2018 Life and Health Sciences Research Expo

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AGENDA THURSDAY, MAY 3

Health Sciences Building, D-Wing,
U of S campus, Saskatoon

8:00 - 9:00 am  Registration for the morning session
D-Wing outside room 1B21, Health Sciences building

9:00 am - 12:00 pm  Morning Poster Session
D-Wing, 2nd & 3rd floors, Health Sciences building
  - Basic Science 1, 2, 3
  - Clinical 2, 3
  - Social Population Health 2

12:00 - 1:00 pm  Registration for the afternoon session
D-Wing outside room 1B21, Health Sciences building

Pizza lunch
D-Wing Atrium, Health Sciences building

1:00 - 4:00 pm  Afternoon Poster Session
D-Wing, 2nd & 3rd floors, Health Sciences building
  - Basic Science 4, 5, 6, 7
  - Clinical 1
  - Social Population Health 1

4:00 - 5:00 pm  Keynote Speaker - Dr. Richard Schulz
B450, Health Sciences building

5:00 - 6:00 pm  Awards & Recognition
B450, Health Sciences building

6:00 - 7:30 pm  Wine & Cheese Networking Reception
D-Wing Atrium, Health Sciences building
WELCOME FROM THE ORGANIZING COMMITTEE

Welcome to the 25th annual Life and Health Sciences Research Exposition (Expo). The Expo is one way that the Health Sciences seek to unite future health professionals and promote collaborative research across the disciplines—dentistry, kinesiology, medicine, nursing, pharmacy and nutrition, rehabilitation sciences, public health, and veterinary medicine. This initiative acknowledges exemplary research and learning activity at the University of Saskatchewan. The Expo is a yearly showcase for interdisciplinary health science research across social population health, basic and clinical sciences. To further bridge disciplinary gaps and enhance discovery, this event is facilitated by the Office of the Vice-Provost Health.

As our University seeks to unlock the research and innovation potential of the university's health ecosystem and works to embrace collaboration in everything we do the Expo is designed to:

- provide an interdisciplinary showcase of student research
- present students with an opportunity to hone their skills with regard to sharing and presenting their research
- highlight the breadth of research currently underway in the Health Sciences
- create an opportunity for new networks and new collaborations to be formed as students engage with each other, faculty and industry judges and interested members of the community

A great deal of work goes into preparing an abstract and poster, so we would like to thank our students for presenting their research today. In turn, we hope all participants enjoy the Expo and have the opportunity to view posters from the various research disciplines. We would like to extend congratulations to the poster prize winners, best paper, and best supervisor winners.

This day would not be possible without help from our sponsors. Thank you to the Saskatchewan Health Research Foundation, the health science colleges, and our other sponsors, for the financial and in-kind support. Another thank you goes to our keynote speaker, who took time out of his schedule to be here and share his story with us. Our final thank you is to the poster and award judges who will help us select the winners in each category; they play a fundamental role in making the day a success.

If you have any questions throughout the day, please contact a member of the organizing committee or email ovph.events@usask.ca.

The organizing committee:

Dr. Jane Alcorn co-chair
Dr. Marek Radomski co-chair
Andrea Knittig
Curtis Larson
Crystal Maslin
GREETING FROM THE INTERIM ASSISTANT VICE-PROVOST HEALTH

It is my absolute pleasure to welcome you to the Life and Health Sciences Research Exposition at the University of Saskatchewan.

This initiative, formerly coordinated by the College of Medicine, has now been adapted by the Office of the Vice-Provost Health to incorporate the often multidisciplinary nature of the health sciences. Additionally, it is becoming increasingly evident that the education, research and clinical care within this field can not—and must not—remain in separate silos. Rather, complex health issues need to be addressed from many angles, to give a multi-perspective, interdisciplinary approach to patient-centered research and clinical care.

Fortunately, the U of S has the key ingredients for successful health research. This includes a full complement of health science disciplines—dentistry, kinesiology, medicine, nursing, pharmacy and nutrition, physical therapy, public health, and veterinary medicine. Within those units are bright faculty minds—leaders in research expertise and clinical practice—supporting our talented students, the next generation of health professionals, and leading discoveries to improve the health of people across Saskatchewan, Canada and the world. The health research is strengthened through collaborations with our colleagues in the colleges of Arts and Science, Agriculture and Bioresources, Engineering and the Library among others.

Aiding in our research success is one of the most scientifically-advanced campuses in the world, including Canada’s only synchrotron; global institutes addressing food and water security; a world-class vaccine development facility; Canada’s largest university-based toxicology centre; one of the largest containment level-3 vaccine research facilities in North America; and of course, the Health Sciences Building, which unites health professionals under one roof to promote collaborative research across the disciplines.

With all this at our fingertips, we are well-positioned to truly excel in health science research and education.

To those presenting posters today, I encourage you to use this opportunity to share your stories and your achievements. Mingle and find out about your colleagues’ projects. That curious, collaborative spirit is the foundation of interdisciplinary initiatives at the U of S and will serve you well as you complete your education here and launch your careers.

Lois Berry
Interim Assistant Vice-Provost, Health
FOREWORD

It is my great pleasure to welcome you to the 25th Annual Life and Health Sciences Research Expo. You will have the opportunity to share in the great work that our trainees are performing at this institution. The work of our trainees is vital to the mission and vision of our university and contributes to sustaining our position as being recognized as one of the most distinguished research-intensive universities in North America.

The University of Saskatchewan is over 110 years old and is rich in history and tradition. It is the largest postsecondary education institution in the province and is recognized nationally and internationally for its creativity, its collaborations and its achievements. Our research is supported by great research infrastructures such as the CLS, Vido-InterVac and the Academic Health Sciences, in addition to the exciting research of its faculty and students. With over 3900 graduate students currently registered in the College of Graduate and Postdoctoral Studies, the health sciences trainees play a vital role as part of our graduate community. Since its humble beginning in 1946, the College of Graduate and Postdoctoral Studies has become an integral part of the institution’s research endeavours. From 2000 onwards, graduate student numbers have doubled, complimenting the University’s mandate of becoming one of North America’s leading research institutions. Graduate students now account for approximately 17% of our student body and, more importantly, bring vitality and excitement to the University through their leading-edge research, new perspectives on the future and engagement with emerging social issues.

Student-centred research conferences are very special events. They provide an opportunity for the students to experience, often for the first time, the excitement of communicating their research to a wider scientific community. These events are also a source of pride for those professors and scientists who have guided the students through their research work. Conferences are an important professional networking opportunity and often lead to links that can influence your future career as a graduate student, academic or professional.

I hope you enjoy this year’s Life and Health Sciences Research Expo.

Trever Crowe, Ph.D., P.Eng.
Dean, College of Graduate and Postdoctoral Studies
University of Saskatchewan
KEY NOTE SPEAKER BIO - DR. RICHARD SCHULZ

Richard (Rick) Schulz is a Professor in the Departments of Pediatrics and Pharmacology at the University of Alberta in Edmonton. A member of the Mazankowski Alberta Heart Institute, the Women and Children’s Health Research Institute, and the Cancer Research Institute of Northern Alberta, Rick is particularly interested in the impact of oxidative stress and matrix metalloproteinases (MMPs) in the heart and vasculature, in both health and disease. Rick’s translational research program is focused on therapies of ischemic heart disease, heart failure, septic shock and Chagas disease, through reducing the impact of oxidative stress and MMP activity. His research is supported by a CIHR Foundation Scheme Award and the Heart and Stroke Foundation of Canada. He serves on the editorial boards for several cardiovascular and pharmacology journals and is a member of many grants and personnel review panels. His research has been recognized with several awards, including his being made a fellow of the British Pharmacological Society.

Rick is an Albertan, born in Calgary, where he did his undergraduate studies in chemistry at the University of Calgary. There he met his wife Petra who was visiting from Germany. After two separate research experiences in Germany he also fell in love with medical research and then returned to the University of Alberta in Edmonton where he did his PhD in vascular pharmacology with David Cook. This was followed by fellowships in nitric oxide biology with Salvador Moncada in London, UK and at the University of Alberta with Gary Lopaschuk and Peter Olley in cardiovascular research, where he has been since, apart from sabbaticals in Italy and Brazil. Along with tinkering with old cars, cross-country skiing, bicycling and camping in his spare time he also tries to get to Mayne Island, BC where he takes care of his peach and olive trees.
1. Treatment of Metastatic Melanoma with Radioimmunotherapy

Presenter: Kevin Allen, College of Pharmacy and Nutrition
Supervisor: Ekaterina Dadachova

**Background:** The approval of 223-Radium chloride (Xofigo) for treatment of metastatic prostate cancer and of 177-Lutetium-labeled somatostatin receptor binding peptides for neuroendocrine tumors, as well as recent successes of 177-Lu-A617 compound in patients with metastatic prostate cancer demonstrate the potential of targeted alpha or beta emitting radionuclides in treatment of cancers resistant to all other therapies.

In 2017, an estimated 7200 Canadians will be diagnosed with melanoma skin cancer. While surgical resection of the primary tumour can be effectively accomplished, there is no satisfactory treatment for late stage metastatic melanoma. This reality projects that approximately 1250 diagnosed Canadians will have succumbed to the disease before the end 2017. It is our goal to utilize radioimmunotherapy (RIT) to treat late stage metastatic melanoma, and improve the current standard of care for patients afflicted with this disease.

**Methods:** C57BL6 female mice were injected subcutaneously with B16-F10 murine melanoma cells into the right flank. Melanin-binding antibody h8C3 was conjugated to CHXA'' and radiolabelled with In-111, Lu-177, and Bi-213. The radiolabelled antibodies were injected into the C57BL6 mice and biodistribution (In-111), imaging (In-111, Lu-177), and therapy (Lu-177, Bi-213) studies were carried out.

**Results:** Biodistribution and imaging studies show that the melanin-binding antibody h8C3 can successfully target B16-F10 melanoma in mice. There is no evidence of uptake in healthy melanized organs such as the eyes or tail in C57BL6 mice. The rate of tumour growth in the Bi-213 treatment group progressed at a slower rate than those of the Lu-177 and the control groups.

**Conclusion:** CHXA'' conjugated h8C3 antibody can successfully target the extracellular melanin in B16-F10 melanoma without any off target effects. Initial results indicate that the alpha emitter, Bi-213, is more effective than the beta emitter Lu-177 for use in radioimmunotherapy of metastatic melanoma

**Keywords:** Radioimmunotherapy. Melanoma. Melanin. Cancer.

2. Cortisol, alpha-amylase, cytokines and treatment-related symptoms in breast cancer survivors submitted to a Swedish massage intervention: preliminary results

Presenter: Emiliana Bomfim, College of Medicine
Supervisor: Kalyani Premkumar

**Background:** Although Massage Therapy (MT) has been providing positive results in the management of cancer Treatment-Related Symptoms (TRS), the quantity and quality of preliminary evidence is not sufficient to build trustworthy clinical guidelines for cancer survivors. The objective of this study is to
investigate the effects of a Swedish massage protocol on quality of life (QoL), sleep, stress, fatigue, immune and endocrine biomarkers in a population of breast cancer survivors.

**Methods:** Females over 18 years who were breast cancer survivors were invited to participate (IRB approval protocol #16-112). Fifteen participants underwent 1 hour/week of a novel Swedish massage protocol for 8 weeks. Data for the study was collected in three main phases: (i) baseline (ii) during an 8-week intervention period and (iii) endpoint. Fatigue, sleep and QoL were assessed through validated questionnaires (FACT-F, FACT-B and Perceived Scale Stress). Sleep was measured with a wrist-worn device (Basic Motionlogger Actigraph Monitor). Saliva was collected to quantify cortisol, α-amylase and cytokines levels. Some physiological parameters such as blood pressure, SpO2 level and pulse were measured.

**Results:** Mean age of participants was 55 years old. A paired-samples t-test was conducted to compare if there was a difference between pre and post-intervention period. There was a significant difference between baseline QoL (M=87.5, SD=14.8) and endpoint QoL (M=99.1, SD=19.3). Fatigue also significantly improved (t(5)=-4.85, p=0.005) from baseline (M=23.5, SD=9.6) to endpoint (M=34.5, SD=9.1). Significant improvement (t(5)=3.369, p=0.020) was also observed in stress from baseline (M=24.1, SD=5.7) to endpoint (M=20.3, SD=8.1). There was a statistically significant improvement in blood pressure following the Swedish massage program from 107.4 ± 8.5 mmHg to 99.8 ± 3.5 mmHg (p=0.047); an improvement of 3.50 ± 1.16 mmHg. Sleep efficiency pre and post-intervention also showed improvement.

**Conclusion:** Our 8-week Swedish massage program showed potential benefits for improvement of TRS.

**Keywords:** integrative oncology, breast cancer, complementary and alternative medicine

3. **Effects of Prior Heavy Exercise in Heart Failure with Preserved Ejection Fraction on VO2 Kinetics**

**Presenter:** Natasha Boyes, College of Kinesiology  
**Supervisor:** Dr. Corey Tomczak  
**Collaborators:** Janine Eckstein, Stephen Pylypchuk, Scotty J. Butcher, Darcy D. Marciniuk, Daliszwe M.K. Dewa, Calvin R. Wells, Mark J. Haykowsky

**Background:** Exercise intolerance and muscle dysfunction characterize heart failure with preserved ejection fraction (HFpEF). Prior heavy exercise (“priming”) speeds pulmonary oxygen uptake (VO2p) kinetics in older adults. PURPOSE: We tested the hypothesis that priming would not speed VO2p on-kinetics in patients with HFpEF due to muscle dysfunction commonly found in patients with HFpEF.

**Methods:** Eight HFpEF, 4 high-fit (CTL-HF), and 5 low-fit matched controls (CTL-LF) performed 2 cycling transitions (3x each): MOD1, rest to 4-min moderate-intensity; and MOD2, 2-min heavy-intensity, 5-min rest, then MOD1. VO2p (pulmonary gas exchange), heart rate (HR), total peripheral resistance (TPR; ModelFlow), and quadriceps tissue oxygenation (TOI) kinetics were measured. Significance was P<0.05.

**Results:** HFpEF VO2p kinetics (45±15s) were slower than CTL-HF (25±6s; P=0.008) but not CTL-LF. MOD2 VO2p kinetics (37±14s) were faster than MOD1 (47±19s; P=0.039), but not in HFpEF alone. HR kinetics were 10s slower after priming (P=0.001). HFpEF TPR was greater than CTL-HF throughout (all P<0.038) with no priming effect. Priming reduced TOI in HFpEF at 30s (P=0.033) and CTL-HF throughout (all P<0.05).

**Conclusion:** Slow HFpEF VO2p on-kinetics may not be speeded by priming exercise despite indications of improved muscle O2 delivery. Heart rate and vascular responses to priming may not account for
speeding of VO2p on-kinetics in older adults. Intracellular mechanisms may limit HFpEF exercise tolerance.

**Keywords:** heart failure with preserved ejection fraction; oxygen uptake kinetics; priming exercise; exercise intolerance; muscle tissue oxygenation; near-infrared spectroscopy

4. An Unusual Finding of Vulvar Ewing Sarcoma - a Case Report & Literature Review

**Presenter:** Dr. Mae Cantos, College of Medicine  
**Supervisor:** Dr. Anita Agrawal  
**Collaborators:** Dr. Rajni Chibbar, Dr. Trina Theorett

**Background:** Superficial Ewing sarcoma/Peripheral neuroectodermal (ES/PNET) family of tumors are rare and have a relatively favourable prognosis compared to the osseous or deep soft tissue extraskeletal ES/PNET. This was first described in 1969 (40). ES/PNET arising in the female genital tract are exceptionally rare with only a few cases reported so far. There are no clear guidelines or prognostic features to guide clinical decision making in vulvar ES. Is vulvar ES another site of cutaneous ES and should be managed similarly or there are differences in clinic-pathological features between these two entities? The purpose of this case report and literature review is to compare clinic-pathological features of vulvar and cutaneous ES/PNET and to identify prognostic features to guide therapy and help patient and clinician discussion in treatment decision, prognosis, and long term follow up.

We report an unusual case of a 52 year old woman with vulvar Ewing’s sarcoma and compare the clinical course and pathological features with cutaneous ES/PNET. Our patient was multiparous, obese (BMI = 57), post-menopausal woman with several medical co-morbidities who presented with a several months history of an enlarging clitoral mass. Biopsy results were reported as ES/PNET. The patient was referred to Gynecologic Oncologist for further management. Staging imaging (CT & MRI) revealed a large heterogeneous mass in the clitoris extending into the crura bilaterally and posteriorly. The bulbous portion of the lesion measured 3.5 x 5.0 cm. The lesion appeared to extend into the superior and anterior vaginal wall and up to the urethra. There were multiple, bilateral, enlarged inguinal lymph nodes (largest measuring 5.0 cm x 1.8 cm on the right and 3.8 x 2.0 cm on the left).

Patient underwent radical anterior vulvectomy. The clitoral mass extended up to the pubic bone and into the bulbocavernous muscle bilaterally as reported by MRI. Histology demonstrated cutaneous variant of extraskeletal Ewing's sarcoma/primitive neuroectodermal tumour. The deep and left bulbocavernous resected margins were focally positive. Imaging (PET/CT) post vulvectomy reported possible residual tumor and bladder involvement.

The patient was discussed in multidisciplinary tumor board and was treated with adjuvant multi-agent chemotherapy. Our patient received nine cycles of adjuvant chemotherapy after surgical excision of the tumor almost two years ago. In the most recent imaging, there is no evidence of local recurrence of disease or any evidence of distant metastasis.

**Methods:** We conducted a literature review using the keywords – Ewing sarcoma, peripheral neuroectodermal, superficial, extraosseus, extraskeletal, cutaneous, vulvar, prognosis and management – to compare and contrast the differences between vulvar and cutaneous ES. Cases of vulvar Ewing sarcoma
were identified and characteristics of the vulvar lesions and their response to treatment were collected. These findings were compared with a review of cutaneous Ewing sarcoma looking at similar categories.

We involved the expertise of Gynecologic Oncology, Pathology and Radiology to interpret our case report alongside the evidence regarding vulvar and cutaneous ES/PNET to support our hypothesis that vulvar is a subset of cutaneous ES/PNET.

**Results:** In comparing vulvar ES/PNET with what is found in the literature regarding cutaneous ES/PNET, we have noted many similarities between the two histopathologies. The incidence of both vulvar and cutaneous ES/PNET is rare with the median age of the case study participants being young at 20 years for vulvar and 15 years for cutaneous. The size of the tumours are also similar with the median measurement of 4cm for vulvar and 4.75 cm for cutaneous and the majority of the studies reporting an initial size of less than 5 cm. (62.5% vulvar, 78.5 cutaneous). Regarding histology, the majority of both vulvar and cutaneous are CD99 + with surgery and chemotherapy being the main arms of treatment. The increased metastasis with vulvar ES/PNET may have to do with the location and proximity of groin lymph nodes. Given the similarity of prognostic factors between vulvar and cutaneous ES/PNET - such as young age at presentation, initial tumour size <= 5cm, good response to multimodal treatment and almost no recurrence rate – it could be inferred that vulvar ES/PNET has the same favourable prognosis as the cutaneous subtype.

**Conclusion:** Because of the rarity of the case, the long term outcome and prognosis is unclear at this point. However, given the literature on cutaneous ES/PNET and that the patient’s vulvar Ewing’s sarcoma is of the cutaneous subgroup of extraskeletal ES/PNET, it is likely that her disease prognosis will be more favourable than non-cutaneous extraskeletal ES/PNET. This case report and review of literature will help clinicians to inform patients of long term outcomes of this rare tumor and assist their patients in making decisions with respect to treatment options and follow up.

As ES/PNET are rare, it is important to know that vulvar ES/PNET may behave as cutaneous ES/PNET and can be treated similarly with the expectation of better outcome. This information can be provided to the patients at the time of initial diagnosis with the assurance that despite being so rare, this cancer has possibility of long term remission with the advised treatment plan of surgery and chemotherapy leading to a possible cure. In addition, knowing that the vulvar ES/PNET is cutaneous subtype and is less likely to have distant metastasis and better overall outcome, may point to using less intensive chemotherapy with less side effects. Increased patient compliance with the treatment plan will result in higher rate of achieving successful treatment completion. The goal would be to tailor treatment for the individual to minimize treatment-related morbidity while maintaining high remission rate and possible cure.

**Keywords:** Ewing sarcoma, vulvar, cutaneous, extraosseous, extra skeletal, prognosis, treatment

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5. **Percentage of alveolar bone and number of teeth in patients taking Simvastatin for the treatment of hypercholesterolemia**

**Presenter:** Brenna Glow and Justin Hennes, College of Dentistry  
**Supervisor:** Dr. Francisco Otero-Cagide

**Background:** Periodontitis is a chronic inflammatory disease of the periodontium which develops in response to bacterial plaque on the neighbouring teeth. Periodontitis results in reduction of alveolar
bone. Recent research suggests a possible connection between statin usage and stopping bone loss, as well as acting to promote bone growth; this ultimately results in increased tooth survival.

**Methods:** Panoramic x-rays will be examined for patients 30 years of age and older, with periodontal disease, who have been taking a dose of simvastatin >20 mg for at least 5 years. The percentage of alveolar bone will be measured, as well as the number of teeth present in the individuals taking simvastatin. This data will be compared to individuals not taking simvastatin, and ANOVA testing will be done.

**Results:** We expect to see increased percentage of alveolar bone in patients taking Simvastatin compared to a matching group who are not. Increased dosage should result in better alveolar bone levels. It is also expected that patients taking Simvastatin will have more teeth than those who are not taking the medication.

**Conclusion:** This study will take a retrospective look at patients who have periodontal disease as well as high cholesterol. Panoramic radiographs will be examined and the percentage of alveolar bone and number of teeth present will be compared to patients who have not been diagnosed with hypercholesterolemia and are therefore not taking Simvastatin.

**Keywords:** Hypercholesterolemia, Periodontitis, Stimvastatin,

6. *Intrapulmonary Delivery of CpG-ODN microdroplets protects neonatal broiler chicks against E.coli septicemia*

**Presenter:** Kalhari Goonewardene, Western College of Veterinary Medicine  
**Supervisor:** Susantha Gomis  
**Collaborators:** Shelly Popowich, Thushari Gunawardana, Ashish Gupta, Shanika Kurukulasuriya, Ruwani Karunarathna, Betty Chow-Lockerbie, Khawaja Ashfaque Ahmed, Suresh K. Tikoo, Marianna Foldvari, Philip Willson

**Background:** Poultry industry is constantly searching for safe alternatives to antibiotics to ensure welfare of the birds and consumer safety. We have previously demonstrated that IM and in ovo injection of CpG-ODN protects neonatal chickens against bacterial septicemia. This study was designed to test the protective efficacy of needle-free intrapulmonary (IPL) delivery of CpG-ODN against E.coli septicemia.

**Methods:** Groups of newly hatched chicks (D0 old) were IPL delivered CpG-ODN (N=40) or saline (N=40). Three-days later chicks were challenged with two doses (1x104 (n=20) or 1x105 (n=20) cfu) of E. coli. Their survivability, clinical condition and bacterial isolation were evaluated.

**Results:** Chicks treated with IPL CpG-ODN had significantly better survival percentage, clinical condition (P<0.05) and lower bacterial load. Protection kicked off as early as 6h and lasted up to 5d post treatment. Protective effect was also dose and exposure time dependent. There were no mortality or harmful effects of CpG-ODN on growth observed up to 42 days of age.

**Conclusion:** Based on these findings it can be suggested that CpG-ODN delivery by IPL route can be a promising alternative to antibiotics for inducing protective immunity in chicks during the critical first week of neonatal life

**Keywords:** Intrapulmonary, CpG-ODN, microdroplets, broiler chicks, poultry, E. coli, septicemia, bacterial infections,
7. Silver Diamine Fluoride Effectiveness for Caries Arrest and Patient Satisfaction in Pediatric Dentistry: A Pilot Study

Presenter: Farah Goubran, Natasha Patel, Ryan Teneycke, College of Dentistry
Supervisor: Dr. Petros Papagerakis and Dr. Mark Berscheid

**Background:** Silver is a potent antibacterial compound that has been used in dentistry for many years, its antibacterial mechanism involves the disruption of the metabolism of bacteria with limited toxicity to human cells. The combination of fluoride and silver has led to the production of Silver Diamine Fluoride (SDF) which uses the favorable properties of both compounds to prevent and arrest dental caries.

**Methods:** SDF will be applied to primary posterior teeth of pediatric patients and its effectiveness will be assessed at 3 and 6 months. Patient and parent satisfaction in terms of time, aesthetics, and comfort during treatment will be assessed through surveys. Clinical evaluation of the effectiveness of treatment will be examined through radiographs to determine caries progression.

**Results:** SDF is expected to arrest caries that extend into the dentin. Patients receiving SDF treatment are expected to report a more comfortable experience compared to those who received traditional restorative treatment.

**Conclusion:** Silver Diamine Fluoride is a treatment option that acts as an antibacterial agent that also promotes remineralization of enamel. Its use in children to prevent and arrest caries has potential to limit invasive treatments in children. Due to its low cost and ease of application, SDF can also be an effective way of addressing early childhood caries in children with limited access to care.

**Keywords:** Silver, Fluoride, Pediatric, Caries, SDF, Dentistry, Early Childhood Caries, Primary Teeth

8. A Neuroimaging Study Investigating Cross-Education for Improving Hemiparesis Post-Stroke

Presenter: Layla Gould, Colleges of Medicine and Kinesiology
Supervisor: Drs. Jon Farthing and Michael Kelly
Collaborators: Justin W. Andrushko, Doug W. Renshaw, Ron Borowsky

**Background:** Based on the current state of knowledge and gaps in the literature we are conducting an intervention study to explore a novel treatment for patients with hemiparesis post-stroke. An intriguing approach to stroke rehabilitation is 'cross-education,' which involves physically training the healthy limb to benefit the injured limb. This study applies cross-education combined with usual care, as part of an easy take home strengthening program to improve hand function post-stroke.

**Methods:** A total of 24 stroke patients over the age of 18 are being recruited to participate in the study and half are performing cross-education. Muscle strength, range of motion, and brain activation patterns are tested at baseline, 12 weeks, and 26 weeks. Changes in brain activation patterns during the strength task are measured using functional MRI (fMRI). A second fMRI experiment is being conducted with healthy participants to examine the test-retest reliability of the paradigm.

**Results:** The results suggest that there is high reliability in the brain activation patterns and strength measures across Time 1 and Time 2.
**Conclusion:** Together, cross-education has the potential to ‘boost’ function of an impaired limb and lead to more complete recovery post-stroke. This study will help define more consistent and effective stroke rehabilitation and lead to better patient outcomes.

**Keywords:** cross-education; stroke; hemiparesis; neuroimaging

**9. Efficacy of a Rinse Containing Tetrapotassium Pyrophosphate and Sodium Tripolyphosphate on Calculus Formation in a Group of Adults**

**Presenter:** Ashley Halstead and Kirsten Hooper, College of Dentistry  
**Supervisor:** Dr. Jay Hoover

**Background:** Plaque is a biofilm that is present within the oral cavity which can undergo mineralization into calculus. Periogen, an anti-calculus rinse, contains tetrapotassium pyrophosphate which binds to calcium and magnesium in the saliva and prevents them from mineralizing plaque into calculus. Sodium tripolyphosphate binds calcium in the saliva to slow down the mineralization of plaque into calculus.

**Methods:** Patients will be selected who meet the criteria. A cleaning will be performed followed by group assignment. Those in the control group will use standard oral hygiene for the duration of the experiment. Those in the experimental group will brush their teeth for 2 minutes, 2 times a day and rinse twice with Periogen. After the 60 day trial period a follow up is needed to record calculus levels.

**Results:** It is expected that those who use the Periogen™ rinse will have statistically significant lower VMI and PI scores and reduced gingival bleeding when compared to those who did not use the Periogen™ rinse. It is expected that the control group will continue normal calculus formation.

**Conclusion:** Supra gingival calculus has an adverse effect on oral health because it acts as a reservoir for more plaque biofilm to accumulate on its surface causing disease progression. Calculus has strong adhesive properties and cannot be removed with regular brushing and flossing. It must be removed by a professional. Having a successful anti-calculus oral rinse could help improve oral health of Canadians.

**Keywords:** Anticalculus, Antitartar, Mouthrinse, Calculus, Periogen, Tetrapotassium Pyrophosphate, Sodium Tripolyphosphate

**10. INTERFRACTIONAL VARIATION IN CANINE HEAD POSITION AFTER IMAGE-GUIDED PATIENT SETUP CORRECTION USING TWO DIFFERENT IMMOBILIZATION DEVICES FOR RADIATION THERAPY**

**Presenter:** Celina Morimoto, Western College of Veterinary Medicine  
**Supervisor:** Monique Mayer

**Background:** Immobilization devices are used to keep the patients in a similar position for radiation therapy, and imaging systems built into the linear accelerator are used to correct the patient’s position prior to treatment. A margin of normal tissue around the tumor is added to account for setup errors. The current margin frequently used is 1 mm, and some radiation oncologists use 0 mm.
Methods: Five spherical lead markers were implanted into bones of the skull of twelve non-brachycephalic dog cadavers prior to immobilization. Six dogs were immobilized with device 1, and six dogs with device 2. Reference CBCT and orthogonal kV images were acquired immediately after immobilizing the dogs, and DRRs were generated from the reference CBCT. The 3D vector accounts for the translational vectors.

Results: The 95th percentile of the 3D vector for the image-guided positioning systems ranged between 2.8-3.6mm for the device 1 tested, and 2.1-2.9mm for device 2. No significant difference was found between MV and no imaging for both immobilization devices (p>0.05). All the other differences were significant (p<0.01).

Conclusion: This study suggests that the current 1-millimeter margin used in veterinary radiation therapy planning for canine brain tumors is smaller than the minimum necessary to ensure that the tumor falls within the treated volume for 95% of patient treatments. This study suggests that the margin should be at least 2 mm.

Keywords: radiation therapy, setup error, residual error, IGRT, head
11. Relationship between root scaling using ultrasonic vibration and the development and/or propagation of micro-cracks on root surfaces

Presenter: Jill Howlett, Courtney Posehn, Shira Lutz, College of Dentistry
Supervisor: Dr. Grazziotin
Collaborators: Dr. Ardenghi, Dr. Hoover

Background: The ideal goal of periodontal instrumentation is to remove plaque and calculus from teeth without causing root surface damage (roughness, cracks and micro-cracks). Scaling and root planning are the basis of periodontal therapy and various instruments have been designed to achieve this goal, such as ultrasonic vibration and curettes. The use of the ultrasonic scaling is an important alternative for daily clinical use. Some of advantages of ultrasonic scaling are: access to furcation, less operator tiredness, appropriate pocket penetration and less time required for scaling and root planning. The current literature is not clear if dentinal defects (such as, micro-cracks) are created or propagated after using power-driven scalers. These dentinal defects may propagate during normal function and result in potential pathways for leakage, sensitivity, pulp disease, or root fractures. Considering the clinical relevance that micro-cracks might have on teeth roots, the purpose of this study is to investigate the relationship of ultrasonic scaling and the development and/or propagation of micro-cracks using micro-computed tomography (Micro-CT)

Methods: 10 human extracted mandibular incisors will be scanned with Micro-CT before and after piezoelectric ultrasonic scaling. There is no control group in this study, because each tooth acts as its own control. Fiji/ImageJ and N-Recon softwares will be used to correct and reconstruct 3D images. The cross-sectional images of the roots (before and after scaling) will be superimposed to verify the presence and/or propagation of a micro-crack. Root micro-cracks are defined as all lines observed on the cross-section root slice, extending from the outer root surface into the dentin. Data will be reported descriptively (frequency and percentages).

Results: our null hypothesis is that there will not have development and/or propagation of root micro-cracks after performing ultrasonic scaling.

Conclusion: N/A

Keywords: Dentistry, Periodontics, Scaling and root planning, Plaque, Calculus, Root fracture, Dentinal defects,

12. The Effects of Sports Drinks on Salivary pH in Long Distance Runners

Presenter: Dylan Jackle, Duke Young, Donovan Shire, College of Dentistry
Supervisor: Mark Berscheid, Phil Chilbeck

Background: It is widely understood that sugary and acidic drinks can cause tooth decay and increase the rate of caries infection. Sports drinks, which are both acidic and high in sugar, are frequently used by endurance athletes as a means of hydration. Prolonged exercise leads to increased activation of the sympathetic nervous system, resulting in decreased salivary pH
Methods: Ideally, the study will have at least 10 participants, with all 10 being both control and experimental subjects. However, the possibility of increasing the number of subjects is feasible. Participants will consist of male and female long distance running athletes. Both test and control trials will have a protocol for fluid consumption, which is approximately 75 ml, at 5 minute intervals.

Results: It is hypothesized that sports drinks consumption during endurance running will cause salivary pH to decrease over time until it reaches a stabilization point. During the endurance running, it is expected that the participants’ salivary pH will drop below the critical pH of 5.5. At this point, enamel dissolution occurs rapidly and the development of caries is at an optimal point.

Keywords: Salivary pH, Endurance running, Sports Drinks, Sympathetic Nervous System, Dentistry, Enamel

13. Targeted therapy of osteosarcoma with radio-labelled monoclonal antibody to an insulin-like growth factor-2 receptor (IGF2R)

Presenter: Sharayu Karkare, College of Pharmacy and Nutrition
Supervisor: Dr Kate Dadachova

Background: Osteosarcoma is the most common non-hematologic primary bone malignancy. It has been reported that it is the most common primary malignant bone tumour and the fifth most common primary malignancy among adolescents and young adults. Recently studies have shown that since there is an inability to improve outcomes using conventional chemotherapy strategies, the need for alternative novel treatment approaches has been highlighted. In this study we investigate a novel therapy for Osteosarcoma utilizing Radio-immunotherapy (RIT) targeted to insulin growth factor receptor type 2 (IGF2R), which has shown a constant over-expression in Osteosarcoma.

Methods: The binding efficiency of the IGF2R specific monoclonal antibody 2G11 to the panel of osteosarcoma cells lines was assessed by flow cytometry with the purpose of selecting the cell lines with the lowest and highest IGF2R expression for the biodistribution will be assessed. Biodistribution studies were performed in osteosarcoma xenografts in SCID B17 mice using Lutetium-177-labeled 2G11 specific antibody and the isotype matching control MOPC21.

Results: Based on the flow cytometry results, OS-17 and 143B were selected for initiation of tumors in SCID mice for biodistribution experiments. The 177Lu-2G11 demonstrated IGF2R-specific uptake in both OS-17 and 143B tumors which was significantly higher than that of isotype matching control MOPC21. 177Lu-2G11 cleared fast from all organs except for the spleen, probably due to the tumor cells invasion into this organ. The therapy studies with 177Lu-2G11 in tumor bearing mice are currently underway.

Conclusion: In conclusion, given the lack of new effective therapies RIT might prove beneficial. Since IGF2R is expressed normally across various tissue types, the constant over-expression in Osteosarcoma recommends that it may serve as a valuable therapeutic target in the treatment of Osteosarcoma.

Keywords: RIT : Radioimmunotherapy
14. Screening for insulin resistance and metabolic abnormalities in clinical practice: a neglected modality in the therapeutic management of women with polycystic ovary syndrome

Presenter: Maryam Kazemi, College of Pharmacy and Nutrition  
Supervisor: Donna R Chizen  
Collaborators: Maryam Kazemi and Donna R Chizen

Background: Polycystic ovary syndrome (PCOS) is associated with insulin resistance (IR), obesity, and metabolic abnormalities. Metabolic syndrome (MetS) is a cluster of risk factors conferring an increased risk for type 2 diabetes (DM2) and cardiovascular disease (CVD). Screening for insulin and metabolic disruptions is often overlooked by clinicians and not a standard practice in the clinical management of PCOS. The present study aimed to evaluate the degree of IR and metabolic aberrations, identified by MetS, between women with PCOS and non-PCOS controls across obesity phenotypes.

Methods: In a prospective cross-sectional study on 151 women aged 18-35 years 111 women with PCOS (Androgen Excess and PCOS Society criteria) and 40 non-PCOS healthy controls were identified and subcategorized to 4 groups based on body mass index (BMI) status: 82 obese and overweight (BMI≥25 kg/m2) women with PCOS (OPCOS); 29 lean (BMI<25 kg/m2) women with PCOS (LPCOS); 11 overweight and obese controls (OC); and 29 lean controls (LC). All women were screened and compared for plasma insulin and glucose levels using a 2-hour 75-gram oral glucose tolerance test (OGTT), clinical, and biochemical measures of metabolic syndrome (MetS). The diagnosis of MetS complied with the 2005 International Diabetes Federation consensus criteria in collaboration with the American Heart Association/National Heart, Lung, and Blood Institute.

Results: The prevalence of IR (the homeostasis model assessment of IR>2.6) was higher in the OPCOS group when compared to the LPCOS group (46.3% [38/82] vs 10.3% [3/29]; P<0.01). No women were identified as insulin resistant in controls. The OPCOS group exhibited an increased and delayed insulin response at all time-points following OGTT when compared with the lean counterparts: two hours following the OGTT the levels of insulin continued rising above the peak 1-hour levels in 41.0% (34/111) of OPCOS group compared with 20.1% (6/29) of LPCOS group (P<0.01). Insulin concentrations returned to <40% of the peak value in all healthy controls 2 hours following the OGTT. The OPCOS group exhibited adverse glucoregulation reflected by higher rates of DM2 (n=5 vs n=0; P<0.05) and impaired glucose tolerance (n=20 vs n=3; P<0.01) following the OGTT when compared with the LPCOS group. Women in the control group exhibited normal glucose tolerance. The prevalence of MetS was approximately 9-fold higher in the PCOS group than age-matched controls: women with PCOS had an overall prevalence of MetS of 45.0% (46/82 in the OPCOS and 4/29 in the LPCOS groups), compared with 5.0% (2/40) of controls who were all from the OC group (P<0.01). The OPCOS group exhibited increased cholesterol to HDL-C ratio (4.39±0.1 vs 3.39±0.4; P<0.001) and decreased HDL-C concentrations (1.2±0 vs 1.4±0.1 mmol/L; P<0.001) when compared to age- and BMI-matched controls.

Conclusion: Reproductive-age women with PCOS have a high prevalence of IR and exhibit exacerbated metabolic phenotype when compared to the general female population of similar age and obesity class. All women with PCOS should be screened for MetS, DM2, and IGT upon diagnosis and when no abnormalities are found, regularly in follow up visits irrespective of obesity and age.

Keywords: insulin, polycystic ovary syndrome, metabolic, lipid, obesity
15. Circadian Disruption, Oral Cancer, and Precision Health

Presenter: Petros Kechagioglou, College of Medicine  
Supervisor: Silvana Papagerakis  
Collaborators: Li Zheng, Petros Papagerakis, Frederick Vizeacoumar, Franco Vizeacoumar

Background: Worldwide, Oral Cancer (OC) continues to be a disfiguring and deadly disease. Currently, there are limited prognostic biomarkers and less than optimal therapeutic options for advanced OC. Disruption of circadian rhythms deregulates cell proliferation and significantly increases cancer risk. Importantly, circadian clock disruption and responses to circadian based-therapies are patient-specific.

Methods: Quantitative Real-Time PCR (qPCR) was used to assess the expression levels of clock genes in Oral Squamous Cell Carcinoma cell lines. The clock genes profiles were analyzed by flow cytometry, while the immunohistochemical staining was performed to various tissue specimens. TCGA analysis of Head and Neck cancer patients was performed regarding clock genes RNA-seq Expectation Maximization levels.

Results: Our data indicated various levels of clock gene expression in OC patients and circadian clock disruption in OC primary cells lines. BMAL1 and CK1ε were the highest expressed in primary tumors derived from oral cavity and oropharynx in the TCGA HNSCC cohort. Their expression levels directly correlated with advanced tumor stage being increased significantly in stages III-IV and poorer survival.

Conclusion: We provide the first comprehensive and circadian rhythms-dependent characterization of the molecular signature of OC patients. We aim to identify statistically significant and clinically relevant changes in the circadian clock genes profiles in OC and provide novel therapeutic targets for precision oncology. This approach could alter the traditional ways of diagnosis and treatment of OC.

Keywords: clock genes, oral cancer, TCGA dataset, circadian clock, precision medicine

16. Daily minutes of physical activity and impact counts are positively associated with 1-year changes in trabecular and cortical bone micro-architecture at the distal radius and tibia in children

Presenter: Anthony Kehrig, College of Kinesiology  
Supervisor: Dr. Saija Kontulainen  
Collaborators: Kelsey Björkman, Amy Bunyamin, Dr. Chantal Kawaiilak, Dr. James Johnston

Background: The Canadian 24-Hour Movement Guidelines for Children and Youth recommend at least 60 minutes of moderate-to-vigorous physical activity (MVPA) per day, and muscle and bone strengthening activities 3 times per week for musculoskeletal health. However, evidence linking objectively measured physical activity with bone growth and development is limited. Particularly the role of physical activity on bone micro-architectural development in children is poorly understood. Our objective is to assess if daily minutes of MVPA and vigorous physical activity (VPA), and impact counts (≥3.9g magnitude) at baseline are associated with 1-year changes in HR-pQCT trabecular and cortical bone micro-architecture at the distal radius and tibia.

Methods: We recorded 7-day activity of 13 children (mean age 10.3, SD 1.3y) at baseline using accelerometers and measured trabecular and cortical bone microarchitecture at the distal radius (7% of
ulnar length) and tibia (8% site) using high-resolution peripheral quantitative computed tomography (HR-pQCT) at baseline and 1-year follow-up (mean follow-up 1.2, SD 0.3 y). We adjusted micro-architectural changes to 1-year for each participant. We tested our hypothesis using Spearman's rho coefficients (p<0.05).

**Results:** Daily minutes of MVPA (mean 37.7, SD 24.9) were positively associated with changes in trabecular thickness (+0.56), cortical bone mineral density (+0.60), and fine cortical thickness (+0.58) at the radius. Daily minutes of VPA (mean 11.7, SD 7.7) were negatively associated with changes in cortical pore volume (-0.56) at the radius, and (-0.56) at the tibia. Daily impact counts (mean 34.8, SD 25.8) were positively associated with changes in cortical bone volume (+0.62) and density (+0.60) at the radius.

**Conclusion:** These findings suggest that children spending more time in MVPA, VPA, or impact activities may have greater annual increases in trabecular thickness, cortical volume, density, and thickness at the distal radius. Children engaged in greater amount of vigorous activity may also experience larger decrease in pore volume at the distal radius and tibia. These preliminary results suggest beneficial relationships between physical activity and trabecular and cortical bone micro-architecture. These findings will guide future prospective studies and exercise interventions aiming to optimize bone micro-architectural development in children.

**Keywords:** children, physical activity, bone, microarchitecture, high resolution pQCT

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17. **Effect of flexibility and walking exercise on blood pressure of older adults with prehypertension or stage I hypertension**

**Presenter:** Jongbum Ko, College of Kinesiology  
**Supervisor:** Dr. Phil Chilibeck  
**Collaborators:** J. Alcorn, T. Hadjistavropoulos

**Background:** Hypertension is one of the most common health risk factors in older adults. Hypertension could develop not only from unhealthy lifestyles (e.g. sedentary lifestyle, unbalanced diet) but also from the natural aging process. Pre-hypertension (130/85 – 139/89 mmHg) and stage I hypertension (140/90 – 159/99 mmHg) are conditions that don't necessarily require drug intervention, and can be improved by simple lifestyle change, such as eating habit modification and regular physical activity. Often, walking exercise is suggested as a first line exercise intervention to improve cardiovascular health because of its convenience and the degree of difficulty compared to other types of exercises. Flexibility training (i.e. stretching) may also provide benefit to blood vessels, improving vascular health, and reducing arterial stiffness and blood pressure. This study compared the effect of walking exercise and flexibility exercise on ambulatory blood pressure of older adults with pre-hypertension or stage I hypertension.

**Methods:** Twenty-five adults over 50 years old with pre-hypertension or stage I hypertension were recruited and randomly assigned to either the 8-week (5d/week) walking intervention at 65% of estimated maximum heart rate for 30 minutes - 1 hour or flexibility training. Twenty-four-hour ambulatory blood pressure was measured before and after the intervention.

**Results:** After the 8-week intervention there were significant group x time interactions for night time systolic and diastolic ambulatory blood pressures (p=0.024 and p=0.01, respectively) with greater reduction in the stretching group (change from 124 to 120 mmHg for stretching and 127 to 132 mmHg for
walking for systolic blood pressure, and 69 to 66 mmHg for stretching and 67 mmHg to 72 mmHg for walking for diastolic blood pressure).

**Conclusion:** Flexibility training may be superior to walking exercise for reducing blood pressure in individuals with pre-hypertension or stage I hypertension.

**Keywords:** cardiovascular, blood pressure, walking exercise, stretching exercise

18. **Effects of Sympathetic Activation on Aortic Stiffness in Young Healthy and Hypertensive Adults**

**Presenter:** Dana Lahti, College of Kinesiology  
**Supervisor:** Corey Tomczak  
**Collaborators:** Shayne Hayward, Calvin R Wells, Erick D McNair, Corey Tomczak

**Background:** Aortic stiffness is a major link between hypertension and cardiovascular risk. Anatomic features of the artery including the smooth muscle regulate aortic stiffness, in part. Importantly, vascular smooth muscle is under sympathetic nervous system control, and thus aortic stiffness may be influenced by the sympathetic nervous system. When exposed to physiological stress, older hypertensive adults demonstrate an exaggerated blood pressure response that may correspond with transient arterial stiffness increases, but this response in young hypertensive adults remains unknown. We tested the hypothesis that sympathetic activation would increase aortic stiffness in young healthy adults (control, CTL), and that aortic stiffness increases during sympathetic activation would be greater in young hypertensive adults (HTN).

**Methods:** Six healthy controls (males=4, females=2; 28.3±5.5 years; BMI: 23.5 ± 3.5 kg/m2) and three young hypertensive participants (males=2, females=1; 28.3 ±6.0 years; BMI: 30.3±8.2 kg/m2) were studied. Mean arterial pressure (MAP) and carotid-femoral pulse wave velocity (PWV) were measured at rest and during 5 min of brachial circulatory occlusion (sympathetic activation condition) that followed isometric handgrip exercise.

**Results:** Resting MAP was higher in HTN (100 ±6 mmHg) than CTL (90 ±5 mmHg; $P=.029$). Occlusion MAP was also higher in HTN (116 ±6 mmHg) than CTL (102±7 mmHg; $P=.016$). Resting PWV was similar between CTL (8.6±1.6 m/s) and HTN (8.1±0.1 m/s; $P=.47$). The increase in PWV from rest to occlusion (1.2±1.4 m/s) in CTL was not significant ($P=.09$), whereas the increase in PWV from rest to occlusion (2.0±0.4 m/s) in HTN was significant ($P=.01$).

**Conclusion:** Sympathetic activation may significantly increase aortic stiffness in young hypertensive adults, but not young healthy adults.

**Keywords:** aortic stiffness, sympathetic activation, hypertension
19. Musculoskeletal risk factors for shoulder dysfunction in breast cancer survivors: can pre-screening predict future dysfunction?

Presenter: Angelica E. Lang, College of Medicine  
Supervisor: Soo Y. Kim  
Collaborators: Clark R. Dickerson, Ian Stavness

**Background:** Approximately one in nine Canadian women will be diagnosed with breast cancer in their lifetime. Fortunately, the survival rate is almost 90%, largely due to improved screening and treatment. However, upper limb dysfunction is common among breast cancer survivors (BCS). It is possible that pre-screening shoulder health may mitigate dysfunction and improve recovery times. The purpose of this study was to determine the musculoskeletal risk factors of shoulder dysfunction among BCS in the first year post-surgery.

**Methods:** Forty-two females with planned breast cancer surgery were recruited from the Breast Health Center in Saskatchewan, Canada. Shoulder range of motion, strength, and posture were assessed by a physical therapist prior to surgery. History of previous shoulder problems was also recorded. Surgical and medical information was obtained from the patients’ charts following their surgery. The Shoulder Pain and Disability Index (SPADI) was completed by each participant pre-surgery and at 3, 6, and 12 months post-surgery. T-tests and non-parametric measures were used to calculate differences between time points and associations of risk factors and disability.

**Results:** Thirty-five participants completed the 3 month post-operative SPADI. Three months post-surgery SPADI scores increased by an average of 7.8% from baseline (p = .002). Seven participants demonstrated a clinically significant 11% increase between these time points, which was moderately associated with history of shoulder problems, restricted humeral extension (average = 37.7° vs 48.9°), and restricted humeral flexion pre-operatively (average = 147.6° vs 151.3°). Twenty-five and twenty-four participants completed the 6 and 12 month SPADI, respectively; scores decreased by 3.4% and 5.0% between the respective time points. Interestingly, of the 10 participants that were lost to follow-up at 6 and 12 months, their 3 month SPADI score was 7% and 12% higher than the 27 women who did respond at the later timepoints.

**Conclusion:** Clinically significant impairments in shoulder function are associated with decreased shoulder extension pre-surgery and history of shoulder problems. These parameters can be used to identify high-risk patients before cancer treatment and direct their rehabilitation. Further investigation is required to confirm these effects.

**Keywords:** breast cancer, shoulder dysfunction, pre-screening, musculoskeletal risk factors
20. Synchrotron analysis of blood clots from stroke patients

Presenter: Vedashree Meher, College of Medicine
Supervisor: Dr. Roland Auer, Dr. Lissa Peeling and Dr. Michael Kelly

Background: Ischemic stroke occurs as a result of vascular occlusion, usually due to thrombus (blood clot) formation which ultimately reduces blood flow to the brain. Deprived of oxygen and nutrients, the brain suffers tissue injury and neuronal death. Ischemic strokes account for 87% of all stroke types and it is essential to treat stroke victims in a time-efficient manner in order to minimize post-stroke damage.

Until recently, one of the most prominent treatments for acute ischemic stroke was, chemically breaking the thrombus by administrating intravenous thrombolytic drug, recombinant tissue-plasminogen activator (rtPA). However, due to several drawbacks associated with rtPA such as, its short treatment window and contra-indication list, only a limited number of patients receive this drug, and there is a low success rate for recanalization (restoring blood flow) for patients with large vessel blockage.

For large vessel occlusions, endovascular therapy (EVT) is a highly effective technique, whereby the thrombus is mechanically retrieved via the femoral artery. In recent years, with technological advances, EVT has demonstrated an improvement in the health outcomes of stroke victims with larger clot burden. However, it is still not clear as to which technique and device combination is the most effective for quick clot retrieval. In an ideal scenario the thrombus can be retrieved quickly and efficiently, however, interventionists occasionally have to perform multiple passes to extract the thrombus using multiple techniques and sometimes are still unable to completely restore intracranial flow. The longer the procedural time and increased complexities, may result in poorer clinical status and higher complication rates.

Defining characteristics of stroke-related thrombus with advanced synchrotron based imaging techniques in combination with conventional histology and immunohistochemistry, may help us better understand the biochemical composition of clots, potentially enabling us to correlate biochemical information with patient information and treatment outcomes, giving us an insight into answering the proposed questions.

The research questions of this project include:

1. Does clot location impact biochemical composition?
2. What makes certain clots denser than the others?
3. Why are some clots much more difficult to retrieve than other clots despite various techniques, approaches and devices used?
4. Which device and technique combination is the most effective for time-efficient retrieval?

We hypothesize that endothelialization, a process whereby endothelial cells cover up the clot, and trapped biological elements result in denser clots, thereby making it difficult to mechanically retrieve them and restore complete intracranial blood flow. Thus, defining composition of dense clots is important to identify effective clot

Methods: Thrombi were retrieved from acute ischemic stroke patients who presented at the Royal University hospital. In order to qualify for EVT, patients had to meet certain radiographic inclusion criteria. Thus, prior to EVT procedure, patients underwent neurological examination and CT angiogram to confirm large vessel occlusion, thrombus size and thrombus location. To examine the status of collateral flow, patients were assigned; 1. National Institute of Health Stroke Scale (NIHSS) score to evaluate stroke
severity, and 2. Alberta Stroke Program Early CT score (ASPECTS) to evaluate the volume of cerebral infarct. To qualify for EVT, candidates required a score greater than 5 for both NIHSS and ASPECTS.

Once the thrombus was retrieved, the sample was flash frozen in 2-methyl butane (isopentane) within 30 minutes of restoring blood flow to preserve the biochemical state of the sample and to avoid damage due to ice crystal formation. The sample was then cryosectioned and adjacent sections were collected for different imaging techniques to define the morphology and biochemical composition. Sections were collected at 7µm thickness on CaF2 discs for Fourier-transform infrared spectroscopy (FTIR) as well as at 7µm thickness for histology, and 30µm thickness on metal-free thermanox coverslips for X-ray fluorescence imaging (XFI).

FTIR enables us to map the distribution of macromolecular metabolites such as glycogen, lactate, proteins, aggregated proteins, lipid esters and glutamate while XFI enables us to map the distribution of elements such as Ca, P, Zn K, Cl, Fe, S and many more. On the other hand, conventional histology enables us to characterize morphology and cellular features such as endothelialization, platelets, red blood cells, white blood cells and fibrin.

Both FTIR and XFI imaging techniques produce a 2-dimensional map to visually compare concentration distributions per pixel for each of the biochemicals individually. Additionally, for each distribution map, a spectrum of energy peaks is produced where each peak defines a specific type of biochemical. For example, for FTIR maps, lipid esters have a specific energy peak distinguishable from proteins or glycogen. Similarly, for XFI maps, each element has its own energy peak distinguishable from other elements.

XFI elements were quantified using Sam’s Microanalysis kit (SMAK) and ImageJ whereas, FTIR spectra and functional group images will be generated and viewed using Cytospec, ImageJ and Orange software. Histological data will be viewed using light microscopy.

All imaging findings will be correlated with patient information and surgical outcomes.

**Results:** This project is a pilot and ongoing project with incomplete data collection and analysis at this point. Data for FTIR has not yet been collected due to beam-time unavailability (i.e. beam-time for FTIR has not yet been allocated for this project). However, preliminary data for XFI and histology has been collected.

For XFI analysis two different clots from two different patients were analyzed to compare their distribution patterns. One of the clot was labelled 007 and the other clot was labelled 004. Both the clot samples exhibited different distribution patterns. For example, clot 007 showed increased distribution of Cl, Fe and Zn on the periphery, while clot 004 showed increased distribution of the same elements, Cl, Fe and Zn inside the clot. Similarly, S and P concentration were minimally observed in clot 007 while for clot 004, the S and P showed high concentration spots throughout the clot.

Histological analysis demonstrated that endothelial cells (labelled with CD31 antibody) were highly spread on the peripheral regions in a way covering up the clot, potentially hardening them. Additionally, endothelial cells were also observed clustering together within some clots. On the other hand, macrophages (labelled with CD68 antibody) were scattered throughout the thrombus. Granular debris were also observed.

**Conclusion:** There are many factors that influence clinical outcomes and EVT success. These factors include infarct/lesion size, recanalization rate, clot size, clot length, size of vessel blockage, location of vessel blockage, collateral flow status, and clot characteristics.

In this project, we are aiming to define clot characteristics to better predict clinical outcomes by minimizing clot-retrieval time and effectively reducing arterial stress by minimizing number of passes.
made during EVT. The long term goal of this project is to reduce post-stroke tissue injury and minimize cell death.

Several previous studies have analyzed clots and defined clot morphology. However, most studies have used conventional techniques. This project is novel because we are employing advanced and sophisticated synchrotron-based imaging techniques, FTIR and XFI to further understand clot composition and build on what is already known from conventional methods.

So far XFI analysis has shown that most elements distribute in higher concentrations at the peripheral regions. This distribution pattern could be a potential indicative factor of denser clots that resist surgical penetration and retrieval. Since this is a pilot project, more samples will have to be analyzed in the coming future to conclusively compare distribution patterns for both FTIR and XFI.

With advances in EVT, and evidence that clearly demonstrates the need for fast and effective clot retrieval, it remains unclear as to which device and technique combination is most effective. Defining clot composition, identifying appropriate targets, and correlating these findings with patient information and surgical outcomes are key steps in improving stroke treatment outcomes.

**Keywords:** Stroke, mechanical thrombectomy, clot, biochemical composition, X-ray fluorescence imaging, histology, endothelialization, biological elements.
Clinical Group 3

21. Relationships between Childhood Arthritis Outcomes and Stressful Life Events

Presenter: Kate Neufeld, College of Medicine
Supervisor: Alan Rosenberg
Collaborators: Elham Rezaei

Background: The role of psychosocial stress in juvenile idiopathic arthritis (JIA) is not well understood, although it has been implicated as a possible factor influencing JIA onset and clinical disease course. Major life events are believed to have a stronger influence in the course of JIA than in adult rheumatoid arthritis.

Factors that influence the occurrence and outcomes of chronic childhood arthritis are likely to include complex interactions among an array of factors that include susceptibility genes, environmental factors and sociodemographic circumstances. Psychosocial stress, infection, hormones, prenatal factors and environmental toxicants have each been implicated as possible exogenous factors influencing the occurrence and outcomes of chronic arthritis in children.

Understanding of the environmental determinants of disease outcomes in JIA remains rudimentary. Therefore, there is an ongoing need for research into the role of these environmental factors, including stress. The ability to predict which children with JIA would have worse outcomes could lead to new preventative strategies, and targeted medical and allied therapies.

The objective of this study was to determine relationships between stressful life events scores at enrolment and clinical outcomes, physical function, quality-of-life and inflammatory biomarkers at 6, 12, 18 and 24 months post-enrolment.

Methods: This study included an inception cohort of 186 new-onset, treatment naïve JIA patients from 11 participating Canadian Rheumatology Programs. The study, titled Biologically-based Outcome Predictors in JIA (The BBOP Study) enrolled participants during the period 2007 to 2012. A broad array of clinical, demographic, family history, psychosocial and environmental variables were collected at enrolment. Stress was measured using a modified Stressful Life Events Questionnaire (StLE) and Hassles Questionnaire, a measure of daily stressors, completed at enrolment by children, adolescents and/or parents.

Enrolment StLE and Hassles scores were analyzed for associations with quality-of-life (Juvenile Arthritis Quality-of-Life Questionnaire [JAQQ]), physical functional ability (Children's Health Assessment Questionnaire [CHAQ]), pain scores, number of active, effused joints, or joints with limited range of motion, serum erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor and a wide range of serum biomarkers including interleukins, matrix metalloproteases, and growth factors at 6, 12, 18 and 24 months post-enrolment.

Data were analyzed using Pearson Correlates with SPSS version 23. P value was set at p< 0.05 for all data outcomes, except biomarker data for which Bonferroni corrected p value was calculated and set at p<0.001. A high JAQQ or CHAQ score represented a low quality of life and low functional ability respectively.
Results: Enrolment child StLE scores (N= 80; X (Mean)= 11.94 +/- 9.23; Mean age: 7.23 years; Male: 36.2%; Female: 63.8%) showed a positive correlation with JAQQ scores at 6 month (N=57; r=0.35; p=0.07), 12 month (N=51; r=0.38; p=0.006), 18 month (N=51; r=0.42; p=0.002) and 24 month (N=40; r=0.45; p=0.003) post-enrolment, indicating worse quality of life as scores increased. Child StLE scores showed a positive correlation with CHAQ scores at 12 month (N=52; r=0.28; p=0.04) and 18 month (N=50; r=0.35; p=0.01) post-enrolment, indicating lower functional ability. Child StLE scores did not correlate with other clinical or biomarker outcomes.

Enrolment adolescent StLE scores (N= 6; X= 9.23 +/- 6.69; Mean age: 12.6 years; Male: 16.7%; Female: 83.3%) could only be calculated using 12 month visit data due to limited data available for statistical analyses at other time points. Adolescent StLE scores only correlated positively with erythrocyte sedimentation rate (ESR) at 12 months (N=5, r=0.91, p=0.035) and pain score at 24 months (N=5, r=0.98, p=0.003).

Enrolment parental StLE scores (N= 78; X= 10.26 +/- 7.44; Mean age: 7.22 years; Male: 34.6%; Female: 65.4%) correlated positively with JAQQ scores at 6 months (N=56, r=0.29, p=0.033), 12 months (N= 50; r=0.46; p=0.001), 18 months (N=51, r=0.44, p=0.001) and 24 months (N=39, r=0.47, p=0.002) visits and CHAQ scores at 6 months (N=56, r=0.29; p=0.033), 12 months (N=51, r=0.46; p=0.016), 18 months (N=50, r=0.37; p=0.008), pain score at 12 months (N=50, r=0.34; p=0.02). Parents’ StLE scores did not correlate with other clinical outcomes or biomarker data.

There was no significant association between mean daily Hassles scores (N = 80; X = 0.57 +/- 0.53; Mean age: 7.23 +/- 3.4 yr; Male: 36.3%; Female: 63.7%) and any of the study outcomes or biomarkers.

Conclusion: Identifying and managing life stressors at first JIA presentation may be important for improving JIA outcomes, especially quality-of-life, functional ability and pain. A multidisciplinary team, including social worker, psychologist, or spiritual support, may help address these needs at onset as they likely impact future disease course in children with JIA. Further research into the role of stress in different subtypes of JIA, and longer-term studies are required.

Keywords: Juvenile idiopathic arthritis (JIA); Stressful life events; Daily stress; Quality-of-life; Functional Outcomes; Pain; Biomarkers
hospital, relatively little is known about the ways in which they participate in safety initiatives. This study sought to describe the personal, interpersonal and organizational factors that influence CKD patients' experiences with and perspectives on safety and safety incidents in acute care settings, as well as their willingness to report incidents utilizing an existing safety reporting system.

**Methods:** Thirty patients with CKD from an acute care facility were recruited for this mixed methods study. Data collection through semi-structured interviews and the Patient Measure of Safety questionnaire were collected over a period of five months. Interviews were audio recorded and transcribed verbatim; accompanied by thematic analyses of the data. Descriptive analysis of the PMOS results offered context.

**Results:** Participants were divided about their expectations of care they should receive in the hospital. Threats to safety from the physical and the socio-emotional care environment were reported by participants. The majority of the participants were unaware of the presence of a safety reporting system. As well, most indicated that they would likely not report safety issues.

**Conclusion:** Participants in this study were able to identify threats to their safety. Most were reluctant or unwilling to report safety issues, due to their dependency on the health care system and providers. As well, the willingness of patients to speak up for their own safety is dependent on the culture of the setting, the relationship with the care providers, and their own personal factors. However, not all patients are healthy enough or have the expertise to participate. This was evident from participants' responses.

**Keywords:** patient safety; patient engagement; chronic kidney disease

### 23. EVALUATION OF RETINAL MORPHOLOGY IN CANINE SUDDEN ACQUIRED RETINAL DEGENERATION SYNDROME USING OPTICAL COHERENCE TOMOGRAPHY AND FLUORESCEIN ANGIOGRAPHY

**Presenter:** Stephanie Osinchuk, Western College of Veterinary Medicine  
**Supervisor:** Bruce Grahn  
**Collaborators:** Marina Leis, Elyse Salpeter, Lynne Sandmeyer, Bruce Grahn

**Background:** Sudden acquired retinal degeneration syndrome (SARDS) is a leading cause of incurable blindness in dogs. Microscopic evaluation is critical in determining the pathogenesis of SARDS and essential for development of evidence-based treatments. This research describes the in vivo optical coherence tomography (OCT) and fluorescein angiography changes in SARDS.

**Methods:** Retinal OCT was performed on 10 SARDS dogs and 8 control dogs. Measurements were collected from the photoreceptor layer, the outer nuclear layer, the outer retina, the inner retina and the whole retina thickness. Sodium fluorescein was injected intravenously and serial fundus photographs were collected for a 5 minute period post-injection.

**Results:** The outer nuclear layer and outer retina measurements were significantly (p<0.05) decreased in SARDS dogs compared to controls. The whole retina thickness was significantly decreased in the temporal retina (p<0.05) but not the nasal retina. All SARDS dogs had a loss of definition of all photoreceptor band signals on optical coherence tomography.
Conclusion: OCT measurements in dogs with SARDS support the previous histopathology findings of apoptosis of the outer nuclear layer and loss of the photoreceptor inner and outer segments. Further work evaluating the retinal pigmented epithelium and photoreceptor outer segment interaction in dogs with SARDS may be valuable.

Keywords: sudden acquired retinal degeneration, canine blindness, amaurosis,

24. Bringing Birth Back

Presenter: Carrie Pratt, College of Nursing
Supervisor: Angela Bowen

Background: "Bringing Birth Back" is a multifaceted research project that serves to implement culturally secure birth for Indigenous women in Saskatchewan. An important outcome of the project is the Indigenous Birth Network (Network). The Network brings together people in Saskatchewan with knowledge and expertise in Indigenous maternal care to inform a model of Indigenous maternal care. The intention is to create a culture of competence and humility of care providers working with Indigenous mothers and their families. Research shows cultural practice serves as a protective health factor. Therefore, the research hypothesis is: supporting Indigenous women to practice their culture during the natal period is a mechanism of health promotion and prevention for the mothers, their babies, and families. If we protect cultural safety for Indigenous mothers of Saskatchewan, it will promote healthy relationships between the baby and its community from the moment it enters the world. Western approaches to healthcare have interrupted the knowledge of reproductive care that exists within Indigenous communities; bringing birth back in a good and meaningful way for Indigenous mothers could have widespread effects for their infants. Ultimately the purpose of our project is to achieve our goal of improving the birth experiences and health outcomes of Indigenous families.

Methods: The team is committed to ethical research and as such will use Patient Oriented Research (POR), and Participatory Action Research (PAR) as a theoretical research framework. PAR is a western-approach to research that is align with the principles of OCAP, Tri-Council Policy Chapter 9, and the University of Saskatchewan's Recommendations for Research with Indigenous People.

The research team will include mothers who will participate in data collection and analysis, and knowledge dissemination activities. The Network, of which our patient and family advisors will be an integral part of, will refine the research plan and design, carry out data collection, and interpret findings. The research project will use multiple tools of data collection to achieve its research goals and to include community partners. Data interpretation will be iterative, with a continuous process of gathering, interpreting, and analyzing the data. It is also important to note data collection methods may alter through the continuous community input. The priorities of the community must take precedence over adherence to methodological rigor. Specific methods will include: online survey, community visits and talking circles, environmental scans of Indigenous midwifery care and education models, collection of data through Medical Health Officer partnership to understand numbers and types of birth for Saskatchewan Indigenous women, and ongoing team and community meetings.

Results: In progress. The research grant proposal was developed after visits to four Indigenous communities in Saskatchewan, including one fly in location. The PI and RA held discussions and focus groups with mothers and health care staff to hear about their birth experiences and what they would like to see and imagine for maternal health care services. While four communities are not nearly
representative of the diversity of Indigenous groups in Saskatchewan, the information gathered was valuable and guided the research grant proposal.

Results will inform the delivery of maternal health care for Indigenous women in tertiary and rural centres, and inform policy briefs for Indigenous, provincial, and federal governments. We expect supporting culturally secure birth for Indigenous mothers will have positive impacts for the mothers, babies, and their families.

**Conclusion:** This research project serves to re-imagine maternal care that serves the unique needs of Indigenous mothers and their families. Colonization processes have created geographical and socioeconomic barriers for Indigenous children to achieve their best health outcomes. It is time to support Indigenous cultural natal care traditions for mothers and infants in Saskatchewan.

**Keywords:** Indigenous, maternal, cultural care, traditional, birthing practices

25. **Teach Me to Feel: A longitudinal study on the development of empathy in students in the Colleges of Dentistry and Medicine at the University of Saskatchewan**

**Presenter:** Hammad Qasim, College of Dentistry  
**Supervisor:** Dr. Petros Papagerakis  
**Collaborators:** Jake Drake and Jory Simpson

**Background:** Various studies have shown a decrease in the level of empathy as students in the health care professions move from their preclinical to clinical courses, while other research has shown a positive effect. The objective of this study is to determine if clinical experience and dental/medical education changes the relative level of empathy in students in the Colleges of Dentistry and Medicine.

**Methods:** Students from the Colleges of Dentistry and Medicine will make up the participant pool. Empathy will be operationally defined using the Jefferson Scale of Empathy. Students will be asked to evaluate their current measurement of empathy and six months later a second questionnaire will be administered. A 2x2 repeated-measures ANOVA will be utilized to measure mean differences.

**Keywords:** Dentistry, Medicine, Empathy, Education

26. **A pilot study to determine the feasibility of using Registered Pharmacy Technicians to identify and correct inhaler misuse**

**Presenter:** Taylor Raiche, College of Pharmacy and Nutrition  
**Supervisor:** Holly Mansell  
**Collaborators:** D. Blackburn, D. Turner, D. Larocque, C. Evans

**Background:** Poor inhaler technique is a pervasive problem among patients with chronic respiratory conditions that has been associated with poor respiratory outcomes. This pilot assessed the feasibility of utilizing registered Pharmacy Technicians (PT) in community pharmacies to assess and correct inhaler technique at inhaler refill pick-ups.
Methods: Assessment and correction of demonstrated inhaler technique was conducted by PTs in three community pharmacies during a 30-day period. All eligible patients who visited the pharmacy for refill pick-ups were asked if they were willing to have their inhaler technique assessed. For each patient interaction, the following data was collected: estimated patient age and sex, type of issue detected (if any), perceived patient response, and length of interaction. Semi-structured interviews were conducted with the PTs and pharmacy managers at the end of the 30-day period to assess perceptions and feasibility of expanding the service. Nvivo software was used to code the data into emerging themes.

Results: Of a possible 231 patients eligible, 47 were offered an independent inhaler technique review by the PT. Eighty-five percent (40/47) of these patients accepted and demonstrated their inhaler technique. More than half of patients (52.5%) demonstrated at least one technical error; all of which the PTs were able to correct. Almost all patients (39/40) were perceived to be either satisfied or very satisfied with the assessment. The median time to review and correct technique was 3 minutes. Five primary themes emerged from the follow-up interviews, including: feasibility, patient benefit, potential to reduce pharmacist workload, professional development/job satisfaction, and barriers.

Conclusion: By examining the use of a PT to identify corrigible inhaler misuse in community pharmacies, this study identified barriers and potential solutions for expansion of the service. Future studies should investigate the benefit of the PT expanded role on clinical outcomes in asthma and COPD.

Keywords: pharmacy, pharmacy technician, inhaler, respiratory disease, asthma, COPD, education, interprofessional, collaboration

27. Development of a Liquid Chromatography Tandem Mass Spectrometry Method for the Identification and Quantification of Cannabidiol and Δ9-Tetrahydrocannabinol in Pediatric Patients

Presenter: Stephanie Vuong, College of Pharmacy and Nutrition
Supervisor: Dr. Jane Alcorn and Dr. Andrew W. Lyon
Collaborators: Deborah Michels, Richard Huntsman, Richard Tang-Wai, and Fang Wu

Background: Up to 30% of children with epilepsy will be refractory to conventional treatment such as anticonvulsant medications and the ketogenic diet, placing the child at risk of having poor long-term cognitive, behavioral, and psychological outcomes. This is particularly true for the epileptic encephalopathies, which are associated with resistance to medical treatment and neurodevelopmental decline. Over the years, Cannabis has been emerging as a therapeutic product for many different health conditions. With the recent interest in Cannabis use as a treatment for refractory epileptic encephalopathy, parents are desperate to obtain medical Cannabis products without adequate knowledge of their safety and efficacy and appropriate dose. By understanding the oral pharmacokinetics of CBD and THC in children, we can better determine dosing regimens for the oral administration of Cannabis oil to children with refractory epileptic encephalopathy. A sensitive and efficient liquid chromatography-tandem mass spectrometry method is under development to identify and quantify cannabidiol, Δ9-tetrahydrocannabinol, and metabolite 11-hydroxy-Δ9-tetrahydrocannabinol in plasma volumes from pediatric patients undergoing Cannabis oil therapy for refractory epileptic encephalopathy.

Methods: Human plasma (190 μL) is spiked with the appropriate cannabinoid concentrations (10 μL). Spiked human plasma undergoes protein precipitation using 75% v/v acetonitrile spiked with internal
standard. Supernatant from samples is dried and reconstituted using mobile phase and 5 μL is injected onto a Zorbax eclipse column, using an Agilent 1290 UPLC to separate analytes for mass spectrometry detection. Gradient elution at a flow rate of 250 μL/min consists of Mobile phase A (water containing 0.1 mM ammonium formate) and Mobile phase B (methanol containing 0.1 mM ammonium formate) as follows: 80% B from 0-3.5 minutes, linear gradient from 80-90% B from 3.5-10 minutes, and decreasing to 80% from 10-13.5 minutes (total run time, 13.5 minutes). Cannabidiol (CBD), Δ9-tetrahydrocannabinol (Δ9-THC), and 11-hydroxy-Δ9-tetrahydrocannabinol (11-OH-Δ9-THC) are quantified by multiple reaction monitoring (MRM), using SCIEX 6500 QTRAP with Turbo Spray electrospray ionization (ESI) in positive ion mode. The following MRM transitions (m/z precursor ion>product ion) are monitored: cannabidiol (m/z 315.1>193.2; 315.1>259.2), Δ9-tetrahydrocannabinol (m/z 315.1>193; 315.1>259.2), and 11-hydroxy-Δ9-tetrahydrocannabinol (m/z 331.1>193.1; 331.1>105.0). Analysis involves use of MultiQuant software from SCIEX.

Results: The method is specific and shows good sensitivity with a lower limit of quantification of 0.49 ng/mL. The calibration curve range of 0.49-125 ng/mL is linear with coefficient of determinations >0.99. Our LC-MS/MS method demonstrates acceptable sensitivity, linearity, precision, and accuracy.

Conclusion: The LC-MS/MS method under development is proving sensitive and robust enough to quantify cannabidiol, Δ9-tetrahydrocannabinol, and 11-hydroxy-Δ9- tetrahydrocannabinol in small plasma volumes collected from pediatric populations. We currently are in process of determining recovery, carryover, and stability. This method will be applied in clinical tolerability and efficacy studies and for oral pharmacokinetic studies that will further help us determine the dosage requirements for oral administration of Cannabis oil in children.

Keywords: LC-MS/MS, plasma, cannabinoids, CBD, THC, epilepsy, pediatrics

28. Web based physiotherapy for moderate to severe multiple sclerosis

Presenter: Shyane Wiegers, College of Medicine
Supervisor: Katherine Knox
Collaborators: Darren Nickel, Sarah Donkers, and Lorna Paul

Background: Access to safe exercise programs for people with advanced disability due to MS can be challenging. In partnership with former SHR and people with MS, we are conducting a randomized-controlled trial of web-based physiotherapy for persons with moderate to severe MS. This interim report assesses acceptability, falls, and symptoms for those in the web-based physiotherapy group over a 3-month period.

Methods: Participants received an in-person assessment and exercise prescription from an experienced neuro-rehab physiotherapist. Those in the web group accessed their individually-tailored exercise program online, with audio, video and text demonstration. Requested frequency was twice per week. Falls and symptoms (Multiple Sclerosis Impact Scale-29) were collected at baseline and 3-month assessments.

Results: 24 participated in the web group; five (21%) withdrew. Median age was 55y (26 to 76y); 11/19 were female. Median disability level was “early cane”. Zero to three falls were reported in the three months prior to baseline (median 0) and between the baseline and 3-month assessment (median 0). Median MSIS29 scores were 69 at baseline and 62 at 3-months. Updated results will be presented in the poster.
**Conclusion:** In a progressive disease where safe exercise is a barrier, web-based physiotherapy may provide an accessible option. Median number of falls and median MSIS29 scores did not worsen over the 3-month intervention, supporting safety and acceptability. Future planned analyses include reasons for program discontinuation, a 6-month follow-up and adherence in comparison to standard home exercise programs.

**Keywords:** Funding Acknowledgement: This investigation was supported by the Hermes Canada | MS Society Wellness Research Innovation Grant.

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### 29. Influence of Endotoxin and Cayston on the Cystic Fibrosis Peripheral Blood Neutrophil

**Presenter:** Nathan Wright, College of Medicine  
**Supervisor:** John Gordon  
**Collaborators:** Donald Cockcroft, John Gjevre, Niki Afseth

**Background:** Cystic Fibrosis (CF) is a genetic disease where the mucosal surface in the lungs is compromised due to an inactive intramembranous chlorine transmitter called the cystic fibrosis transmembrane conductance regulator (CFTR). Pulmonary issues in CF present with a thickening of mucus, impaired lung function, and recurring bacterial pneumonia and inflammation. In CF increased inflammation caused by recurrent neutrophil recruitment is a central contributor to exacerbation of lung pathology, and eventually morbidity, and mortality. Chronic activation of peripheral blood neutrophils could play an important role in the neutrophilic lung inflammation seen in CF. CF blood neutrophils are suspected to be activated or primed when compared to neutrophils from individuals without CF. This study aims to identify the cause of this activation and the mechanism or signaling that it involves.

**Methods:** Medical chart data and blood samples were collected from 30 CF patients (ΔF508) and 21 non-CF volunteers, from which both plasma and neutrophils were isolated. The plasma was analysed for G-CSF and endotoxin. The activation status of inflammatory signalling pathways, in the isolated neutrophils, was investigated using kinome array approaches.

**Results:** Neutrophilia, plasma endotoxin levels, and treatment with the inhaled antibiotic Cayston were associated with activation or signalling through the TLR4 pathway in circulating CF neutrophils. Our kinome array analyses revealed this pathway to have one of the strongest links to neutrophil activation in CF.

**Conclusion:** These results present an interesting link between neutrophil stimulating factors in the blood, activation of the TLR4 pathway in the peripheral blood neutrophil, and disease progression in CF. Understanding the pathways involved in this signalling and how they are initiated provides insights into CF and other inflammatory diseases wherein the neutrophil response plays a deleterious role.

**Keywords:** Neutrophil, Cystic Fibrosis, TLR4, Signalling
30. External Pacing in Motor Learning and Cross-Education of Skill

Presenter: Dakota Zirk, College of Arts and Science  
Supervisor: Jon Farthing  
Collaborators: Justin Andrushko, Doug Renshaw

Background: Cross-education (CE) is the phenomenon that ensues when strength or skill training of one limb leads to improved performance in the opposite untrained limb. While externally pacing a motor task can enhance CE, the influence of different pacing methods is unknown. This study looked to explore the difference in CE effects when comparing visual (VP) and auditory pacing (AP) in a visuo-motor force target matching task. Two hypotheses were constructed. One predicted AP would lead to greater CE because for synchronizing tasks and planning motor movements, AP has been found to be more efficient in comparison to VP. The secondary hypothesis was exploratory, as it was concerned with the potential difference in direction of transfer. Previous research has demonstrated that when using a timing anticipation aspect (i.e., pacing) the direction of transfer (dominant [D] to non-dominant [ND] limb, or ND to D limb) can be more symmetrical (equal transfer in either direction). However, in a visuo-motor task like this, prior work would suggest a trend of increased transfer from only the direction of D to ND limb. This led to the exploratory hypothesis that the transfer would be stronger from D to ND for the visuo-motor task in this study.

Methods: Twenty-three participants were block randomized into four conditions. Condition 1 consisted of VP and training with the D hand (n=6). Condition 2 was also VP but trained with their ND hand instead (n=6). Condition 3 was AP with the D hand (n=6), whereas condition 4 was AP with ND hand training (n=5). Maximum voluntary contractions for force output were recorded to set individual force target values for each participant during the task. Baseline scores were then collected for both hands. These scores were calculated by having the participant attempt to match the amount of force displayed on screen (target), by pushing their index finger into a load cell. The difference score either above or below the intended force target was the dependent variable, represented by the amount of error for an individual target. Each testing period and trial consisted of 20 targets, where a cumulative error score was produced upon completion. For baseline testing, 20 targets were presented to both hands and two different error scores were produced. For the training period, 10 trials of 20 targets (200 targets total) were practiced with either the D or ND hand. Post-testing occurred again in both hands (20 targets each) to determine the amount of CE and motor learning that had occurred.

Results: One-way ANOVA identified a significant baseline difference between the pacing type and the trained hand, F(1,22) = 15.482, p = 0.01, with the AP group scoring lower (AP, M = -107.05 vs VP M = -198.54). Subsequently, a mixed factorial ANCOVA was used to account for the baseline differences, with the change in error after training as the dependent variable. A main effect for transfer was identified F(1,17) = 5.187, p = 0.036 indicating that CE had occurred for both AP and VP. However, a significant interaction for hand (trained and untrained) and group (AP or VP) was also identified, F(1,17) = 9.914, p = 0.006, indicating a stronger CE effect was observed for the untrained limb with VP when compared to AP. This finding was particularly interesting, as the trained hands improved similarly between pacing types (AP: M = -59.025, SD = 21.48 vs. VP: M = -57.841, SD = 31.61). From this result, it can be inferred that pacing type had an influence only for the untrained hand (CE effect). No significant directional effects were identified F(1,17) = 2.297, p = 0.148, indicating that regardless of pacing method or hand trained (D or ND), the task elicited symmetrical transfer.

Conclusion: VP for a visuo-motor force target task elicited greater CE than AP, which contrasted the initial prediction. Two explanations may be offered: One is that baseline differences between groups,
where AP showed less error than VP, could indicate that the VP task was more difficult. This increased difficulty may have enhanced CE effects, as more complex or novel tasks often lead to greater transfer. Second, there could be a ceiling effect for the task itself, in that participants could only improve a certain amount before a plateau. Since AP was better at baseline, there could be less room for improvement and ultimately less skill to transfer. The finding of no directional effects for pacing type suggests that the timing anticipation factor, and little baseline asymmetry in performance created more symmetrical transfer. This is important as other tasks that typically show unidirectional transfer could be modulated to transfer in either direction by adding a timing component. Doing so may be beneficial for clinical populations, where tailored rehabilitation programs for specific limbs and direction of transfer may be required (i.e., immobilization models, stroke recovery, neurological damage resulting in loss of function for one limb, etc).

**Keywords:** Cross-Education, Pacing, Motor Learning, Symmetry/Asymmetry of Cross-Education
31. The planned menus in childcare centres across the province fall short of meeting the Saskatchewan Childcare Nutrition Guidelines

Presenter: Lila Abobakar, College of Pharmacy and Nutrition
Supervisor: Dr. Hassan Vatanparast
Collaborators: Anne Leis, Amanda Froehlich Chow, Mathieu Bélanger, Rachel Engler-Stringer, and Stephanie Ward

Background: Recent statistics estimate that close to one-third (29.8%) of Canadian preschoolers (ages 2-5 years) are overweight or obese. Over half (52%) of Canadian children attend childcare centres regularly, thus these facilities play an important role in shaping the eating habits of a large proportion of young children. To date, little is known about the quality of food served in Canadian childcare centre. This study was conducted to assess the extent to which the planned menus in Saskatchewan’s childcare centres adhere to the Saskatchewan childcare nutrition guidelines.

Methods: Overall, 39 licensed childcare centres were selected through a cluster randomized control trial to evaluate the impact of the HS/DS intervention. The baseline food menus of these centres were analyzed and compared to the Saskatchewan Childcare Nutrition Guidelines (SCNG). Descriptive analyses were performed to determine the characteristics of the menus and the percentage of adherence to the guidelines.

Results: The results of our study indicated that only 15.3% of the centres met the lunch and snacks guidelines. Overall, 61.5% of the centres met the milk guideline and 35.9% met the processed food limitation recommendations. Furthermore, among the centres that listed breakfast meals on their menus, 69% met the breakfast guideline recommendation. The analysis of the rate of adherence to each guideline showed that both the lunch and snacks guidelines are the benchmark that centres most frequently failed to meet.

Conclusion: The analysis of the rate of adherence to each guideline showed that both the lunch and snacks guidelines are the benchmarks that centres most frequently failed to meet. Without any targeted intervention, the planned menus in childcare centres across the province fall short of meeting the SCNG. This study provides a baseline of evidence for further monitoring of menu compliance in other provinces across Canada and revealed the needs for menu planning programmes targeting the childcare centres. Findings from this study contribute to the overall evaluation of the nutrition practices at childcare centres and to ongoing studies aimed at improving the menu planning and the food served throughout Phase III of the HS/DS intervention.

Keywords: Childcare, food menu, and Saskatchewan Childcare Nutrition Guidelines.
32. Factors influencing disease modifying medication use among individuals with multiple sclerosis

Presenter: Khrisha B. Alphansus, College of Graduate and Postdoctoral Studies
Supervisor: Dr. Carl D’Arcy

Background: Multiple sclerosis (MS) is a chronic autoimmune disease which affects the central nervous system causing neurological deterioration over time. Adherence to medication is crucial since it can reduce disease progression, lower rates of emergency department visits and in general improve overall quality of life. The primary objective of this study was to examine the association between complementary treatment, rehabilitation therapy, counselling/psychotherapy services, and having co-morbid health conditions on disease modifying medication use among individuals with MS.

Methods: The Survey on Living with Neurological Conditions in Canada (SLNCC) 2011 which is a cross sectional survey was linked to the Canadian Community Health Survey (CCHS) 2010-2011 cycle. There were 630 respondents with multiple sclerosis (MS). The predictors that were assessed were demographic factors (age and sex), socioeconomic factors (income and education), types of treatments (complementary treatment, rehabilitation therapy and counselling /psychotherapy), psychological factors (mood disorder, anxiety disorder, and depression), and health conditions (back problems, arthritis, heart disease and blood pressure) as well as age when MS was first diagnosed. The outcome variable was whether or not the individual used MS medication. Univariate and multivariate analysis was carried out using STATA IC 14. In order to take into account the survey design, replicate sampling weights and bootstrapped variance estimation as recommended by Statistics Canada were used. A set of (n=500) replicate weights were used in order to estimate variance and adjust for non-response and out of scope status.

Results: In the multivariate analysis complementary treatment was associated with lower odds (OR=0.18; 95% CI: 0.05 - 0.67) of medication use, however individuals who had underwent rehabilitation therapy were 3.94 times 95% CI (1.10-14.20) more likely to use medication for MS. In addition, individuals who had a mood disorder were 6.4 times 95% CI (1.47-28.72) more likely to take MS medication.

Conclusion: The use of complementary treatment is associated with a lower odds of MS medication use. Efforts should be taken by health care practitioners to inform patients about the benefits of disease modifying medications and why it should never be substituted with other treatments.

Keywords: Multiple sclerosis, Disease modifying medication, Complementary treatment, Rehabilitation therapy, Counselling services Psychotherapy services

33. Conflicting or facilitating goals: Differences in adults' social cognitions and exercise over time

Presenter: Jocelyn Blouin, College of Kinesiology
Supervisor: Nancy Gyurcsik

Background: A better understanding of the self-regulation of exercise is needed since most adults do not meet the public health recommendation of 150+ minutes of moderate–vigorous exercise each week. Exercise does not occur in isolation, as adults often set multiple concurrent exercise and non-exercise
goals that they wish to pursue during their leisure time. Social cognitive theory (SCT) contends that whether concurrent goals are perceived to be in conflict or facilitation with one another may affect successful exercise self-regulation; conflicting goals may be more challenging to regulate than facilitative goals. As a result, adults who hold concurrent conflicting goals may report lower adherence-related social cognitions, including self-regulatory efficacy and the likelihood and value of positive proximal outcome expectations and exercise less than those holding facilitative goals.

**Methods:** Our prospective SCT-based study examined whether adults (N=191; Mage=31±12 years) who reported their exercise and non-exercise goals conflicted or facilitated differed in their self-regulatory efficacy to manage multiple goals at the same time, outcome expectations, and exercise. Participants completed online measures of efficacy, outcome expectations, and exercise at study onset. Exercise was assessed again one month later. Participants who perceived their goals conflicted (n=100) or facilitated (n=91) formed comparison groups. A between groups MANCOVA with Time 1 exercise as a covariate and social cognitions and exercise as the dependent variables was conducted to examine the study purpose.

**Results:** The resultant overall MANCOVA model was significant, (p<.0001, η2partial=.17). Follow-up ANOVAs revealed that the group with conflicting goals reported significantly lower self-regulatory efficacy and exercised less at Time 2 compared to the group with facilitating goals (p’s<.05, η2partial=.14 and .03). Outcome expectations did not significantly differ between groups.

**Conclusion:** Findings provide first evidence that self-regulatory efficacy is a key differentiating social cognition between those who hold conflicting or facilitating goals. If study findings are replicated, at least two intervention avenues exist. First, when individuals have conflicting goals, increasing their self-regulatory efficacy may be beneficial. Second, intervening to help adults set at least some facilitative goals (e.g., exercise and socialize at the same time) may also be beneficial. Such intervention approaches should help adults learn to better self-regulate their exercise alongside their non-exercise leisure time goals.

**Keywords:** Multiple goals; Social Cognitive Theory; Concurrent Self-Regulatory Efficacy; Outcome Expectations; Exercise

34. Bachelor of Science in Pharmacy Student Perceptions of the Entry-Level Doctor of Pharmacy Degree: A Qualitative Study

**Presenter:** Thomas Brownlee, College of Pharmacy and Nutrition
**Supervisor:** Holly Mansell
**Collaborators:** Anan Ahmed, Kerry Mansell, Holly Mansell

**Background:** Canadian academic pharmacy institutions are undergoing a credential shift from a baccalaureate degree to an entry-level Doctor of Pharmacy (ELPD). Little is known about how Bachelor of Science in Pharmacy (BSP or equivalent) students perceive this transition.

**Methods:** All students in the BSP program at the University of Saskatchewan during the 2017-18 academic year were eligible to participate. Students were randomly assigned a number based on their year in the program, and eight participants were selected from each year (Year 2 to 4) by a third party using a table of random numbers. Face to face interviews were conducted by a research assistant, using a semi-structured interview guide to characterize students' perceptions of the PharmD program. Interviews were
audiotaped and transcribed verbatim. Thematic analysis was performed using NVivo qualitative analysis software.

**Results:** Twenty-four interviews were conducted during the months of September through November, 2017, lasting a mean of 15 minutes. Students' opinions on the impact of the implementation of the PharmD program varied, and six themes emerged from the interviews: positive academic and social experiences, perceptions of the PharmD program, insecurities of BSP students, impact on future employment, mixed plans to pursue PharmD, and suggestions for improvement. Participants were primarily concerned about PharmD graduates being preferentially hired for hospital pharmacy jobs (n=20), and claimed this as a common motivator for pursuing a post-baccalaureate PharmD. Participants that expressed most confidence in their ability to secure employment based on experience were in later years of the program.

**Conclusion:** Increased dialogue between Canadian pharmacy faculties and students is necessary to provide reassurance. The credential shift to PharmD should not deter BSPs' desire to work in a specific practice setting.

**Keywords:** qualitative study, undergraduate pharmacy education, pharmacist employment

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35. **Assessment of oral health of Syrian refugees settled in Saskatoon during 2015-2017**

**Presenter:** Oleksandr Boyko, Daniel de Jong, Nazli Abtahi, College of Dentistry  
**Supervisor:** Dr. Gerry Uswak

**Background:** Due to language, cultural and financial barriers, access to oral health care may be decreased among refugees. To provide adequate care and avoid potential strain on the public health care system, an accurate estimate of their oral health needs prior to their intake to Canada is required. Based on recent Syrian refugee (SR) intakes, our study evaluates oral health needs of refugees to Canada.

**Methods:** A total of 140 SR records from the University of Saskatchewan College of Dentistry from 2015-2017 were analysed. The records were divided by age to match those used in the Oral Health Component of the CHMS. Oral health status was assessed using DMFT and PUFA indexes, as well as estimated urgency of needed care. The data was compared against the Canadian population using the CHMS and FNOHS.

**Results:** Presence of oral disease was significantly higher for all age groups of SR when compared to the Canadian population. Overall, SR between the ages 3 and 19 had a significantly higher prevalence of DMFT than the Canadian population, as well as a larger number of untreated decayed teeth. While 90% of the SR were identified as those in need of dental care, 43% required urgent dental care.

**Conclusion:** There is a very high prevalence of dental decay among SR that coincides with a high urgency of care. Since the high DMFT scores were due to untreated decay, SR have the potential to add stress to the health care system if the resources to manage are insufficient or not available. Insurances and programs such as the IFHP may require updating or improving to meet the needs of refugee populations.

**Keywords:** Syrian refugees, Oral health, Public health, Dentistry, DMFT, PUFA
36. Determinants of Job Satisfaction in Canadian Correctional Officers

Presenter: Rochelle Ferron, College of Medicine
Supervisor: Dr. Bonnie Janzen

Background: Job satisfaction refers to the gratification or fulfillment of needs associated with a person's occupation and consists of the degree to which a person likes or dislikes their job. Job satisfaction influences employee commitment and institutional performance, and it may affect on-the-job behavior. Job satisfaction has also been linked with employee health and general quality of life. The Correctional Service of Canada (CSC) aims to provide the public a safe environment of living by encouraging and assisting offenders to obey law through safe, secure, and humane approaches.

Correctional officers within the CSC are typically frontline workers who guard inmates and maintain safety and order.

The determinants of job satisfaction among correctional officers have been widely researched internationally. In Canada, however, only a limited number of studies have been conducted which focus specifically on corrections officers' job satisfaction. In addition, few studies have considered job training as a potential determinant of job satisfaction.

Methods: The data source for this study is the 2014 Public Service Employee Survey (PSES), a cross-sectional survey conducted by Statistics Canada. I will be accessing the survey through the Saskatchewan Research Data Centre. Analyses will be restricted to correctional officers employed by the CSC. The dependent variable is job satisfaction. Based on my conceptual framework, independent variables will be selected to best reflect the hypothesized individual, job-specific and structural determinants of job satisfaction. Job training will be positioned as a primary exposure of interest. Multiple logistic regression will be the main analysis conducted. SPSS will be utilized to perform the analysis, applying the appropriate weights provided by Statistics Canada.

Results: Forthcoming.

Conclusion: Forthcoming.

Keywords: Forthcoming.

37. An Investigation into Saskatchewan's HIV-1 Epidemic: A population based study of APOBEC3 repertoires and effects of genotypic variation on retroviral replication

Presenter: Tyson Follack, College of Medicine
Supervisor: Dr. Linda Chelico

Background: HIV-1 prevalence in Saskatchewan has risen to over two times the National average, with observable infection bias towards rural indigenous populations. Current literature shows us that the APOBEC3 repertoires are variable in all populations, but have observable genotypic trends correlated with human ancestry. These genotypes can be used to determine HIV-1 susceptibility within a population.
**Methods:** Using Sanger sequencing we have genotype the APOBEC3 locus from patient PBMCs. Using sequencing software programs we determine the allelic SNPs. We then clone the prevalent population based A3 SNPs into plasmid expression vectors to be expressed in cell culture. We then do infectivity based experiments to determine the effects of each A3 with HIV challenge, then look for A3 induced deaminations.

**Results:** As expected, we have found that A3G, A3H, and A3F allelic frequencies in the Saskatoon Health Region correlate to a mixed population, however upon whole genotype analysis, we found that heterozygous expression of A3F I231/V231 is dominant in population. Furthermore, In cells this genotype appears to act synergistic-ally with other A3s to restrict retroviral replication.

**Conclusion:** When examining population based genetics of innate retroviral restriction factors, as well as in-cell/ and primary cell assays, studying APOBEC3 enzymes in combination is a necessity, as we have shown that the co-expression of known A3F SNPs results in a more robust restriction of HIV-1 replication. This information can help determine predispositions for HIV susceptibility.

**Keywords:** HIV-1, retrovirology, APOBEC3, deaminase, deamination, innate immunity, Saskatchewan Health, Public Health

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38. **Risk Factors Associated with Single and Recurrent Falls among Community-Dwelling Elderly in Canada**

**Presenter:** Edris Haghir, College of Graduate and Postdoctoral Studies  
**Supervisor:** Dr. John Moraros  
**Collaborators:** Dr. Cindy Feng, Dr. Yelena Bird

**Background:** Falls are a major public health concern among community-dwelling elderly in Canada. Falls can have a considerable impact on an older person's quality of life and health, causing potential disability, chronic pain, loss of independence and even death. Despite an increased public awareness that the Canadian population is aging, research in this area is lacking.

**Objective:** This study aimed to identify and compare the risk factors associated with single and recurrent falls among elderly in Canada.

**Methods:** This is a cross-sectional study that uses data from a large-scale, population-based, nationally representative survey, the Canadian Community Health Survey – Healthy Aging. It included 16,369 individuals aged 65 years and older. Data related to the incidence of single (one fall) and recurrent falls (≥ 2 falls) in the previous 12 months, as well as associated factors from selected variables (demographics, general health and functional condition, chronic conditions, medication use, and fall history) were examined by univariate analysis and multinomial logistic regression modeling.

**Results:** This study found that 19.8% of the participants had experienced falls in the past year with 7.2% of them being recurrent fallers. The multinomial logistic regression modeling showed that participants who were males and perceived their health as being poor to fair (OR=1.4; 95% CI, 1.1 to 1.8) were more likely to experience recurrent falls when compared to single falls. Relative to single fallers, recurrent fallers were also more likely to have arthritis (OR=1.3; 95% CI, 1.0 to 1.7), urinary incontinence (OR=1.4; 95% CI, 1.1 to 1.9), use of ≥ 4 medications (polypharmacy) (OR=1.6; 95% CI, 1.2 to 2.1) and fear of falling (OR=1.6; 95% CI, 1.2 to 2.1).
Conclusion: Falls and their related injuries represent a significant health, safety and financial concern for elderly Canadians. The findings of this study suggest that fall prevention efforts should consider a variety of risk factors in order to ensure the most effective interventions for this rapidly increasing and vulnerable population.

Keywords: Falls (single and recurrent); risk factors; elderly; Canada


Presenter: Bethany Hase, College of Kinesiology
Supervisor: Dr. Saija Kontulainen
Collaborators: Kate Thompson, Anthony Kehrig, Dr. Colleen Dell, Dr. Darlene Chalmers

Background: Children and youth with Autism Spectrum Disorder (ASD) have greater fracture risk which may relate to deficits in bone strength development (Neumeyer et al. J Autism Dev Disord 2015; Neumeyer et al. Bone 2017). Literature from typically developing children suggest; a) that engaging more time in moderate to vigorous physical activity (MVPA), vigorous physical activity (VPA) or impact activities will provide bone benefits and; b) activities in outdoor (greenspace) environment are associated with more intense activity (Kehrig et al. JMNI 2017; Ward et al. Health Pl 2016). Our objectives were to compare minutes of MVPA and VPA and number of bone impacts between an outdoor and indoor exercise sessions in children with ASD.

Methods: We recruited 8 children with ASD (5 boys), mean age 10.4 (SD 2.9). We executed two 45-minute exercise sessions including same activities first in outdoors and a week after indoors. During each session children wore activity monitors (accelerometers). Two therapy dogs and handlers participated in both sessions to enhance children’s adherence and engagement with activities. We used a cross-over design and paired t-tests to compare the minutes of MVPA, VPA and number of bone impacts between outdoor and indoor sessions (p<0.05).

Results: Minutes of MVPA and VPA in the indoor session (mean 10.9, SD 8.3 and mean 4.3, SD 4.0) did not differ from minutes spent in MVPA and VPA in the outdoor session (11.5, 7.2 and 3.2, 3.4). The number of impacts was greater indoors (45.0, 34.2) when compared to outdoors (22.1, 24.2).

Conclusion: Findings suggest that indoor rather than outdoor physical activity interventions during the winter months may be more beneficial to increase bone impacts in children with ASD. Future interventions may benefit implementing outdoor (greenspace) physical activity interventions during the warmer months. These findings guide design of exercise interventions aiming to optimize bone development in children with ASD.

Keywords: Children, Bone, Autism spectrum disorder, Physical activity,
40. Sociocultural Determinants of Physical Activity Within Indigenous Populations of Canada

Presenter: Avery Ironside, College of Kinesiology
Supervisor: Dr. Heather J.A. Foulds
Collaborators: Dr. Leah J. Ferguson

**Background:** It is recognized that certain social and cultural factors play key roles in determining a person’s physical activity (PA) level. Little research is available on the social and cultural determinants of PA in Indigenous peoples. These determinants of PA could be used to increase effectiveness of Indigenous PA interventions, thus decreasing the risk of chronic diseases.

**Methods:** In-person interviewer administered questionnaires and online self-administered questionnaires will be used to collect information on social and cultural determinants of PA. Demographic and anthropometric data will also be collected. Participants will include self-identifying Indigenous students, staff, and faculty. Recruitment will be completed through our partnering Indigenous community groups.

**Results:** Main outcomes include: PA levels, social support, cultural connectedness, cultural identity, cultural affinity, sedentary behaviours, mentor/role model, family influences, traditional activities, leaving community, experiences of racism, income, education, alcohol & tobacco use, gender, and sex. Demographic measures: body mass index, waist circumference, blood pressure, hand grip, aerobic fitness.

**Conclusion:** The primary objective is to determine the associations of many under researched sociocultural factors and Indigenous peoples of Canada's PA levels. The overall purpose of this study is to provide the Indigenous Saskatchewan community with identification of meaningful social and cultural determinants of PA that can be used to increase effectiveness of Indigenous PA programs and interventions.

**Keywords:** Physical Activity, Indigenous Health, Cultural Connectedness, Social Determinants, Cultural Determinants, Chronic Disease, Sedentary Behaviours,

41. Efficacy and Effectiveness of Behavioral Intervention Programs for STIs at Educational Settings (Systematic Review and Meta-Analysis)

Presenter: Nway Mon Kyaw Soe, School of Public Health
Supervisor: Jean Moraros

**Background:** The last decade has seen an increase in sexually transmitted infections (STIs) and an emergence of drug resistant STIs (gonorrhea) globally including developed countries like the US, Canada and Australia. Canadian national data suggested chlamydia cases have doubled, gonorrhea cases have increased by 61.3% and syphilis cases have shown a 95% increase between 2005 and 2014 with 307.4 cases/100,000, 45.8 cases/100,000 and 6.63 cases/100,000 respectively in 2014. Furthermore, the prevalence of HIV infections is increasing in Canada and approximately 21% of individuals infected with HIV are unaware of their infection. These developments pose a major public health concern. Adolescent and young adults are at a higher risk to contract STIs for various reasons including: risky behaviours (substance use and unsafe sexual practices) and limited access to healthcare services. Therefore,
educational institutions may be ideal settings to implement effective strategies to help reduce the incidence and prevalence of STI.

This systematic review and meta-analysis examines the efficacy and effectiveness of current STI preventive interventions at educational settings.

**Methods:** A systematic review and meta-analysis of relevant databases was conducted including: PubMed, Medline, Embase, Public Health Database and Cochrane Library. Information relating to studies (e.g. type, published year, location), programs (e.g. characteristics, providers, total hours, theories underpinning) and outcome variables with quantitative data were extracted. Risk of bias was assessed using criteria presented by the Agency for Healthcare Research and Quality (AHRQ). Finally, meta-analysis was performed using Comprehensive Meta-Analysis (CMA) software.

**Results:** There were 18 articles included in the systematic review and meta-analysis. The outcomes were classified into behavioural and psychosocial categories. The behavioural category included sexual partners, sexual activity, condom practice and testing. The psychosocial category consisted of knowledge, motivational factors (attitudes, norms and beliefs, risk perceptions and intentions) and skills (condom efficacy, refusal self efficacy, partner communication and parental communication). Preventive interventions had a positive impact on both behavioural and psychosocial outcomes. The intervention effect was more prominent for promoting knowledge (OR=2.76), followed by enhancing motivational factors (OR=1.58), skills (OR=1.35) and behaviours (OR=1.22). The use of gender blind approach interventions was not effective for males. There was no difference in the effectiveness between peer involved and non-peer involved interventions. Findings of this review were inconclusive as to whether there was a difference between tech-based and face-to-face interventions.

**Conclusion:** Behavioural intervention programs at educational settings addressing STIs showed favourable impact on psychosocial factors and behaviours related to sexual practice. Educational authorities, policy makers and health promotion personnel can use insights and information from this review in crafting and modifying STIs prevention programs at educational setting to attain better results. However, information from this systematic review should not be generalized to adolescents and young adults who are not in school because we focused only on the student population. More studious researches are needed to examine the impact of behavioural interventions on the epidemiological outcomes and the sustainability of the effectiveness of the interventions.

**Keywords:** Sexually transmitted diseases, chlamydia, gonorrhea, syphilis, HIV, health promotion, health educations, preventive health services, health knowledge, attitudes and practice, program effectiveness, evaluation studies, adolescents, young adults, schools, universities, colleges, students.
42. Handgrip is a predictor of upper extremity eccentric but not concentric strength in older adults

Presenter: Hayley S Legg, College of Kinesiology
Supervisor: Dr J Lanovaz & Dr C M Arnold
Collaborators: Dr J P Farthing

Background: Age-related declines in upper extremity muscle strength may reduce an older adult's functional independence and ability to control a forward fall descent using the arms. Handgrip (HG) dynamometry is widely utilized to assess overall strength and predict functional decline in older adults; however, less is known regarding the relationship of HG to concentric (CON) and eccentric (ECC) strength.

Methods: Sixty-eight older adults (34 females, age-matched to 34 males; age range: 60-93 yr, mean: 73±8 yr) performed maximal single-arm press movements on a dynamometer-controlled device. Peak right arm CON and ECC strength (NORM dynamometer), maximal right arm HG strength (Jamar dynamometer) and BMI were recorded. Separate stepwise linear regression analyses determined predictors of CON and ECC strength.

Results: For CON strength, age was the only significant independent predictor (females adj r²=0.365, males adj r²=0.374). HG and age were significant independent predictors of ECC strength (females adj r²=0.504, males adj r²=0.495).

Conclusion: In summary, age was a predictive factor for both CON and ECC strength; however, HG was a significant independent predictor only for ECC strength. Determining the factors associated with upper extremity ECC strength may play an important role in predicting declines in functional ability and fall arrest capacity. HG strength may be an important predictor of upper extremity ECC strength declines.

Keywords: Strength, aging, handgrip, upper extremity.
43. Factor Structure and Psychometric Properties of ALS-18 in Pregnant and Postpartum Women

Presenter: Hua Li, College of Medicine  
Supervisor: Angela Bowen  
Collaborators: Rudy Bowen MD, Cindy Feng PhD, Lloyd Balbuena PhD, and Nazeem Muhajarine PhD

**Background:** Investigating the dimensions of affective lability may help to explain possible etiology and outcomes for mental disorders. The Affective Lability Scale -18 (ALS-18) is a widely utilized measure of labile affect, and its psychometric properties have been studied in non-clinical and clinical populations. However, the psychometric properties have not previously been examined in pregnant and postpartum women despite the fact that affective lability is a prominent feature in pregnant and postpartum women. In this study, we used a sample comprised of pregnant and postpartum women with various mood symptoms to explore the psychometric properties of the ALS-18.

**Methods:** 113 pregnant and postpartum women with mood symptoms participated in this study. A confirmatory factor analyses (CFA) were performed to compare the fit of alternative models.

**Results:** The three-factor structure of the ALS-18 presented a nearly acceptable model fit and a high internal consistency, while the six-factor model of the ALS-18 displayed a good model fit and an acceptable to high internal consistency.

**Conclusion:** Our findings from pregnant and postpartum women with mood symptoms showed evidence for six underlying factors of ALS-18, and a close to acceptable model fit of three-factor ALS-8. ALS-18 can be used as an instrument of measuring affective lability in perinatal women. Further research is needed to test the three-factor substructure of the ALS-18 against alternative factor models in a larger sample of pregnant and postpartum women.

**Keywords:** Perinatal women, affect lability, measurement, psychometric properties

44. Precipitation, demographic correlates and built environment features are associated with increased sedentary behaviour in 9-14 year old children

Presenter: Larisa Lotoski, College of Medicine  
Supervisor: Dr. Nazeem Muhajarine  
Collaborators: Dr. Daniel Fuller, Dr. Kevin Stanley, Dr. Daniel Rainham

**Background:** The average Canadian youth spends 8.6 waking hours of their day in a sedentary state, and consistently do not meet recommended leisure time sedentary limits of 2 hours per day. This longitudinal study seeks to establish: a) How changes in weather conditions affect total sedentary behaviour (SED) in children, and b) How SED effects are moderated by urban design.
**Methods:** Families with children aged 9-14 years were recruited from the prairie city of Saskatoon, Canada (n=816). Location-specific SED was measured in children over three time frames (Sept-Dec; Jan-April; May-July) using GPS equipped accelerometers. Neighbourhood level built environment features were assessed using the audit tool, Irvine Minnesota Inventory (IMI), the Neighbourhood Active Living Potential (NALP), neighbourhood era design and Walk Score®. A multilevel modeling approach was taken to understand the relationship between weather conditions, demographics, built environment and total daily SED of children.

**Results:** On average, children with valid accelerometry data accumulated 4.5 hours of sedentary time per day (n=620). In random-intercept multilevel models, increased levels of light physical activity (LPA) and moderate-to-vigorous physical activity (MVPA) were negatively associated with increased accumulation of SED (LPA p<0.0001, MVPA <0.0001). Overweight and obese children were significantly more likely to be sedentary in comparison to normal weight children (Overweight p=0.0162; Obese p<0.0001). With increased age, the level of SED increased at a greater rate in females, in comparison to males (p=0.0166). Higher total daily precipitation was significantly associated with increased levels of SED (p=0.0065), but children’s SED patterns were differentially moderated by both neighbourhood NALP universal accessibility (p=0.0185) and IMI active living cumulative score (p=0.0070). Pedestrian access was positively associated reduced sedentariness in females, but increased sedentariness in males (p=0.0157).

**Conclusion:** Interventions targeting SED in youth may require specific population targeting to be most effective. Disruptive positive interventions to minimize SED in both boys and girls, especially as they age, may provide the greatest benefit when done so in our youngest populations. This project provides necessary information to relevant public health policy architects.

**Keywords:** sedentary behaviour, health, children, adolescents, physical activity, built environment

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45. **Asthma diagnosis along an urban-rural gradient in Saskatchewan, Canada**

**Presenter:** Oluwafemi Oluwole, College of Medicine  
**Supervisor:** Joshua A. Lawson  
**Collaborators:** Donna C. Rennie, Ambikaipakan Senthilselvan, Roland Dyck, Anna Afanasieva, Darryl Adamko

**Background:** Most studies investigating childhood asthma have reported a lower prevalence in rural compared to urban areas. Environmental factors have mostly been implicated for these differences. However, the association could also be linked to possible under-diagnosis of asthma in rural children. The aim of this study was to investigate if rural children experience more asthma under-diagnosis compared to urban children.

**Methods:** The study population was comprised of 335 schoolchildren (diagnosed asthma = 28.4%; at-risk-for-asthma = 36.1%; no asthma = 35.5%). Location of dwelling was 73.4% large urban, 13.7% small urban, and 12.8% rural. Overall, percent predicted FEV1 was lower in rural children compared to small urban and large urban children [Mean (SD) = 89.3% (12.9), 98.2% (10.0), and 96.0% (13.3), p<0.05, respectively] as was FEF25-75 [Mean (SD) = 78.8% (20.4), 91.6% (20.2), and 88.6% (23.1), p<0.05, respectively]. Lower mean values for FEV1 and FEF25-75 observed in the rural group were only found in the at-risk-for-asthma children and not in the diagnosed asthma or no asthma groups. Among those not classified as diagnosed
asthma by survey, the validated algorithm further identified the presence of asthma in 5.5% of large urban, 8.1% of small urban, and 18.8% of rural children (p = 0.026).

**Results:** The study population was comprised of 335 schoolchildren (diagnosed asthma = 28.4%; at-risk-for-asthma = 36.1%; no asthma = 35.5%). Location of dwelling was 73.4% large urban, 13.7% small urban, and 12.8% rural. Overall, percent predicted FEV1 was lower in rural children compared to small urban and large urban children [Mean (SD) = 89.3% (12.9), 98.2% (10.0), and 96.0% (13.3), p<0.05, respectively] as was FEF25-75 [Mean (SD) = 78.8% (20.4), 91.6% (20.2), and 88.6% (23.1), p<0.05, respectively]. Lower mean values for FEV1 and FEF25-75 observed in the rural group were only found in the at-risk-for-asthma children and not in the diagnosed asthma or no asthma groups. Among those not classified as diagnosed asthma by survey, the validated algorithm further identified the presence of asthma in 5.5% of large urban, 8.1% of small urban, and 18.8% of rural children (p = 0.026).

**Conclusion:** The study revealed evidence of asthma under-diagnosis in rural areas and further supports the use of objective measures in addition to symptoms history when investigating asthma burden across an urban-rural gradient. This may have direct implications for better childhood asthma management, especially in rural populations

**Keywords:** Asthma algorithm, asthma, diagnosis, pulmonary function, schoolchildren, urban-rural gradient

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46. **Nursing Home Ownership Changes and Care Quality in the United States**

**Presenter:** Tyler Pittman, School of Public Health  
**Supervisor:** Michael Szafron

**Background:** Ownership type of nursing homes influences resident care quality, with investor-owned facilities averaging higher deficiencies than government-ran or non-profit enterprises. Changes in the ownership structure of convalescent homes has implications on resident care quality. Agents may disseminate through environmental factors and be expressed in care determinants such as the reported number of deficiencies, the percentage of long-stay or short-stay residents with disability outcomes, to ratios of nursing home staffing.

**Methods:** Information is obtained from the Centers for Medicare and Medicaid Services (CMS) Nursing Home Compare (NHC) datasets on Medicare and Medicaid reimbursed nursing homes from March 2016 to March 2018. Structural equivalence analysis (SEA) is applied to identify facilities that are managed by the same group of owners, and to distinguish groups of nursing homes that have similar ownership structure.

**Results:** It is hypothesized that networks with a high degree of connectivity within subgroups are exhibited among facilities and owners. Inter-generational collaboration may be more important than intra-generational association for better care quality in nursing homes, after accounting for ownership duration of managers.

**Conclusion:** Our findings will provide evidence that owners occupying a central position in a syndication network have greater awareness of spatially obscured resources for expansion.

**Keywords:** nursing homes, care quality, social network analysis, United States
47. **Secondary Trauma and Trauma-informed Practice Competency in Remote Northern Saskatchewan Therapists. A Mixed Methods Study.**

Presenter: Wanda Seidlikoski Yurach, College of Medicine  
Supervisor: Dr. Caroline Tait

**Background:** Mental health therapists providing trauma supports in remote northern First Nations communities in Saskatchewan work in isolation, which has been identified as one of the most significant challenges of this work and has been linked to vulnerability to secondary traumatic stress (STS). STS is the distress a person experiences when exposed indirectly to the trauma of others.

Trauma-informed practice competency involves understanding trauma symptoms, its impact on clients and the helper and the practice tools required to support recovery and healing for each. Therapists are generally approved through First Nations Inuit Health Branch (FNIHB) of Health Canada to provide short-term crisis counselling or negotiate contracts directly with communities to provide longer-term supports. Therapists are a limited resource and tend to have a more generalist background such as social work. With no studies to date on therapists working in Saskatchewan communities, it is of great interest to explore their experiences in relation to vulnerability to STS.

**Methods:** A mixed method explanatory sequential design will be employed in this study. In the first phase, quantitative data will be collected by mailing out the Secondary Traumatic Stress Scale, Trauma Informed Practice Competency Scale and demographic information questionnaire to participants. Participants in phase one are all approved FNIHB therapists and social workers registered with the Saskatchewan Association of Social Workers who have provided trauma support in remote northern First Nations communities in Saskatchewan. This will be followed by qualitative data being collected from a purposeful sample of participants drawn from the same group of therapists and interviewed in person using semi-structured, open-ended questions to explain and elaborate on the quantitative results.

**Results:** Expected results of the STSS will indicate therapists are experiencing symptoms of STS. Contributing factors will likely be identified as high trauma caseloads and being isolated from peer supports or clinical supervision. Protective factors will likely be identified as: trauma-informed practice competency, self-care resources, competent supervision, networking, spirituality and regularly scheduled debriefings.

**Conclusion:** Examining the experiences of therapists working in remote northern First Nations communities in Saskatchewan will aid in understanding this work and provide evidence-based recommendations for supports and policy changes that include trauma-informed practice competency to reduce vulnerability to STS.

**Keywords:** Secondary trauma, First Nations, mental health therapists, northern Saskatchewan, trauma-informed competency
48. Components of Success and Barriers to Indigenous Health Programs and Frontline Worker Input in the Health Program Process: A Narrative Literature Review

Presenter: Charlene Thompson, School of Public Health
Supervisor: Dr. Michael Szafron

Background: To address the burden of Indigenous health inequity it is important to include authentic Indigenous engagement to understand how Indigenous health programs (IHPs) can be implemented effectively. Community input, including the input of frontline workers (FLWs), can actualize Indigenous inclusion and is essential to successfully implementing health programming. The purpose of this literature review is to identify the components of success and barriers of IHP implementation and examine the inclusion of FLWs in Indigenous communities.

Methods: Scholarly data bases and grey literature sources were searched. Search terms included “health programs”; “intervention”; “health intervention”, combined with Indigenous search filters; “Indigenous”; “American Indian”; and “Aboriginal”.

Results: Findings from the literature suggest: (1) components associated with program success include community engagement, cultural considerations, community ownership, and a community-based/multi-sectoral approach; (2) challenges to successful programs include contextual, resource, and community barriers; (3) FLWs have been left out of health program decision-making and their level of inclusion could be improved; and (4) the input of local FLWs increases the likelihood of programs to align with local community values and Indigenous knowledge resulting in more positive health outcomes.

Conclusion: FLWs hold local community knowledge that can potentially contribute to the components of success and the modification of some program barriers. The findings from this literature review may be used to inform the IHP process and possibly foster program success. Additionally, this review will inform a larger research project involving on-reserve frontline workers and IHPs.

Keywords: Indigenous health, health programs, frontline workers, health equity

49. E-cigarettes: a survey of perceived use, attitudes and knowledge among a group of adults attending a Canadian dental school.

Presenter: Kyla Tzupa and Lisa Rumpel, College of Dentistry
Supervisor: Dr. Jay Hoover and Dr. Diego Ardenghi

Background: Electronic cigarettes (e-cigarettes) are a newly emerging, safer alternative to cigarette smoking and its use among Canadian teens and young adults has been steadily increasing. Recently however, studies have revealed that e-cigarettes have harmful effects on both systemic and oral health. There is limited published data on the use of e-cigarettes among an adult Canadian population.

Methods: The aim of this study, therefore, is to assess by means of a questionnaire, the use and attitudes surrounding e-cigarettes, and knowledge concerning its effect on the general and oral health, among a group of adults attending a Canadian dental school.
Results: The results could perhaps help educate the public of the potential detrimental effects of e-cigarettes on the periodontium of natural teeth and dental implants. It is expected that our survey population will believe e-cigarettes are a safer alternative to smoking cigarettes and less detrimental to both oral health and systemic health.

Conclusion: We hypothesize that we will concluded people believe e-cigarettes to be a safer alternative to smoking. Likewise, it is probable that an older adult population will demonstrate a lower prevalence of e-cigarette use compared to teens and young adults.

Keywords: oral health, systemic health, e-cigarettes, cigarettes, survey, knowledge, attitudes

50. Proposal: The Influence of Welfare Generosity on Preventative Health Interventions

Presenter: Mary Ellen Walker, College of Nursing
Supervisor: Dr. June Anonson & Dr. Michael Szafron

Background: The political and economic contexts in which people live have important implications for their lives. Welfare policy may reflect this political-economic context, as it can also impact peoples’ lives, including their health. Previous research has explored how welfare policies influence health, but no research has explored how welfare generosity influences the relationship between a health intervention and its associated outcome. Furthermore, no research on welfare policy has used spatial analysis.

Methods: This proposal suggests a methodology to address these literature gaps while providing a template for spatial analysis, making it accessible to other health researchers. This study will explore the influence of welfare generosity on the relationship between measles vaccination rates and measles cases over time and geographic location while adjusting for female employment rate, world region, gross domestic product per capita, level of democracy, and the Gini inequality index. The statistical methods used to develop the methodology may include generalized linear mixed model regression to quantify the relationship between welfare generosity and health interventions and spatial models to determine the influence of geography on this relationship.

Conclusion: This research will allow nurses and other public health professionals to consider new ways of looking at the larger influences on health. It also provides public health professionals with examples of countries where welfare generosity policies are having a positive influence on prevention interventions for health. This research may inspire further study of the influence that policies have on health interventions.

Keywords: measles, prevention, spatial analysis, vaccination, welfare generosity
51. Towards the conceptualization of patient empowerment within digital health

Presenter: Jeremy Young, College of Nursing
Supervisor: Tracie Risling
Collaborators: Juan Martinez

Background: Recent efforts to shape and sustain patient-centered care have been associated with an increased demand to conceptualize patient empowerment. A lack of conceptual clarity has complicated the operationalization and subsequent measure of patient empowerment, and there are ongoing calls to develop comprehensive and valid tools to further explore this concept in relation to digital health interventions. The inclusion of patient voice to further delineate the concept of patient empowerment is urgently needed. This is relevant in Saskatchewan, as patient-centred digital health solutions emerge such as the Citizen Health Information Portal (CHIP).

Methods: A multi-method approach was utilized to explore patient empowerment in digital health. From the Levac and Colquhoun framework, a scoping review was conducted to identify current practices of empowerment measures in relation to the use of tethered patient portals. The use of Interpretive Description methodology guided a qualitative exploration of experiences and views related to empowerment of (n=26) Saskatchewan participants engaged in the CHIP to access health information contained in their electronic health record.

Results: From an initial count of 1,387 publications, the scoping review identified 19 empirical studies pertaining to patient empowerment in relation to the use of digital health solutions. Of the 19 empirical articles, only four articles were found to have used specific patient empowerment measures with significant variety in their identified conceptual elements. Interpretative work on empowerment related to the experiences of the CHIP participants were thematically categorized into Being Heard (Knowing More and Seeing What They See) and Moving Forward (Owning Future Steps and Promoting Future Care).

Conclusion: The lack of a definitional consensus on patient empowerment persists within the scope of patient empowerment research in digital health. Operationalization of patient empowerment remains unclear, and is further complicated with the interchangeable use of the terms of empowerment, engagement, and activation. To support innovative e-health solutions for optimal patient-centred care, the challenges of operationalizing patient empowerment and incorporating patient voice should be addressed.

Keywords: empowerment, digital health, scoping review, qualitative, Interpretative Description
52. Development of a feasible field implementation strategy using fortified lentils to improve the iron status (Fe) status of adolescent girls in Bangladesh.

**Presenter:** Fakir Yunus, College of Pharmacy and Nutrition  
**Supervisor:** Gord Zello  
**Collaborators:** Marywood University, USA

**Background:** The purpose of this crossover study was to establish the methodology and logistics required to conduct a large-scale community-based efficacy study using fortified lentil as a means to improve iron status in Bangladeshi adolescent girls.

**Methods:** A crossover trial was carried out among 100 adolescent girls (12.9±2.0 years of age) consumed cooked fortified lentil consisting of 2 different cooking preparation styles (thick vs. thin) and 3 different portion sizes of lentil (raw weight 25g, 37.5g and 50g) in a counter-balanced manner. Lentils were served 5 days a week over 12 weeks with 250g of cooked rice.

**Results:** Thick preparation of cooked lentil at the 37.5g portion (equal to 200g cooked dal) had higher Visual Analog Scale ratings compared to all thin preparations. Considering both the amount served and contribution of dietary Fe, the thick preparation of lentil at 37.5g would provide 6.9 mg Fe/d. This would provide approx. 86.3% and 46% of the RDA for Fe for adolescent girls aged 9-13 and 14-18 yrs.

**Conclusion:** Although both 50g and 37.5g serving of thick lentil provided similar results, a serving of 37g of thick lentil was deemed more feasible in the implementation of a larger scale human efficacy study. This preparation of cooked lentil served as a portion size of 200g dal would require less fortified lentils and still provide dietary levels of Fe that along with other foods eaten would meet their RDA.

**Keywords:** Fortification, Iron, Community-based trial, Lentils, Study Design.
Can we reliably monitor muscle strength development in children?

Presenter: Yuwen Zheng, College of Kinesiology
Supervisor: Dr. Saija Kontulainen
Collaborators: Kelsey Bjorkman, Dr. Joel Lanovaz

Background: Muscle forces provide the largest voluntary loading on bone. Reliable monitoring of muscle strength development is therefore fundamental in pediatric bone studies. We aimed to assess reliability of muscle strength measurements in children by 1) defining precision errors, and contrasting these errors to annual muscle strength development and 2) determining monitoring time intervals (MTI) for muscle strength measures in children.

Methods: To define short-term precision errors, we measured maximal push-up force, number of endurance push-ups, maximal grip force, countermovement and long jump peak forces, power and impulse, and long jump length on two different occasions (approximately 1 month apart) from 33 children (18F) with mean age of 10.5, SD 1.8yrs (precision cohort). To define annual change, we obtained the same measures approximately one year after the first visit from 33 (19F) participants (1-year follow-up cohort). We assessed precision errors by calculating root-mean-squared coefficient of variation (CV%RMS) and assessed annual changes with paired t-test (p<0.05). We then contrasted %-annual changes to precision errors. We determined MTIs by dividing least significant change (calculated from CV%RMS) by median annual change.

Results: For the maximal push-up force, precision error was 9% and annual increase was 29% (p<0.01). Number of endurance push-ups had the highest precision error (27%) with an annual increase of 43% (p<0.01). For the maximal grip force, precision error was 14% and annual increase was 38% (p<0.01). For force related measures in the countermovement jump, precision error ranged from 11% - 23% and annual increase ranged from 18% - 68% (all p<0.01). For the long jump, vertical and horizontal force related measures had precision errors ranging from 6% - 25% while annual increases ranged from 16% - 92% (all p<0.01). Long jump length had the lowest precision error (6%) and annual increase (8%) across all measures. Number of endurance push-ups had the longest MTI (2.7yrs), while MTIs ranged from 1 - 2yrs for all other upper and lower extremity measures.

Conclusion: Annual increases in the tested muscle strength measures exceeded related short-term precision errors in children. Estimated MTIs ranged from 1 - 2yrs for all upper and lower extremities measures except for endurance push-ups. These findings indicate that annual monitoring over two years will reliably capture muscle strength development in children when recording force from the push-up, grip strength, countermovement and long jump tests.

Keywords: Growth and Development; Musculoskeletal Health; Force; Power; Testing; Precision; Monitoring Time Interval
BASIC SCIENCE GROUP 1

54. Sphingosine Kinase 2 as a Potential Therapeutic Target in Telomerase Overexpressing Cancers

Presenter: Omar Abuhussein, College of Pharmacy and Nutrition
Supervisor: Franco Vizeacoumar

Background: The catalytic subunit of human telomerase reverse transcriptase (hTERT) is overexpressed in about 90 percent of all tumors. The role for the enzyme telomerase in multiple cancers and its up-regulation is linked to tumorigenesis. While this indicates inhibition of telomerase as a potential therapeutic strategy, disappointingly, there is no clinically potent and specific inhibitor of telomerase that has progressed into clinics yet. Rather than targeting telomerase, here we use synthetic dosage lethality (SDL) to target hTERT overexpressing tumors rather than targeting the hTERT itself. Cancer cells overexpressing hTERT would be killed when the expression of another gene is silenced/inhibited. Importantly, normal cells would be spared as the gene whose expression is silenced is not essential for its survival. Through a genome wide SDL screen using pooled shRNA platform, we were able to identify sphingosine kinase 2 (SK2) as a potential hit for targeting telomerase overexpression. SK2 is one of two kinases responsible for two sphingosine kinase isozymes that catalyze the phosphorylation of sphingosine into sphingosine 1-phosphate. Sphingosine 1-phosphate mediates many cellular processes including migration, proliferation and apoptosis, and also plays a role in several types of cancer by promoting angiogenesis and tumorigenesis. Considering the role SK2 has in cancer, we investigated if we can target telomerase overexpressing cancer cells by inhibiting SK2 activity.

Results: Our results show that a knockdown of SK2 significantly reduced the growth, colony formation ability of hTERT overexpressing cell line but not in the parental cell line. A Pharmacological inhibitor of SK2 by ABC294640 decreased the growth of hTERT overexpressing cell line to a greater extent than parental cell line. Thus, our data suggest that targeting SK2 inhibits cell proliferation, hTERT overexpressing cell line.

Keywords: Telomerase overexpression, Synthetic dosage lethality (SDL), Genome wide SDL screen, Sphingosine Kinase 2

55. Alpha-synuclein Binding 18F Labelled Bifunctional Agents as Positron Emission Tomography Imaging Probes for Parkinson's disease

Presenter: Aigbogun, Omozojie Paul, College of Arts and Science
Supervisor: Dr. Ed S. Krol, Dr. Christopher P. Phenix

Background: The misfolding, aggregation, and fibrillation of the intrinsically disordered alpha-synuclein protein is associated with the pathophysiology of Parkinson's disease. Recently we have developed dimer drugs that bind to alpha-synuclein and protect yeast cells from alpha-synuclein mediated toxicity. The alpha-synuclein binding properties of these dimers may also be useful as a non-invasive research and diagnostic tool for Parkinson's disease. Positron Emission Tomography (PET) imaging has a rich history in studying neurological disorders but requires the injection of radiotracers labeled with short-lived
radioisotopes such as $^{18}\text{F}$, $^{11}\text{C}$, $^{15}\text{N}$. $^{18}\text{F}$, which has a half-life of 109mins, is the most commonly used PET isotope for labeling radiotracer candidates. Our research objectives are to develop and optimize synthetic routes to incorporate $^{18}\text{F}$ into several of the dimers (C(8)-6-N, C(8)-6-I) to assess their biodistribution in vivo and to investigate whether they may serve as PET imaging probes to non-invasively evaluate alpha-synuclein aggregation in Parkinson's disease.

**Methods:** We have adapted a method for C(8)-6-N-$^{18}\text{F}$ synthesis in which we will carry out fluoride-mediated nitro displacement from the pyridine ring of nicotine. We are currently developing two approaches for labelling of C(8)-6-I. In one approach, we will incorporate $^{18}\text{F}$ on the indan aromatic ring C(8)-6-I-$^{18}\text{F}$ by making a reactive intermediate (spirocyclic hypervalent iodine precursoor). Our second approach will introduce the $^{18}\text{F}$-label on a N7 substituted propyl chain on the caffeine moiety (C(7)-$^{18}\text{F}$-(8)-6-I. $^{19}\text{F}$-labelled analogues will be initially prepared and assessed for their binding to alpha-synuclein through nanopore and isothermal titration calorimetry methods to determine the influence of fluorine on the labelled compounds.

**Results:** We are optimizing a synthetic pathway, adaptable to $^{18}\text{F}$ radiolabeling chemistry, and have determined that the key reaction in the successful synthesis of the C8-6-N is a mesylation reaction which proceeds to give a mono-mesylate and dimesylate that cannot be purified using conventional chromatographic methods.

**Conclusion:** A model synthetic route for C(8)-6-N has been designed and optimized. Our next step is the introduction of NO2 leaving group on Nicotine (C(8)-6-N) to facilitate fluorine incorporation to obtain C8-6-N-$^{19}\text{F}$. This will enable our long-term goal of C8-6-N-$^{18}\text{F}$ synthesis and PET imaging in mice to examine biodistribution.

**Keywords:** PET - Positron Emission Tomography, $^{18}\text{F}$- $^{18}$Fluorine, C(8)-6-N- Caffeine-Nicotine, C(8)-6-I- Caffeine-amino indan

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56. **Lysine functionalized nanodiamonds for gene delivery: investigation of internalization pathways and optimization of chemical design**

**Presenter:** Saniya Alwani, College of Pharmacy and Nutrition  
**Supervisor:** Ildiko Badea  
**Collaborators:** Raj Rai, Nancy Hua, Deborah Michel, Larhonda Sobchishin, Chithra Karunakaran, Narayan P. Appathurai

**Background:** We have utilized nanodiamonds (NDs), the most biocompatible member of the carbon nano-family which offers several advantages to be utilized as a carriers for targeted therapeutics. However, high degree of aggregation is a major limitation for its utilization. Covalent functionalization of ND surface with basic AA ‘lysine’ limits aggregation by dominating electro-repulsive forces and imparts a primary amine rich surface capable of binding negatively charged genetic materials forming ‘diamoplexes’. In order to understand the cellular interaction of functionalized NDs and diamoplexes, series of complimentary techniques are used to: (1) visually record plasma membrane activity highlighting specific pathways and (2) quantify the changes in cellular association of fluorescent siRNA conjugated as diamoplexes resulting from general and targeted endocytic inhibitions. Furthermore, final distribution patterns of various ND based treatments in cancerous cells are also recorded. Based on observations from above cellular assays, chemical design modification is performed to introduce a pH sensitive amino acid in the system which...
may limit endosomal entrapment and subsequent lysosomal degradation of genetic materials by inducing endosomal membrane rupture upon protonation of the imidazole ring.

**Methods:** NDs were covalently functionalized with lysine and lysyl-histidine via 3 carbon chain linker. 1HNMR and infrared spectroscopy (IR) were performed for validation. Surface loading was calculated using thermogravimetric analysis (TGA) to quantify the extent of functionalization (at this stage for lysine NDs only). Physicochemical stability was tested in different media through particle size and zeta potential measurements. siRNA was used as model genetic material and diamoplexes were created at various mass ratios. Formation of diamoplexes, their cellular internalization and uptake mechanism were studied through electrophoresis, flow cytometry, scanning transmission X-ray microscopy (STXM) and transmission electron microscopy (TEM). Gene expression efficacy and biocompatibility were analysed via flow cytometry.

**Results:** Functionalization of NDs with lysine (lys-NDs) was confirmed using above mentioned techniques with surface loading ranging from 1.97 to 2.22 mmoles/g. Our study is a first to quantify the relative extent of biomolecular functionalization. In all batches, the surface loading of lys-NDs and reoxidized NDs (with Carboxylated surface) were consistent, indicating maximum ND surface covering. Aqueous dispersion of lys-NDs exhibited excellent stability over the course of 25 days and formed diamoplexes with pDNA and siRNA at 1:1 and 1:20 mass ratios. Flow cytometry showed a dose dependent uptake of NDs and successful intracellular delivery of fluorescent siRNA (3-fold increase over the background fluorescence in two human cancer cell lines). Clathrin mediated endocytosis and macropinocytosis were the main pathways of internalization as confirmed through flow cytometry and TEM. STXM spectra of ND-treated cells showed diamond-specific absorption peaks. Colour-composite maps indicate the distribution of NDs and diamoplexes in the cytoplasm and some entrapped in lysosomes. Based on observations from above cellular assays that diamoplexes get entrapped in the endosomes, lysyl-histidine AA moiety was designed, confirmed through 1HNMR and is now covalently attached to NDs. Physicochemical analyses and biological interaction studies are under way for characterization.

**Conclusion:** This study is first in the field of ND research to demonstrate that covalent functionalization of NDs with AAs minimizes aggregation and make them capable of carrying therapeutic genes along with maintaining their innate biocompatibility.

**Keywords:** nanodiamonds, lysine, lysyl-histidine, Scanning transmission X-ray microscopy, gene delivery, siRNA, cellular uptake, endosomal entrapment

57. **Chronic A1R Stimulation Increases Microglia Activation and Neurodegeneration**

**Presenter:** Adelaide Amah, College of Medicine  
**Supervisor:** Dr. Francisco S. Cayabyab  
**Collaborators:** Olivia Friesen

**Background:** Elevation of adenosine during stroke results in widespread neuronal damage, after which microglia and other immune cells may become hyper-activated and induce/exacerbate further neuronal damage. While much has been uncovered about how microglia produce neuronal damage in the hippocampus, little is known about what initiates microglia hyper-activation. We hypothesized that stimulation of adenosine A1 receptors (A1R) on microglia elicits microglia hyper-activation causing
hippocampal neuronal damage, and therefore blocking microglia activity would improve neuronal cell survival following supraphysiological adenosine increases.

Methods: Young male Sprague Dawley rats (PN day 35, weighing 200-250g) received once daily intraperitoneal injections over a 48 hour time period with: 1. DMSO/Saline (vehicle control), 2. A1R agonist N6-Cyclopentyladenosine (CPA), 3. A1R antagonist 8-Cyclopentyl-1,3-dipropylxanthine (DPCPX)+CPA, 4. Minocycline (microglia inhibitor)+CPA. Rats underwent Y-maze behavioural testing to measure hippocampal-dependent spatial memory and open field and forced swim testing to assess anxiety and depressive behaviours, respectively. Following animal euthanasia, hippocampal brain slices of these animals were assessed for measures of neuronal damage and immune cell infiltration with immunohistochemistry and confocal imaging techniques. These parameters were compared between groups to investigate the overall effect of these drugs.

Results: Minocycline and DPCPX improved the CPA-induced cognitive deficits and anxiety/depressive behaviours. Imaging of hippocampal brain slices revealed substantial neuronal loss in CPA-treated rats in conjunction with increased microglia infiltration. However, co-administration of either DPCPX or Minocycline was found to provide neuroprotection against the harmful effects of CPA.

Conclusion: These results suggest that hippocampal neurodegeneration after prolonged A1R stimulation is, in part, mediated by microglia activation via A1Rs. Whether chronic A1R stimulation in microglia shifts microglia polarization to the pro-inflammatory phenotype, which leads to neurodegeneration, remains to be further examined.

Keywords: Adenosine, Hippocampus, Inflammation, Microglia

58. Effects of the type 1 cannabinoid receptor positive allosteric modulator GAT211 on absence seizures and the anxiety-like phenotype of Genetic Absence Epilepsy Rats from Strasbourg.

Presenter: Michael Anderson, College of Medicine
Supervisor: John Howland
Collaborators: Mariam Alaverdashvili, Quentin Greba, Andrew J. Roebuck, Wendie N. Marks, Sumanta Garai, Terrance P. Snutch, Ganesh A. Thakur, Robert B. Laprairie, John G. Howland

Background: Absence epilepsy is characterized by recurring seizures that lead to brief lapses of awareness. The most widely accepted treatments for the syndrome are ethosuximide, which can produce drowsiness and confusion; and valproic acid, which displays hepatotoxicity. The type 1 cannabinoid receptor (CB1R) is considered a potential therapeutic target for many forms of epilepsy, including absence seizures.

Methods: In the first experiment, adult male Genetic Absence Epilepsy Rats from Strasbourg (GAERS) were implanted with recording electrodes in sensorimotor cortex and hippocampus. They were then treated with GAT211 or vehicle. In the second experiment, male and female GAERS and non-epileptic controls (NEC) were treated with either vehicle or GAT211 and tested on the elevated plus maze and acoustic startle.

Results: Analysis based on electrode implantation revealed that GAT211 treatment decreased the total duration of seizures for 1 h after treatment. Vehicle-treated GAERS showed decreased open arm time on
the elevated plus maze, representative of lower anxiety, and increased startle compared to NEC. Importantly, GAT211 treatment normalized both behaviours in GAERS without significant effects in NEC.

**Conclusion:** These results suggest that positive allosteric modulation of CB1R may be therapeutically effective target for ameliorating absence seizures, as well as their comorbidities such as anxiety.

**Keywords:** Cannabinoid; type 1 cannabinoid receptor (CB1R); GAERS; allosteric modulator; behavioral pharmacology

59. Specificity of sparing effects with cross-education in an immobilized limb

**Presenter:** Justin W. Andrushko, College of Kinesiology
**Supervisor:** Jonathan P. Farthing
**Collaborators:** Joel L. Lanovaz, Kelsey M. Björkman, Saija A. Kontulainen

**Background:** Cross education (CE) occurs after unilateral training whereby performance of the untrained contralateral limb is enhanced. A few studies have shown that CE can preserve or “spare” strength and size of an opposite immobilized limb, but the specificity (i.e., trained homologous muscle and contraction type) of these effects is unknown. The purpose was to investigate specificity of CE “sparing” effects with immobilization.

**Methods:** The nondominant forearm of 16 participants was immobilized with a cast, and participants were randomly assigned to a resistance training (eccentric wrist flexion, 3 times/week) or control group for 4 weeks. Pre- and posttesting involved wrist flexors and extensors eccentric, concentric and isometric maximal voluntary contractions (via dynamometer), muscle thickness (via ultrasound), and forearm muscle cross-sectional area (MCSA; via peripheral quantitative computed tomography).

**Results:** Only the training group showed strength preservation across all contractions in the wrist flexors of the immobilized limb (training: −2.4% vs. control: −21.6%; P = 0.04), and increased wrist flexors strength of the nonimmobilized limb (training: 30.8% vs. control: −7.4%; P = 0.04). Immobilized arm MCSA was preserved for the training group only (training: 1.3% vs. control: −2.3%; P = 0.01). Muscle thickness differed between groups for the immobilized (training: 2.8% vs. control: −3.2%; P = 0.01) and nonimmobilized wrist flexors (training: 7.1% vs. control: −3.7%; P = 0.02). Strength preservation was nonspecific to contraction type (P = 0.69, ηp2 = 0.03) yet specific to the trained flexors muscle.

**Conclusion:** These findings suggest that eccentric training of the nonimmobilized limb can preserve size of the immobilized contralateral homologous muscle and strength across multiple contraction types.

**Keywords:** Cross-education, muscle size, muscle strength, immobilization
60. Discovering the architecture of a new p63 gene regulatory network regulating tooth formation

**Presenter:** Cassy Appelt, College of Medicine  
**Supervisor:** Dr. Julia Boughner  
**Collaborators:** Aunum Abid

**Background:** Congenital facial and dental defects are among the most common birth defects in Canada. The p63 transcription factor is an evolutionarily ancient member of the p53 family of tumor suppressors. Expressed in epithelium, p63 helps mediate the healthy differentiation of epithelium-derived structures such as hair, skin, glands, teeth, and limbs. Inherited heterozygous p63 mutations cause a range of syndromes such as: Limb mammary syndrome, Ankyloblepharon-ectodermal deficits–cleft lip/palate syndrome, Rapp-Hodgkin syndrome, Acro-dermato-unguinal-lacrimal-tooth syndrome, and Ectrodactyly, ectodermal dysplasia, cleft lip/cleft palate syndrome. Notably, these syndromes all have orofacial clefting, ectrodactyl hand/foot malformations, and other complications arising from the failed development of epithelium-derived structures in common. Knocking out p63 in mouse models causes similar malformations. Mice are born with underdeveloped skin, hair, glands and limbs, and with craniofacial defects such as cleft palate. Additionally, p63-null mice fail to develop teeth; these are arrested in the placode stage of early odontogenesis, meaning that the dental epithelium thickens but fails to progress further towards a tooth organ. Our lab has revealed a novel gene regulatory network (GRN) controlled by p63 that drives odontogenesis, linking for the first time several genes to both odontogenesis and p63. To investigate this GRN further, we aimed to test for expression of novel genes in developing tooth organs in mouse, an established model for human odontogenesis. Teeth are homologous structures among jawed vertebrates, appearing first in the oral jaws of ancient gnathostomes; p63 and its function mediating the development of epithelium-derived structures is also ancient and conserved, likely present at the time that jawed fishes first evolved. The premise that this GRN is also ancient and conserved has merit as most of the GRN members are homologous in most of the major vertebrate classes. We tested this by probing for the same genes' expression in gar. Gar belong to an order of ancient bony fishes that have retained oral teeth homologous to mammalian teeth. Thus gar is an excellent model to query whether our p63 GRN is ancient and conserved. Next, we are building the architecture of this GRN; notably, determining how P63 interacts with each of its 30+ downstream targets. My master's project uses Next Generation ChIP- Sequencing to identify which genes are primary binding targets of P63, and which are secondary targets transcriptionally controlled by other GRN members. Building the specifics of this p63-driven GRN will help explain how p63 mediates normal tooth and craniodental development on a broader scale.

**Methods:** We completed immunohistochemistry (IHC) assays to define the expression of 5 novel genes (Fermt1, Krt15, Cldn23, Cbln1, Prss8) in mouse and gar fish. p63 +/+ Mouse embryos (n=4) were collected at embryonic day (E)12 and E14; gar embryos (n=2) were gifted to our lab by Eames lab, and euthanized at 14 days post fertilization (dpf). Embryos were fixed in 4% paraformaldehyde and stored in 70% (mouse) and 100% (gar) ethanol. From storage, embryos were processed in xylene (mouse) and chloroform (gar) and embedded in paraffin blocks. Following embedding, the blocks were sectioned at 7microns thickness and slide mounted. Slides were prepared with 3 adjacent sections; one section used as the experimental replicate, and the other two for controls. Negative controls included no secondary or primary antibody application, and secondary antibody-only conditions. An additional, positive control applied only a primary antibody. Gar slides included a fourth section of mouse tissue for an additional p63-positive control. The presence of tooth tissues in the experimental series was confirmed with H&E sections. Protocol for IHC assays included a 10 minute Bloxall application to block endogenous peroxidases,
followed by 5 minute 2.5% natural horse serum to block non-specific binding. Next, the primary antibody was applied to tissues for 30 minutes, secondary antibody application (conjugated with HRP) for 10 minutes, and finally a 10 minute NovaRed application to effect a chromogenic reaction. Slides were graded to absolute ethanol, cleared in xylene, and glass mounted using entellan. Visualization of slides was done using a high-powered scope. Moving forward, we will be using ChIP-seq techniques to analyse the architecture of this GRN, distinguishing which gene members are primary targets (gene targets and regulatory transcription factors) and which are secondary targets (influenced by other GRN members). Embryos (n=4/condition) will be collected at E10 and E12, corresponding to the initiation and early stages of odontogenesis. Jaw primordia will be excised, the epithelium separated, and epithelium cells isolated using Dispase II. Cross linking will be effected with 4% PFA, and immunoprecipitation (IP) will be completed with a ChIP-validated antibody for P63. After confirming motif enrichment via qPCR, purified DNA will be sent to IRIC (Univ. Montreal) for Next Generation Sequencing on MiSeq/HiSeq2500 platforms (Illumina). Controls will include non-dental epithelium and DNA post-fragmentation but pre-IP. The GRN will be built using guidance from IRIC's Bioinformatics Services and free software (e.g., MACS, Harvard).

**Results:** Our results were positive for the protein expression of our 5 genes-of-interest in both developing tooth organs of mouse and gar. These genes were expressed in the same domain as p63; that is, in the tooth epithelium, and as such, their expression also overlapped at least somewhat. These gene expression domain results are novel; previously, only our lab has connected Krt15, Fermt1, Cldn23, Cbln1, and Prss8 with tooth development through microarray screens and RNA-seq experiments comparing gene expression in edentulous p63/- mouse with heterozygote littermates.

**Conclusion:** Our study provided additional, strong support for a p63-driven gene regulatory network recently identified by our lab, and generated new expression data for 5 genes not previously known to be expressed in developing tooth. Because these genes are functional in the developing tooth of mouse, which exhibits stages of odontogenesis very close to humans, our work implicates these 5 genes in human tooth development. Because we also saw expression of these same 5 genes in fish tooth (gar), our work supports that this GRN and its members are deeply conserved, ancient in origin, and may work to drive tooth development in all jawed vertebrates.

**Keywords:** Craniodental development, tooth development, odontogenesis, p63, tp63, tooth evolution, craniofacial evolution,

61. **TLR9 agonist enhances radiofrequency ablation-induced CTL responses leading to potent inhibition of primary tumor growth and lung metastasis**

**Presenter:** Fatma Babikr, College of Arts and Science  
**Supervisor:** Jim Xiang

**Background:** Radiofrequency ablation (RFA) is the most common approach in thermal ablation cancer therapy. In specific cancer cases, such as small liver tumor-metastasis, RFA therapy produces clinical outcomes comparable to surgical operation. Overall, RFA offers some significant advantages compared to the surgical procedures, including low morbidity, lower costs and better preservation of surrounding tissues. However, its common drawback is an incomplete tumor ablation, leading to cancer recurrence.

**Methods:** Preparation and characterization of heat-treated EG7 cells:
EG7 cells were resuspended in complete medium at 10 million cells/ml. culture tubes were submerged in a water bath and incubated at 45 or 65 degrees for 20 min, which was an optimal exposure time.

**Results:** This study demonstrate that more EG7 tumor cell-death by necrosis is achieved by incubation of these cells at 65 degrees compared to the treatment at 45 degrees. These 65 degree-treated cells are more effective than the 45 degree-ones in inducing antigen-specific CD8 cytotoxic T lymphocyte (CTL) responses after being injected into mice. The phagocytosis of 65 degree-treated EG7 tumor cells by Dendritic cells (DCs) induce their maturation with upregulated la b and CD80 expression and they become capable of efficiently inducing effector CTLs in mouse tumor models.

**Conclusion:** RFA (65 degrees) therapy of EG7 tumors induces large areas of tumor necrosis and stimulates CTL responses, however, it fails to suppress larger-size (~ 350 mm cubic) tumors. Administration of Toll-like receptor-9 (TLR9) agonist, unmethylated Cytosine-phosphorothioate-Guanine (CpG) oligonucleotide, to DCs phagocytosing 65 degree-treated EG7 cells, enhances both expression of la b, CD40 and CD80 by DCs and the DC- induced stimulation of CTL responses. Importantly, intratumoral administration of CpG following the RFA treatment also leads to potent inhibition of primary tumor growth and tumor lung metastasis in mice bearing larger-size tumors. Overall, these data indicate that CpG administration, which enhances RFA-induced CTL responses and ultimately potentiates inhibition of primary tumor growth and lung metastasis, is a promising strategy for improving RFA treatment, which may assist in optimizing this important cancer therapy.

**Keywords:** RFA, CTL responses, TLR9 agonist, anti-tumor immunity, metastasis

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62. Learning form an evolutionary host: IRF3 signaling is critical to prevent Middle East respiratory syndrome (MERS) coronavirus propagation in big brown bat cells.

**Presenter:** Arinjay Banerjee, Western College of Veterinary Medicine  
**Supervisor:** Dr. Vikram Misra  
**Collaborators:** Dr. Darryl Falzarano, Noreen Rapin, Jocelyne Lew and Dr. Scott Napper

**Background:** Insectivorous bats are speculated to be evolutionary hosts of Middle-East respiratory syndrome (MERS) coronavirus (CoV). MERS-CoV causes disease in humans with a thirty-five percent mortality. Since bats experimentally infected with MERS-CoV do not develop disease, we tested the hypothesis that MERS-CoV cannot subvert antiviral responses in bat cells.

**Methods:** We infected bat and human cells with MERS-CoV and quantified virus propagation by TCID50. We monitored innate antiviral responses by quantitative real time PCR. We studied the function of Interferon response factor 3 (IRF3) in bat cells by immunofluorescence and immune blots. Finally, we knocked-down IRF3 in human and bat cells using small interfering RNA (siRNA) to identify its antiviral role.

**Results:** MERS-CoV propagated significantly more in human cells than bat cells. MERS-CoV effectively suppressed antiviral interferon beta (IFN) response in human cells, unlike in bat cells. Bat IRF3 responded to poly(I:C) by phosphorylation and nuclear translocation; hallmarks of IRF3 activation. Finally, MERS-CoV propagated to significantly higher levels in IRF3 knocked-down bat cells.

**Conclusion:** Our study was able to identify a unique IRF3 mediated antiviral signaling process in bat cells that is resistant to subversion by MERS-CoV. Future studies will enable us to adapt these strategies to restore antiviral signaling in coronavirus infected human cells.
63. Determining glycogen degradation and utilization capabilities of Gardnerella vaginalis

Presenter: Pashupati Bhandari, Western College of Veterinary Medicine  
Supervisor: Dr. Janet E. Hill

**Background:** Glycogen is a major carbon source available to vaginal microbiota and is break by human amylases. Role of bacterial amylase in this breakdown is not known. Previous reports on glycogen fermentation in G. vaginalis are inconsistent, which suggests this trait may be subgroup-specific. Competition for glycogen and its breakdown products may be a key factor in determining microbial community structure.

**Methods:** Representative isolates from each subgroup were grown on BHI agar containing 1% glycogen or 1% starch and incubated anaerobically at 37°C. Presence of a clear zone around the colonies after adding iodine indicator indicates α-amylase activity. Glycogen utilization activity determined by growth curve experiments performed in BHI broth with and without 2% maltose or 2% glycogen.

**Results:** All 35 strains tested from four subgroups (A (11), B (11), C (9) and D (4)) were found to be α-amylase positive. Growth rates of 6/8 isolates were greatly enhanced by the presence of glycogen indicating their ability to degrade and utilize this complex substrate. No enhancement of growth of vaginal Lactobacillus controls was observed.

**Conclusion:** Presence of amylase enzyme and ability to utilize glycogen can give Gardnerella vaginalis competitive advantage over lactobacilli in glycogen containing environment.

**Keywords:** Gardnerella vaginalis, Glycogen, amylase, maltose
**BASIC SCIENCE GROUP 2**


**Presenter:** Harkirat Bhullar, College of Arts and Science  
**Supervisor:** Dr. Anthony Kusalik, Dr. Jo-Anne Dillon  
**Collaborators:** Kimberly MacKay, Dr. Jinhong Shi, Katie Ovens

**Background:** Antimicrobial resistance (AMR) is a major threat to global public health with 10 million people at risk of dying from AMR-related causes by 2050. Understanding the underlying biological factors of resistance is crucial in the battle against AMR driven “superbugs”. Unfortunately, existing computational techniques used to uncover these factors lack novel insights and have inadequate biological interpretability. The objective of this work was to develop a fast, accurate and interpretable computational framework that utilizes machine learning to identify novel (and validate known) resistance factors from whole-genome sequencing (WGS) data.

**Methods:** The developed framework used decision tree models to identify resistance factors. Genomic features (short genetic variations [SGVs]) were extracted from WGS data. These features were used as input into 4 decision tree models (reduced error pruning tree, C4.5 tree, alternating decision tree and logistic alternating decision tree) to predict AMR. Each model’s performance was evaluated with 10-fold cross-validation. The structure of the model with the highest performance was probed to identify genomic features predictive of resistance.

**Results:** To demonstrate the power of the developed framework, it was used to identify resistance factors for 5 antibiotics (ciprofloxacin, azithromycin, cefixime, penicillin and tetracycline) in Neisseria gonorrhoeae (the bacterium responsible for the sexually transmitted infection gonorrhea). Specifically, 38683 SGVs were extracted from the genomes of 676 Neisseria gonorrhoeae strains and used to build the decision tree models. The alternating decision tree model reported the best performance with an average accuracy of 95% and 90.9% for resistant and susceptible strains respectively. Overall, the framework uncovered 45 novel (and validated 6 known) resistance factors across all 5 antibiotics.

**Conclusion:** This is the first-ever interpretable machine learning framework for predicting AMR from WGS data. Overall, it has the potential to provide unprecedented insight into the underlying biological mechanisms of AMR. This framework could also be used to facilitate targeted antimicrobial treatment and drive drug development, both of which would help in the battle against AMR driven “superbugs”.

**Keywords:** Antimicrobial Resistance, Machine Learning, Antibiotics, Gonorrhea, Whole Genome Sequencing
65. **CNQX Blocks Reelin's Fast-Acting Antidepressant Effects in a Preclinical Animal Model of Depression**

**Presenter:** Kyle Brymer, College of Arts and Science  
**Supervisor:** Lisa Kalynchuk

**Background:** Previous work in our lab has shown that a single intrahippocampal infusion of the extracellular matrix protein reelin rapidly reverses depressive-like behavior in the forced swim test, alters hippocampal neurogenesis, and increases the number of GLUA1-ir cells in the SGZ. Here, we tested the involvement of AMPA in the fast-acting antidepressant effects of reelin by administering CNQX.

**Methods:** We conducted stereotaxic surgery to implant an indwelling cannula into the dorsal hippocampus. Rats received 21 days of 40 mg/kg CORT/vehicle injections, in addition to infusions of reelin (1 µg/1µl) or reelin+CNQX (1.25 µg/1µl). The FST was then conducted, and rats were immediately sacrificed. Post-mortem analyses were conducted to evaluate changes in neurogenesis, Fos expression, and microglia.

**Results:** A single intrahippocampal reelin infusion decreased time spent immobile in the FST, increased the number but not the complexity of DCX-ir cells, and contributed towards an active microglia phenotype. A single intrahippocampal CNQX infusion following reelin blocked reelin's widespread effects on both behavior and neurobiology.

**Conclusion:** These novel results demonstrate that CNQX blocks reelin's fast-acting antidepressant effects on the FST without altering reelin's effects on hippocampal neurogenesis or microglia morphology.

**Keywords:** Depression, Reelin, AMPA, Neurogenesis

66. **Rats and Mice Present Different Post-Traumatic Behavioural Responses to The Predator-Scent Psychosocial Stress (PPS)**

**Presenter:** Jacob Cohen, College of Medicine  
**Supervisor:** Yanbo Zhang  
**Collaborators:** Zeilan Wei, Olunbuni Adebyi

**Background:** Post-Traumatic Stress Disorder (PTSD) is a debilitating psychiatric disorder whose features include severe anxiety, hyperarousal, as well as cognitive and mood changes after experiencing or witnessing a traumatic event. To date, a precise cause of PTSD has not been elucidated. Animal models producing PTSD-like symptoms are valuable tools for studying the neurobiology of PTSD and treatment development. The predator psychosocial stress (PPS) animal model integrates predator exposures and inadequate social support into one PTSD model, which produces PTSD-like symptoms in all stressed rats. The PPS model is particularly suitable for treatment development because it provides more consistent PTSD-like symptoms and reduces the animal use and research expenses. Compared to rats, mice are more cost-effective. Besides, genetically modified mouse strains can be used to study the roles of specific genes in developing PTSD. However, the effects of PPS on mice is rarely explored. This project sought to establish the validity of PPS mouse model of PTSD. We applied an identical PPS protocol to both mice and rats and compared PTSD-like symptoms, sizes of adrenal gland and serum cortisol levels. We found that 70% rats
and 40% mice met the pre-set PTSD score. Rats are more sensitive and produce a better PTSD model for treatment development. Mice are more resilient to the same stress compared to rats. These findings warrant future studies to identify underlying mechanisms for the resilience using PPS mice model.

**Methods:** Animals were given a 7-day acclimatization period before beginning the study. PPS animals were exposed to cat urine soaked litter 1 hour on day 2 and day 11. PPS animals were given social stresses by randomized changing their cage mate(s) daily from day 2 to day 30 (Figure 1). The control animals were exposed to saline soaked litter 1 h on day 2 and day 11 and stayed in their home cage with original cage mates during the experiment.

**Predator Psychosocial Stress (PPS)**

On day 2, PPS groups were exposed to soiled cat litter for 1 h during the light cycle 07:00 – 19:00). The soiled cat litter were collected from cat housed at Western College of Veterinary Medicine (WCVM), University of Saskatchewan. Clean litter was weighed dry before being placed into the box and re-weighed upon collection to estimate the urine volume. A total 1.2 L of urine was collected from six litter boxes and mixed before use. The litter containing 150 ml of urine was put on the bottom of an animal cage. A metal grate was placed above the litter. Animals were placed on top of the metal grate to separate them from physically contacting the cat litter. Animals were exposed for 1 hour and then returned to the home cage. On day 3, control groups were exposed to regular cat litter wet with 150 ml of deionized water. Control groups were also placed in a closed cage on top a metal grate to separate them from the damp litter. Exposure lasted 1 h, and they were returned to the home cage. On day 11, all procedures were repeated identically, but during the dark cycle (19:00 – 07:00). Animals were weighed twice weekly beginning on day 1 until day 30 and before sacrifice to measure the growth rate.

**Results:** This study shows that although the mice model can be a valuable model, the rat model produces a more definite picture overall. This may be because the rat is more sensitive and perhaps more resilient to traumatic stressors than the mouse. Chronic stress is known to cause an increase in adrenal gland weight due to hypertrophy and a reduction in thymus weight. Both factors contribute to reducing the level of basal cortisol. These factors have a significant impact on the hypothalamic-pituitary-axis (HPA) which is involved in sleep and mood regulation (10; 11).

Rats seem to be either more sensitive or perhaps less resilient to traumatic experiences that mice. Many theories and suggestions have been made regarding these differences, but they have been poorly studied (12). Rats are more social than mice (13). Certain strains of mice are known to display extreme aggression towards other mice within their litter, which is far less seen in rats (14). Mice also take longer and have more difficulty than rats to learn (15). A study completed by Maren et al. in 2012 (14) showed that rats learned significantly faster and were less affected by distractions than mice when learning a food reward task than the involved location of a food reward in one of two bowls that differ in two dimensions (16). There are profound chemical receptor differences in the brains of rats compared to mice. Rats have more serotonergic receptors and less CB2 receptors compared to mice, which can explain differences in mood, cognition and learning (17-19). As we know in animals, PTSD is complicated to diagnose and affects all patients in different ways. Both models produce a wide array and varying degrees of PTSD-like symptoms, but the distribution is more transparent in the rat model. The rat model may, therefore, be more effective in translational pharmacological experiments (20).

**Conclusion:** We can conclude from this study that although the mice model can be a valuable model, the rat model produces a more definite picture overall. This may be because the rat is more sensitive and perhaps more resilient to traumatic stressors than the mouse. Future directions include determining the precise reason for the resilience and further studies into a genetic factor for resilience. Replication of the model should be made in an acute model of PTSD to determine the effect of extinction on various...
parameters and data acquisition. It is of critical importance to establish a common pathway between rats and mice before proceeding to human clinical trials. Many animal models have used only one species in their findings. Determining pathways and factors common to both species will provide a more robust foundation for translational experiments.

**Keywords:** Post-Traumatic stress disorder, Stress, Behavior, Learning, Anxiety

### 67. Cytotoxicity profiles of lanthanide compounds within human kidney (HEK-293), liver (HEPG2), and osteoblast (HOb) cells in addition to murine pre-osteoclast (RAW 264.7) cells

**Presenter:** Grace Cuddihy, College of Pharmacy and Nutrition  
**Supervisor:** Dr. Kishor Wasan  
**Collaborators:** Yunyun Di, Jacqueline Cawthray, Ellen Wasan, Chris Orvig, Thomas. I. Kostelnik, David Cooper

**Background:** Our team has developed a promising lanthanide compound (LaXT) that has the potential to treat bone density disorders such as osteoporosis. Recently published animal studies found that La3+ preferentially accumulates in tissues and particularly in bone. The purpose of this study is to develop a cytotoxicity profile for the lanthanum compounds in human kidney and liver cells as well as bone-related human osteoblast cells after a preliminary investigation into the IC50 of the compound in a prostate cancer cell line (C4-2).

**Methods:** For all cell lines, 5000 suspended cells in 100 µL of complete culture medium, were seeded in 96-well plates and allowed to attach overnight. Subsequently, cells were treated with varying concentrations of each lanthanum compound for 48 or 72 hours then cell viability was determined using CellTiter 96® AQueous One Solution Cell Proliferation Assay (MTS). Data were plotted in GraphPad Prism5 and analyzed using two-way ANOVA with Bonferroni post hoc tests.

**Results:** Preliminary investigation into the cytotoxicity of LaXT in C4-2 cells demonstrated that the concentration when 50% of cell death occurred was 355.3 µM. Limited toxicity was observed in HEK-293 human kidney cells, HepG2 human liver cells, and RAW264.7 murine pre-osteoclast macrophage cells treated with <300 µM of LaXT or LaCl3 (docetaxel 25nM and 1% (v/v) Triton X-100 were positive controls used to achieve an average of approximately 60% and 99% cell death respectively). In HOb bone-related human osteoblast cells, no significant reduction in cell viability occurred until concentrations of LaXT or LaCl3 ≥1000 µM).

**Conclusion:** The present study shows that the LaXT compound has only limited in vitro toxicity at very high concentrations in the human kidney and liver cells with similar toxicity profiles in bone-related human osteoblast and murine pre-osteoclast cell lines.

**Keywords:** lanthanide, cytotoxicity, osteoporosis
68. Exploiting the synthetic dosage lethal interactions of Polo-like Kinase 1 for cancer therapeutics

Presenter: Chelsea Cunningham, College of Medicine  
Supervisor: Franco Vizeacoumar  
Collaborators: Andrew Freywald

**Background:** Targeted therapies are crucial for personalizing cancer treatment but identification of effective targets is a challenge. PLK1 is overexpressed in nearly all cancer types. Clinical trials of PLK1 inhibitors are generally terminated due to poor response or side-effects. Applying synthetic dosage lethality can overcome these issues and identify targets that kill only cancer cells overexpressing PLK1.

**Methods:** A genome-wide shRNA screen was utilized to identify interactions in an inducible PLK1 model cell line. This screen identified 960 significant possible hits. An array of computational validations narrowed the list of hits to 122. These 122 genes were further validated using an in vivo screen and individual knockdowns by shRNA and CRISPR in cell lines of different origin and varying levels of PLK1.

**Results:** Our computational validation successfully identified a previously characterized synthetic dosage lethal interaction between PLK1 and PPP2R5D, showing the strength of the unbiased approach of selecting hits for validation. Experimental validation using a variety of cell lines, models, and genome-editing techniques provides robust validation of our identified hits as the strongest potential targets.

**Conclusion:** Synthetic dosage lethality is valuable in identifying new and effective therapies to specifically target cancer by taking advantage of its genetic vulnerabilities. Our results will generate highly validated set of therapeutic targets for a variety of solid tumours in the context of PLK1 overexpression, and potentially lead to the identification of therapeutic compounds for pre-clinical studies.

**Keywords:** Synthetic dosage lethality; polo-like kinase 1; cancer therapeutics; genomic instability

69. Cellular Effects Linked to Mammalian Lignan Enterolactone Modulated Lipid Homeostasis

Presenter: Franklyn De Silva, College of Pharmacy and Nutrition  
Supervisor: Jane Alcorn  
Collaborators: Martin Reaney

**Background:** Impairment of physiological regulatory mechanisms of cholesterol and lipid homeostasis is a feature of cardiovascular disorders, various neurodegenerative disorders, diabetes, and cancer progression. Furthermore, dysregulated cells can exhibit elevated endoplasmic reticulum (ER) stress as an adaptive survival mechanism. A link between flaxseed lignans (FLN) anti-cholesterolemic and anti-cancer effects might exist through the ability of FLN to modulate both ER stress and cholesterol homeostasis as FLN are known to modulate multiple targets in dysregulated cellular signaling pathways. This study aims to identify the molecular targets responsible for enterolacone (ENL), flaxseed lignan mammalian metabolites' ability to modulate ER stress and cholesterol homeostasis in dysregulated cell types such as cancer.
Methods: Key targets involved in cholesterol metabolism, ER stress, cell survival, and vesicular cholesterol trafficking were evaluated using a battery of in vitro assays such as qPCR, western blot, fluorescence microscopy, gene reporter assay, and substrate uptake assay using various cell lines.

Results: Gene reporter assay and glucose uptake assay revealed ENL as a PPARγ inducer. ENL modulated cholesterol and lipid metabolism targets (FASN, SREBPs, INSIG-1, LDLR, PPARγ) and ER stress markers (ATF4, CHOP, GADD34 and GRP58). ENL reduced mitochondrial redox function and caused mitochondrial toxicity. ENL enhanced ability of select anticancer drugs (e.g: microtubule inhibitors such as taxols) to decrease cell viability. Fluorescently labeled cholesterol treated cells along with ENL revealed altered intracellular vesicular trafficking linking the actin cytoskeleton.

Abbreviations: peroxisome proliferator-activated receptor gamma (PPARγ), fatty acid synthase (FASN), sterol regulatory element-binding proteins (SREBPs), insulin induced gene 1 (INSIG-1), low density lipoprotein receptor (LDLR), Activating transcription factor 4 (ATF4), CCAAT-enhancer-binding protein homologous protein (CHOP), growth arrest and DNA damage-inducible protein 34(GADD34), glucose-regulated protein 58-kD/ protein disulfide-isomerase A3 (GRP58).

Conclusion: A novel role may exist between the regulation of PPARγ, lipid and cholesterol metabolism, and ER stress. Reduced mitochondrial redox function and caused mitochondrial toxicity may aid in ENL induced apoptosis and reduced cancer cell viability. These findings warrant further investigations to support FLN’s ability to modulate ER stress as the key mechanism involved in the disruption of dysregulated cellular signaling. ER stress and PPARγ mediated signaling can influence cholesterol and lipid metabolism and therefore are relevant targets in drug discovery.

Translational Relevance: Lignans are safe, and therefore are good candidates for adjuvant therapy that could improve patient longevity and quality of life. Additionally, an appropriate lignan enriched product can provide a clinically relevant dose without significant toxicities.

Keywords: Natural Products, Lignans, Flaxseed, Endoplasmic reticulum stress, Metabolism, Adjuvant therapy

70. Structural and Biochemical studies of H. pylori chaperone-substrate protein complexes

Presenter: Poonam Dhindwal, College of Medicine
Supervisor: Stanley A. Moore

Background: H. pylori is a gram negative motile pathogenic bacterium. The presence of flagella is essential for motility and persistent colonization in the stomach, which causes ulcer formation. The chaperone FlgN and its substrate FlgK are crucial flagellar proteins which forms the hook filament junction of the flagella. Knocking out of either of the two proteins result in compromised flagella formation.

Methods: FlgK and FlgN genes were cloned by traditional and Ligation independent cloning respectively. The proteins were purified using affinity and ion exchange chromatography. Interaction studies were done using pull down technique. The FlgK protein was crystallized using hanging drop and micro-seeding method. The protein crystals were diffracted and data was collected at the CMCF ID beamline at the CLS.

Results: The His-FlgN chaperone and GST-FlgK substrate protein interaction was shown using pull down study. The crystals obtained for FlgK protein were highly birefringent and clustered in nature. The crystals
diffracted up to 2.5 Å... and belonged to the P1 triclinic space group. The structure of the protein was determined using molecular replacement.

**Conclusion:** The FlgN protein dimer dissociates into monomer to facilitate the interaction with FlgK protein in 1:1 ratio. The conformational flexibility of FlgN will be further studied using co-crystallization of FlgN protein with FlgK protein. The overall H. pylori FlgK structure is similar to C. jejuni FlgK structure. The conserved structural features indicate likely specific functional relevance.

**Keywords:** H. pylori, Flagella, Chaperone, Crystallization, CLS

71. **Knockdown of Scavenger Receptor Class B Type I (SR-BI) reduces uptake of Vyxeos into K562 leukaemia cells**

**Presenter:** Yunyun Di, College of Pharmacy and Nutrition  
**Supervisor:** Kishor M. Wasan  
**Collaborators:** Ellen K. Wasan, Jacqueline Cawthray

**Background:** The Scavenger Receptor class B type I (SR-BI) plays an important role in mediating the uptake of high-density lipoproteins. The purpose of this study is to assess the role of the cell surface lipoprotein receptor SR-BI in the uptake of Vyxeos liposomes (Jazz Pharmaceuticals) into K562 leukaemia cells. Vyxeos liposomes encapsulate a fixed ratio of daunorubicin and cytarabine, and is approved for use in acute myeloid leukaemia.

**Methods:** K562 cells were treated with 10nM Stealth RNAi duplexes targeting the SR-BI gene (SR-BI kd) or 10 nM low GC negative control Duplexes (NC), premixed with Lipofectamine RNAiMAX reagent. Cells were collected every 24 hours to determine the SR-BI gene expression levels by RT-PCR. Uptake of Vyxeos within K562 cells was determined using flow cytometry by tracking daunorubicin. Vyxeos at concentrations of 0, 10, 20, 30 and 50 ng daunorubicin/mL were incubated for 24, 48 or 72 hours after siRNA transfection to downregulate SR-BI. At each time point, cells were collected and analyzed at λex/λem=480/590 nm on a CytoFLEX Multicolour flow instrument to determine cellular uptake of daunorubicin. Experimental data were plotted as mean±SD using GraphPad Prism (Version 5.0). Data were analyzed using two-way ANOVA with Bonferroni multiple comparisons. Significance was set at p<0.05.

**Results:** The SR-BI gene expression levels were significantly decreased by > 75% in the cells treated with 10 nM siRNA for at least 48 h, and maintained up to 120 h, compared to K562 cells treated with medium only (Figure 1). Uptake of daunorubicin into K562 cells treated with Vyxeos was significantly decreased in the cells where expression of SR-BI was knocked down by siRNA, compared with cells treated with low GC Negative Control Duplexes (NC) at 24, 48, and 72 h. A 75% reduction in SR-BI gene expression (72h post siRNA transfection) resulted in a 30% reduction in Vyxeos (50ng/mL) uptake (Figure 3 and Table 1).

**Conclusion:** These preliminary studies suggest that SR-BI may be one potential mechanism by which Vyxeos is taken up into K562 cells.

**Keywords:** SR-BI, Liposome, Leukaemia
Effects of exercise and screen time on sleep in middle age.

Presenter: Rueben Dreher, College of Kinesiology  
Supervisor: Heather Foulds

**Background:** Sleep is an important process for good health. Previous studies found sleep facilitation with aerobic exercise rather than resistance and afternoon exercise rather than morning or evening. Previous research suggests a negative affect of screen time on sleep, however those with high screen time and high physical activity have lower risks of sleep problems. The purposes of this study are to; explore the relationship between screen time, exercise and sleep in middle age (age 30-55yrs), evaluate the effect that different quantities have on sleep in middle age (low, moderate, and high screen time), and explore how time of day (morning, afternoon, and evening) of exercise and exercise type (aerobic vs. muscle strengthening) influences sleep in the same middle aged population.

**Methods:** Descriptive information was collected via physical measures (height, weight, etc.) and survey questions. Study variables (sleep, exercise, etc.) where collected via survey. Independent samples t-tests were preformed to discern differences between descriptor variables of exercisers (those that exercised >150 mins of moderate/moderate-vigorous exercise per week) and non-exercisers (those that did not meet the 150 mins). Independent samples t-tests compared muscle strengthening activity (MSA) participants and non-MSA exercisers. One-way ANOVA’s compared the sleep variables of the time of day, screen time and exercise and screen time groups (the 3 screen time groups only including exercisers).

**Results:** Statistically significant differences in body mass index was found between exercisers (24.52 ± 4.58) and non exercisers (27.94 ± 8.46)(n=97). MSA participants woke significantly more during the night (2.04 mean waking's compared to 1.06 mean waking's, n=21, t=0.015). No significant differences where found in the sleep data comparing time of day of exercise, screen time overall and screen time in exercisers.

**Conclusion:** The difference in waking amount with MSA participation agrees with previous research. Other findings suggest that exercise and screen time might not be central factors to middle aged sleep moderation. Limitations include indirect measures (surveying) and small participant numbers in later questions.

**Keywords:** sleep, middle age, exercise, kinesiology

The Impact of Pilates Exercise in Multiple Sclerosis: A Randomized Controlled Trial

Presenter: Whitney Duff, College of Medicine  
Supervisor: Phil Chilibeck  
Collaborators: Justin Andrushko, Doug Renshaw, Philip Chilibeck, Jonathan Farthing, Jana Danielson, Charity Evans

**Background:** Pilates is a series of exercises based on whole-body movement, and may improve mobility in people with multiple sclerosis (MS). The purpose of this study was to determine the effect of Pilates on walking performance in people with MS.
Methods: Thirty individuals with MS, and who were not restricted to a wheelchair or scooter (Patient-determined Disease Steps <7), were randomized to Pilates (twice weekly) and massage therapy (once weekly), or once-weekly massage therapy only (control). The Pilates was delivered in a group setting, with 5-10 participants in each session. The primary outcome was the change in walking performance (6-minute walk) after 12 weeks. Secondary outcomes included functional ability (timed-up-and-go test), balance (Fullerton Advanced Balance Scale), flexibility (sit and reach), body composition (dual energy x-ray absorptiometry), core endurance (plank-hold), and muscle strength and voluntary activation (quadriceps). Intention-to-treat analysis was performed using a two-factor repeated measure ANOVA.

Results: Walking distance increased by 52.4 (SD 40.2) meters in the Pilates group compared to 15.0 (SD 34.1) meters in the control group (group × time; p=0.01). The time to complete the timed-up-and-go test decreased by 1.5(SD 2.8) seconds in the Pilates group compared to an increase of 0.3 (SD 0.9) seconds in the control group (group × time; p=0.03). There were no other significant differences between groups over time.

Conclusion: Pilates improved walking performance and functional ability in persons with MS, and is a viable exercise option to help manage the disease.

Keywords: Pilates, Multiple Sclerosis
Basic Science Group 3

74. Common bean seed coats as a sustainable source of polyphenols

Presenter: Fatma Elzahraa M. Elessawy, College of Pharmacy and Nutrition
Supervisor: Drs. Randy Purves & Anas El-Aneed

Background: Polyphenols are a diverse family of plant secondary metabolites that can be used in various applications in industry and medicine. Pulses are gaining importance in Canada because of their rich content of protein, fiber, minerals and micronutrients, such as polyphenols. In spite of their potential value as sources of polyphenols, pulse crop seed coats are often discarded as food waste not effectively used. Common bean (Phaseolus vulgaris L.) is one of the emerging pulses grown in Canada. Although common bean seed coats could represent a potential source to obtain high quantities of beneficial polyphenols, there is limited information about polyphenol types and concentrations in seed coats. This study aims to analyze polyphenols of seed coat extracts from four different common bean market classes, and to estimate their antioxidant capacity. The selected genotypes are envoy (N1), CDC Jet (N2), sol (N3) and CDC WM-2 (N4) which have white, black, yellow and pinto seed coat colors, respectively.

Methods: Polyphenol extraction procedure is simple and fast which involves mixing 70% acetone with the pulverized seed coats for one hour, followed by centrifugation, taking the supernatant and drying it down. Dried-down extracts were reconstituted in 10% methanol to be ready for further analysis. Liquid chromatography (LC) coupled to mass spectrometry (MS) was applied for semi-quantitative analysis of polyphenols. DPPH (2,2-diphenyl-1-picrylhydrazyl radical) assay is used for antioxidant activity screening which mainly depends on the capability of the sample to bleach the dark purple color of the DPPH reagent. Effective concentration required to obtain 50% antioxidant effect (EC50) is a typical parameter to express the antioxidant capacity and to compare the activity of different samples or compounds.

Results: LC–MS semi-quantitative analysis of 97 polyphenols showed that the major polyphenol subclasses among different genotypes of common bean seed coats were anthocyanins, flavonols, procyanidins and flavan-3-ols. In the common bean seed coat extracts, the major anthocyanins found were delphinidin-3-β-glucoside, delphinidin-3,5-di-O-glucoside, kuromanin, cyanidin-3-,5-di-O-glucoside malvidin-3-O-glucoside, malvidin-3-O-galactoside and malvidin-3,5-di-O-glucoside. Kaempferol, kaempferol-3-O-glucoside, quercetin, quercetin-3O-glucoside and myricetin were the main detected flavonols. Procyanidins B1, B2, B3 and C1 were found with relatively high concentrations. In addition, catechin, gallocatechin and epigallocatechin, as flavan-3-ols, were found abundantly. Polyphenol distribution and relative abundances are variable depending on the seed coat genotype. For DPPH antioxidant activity, black-colored CDC Jet seed coat extract (N2) showed the highest antioxidant activity compared to other seed coat extracts. Its EC50 was 0.93 representing the strongest radical scavenging capability.

Conclusion: Black-colored CDC Jet seed coats is considered as a potential source for beneficial polyphenols with high antioxidant activity.

Keywords: polyphenols, common beans, DPPH, antioxidant capacity and EC50.
75. The effect of a low glycemic index diet on body composition during bed rest

Presenter: Ruirui Gao, College of Kinesiology
Supervisor: Phil Chilibeck

Background: Bed rest is sometimes necessary for medical conditions, but even a short period of inactivity (3-4 days) can cause many harmful conditions including bone loss and muscle loss. Pulses (i.e. lentils, chickpeas, peas, beans), having a low glycemic index and high quality proteins that do not induce metabolic acidosis, may be superior to typical hospital diets in preventing these harmful effects. Our study purpose was to determine the effects of a pulse-based diet compared to a Western diet of typical hospital foods on body composition during bed rest.

Methods: Using a randomized, counter-balanced cross-over design, 6 healthy individuals (mean age 30 SD 12 y; BMI 23.3 SD 4.5 kg/m²) consumed one of two diets for four days of bed rest, followed by a one-month washout, and then the second diet for another four days of bed rest. The day before and the day after the bed rest period, body composition was assessed by dual-energy X-ray absorptiometry.

Results: There was no difference between diets. Time main effects were found for lean tissue mass (pre-bedrest mean 41.0 SD 10.9 kg, post-bedrest mean 39.5 SD 10.7 kg; p=0.002), body mass (pre-bedrest mean 59.9 SD 14.9 kg, post-bedrest mean 58.4 SD 14.6 kg; p=0.001), and %fat (pre-bedrest mean 27.7 SD 10.6%, post-bedrest mean 28.6 SD 10.9%; p=0.044). There were no changes in bone mass.

Conclusion: We conclude that four days of bed rest has significant negative effects on body composition, and that a pulse-based diet was not effective for attenuating these negative effects.

Keywords: nutrition, glycemic index, pulse, diet, bed rest, body composition

76. BAM32-DEPENDENT REACTIVE OXYGEN SPECIES PRODUCTION IS CRITICAL IN BACTERIAL PEPTIDE WKYMVM-INDUCED MICROVASCULAR HYPERPERMEABILITY

Presenter: Li Hao, College of Medicine
Supervisor: Lixin Liu

Background: Bam32 (B cell adaptor molecular of 32 kDa) has been indicated in regulating lymphocyte proliferation and recruitment during inflammation. However, its role in neutrophils and neutrophil-driven microvascular leakage remains unknown.

Methods: Using intravital microscopy in mice, we examined the role of Bam32 in bacterial formyl peptide WKYMVM- and chemokine CXCL2-induced permeability changes in post-capillary venules and assessed simultaneously neutrophil adhesion and emigration in murine cremaster muscle in both Bam32 knockout (KO) mice and wild-type (WT) mice.

Results: We observed significant decrease in WKYMVM-induced microvascular hyperpermeability in Bam32KO mice, accompanying by remarkably decreased neutrophil emigration. On the contrary, we found significant increase in CXCL2-induced microvascular hyperpermeability in Bam32KO mice at early
time points (15 min, 20 min and 25 min) with significantly decreased neutrophil adhesion at 60 min. Furthermore, we uncovered that Bam32 was critically required for WKYMVm- but not CXCL2-induced intracellular and extracellular reactive oxygen species (ROS) production in neutrophils. Pharmacological inhibition of local oxidative stress eliminated the difference in WKYMVm-induced hyperpermeability between Bam32KO mice and WT mice without diminishing the difference in neutrophil emigration.

**Conclusion:** In conclusion, our study reveals Bam32-dependent ROS generation is critically important in bacterial formyl peptide-induced microvascular hyperpermeability during acute inflammation.

**Keywords:** Bam32, neutrophil, WKYMVm, microvascular permeability, reactive oxygen species

77. **Enterolactone Modulates Cholesterol Trafficking in HepaRG Cells**

**Presenter:** Ahlam Hawsawi, College of Pharmacy and Nutrition  
**Supervisor:** Dr. Jane Alcorn

**Background:** Cardiovascular disease (CVD) is a cause of significant morbidity and mortality world-wide. High blood cholesterol (HBC) is one of several non-genetic causes of cardiovascular disease (CVD), which doubles the chance of having heart disease. Life style changes and drugs (Statins mainly) are mainly advised by practitioners to manage cholesterol; however, there is an increasing shift towards safer alternatives such as natural products. Flaxseed supplementation may serve as an alternative natural product treatment for mild to moderate hypercholesterolemia or in combination to statins in severe conditions. Studies suggest a putative improvement in cholesterol blood profile following consumption of flaxseed; however, the underlining mechanism by which flaxseed lignan or its active metabolites modulate blood cholesterol level is not yet known. This study examines the possible underlying mechanism by which flaxseed lignans or the active metabolites may influence cholesterol trafficking in liver. In addition, possible concomitant administration of statins and flaxseed lignans raises a possible role of intestinal efflux transporter, multidrug resistance-associated protein 3 (ABCC3 or MRP3), and/or hepatic uptake transporters (OATP1Bs) in a potential important drug-drug interaction which cannot be ignored.

**Methods:** We studied the possible effect of flax lignan metabolites, Enterolactone (ENL) and Enterolactone glucuronide (ENL-Gluc), on hepatic trafficking of fluorescing cholesterol, using the HepaRG cell line as an in vitro liver model. We also screened for genetic modulation of INSIG-SREBP cholesterol genetic regulation pathway in liver cells after treatment with ENL and ENL-Gluc by screening some transcriptional changes in genes important in cholesterol metabolism and trafficking such as, INSIG-1, SREBP, HMGCoA-R and LDL-R. We used western blot analysis to confirm qPCR results. In addition, since organic anion transporter possess high impact on statin pharmacokinetics, a possible interaction was investigated by studying the inhibitory effect of ENL and ENL-Gluc on the uptake of organic anion transporting polypeptides 1B1 and 1B3 substrate (fluorescein Methotrexate-FMTX) in HEK293 cells overexpressing human OATP1B1 & OATP1B3 transporters.

**Results:** Both ENL and ENL-Gluc treatment minimized uptake of fluorescent cholesterol into hepatocyte. In comparison to vehicle control treated with 1% DMSO only, treatment with 20 µM ENL and 20 µM and 40 µM ENL-Gluc reduced cholesterol uptake by 1.78, 1.96 and 2.11 fold, respectively. This was confirmed by observing a surge in NBD-cholesterol retention in endoplasmic reticulum (ER) following treatment with different concentrations of ENL and ENL-Gluc. In addition, a preliminary evaluation a concentration dependent inhibition by ENL-Gluc on OATP1B1 and OATP1B3 transporter mediated liver uptake of FMTX was observed at levels comparable with alternative inhibitors described in the literature.
**Conclusion:** Phenotypically, ENL and ENL-Gluc alters cholesterol metabolism through increasing fluorescing cholesterol (NBD-Cholesterol) retention in endoplasmic reticulum and lysosomes in hepatocytes. Further confirmation of these changes will be available via screening the relative genetic expression of multiple target genes that are responsible for activation of a membrane bound transcription factor SREBP as well as protein level measurements, which will be obtained by western blot analysis. In addition, the concentration dependant uptake inhibition of a fluorescence substrate of OATP1B1 and 1B3 by ENL and ENL-Gluc will be completed.

**Keywords:** Flaxseed lignans, Enterolactone glucuronide, Enterolactone, HMG-CoA-R, LDL-R, OATP1B1 transporter, OATP1B3 transporter, Hepatic cholesterol trafficking, HepaRG cell.

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**78. Relative protection by cyanidin and its degradation products against doxorubicin cytotoxicity in H9c2 cardiomyocytes**

**Presenter:** Muath Helal, College of Pharmacy and Nutrition  
**Supervisor:** Brian Bandy and Jane Alcorn

**Background:** The cyanidin pigments found in purple berries are believed to have potent antioxidant activity when tested in many different in vitro and in vivo assays. Despite these features, cyanidin is claimed to degrade rapidly at neutral pH to produce protocatechuic acid (PCA) and phloroglucinaldehyde (PGA) passing through different intermediate chemicals. A general belief exists that the health benefits of cyanidin arise from PCA and PGA. Previous in vivo observations in our laboratory have led us to hypothesize that the parent compound persist for sufficient periods to exert a cytoprotective activity against pro-oxidant insults, such as that produced by doxorubicin on heart mitochondria.

**Methods:** To investigate this hypothesis further, we investigated the cytoprotective activity of cyanidin against doxorubicin induced cytotoxicity in H9c2 cells and compared it to that of PCA and PGA. The protective mechanism was also investigated by determining the effects of cyanidin mitochondrial function after a doxorubicin insult. Reactive oxygen species, mitochondrial superoxide levels and mitochondrial membrane potential were determined to establish the protective mechanism of cyanidin against doxorubicin.

**Results:** In differentiated H9c2 cells exposed to doxorubicin, a cyanidin solution resulted in considerably higher cytoprotection against doxorubicin compared to a PCA and PGA mixture solution. In addition, cyanidin caused lowering in ROS, mitochondrial superoxide levels and mitochondrial membrane potential.

**Conclusion:** These results suggest that cyanidin parent compound, not only PCA and PGA, survives long enough in culture media to accumulate in cells and exert a cytoprotective activity. Reversing the mitochondrial damage caused by doxorubicin might present a major protective mechanism. To substantiate this observation, future studies are required to identify the presence of these intermediate compounds in a biological system.

**Keywords:** Cyanidin, doxorubicin, heart, cytoprotection, mitochondria
Chronic and prolonged administration of adenosine A1 receptor agonist stimulates alpha-synuclein expression in the hippocampal and substantia nigral neurons.

Presenter: Elisabet Jakova, College of Medicine
Supervisor: Francisco Cayabyab
Collaborators: Adelaide Amah, Siddarth Nosib

Background: Destruction of dopaminergic neurons due to Alpha-Synuclein (AS) misfolding in the substantia nigra pars compacta (SNc) underlies the motor deficits observed in Parkinson's disease (PD). Although various therapeutic strategies are available to alleviate the symptoms of PD, including dopamine replacement therapy and monoamine oxidase inhibitors, none of these therapies slows aggregation of the AS. Since we recently reported that adenosine contributes to neuronal damage in in vivo and in vitro stroke models, we now hypothesize that aging-related elevation of cerebral adenosine leads to dopaminergic neuron damage in substantia nigra pars compacta. We also hypothesize that pharmacological inhibition of A1Rs or administration of the drug, 1-aminoindan, which was previously implicated in preventing AS misfolding (Jakova et al., 2016), can prevent the neurotoxicity-enhancing effects of increased AS in hippocampal and SNc neurons.

Methods: Using male postnatal 28-35-day old Sprague-Dawley rats, we administered an adenosine-mimicking compound (AMC) for 7 days by intraperitoneal injection and tested the effects of novel neuroprotective agents in hippocampal and SNc neurodegeneration. Behavioural tests were conducted after day 8. Animals were then euthanized and perfused with 4% paraformaldehyde for subsequent immunohistochemical and confocal imaging with Zeiss confocal microscope. Additional biochemical and biophysical techniques, such as nanopore analysis and electrophysiology, were used to determine the binding sites of our compounds to AS, as well as to measure the effects of these compounds on synaptic transmission by fEPSP recordings.

Results: Compared to vehicle controls, systemic administration of the AMC for 7 days caused hippocampal-dependent learning deficits (Y-maze test) consistent with increased neurodegeneration of hippocampal neurons (FluoroJade B staining and NeuN labelling). AMC-treated rats also showed significant motor impairment and increased depressive behaviour (forced swim test), which was prevented by A1R antagonist DPCPX, 1-aminoindan (a metabolite of Rasagiline) but not by the amphetamine analog 2-aminoindan (structurally similar to 1-aminoindan). Both DPCPX and 1-aminoindan prevented AMC-mediated increase of AS. Using nanopore and confocal imaging analyses, we determined that the neuroprotective compounds 1-aminoindan and DPCPX exerted their effects by binding directly to AS and preventing AS misfolding and aggregation. Additionally, untreated hippocampal CA1 neurons showed enhanced baseline synaptic transmission (increased fEPSPs) in the presence of 100nM 1-aminoindan, which was similar to the excitatory effects of A1R antagonist DPCPX. The 1-aminoindan decreased paired pulse ratio, indicating facilitation of transmitter release.

Conclusion: Taken together, these data suggest that adenosine signalling plays a major role in neurodegeneration, motor and cognitive deficits. AMC agonists/antagonists may also directly regulate alpha synuclein conformation and expression.

Keywords: Alpha-Synuclein, adenosine A1 receptor, neuroprotective, neurotoxic, hippocampal neurotoxicity, field excitatory postsynaptic potentials, persistent synaptic depression.
Phosphorylation state of NS5A modulates HCV translation differently

Presenter: Mangyung Kandangwa, School of Public Health
Supervisor: Dr. Qiang Liu

Background: Hepatitis C virus (HCV) infection is the major risk factor for the development of liver cirrhosis and hepatocellular carcinoma (HCC) and estimate of 2.8% of world population are HCV infected. There is no prophylactic vaccine but very effective treatment strategy: Direct Acting Antiviral (DAA) regimen is available. Access to DAA’s is restricted in several countries due to its high cost, resulting in death of 1000 people every day.

HCV has a single-stranded positive-sense RNA genome encoding a polyprotein from which 3 structural and 7 non-structural viral proteins are generated upon proteolytic cleavage. The non-structural protein 5A (NS5A), a pleiotropic viral protein is known to be essential for HCV replication and assembly. However, its role in translation is unclear. Previously, HCV-1b NS5A was demonstrated to downregulate viral translation through a mechanism that requires the polyU/UC region at the 3'UTR where NS5A can bind. NS5A is a phospho-protein and exists in hypo- and hyper-phosphorylated forms. NS5A hyper-phosphorylation has been reported to occur through phosphorylation of serine residues cluster in the LCS I of NS5A. In this study, we show that phosphorylation state of NS5A modulates the HCV-1b translation differently.

Methods: Plasmids expressing NS5A mutants mimicking either hypo- and hyper-phosphorylated NS5A were constructed by phospho-mimetic (S-A) or phospho-ablatant (S-D) mutation of the serine residues S222, S225, S229 and S232A present in the LCS I of NS5A. These plasmids were co-transfected with HCV-1b RNA translation Renilla luciferase reporter RNA in Huh-7 cells and luciferase assay was performed to study the effect of the NS5A proteins in the HCV-1b translation.

Results: When plasmids expression NS5A mutants mimicking either hypo- and hyper-phosphorylated NS5A were co-transfected with HCV-1b RNA translation Renilla luciferase reporter RNA, the hypo-phosphorylated NS5A downregulated the translation similar to wild-type NS5A in a dose-dependent manner and the presence of polyU/UC was important for this effect. Unlike the wild-type NS5A, the hyper-phosphorylated NS5A did not inhibit viral translation, suggesting that hyper-phosphorylated NS5A has a negative role in translation downregulation by wild-type NS5A. To further investigate the mechanism behind the translation modulation by NS5A, we studied the effects of phospho-mimetic (S-A) or phospho-ablatant (S-D) single serine NS5A mutant on the HCV-1b translation. We found that the NS5A mutant S229A and S229D both downregulated the translation similar to wild type and hypo-phosphorylated NS5A with S229D having a more profound effect than S229A. Interestingly, while the S225D mutant retained the ability to downregulate HCV translation, S225A could no longer to do so. We are currently investigating the underlying mechanism. We are also studying the effects of additional serine residues within the phosphorylation cluster on HCV translation.

Conclusion: The hypo-phosphorylated NS5A downregulates the translation of HCV-1b similar to wild type NS5A in a dose-dependent manner while the hyper-phosphorylated NS5A does not downregulate the translation. This suggest that the phosphorylation state of NS5A modulates the HCV translation differently.

Keywords: HCV, NS5A, phosphorylation, RNA translation
81. Development of Protein Based Inhibitors Targeting HIV-1 Viral Infectivity Factor (Vif)

Presenter: Muhammad Khalil, College of Medicine
Supervisor: Linda Chelico
Collaborators: Maruti Uppalapati

Background: New treatments are needed to prevent the spread of HIV infection. We propose the development of inhibitory peptides that are based on protein scaffolds to prevent HIV-1 Viral Infectivity Factor (Vif) from promoting the degradation of human anti-HIV restriction factor APOBEC3G (A3G) and APOBEC3F (A3F). Preventing APOBEC3 degradation will help restrict HIV replication. The project will start with identifying potential inhibitory protein scaffold libraries that will be used to inhibit Vif interaction with A3G and A3F. The project is divided into three important parts: (i) development of affinity reagents using combinatorial protein scaffold libraries; (ii) engineer a chimeric APOBEC3 (A3) -Vif binding domain; (iii) validate affinity reagents during viral replication.

Methods: The accomplish the objectives of this study we will use phage display method to select binders specific to our target. After identifying the binder, single cycle infectivity assays will be carried out to test binders ability to restrict HIV infection in a 293 T cell system.

Results: Currently, we have isolated 10 binders that show various levels of specificity to the HIV-VIF target through the phage display system. Next, we will test these binders in a cell system.

Keywords: HIV, VIF, APOBEC3, BINDER, PHAGE DISPLAY
82. **Interactions between cpn60-defined subgroups of Gardnerella vaginalis**

Presenter: Salahuddin Khan, Western College of Veterinary Medicine  
Supervisor: Janet E. Hill

**Background:** Gardnerella vaginalis is a hallmark of Bacterial Vaginosis, a loosely defined dysbiosis of the vaginal microbiome. G. vaginalis has four cpn60-defined subgroups: A, B, C and D, that potentially differ in their virulence. Subgroup mixtures are common but the dominant subgroup varies. When G. vaginalis is abundant, direct interactions would be common that may contribute to abundance of subgroups.

**Methods:** To detect contact independent interaction between subgroups of G. vaginalis, strains representing all four subgroups were grown in NYC III and BHI + 1% glucose supplemented with 10% cell free supernatant derived from isolates of different subgroups and were also grown without CFS as control. Total and planktonic growth was measured by optical density and biofilm formation was quantified at 48h.

**Results:** A total of 111 combinations of 27 strains were tested in a pairwise fashion. No effects of CFS vs. control cultures were observed. To detect contact dependent effects on growth using co-culture experiments, growth conditions were optimized for biofilm formation and subgroup specific qPCR assays for quantifying input and output of subgroups in mixtures were validated.

**Conclusion:** G. vaginalis isolates are not producing effector molecules affecting the growth of closely related strains.

**Keywords:** Biofilm formation, Effector molecules, Direct interactions, Abundance

83. **Gamma Burst Oscillations (GBOs) Using Low Field Magnetic Stimulation (LFMS) Improves Post-Stroke Cognitive and Psychiatric Deficits in an Animal Stroke Model.**

Presenter: Hye Ji (Jay) Kim, College of Medicine  
Supervisor: Francisco Cayabyab  
Collaborators: Michael Zaki, Jocelyn Stockwell, Francisco Cayabyab, Yanbo Zhang

**Background:** Stroke survivors often suffer from disability, including motor, psychiatric, and cognitive deficits. Early therapeutic intervention with the clot-busting agent TPA can indeed be effective, but the few who receive this treatment still suffer from neurological deficits. We hypothesize that neuroprotective adjunct therapy is required to reduce post-stroke adult disability. The potential non-invasive stroke treatment involving low field magnetic stimulation (LFMS) is under investigation, and we are delineating the cellular mechanisms involved in the therapeutic benefits of this novel treatment in our animal model of post-stroke depression.

**Methods:** Using an established focal cortical pial vessel disruption (PVD) stroke model in Sprague-Dawley rats, we studied the efficacy of gamma burst stimulation or LFMS (40 Hz, <0.1 Tesla) in reducing hippocampal neuronal damage and associated behavioural deficits. Levels of anxiety, depressive and cognitive behavioural deficits were measured using the open field test (OFT), forced swim test (FST) and
Y-maze, respectively. In vitro electrophysiological recordings were performed to correlate cognitive deficits with changes in hippocampal synaptic plasticity. Various tissue staining methods followed by confocal microscopy were employed to visualize the effects of PVD and LFMS on hippocampal protein and cell expression. Western blotting was then used to quantify these expressions.

**Results:** PVD treatments produced hippocampal-dependent spatial memory deficits, which were associated with decreased long-term potentiation in hippocampal brain slices. Increased anxiety and depressive behaviours were observed in PVD-treated animals but not in sham animals (similar surgical procedures but with pial vessels left intact). Increased neuronal damage was confirmed using propidium iodide and Fluro-jade C labeling followed by confocal imaging. In contrast, all animals that received daily LFMS (20min, 3d) showed significant improvements in their depression, anxiety, and spatial memory impairments.

**Conclusion:** The results showed that restoring gamma oscillations with LFMS counters the damaging effects of pro-neurotoxicity pathways after stroke. Clinical implications of this non-invasive therapy include potential treatments of post-stroke depression and dementia, and other neurodegenerative diseases.

**Keywords:** neurology, neuroscience, psychiatry, stroke, low-field magnetic stimulation, post-stroke depression, post-stroke anxiety, post-stroke spatial memory
**BASIC SCIENCE GROUP 4**

84. The role of the bovine adenovirus (BAdV)-3 protein VII (pVII) in virus life cycle

**Presenter:** Shermila Kulanayake, School of Public Health  
**Supervisor:** Dr. Suresh Tikoo

**Background:** Bovine adenovirus-3 is non-enveloped, double-stranded DNA virus, belongs to Mastadenovirus genus. The genome divides into early, intermediate and late regions. Protein VII is a late protein belongs to late region of the genome and it is the most abundant core protein. Mature pVII tightly attaches with DNA and enters the nucleus and act as template for early viral gene transcription.

**Methods:** We are investigating the role of BAdV-3 protein VII in modulating the viral life cycle by characterizing the BAdV-3 pVII in detail, identifying the viral and cellular protein interaction with pVII and study the biological significance of these interactions, and determining the importance of protease cleavage of protein VII for the BAdV-3 life cycle.

**Results:** BAdV-3 pVII was expressed at 26 kDa between 12 to 24 hours post BAdV-3 infection. Bioinformatics analyses were predicted 4 potential nuclear localization signals (NLS) and pVII localizes in nucleus of transfected cells. Once NLS were deleted individually, pVII localization was limited to cytoplasm of transfected cells.

**Conclusion:** BAdV-3 pVII is a late protein sized 26 kDa. pVII contains 4 non-functionally redundant NLS and one potential protease cleavage signal. pVII localizes nucleus but not nucleolus by active transportation with the help of NLS and it does not need other viral proteins for nuclear localization.

**Keywords:** BAdV-3, pVII, protease cleavage, nuclear localization, strep tag

85. Determining the correlates of protection that prevent MERS-CoV infection in camels.

**Presenter:** Swarali Kulkarni, Western College of Veterinary Medicine  
**Supervisor:** Dr. Darryl Falzarano

**Background:** Middle East respiratory syndrome coronavirus (MERS-CoV) known to infect humans. Dromedary camels appear to be a host for MERS-CoV and have been found to have very high seropositivity. It has been speculated that MERS-CoV transmission to humans occurs as a result of close contact to camels. Our lab is focused on developing a vaccine against MERS-CoV to be used in camels as a way of preventing transmission to humans. My project specifically focuses on developing assays that will help us understand systemic and mucosal immune responses that result in protection against MERS-CoV infection in alpacas. Camelids have three isotypes of IgG: IgG1 is a conventional antibody, while IgG2 and IgG3 possess heavy chains only, a feature that is unique to camelids. From previous observations in our lab, IgG1 and IgG3 against the MERS-CoV spike protein are induced following MERS-CoV challenge, while IgG2 is only observed following re-challenge. Furthermore, as MERS-CoV follows a mucosal route of infection we speculate that IgA also may play a role in protection.
Methods: To determine the role of each IgG isotype on virus neutralization I will first separate the IgG isotypes from alpacas by using affinity chromatography and subsequently determine the neutralization titre per unit of each IgG isotype in a microneutralization assay. In addition, I will also develop assays to purify IgA from alpacas. Purified IgA will be used to immunize rabbits for the generation of secondary antibodies. We will use these antibodies to determine the role of mucosal IgA against MERS-CoV in response to vaccination and infection.

Results: To determine the IgG isotype(s) that is responsible for neutralizing activity against MERS-CoV, three IgG isotypes were separated by using protein A and protein G affinity chromatography using pulled serum collected from non-infected healthy alpacas. From literature we know that IgG1 and IgG3 has a great affinity for protein G and protein A. In contrast, IgG2 has an affinity for only protein A column (11). Serum samples were collected from non-infected healthy alpacas and pulled. This pulled serum from alpaca (1ml) was absorbed onto 1ml protein G – sepharose column and washed with 20mM phosphate buffer pH 7.0. After subsequent cycles of washing IgG3 was eluted with 0.15M NaCl, 0.58% acetic acid (pH 3.5) and IgG1 was eluted with pH2.7 0.1 M glycine –HCl. The fraction not absorbed on protein G column was loaded on protein-A sepharose column. After washing with phosphate buffer, IgG2 was eluted with 0.15 M NaCl, 0.58% acetic acid (pH 4.5). IgG elutes were analysed with ELISA using monoclonal antibodies specific for each IgG isotype (Fig.4.2.a). Purified IgG isotypes were also analysed with western blotting with same monoclonal antibodies. After reduction we observed 50.1K heavy chain and 22.7K light chain in IgG1 elute and IgG2 elute. The IgG2 fraction upon reduction showed 40.9K heavy chain band in only IgG2 elute. In IgG3 43K band was observed in IgG3 and IgG2 purified elutes (Fig4.2.b). Western blot analysis showed that each IgG isotype elute was pure and not contaminated with each other. IgG1 level was observed with high absorbance in chromatogram as compared to IgG3 and IgG2.

Conclusion: Based on previous experiments in Alpacas, IgG1 and IgG3 were induced in infection with MERS-CoV and IgG2 was induced in re-infection with same strain of MERS-CoV.

Keywords: MERS-CoV Middle East respiratory syndrome coronavirus

86. Mapping the region on the Hepatitis C virus (HCV) genome to which miR-122 and other small RNA annealing promotes virus replication

Presenter: Rasika Kunden, College of Medicine
Supervisor: Dr. Joyce Wilson

Background: Terminals of HCV genomic RNA consists of a 5'UTR and a 3'UTR. Its replication requires host miR122 (small-RNA) annealing to two sites on its 5' UTR, but the mechanism by which miR122 promotes HCV replication is poorly understood. We found that annealing of perfect match siRNAs to HCV 5'UTR can also promote HCV replication as efficiently as miR122, when siRNA cleavage was abolished, in Ago2 KO cell

Methods: The above finding provided us with a method to test other small RNAs and map the locations on the HCV genome to which small-RNA annealing can promote HCV replication. Therefore, several 19bp siRNA duplexes targeting different sites on HCV genome were tested. Replication promotion was assessed in Ago2 KO cells and the activity of miR-122 was blocked using miR-122 antagonists.

Results: siRNA annealing between, 13-44nts in HCV 5'UTR can promote replication, and siRNAs within IRES, NS5B and 3'UTR cannot. Replication promotion required at least 13nts and an siRNA that targeted
19-37nts promoted replication more efficiently than miR-122. Replication efficiency decreased as the siRNA target site moved away from this region, and was abolished if the siRNA target included nucleotide 45.

**Conclusion:** We have defined an RNA domain that is influenced by small-RNA annealing. RNA structure predictions with small-RNA that promote HCV replication, suggests a structural change of the identified domain. In future, we will look at how HCV translation, genome stability, RNA structures, and protein binding are modulated by small-RNA to understand the mechanism of HCV replication promotion by miR122.

**Keywords:** Hepatitis C Virus, miR122, Argonaute 2 (Ago2), Knockout (KO) cells, siRNA, Nucleotides (nts), Untranslated region (UTR).

87. **Expression and characterization of a putative extracellular sialidase enzyme in Gardnerella vaginalis**

**Presenter:** Shakya Kurukulasuriya, Western College of Veterinary Medicine  
**Supervisor:** Janet Hill

**Background:** Bacterial Vaginosis (BV) is a condition that occurs when the healthy, Lactobacillus spp. dominated vaginal microbiota is replaced by BV related bacteria. BV is highly prevalent in women in their reproductive age and known to be associated with infertility, preterm delivery, cervical cancer and increased susceptibility to sexually transmitted diseases. High abundance of Gardnerella vaginalis is often found in cases of symptomatic BV. G. vaginalis consists of four different subgroups (subgroup A–D) with potentially different virulence, which could explain why G. vaginalis is also found in some healthy women. Sialidase is recognised as an important virulence factor in G. vaginalis that contributes in degradation of the mucus layer, but genomic determinants of this activity are not known. We hypothesize that extracellular sialidase activity shown by some G. vaginalis isolates is due to an enzyme encoded by Gene 2. Previous work in our lab has confirmed that the presence of Gene 2 strongly correlates with extracellular sialidase activity. The objective of the study is to demonstrate that Gene 2 encodes a sialidase with extracellular activity.

**Methods:** The predicted sialidase domain sequence was amplified by PCR and ligated into expression vector pQE-80L. The construct was then transferred into competent E.coli and the transformants were screened using PCR and sequencing. A selected clone was cultured and protein expression was induced with IPTG at 37°C for 5 hours. The protein profiles of induced and uninduced cells were examined by SDS PAGE.

**Results:** A putative extracellular sialidase domain was identified within the Gene 2 sequence using NCBI conserved domain database, and PCR primers were designed to amplify this region for cloning and expression. The presence of the insert in-frame with the 6x-His tag of the cloning vector was confirmed. The target protein expression level was not substantial.

**Conclusion:** Although the sialidase domain was precisely cloned, the expression level under the conditions we used so far is not optimal. Currently, we are trying to improve the expression in E.coli using different conditions and different stains. The His-tagged protein will be purified using a Ni-affinity column and will be used to produce polyclonal antibodies to localize the enzyme in G. vaginalis. Sialidase
activity will be determined qualitatively and quantitatively using 2'-(4-methylumbelliferyl) α-D-N-acetylneuraminic acid as a fluorogenic substrate.

**Keywords:** Bacterial Vaginosis, Gardnerella vaginalis, extracellular sialidase,

### 88. Development of a mouse disease model for the highly pathogenic avian H7N9 influenza

**Presenter:** Shelby Landreth, School of Public Health  
**Supervisor:** Yan Zhou  
**Collaborators:** Yao Lu, Amit Gaba

**Background:** H7N9 influenza virus is a threat to public health and has generated over 1000 cases as of July 2017. In order to develop a novel vaccine, one must first understand the pathogenesis through the development of a mouse disease model. The influenza virus that was evaluated was the highly pathogenic avian influenza A/British Columbia/2015 (H7N9) virus.

**Methods:** Four groups of 12 BALB/c mice each were infected intranasally with either a mock (PBS) or three different doses of H7N9: 10^3 pfu, 10^4 pfu and 10^5 pfu per mouse. Body weight, survival rate and clinical scores were evaluated daily. Mice were euthanized and organs collected when they either lost 20% of their total body weight, or their clinical score reached a score of three.

**Results:** All three doses of H7N9 rapidly lost weight with the 10^5 pfu group all euthanized by day 5, the 10^4 group by day 6 and the 10^3 group by day 8. TCID50 titres were determined for the lungs with high titres present after infection, then decreased as the days progressed. No detectable virus was in brain or spleen. Cytokines and chemokines were profiled, with significant differences noted.

**Conclusion:** The knowledge acquired from the development of the mouse model for highly pathogenic avian H7N9 influenza is a prerequisite in order to evaluate various vaccine candidates. Establishment of this model will allow us to understand the pathogenesis of H7N9 and the immune response which will aid in the development of an effective vaccine.

**Keywords:** H7N9 influenza virus, mouse disease model, TCID50, cytokines, chemokines, novel vaccine, body weight, survival rate, clinical score

### 89. Peptide Microarray Quality Control

**Presenter:** Conor Lazarou, College of Graduate and Postdoctoral Studies  
**Supervisor:** Dr. Tony Kusalik  
**Collaborators:** Dr. Scott Napper

**Background:** Peptide microarrays are fast becoming a go-to tool for high-throughput biological research, with researchers increasingly applying them to investigate various protein-protein and protein-substrate interactions. Kinome microarrays are one such example, wherein the activity of hundreds of kinases are simultaneously measured. The deluge of data this technology provides gives researchers unprecedented breadth of coverage, but the sheer volume of data has the potential to mask errors that would otherwise be obvious in smaller datasets.
**Methods:** Here we present an overview of three common microarray sources of error, their diagnosis, and techniques for their mitigation. These include location bias, spot-feature-misalignment, and insufficient signal-to-noise ratio. Location bias was identified through the use of contour maps and visual inspection after array normalization; large islands of high or low-intensity correspond to a biased array. Spot-feature-misalignment was diagnosed by comparing the mean and median intensity of spots, with significant differences between the two resulting from improper alignment. Signal-to-noise ratio was estimated using the zero-inflated normexp statistical model, resulting in two quality metrics for overall array evaluation.

**Results:** While still early in development, these three diagnostic techniques are already proving useful for biological researchers. While previously low-quality arrays would result in countless wasted hours of analysis, and in the worst of cases false conclusions, the application of these diagnostic tests can identify errant arrays in minutes and streamline the overall peptide microarray pipeline, reducing analysis time and improving result quality.

**Conclusion:** These three issues can be major nuisances to researchers if left undiscovered; fortunately, an understanding of their symptoms makes for a quick diagnosis, improving the overall quality of results. These techniques will be combined into a web-based array analysis tool for the peptide microarray community at large.

**Keywords:** peptide array, kinome microarray, statistics, data visualization

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**90. RGDSK Peptide Functionalized Helical Rosette Nanotubes (RGDSK-HRNs) Inhibit E. coli Adherence to Jejunal Epithelium by Blocking Integrin αvβ3**

**Presenter:** Nguyen Phuong Khanh Le, Western College of Veterinary Medicine  
**Supervisor:** Baljit Singh and Volker Gerdts  
**Collaborators:** Chi Cuong Quach, Gurpreet Aulakh, Hicham Fenniri

**Background:** There is an ongoing effort to find ways to reduce the intestinal colonization of pathogens in both animals and humans. Integrin αvβ3, recognizing arginine-glycine-aspartic acid (RGD) sequences, has important functions in cell adhesion, signaling, and survival. However, the role of this protein in the adhesion of bacteria, particularly E. coli to the jejunum, remain elusive.

**Methods:** Therefore, to explore the expression of integrin αvβ3 and its role in interaction with a novel treatment - RGDSK-HRNs in E. coli binding, we performed a series of experiments using porcine jejunum, intestinal porcine epithelial 1 cell line (IPEC1) and E. coli K88.

**Results:** Immunohistochemistry staining results showed that the normal porcine jejunum strongly expressed integrin αvβ3 on the nucleus and apical surface of epithelium and gland cells. The expression of integrin αvβ3 decreased in the epithelium of the jejunum infected with E. coli or E. coli associated with Salmonella. Using immune-gold staining with the integrin αvβ3 antibody, we recognized that integrin αvβ3 was expressed on the plasma membrane, cytoplasm, and nucleus of IPEC1. In the porcine jejunum, integrin αvβ3 was also found in epithelial microvilli. Immuno-precipitation and western blot data showed that the expression of integrin αvβ3 on IPEC1 decreased at 15 minutes but returned to normal after 90 minutes of infection with E. coli K88 (P<0.05). We also found that the E. coli K88 had a protein-like integrin αvβ3.
In this study, we reported that dose-dependent RGDSK-HRNs mediated the attachment of E. coli to IPEC1 (P<0.001). Interestingly, RGDSK-HRNs slightly induced IPEC1 apoptosis compared to the normal untreated group but significantly enhanced the survival of IPEC1 upon E. coli infection compared to the E. coli infection group (P<0.05). Data from binding assays on 96-well plates showed that the number of E. coli binding on the integrin αvβ3 coated wells was significantly higher than that binding on uncoated ones with the same dose of E. coli (P<0.05). We then performed ex-vivo villus adhesion assays on scraped villi from porcine jejunum. Data showed that in F4 receptor positive villi, RGDSK-HRNs significantly reduced the number of adhering E. coli up to 12 hours compared with the E. coli-only challenging group (P<0.05). Both RGDSK peptide and monoclonal antibody anti integrin αvβ3 control groups remained effective in inhibiting the E. coli binding to villi up to 24 hours. Confocal images confirmed the binding of RGDSK-HRNs-FITC to both villi and E. coli.

**Conclusion:** These are the first data to show the role for the integrin αvβ3 in the adherence of E. coli to the intestinal epithelium, and that novel RGDSK-HRNs, a potential alternative to antibiotics, can inhibit the attachment of E. coli to the intestinal epithelium.

**Funding:** Saskatchewan Agriculture Development Fund and NSERC.

**Keywords:** integrin αvβ3, intestine, nanomedicines, E. coli

### 91. Variant Infectious Bursal Disease Virus (varIBDV)- SK09: A Potential Vaccine Candidate to Control IBDV Infection in Canada

**Presenter:** Mengying Liu, Western College of Veterinary Medicine  
**Supervisor:** Susantha Gomis  
**Collaborators:** Shanika Kurukulasuriya, Khawaja Ashfaque Ahmed, Kalhari Goonewardene, Ashish Gupta, Ruwani Karunarathna, Shelly Popowich, Thushari Gunawardana, Lisanework Ayalew, Betty Chow-Lockerbie, Davor Ojkic, Philip Willson, Suresh K. Tikoo and Susantha Gomis

**Background:** Infectious Bursal Disease (IBD) is an immunosuppressive disease that occurs throughout the world. The etiological agent is Infectious Bursal Disease Virus (IBDV) which is grouped under the family Birnaviridae. Serologically, IBDV is divided into serotype 1 and serotype 2. Serotype 1 is pathogenic in poultry and is sub classified as classical, variant (varIBDV) and very virulent (vvIBDV) strains based on virulence.

The main circulating IBDV strain in North America is varIBDV, except for the incidence of vvIBDV in California. Even though varIBDV does not result in huge mortality as vvIBDV does, subclinical infections lead to severe immunosuppression. Consequently, infected birds become easily susceptible to secondary infection leading to considerable economic loss. Previously, we reported that varIBDV infection in 43% broiler chicken farms in Saskatchewan, Canada, which was associated with high mortality and higher condemnation and lower meat production. Hence, Saskatchewan has been losing approximately 3.9 million kilograms of meat per year. Despite the huge cost in disease prevention, commercially available vaccines in Canada fail to provide full protection for broilers due to the antigenic difference between the vaccine and circulating varIBDV strains. We isolated five main varIBDV strains from Western Canada, namely varIBDV-SK09, SK10, SK 11, SK12 and SK13. The most prevalent strain is varIBDV-SK09 (60%) which exhibited potential to be a vaccine candidate.
A variety of vaccine strategies have been applied for prevention of IBD in poultry industry. For broiler vaccination, live attenuated, recombinant and immune complex (Icx) vaccine are practiced. For hyperimmunization of broiler breeders, live vaccine priming followed by boosting with inactivated vaccine is widely applied to ensure adequate transfer of neutralizing maternal antibody to broiler progeny.

The concept of immune complex vaccination against IBDV was first proposed by Haddad et al., in 1994. The vaccine was developed by combining live IBDV with virus specific antibody. The vaccine provides protection for broiler chicks with reduced bursal damage and work in the presence of preexisting antibody.

Since existing commercial vaccines are not effective in preventing IBD caused by varIBDV in broilers, this study was carried out to develop effective breeder vaccines to control varIBDV in broilers via efficient transfer of neutralizing maternal antibodies.

**Methods:** Four groups of breeders (n=20/group) were treated with SK09-based immune complex, live, live plus inactivated vaccine or saline, respectively. Progenies (n=30/group) from each breeder group were in parallel with commercial broilers (n=30). All broilers were challenged by SK09 and examined for maternal antibody, bursal weight to body weight ratio and viral load to determine the protection.

**Results:** Antibody productions was detected in SK09 vaccinated breeders and maternal antibody transfer was conferred in respective progenies. Bursal atrophy was delayed in SK09 vaccinated progenies. Moreover, no virus was detected in the bursae of SK09 vaccinated progenies.

**Conclusion:** varIBDV-SK09 exhibited great potential to be a breeder vaccine candidate.

**Keywords:** variant IBDV, breeder vaccination, immune complex
92. Development of pre-pandemic influenza vaccine against highly pathogenic H5 strains

Presenter: Yao Lu, Western College of Veterinary Medicine
Supervisor: Yan Zhou
Collaborators: GuanQun Liu, Shelby Landreth, Amit Gaba, Robert Brownlie

**Background:** The emergence of highly pathogenic avian influenza A viruses (HPAI) and their spillover into human population poses substantial economic burden and public health threats. H5 viruses are of particular concern given their global spread and pandemic potential. In this study, the first North American HPAI H5N1 strain (A/Alberta/01/2014) was selected for recombinant H5 hemagglutinin (HA) design.

**Methods:** Recombinant H5 HA is expressed in both mammalian and bacterial system for comparison of H5 antigenicity from distinct expression hosts. Mouse diseases model was established for the HPAI H5N1 virus (A/Alberta/01/2014) with 3 different doses. The morbidity and mortality of the mice was recorded daily after H5N1 challenge. Viral replication of mice lungs and spleens were quantified by TCID50.

**Results:** HA immunogen was successfully purified from mammalian system. Soluble HA immunogen was successfully obtained in bacterial expression system. In dose determination challenge model, mice are highly susceptible to A/Alberta/01/2014 (H5N1) virus infection as determined by rapid weight loss and mortality. Viruses could be detected from lungs and brains of the mice challenged at 10^3 PFU.

**Conclusion:** In this study, we aimed at developing a novel pre-pandemic H5 influenza vaccine that is of potential importance in improving pandemic preparedness. Soluble HA immunogen was obtained from mammalian and bacteria system. HPAI H5N1 virus induced a systematic disease progression in mice with rapid weight loss and high mortality.

**Keywords:** Influenza, H5 vaccine, glycosylation
93. Relationship between porcine reproductive and respiratory syndrome virus (PRRSV) load in fetal tissues and intrauterine growth retardation (IUGR)

Presenter: Carolina Maciel Malgarin, Western College of Veterinary Medicine
Supervisor: John Harding
Collaborators: Roman Nosach; Muhammad Suleman; Susan Detmer; Daniel J. MacPhee

Background: A previous study has suggested that intrauterine growth retarded (IUGR) fetuses have lower PRRS viral load (VL) in thymus and adjacent endometrium than larger fetuses when collected at 21 days post inoculation (DPI). The objectives of this study were to confirm those results at five different DPI and to extend the results to other fetal tissues.

Methods: Pregnant gilts were inoculated with PRRSV and euthanized at 5 different DPI. The fetal status was recorded, and fetal brain and liver were weighed. Endometrium, placenta, serum, thymus, umbilical cord, and amniotic fluid were collected from each fetus. PRRS VL was quantified (RT-qPCR). Fetuses were categorized by their brain-to-liver weight ratio as: G1 (non-IUGR), G2 (average), G3 (IUGR).

Results: Significantly more G1 fetuses were dead compared to G2 and G3. Fetuses G1 had significantly higher VL in sera, thymus, umbilical cord, and amniotic fluid at 14 DPI. There were no differences of VL among the three groups in endometrium and placenta. The absence of group differences before 14 DPI, is likely because insufficient time had elapsed for transplacental infection and replication.

Conclusion: No differences in endometrium end placenta indicates that the consequences of IUGR affect only the fetal compartment. We hypothesize that IUGR fetuses have lower VL due to their smaller placenta and consequently lower vascularization and opportunity for viral transplacental transmission and replication in the fetal tissues.

Keywords: swine; virus; reproduction; qPCR.

94. The physiological impact of arginine supplements in rats: effects on basal formation of methylglyoxal

Presenter: Sarah Martin, College of Medicine
Supervisor: Dr. Kaushik Desai

Background: Several amino acids including arginine are used as oral supplements. However, the physiological impact of arginine on the body, its own metabolic pathways and its potential adverse effects have not been scientifically studied. Arginine is a semi essential amino acid, meaning it is produced in the body and derived from the diet. Endogenous arginine is primarily produced via the intestinal-renal axis. Additionally, the liver produces arginine within the urea cycle. As a substrate for a variety of enzymes, arginine is a precursor for many molecules including nitric oxide (NO), urea, ornithine, polyamines, proline, glutamate, creatinine and agmatine. NO, a product of L-arginine conversion via nitric oxide synthase (eNOS), has several positive effects on the body including increased blood flow and scavenging of free radicals. Arginase exists in two isoforms, both of which compete with eNOS for L-arginine as a substrate. Arginase I detoxifies ammonia within the liver, while Arginase II ultimately produces polyamines.
in non-hepatic tissues. Additional enzymes requiring L-arginine as a substrate include arginine: glycine aminotransferase and arginine decarboxylase, which produce creatinine and agmatine, respectively. Agmatine, has diverse physiological roles and can be further metabolized to the polyamine putrescine.

L-arginine is a supplement used by many to treat several conditions. Additionally, healthy people and athletes ingest oral arginine as a preventative and performance enhancer. However, despite its wide use, no scientifically backed minimum or maximum daily dose of L-arginine exists.

MG is a toxic glucose and fructose metabolite. Under physiological conditions, MG is degraded into inert D-lactate via the glyoxalase system, aided by reduced glutathione. However, during chronic hyperglycemia, MG levels rise in such excess that enzymes of the glyoxalase system become saturated and the excess MG binds other proteins, interfering with their normal functioning. High levels of MG have been implicated in chronic diseases such as diabetes and hypertension. Additionally, MG is a major precursor of advanced glycation endproducts (AGEs) which cause inflammation, contribute to the aging process and catalyze free radical production. L-arginine has a high affinity for MG making it an effective scavenger of this reactive molecule. D-arginine while thought to be metabolically inert in respect to L-arginine metabolic pathways, is also an effective scavenger of MG. However, the impact of oral L-arginine on basal MG and AGE formation is not known. L- and D-arginine have been shown to inhibit pathological effects of MG in vitro in addition to decreasing oxidative stress and AGE formation.

Methods: Study is performed in vivo in the whole animal and in vitro from isolated tissues/organs collected from male Sprague-Dawley (SD) rats. Using the following protocol, phase I and II consist of chronic arginine administration for pharmacodynamic studies. In phase I rats received a low dose of 500mg/kg/day for 4 weeks. In this phase, 9-week-old male SD rats (10 per group) were randomly assigned to one of the following treatment groups: (1) control: normal saline, (2) L-arginine: 500 mg/kg/day via drinking water, (3) D-arginine: 500 mg/kg/day via drinking water. In phase II, the same treatment groups and protocol will be used but with a higher dose of 1000mg/kg/day for 12 weeks. Long and short-term administration has been implemented to observe any possible adaptive changes regarding enzymes and metabolic pathways. Additionally, the use of both a low and high does allows for any potential toxicity and differences in distribution to be assessed. All phases end in terminal experiments. 24 hours prior to the terminal experiment, urine is collected and frozen. Rats are then anesthetized under isoflurane for blood vessel cannulation and subsequent blood sample collection. Following euthanasia, adipose tissue, skeletal muscle, pancreas, aorta, kidney, heart, liver, lungs, brain, spleen and small intestine are collected and frozen for later analysis.

To determine distribution of L- and D-arginine, plasma, urine and tissue/organ concentrations were measured using high performance liquid chromatography (HPLC). MG in tissue samples was also analyzed via HPLC. Expression of enzymes including arginase I, arginase II, arginine decarboxylase, agmatinase and glyoxalase I were quantified in various organs using western blotting. ELISA assay kits with fluorescence detection were used to quantify both polyamine and d-lactate levels in the plasma, urine and various tissues. Statistical analysis and descriptive statistics (i.e., mean ± standard error of the mean) were used to report results. Additionally, one-way ANOVA with Tukey’s test for pair-wise multiple comparisons was used with P<0.05 being considered significant.

Results: Within the arginase pathway our data shows significantly decreased arginase expression compared to control by D-arginine in the liver and by both L- and D-arginine in the ileum. Looking at the arginine decarboxylase (ADC) pathway, ADC expression was significantly increased in the liver by L-arginine treatment compared to control. We also see a trend towards increased ADC expression in the D-arginine group compared to control. Finally, in the brain while not significant due to a low N value, we also see a trend towards increased ADC expression in both the L- and D-arginine as compared to the control group. Quantification of agmatinase expression shows no change in either the L – or D-arginine
treatment groups across all organs except in the liver where D-arginine causes a significant decrease in agmatinase expression as compared to control. Looking at polyamine levels which are metabolites of both the arginase and ADC pathways we do not see any significant changes in the brain, kidney or ileum. However, within the plasma we do see a significant increase in polyamines present in the D-arginine group as compared to the controls. Within the liver a significant increase in polyamine concentration was observed in the L-arginine group as compared to the control group. Additionally, we see a significant decrease in polyamines in the D-arginine group as compared to the L-arginine group. Within the liver we observed a significant increase in MG levels as compared to control for the D-arginine group. Furthermore, we observed significant decreases in the expression of glyoxalase I (GLO1) in the L- and D-arginine groups as compared to controls without any changes in D-lactate concentrations. Looking at the kidney, we see increased MG levels in the D-arginine group as compared to control. While there were no significant changes in GLO1 expression, we do see a significant increase in D-lactate within the D-arginine group as compared to control. Within the ileum both the L- and D-arginine groups significantly decreased MG and GLO1 expression as compared to the control without any changes in D-lactate levels. In the brain we observed a trend towards increased MG in both the L-and D-arginine group as compared to control. We also saw a significant decrease in both GLO1 and D-lactate within the L-arginine group. Finally, looking at D-lactate levels in both the plasma and urine, we only see a significant change within the L-arginine treatment group which is increased compared to

**Conclusion:** Oral arginine supplements are most often taken by the public in the hopes of improving cardiovascular performance and exercise capacity via increased nitric oxide (NO) production. However, when taken solely for this purpose, these supplements may not be completely safe. Caution should be taken because as my research shows, oral arginine supplements have effects on enzymes and metabolites beyond the NO pathway. For example, with oral L- and D-arginine administration we see significantly decreased expression of arginase. This may be due to the inhibitory actions of the NO intermediate N-hydroxy-l-arginine or feedback inhibition by arginase metabolites such as urea and L-ornithine. As the arginase pathway is quantitatively the largest source of polyamines in the body it follows that decreased expression of the arginase enzyme would result in a compensatory upregulation in the arginine decarboxylase pathway as was observed in both the L- and D-arginine groups. Furthermore, it is important to note that while D-arginine is traditionally thought to be inert in respect to arginine metabolic pathways, my data confirms that D-arginine is able to alter the expression of arginine related enzymes and their metabolites. Finally, our research into the affect of oral arginine supplements on methylglyoxal (MG) and the glyoxalase pathway is novel. While we do observe a general trend towards increased MG levels and decreased glyoxalase expression in both the L- and D-arginine treatment groups, further research into glyoxalase activity and optimizing MG analysis needs to be performed before any final conclusions can be made.

**Keywords:** Arginine, methylglyoxal, hypertension, pharmacokinetics and pharmacodynamics
BASIC SCIENCE GROUP 5

95. An interaction between monoglycosylated form of PrPc and GluA2 regulates Ca2+ impermeable AMPA receptor trafficking to the neuronal lipid rafts

Presenter: Hajar Miranzadeh-Mahabadi, College of Medicine
Supervisor: Dr. Changiz Taghibiglou

Background: Lipid rafts are microdomains of the plasma membrane (PM) with high concentration of cholesterol, saturated phospholipids, sphingolipids, glycolipids and lipidated proteins in which specific lipid-lipid, protein-lipid, and protein-protein interactions occur. GluA2-containing AMPARs are distributed in both lipid rafts and non-rafts compartments of neuronal PM. We discovered that GluA2-containing AMPA receptor (AMPAR) requires an interaction with mono-glycosylated form of cellular prion protein (PrPc) for trafficking to the neuronal lipid rafts. The N-terminal polybasic region of PrPc interacts with N-terminal domain of GluA2.

Methods: PrPc Tat-fused peptide was administered to neuronal cells (Invitro and Invivo). Control group received Scrambled Tat-fused peptide. Brain/neuronal cells were collected and subjected to co-immunoprecipitation, biotinylation and lipid raft isolation to study the interaction between PrPc and GluA2 subunit of AMPAR. Further, behavioural analysis for animals were conducted.

Results: Our data indicate that this interaction occurs co-translationally and is necessary for GluA2-containing AMPAR trafficking to the lipid rafts and its localization/anchoring there. Any disruption of this interaction triggers GluA2 subunit endocytosis. Confocal imaging and electron microscopy confirmed the colocalization of PrPc/GluA2 and the importance of polybasic region in this interaction. These observations were also confirmed in lipid rafts and non-raft isolated fractions from PrPc-KO mouse cortices when compared with the wild type mouse cortices. We also noticed a significant behavioral change in wild type mice after intraperitoneal injection of the TAT-fused interfering/disrupting peptide.

Conclusion: Together, these results showed a previously unknown functional interaction between mono-glycosylated form of PrPc and GluA2 subunit of AMPA receptor with physiological and behavioral consequences.

Keywords: PrPc, GluA2-containing AMPA receptor, Interaction, lipid rafts

96. 3D-printed dual-compartment scaffolds for enamel and dentin tissue engineering

Presenter: Fatemeh Mohabatpour, College of Dentistry
Supervisor: Petros Papagerakis, Daniel Chen
Collaborators: Silvana Papagerakis, Peter Ma

Background: Tooth loss, caused by trauma, aging or disease, has severe physiological and psychological impacts. Tooth is composed of three main layers consisting enamel, dentin and pulp. Enamel is produced
by dental epithelium stem cells (DESCs) differentiated into ameloblasts, which are lost after tooth appearance and incapable of self-renewal. Dentin is formed by dental pulp mesenchymal stem cells (DPSCs) differentiated into odontoblasts and exhibits limited capacity for regeneration. Consecutive and mutual interactions between epithelial and mesenchymal cells are essential for tooth development. Enamel and dentin composite tissues regeneration is required to biologically restore dental crown defects. Our objective is to fine-tune the optimal conditions to regenerate dental enamel and to promote enamel–dentin integration.

**Methods:** Self-cross-linkable hydrogels made of different ratios of oxidized alginate (OAlg) and carboxymethyl chitosan (CMC) were developed and swelling, gelation time were measured. hDPSCs and hDESCs were mixed in 1:1 ratio within the Matrigel and the construct was inoculated on mice. In addition, hDEPC with hDPSC were co-cultured in vitro and examined for mineralization and amelogenin expression. HAT-7 cells were transfected with Dlx3, Runx2, Tbx1, or empty (control) expression vectors and 48 hours later mRNA was extracted and tested for cell proliferation and amelogenin expression. DPSCs were also cultured in media with and without BMP2 and tested for odontogenic differentiation.

**Results:** The gelation time was decreased by increasing the ratio from 4.7 min for 2:1 ratio to 2.3 min for 4:1 ratio and also swelling ratio was decreased by increasing the ratio of OAlg to CMC. The ration of 2:1 was selected as a cell carrier. Amelogenin mRNA relative expression level and also HAT-7 proliferation were much more higher in TBX1 group compared to other groups. It showed evidence that TBX1 is a strong inducer of dental epithelium cell proliferation and differentiation in HAT-7 DESC cells. In addition, the BMP2 promotes DPSCs Differentiation into odontoblasts. The formation of mineralization nodules in vitro and induction towards an ameloblastic phenotype and organoid formation in co-cultured hDESC and hDPSC indicated that co-culture is necessary to produce regenerated Enamel and Dentin.

**Conclusion:** We anticipate that two-compartment scaffolds will support simultaneous formation of human enamel and dentin in vivo, which is an essential step towards the biological repair of diseased or missing tooth parts.

**Keywords:** Tissue Engineering, tooth regeneration, Enamel, Dentin, 3D printed scaffolds

97. Role of APOBEC3 enzymes in HIV-1 evolution

**Presenter:** Nazanin Mohammadzadeh, College of Medicine  
**Supervisor:** Dr. Linda Chelico

**Background:** Human immunodeficiency virus (HIV) is a major global health issue. There has not been any report on the conventional cure but we can benefit from pharmacological (Antiretroviral drugs) and immunological (APOBEC3s) barriers. APOBEC3 enzymes are inhibited by HIV-1 vif but their mutagenic activity can potentially contribute to the evolution of the virus.

**Methods:** To determine role of APOBEC3 enzymes in HIV-1 evolution we used wide range of virological experiments like single cycle infectivity assays, spreading infections and next generation sequencing.

**Results:** APOBEC3 enzymes could mutate the specific region of reverse transcriptase that is responsible for drug resistance. Spreading infection assays show that the viable virus with drug resistance mutation couldn’t thrive when the mutagenic agent was APOBEC3 enzyme.
Conclusion: Although APOBEC3 enzymes can cause mutations more than Reverse transcriptase enzyme (background) since they caused nonsense mutations and premature stop codons beside the drug resistance mutations their role in the contribution is minimal.

Keywords: HIV-1, Viral evolution, APOBEC3, Antiretroviral drugs, Drug resistance mutations.

98. Development of mycophenolate mofetil (MMF) immunosuppressant as sustained release oral nanoparticles

Presenter: Munawar Mohammed, College of Pharmacy and Nutrition
Supervisor: Dr. Ellen Wasan

Background: To reduce dosing frequency and improve drug adherence, mycophenolate mofetil was formulated as sustained-release mucoadhesive oral polymeric nanoparticles (CS-PNPs).

Methods: MMF nanoparticles (CS-PNPs) were prepared by a modified single-emulsion solvent evaporation method with low, medium and high molecular weights of acid-capped polylactic-co-glycolic acid (PLGA) or polylactic acid (PLA), coated with chitosan. Surfactant type, surfactant concentration and polymer concentration were varied in a limited matrix study to optimize particle size, encapsulation efficiency and in vitro drug release in simulated gastric fluid (2h) followed by simulated intestinal fluid (22h). Encapsulation efficiency and release of MMF were measured by HPLC. Differential scanning calorimetry (DSC), scanning electron microscopy (SEM) and mucin binding by zeta potential were also conducted.

Results: Nanoparticles of PLA (MW 18K-24K) and polyvinyl alcohol 0.5% as the surfactant, achieved encapsulation efficiency of 71-97% at drug-polymer ratios (w/w) of 1:3 to 1:7. Particle size varied by composition. Two optimal formulations [PLA 18-24K MW, medium MW chitosan, drug: polymer ratio 1:7 (w/w) and PLGA 24-38K MW, high MW chitosan, drug: polymer ratio 1:7 (w/w)] had high encapsulation efficiency (94.34% and 75.44% respectively) and sustained drug release with a minimal burst phase (Fig 1). DSC experiments reveal crystalline to amorphous transformation of MMF in the optimal formulation. Surface morphology of CS-PNPs shows spherical nanoparticles with minimal porosity. Mucin binding was demonstrated by change in zeta potential.

Conclusion: Two CS-PNP formulations of MMF containing PLA: medium molecular weight chitosan (1:7 w/w) and high MW PLGA: high MW chitosan (1:7 w/w) prepared by a solvent evaporation method is a potential approach towards achieving once, rather than twice daily oral sustained delivery of MMF.

Keywords: polymeric nanoparticle, chitosan, sustained drug release, encapsulation efficiency, mucoadhesiveness
The effects of low field magnetic stimulation on cognitive impairment and depressive symptoms of a mouse model of demyelination

Presenter: Ali Mooshekhian, College of Medicine
Supervisor: Dr Yanbo Zhang

Background: Although the etiology of MS is not clear, different mechanisms have been introduced as possible aetiologies. The Neuropathology of MS is generally based on three pillars: 1) demyelination 2) microglia activation and 3) impaired remyelination. As for demyelination, there has been many studies done both on human brain samples and animal tissue all of which show that excitotoxicity contributes to oligodendrocyte (OL) death, demyelination and tissue damage in MS. Demyelinated axons are exposed to neurotoxic insults, oxidative stress, and energy deficiency, and are therefore vulnerable to further injury, resulting in irreversible axonal damage. Recent studies showed a selective loss of GABAergic parvalbumin-positive (PV+) interneurons in both animal models of MS and post-mortem studies. PV+ interneurons generate the gamma band oscillations (GBOs, 30–120 Hz) by synchronized inhibition of large pyramidal cell ensembles. GBOs (especially 40 Hz) play critical roles in maintaining synaptic plasticity and cognitive task. Abnormal GBOs is strongly linked to CI in the patients with autism, schizophrenia and Alzheimer's disease. In general, Multiple Sclerosis has four distinguished forms based on the progression pattern of the lesions and clinic: Relapsing Remitting (RRMS), Primary Progressive (PPMS), Secondary Progressive (SPMS) and Progressive Relapsing (PRMS). Among the four existing variations of MS, the progressive forms are more commonly associated with cognitive impairment. In clinical setting, this impairment is usually observed in certain domains of cognition than others. Memory, specially working memory and long-term memory, Learning, attention and information processing are considered to be the most common areas of cognitive disruption in MS. But, other aspects of cognition are not spared including: language, executive functioning, conceptual reasoning and recognition memory. Unfortunately, in spite of our detailed knowledge regarding the prevalence and clinical features of cognitive impairment in MS patients and the debilitating impact of this impairment on patients’ quality of life, no pharmacological treatment has been approved for this impairment and older non-pharmacological treatments like rTMS are currently the only option, but its efficacy is controversial. Depression is one of the most common psychiatric symptoms of MS and the association of depression with inflammation caused in the brain has been documented. Depression has also been shown to be quite close to CI in MS both in clinic and pathology.

Methods: The design: The mice (C57bl/6) were randomly assigned to four different groups: 1) Control which received normal chow and no LFMS treatment, 2) Control/Treatment that received normal chow plus LFMS treatment, cuprizone which were given cuprizone diet but no LFMS treatment and Cuprizone/Treatment that were fed with cuprizone diet and received LFMS treatment. Cuprizone groups were given chow infused with 0.2% cuprizone. Treatment groups were treated with LFMS on a daily basis for 20 minutes. The food was given in regular fixed portions to all groups and the mice were weighed twice weekly during the whole period of the experiment. Subjects accommodation and maintenance were provided according to the regulations of the University of Saskatchewan animal ethics committee. By the end of the sixth week, behavioural tests were done, animals were afterwards humanly euthanized by trans-cardiac perfusion and their brains were harvested.

Behavioural test: different behavioural tests were carried on in order to study the cognitive impairment and depressive symptoms. In order to assess the working memory Y-maze was chosen. Tail suspension test (TST) and forced swim test (FST) were applied to measure the depressive symptoms of the mice and
the results were recorded and analyzed by “Anymaze”. Anxiety-related behaviours were assessed by an open-field test (OFT). The OFT conflict between the desire to explore and the desire to avoid the anxiogenic stimuli of open spaces in rodents. Western blot: Various antibodies will be used to examine the protein levels that indicate inflammation (iNOS, GFAP, Iba-1) and remyelination (MBP). Membranes will be read and analyzed using “Image-J”.

Myeline and OL pathology: Luxol Fast Blue (LFB) for myelin will be used to detect the severity of WM demyelination and remyelination in corpus callosum. The intensities of myelin basic protein (MBP) immunostaining will be used to identify cortical and hippocampal myelin tracts and GM demyelination and remyelination. The assembling and structure of Node of Ranvier indicate myelin sheet integrity and functioning, which will be assessed through a double-labelling of sections with antibodies against Caspr (paranodes) and Nav1.6. Immunostainings of OL cell markers will be used to identify cells in OL lineage (Olig2), mature OL (GST-Î€) and OPCs (NG2).

Statistical Analysis: One or two-way ANOVAs will be used depending on the experimental design, followed by Tukey’s post hoc test or two-tailed Student’s t-test to compare individual mean values of behavioural and pathological data among treatment groups with the control.

**Results:** The research is still going on but fortunately the results that we have so far, which are from behavioral tests and western blots, are quite promising. The behavioral tests demonstrate that there is a significant difference between the results of Y-maze in our cuprizone control group and the cuprizone treatment group who were treated by LFMS. Meaning that the working memory of the cuprizone/Treatment group has been significantly preserved in spite the ingestion of cuprizone. This indicates that our treatment has been successful in playing a protective role in the treatment group against the demyelinating effects of cuprizone.

Moreover, our western blot results for Myelin Basic Protein (MBP) came back and it shows that in cuprizone plus treatment groups there is a significant difference in the amount of MBP compared to those mice that merely received cuprizone. In other words, our LFMS treatment has been successful in significantly protecting the prefrontal cortex of our subjects against the demyelinating effects of cuprizone. More tests including immunohistochemistry are due in a few months and we hope to get more satisfying results from them.

**Conclusion:** Based on our experiment results we can claim that LFMS has the potential to be considered for more studies and hopefully with gathering more solid results a potential might rise for LFMS to be considered for new clinical trials aiming to study the effects of LFMS on humans and it could be considered for clinical studies on cognitive impairment and depressive symptoms in demyelinating diseases, specially multiple sclerosis.

**Keywords:** Demyelination, multiple sclerosis, Low Field Magnetic Stimulation, Cuprizone, cognitive impairment, depressive symptoms.
100. A comparison of the bactericidal efficacy of silver diamine fluoride and sodium hypochlorite against Enterococcus faecalis as an endodontic irrigant- an ex-vivo study.

Presenter: Zekria Muradi and Jason Lee, College of Dentistry  
Supervisor: Petros Papagerakis  
Collaborators: Petros Kechagioglou, Renata Grazziotin Soares

**Background:** Endodontic therapy has largely relied on mechanical instrumentation and disinfection of root canals to eliminate bacteria causing periapical infections. This ex-vivo study aims to compare the antimicrobial effects of silver diamine fluoride and sodium hypochlorite against Enterococcus faecalis in root canal therapy on extracted single rooted teeth.

**Methods:** Ten single rooted extracted teeth were decoronated and had their root canals standardized in length and diameter and autoclaved. All teeth (except negative controls) were inoculated with Enterococcus faecalis for 72 hours and subsequently treated with the assigned medicament. After 24 hours, shavings of the teeth were collected and grown on agar plates. Colony forming units were compared.

**Keywords:** root canal, enterococcus faecalis, silver diamine fluoride, sodium hypochlorite

101. Depth-specific subchondral bone density measures in osteoarthritic and normal distal femora: in vivo precision and associations with pain

Presenter: Atieh Najafi Semnani, College of Engineering  
Supervisor: Dr. James Johnston, Dr. Saija Kontulainen

**Background:** Knee osteoarthritis (OA) is the leading cause of pain. OA is commonly characterized by changes in bone mineral density (BMD). The alterations are thought to be involved in the OA pain process. However, the relationship between joint pain and BMD at the distal femur has not yet studied. My objective is developing an image processing method for assessing BMD of the distal femur.

**Methods:** For analyzing depth-specific measures of subchondral bone, I will develop a variation of imaging processing methods developed by Johnston et al., Speirs et al., and Wright et al. This method will account for curvature of the distal femur. I will manually segment these regions. I will use Matlab to conduct regional analyses of these features across the distal femur.

**Results:** The research is currently ongoing. Methodologies are currently being established.

**Conclusion:** Further, as pain is the reason patients seek medical care, rational treatment targeting requires specific understanding of which structures contribute to pain [10]. This research will strive to clarify the role of bone in OA-related pain. As well, findings may be valuable in guiding outcome selection in OA studies addressing subchondral bone and pain, particularly in determining regions of interest for future prospective studies.

**Keywords:** Bone Mineral Density, Osteoarthritis
102. Structural investigation of the oligomeric domain of the psychiatric risk protein DISC1

Presenter: Anand Krishnan Nambisan, College of Graduate and Postdoctoral Studies
Supervisor: Dr. Adelaine Leung

Background: Disrupted in Schizophrenia 1 (DISC1) is a psychiatric disease risk gene, implicated in numerous mental disorders such as bipolar disease, autism spectrum disorder, major depressive disorder and schizophrenia. Many isoforms of DISC1 is found in the human brain. The longest isoform of DISC1 contains 854 residues. DISC1 functions like a scaffold, interacting with hundreds of protein partners to dynamically coordinate different stages of brain development. The N-terminal domain of DISC1 is predicted to be unstructured on its own, whereas the C-terminal domain contains a number of coiled coil domains. DISC1 exists in different oligomeric species in solution. The functional significance of this is unclear. DISC1 interacts with at least one of its partners as an octamer.

Methods: Overexpression of C-terminal domain (300-854 residue) of DISC1 in E.coli cells and it subsequent purification by a series of chromatography experiments. Structural studies of the target protein mainly involve electron microscopy negatively stained protein sample

Keywords: DISC1, schizophrenia, oligomerization, C-terminal domain, structural characterization

103. Unraveling the Metabolic Fate of Potential Therapeutic Dimer Compounds For Parkinson's Disease

Presenter: Chukwunonso Nwabufo, College of Pharmacy and Nutrition
Supervisor: Edward Krol

Background: Disease-modifying treatments and improved diagnostic tools are a major focus of research in Parkinson's disease (PD). Alpha-synuclein (AS) has been identified as a putative target for drug discovery and diagnosis in PD. Recently, we reported that two dimer compounds comprising of a caffeine scaffold attached to nicotine (C8-6-N), and 1-aminoindan (C8-6-I) were the most promising candidates in preventing AS-induced cell death in a yeast model of PD. Although Caffeine linked to Caffeine (C8-6-C8) did not show therapeutic potentials, its sufficient binding to AS makes it a suitable candidate for the development of imaging probes for diagnosis of PD. Given the therapeutic and diagnostic potentials of these novel compounds, it is of great importance to understand their metabolic profile. We are investigating the in vitro metabolic profile of these compounds in human liver microsomes (HLM), rat liver microsomes (RLM), and mouse liver microsomes (MLM), and will use the information obtained from this study to guide our design and development of Fluorine-18(18F) labeled dimer compounds towards their use in treatment or diagnosis of PD. In addition, comparison of the metabolic profile of C8-6-N, C8-6-I, and C8-6-C8 in RLM and MLM with those of HLM will help to identify the most relevant model for future toxicological studies.

Methods: We performed in-vitro incubations of C8-6-N, C8-6-I, and C8-6-C8 using HLM, MLM, and RLM at 37oC for 60 minutes. Chlorzoxazone conversion to 6-hydroxychlorzoxazone was used as a positive control for HLM, MLM, and RLM viability, negative controls included incubations in the absence of NADPH or with heat-inactivated microsomes. The metabolites were identified and confirmed with accurate mass
measurement and tandem mass spectrometry using a quadrupole/time of flight mass spectrometer (QToF).

**Results:** Two metabolites were identified for both C8-6-I and C8-6-N, whereas no metabolite was observed for C8-6-C8. The metabolites identified for C8-6-I were generated from de-alkylation (M1) and hydroxylation (M2) while for C8-6-N, the metabolites corresponded to de-alkylation (M3) and hydroxylation (M4).

**Conclusion:** Although C8-6-N and C8-6-I are metabolized in HLM, MLM, and RLM, C8-6-N undergoes extensive metabolism as it was depleted within the 60 minutes incubation period. Furthermore, the metabolism of C8-6-N and C8-6-I is dependent on NADPH and active liver microsomes. The same metabolic profile was observed for C8-6-N and C8-6-I in HLM, MLM, and RLM. Consequently, mouse and rat may be useful models for future toxicological studies of C8-6-I and C8-6-N. The tandem mass spectrometric information obtained from this study may be useful for future pharmacokinetic studies of C8-6-N, C8-6-I, and C8-6-C8.

**Keywords:** Disease-modifying treatments, Parkinson's disease, Alpha-synuclein, imaging probes, accurate mass measurement, tandem mass spectrometry

104. Long term effects of high-sucrose consumption and low-grade LPS administration on behaviour and late-onset Alzheimer's disease pathology in wild-type mice

**Presenter:** Anthony Pacholko, College of Graduate and Postdoctoral Studies  
**Supervisor:** Lane Bekar  
**Collaborators:** Caitlin Wotton

**Background:** Canadian dementia cases are expected to more than double over the next generation. If this growing problem is to be addressed, the impact of modern lifestyles and diets on the etiology and progression of Alzheimer's disease (AD) must be explored. At present, much of the research surrounding AD is centered on the use of transgenic animal models reliant on humanized genetic mutations that account for less than 10% of all AD cases. Given the relative rarity of these familial AD variants within our population, it seems likely that environmental factors - not genetic predisposition – are chiefly responsible for the observed rapid escalation in the incidence of late-onset neurodegeneration. Thus, animal models that explore the impacts of these environmental factors on neurodegeneration are needed to better elucidate the etiology behind late-onset AD.

Diabetes, chronic stress, sleep deprivation and inflammation (Crohn's, arthritis, etc.) are quickly becoming the norm in our society rather than the exception. Worryingly, each of these stressful conditions has been shown to contribute to mild neurodegeneration in isolation, which thus begs the question: what havoc might these combined stressors have on the human brain when present for multiple decades? Could these rising conditions be responsible for the growing AD epidemic? This project explores this possibility through the utilization of a long-term combination of high-sucrose diets and LPS-induced inflammation to accelerate neurodegeneration in the pursuit of generating an AD-like phenotype.

The Public Health Agency of Canada estimates that one in five Canadians over the age of 65 now have diabetes. The prevalence of diabetes/pre-diabetes is noteworthy, as it has been observed that the degree of neurodegeneration in AD patients correlates closely with the severity of brain insulin resistance, a state
intimately associated with the gluco-regulatory impairments induced by diabetogenic diets. Further compounding the issue, high-sucrose consumption may also exacerbate pro-inflammatory pathways in the brain; neuroinflammation is an integral component of AD pathogenesis. It is therefore possible that sugar filled diets and inflammatory events (disease, stress, lack of sleep) intersect to both initiate and drive forth the development and progression of AD, which may in part explain the rising incidence of the disease. Intriguingly, there may be a non-invasive way to counteract these processes: sub-therapeutic supplementation with lithium orotate. Lithium is a highly neuroprotective mineral with the potential to inhibit many of the processes involved in AD pathogenesis.

**Methods:** Two cohorts (one male and one female) comprised of six groups of 10 C57/Bl6 mice (12 weeks old) will form the basis for this study. Each cohort will be subjected to identical treatments. Groups 3, 4 and 6 will receive intraperitoneally delivered LPS injections, while groups 1, 2 and 5 will receive saline. Saline and LPS (0.1 mg/kg) injections will be performed once monthly for 3 months, beginning one month into the experimental regimen. Groups 2, 4 and 6 will be provided with 20% sucrose drinking water for the duration of the study. Groups 5 and 6 will have lithium orotate (1 mg/L) added to their drinking water to assess the prophylactic potential of lithium in halting the progression of neurodegeneration. The groups will thus be labelled according to the treatment received: control (group 1), high-sucrose (group 2; hS), lipopolysaccharide (group 3; LPS), high-sucrose-lipopolysaccharide (group 4; hSL), lithium (group 5; Li), and high-sucrose-lipopolysaccharide-lithium (group 6; hSLLi). Following 6-months of treatment, each group will be subjected to the Barnes maze, Y-maze, Open Field and Forced Swim behavioural tests for the assessment of spatial memory, anxiety and despair, respectively. Post-behavioural testing, each animal will be sacrificed for the immunological, biochemical, and histological analysis of markers for inflammation, insulin resistance and AD pathology.

**Results:** On account of the early-stage nature of our data collection, our results are minimal at present. However, the results thus far obtained are as follows:

**Open Field:**

No significant differences observed between the control, hS, hSL and hSLLi groups on measures of latency to center, frequency of entry into center, duration in center, and duration of immobility. However, Li animals appeared to spend more time in the center of the maze than do the controls, suggesting a potential anxiolytic effect of lithium supplementation (~5-8x below the therapeutic dose).

**Forced Swim Test:**

No significant differences were observed on measures of frequency, latency to first, and duration of immobility. No evidence of despair was observed.

**Spontaneous-alternation Y-maze:**

No significant differences were observed on measures of total alternations, alternation indices, and indirect revisits. No evidence of impaired spatial memory was observed.

**Barnes Maze:**

LPS animals appeared to demonstrate an increase in latency to escape relative to controls, with the greatest differences observed on days 4, 5 and 7. No significant differences were observed in the latency of escape between control, hS, hSL and hSLLi groups. To sum, LPS animals demonstrated possible signs of cognitive decline and impaired spatial memory relative to controls, while hS, hSL and hSLLi groups did not.

**Conclusion:** The present study is still very much underway, but early behavioural results appear to suggest a lack of a high-sucrose and inflammation-induced sporadic AD-like phenotype in male wild-type mice. With that being said, behavioural tests are highly susceptible to confounding variables, of which
there were several. Chronic stress in the form of fire alarms, injections and room changes may have disrupted the effects of our low dose LPS treatments, and contributed to the induction of stress-related processes across all groups. Some possible evidence for the involvement of chronic stress was observed in the form of obese controls that exhibited similar weight gain to our high-sucrose treated animals (indicative of chronic stress).

The histological and biochemical data from our male mice (to be acquired) will provide a clearer picture of the issues at play. It remains entirely possible that 20% sucrose consumption and LPS administration do not produce an AD-associated cognitive deficit, though such results would counteract the numerous studies that have established high-sucrose diet-fed mice as a model for neurodegeneration. Any conclusions regarding the effects of these treatments will be withheld until completion of the appropriate histological and biochemical assessments. Also of note, the female behavioural results may prove to be in disagreement with the data collected during the male trials. To sum, male behavioural results indicate a lack of an AD-like phenotype, with the female behavioural and male/female histological/biochemical assessments yet to be completed.

Keywords: Neurodegeneration, Alzheimer's disease, High-sucrose, Inflammation, Insulin resistance, Diabetes, Behaviour

105. Lung inflammation following glyphosate and lipopolysaccharide (LPS) exposure

Presenter: Upkardeep Pandher, College of Medicine
Supervisor: Shelley Kirychuk
Collaborators: David Schneberger, Brooke Thompson

Background: Agricultural workers are commonly exposed to both endotoxin (LPS) and herbicides. Endotoxin (LPS), a constituent of gram-negative bacteria, is a common exposure in agricultural production. Herbicides are a common weed control application in both occupational and non-occupational settings. Exposure to herbicides and endotoxin individually and in combination are therefore common. Exposure to herbicides at low concentrations have been shown to induce lung inflammation. Glyphosate is the most common active ingredient in herbicides and products containing glyphosate are most commonly applied in agriculture worldwide. Despite the benefits for food production, exposure to glyphosate has been linked to health effects including respiratory symptoms in exposed agricultural workers. However, there is little information on lung inflammation related to glyphosate exposure. LPS, a purified form of endotoxin, is a well-known stimulant for lung inflammation. Thus, we hypothesized that glyphosate exposure can induce lung inflammation and that co-exposure to glyphosate and LPS can further enhance the inflammatory response.

Methods: Both in-vitro and in-vivo experiments were performed to study the inflammatory response of glyphosate and LPS, individually and in combination. Human alveolar epithelial cells (A549) were treated for 24 hours with varying concentrations of glyphosate (0.1 mM, 1 mM, 10 mM) and LPS (1 µg, 100 µg), individually and in combinations. Supernatants were harvested and assessed for interleukin-8 (IL-8) cytokine using ELISA. RNA was isolated from treated cells and tested for expression of A20 (also known as tumour necrosis factor alpha-induced protein 3) with Real Time PCR to assess the potential for inhibition of nuclear factor kappa B (NFκB) gene expression. C57BL/6 mice (4 groups; 5 animals per group) were treated intranasally and observed for 4-hours. The four groups included: (1) LPS (0.5 µg); (2) glyphosate
(1 µg); (3) combined treatment (LPS = 0.5 µg + glyphosate = 1 µg); and (4) control group. Post 4 hours, mice were euthanized and samples were collected (blood, broncho alveolar lavage fluid, and lungs).

**Results:** A549 cellular treatments showed that glyphosate alone had no effect on IL-8 release at any of the concentrations (0.1 mM, 1 mM, 10 mM). However, there was a significant reduction in IL-8 in cells co-treated with LPS (100 µg/ml) and glyphosate (10 mM). Further, we found an increase in expression of A20 on co-treatment of glyphosate and LPS, with no significant reduction in viability of A549 cells. Evaluation of in-vivo experiment results for the assessment of inflammatory markers is currently underway.

**Conclusion:** Taken together, our A549 results suggest that glyphosate co-exposure may inhibit LPS mediated lung inflammation, and A20 may be an important regulator. Results of in-vivo experiment will augment the findings of inflammatory effects of glyphosate and LPS co-exposure.

**Keywords:** Lung inflammation, glyphosate, LPS, human lung epithelial cells, mouse model
106. Translational alteration of HCV genome promotes miR-122-independent replication of the virus.

Presenter: Mamata Panigrahi, College of Medicine
Supervisor: Dr. Joyce Wilson

**Background:** miR-122 is a liver-specific microRNA (miRNA) that binds to two sites on the 5' untranslated region (UTR) of the hepatitis C virus (HCV) genome and promotes the viral life cycle. It positively affects viral RNA stability, translation, and replication, but the mechanism is not well understood. Work from our lab demonstrates that, unlike the wild-type HCV genome, some full length RNAs with mutations in the 5' UTR and bicistronic HCV replicons containing an additional IRES can replicate at low rates in miR-122-deficient cells. Although there are reports of miR-122-independent replication of HCV, no mechanism for independent replication has been proposed. In this study, we hypothesize that an alteration in translation regulation affects viral propagation and, in-turn, promotes miR-122-independent replication.

**Methods:** To unravel the role of miR-122 in translation regulation we have used Huh 7.5 miR-122 knock out cells to perform translation study of in vitro transcribed replication defective HCV RNA genome with mutations in the 5'UTR. We have also used FACS and Confocal microscopy to characterise cells supporting miR-122-independent replication. Inverse PCR and cloning was done to delete specific structural genes from HCV genome, in vitro transcribed and electroporated with or with out miR-122 to study viral propagation.

**Results:** We observed that the presence of an extra IRES and mutations in the 5'UTR that enhance HCV genome translation efficiency also promoted miR-122-independent replication. We also observed that deleting the structural genes of the virus increased its overall replication efficiency and promoted low levels of replication in miR-122-deficient cells, however, deleting individual structural genes did not promote miR-122-independent replication. Finally, analysis of cells supporting miR-122-independent HCV replication by microscopy and flow cytometry revealed efficient replication (similar to miR-122-dependent replication) in a small number of cells, instead of low-level replication in all cells.

**Conclusion:** These findings support the role of miR-122 in regulating HCV translation and also suggest that establishment of replication in a high proportion of cells requires miR-122, but for genomes capable of miR-122-independent HCV replication, establishment of an infection is inefficient in the absence of miR-122. Thus, we speculate that miR-122 promotion of virus translation functions to establish virus replication, but that miR-122 may be dispensable for ongoing replication of some HCV genomic RNAs.

**Keywords:** HCV, miR-122-independent replication, IRES,
107. Role of Low Field Magnetic Stimulation on cognitive and motor functions in Traumatic Brain Injury Mouse Model

Presenter: Amir Parvizi, College of Medicine  
Supervisor: Changiz Taghibiglou

**Background:** Traumatic brain injury/concussion (TBI) is a growing epidemic throughout the world. Memory and neurobehavioral dysfunctions are among the sequela of TBI. TBI has been increasingly accepted as one of the major external risk factor in the development/progression of neurodegenerative diseases. Low-field magnetic stimulation (LFMS) is a new non-invasive transcranial magnetic stimulation (TMS) technique that generates deep brain magnetic stimulation. In the present study, the role of LFMS on cognitive and motor functions were investigated in a weight drop induced TBI mouse model.

**Methods:** Repeated traumatic brain injury (TBI) was induced to respective animals using weight-drop (60 g, on the right side of the head) machine, once daily for 3 days. LFMS treatment was given to the respective animals immediately following first induction and then once daily for 3 days. On day 4, animals were assessed for cognitive and motor functions. Following behavioral tests, the animals were sacrificed, and brains were collected for further analysis.

**Results:** LFMS treated TBI mice covered longer distance in open field when compared to vehicle treated TBI mice. In addition, they moved center squares like normal control and LFMS control mice, whilst vehicle treated TBI mice spent less time in the center squares of open field. Further, LFMS treated TBI mice withstand more time on the rotating rod, whilst vehicle treated mice fall in short time compared to normal control mice. In Novel location task, LFMS treated mice spent more time in the novel location compared to vehicle treated mice. In our previous studies, we reported the release of cellular prion protein (PrPc) from brain to peripheral circulation following sport concussion and blast-induced brain injury which may serve as a biomarker for TBI. Here, we observed increased PrPc levels in LFMS treated mice brain compared to vehicle treated which shows the restorative effect of LFMS.

**Conclusion:** Thus, the results obtained from the study suggest that LFMS may improve subject's neurological conditions following TBI.

**Keywords:** LFMS; Weight-drop TBI; Mouse model; PrPc; behavior; Neuroprotection

108. Liposomal formulations of phytosterols and tocopherols into functional food

Presenter: Asmita Poudel, College of Pharmacy and Nutrition  
Supervisor: Dr. Anas El-Aneed and Dr. Ildiko Badea  
Collaborators: Dr. Zafer Dallal Bashi

**Background:** Phytosterols and tocopherols extracted from canola oil waste stream can be a potential component of functional food due to their cholesterol lowering abilities and antioxidant properties respectively. However, their lipophilic nature as well as heat and light sensitivity makes it challenging to incorporate them into functional food. The aim of this study is to develop bifunctional liposomes of phytosterols and tocopherols and incorporate them into functional food.
Methods: Liposomes containing phytosterols and tocopherols were created using three different approaches- homogenization, ultrasonication and heating methods. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) quantitative method was developed and validated to apply for determining the incorporation efficiency into liposomes.

Results: The particle size was significantly larger when employing the heating method (258nm) compared to homogenization (192nm) and ultrasonication (195nm) method. Whereas zeta potential were comparable among the three formulation (-15mv to -18mv). Linearity (R2= 0.998) and adequate sensitivity (0.005µg/ml) was achieved by quantitation method. In addition, the method was validated as per the ICH guideline, ensuring robustness of analytical platform. Incorporation efficiency was around 95% with homogenization approach as measured by LC-MS/MS method.

Conclusion: All three-formulation strategies showed size and zeta potential suitable for colloidal stability and oral drug delivery. Robust analytical method was developed and validated and applied to measure incorporation efficiency. The optimized liposomes will be incorporated into orange juice. Formulation stability in pasteurized orange juice will be evaluated for 60 days.

Keywords: Functional food, Canola, Phytosterols, Tocopheros, Liposomes, Liquid Chromatography Tandem Mass Spectrometry

109. Engineering functionalized diamond nanoparticles for drug/gene delivery: biodistribution studies

Presenter: Raj Rai, College of Pharmacy and Nutrition
Supervisor: Dr. Ildiko Badea

Background: Pharmaceutical research and development greatly focuses on non-viral drug delivery systems as they are safer compared to viral vectors. Inorganic nanoparticles that can be used as drug carriers are silica, gold, carbon nanotubes are also a major area of interest. Nanodiamonds have emerged as new drug carriers due to their excellent physical and chemical properties. Surface modifications nanodiamonds can achieve targeted drug delivery. To engineer lysine-functionalized nanodiamonds (lysyl-NDs) as biocompatible and efficient gene carriers. Optimization of the design was carried out by grafting histidine as an endosomal membrane destabilizer onto the lysyl-NDs (lysyl-histidyl-ND). However, their specific interactions with the biological system are yet to be defined. Biodistribution studies will help to elucidate their fate at organ levels and monitor their pharmacokinetics. A suitable chelating agent (deferoxamine, DFO) was attached to the functionalized NDs to assist with radio labelling with 89Zr to study the biodistribution in animal models.

Methods: 1HNMR is used to confirm synthesis of amino acid conjugates at all steps. The lys-nanodiamonds are characterized by size and zeta potential measurements. To provide evidence of functionalization of nanodiamonds with the lysine linker, Raman spectroscopy of pristine nanodiamonds (pNDs), reoxidized nanodiamonds (rNDs), functionalized nanodiamonds (fNDs), is performed. Thermogravimetric analyses is performed to provide quantitative estimates of the surface loading of functional groups attached to the NDs. Gel electrophoresis is done to examine the binding efficiency of the fNDs to the siRNA. Positron emission tomography is applied to study the biodistribution; therefore, functionalized NDs are conjugated to a radionuclide-chelating agent (desferoxamine) and labeled with 89-Zr for imaging in experimental animals.
Assessment of biodistribution will inform us whether the nanoparticles accumulate in certain organs (liver, kidney, lungs, spleen), able to penetrate biological barriers (such as blood-brain barrier) and reside in the body for prolonged time. This fundamental knowledge will guide selection of target diseases amenable to gene therapy and future re-design of nanoparticles, if needed.

**Results:** Several batches of lys-NDs revealed a surface loading of 1.67 mmoles/gm of ND. The average particle size was 66 nm and zeta potential of +21 mV, showing consistency in all batches and validating the reproducibility of the designed protocol. 1HNMR revealed that the tagged NDs show all DFO protons of the aliphatic chain along with 4 protons of the benzene ring in the aromatic region, confirming the DFO-lysine-linker conjugation. Similarly, lysyl-histidine chemical moiety was synthesized and confirmed using 1HNMR through characteristic peaks at $\delta$ 7.34, $\delta$ 7.45 (t, 2H, imidazole side chain) as well as presence of 3 Boc protecting groups at $\delta$ 1.4 (s 27H).

**Conclusion:** This study establishes that lysyl- and lysyl-histidine functionalized NDs, as potential carriers for gene therapy, can be labeled with radiotracers for assessment of biodistribution and pharmacokinetic analyses. Understanding the in vivo behavior of the functionalized NDs is critical for their translation from benchtop to clinical applications.: As nanodiamonds are relatively new to drug therapy, little is known about their specific interaction with living systems. It is known that the targets of many therapeutic agents are localized inside the cells in subcellular compartments; therefore, it is vital to engineer nanoparticles that can carry the drug to the affected tissues and inside of the diseased cells in the body. We have already demonstrated that nanodiamonds are capable of introducing siRNA into mammalian cells and cause no toxicity. Moving forward, elucidation of the biodistribution of nanodiamonds brings the opportunity to better understand the risk that these systems may pose in complex living system and provides an important basis for designing a ND- based drug delivery systems. With rapid advances of nanoscience in drug delivery, the application of functionalized nanodiamonds to make target-specific drug delivery in cancer could revolutionize the way current cancer treatment work. It could help the province to mitigate the therapeutic outcome of more than 5800 new cancer cases per year effectively.

**Keywords:** Lysine, Histidine, Biodistribution, PET
110. The Implications of Calcium Release Activated Calcium Channels in Amelogenesis

Presenter: Raed S. Said, College of Medicine  
Supervisor: Petros Papagerakis  
Collaborators: Silvana Papagerakis and Li Zheng

**Background:** Dental enamel formation (Amelogenesis) largely depends upon the trans-cellular transport of (Ca2+) by ameloblasts but it remains unclear how (Ca2+) channels regulate amelogenesis. Stromal interaction molecule 1 (STIM1) is the main sensor of the calcium concentration in the endoplasmic reticulum. Depletion of endoplasmic reticulum calcium stores activates STIM1 protein which, in turn, binds and opens calcium channels in the plasma membrane formed mainly by ORAI Calcium Release-Activated Calcium Modulator 1 (ORAI1) protein. Humans with mutated ORAI1 or STIM1 present with hereditary combined immunodeficiency, congenital myopathy and anhidrotic ectodermal dysplasia, including severely affected enamel. This study aims to characterize the roles of Orai1/Stim1 during early (ameloblast differentiation) and late (enamel formation) amelogenesis in terms of gene expression control, calcium influx and enamel thickness and mineral content. Our aim is also to gain novel insights regarding Ca2+ channels roles in regulating synchronized ameloblast differentiation and functions.

**Methods:** We evaluated the degree that Orai1/Stim1 controls ameloblast differentiation and function by targeting calcium-dependent gene expression in vitro and in vivo. By using ameloblast cell line (HAT-7) we measured the potential effects of Orai1 shRNA knockdown and on the ameloblast differentiation-related gene expression. We also fully evaluated the effects of Ca2+ channels on enamel formation by generating unique conditional knock out (cKO) mice models of Stim1flox/Amelx-cre in which Stim1 was selectively deleted from enamel forming cells. We evaluated enamel thickness and mineralization in the mice models by micro-CT; SEM EDS; x-ray and enamel gross morphology.

**Results:** Our results demonstrated that ablation of Ca2+ channels disrupts dental cell differentiation and significantly reduce their proliferation rates. Knock-out of STIM1 gene also resulted in significant changes in gene expression, mineralization rates, and overall enamel morphology. STIM1 cKO mice showed much shorter incisors with significant attrition in their molar enamel. micro-CT and SEM analysis revealed that STIM1 cKO incisors and molars display an abnormal prismatic enamel structure with dramatically reduced mineral densities as compared with control.

**Conclusion:** Our data indicate that in addition to their importance in enamel mineralization, Ca2+ channels play key roles in regulating ameloblasts gene expression and enamel formation. Understanding the role of these complex channels is essential for setting up successful protocols of dental tissue regeneration.

**Keywords:** Dental Enamel, Ameloblasts, Calcium, Stim1, Orai1.
111. Investigating the Effects of Selective Pacemaker Channel (Ih) Blocker ZD7288 in Epileptogenesis and Adenosine A1 Receptor Mediated Hippocampal Neuronal Damage

Presenter: Jasleen Saini, College of Medicine
Supervisor: Francisco Cayabyab

**Background:** Hyperpolarization-activated cyclic nucleotide-gated (HCN) channels or pacemaker channels conduct the Ih current in the brain. Several important studies found that pharmacological inhibition of Ih or genetic deletion of HCN1 channels increases excitability in neocortical and hippocampal pyramidal neurons. Previously, the Cayabyab lab showed that prolonged adenosine A1 receptor (A1R) stimulation induced persistent hippocampal synaptic depression and neurodegeneration. We hypothesize that the inhibition of HCN1 channels with ZD7288 in presence of A1R agonist N6-Cyclopentyladenosine (CPA) serves a neuroprotective role by prolonging the latency to pilocarpine induced status epilepticus (SE) and enhancing synaptic function.

**Methods:** Male Sprague-Dawley (SD) rats were given intraperitoneal (IP) injections of 5 mg/kg body weight of the A1R selective agonist CPA or DMSO/Saline, as well as intranasal (IN) administration of 1 mg/kg body weight of the selective HCN1 blocker ZD7288. The perfused brain tissue was cut at 40 μm and was probed with appropriate antibodies or Fluoro-Jade B.

**Results:** Fluoro Jade B staining showed that IP CPA + IN DMSO increased neurodegeneration in the hippocampus, which was blunted by IN ZD7288 co-treatment with IP CPA. These changes in neuronal health were associated with reduced A1R and increased HCN1 expression (IP CPA + IN DMSO) or increased A1R and decreased HCN1 expression (IP CPA + IN ZD7288). Results obtained from FJB and IHC suggest that inhibition of HCN1 or Ih current with ZD7288 serves a neuroprotective function against the neuronal damage caused by chronic A1R stimulation. The rats that received IP CPA + IN DMSO also spent less time in the novel arm during the Y maze test, which examines hippocampal-dependent spatial memory. Whereas, the rats that received IP DMSO + IN ZD7288 spend the majority of their time in the novel arm. Lastly, we found that IP DMSO + IN ZD7288 administration decreases the latency to pilocarpine-induced SE as opposed to prolonging it.

**Conclusion:** Since adenosine elevation occurs after stroke and post-stroke seizures are observed in some stroke survivors, these results suggest a role for A1R-mediated changes in HCN channels associated with epileptogenesis.

**Keywords:** HCN1 Channels, Adenoside A1 Receptor

112. Binding Kinetics Study of DISC1-44mer Fragment to GSK3b

Presenter: Stephanie Saundh, Western College of Veterinary Medicine
Supervisor: Dr. Adelaine Leung
Collaborators: Steve Gagné & Narsimha Pujari

**Background:** GSK3B is a multipurpose serine-threonine kinase which plays a role in many signaling pathways. Abnormal SK3B function has been implicated in a number of diverse disease states including metabolic diseases, cancer, and neuropsychiatric diseases. Its role in neurological disease stems from its
abnormal activity within the WNT/B-catenin signalling pathway. One of the binding partners of GSK3B within the WNT pathway is DISC1. Mutations within the DISC1 protein have been suspected to play a role in individuals presenting with mental illness. Research in this area is lacking in the amount of information known about how DISC1 interacts and influences the activity of GSK3B. This poster aims to display the work in progress towards identifying a potential binding site on GSK3B for a small 44 base pair fragment of the DISC1 protein (DISC1-44mer). The ability to determine the location of DISC1 binding is essential to better understanding the mechanism behind DISC1s ability to inhibit GSK3B. Binding interaction studies using Surface Plasmon Resonance (SPR) technology were conducted to determine the binding kinetics of DISC1-44mer. The DISC1-44mer kinetics were compared to the kinetics of a different peptide fragment (FRATtide) that has been shown to bind to GSK3B outside of the substrate binding pockets. SPR was used to determine if binding of DISC1-44mer and FRATtide to GSK3B is competitive in nature. Any indications towards competitive binding between these peptides would indicate that the binding sites of overlap. These studies contribute to our overall understanding of how DISC1 functions to modulate the activity of GSK3B.

**Methods:** Surface Plasmon Resonance technology was utilized to study the binding kinetics. His-GSK3B-His construct was bound to a NiNTA chip. A synthetic version of the DISC1 44-mer peptide fragment was flowed over the captured protein and the resulting binding kinetics were analyzed. The synthetic version of the FRATtide peptide was flowed over bound GSK3B and the resulting binding kinetics were analyzed. A mixture of DISC1 44-mer peptide and FRATtide together were analyzed and the results were compared.

**Results:** Binding curves and dissociation constants were obtained for all three test conditions.

**Conclusion:** Results indicate that DISC1 44mer peptide fragment and FRATtide have similar binding sites that may overlap.

**Keywords:** GSK3B, DISC1, SPR, Kinetics

113. **Effect of Low Field Magnetic Stimulation on Restoring Neuronal and Glial Function Against 1-Methyl-4-Phenyl-1,2,3,6-Tetrahydropyridine Induced Parkinson's Disease Mouse Model**

**Presenter: Sathiya Sekar, College of Medicine**  
**Supervisor: Changiz Taghibiglou**

**Background:** Parkinson's disease (PD) is a progressive neurodegenerative disorder affecting approximately 1% of population over the age of 60 years world-wide. PD is clinically characterized by slow or decreased movement, resting tremor, postural instability and various other symptoms, and is primarily caused by the degeneration of dopaminergic neurons in substantial nigra pars compacta (SNpc) and depletion of dopamine in striatum (ST). Current approved treatments of PD only decrease symptoms but do not affect disease progress. Numerous medications developed for rescuing dopaminergic neurons and restoring motor and non-motor functions have failed in clinical trials because of low efficacy or adverse effects. Recently, researchers showed that transcranial magnetic stimulation (TMS) improves cognitive and motor functions in PD patients. Low-field magnetic stimulation (LFMS) is a new non-invasive TMS technique that generates deep brain magnetic stimulation. In the present study, the effect of LFMS on neuronal and glial activities, in turn motor function in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced PD mouse model was investigated.
**Methods:** Animals were acclimatized for 7 days to the laboratory conditions before experimentation. Following acclimatization, animals were pre-trained for beam walk test until ceiling performance was reached. Then the animals were randomly assigned to one of the following groups (12-13 mice/group): I - Normal control, II - MPTP, III - MPTP + LFMS and IV - LFMS.

MPTP was administered to group II and III, intraperitoneally (i.p.) at 35 mg/kg, once daily for 5 days. Normal saline (NS) was administered i.p., once daily for 5 days to normal control and LFMS groups. LFMS treatment (20-min) was given to the respective animals, 4 h after first MPTP or NS injection and then once daily for 6 days.

Animals were assessed for motor functions at the end of treatment period. Following motor function tests, animals were sacrificed, and brains were collected for western blot and immunohistochemistry analysis.

**Results:** LFMS treated MPTP mice improved motor function compared to vehicle treated MPTP mice, as evidenced by stride length, beam walk, rotarod and open field tests. Further, LFMS treated mice showed significant increase in tyrosine hydroxylase (TH) and decrease in microglial marker (IBA1) levels when compared to vehicle treated MPTP mice, whilst no difference in astroglial marker (GFAP) level was observed between them. In addition, apoptotic marker like caspase 3 and inflammatory markers like TNFα and IL-1β levels were found to be ameliorated in LFMS treated MPTP mice brain compared to vehicle treated MPTP mice.

**Conclusion:** The results obtained from the study clearly reveal the unswerving involvement of LFMS in restoring neuronal and glial activities, in turn motor functions in MPTP intoxicated mice. Thus, we suggest that LFMS may serve as a potentially effective therapeutic intervention in the treatment of PD. Further studies may warrant to clearly elucidate the underlying molecular mechanisms of LFMS in protecting dopaminergic neurons against PD pathogenesis.

**Keywords:** LFMS; MPTP mice; Parkinson's disease; Neuronal-glial function

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**114. Identification of Bacterial Zoonotic Pathogens in the Oral Environment of Dogs Fed a Raw-Food Diet**

**Presenters:** Jessa Drury, Lisa Bachiu & Susanne Skulski, College of Dentistry  
**Supervisor:** Dr. Candace Lowe  
**Collaborators:** Dr. Doug Brothwell

**Background:** It is known that various bacterial zoonotic pathogens are present at elevated levels directly in raw meat-based dog foods as well as the fecal matter of dogs fed these foods. This study seeks to identify the presence of such bacterial zoonotic pathogens in the oral environment of dogs fed raw food-based diets - potentially constituting a significant route of pathogen transfer to humans.

**Methods:** 25 dogs fed raw food diets as well as 25 fed traditional kibble diets will be recruited through the Western College of Veterinary Medicine based on their reported diet. Saliva samples will be collected from the dogs using swabs and following a swabbing protocol. These swabs will be cultured to determine if bacterial species such as E.coli, Salmonella and Camylobacter sp. are present in the saliva.

**Results:** The study has not yet been executed but the results expected to be seen are that the dogs being fed raw-food diets will have an increased likelihood of zoonotic pathogens being present in their saliva compared to the control group, the kibble fed dogs.
Conclusion: The purpose of this study is to potentially identify zoonotic pathogens in the saliva of raw food fed dogs. The presence of said pathogens could adversely affect human health through the potential transmission of bacteria from the dogs mouth to their owners. The first step in identifying the risk of transmission is to first observe the presence of these zoonotic pathogens in the saliva of dogs.

Keywords: Escherichia coli, Salmonella, Camylobacter species, Dog, Zoonotic Pathogen, Oral Cavity, Saliva

115. Co-infection of bats with coronavirus and the White Nose Syndrome causing fungus may influence the severity of the disease and/or increase virus shedding

Presenter: Sonu Subudhi, Western College of Veterinary Medicine
Supervisor: Dr. Vikram Misra
Collaborators: Environmental and Life Sciences Graduate Program, Trent University; Ontario Ministry of Natural Resources and Forestry, Wildlife Research and Monitoring Section, Trent University; Department of Biology, University of Winnipeg; Canadian Wildlife Health Coo

Background: In recent years, viruses found in bats are thought to have spilled over to humans and other mammals, causing fatal disease. These spill-overs appear to be associated with increased contact between bats and other animals as well as increased shedding of virus by bats.

Methods: Our lab tested the prediction that little brown bats (Myotis lucifugus) co-infected with the M. lucifugus coronavirus (Myl-CoV) and with Pseudogymnoascus destructans (Pd - the fungus that causes bat white-nose syndrome (WNS)) exhibit different disease severity, viral shedding and molecular responses than singly-infected or mock-infected bats.

Results: We showed that more than 30% of either mock-infected or experimentally infected bats (with Pd) were persistently infected with the Myl-CoV. However, the intestines of bats co-infected with Pd and Myl-CoV, contained on average 60-fold more viral RNA than singly-infected bats (which correlated with the pathology). Coinfected bats had lower levels of interleukin genes (anti-viral genes).

Conclusion: Our results suggest that the systemic effects of WNS may down-regulate anti-viral responses in persistently infected M. lucifugus, and increase the potential of virus shedding or that co-infection increases the severity of WNS.

Studies with wild-caught bats to determine if natural environmental stressors influence viral shedding are underway.

Keywords: Little brown bats, Coronavirus, white nose syndrome, spillover, zoonosis, stress, coinfection
BASIC SCIENCE GROUP 7

116. A mucoadhesive lipidic delivery system of the adjuvant innate defense regulator (IDR)-1002

Presenter: Jaweria Syeda, College of Pharmacy and Nutrition  
Supervisor: Ellen Wasan  
Collaborators: VIDO-Intervac

Background: To design a mucoadhesive nasal formulation of the vaccine adjuvant innate defense regulator (IDR)-1002 peptide, previously used systemically as a triple complex with poly(I:C) and polyphosphazene (TriAdj).

Methods: The binding properties of the TriAdj mixture were characterised by gel electrophoresis and fluorescence quenching using rhodamine-poly(I:C). Cationic liposomes comprised of didodecyl dimethylammonium bromide (DDAB), dioleoyl phosphatidylethanolamine (DOPE) (60:40 mol:mol) and DDAB, L-α-phosphatidylcholine (egg PC) and DOPE (45:45:10 mol:mol:mol) were prepared by the thin-film extrusion method. The liposomes and TriAdj were combined by simple mixing. The formed complex was characterized by dynamic light scattering, zeta potential, mucin binding and cytotoxicity in RAW267.4 macrophage cells by MTS assay. Mice were administered the complex intranasally with ovalbumin as antigen, and the immunogenic response was measured by ELISA (plasma IgG1, IgG2) and Elispot assays (spleen IL-5, INF-γ).

Results: IDR-1002 peptide, polyphosphazene and poly(I:C) self-assembles in solution forming an anionic complex, demonstrated by altered electrophoretic mobility in agarose gel, co-elution on size exclusion chromatography and fluorescence quenching of rhodamine-labeled poly(I:C). TriAdj+ cationic liposomes were prepared at several molar ratios to determine optimal size stability and desired positive charge. Stable particles (IgG2, a dose-response with the IDR-002 peptide content (2µg vs 10µg/dose), and a differential IgG1 vs IgG2 response based on the lipid composition.

Conclusion: A mucoadhesive cationic lipid-based formulation of the TriAdj IDR-002 peptide adjuvant is a potential approach for nasal administration of a vaccine product.

Keywords: IDR-1002 Peptide, poly I: C, polyphosphazene, TriAdj, liposomes, mucoadhesive

117. Oral Health and Its Relation to Oral Cancer In Saskatchewan: A Literature Review

Presenter: Wyatt Goldade, Joel Scott, Ryan Turple, College of Dentistry  
Supervisor: Dr. Silvana Papagerakis  
Collaborators: Dr. Petros Kechagioglou

Background: Oral and Oropharyngeal Cancer (OPC) is the most common malignancy of the upper digestive tract and it is one of the fastest growing cancers in the world. OPC continues to be a disfiguring and deadly disease with a 5-year disease specific survival of a dismal 57%. In Canada, OPC incidence is on raise in both men and women, as well as its morbidity and mortality are high.
Methods: Our study reviewed the epidemiological data available from the Canadian Cancer Society, GLOBOCAN and World Health Organization in regard with Saskatchewan OPC incidence and mortality comparatively with national and worldwide figures. We have also reviewed information regarding access to oral health care, awareness of OPC and socio-demographic profile.

Results: Our study revealed increasing OPC incidence and mortality in both sexes in Saskatchewan. Alarmingly, the OPC incidence rate is higher than the national figures in younger females, starting as young as 25 of age. Across Canada, the incidence rate of human papillomavirus (HPV)-related OPC has increased significantly in both sexes over the last 20 years, with a peak in the 60-69 age group.

Conclusion: Because the lack of information on this topic, our study aims to provide up-to-date information on the burden of OPC in Saskatchewan to guide future OPC prevention strategies. Prediction of OPC incidence rates indicates a significant increase in both sexes; the rate of OPC in males is expected to surpass the rate of cervical cancer in females in the near future.

Keywords: oral cancer, oropharyngeal cancer, human papilloma virus, Saskatchewan

118. Generation and Characterization of Small Protein-Based Affinity Reagents for Cancer Imaging

Presenter: Arunkumar Annan-Sudarsan, College of Medicine
Supervisor: Maruti Uppalapati
Collaborators: Vizeacoumar F and Geyer CR

Background: Small protein-based affinity reagents are useful for diagnostic imaging applications as they have better tumor penetration and bio-distribution than antibody-based affinity reagents.

Methods: Kunkel mutagenesis, Phage display, ELISA, Affinity chromatography, Bio-layer interferometry, Circular Dichroism spectroscopy and Flow cytometry

Results: In this work, we designed a small-protein domain library named SKSCF7, based on the well-established 3-helical alpha-bundle scaffold. We identified eleven surface-exposed residues on the protein scaffold, which are involved in protein-protein interactions. We diversified these eleven amino acid positions and displayed the library on M13 phage particles. We assessed the quality of the small-protein library using Ion torrent next-generation sequencing. We panned the SKSCF7 library against three disease-relevant cell surface receptor ectodomains: Nectin-4, PDL1 and CEACAM. We isolated specific small-protein binders to all three protein targets using phage-ELISA and decoded the identity of the binders using Sanger sequencing. We over-expressed and purified small-protein binders from E. coli using affinity chromatography. In bio-layer interferometry experiments, SKSCF7-based small-protein binders exhibited high affinity (low-nM KDs) and high specificity for the target proteins. The Circular dichroism spectroscopy experiments showed, that the SKSCF7 small-protein binders had higher Tm (58-68 degrees) than the wild-type scaffold. Currently, we are conducting flow cytometry studies to measure the binding affinity of these small-protein binders to cancer cell-surface receptors.

Conclusion: We designed and constructed a new phage-displayed small-protein library named SKSCF7 and identified high-quality protein binders against three cancer cell-surface receptors for applications in cancer imaging.

Keywords: Small-protein engineering, Phage display, Alpha-helical bundles and Cancer imaging
119. Avian-origin PB1 gene of influenza A virus confers selective advantages to enhance 2009 pandemic H1N1 virus RNA transcription and replication

Presenter: Fangzheng Wang, Western College of Veterinary Medicine  
Supervisor: Yan Zhou

**Background:** Polymerase functions of avian influenza viruses were restricted in mammals due to host restrictions. PB1 gene originated from avian strains has been frequently observed in seasonal strains, 1957 and 1968 pandemic strains. However, the biological significance and corresponding molecular mechanism by which avian-origin PB1 emerged in these strains have long been elusive.

**Methods:** Using recent 2009 pH1N1 virus which naturally lacks avian-origin PB1 segment and the canonical PB2 E627K mutation, we show that avian-origin PB1 can enhance polymerase activity and compensate the defect in avianized pH1N1 polymerase.

**Conclusion:** Polymerase functions of avian influenza viruses were restricted in mammals due to host restrictions. To overcome restrictions on heterotrimeric polymerase complex, diverse adaptive strategies has been deployed by viruses. PB1 gene originated from avian strains has been frequently observed in seasonal and pandemic strains. Nevertheless, the biological significance and corresponding molecular mechanism by which avian-origin PB1 emerged in these strains have long been elusive. Using 2009 pH1N1 virus which naturally lacks avian-origin PB1 segment and the well characterized PB2 E627K mutation, we show that avian-origin PB1 can enhance polymerase activity and compensate the defect in avianized pH1N1 polymerase. The results of viral ribonucleoprotein reconstitution assay and cRNA stabilization assay indicated that avian-origin PB1 can elevate RNA transcription activity and vRNA replication from cRNA template. Furthermore, our data suggest that the previously identified argumentation in polymerase activity by ANP32A, one of the critical host factors underlies species differences, occurs globally when the polymerase is defective.

**Keywords:** Influenza A virus, viral polymerase, mammalian adaptation

120. New insight into Salmonella pathogenesis in chicken revealed through bioluminescent imaging

Presenter: Dinesh Wellawa, Western College of Veterinary Medicine  
Supervisor: Dr. Wolfgang Koester  
Collaborators: Dr. Brenda Allan, Dr. Aaron White, Dr. Heather Wilson

**Background:** Salmonella enterica serovar Enteritidis (SE) is a Gram negative facultative anaerobic bacterium belonging to the family of Enterobacteriaceae. SE can infect and colonize many animals including humans, rodents, bovine and swine species, and wild birds. The domestic chicken (Gallus gallus domesticus) acts as a reservoir for SE and represents a major ecological niche thus allowing transmission to human population resulting in salmonellosis globally. Growing concerns of antibiotic resistance found in “superbugs” have initiated the search for alternative therapeutic strategies such as vaccines. Current opinion to control these pathogens at farm level is to implement strict biosecurity measures and vaccination protocols which provide efficient protection in birds. Our understanding of Salmonella
pathogenesis in chicken is not sufficient and we believe that knowledge regarding key virulence factors of SE will lead us to novel therapeutic targets. Recent data suggest that Salmonella may deploy strategies to colonize and persist in chickens different from those in mammals. The phenomenon of bioluminescence imaging (BLI) has been applied to study host pathogen interaction. Contag et al., 1995, became pioneers in live imaging using mice infected with a Salmonella Typhimurium strain harbouring a plasmid which constitutively expressed luxCDABE genes from Photorhabdus luminescens. To our knowledge no live imaging system has been reported in chickens. A major focus of this study is to establish the BLI system in chicken and characterize some of the putative virulence genes in the context of colonization, infection, and persistence of Salmonella Enteritidis (SE) in the host. Virulence genes of interest include: Salmonella Pathogenicity Island 1 (SPI-1), SPI-2, ferric uptake regulator (fur), pagN (i.e., PhoP/Q regulated genes) and tonB (which encodes the energy transducer to facilitate Fe3+ uptake). SPI-1 encodes for both type three secretion system apparatus (T3SS-1, a molecular syringe) and effectors proteins secreted from the bacterium in to the host. The role of SPI-1 is to facilitate cell invasion and subsequent colonization in phagocytic and non-phagocytic cells. The key role of SPI-2 is to aid bacterium's survival inside the phagocytic cells like macrophages, neutrophils and dendritic cells. PagN is an outer membrane protein which act as an adhesin molecule. Fur acts as the global iron regulator which coordinates iron homeostasis inside the bacterium. For example under iron starvation it upregulates various iron uptake system including tonB dependant Fe3+ uptake systems.

Methods: Single gene mutation was accomplished using lambda red system. All mutations were confirmed by DNA sequencing. The lux operon (luxCDABE) from Photorhabdus luminescens was integrated into the SE wildtype and mutant strains, and expressed under a constitutive promoter (sigma 70) to generate a continuous light signal. Chromosomal integration was gained through MiniTn7 vector based transposon method. Specific pathogen free eggs were incubated for 21 days in the VIDO-InterVac animal facility in direct accordance with guidelines drafted by the University of Saskatchewan's Animal Care Committee and the Canadian Council on the Use of Laboratory Animals. Six groups of day-old birds (9 birds per group) were reared in separate rooms with strict biosecurity control avoiding cross contamination. Birds in each group obtained an oral challenge dose of 109CFU of either wildtype or mutant strains. They were euthanized at days 4 and 5 post challenge. At each sampling day birds were subjected to BLI imaging using IVIS Lumina II (PerkinElmer). Cecum content, liver and spleen were sampled for direct SE enumeration on brilliant green agar plates. Selenite broth was used as the enrichment medium to detect Salmonella which were below the detection limit on brilliant green agar plates.

Results: IVIS Lumina II (PerkinElmer) was able to detect bacteria along the digestive tract. Strong bioluminescent signals were detected through ileum, cecum, colon and yolk. None of the mutations in SE did affect the colonization in cecum at both sampling days compared to the wildtype. This observation was confirmed through BLI imaging where cecum generated bioluminescent signals ranging from 1000-2000 cps. The wildtype strain was able to 100% systemically infect both liver and spleen at days 4, 5 post challenge. Compared to the wildtype type reporter strain, the ΔSPI-2 mutant showed significant reduction in colonizing spleen and liver at day 4 post challenge as determined by direct plate counts. Similar results were obtained for the ΔSPI-1 mutant. Even though direct plate results suggested that most of the birds were negative for ΔSPI-1 and ΔSPI-2 mutants, enrichment data revealed that all the birds were systemically infected. Interestingly, the Δfur mutant did not systemically infect all the birds at day 4 post challenge which was confirmed through enrichment using selenite broth. Deletion of TonB showed no significant difference in colonization of spleen and liver compared to the wildtype strain. Similarly, ΔpagN did not affect systemic site colonization at day 4, 5 post challenge. IVIS Lumina II (PerkinElmer) was unable to detect signals from sites of systemic infection such as liver and spleen.
**Conclusion:** Our current bioluminescent reporter system facilitated ex vivo imaging in chicken yet needs further enhancement to improve the detection limit. SPI-1 and SPI-2 have been known to play a major role in colonization and subsequent systemic spread in mammalian models, but in chicken both systems may not be essential. The ferric iron uptake system facilitated through TonB dependent outer membrane receptors may not be important in cecal colonization or the systemic phase of infection during early life of the chicken. The role of outer membrane protein PagN has been described as an invasin and thought to play a T3SS-1 independent mode of invasion in mice. But our data shows that it might not play a role in infection and colonization in day-old chickens. Bacterial global iron regulator gene fur seems to be important in the systemic phase of infection but did not influence cecal colonization in day-old chickens. Further investigation with an extended timeline of monitoring is warranted to elucidate the role of these genes in virulence and persistence in chickens.

**Keywords:** Salmonella Enteritidis, virulence, bioluminescent imaging, chicken

121. Biochemical Characterization of the Human Cytidine Deaminase APOBEC1

**Presenter:** Lai Wong, College of Medicine  
**Supervisor:** Linda Chelico

**Background:** Humans produce many enzymes that can modify the sequences of DNA and RNA to enrich the coding capacity of these biological molecules. APOBEC1 is one of the first modification enzymes identified and was initially discovered to play an essential physiological role in lipid metabolism by enabling two proteins with distinct functions to be produced from the same single-stranded RNA molecule through cytidine deamination into uridine. Since this discovery, APOBEC1 has been found to modify many other RNA and DNA molecules, but the molecular basis by which this is achieved and how the enzyme selects and differentiates between DNA and RNA targets is not known. Importantly, APOBEC1 can exist in cells at the wrong time and place, and under these circumstances it may mutate the genomic DNA driving the cell to a cancerous form. For example, APOBEC1 has been implicated in various cancers including lung, pancreatic, and rectum in which they have been found to contain upregulated levels of APOBEC1. In contrast to the human small intestine where it is primarily expressed, APOBEC1-induced cancers are not observed. We therefore hypothesized that off-target mutations caused by APOBEC1 contributed to cancer mutagenesis and undertook biochemical and structural techniques to study the molecular basis of APOBEC1 function and regulation in normal and diseased cells, particularly to understand how APOBEC1 may access and harm the genomic DNA providing information essential for the development of therapies to prevent this pathogenic activity.

**Methods:** GST tagged-APOBEC1 was expressed in a recombinant baculoviral-Sf9 system and purified using a glutathione resin. APOBEC1 was subjected to thrombin digestion for removal of the GST tag. A deamination assay is used to determine the mechanism(s) in which APOBEC1 uses to search for its target motif as well as processivity. Synthetic fluorescein-labelled single-stranded DNA (ssDNA) with varying distances between two target motifs are utilized. Shorter substrates are ideal for one-dimensional sliding movements whereas longer substrates are ideal for three-dimensional translocations such as jumping and intersegmental transfer. Reactions are carried out at single-hit conditions (<15% substrate usage) to enable determination of a processivity factor. A cycling assay is used to determine the ability for APOBEC1 to cycle on/off fluorescein-labelled ssDNA substrates in the presence of unlabelled trap DNA. Varying concentrations of unlabelled DNA are used in the reaction. Enzymes that can cycle can will not observe a
drastic decrease in percent deamination in contrast to those which cannot. Deamination in the presence of RPA (replication protein A) was assayed similarly to determine if APOBEC1 can displace RPA to access its target motifs. Steady state fluorescence depolarization (rotational anisotropy) is used to determine the binding affinity of APOBEC1 on fluorescein-labelled ssDNA. Enzyme is titrated into a reaction mixture until saturation. Apparent dissociation constants were obtained by fitting to a rectangular hyperbola or sigmoidal curve. Size exclusion chromatography is used to determine the oligomerization states of APOBEC1. Fractions are resolved by SDS-PAGE followed by immunoblotting. Gel band intensities are measured and the molecular weights as well as oligomerization states are calculated from a standard curve.

**Results:** Previous studies with APOBEC3G determined the inhibitory role of RNA and therefore we sought to determine if this was the case for APOBEC1. Treatment of APOBEC1 with various endonucleases found that RNA was present in our purified protein but not DNA. Therefore, we conducted experiments in the presence or absence of RNase A treatment. Size exclusion chromatography revealed that RNase A treated APOBEC1 existed in 4 forms: large oligomer, tetramer, dimer and monomer with the large oligomer being the predominant form. Untreated APOBEC1 was also predominantly expressed as a large oligomer as well as monomer; however, the dimeric and tetrameric forms were not observed. Deamination assays revealed that APOBEC1 was a processive enzyme that utilized a three dimensional jumping mechanism to scan ssDNA but was unable to perform one dimensional localized sliding. The specific activity and processivity was not affected regardless of RNase A treatment which suggests that RNA does not play an inhibitory role unlike previous studies performed with APOBEC3G. Cycling assays revealed that APOBEC1 is able to cycle on/off substrates because it had a minimal decrease in deamination activity in the presence of unlabelled “trap” ssDNA in contrast to APOBEC3G which has been previously shown to be unable to cycle. Deamination experiments in the presence of saturating amounts of RPA on ssDNA revealed a 6-fold decrease in specific activity. A binding constant of approximately 350 nM was determined for APOBEC1 and was unaffected by RNase A treatment. However, a loss of cooperative binding was observed after RNase A treatment.

**Conclusion:** APOBEC1 is a processive enzyme that is able to utilize a three-dimensional jumping mechanism to scan ssDNA but not one-dimensional localized sliding. RNA does not have an inhibitory effect on APOBEC1 unlike previous studies performed on APOBEC3G since it did not affect its processivity as well as specific activity. APOBEC1 is able to cycle on/off ssDNA substrates with a minimal decrease in deamination activity in the presence of trap ssDNA. In contrast with an enzyme that cannot cycle, we saw a large decrease in deamination activity in APOBEC3G. This suggests that APOBEC1 may be able to access ssDNA during dynamic processes such as replication or transcription. However, deamination assays performed in the presence of RPA found that APOBEC1 is unable to displace RPA to effectively deaminate ssDNA and had resulted in a 6-fold decrease in specific activity. This suggests that RPA is a substantial roadblock in reducing APOBEC1 deamination activity on ssDNA. RNase A treated APOBEC1 exists in large oligomeric, tetrameric, dimeric and monomeric forms with the large oligomer being its predominant form. Untreated APOBEC1 existed as an even larger oligomer with noticeably decreased monomeric form. An apparent dissociation constant of 350 nM was determined and was unaffected by RNase A treatment but resulted in a loss of cooperativity. APOBEC1 may be utilizing RNA to oligomerize but since no decrease in processivity or specific activity was observed in our deamination assays, it may suggest that the presence of DNA may be breaking apart large oligomer into smaller active forms. These data provide insights into the biochemical mechanisms in which APOBEC1 may access ssDNA to induce genomic damage.

**Keywords:** APOBEC1, cytosine deamination, enzyme mechanisms, cancer mutagenesis
122. Serotonin effects on inhibition are partially mediated by astrocytic purine release

Presenter: Caitlin Wotton, College of Medicine
Supervisor: Dr. Lane Bekar

**Background:** It is well established that serotonin (5HT) plays a critical role in shaping cortical network activity by affecting inhibition. However, we call in to question the mechanism through which this is thought to occur. Many would argue that 5HT is having its effects via direct action on interneurons. While this may occur, limitations in neuromodulator diffusion, such as degradation and uptake, would limit the ability of 5HT to have rapid actions on these inhibitory networks. We propose that astrocytes, which possess 5HT receptors, the means to influence inhibitory networks via purinergic signaling, and are each in contact with over 100,000 synapses are the ideal intermediary to aid 5HT in rapidly modulating cortical inhibition. Previous publications from our lab indicate 5HT is affecting cortical inhibition via purinergic and GABAergic mechanisms. This study sought to narrow down those mechanisms and establish a role for astrocytes in the 5HT effects on inhibition.

**Methods:** We used both whole-cell patch-clamp technique and field recordings in acutely isolated mouse brain slices.

**Results:** Our results thus far indicate that adenosine A2A and ATP P2Y receptors, which are both previously established to depolarize interneurons, are playing a role in the 5HT effect on cortical networks. In patch recordings, we see that antagonists at the P2Y and A2A receptors block the 5HT increase in spontaneous inhibitor currents. Alternatively, using agonists at these same receptors produces an effect similar to 5HT in field recordings. Finally, a known antagonist of astrocyte metabolism, iodoacetate, was also found to attenuate 5HT effects on inhibition.

**Conclusion:** These results provide evidence for a novel role of astrocytes in shaping the flow of information in the cortex.

**Keywords:** Serotonin, Astrocytes, Whole-cell patch clamp, Electrophysiology, Cortical inhibition

123. Are Enterolactone and Certain TKI Drugs (Ibrutinib, Dabrafenib, and Gefitinib) PPARγ Partial Agonists?

Presenter: Xiaolei Yang, College of Pharmacy and Nutrition
Supervisor: Jane Alcorn

**Background:** Hepatic fibrosis, defined as a wound-healing response, threatens human health worldwide due to the risk of fatal complications such as cirrhosis, liver dysfunction, and hepatocarcinoma. Currently, effective treatments remain elusive. As a wound-healing response, the pathology of hepatic fibrosis is quite complicated and includes inflammatory responses, proliferative dysfunction, and dysregulated protein production and lipid homeostasis. The peroxisome proliferator-activated receptors (PPARs), described as a member of ligand-activated nuclear hormone receptor superfamily, is reported to modulate inflammation, cell proliferation, lipid homeostasis, and wound healing response, and thus plays a role in the pathogenesis of fibrosis. Both literature evidence and previous studies of our lab suggest that lignans and tyrosine kinase inhibitors (TKIs) may bind to PPARγ. Our study aims to confirm whether
enterolactone, an active polyphenolic metabolite of plant lignans, and certain TKIs, multi-target drugs primarily marketed for cancer therapy, are PPARγ agonists or partial agonists prior to their evaluation as possible treatments in hepatic fibrosis.

**Methods:** A PPARγ competitive binding assay was done to assess the binding affinities of enterolactone and three TKIs (ibrutinib, dabrafenib, and gefitinib) to the PPARγ binding site of Rosiglitazone, a known PPARγ agonist. A transactivation assay was applied to detect the transactivities of the compounds in PPARγ-transfected HepG2 cells. Both assays used rosiglitazone and FMOC-L-leucine as controls, which are known PPARγ full and partial agonists, respectively. Subsequently, adipogenesis and glucose uptake assays were performed to confirm the biological function of these compounds, using rosiglitazone and FMOC-L-leucine as controls.

**Results:** The PPARγ competitive binding assay showed that enterolactone and the TKIs, ibrutinib, dabrafenib, and gefitinib, have limited binding affinities to PPARγ. In PPARγ-transfected HepG2 cells, enterolactone, ibrutinib, dabrafenib, and gefitinib showed weak transactivation potential in comparison to rosiglitazone, but similar transactivation as FMOC-L-leucine. The adipogenesis and glucose uptake abilities of enterolactone, ibrutinib, dabrafenib, and gefitinib were similar as that of the PPARγ full and partial agonists.

**Conclusion:** Enterolactone, ibrutinib, dabrafenib, and gefitinib are potential PPARγ partial agonists with similar biological responses in the modulation of PPARγ-related processes in comparison to the known PPARγ full and partial agonists.

**Keywords:** PPARγ, partial agonist, TKIs, enterolactone, hepatic fibrosis

**124. The energy storage and metabolic enzymatic effects of acute naphthalene and pyrene exposure in adult zebrafish (Danio rerio).**

**Presenter:** Chanel Yeung, College of Graduate and Postdoctoral Studies  
**Supervisor:** Lynn Weber

**Background:** Benzo-a-pyrene (BaP), a representative polycyclic aromatic hydrocarbon (PAH), causes adverse cardiorespiratory and metabolic effects in adult zebrafish (Danio rerio), while PAHs such as naphthalene (NAP) or pyrene (PYR) are not well characterized.

**Methods:** We hypothesized that NAP and PYR will cause similar sublethal metabolic impairment to BaP, but via differing mechanisms of oxidative stress and aryl hydrocarbon receptor (AhR) activation, respectively. Adult zebrafish were aqueously exposed to NAP and PYR for 48h (n=16 fish/group).

**Results:** NAP increased citrate synthase expression, yet glycogen stores were unchanged. Fish were unable to metabolize lipids; increase in triglycerides and HOAD in the heart and skeletal muscle. Changes in HOAD expression after PYR do not predict the changes observed in lipid content in all three tissues. CYP4501A expression significantly increased in skeletal muscle and heart, but paradoxically not liver.

**Conclusion:** In conclusion, effects on key metabolic enzymes and energy stores in different tissues in acutely exposed adult zebrafish showed some resemblance to previously reported effects of BaP, but differences were noted among all three PAHs. Surprisingly, the mechanisms of action may involve AhR activation for NAP, but not PYR.

**Keywords:** Naphthalene, Pyrene, Zebrafish
125. Could Targeting Ligands' Size Affect the Delivery of Docetaxel to HER2 Breast Cancer

Presenter: Ayat Zagzoog, College of Pharmacy and Nutrition
Supervisor: Azita Haddadi
Collaborators: Mehran Yarahmadi and Pedram Rafiei

**Background:** This research focuses on the effect of various formulation parameters on targeting human epidermal growth factor receptor-2 (HER2), specifically in breast cancer. Poly (D, L-lactide-co-glycolide) (PLGA) polymer, which is approved by FDA and used to form nanoparticles (NPs) encapsulating docetaxel (DOC) as chemotherapy. The HER2 antibody was decorated on the PLGA NPs, as either whole IgG (TrAb) or fragments (ScFv), and investigated regarding their ability to target HER2 breast cancer cells.

**Methods:** A solvent evaporation technique was adapted to design NP formulations. Incorporation of ligands (TrAb or ScFv) was conducted through chemical conjugation processes. Executing the physicochemical characterization of formulations, so as performing Fourier transform infrared spectroscopy (FTIR) to assess the attachment of different ligands. Also, fully validated mass spectrometry analysis method was used to quantify the loading of DOC. In vitro drug targeting assessed by performing Fluorescence-activated cell sorting (FACS) and western blot.

**Results:** Particle size was measured to be below 400 nm for the modified PLGA NPs with approximately neutral zeta potential. Encapsulation efficiency for DOC reached up to 85% for some formulations, and the amount of anti-HER2 attachment efficiency exceeded 40%. The cellular targeting of nanoparticles was studied using two cell lines (MCF-7 and SK-BR-3), which express different levels of HER2. The significant reduction in the level of HER2 expression was observed for modified NPs in HER2 overexpressed SKBR-3 cells.

**Conclusion:** Our data demonstrated a prospective potentiality for this NPs against different cell lines. Thus, ligand modified structurally concealed PLGA NPs could be a promising delivery tool for targeting HER2 breast tumor in vitro that improves the release of chemotherapy while reducing the side effects.

**Keywords:** PLGA (Poly (D, L-lactide-co-glycolide), Targeting Drug Delivery, Nanoparticles, Human Epidermal Growth Factor Receptor-2 (HER2), Breast cancer

126. The Neuroprotective Effects of Non-competitive AMPA Receptor Antagonist (Perampanel) and A2A Receptor Antagonist (Istradefylline) in a Small Vessel Stroke Model t (Istradefylline) in Ischemic Stroke

Presenter: Michael Zaki, College of Medicine
Supervisor: Francisco S. Cayabyab

**Background:** Extracellular brain adenosine concentrations increase more than 100-fold after pathological trauma such as head injury, hypoxia and ischemia. The neuroprotective effect of adenosine through A1R is short lived as A1R desensitization occurs after 12-24 hour of chronic A1R stimulation. Therefore,
Ischemic stroke is associated with low expression of the neuroprotective inhibitory A1R and high expression of A2AR, which enhances neuronal excitability and glutamate-induced neurotoxicity. We hypothesize that induced neurodegeneration in our in vivo focal cortical stroke model, is mediated by action of elevated adenosine and glutamate on the highly expressed A2AR and calcium-permeable AMPAR, respectively. This can be prevented by administration soon after a stroke of a clinically approved drug Perampanel, a non-competitive AMPAR blocker, or Istradefylline a selective A2AR antagonist.

**Methods:** 1- Pial vessel disruption (PVD) surgery of male Sprague-Dawley rats was used as a model of small vessel stroke, and Perampanel or istradefylline at dose 3 mg/kg was administered by intraperitoneal (IP) injection 1 hr after the surgery.

2- Immunohistochemistry followed by confocal imaging of hippocampal slices was used to assess changes in nNOS and the AMPAR subunits GluA1 and GluA2.

3- Neurodegeneration and non-discriminant hippocampal neuronal damage were as assessed by FluoroJade C and propidium iodide (PI) staining, respectively.

4- Biochemical changes in levels of nNOS and AMPAR subunits were monitored using Western blot analysis, and changes in synaptic transmission was assessed using extracellular field potential recordings (fEPSP) from hippocampal brain slices.

**Results:** Propidium Iodide and Fluoro-Jade C staining showed increased neurodegeneration in hippocampus in PVD group compared to SHAM, Perampanel- and Istradefylline-treated groups. SHAM, perampanel and istradefylline treated groups have lower expression of both nNOS and GluA1 compared to PVD group.

Finally, 200 nM Perampanel significantly inhibited the post-hypoxic synaptic potentiation in fEPSP that occurs after hypoxia/reperfusion and returned the potentiated fEPSP back to baseline levels.

**Conclusion:** Perampanel and Istradefylline exhibit a neuroprotective effect in PVD model, by inhibiting glutamate excitotoxicity mediated by the upregulated expression of calcium-permeable AMPARs and A2AR after ischemic stroke.

**Keywords:** Ischemic stroke, Perampanel, AMPA, A2AR, Adenosine
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