knee joint, such as anterior cruciate ligament (ACL) tears and/or menisci damage, often results in accelerated development of osteoarthritis (OA). It is thought that there may be an injury-induced, mechanical abnormality of the injured joint and subsequent interplay between altered mechanics and/or biological changes, such as inflammation, which may lead to cartilage damage. Dexamethasone (DEX) is a synthetic steroid with anti-inflammatory properties that could be a possible treatment strategy for controlling inflammation. The purpose of this study was to characterize inflammation and joint mechanics following idealized ACL reconstruction (ACL-R) surgery after DEX injection.
Methods: A small pilot study was conducted in untrained sheep (n=2 ACL-R, n=2 controls). Surgeries involved an arthrotomy to the right stifle joint, with the left joint serving as the control. DEX was given immediately after ACL-R by an intra-articular injection (0.5 mg/kg body weight). Animals were sacrificed 2 weeks after surgery and tissues, synovial fluid and blood were collected. Gross morphological grading was conducted for gross cartilage defects, osteophyte formation, and meniscal damage. Histology of synovium was evaluated for microscopic changes with Hematoxylin and Eosin staining.
This pilot study is the start of a large-scale project: 20 sheep divided into three groups: ACL-R+DEX (n=8); ACL-R (n=8); and, controls (n=8). Furthermore, an *in vivo* motion analysis system (instrumented spatial linkage) will measure kinematics. mRNA expression of inflammatory cytokines will be measured by real-time polymerase chain reaction.
Results: Combined gross morphological score in the ACL-R+DEX group was lower than that of the control for cartilage damage/defects, osteophyte formation, and meniscal damage. Mean aggregate synovitis score consisting of sub-intimal fibrosis, intimal hyperplasia, and cell infiltration in the ACL-R+DEX group was similar to that of the control group.
Conclusion: Preliminary results demonstrate that even one injection of DEX immediately after ACL-R surgery is sufficient to completely block induction of cartilage damage and synovitis in this experimental animal model.

Characterizing hypoxic vascular lesions using susceptibility weighted MRI in a model of multiple sclerosis

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Introduction*:* Multiple sclerosis (MS) is an inflammatory and demyelinating neurological condition. Susceptibility weighted imaging (SWI) is a magnetic resonance imaging (MRI)

method that is sensitive to iron in hemosiderin, ferritin and deoxyhemoglobin (dHb) and that has detected lesions not seen with conventional MRI in MS patients. Previously, SWI has been used in the experimental autoimmune encephalomyelitis (EAE) mouse model of MS where two types of lesions were detected: 1) vascular lesions (or hypointensities), due to dHB; and, 2) parenchymal white matter lesions, due to iron deposition/demyelination. Here, we aimed to determine if vascular and parenchymal lesions could be differentiated using SWI by increasing the inspired oxygen to reduce dHb in the blood. Vascular lesions would alter in appearance with high oxygen, whereas parenchymal lesions would not.

Methods*:* Control and EAE mice were imaged at 9.4 T using 3D gradient echo with flow compensation (for SWI) with 30% O_2/70% N_2 then 100% O_2. A subset of mice were imaged with these gases and then after perfusion (to remove blood). Lesions were counted and compared between control and EAE mice, and the number of lesions seen with 30% O_2 was compared with the number that remained unchanged with 100% O_2. Iron deposition was assessed using DAB-enhanced Perl's staining.

Results*:* Most lesions (hypointensities) seen with 30% O_2 altered in appearance with 100% O_2 in control (p<0.001) and EAE mice (p<0.01). Hypointensities that changed in appearance with 100% O_2 also disappeared after perfusion, supporting that they are due to dHb. Parenchymal white matter lesions appeared dark in MRI and did not change in appearance with high oxygen.

Conclusions*:* Changing the inspired oxygen concentration differentiates between vascular and parenchymal lesions in the EAE model *in vivo*. This method can be applied in MS patients, paving the way to investigate the pathophysiology of venous hypoxia and iron deposition in MS.

Rebuilding the Calgary Student Run Clinic: A model for sustainability

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Introduction: Since May 2012, The University of Calgary Student Run Clinic (SRC) has been rebuilding and restructuring its programs in order to create a sustainable and diverse clinic model. The goal of the clinic is to provide high quality, accessible health care to low income, marginalized and/or homeless clients, as well as to provide educational opportunities and clinical exposure to medical students. **Methods:** Through an "umbrella" model, the SRC aims to act as a platform organization facilitating student involvement at multiple clinic sites. Each site offers services to a specific marginalized population, including children at a family emergency shelter, new Canadians at a refugee clinic, and older male patients experiencing addictions and homelessness on board a mobile clinic. Methods for sustainability include securing multiple sites, preceptors and funding sources. **Results:** Today's SRC utilizes a two-pronged approach to delivery of care, focusing on inter-professional collaboration to provide primary care to its patients in various clinic settings, as well as engaging in health promotion initiatives in the community. With respect to health promotion, the SRC has developed a literacy program, a child care program at the family shelter site, a health education series, a community services night for low income women, and is an active participant in a health and community fair for Calgary's homeless population. **Conclusions:** The SRC umbrella model has provided a framework for sustainability, both for its target population and for medical students and health professionals, where it provides a professional, engaging clinical experience. As a result, there has been a marked increase in capacity, with student participants growing from twelve to thirty. The number of permanent preceptors has increased from one to four, and the number of clinic sites has increased from one to three. This model has strengthened partnerships with the community and has led to increased opportunities for funding and expansion.

Viscosity of Lubricin: Effects of Concentration, Structure and Interaction with Hyaluronan

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Introduction: The viscosity (resistance to flow) of synovial fluid (SF) is essential for its ability to provide lubrication and cushioning to articular joints. Hyaluronan (HA) is a large gly-

cosaminoglycan that contributes significantly to the viscosity of SF. HA also works synergistically with lubricin (a mucin-like glycoprotein) to provide SFs lubricating ability. HA is currently used as an intra-articular treatment for pain relief of osteoarthritis (OA), a painful and debilitating disease affecting 13% of Canadians. Lubricin has demonstrated ability to slow cartilage degradation in animal injury models of OA; however, the viscosity of lubricin alone and lubricin+HA solutions are unknown. The objective of this study was to measure the viscosity of 1) lubricin alone, 2) lubricin with its naturally-occurring disulfide bonded multimers broken by reduction and alkylation (R/A), and 3) lubricin+HA solutions.

Methods: Viscosity analyses of lubricin±R/A, HA, and lubricin+HA solutions were performed with high molecular weight HA and lubricin purified from media conditioned by bovine cartilage explants.

Results: Lubricin, at physiologically normal concentrations, demonstrated concentration- and multimer-dependent shear thinning behaviour (decreasing viscosity with increasing rate of deformation, like paint); however, lubricin at low concentration and lubricin+R/A viscocities were similar to that of water. When lubricin was added to low concentrations of HA, viscosity increased in a manner independent of lubricin concentration but dependent on multimeric structure. Viscosities for lubricin+R/A and lubricin+HA were similar to those of HA alone.

Conclusions: These results demonstrate that the disulfide bonded structure of lubricin is essential in the unknown mechanism of lubricin+HA interaction. They suggest that intra-articular treatment with lubricin might increase the viscosity of diseased SF; this is the objective of current HA treatments. Characterization of the viscosity of lubricin+HA solutions will contribute to the understanding of SF function in health and disease, and will be necessary for new lubricin±HA biotherapeutic treatments.

Harmless Commensal Microbial Neighbours Synergistically Trigger Pseudomonas aeruginosa Virulence Genes in Cystic Fibrosis

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Rationale: Cystic fibrosis (CF) is the most common lethal genetic disease among Caucasians: 90% of CF patients succumb to pulmonary failure from chronic respiratory infections. Traditionally, research has focused on a narrow spectrum of microorganisms as principal pathogens, such as *Pseudomonas aeruginosa* (PA). The oropharyngeal flora (OF) have been implicated in enhancing pathogenesis of PA while acting as benign commensals, otherwise known as "synergens". These interactions may skew the balance between clinical stability and acute pulmonary exacerbation, leading to hospitalization. The objectives here were to evaluate these interactions and construct synergen mutants to identify the pathway(s) involved.

Methods: Seven oropharyngeal-derived microbes were isolated from sputum of adult CF patients (*Streptococcus*. sp, *Rothia*. sp and *Actinomyces*. sp) and screened *in vitro* for affecting PA virulence gene expression in co-cultures. The ability of these benign microbe synergens to stimulate PA virulence genes was evaluated using transformed PA reporters harboring luciferase constructs for known virulence gene promoters. The luciferase light production caused by the co-culture *vs*. monoculture of PA was monitored to quantify synergen activity by measuring changes in light production. Transposon libraries in the synergens were constructed with 8000 mutants screened.

Results: Up-regulation of PA virulence gene expression was seen for all seven synergens tested. The virulence pathways affected were for quorum sensing or bacterial communication. The highest up-regulation was by *Streptococcus*. sp, with 1800-fold increased virulence gene expression in co-culture as compared with PA alone. From 8000 synergen mutants, 526 were isolated as hits involved in co-culture. Sixty one of these mutants were conserved in all PA reporters, suggesting common interaction pathway(s) triggered by the synergens. Thirty five mutants displayed 10-fold or greater activation in co-culture as compared to the wild-type, demonstrating a gain-of-function mutation.

Conclusion: Seemingly harmless non-pathogenic oropharyngeal synergen microbes can trigger virulence genes in PA found in CF patients. The production of secondary signaling molecules have been shown to influence pathogen virulence profiles

by modulating bacterial cell-cell communication pathways. Understanding the way in which commensal microbes synergistically trigger virulence will lead to better treatment and management of CF.

Characterization of the aspartic protease, nepenthesin, as a therapeutic for the treatment of celiac disease

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Background: Celiac disease (CD) is a highly prevalent autoimmune disorder that is triggered by the incomplete digestion of immune stimulatory peptides in the gliadin fraction of dietary gluten. The basis for gliadin resistance to digestion is due to the abundance of P (~15%) and Q (~30%) residues in its protein sequence. Currently, no therapeutic product for CD exists but oral proteases aimed at efficiently digesting gliadin throughout the gastrointestinal tract have shown promise in advanced clinical trials. In this study, the potential of a novel aspartic protease from *Nepenthes* plant extracts, nepenthesin, whose properties appear suited for an oral protease therapeutic for CD was evaluated.
Methods: Both isoforms of nepenthesin (I and II) were recombinantly expressed in *E. coli* and purified from inclusion bodies. Functionality was assayed by comparing cleavage specificities of recombinant nepenthesins to native plant extracts. Gliadin was digested *in vitro* with various concentrations of recombinant nepenthesins under simulated stomach-like conditions and analyzed by LC-MS/MS. Digestion of a immunodominant 33-mer peptide was quantified by indirect ELISA.
Results: The cleavage specificities of native plant extracts vs. recombinant nepenthesins showed that cleavage N- and C-terminal to all residues are retained except cleavage C-terminal to proline. *In vitro* digestions of gliadin showed that the average length of peptides, including all immunogenic epitopes, decreased in a dose-dependent manner at clinically relevant nepenthesin doses as compared with leading clinical oral protease candidates. Quantification by indirect ELISA showed that the immunodominant 33-mer peptide within gliadin extracts was digested by nepenthesin in a dose-dependent manner. In addition, digestion maps show cleavage within all known immunogenic epitopes, including the 33-mer peptide.
Conclusions: Preliminary results from the identification and initial characterization of the first aspartic protease, which appears to efficiently process gliadin in all known immunogenic regions and act optimally in the stomach, supports nepenthesins potential as an effective oral therapeutic candidate for CD.

A model for chronic consequences of acute enteric infection: the role of pathogen-mediated disruptions in the intestinal microbiota

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Introduction: *Giardia duodenalis (G. duodenalis)* is a leading cause of water-borne infectious dysentery that is encountered worldwide. Following a number of recent outbreaks, the symptomology profile of giardiasis has been extended to include the development of both chronic and long-term gastrointestinal complications characteristic of post-infectious irritable bowel syndrome (PI-IBS). Despite its occurrence in upwards of 40% of individuals who have experienced previous enteric infection, the mechanisms underlying the generation of PI- IBS remain obscure. Disruptions in the normal species distribution of the intestinal microbiota in IBS patients have been observed, but remain incompletely characterized. Moreover, novel insights into the ability of enteropathogens to modify the phenotype of the mucosa-associated microflora, normally existing as a series of biofilm communities, must be expanded in order to fulfill an all-encompassing view of the poly-microbial interplay that can elicit gastrointestinal disease.
Objective: This study measured the presence of *G. duodenalis* in colonic biopsies to examine the impact of an acute enteropathogen on the structure, species composition, and resulting pathogenic profile of human mucosal biofilm communities.
Methods: Representative intestinal mucosal biofilms were cultivated from human colonic mucosal biopsy samples collected during routine colonoscopy procedures.
Results: *Giardia*-exposure results in a loss in diversity in the species composition of microflora biofilms, when compared to

control-communities. Additionally, *Giardia* promotes a phenotypic switch from the normal biofilm mode of bacterial growth, to planktonic growth in microflora biofilms via a disruption in normal extracellular matrix production, characteristic of biofilm communities. Finally, *Giardia*-exposed biofilm communities induce higher levels of enterocyte apoptosis, and promote changes in Caco2 monolayer permeability.
Conclusion: Human mucosal biofilm communities exposed to *Giardia* exhibit an alteration in the normal biofilm phenotype, as well as species composition. Furthermore, the detrimental effects of *Giardia*-exposed mucosal biofilms on enterocyte homeostasis outlines the potential consequences that complex poly-microbial interplay may have in initiating functional gastrointestinal disorders, such as PI-IBS.

The role of NCX in the regulation of endothelial-dependent flow-mediated dilation

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Introduction: Appropriate release of nitric oxide (NO) from the endothelium is critical for normal physiological functioning of the cardiovascular system. Although changes in intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$) due to Ca^{2+} influx are thought to lead to activation of nitric oxide synthase (eNOS) and the release of NO, the molecular mechanism(s) underlying endothelial Ca^{2+} influx is (are) poorly understood. Transient receptor potential (TRP) channel proteins are widely viewed as molecular candidates for the Ca^{2+} entry pathway; however, the non-selective nature of TRP channels for cations indicates that TRP channels can also act as a Na^+ entry pathway. Na^+ accumulation under the plasma membrane could then facilitate sodium-calcium exchanger (NCX) activity in the reverse, Ca^{2+} entry mode. Although NCX has been implicated as a Ca^{2+} influx pathway, its role in endothelial cells, specifically flow-mediated dilation (FMD) has not been elucidated. Here, the molecular mechanisms responsible for regulating endothelial $[Ca^{2+}]_i$ and their role in controlling NO production and release during FMD were characterized.
Methods: The effect of flow on arterial diameter was studied using pressurized myography in endothelium-intact rat cerebral arteries (RCAs). Co-localization of proteins was assessed using proximity ligation assay (PLA). A three-step method of western blotting was utilized to detect eNOS phosphorylation at Ser1177.
Results: The eNOS inhibitor, L-NAME, significantly reduced the magnitude of FMD, suggesting a role for NO in FMD. Inhibition of endothelial NCX by intraluminal perfusion of KB-R7943 or 6H2 NCX antibody also significantly reduced FMD. Moreover, FMD was associated with the phosphorylation of eNOS at serine 1179, which was inhibited in the presence of NCX blockers. PLA data indicated the presence of TRPV4/C1-NCX1 co-localization in intact RCA endothelium.
Conclusions: Our findings provide unique insight concerning the molecular mechanisms underlying regulation of endothelial $[Ca^{2+}]_i$ and FMD. The data suggest that a TRP-NCX signaling complex mediates Ca^{2+} influx, leading to a rise in $[Ca^{2+}]_i$, activation of NOS and release of NO to evoke cerebral arterial FMD.

Psychosocial stress partially mediates the association between race and prenatal depressive symptoms in a sample of pregnant women in Alberta

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Introduction: Prenatal depression is a serious maternal-child health concern and risk factors and health consequences appear to be more prevalent in Aboriginal communities and among ethnic minority groups; however, research on these populations is limited. The following research questions were examined: A) How do pregnant Aboriginal women, ethnic minority women and white/Caucasian women compare on levels of depressive symptoms, and on major risk and protective factors? B) Is non-dominant race associated with higher de-

pressive symptoms? C) Through what pathways does race operate to contribute to depressive symptoms?
Methods: Data were from the *All Our Babies* study (n=3354 pregnant women from Alberta recruited between 2008-2011). Depressive symptoms were measured with the Edinburgh Postnatal Depression Scale (EPDS). Descriptive statistics and multivariable regression methods were used to assess the following hypotheses: Aboriginal and ethnic minority women would have significantly higher mean EPDS score estimates relative to white/Caucasian women. The association between race and EPDS score was hypothesized to be partially mediated by risk factors such as social and economic factors, health background, negative life experiences, including discrimination and domestic violence, and psychosocial stress. Potential confounders were age, marital status and parity. Protective factors (diet, social support and optimism) were hypothesized as buffers between stress and depressive symptoms.
Results: White/Caucasian women appeared to have higher incomes, better employment, higher social support and higher levels of optimism, and have significantly lower depressive symptoms. The association between race and depressive symptoms appeared to be partially mediated by socioeconomic factors and psychosocial stress; the attenuation with addition of stress in the model, in particular, was quite striking. Race remained highly statistically significant as a predictor.
Conclusion: Mental health inequities between pregnant white/Caucasian women and other women are driven by social inequities. A better understanding of the determinants of prenatal depression in specific populations may facilitate more effective public health and clinical interventions.

Kawasaki disease disguised as retropharyngeal abscess

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Introduction: Kawasaki disease is an acute and self-limited inflammatory vascular condition of undetermined etiology that primarily affects young children and infants. Cardiac complications of the disease can be severe and life threatening; however, the risk of the most severe cardiac complication, coronary artery aneurysm, can be significantly reduced by treatment with intravenous immunoglobulin (IVIG) within a 10-day window of fever onset. A prompt diagnosis is essential in ensuring good outcomes. In order to diagnose Kawasaki disease, clinicians rely on a classic pattern of symptoms; however, many children present with non-specific findings or symptoms that mimic other disease processes. In these cases, erroneous diagnoses may lead to delay in treatment of Kawasaki disease.
Case Description: A 3-year-old unimmunized boy presented to hospital with four days of fever, irritability, and neck pain. On physical exam, the child was febrile, had a rigid neck and bilateral non-purulent conjunctivitis. Laboratory and radiological findings were consistent with retropharyngeal abscess and the patient was started on intravenous antibiotic therapy. Despite 48 hours of intravenous antibiotics, the patient remained febrile. His symptoms slowly began to evolve - he developed prominent right anterior cervical chain lymphadenopathy, bilateral edema of the hands and a polymorphous rash. A diagnosis of Kawasaki disease was made. While the patient had a normal echocardiogram and a positive treatment outcome, appropriate high-dose aspirin and IVIG therapy was delayed by four days because of the atypical presentation.
Conclusion: Unusual clinical symptoms and radiographic findings in Kawasaki disease can be misleading and may contribute to delayed diagnosis and treatment. By recognizing that Kawasaki disease can initially present with specific head and neck manifestations such as retropharyngeal abscess, physicians may consider the diagnosis sooner, ultimately reducing the risk of cardiac sequelae in affected children.

Frontal Lobe Epilepsy Alters Functional Connections Within the Brian's Motor Network: A Resting-state fMRI Study

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Introduction: Patients with frontal lobe epilepsy (FLE) often experience motor deficits. Previous studies have associated impairments in patients with epilepsy with changes in resting-state connectivity; a technique that examines temporally-correlated brain regions at rest using modalities such as functional magnetic resonance imaging (fMRI). It is not known whether patients with FLE have altered motor networks, and if such alterations could contribute to functional motor deficits; therefore, resting-state motor networks were examined in participants with FLE using fMRI.

Methods: Thirteen patients (seven right FLE, six left FLE) and ten control participants were examined. While in the MR scanner, participants concentrated on a fixation cross for five minutes. fMRI data was analyzed using FSL. First, the left and right sensorimotor cortices were identified as regions of interest (ROI). The average BOLD signal from voxels in the ROI was compared to every voxel in the brain to determine the temporal correlation between BOLD signals. Mean maps were generated for each group and compared to determine voxels exhibiting a significant difference ($Z>2.3$, corrected cluster significance $p=0.05$). Laterality indices from resting-state maps were calculated for each patient and correlated with years since diagnosis, lifetime seizures, seizures in past year, and months since last seizure to determine significant relationships.
Results: Patients with FLE had significantly decreased connectivity between the left and right sensorimotor cortices compared with controls ($Z>2.3$). Laterality indices were significantly correlated to total lifetime seizures (left FLE: $r_s=0.89$, right FLE: $r_s=1.00$). As patients experienced more seizures, the healthy hemisphere sensorimotor cortex became less connected to the epileptic hemisphere sensorimotor cortex.
Conclusions: Resting-state motor networks are altered in patients with FLE compared with controls, and differences become more pronounced when patients had experienced more lifetime seizures. These results have important implications for understanding the mechanisms behind daily motor deficits experienced by patients with FLE.

Evaluation of haptic controller dexterity with regards to driving surgical performance in teleoperated robotic-assisted surgery

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Introduction: In robotic-assisted surgery, the surgeon's interface is the component connecting the surgeon to their tools and environment. The interface is required to be responsive, intuitive, and ergonomic in order to optimize the advantages of robotic systems, and streamline transition from conventional surgical techniques. It can represent a significant bottleneck if not designed appropriately, which would correlate negatively for patient outcomes. Surgeons require precision hand controllers that provide kinesthetic and in some cases tactile feedback, which also feature a wide range of motion and ergonomic considerations. Robotic systems without the sense of touch (haptics), have been recently introduced into medicine (e.g., da Vinci, Intuitive Surgical Ltd). The lack of haptic interaction has been identified as a major drawback of most current robotic-assisted surgical systems, and a satisfactory solution has yet to be developed. The purpose of this study was to evaluate existing haptic devices and drive design considerations for the development of a new surgical interface created specifically to enable robotic-assisted surgery.
Methods: Seven commercially available haptic hand controllers were procured for this study. Previous literature and experience within the neuroArm team identified dexterity as a key metric of haptic controller performance. Study design and performance metrics are also outlined for a future trial involving surgeons from numerous surgical disciplines immersed in simulation-based (virtual reality) surgical skill-testing scenarios. The project consists of several components: quantitative analysis, where dextrous workspace analysis of each hand controller was conducted; empirical study, via performance evaluation through simulation-based test-cases performed by surgeons from multiple surgical disciplines; subjective assessment, in which qualitative assessment of user-perceived performance was considered. We assessed performance based on several metrics: task completion time, errors (e.g., excessive force and slip), clutching frequency, path deviation from optimal trajectory and total traveled trajectory.
Results: Results included dexterity quantification in the form of isodexterity mapping and global conditioning indices, which showed that the hand controllers with greater ranges of motion also had lower values of GCI.
Conclusion: Further study will investigate how this correlates with performance in surgical scenarios.

Giardia cathepsin B proteases degrade interleukin-8 and attenuate neutrophil chemotaxis.

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Introduction: During acute inflammatory responses, the secretion of interleukin-8 (CXCL8) by intestinal epithelial cells (IECs) recruits extravasted neutrophils (PMN) to the basolateral membrane of the intestinal epithelium. Several parasitic organisms modulate aspects of their host's acute inflammatory immune response. *Giardia duodenalis* is a non-invasive protozoan parasite of the upper small intestine of many animals including humans. During *Giardia* infections, the small intestinal mucosa is devoid of signs of overt inflammation despite trophozoite numbers exceeding 10^6 per centimetre of intestine. Moreover, infections have been associated with decreased intestinal inflammatory responses via unknown mechanisms. The *Giardia* genome contains genes for 23 cathepsin-like cysteine proteases, most of which have no known function. The purpose of this study was to determine if *Giardia* cathepsin-like cysteine proteases modulate CXCL8 secretion from IECs and attenuate CXCL8-induced PMN chemotaxis.
Methods: *Giardia* trophozoites (assemblage A: NF, WB or assemblage B: GS/M) were co-incubated *ex vivo* with small intestinal mucosal biopsy tissues or *in vitro* with Caco-2 monolayers. After 2 hours, groups were administered recombinant interleukin-1β (IL-β) (1.0 ng/ml), CXCL8 (1.0 ng/ml), or *Salmonella typhimurium* (MOI 100:1). Samples were processed for various assays, western blotting, qPCR, and PMN chemotaxis assays.
Results: Co-incubation of assemblage A *Giardia* trophozoites with small intestinal mucosal biopsy tissues or *in vitro* Caco-2 monolayers resulted in attenuation of IL-1β-induced CXLC8 secretion; similar results were obtained when Caco-2 monolayers were apically administered *S. typhimurium*. *Giardia* assemblage A trophozoites decreased levels of recombinant CXCL8 administered to supernatants in the presence or absence of Caco-2 monolayers, while *Giardia* assemblage B trophozoites did not. Inhibition of cathepsin B proteases prevented assemblage A trophozoites from degrading CXCL8. Supernatants from the co-incubation of *Giardia* assemblage A trophozoites and Caco-2 monolayers with CXCL8 significantly attenuated CXCL8-induced PMN chemotaxis; these effects were reversed when cathepsin B activity was inhibited in *Giardia* trophozoites.
Conclusion: *Giardia* assemblage A cathepsin B-like proteases degrade CXCL8 and attenuate CXCL8-induced PMN chemotaxis.

Exploiting the Immunomodulatory Capacity of the Rat Tapeworm Hymenolepis diminuta to Treat Colitis

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Background: Epidemiological and proof-of-principle data support the concept of helminth therapy for several autoimmune disorders prevalent in Westernized societies. One goal is to isolate and characterize immunomodulatory molecules from parasitic helminths for drug development. We utilized the *Hymenolepsis diminuta* (*H. diminuta)*-mouse model system to explore novel anti-inflammatory possibilities. We hypothesize that one or more anticolitic molecules can be isolated from *H. diminuta*. To test this, mice are infected with *H. diminuta,* or injected with a crude extract thereof (HdAg), and the impact on dinitrobenzene sulphonic acid (DNBS)-induced colitis assessed.
Methods: Male Balb/C mice (n=7-8/group) were treated as follows: (1) infected with 1, 3 or 5 cysticercoids of *H. diminuta* and colitis induced 8 days later with DNBS (3 mg in 100 μL 50% ethanol., ir.); (2) given one injection (ip., sc. or im.) of 1 mg of PBS-soluble HdAg 6 h after DNBS; or, (3) given 10 μg, 100 μg or 1 mg of HdAg ip. 6 h after DNBS. Mice were monitored daily for 3 days, then necropsied and colitis assessed.
Results: Infection with even one *H. diminuta* protected mice from DNBS-induced colitis. This anticolitic effect was accompanied by increased IL-4, IL-5 and IL-10, typical of the mammalian helminth infection response. Moreover, a single ip. or sc. (but not im.) injection of HdAg was as effective as a prophylactic as viable 5 cysticercoid infection of *H. diminuta* at inhibiting DNBS-induced colitis. A threshold dose of 100 μg HdAg was needed for significant colitis inhibition.
Conclusion: The rat tapeworm, *H. diminuta*, is identified as a remarkably potent anticolitic stimulus of DNBS colitis. We conclude that (a) infection with viable *H. diminuta* could be developed as a therapy for IBD, and (b) that *H. diminuta* has at least one effective anti-colitic molecule, the isolation and purification of which could result in a novel therapeutic immunomodulator.

Multimodal Quantitative MR Imaging in Acute Ischemic Stroke: Mapping Tissue Fate

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Introduction: Stroke therapies are available within a "time window" (4.5 hours) of stroke onset with concerns about hemorrhagic transformation. We hypothesized that quantitative (q) implementations of conventional T1- and T2-mapping with magnetic resonance (MR) imaging could provide a more accurate depiction of tissue at risk of dying. Prediction of tissue fate is a step towards a "tissue window" paradigm of therapy where response to treatment is stratified by the "tissue properties" of ischemic brain.
Methods: Acute ischemic stroke patients were imaged within 6 hours of symptom onset and at 24 hours with a 3 T MR scanner. T1 mapping was performed with a 3D-GRE-LL sequence (22 phases) or a DESPOT1 sequence (two spoiled-gradient acquisitions). T2 mapping was performed using a CPMG sequence with 8 echoes (30 ms intervals) or 16 echoes (15 ms intervals). Typical diffusion-weighted imaging was also performed to provide apparent-diffusion coefficient (ADC) maps. Volumetric and absolute value analysis of the infarct core was conducted on the ADC, T1 and T2 maps.
Results: Fourteen patients were included with a median time from onset to first MR exam of 228 min. Eleven had detectable ADC lesions; median infarct volume on ADC increased from 13 ml at baseline to 29 ml at 24 hours. Nine patients had visible qT2 changes. Eight patients showed early qT1 changes. Distinct differences in ADC, qT1 and qT2 evolution were observed: qT1 reversal occurred in three patients; qT2 changes increased in all patients by 24 hours; qT1 and qT2 depicted changes in different areas of the suspected ischemia compared to ADC.
Conclusion: Distinct qT1 and qT2 changes occur in response to acute ischemic stroke. The presence of qT2 concurrent with reduced ADC suggests a more complicated process than cytotoxic edema, with the influence of blood-brain barrier compromise. These findings suggest qMR can define ischemic tissue properties, and may help in determining tissue fate.

A comprehensive case study of an orthopaedic surgery referral service in the Winnipeg Regional Health Authority: A single-entry model to manage waiting times for total joint replacement surgery of the hip and knee.

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Introduction: Single-entry is a wait time management strategy that consolidates multiple queues into one. When used for surgery, patients are referred to see the next-available surgeon. Gaining popularity across Canada, single-entry models (SEMs) have been shown to reduce wait times and improve patient experience but it is not clear how this model affects other aspects of quality of care such as acceptability, appropriateness and safety.
Methods: The Winnipeg Central Intake Service (WCIS; a SEM for hip and knee replacement) will be evaluated using a pre/post case study approach. Semi-structured telephone interviews will be conducted with multiple stakeholders: patients; family physicians,;surgeons,; surgical office assistants; and, those who designed the WCIS. Regression analysis will be applied to administrative data to measure changes in quality of care. This will be based on six dimensions of quality - acceptability, accessibility, appropriateness, effectiveness, efficiency and safety - and 20 quality of care indicators. Subsequent interviews (Round 2) and data analysis in 2014 will provide greater insight into the uptake, acceptability and performance of the model.

Results: Seventy stakeholder interviews have been completed (Round 1). Policy-makers and patients are in favour of the model because of reduced wait times and better availability of information related to patient care (appointment dates, preparation for surgery, etc.). Family physicians and surgeons appreciate the streamlined referral process but remain concerned about loss of autonomy and question the model's ability to permanently improve access. Surgical office assistants were initially opposed and faced an increase in administrative workload, but with ongoing support from the WCIS team and simplified processes, they are optimistic. Greater emphasis on assessment of capacity for change and readiness would have improved initial uptake and awareness among stakeholders.
Conclusion: Stakeholder expectations have been divergent and acceptance of SEMs has been conditional not universal. Continual improvement based on stakeholder feedback will be critical for sustained success.

Should pollution be considered when identifying human and animal populations at high risk for emerging infectious disease?

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Objectives/Introduction: Emerging infectious diseases (EID) have important impacts on human health and animal conservation and productivity. Most recent human EIDs are of animal origin. Organizations worldwide are focussed on predicting high risk areas of disease emergence to enable preparedness for EIDs before clinical and population impacts. Although it is known that exposure to chemical pollutants can cause immunomodulation in both humans and animals, little effort has been focussed on determining if pollution is a shared environmental exposure for EID risk.
Methods: A scoping literature review was undertaken to determine whether data and experiences in human and veterinary medicine supported the hypothesis that variation in environmental contaminants could affect vulnerability to EIDs. We also took a more in-depth look at the body of knowledge surrounding four cases.
Results: (1) Synergies and/or associations between rates of infectious diseases and levels of patient contamination could be found in both the veterinary and medical literature; (2) these trends could be found for multiple different species, exposure routes, diseases, and pollutants; (3) some associations could be found for the same contaminant in both people and animals; (4) biologically plausible and demonstrable mechanisms for these associations were present in the literature; and, (5) pollution patterns are not homogenous globally and some of the more highly polluted regions have experienced EID events.
Conclusions: The literature supported our hypothesis and suggested that pollution tracking and control should be managed in concert with medical and veterinary programs intended to predict EID risk globally and reduce the impacts of infectious diseases.
This work was funded by the Dr. D. Grant Gall Award in Global Health

Role of Serine Protease Inhibitor (SERPINB3) in Radiation Response in Squamous Cell Carcinoma of the Cervix

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Introduction: Cervical cancer remains a significant global health problem: it is the second leading cause of cancer death in women worldwide. Currently, the primary treatment for patients with locally advanced disease (FIGO IB2-IVA) is high dose radiotherapy (RT), with chemotherapy. Unfortunately, a subset of patients are not cured, likely due to radiation resistance. There is an urgent need to develop better prognostic and predictive information for response to RT, in an effort to improve patient outcomes and reduce toxicities. The aim of this project is to identify and validate the candidate radiation response tumour biomarker SERPINB3 (a serine protease inhibitor found to protect tumors from apoptosis) in clinical specimens, and determine its role in clinical outcome in patients treated with RT.
Methods: Patients treated with radical RT for locally advanced cervical cancer were identified from a retrospective database; pre-treatment formalin-fixed paraffin-embedded tumour biopsies were retrieved. Cervical cancer specimens that passed GeneChip and Data QC were further tested: eleven non-responder samples (patients with cervical cancers that did not respond to RT) were evaluated versus twelve responder samples (patients with cervical cancers that responded to

radiation). These raw scores were analyzed with SERPINB3 probe sets in SPSS statistical software. Parametric and non-parametric analyses of these scores were correlated with histological, overall survival (OS) and progression-free survival (PFS). Finally, real time PCR analysis on ten cervical cancer specimens and normal cervix (control) were used to verify microarray dataset.

Results: Our microarray dataset demonstrates SERPINB3 levels were upregulated in responders and down-regulated in non-responders. This data was further supported by statistical analysis in which higher levels of SERPINB3 was correlated significantly (p=0.033) with responders. Furthermore, patients with higher levels of SERPINB3 (6.77-362.43) demonstrated significantly (p=0.000) better overall and progression-free survival (p=0.001). Real-time PCR results on ten blind cervical cancer specimens demonstrate similar results when compared with normal cervix data.

Conclusion: In this pilot study, we found that SERPINB3 was upregulated in responders and was associated with better clinical outcome. Follow-up with a larger dataset will be required to confirm these findings. In addition, further studies are required to determine the molecular role of SERPINB3 in response to RT.

A Systematic Literature Review of the Trail-Making Test and its Effectiveness in Identifying Cognitively Impaired Drivers

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Introduction: The medical community is well-placed to identify cognitively-impaired drivers who may no longer be safe to drive; however, the validity of commonly used screening tools for identification of cognitive impairment for *decisions about driving* is not well established. The primary objective of this research was to examine the accuracy of the Trail Making Test (Parts A and B) [TMT] for determination of driving competency.

Methodology: Using established systematic review methodology, a search of six electronic databases was conducted, with studies from database inception to June 2011 included. Key terms to identify studies using the TMT as a predictor variable for driving performance were used, with pre-defined inclusionary/exclusionary criteria used for study selection. Rigorous full-text review with data extraction was conducted by both investigators blinded to each other's results.

Results: From an initial sample of 4,441 studies, 30 articles met the inclusionary/exclusionary criteria and were included in the systematic review. The results from the 30 empirical studies yielded 46 unique data points. The majority (n = 36) of data points had on-road evaluation as the outcome measure, with 10 data points having crashes (n = 5) or simulator results (n = 5) as the outcome measure. The vast majority of studies relied on correlational analyses, with only four studies using cutpoints. Only one of the four studies using cutpoints examined sensitivity and specificity, with a reported sensitivity of 45% and a specificity of 86%.

Conclusion: The results from the 30 empirical studies reveal that TMT-A and -B scores are *associated* with driving outcomes; however, knowledge of that association provides little in the way of information for decision making on driving competency in the clinical setting. Without the aid of empirically determined cut points, the use of the TMT for decision making on medical fitness to drive is questionable.

Does Land-Based Exercise Decrease Pain and Improve Function in Hip Osteoarthritis Patients? A Systematic Review and Meta-Analysis

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Introduction: Therapeutic exercise is commonly prescribed as treatment modality in the management of lower extremity osteoarthritis (OA). To date, however, there is conflicting evidence as to whether exercise is effective in reducing pain and improving function in hip OA patients. Given the disparate findings, the purpose of the present study was two-fold: 1) to determine whether land-based exercise is an effective intervention for decreasing pain and improving function in individuals with hip OA; and, 2) to determine whether semi- tailored exercise programs are more efficacious than generic exercise interventions with respect to pain and function outcomes.

Methods: Systematic review and meta-analysis of randomized controlled trials (RCTs) compared land-based exercise to a control intervention in people with hip OA not awaiting surgery. Group means, standard deviations and sample sizes were extracted from each study. From these data, mean differences, standardized mean differences (SMD = mean difference divided by the pooled standard deviation) and their 95% confidence intervals were calculated. When ≥2 studies measured the same outcome at time points within 6 weeks of each other, meta-analyses of their SMDs were performed. Confidence intervals that included zero were interpreted as having no effect. The PEDro quality index scale was used to determine the quality of the evidence.
Results: Eight RCTs involving 570 participants with hip OA were identified and included in the review. The eight identified RCTs scored an average of 7.5/10 on the PEDro quality index score indicating sound methodological quality. Pooled data revealed that exercise interventions had no effect on pain outcomes (SMD = -0.15 (-0.60 to 0.29) post-intervention or at follow-up (SMD = -0.15 (-0.55 to 0.25)) when compared with controls and no effect on self-reported function post intervention (SMD = -0.10 (-0.41 to 0.22), at 6-months (SMD = -0.13 (-0.43 to 0.18) or 10-12 months follow-up (SMD = -0.15 (0.55 to 0.26) and no effect on performance-based physical function. When only those studies that prescribed a semi-tailored exercise program were considered, data pooling of three studies revealed that exercise resulted in moderate improvements in pain (SMD = -0.78 (-1.21 to -0.35)) immediately post-intervention.
Conclusions: Low risk of bias studies provided no evidence of an effect of land-based exercise on pain and function (both self-reported and performance-based) post-intervention; however, exercise that is based on patient assessment findings (semi-tailored) does appear to impart a moderate beneficial effect on pain post-intervention and should be considered an important component of exercise based interventions in hip OA populations.

Dynamic Link Between Communication and Computation in an in vitro model of the human temporal neocortex.

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Objectives/Introduction: The role of theta frequency inter-laminar oscillations of the human neocortex and their role in the coordination of communication and computation is not well understood. We hypothesized that the requisite circuitry for both local computation and long-range communication should overlap and be related in a dynamic and functional way.
Methods: Electrical activity was measured from dual electrophysiological recordings from the deep and superficial lamina of human temporal neocortical slices resected during surgery for epilepsy. Cross frequency coupling (CFC), which is thought to represent a neural code implicated in local neuronal computation, and a variety of behavioural and cognitive correlates such as spatial awareness, sensation and memory were measured. Inter-regional oscillatory coherence is thought to be marker for long-range communication, and is encapsulated in what is known as the communication through coherence (CTC) hypothesis. Phase-dependent power correlations (PDPC), which was generated from the CTC hypothesis, were measured..
Results: There is a strong correlation between the strength of CFC and CTC between trials of oscillatory activity at theta (4-15 Hz) frequency. This correlation was particularly marked between CFC in the deep cortical layers and CTC between layers, indicating that deep layers may play a preferential role in driving inter-laminar communication.
Conclusions: For the first time, a quantitative correlation has been demonstrated between local computation and long-range communication. This result supports further research into an integrative approach to studying brain activity, whether *in vivo*, *in vitro* or *in silico*. Furthermore, such communication occurs at theta frequency, a frequency well known to be involved in both interlaminar and cortical-subcortical communication processes.

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A Prescription that Addresses the Decline of Basic Science Education in Medical School

Abstract

Over 30 years ago a cry rang out through the proverbial halls of academia; "The clinician scientist is an endangered species." These prophetic words have been reverberated in the ears of every specialty and every general medical organization in deafening tones. Why is the role of the clinician scientist or clinician investigator so important that this phrase has been repeated subsequently in medical and educational journals? Simply put, the clinician scientist bridges the ravine between the ever-growing mountain of scientific knowledge and the demanding patient centered clinical care. Here, we describe the current educational model established by the University of Calgary, Leaders in Medicine Program. Our program seeks to train future physicians and clinician scientists by incorporating training in basic science, translational and clinical research with clinical and medical education in a longitudinal program to students of traditional MD/PhD, MD/MSc or MD/MBA stream as well as interested Doctor of Medicine students.

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Over 30 years ago a cry rang out through the proverbial halls of academia; "The clinician scientist is an endangered species." These prophetic words have been reverberated in the ears of every specialty and every general medical organization in deafening tones. Why is the role of the clinician scientist or clinician investigator so important that this phrase has been repeated subsequently in medical and educational journals? Simply put, the clinician scientist bridges the ravine between the ever-growing mountain of scientific knowledge and the demanding patient centered clinical care.

The role of the clinician scientist becomes more poignantly emphasized in the medical profession as changes in schools of medicine continue to occur. In April 2012, an editorial published by The Lancet entitled the "Catastrophic neglect of the basic sciences in medicine" [1] outlined the systematic erosion of basic sciences in medical schools through multiple politically driven policies. The authors felt that neglect and marginalization of the basic medical sciences in medicine will have damaging and far reaching effects on clinical care [1]. To quote the authors parting sentiments;

"The basic science of medicine, and the future of safe and effective patient care, relies on smart people working in laboratories to answer questions about which they are passionate. We seem to have forgotten that lesson. We need to relearn it quickly."[1][1]

Clearly, as we see further advances in the scientific literature and the absence or dilution of the basic sciences in our medical schools, it becomes imperative that we graduate physicians skilled in both clinical medicine as well as the basic sciences to bridge the widening gap between scientific literature and clinical care. Thus enters the clinician scientist. The clinician scientist, trained with the academic rigor of graduate studies melded with the frontline medical skills of physicians and surgeons, is perfectly poised to facilitate the translation of knowledge from the basic sciences to the clinical practice, while providing the observations of clinical practice that form the basis for further research and innovation. This type of individual fulfills the vision early medical educators must have had of the future of medicine. In the sections that follow, we provide an overview of our approach: (1) to generate such 'dually-trained' physicians and (2) to remedy with the decline of the teaching of the basic sciences in our medical schools, not only for our combined program trainees but also for our MD class in general. Our approach is embodied in our Leaders in Medicine program; thus, our overview is focused primarily on our own experience at the University of Calgary Faculty of Medicine, and is not intended to provide a general overview of the MD-PhD program.

The Leaders in Medicine (LIM) program at the University of Calgary was established to facilitate the training of clinician scientists. This joint degree stream allows interested individuals to pursue the doctor of medicine degree while simultaneously obtaining either a PhD, MSc or even an MBA, in an integrated, protected training stream and is the penultimate realization of incorporating scientific and medical education envisioned by Flexner in his report of 1910 [2].

Training research-oriented physicians

The Flexner report, which revolutionized medical education, still has a major impact on the way we select and train our physicians of the future. Flexner was acutely aware of (1) the importance of evidence-based data as an essential component of clinical practice and (2) the key role for research in advancing medical care [2]. What he did not deal with was the critical issue of ensuring the life-blood of the enterprise that is necessary (1) to generate new knowledge that will mitigate the negative impacts of disease; and, (2) to take the disease-altering discoveries (whether derived from 'test tube' studies or from patient sources) to bear on the needs of a general patient population. For that process to thrive, our medical faculties must foster all of the three personality types that are necessary for developing the 'new knowledge' for improving human health, as described by Goldstein and Brown [3]: (1) the individual involved in curiosity-oriented 'basic research'; (2) the individual focused on 'disease-oriented' research that does not directly involve patient participation (e.g., dealing with cell cultures, tissue samples or clinical-epidemiological data); and, (3) the individual who works directly with patients, either to gain insight into their pathology or to implement and test new therapeutic modalities in the clinic – the illusive clinician scientist. The goal of our LIM program is to develop all three types of individuals who will be 'bilingual'- in terms of human pathophysiology and in an allied discipline that will generate new approaches for improving human health.

The development of individuals in the first two categories listed above (basic and disease-oriented research) appears secure; however, those in the third category, research-trained physicians who work directly with patients, are perceived as an 'endangered species' [4]. Much has been written about the challenges of fostering clinical investigators who do patient-oriented research [3, 5, 6] and we believe that part of the answer to addressing this issue is to capture the imagination of our trainees early on to develop the passion for research that is one of the 'Ps' (Passion, Patients and Patience) that Goldstein and Brown suggest are the essential traits for a successful clinician scientist involved in patient-oriented research [3]. In our

LIM program, our goal is to develop that passion in those who will fit into all three research categories outlined above, including the patient-oriented 'clinician scientist'.

To generate that passion for furthering the future of biomedical research, we involve our students in several programs: (1) research-in-progress sessions, in which each trainee presents their research work or new ideas; (2) translational research rounds, which emphasize patient-oriented research and converting new basic science into enhanced patient care; and, (3) a visiting speaker series, developed by the trainees to host research-oriented physicians who present the latest in important areas of current biomedical research and who interact directly with them in an informal setting as clinician-scientist role models. Finally, our trainees organize an annual 'Research Day' that highlights work done not only by our LIM students but also by those in our MD class at large who are also engaged in research activities during the academic year. These student-led programs have had a substantial impact on all of the MD trainees in our faculty: (1) amplifying the basic science component of their education; and, (2) raising the profile and impact of clinically-oriented research in general. We believe that this prescription for capturing the imagination of our LIM students is not only creating a passionate 'ownership' in our LIM trainees for furthering the future of biomedical research, but is also responsible for a positive 'bystander effect' that is furthering the commitment to research endeavors in all of the other MD trainees in our student population.

The LIM Program, supported by the Graduate Science Education Department within the Faculty of Medicine at the University of Calgary is run largely by the students. The program has grown to 90-125 students per year (Fig 1). At present there are 63 active joint degree students (MD/MSc or MD/PhD) and 58 Affiliate (medical degree only) students. The program has evolved continuously over the years, based on student input, and directly addresses the "catastrophic neglect of the basic sciences in medicine". To enter the joint degree program a student must be accepted into both the medical school and a graduate program at the University of Calgary. Students can apply to the medical program any time before or during graduate school. The Affiliate Program was initiated at the request of the medical student body. The Affiliate Program was initiated at the request of the medical student body and welcomes all students, including those that have already completed graduate degrees, to attend and participate in all LIM activities. On average, 20% of students that enter into medical school in Canada have a graduate degree [7], including our students in the LIM Program (via the Affiliate Program), and this increases the depth and diversity of our LIM student body. The Affiliate Program has allowed students with interests in basic science or other pillars of science to continue, or to enhance, their interests by interacting with like-minded students and staff. A number of our Affiliate students who do not yet have a graduate degree take advantage of our LIM program to step away from their MD curriculum to pursue a joint MD/MSc or MD/PhD and then later re-enter the medical school stream.

The unique aspect to the University of Calgary Medical School is that it accepts applicants who are currently in graduate school. Many medical schools in Canada do not allow this and require students to complete their graduate degree before entering into medical school. We feel it is restrictive to bar students from applying to medical school during graduate work, since most students that gain entry to medical school apply more than once: on average, a student who gains entry into medical school in Canada has applied 3 times [8]. At other universities, a student keen to pursue an MD and PhD, for example, will do 4 years of undergraduate work then 4-6 years of graduate studies (PhD) before even being eligible to apply to medical school. If all goes well, with no delays, the 18 year old high school student will be 26-28 years old before they can possibly get into medical school, and if they have average success at getting in then they will be 29-31 years old making them older than the average medical student at most universities in Canada [7, 8]. If they do not get into medical school on their first attempt, then these students can be left in limbo. Some go back and redo undergraduate courses to raise their marks, some are underemployed and some commit themselves to a post-doctoral program. Another possible constraint in the training of clinician scientists is the rigid format of joint degree completion, usually consisting of a 4-year window for graduate studies flanked at the beginning by 2 years of pre-clerkship medical studies and at the end by 2 years of clerkship. The average completion for a conventional PhD in North America is well above 4 years, and therefore this strict timeline might persuade students to defend their theses before their thesis can be as thoroughly explored as their supervisors would wish.

The University of Calgary LIM program encourages students to complete both components of their joint degrees in whatever format is best suited for the student and supervisor, provided that the total program is completed within 8 years, starting from the time they gain entrance into medical school. It is our opinion that students get most out of their program by completing each part in whole blocks, while participating in LIM events during both parts (MD and graduate training). This sequence of study keeps the student informed of what their colleagues in different stages of the program are doing and the program enhances both their science and medical

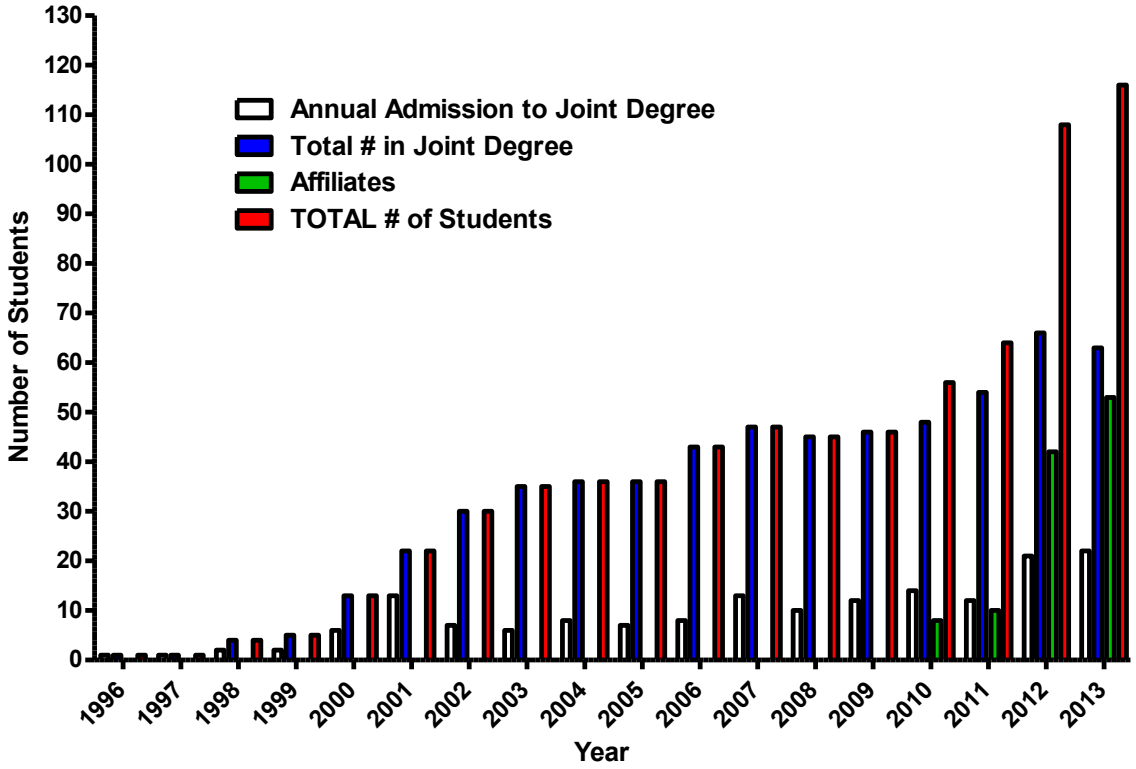

FIGURE 1. Student enrollment in the Leaders in Medicine Program
The Affiliate program was started in 2010 at the request of the medical school student body.

knowledge base. In some situations, we feel a student may benefit from having flexible timelines as research is often unpredictable. By enforcing a strict timeline, there is the potential liability that combined MD/PhD program students might generate lower calibre graduate projects since they would be expected to complete a PhD in a shorter time than other doctoral trainees. More importantly, students and supervisors should be given some flexibility to explore a curiosity-driven side project or follow-up on an unprecedented result, giving rise to future avenues of research interests. Again, this option may be limited in a strict four year format for a PhD flanked by MD training.

Structure

The University of Calgary Medical School is a three year program and the LIM program had been developed at the University of Calgary over the last 25 years. Initial students were given the authorization to complete their graduate work as they attended medical school. Over the past 18 years, we have developed a formal joint degree program with the hallmarks of flexibility and acceptance. This flexibility applies both to the acceptance of students into the MD program and to the sequence of studies (graduate plus MD) selected by each trainee. The program has grown markedly since 2000 (see Fig. 1), where there were 13 students in the program pursuing joint degrees, to 2013, where there were 22 new admissions to the joint degree program, with a total of 63 pursuing joint degrees and 53 Affiliate members for a total enrollment of 116 students. Of these 116 students, some will be pursuing their graduate training while others will be participating in the MD courses. Each year approximately 50% of joint degree students are in MD/PhD and 50% in the MD/MSc stream. To date, we have also had three MD/MBA students. See Fig. 2 for details on program structure.

Translational Journal Club

Translational research has become an important area of investigation, and funding agencies have increasingly supported this research in hopes of enhancing patient-relevant discoveries. The definition of translational research remains nebulous and the specifics of how to perform this research are unclear. The key principle of this research relates to understanding how to

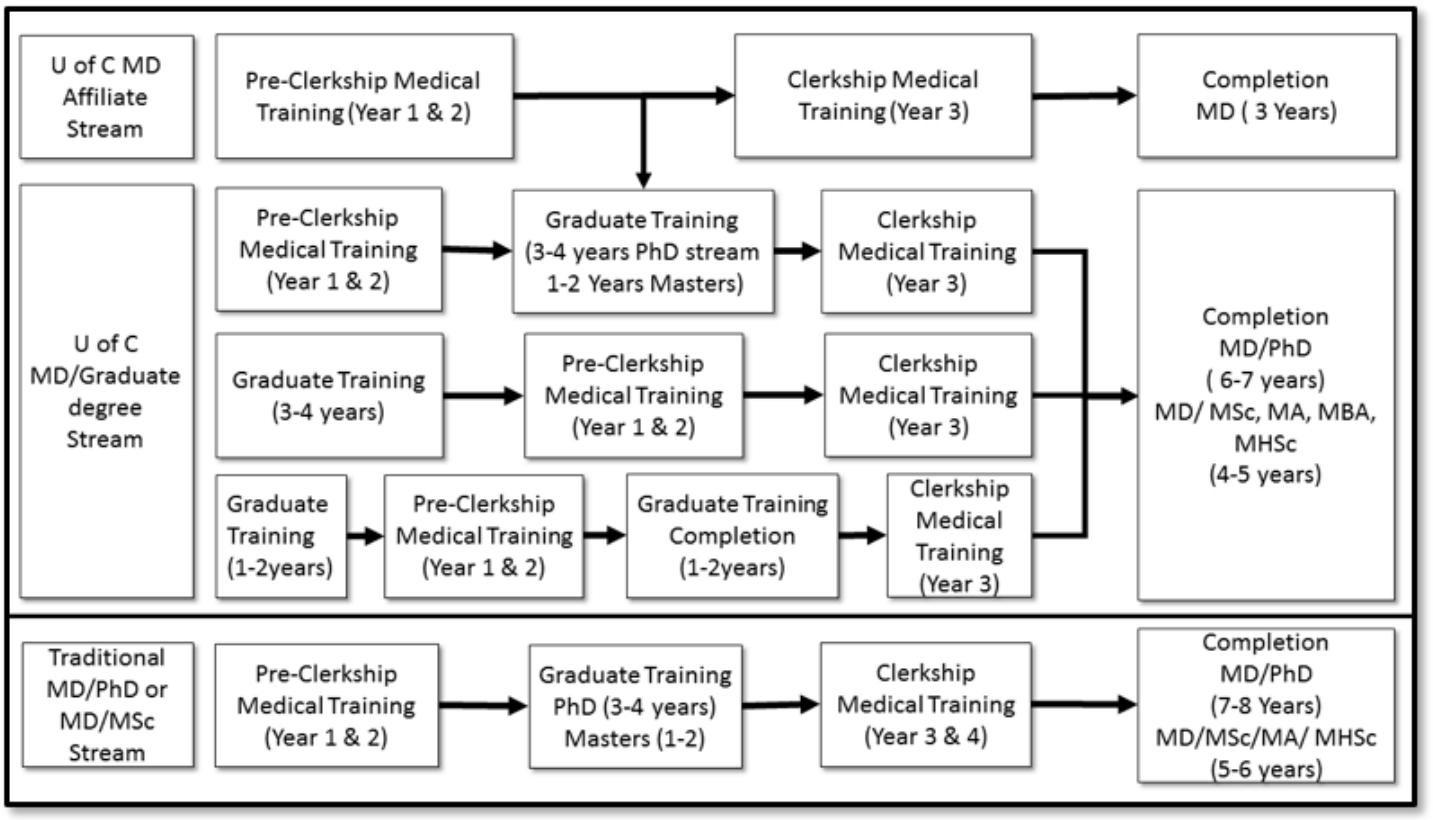

FIGURE 2. Overview of the University of Calgary Leaders in Medicine and Leaders in Medicine Affiliate program and comparison of traditional MD/PhD training programs

convert, or translate, scientific discovery into medical patient utility. Cleary, clinician scientists are well positioned to accept the challenge of translational research. At the University of Calgary, we have developed a highly focused translational journal club that differs from traditional discipline-based journal clubs. Following careful article selection from any of the research disciplines, key questions are posed to the trainees. These questions reflect previously well-developed strategies for conceptualizing translation research [9]. A clinician scientist trainee presents the article during the first half of the seminar, followed by small group discussion of the posed questions, ending with a full group discussion. Major questions addressed include the following:

- Can a medical need be clearly defined?
- How good is the scientific evidence supporting the article's discovery?
- What intellectual property issues exist that impact financial investment?
- What regulatory and bioethical challenges exist in performing human investigations based on the article findings?
- Can a definitive efficacy phase III clinical trial be conceived to justify continued investment in the discovery?

To better prepare the trainees to evaluate translational research, a longitudinal didactic lecture series runs concurrently. Here, experts are invited to lecture on patent law, intellectual property, health regulatory requirements, clinical trial design and product development. This directed approach to evaluating translational research is essential to building the skills necessary for future clinician scientists.

Research in Progress/brief presentation "TED Talks style"

The LIM program at the University of Calgary, in addition to the variety of other activities, runs a monthly Research in Progress (RIP) session. These RIP sessions allow several students to present (1) their own research, (2) interesting research observed in any area relevant to clinical medicine and (3) clinical case studies/presentations, or other topics. The presentations of these RIP sessions are done in a brief presentation in a "TED talk" style. The benefit of such a format is, firstly, that multiple students in each session are able to present, allowing diverse

topics to be showcased. Secondly, the dissemination of research in this format allows ample opportunity for obtaining feedback from both peers and faculty as well as for building connections for future projects. The plethora of topics that have been presented at these sessions include radiology profiles, medical business models, the use of mass media in clinical research, the use of literacy in mental illness, as well as more traditional basic science presentations. The RIP sessions are open to all those interested including LIM students, MD students and faculty; thus, this forum facilitates a dynamic conversation following presentations. The ability to convey research and scientific literacy is the backbone of successful clinician scientists. With the LIM program's dedication and commitment to building these skills in the context of the activities described above, students will be poised to have this understanding into residency and further on with their careers.

Visiting Speakers Series

An important aspect of the LIM program is the active promotion of mentoring opportunities for its students. Often, research-oriented institutions have a sizable fraction of faculty involved in clinical research; however, a constant challenge in training the next generation of clinician scientists is to provide suitable role-models and to enable and nurture mentoring connections that can develop over the course of the training program. Furthermore, obvious time limitations (on both the part of the student and faculty) can limit these opportunities to the detriment for those interested in pursuing a clinical investigator career path; thus, the program has made it is priority to provide these opportunities through monthly seminars with local clinician scientists. Specifically, faculty members are asked to discuss training and career paths as well as their current research with a group of trainees in a regularly planned series of 'Visiting Medical Educator' sessions. This seminar series has dedicated LIM funding to bring individuals from either local or off-campus institutions to meet with our trainees. The invitees are selected by our students. This format is highly engaging, as students are encouraged to openly ask questions that normally would not come up outside of these sessions. Questions include: What were their greatest challenges? and What is the most rewarding part of their job or their most difficult career decision. Often, feedback from faculty members is as positive as it is from students and, furthermore, students are exposed to branches of medicine that they may not have previously considered.

We feel these sessions provide a unique opportunity (1) to broaden the students' understanding of the career of a clinician scientist and (2) to introduce the students to role model individuals who may possibly become mentors for them in the future. This kind of impact between role models, potential mentors and students is difficult to achieve through traditional didactic seminars presented by visiting speakers.

LIM Research Symposium and Related Conferences

The University of Calgary LIM Program has presented an annual research symposium for the past five years. This half-day symposium is student-organized and features oral and poster presentations by students along with a keynote address by an invited clinician scientist. This well-attended event fulfills several key objectives for our program. (1) To showcase the impressive variety of projects undertaken by students in the LIM Program as well as U of C medical students. All types of research projects (e.g., clinical, basic and case reports) are accepted into the symposium and students in the medical class are encouraged to participate in addition to our students. All accepted abstracts are published in a symposium abstract booklet and awards are given out to highlight particularly remarkable work. (2) To encourage medical student participation in research and special projects. The symposium is an enjoyable event that provides students with an opportunity to present research that may not be published or presented elsewhere. The poster session is highly interactive and allows students with similar research interests to forge connections. (3) To inform students and faculty about the diversity of opportunities available for research and special projects during medical school and beyond.

We strive to involve university faculty in the symposium to showcase student research and provide students with opportunities for networking. Approximately two dozen faculty members participate as judges in the poster session, with representation from a wide range of departments and specialties. In recent years, individuals from the Clinician Investigator Program have also been invited to judge. The keynote speaker serves as an inspirational model of a successful clinician scientist, with past keynote speakers including NASA Flight Surgeon Dr. Douglas Hamilton and former Canadian Medical Association president Dr. Hugh Scully. LIM students are given the opportunity to attend career development sessions prior to the symposium where they can ask the keynote speaker about career management, life-work balance and other issues crucial to aspiring clinician scientists. Upon conclusion of the symposium, students are asked to provide formal feedback to help with the growth of this symposium. Future directions for the symposium include: separate award categories for medical students, a "three-minute thesis" competition, and further strategies to expand faculty involvement.

In addition to hosting our own symposium, the LIM program routinely sends delegates to two annual, national conferences: the joint Canadian Society of Clinical Investigation (CSCI)- Clinical Investigator Trainee Association of Canada (CITAC) Young Investigators Day Symposium and the Canadian Medical Students Research Symposium (CNMSRS). Both conferences have national prominence and showcase research by active clinician scientists in Canada. Moreover, these conferences provide excellent networking and mentoring opportunities at a national level that would otherwise be limited at individual institutions. Importantly, students are exposed to the challenges faced by new investigators in simultaneously managing both scientific and clinical careers. Often, these directed, small group sessions have much greater impact than engaging a larger audience. We therefore encourage and finance students to join CITAC and attend the annual CSCI-CITAC meeting where they meet like-minded students and staff from across Canada. The joint CSCI-CITAC meeting has specific workshops on career development (industry, clinical and research), mentorship and career planning, including specific session on "finding your first faculty position", "signing your first contract" and "how to protect time for research". Thus, it is and will be a continued priority for the LIM program to have strong representation at these gatherings.

Mentorship

Mentorship is a critical aspect of the LIM program. The directors (Dr. Beck and Dr. Hollenberg), associate director (Dr. Yipp) as well as our program administrator (Ms. Selman) frequently meet with students on a one on one basis. We have 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 and research. We have also started a program where LIM graduates (some residents and some in junior staff positions) lead sessions to discuss career development, balancing research career with residency/clinical work and family. We have now set up a "mentorship flow" process involving our own graduates, where we help to identify mentors for the students to guide them through their graduate program, medical school, clerkship, residency and, ideally, into their first faculty position. We have identified LIM graduates and/or others at universities across Canada and many in the United States who can mentor our students. A list of willing high level mentors is posted on the LIM website and is given to students on a yearly basis. Developing this list of mentors from across North America has been crucial in aiding students when they start a new position or at a new university. The assigned mentors enable our trainees to get involved in research groups and to develop strong local, discipline-specific guidance. Many LIM students who have graduated still contact our program directors for advice, mentorship and career planning.

Funding

Financial issues can dramatically affect one's ability to pursue a career as a clinician-scientist; thus, minimizing debt-load due to the long training time frame of a clinician scientist is an important goal of our LIM program. Early in the history of the LIM Program we received an anonymous donation and the Faculty of Medicine matched this donation, allowing us to provide some financial support for students throughout their program. At present, tuition awards are available to all joint MD/PhD students and funds are available for all LIM students (and Affiliates) to attend conferences. We have recently added a competition where MD/MSc students can also apply for tuition support. The program is also supported by Canadian Institutes of Health Research (CIHR) from whom we receive one or two MD/PhD stipend awards annually (each award provides six years of funding). Alberta Innovates Health Solutions (AIHS) also has a MD/PhD program that supports many of our students. We also award two AIMs (Achievers in Medical Science) awards to graduating MD/PhD students, which we hope will reduce their financial burden allowing them to further pursue their goal of becoming clinician-scientists as they enter their residencies.

Success

Success of a program such as LIM can be measured according to several outcomes; however, our outcomes data are limited since our program is relatively new, with many of our students still involved in their residency training , some in the process of returning to academic positions and a few already established as very successful career clinician-scientists. We are just now seeing evidence of success of the program: the contributions of our students to medicine and science can already be seen in terms of their roles as authors of peer-reviewed manuscripts, teachers, expert physicians as well as administrators. One of our first graduates, Dr. Douglas Hamilton, has served as the NASA flight surgeon for many years - overseeing many space missions as well as developing several associated programs within NASA on space travel-related medical issues. Dr. Hamilton has recently returned to our Faculty, where he is contributing to our LIM program. We look forward to comparable contributions by our other graduates, who will have expertise in many areas, including those who have completed joint MD/

MBA degrees. We look forward to their successes in medicine, research, administration and health care delivery.

In our most recent in-depth assessment, which was completed for 2011-12, our 54 full LIM students (joint MD/PhD, MD/MSc) and 33 Affiliates were extremely successful. (1) Matching to training programs: most of our LIM students do extremely well in the residency matching competition, with approximately 90% landing their first choice of program and location. (2) Peer-reviewed publications: In 2011-2012, our LIM students published 59 papers (many in very high impact journals) and 21 more were in-submission and in-review. (3) Book chapter and abstract publications associated with meeting presentations: They also published six book chapters and 100 abstracts, and were responsible for 118 presentations at local (69) at national/international meetings (49). These students won 95 awards, many that were at the provincial and national level and some at the international level! We have set up a database to track our students and measure success. (4) Program completion rate and job placement: Unfortunately, there are limited data on the outcomes of our other graduate education programs for comparison with our LIM trainees. For the LIM program, we have a dropout/noncompletion rate of less than 5%. In contrast, non-LIM trainees in our faculty MSc/PhD programmes have a dropout/non-completion rate of from 20-25%. The best index of success for clinician-scientist training in Canada has come from the Canadian Child Health Clinician Scientist Program at the Hospital for Sick Children at University of Toronto, where they reported that all but 1 of 18 graduates went on to seek a junior faculty position as a clinician scientist [10]. This is a much smaller and more intensive and specialized program than the LIM but it is clearly remarkably successful. Although we do not have data for Canadian post-doctoral programme trainees, in the United States it is estimated that only about 20% of post-doctoral fellows advance to a tenure-track academic, research position [11]. Although it is too early for us to document, we project a much higher success rate of our graduates in terms of playing key roles in academic leadership and in furthering medical practice.

In summary, the LIM Program at the University of Calgary is committed to enhancing science education in medical school and committed to training clinician scientists and MD/MBA students. We have developed a unique program that not only trains clinician scientists but also aims to enhance basic science education and research in the undergraduate medical school curriculum.

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