Summer Student Poster Day

Thursday, July 28
2016

Celebrating Excellence in Our Talented Research Community

Welcome to the 2016 Poster Day for the Summer Student Research Program. Each year we host this event to showcase unique and innovative research being conducted by undergraduate and medical students on the Oak Street campus over the summer.

The research community at BC Children's Hospital provides students with a true 'bench to bedside' opportunity for research. Since the early 1990s the Summer Student Research Program has provided 1,000+ undergraduate and medical students an opportunity to participate in research projects related to children's and women's health.

The diversity of the research here is remarkable, it is amazing to see the activities the students are involved with, including basic science, clinical and population health research. Poster Day provides a wonderful preview of the interdisciplinary work our students will pursue as they progress into their own careers as scientific and clinical investigators.

We are proud of the students here and we are pleased to be able to help them become leaders in their respective fields.

Jennifer Myers
Manager, Research Education
BC Children's Hospital, *an agency of the Provincial Health Services Authority*

Thursday, July 28

Poster Presentations
10:00pm
Chieng Family Atrium

Awards Ceremony
1:00pm
Chan Centre for Family Health Education

The ceremony will include the Poster Presentation Finalists

Join us in celebrating the accomplishments of our colleagues and the positive impact of research taking place on the Oak Street campus

Summer Studentships

Congratulations to the following students who received external funding from national, provincial or regional funding agencies for the summer

Ruky Agbahovbe - Deans International Summer Research Scholarship, UCD School of Medicine

Arshia Beigi - NSERC Undergraduate Student Research Award

Anna Black - Michael Cuccione Cancer Research Program Summer Studentship

Ingrid Blydt-Hansen - Childhood Diseases Summer Studentship

Christina Botros - Centre for International Child Health Summer Studentship

Mackenzie Campbell - BC Children's Hospital Research Summer Studentship

Rayleigh Chan - UBC Faculty of Medicine Summer Studentship

Caitlin Courchesne - BC Children's Hospital Research Summer Studentship

Xiaoning Guan - BC Children's Hospital Research Summer Studentship

Jack Huang - BC Children's Hospital Research Summer Studentship

Nicole Janusz - Healthy Starts Summer Studentship

Farnaz Javadian - NSERC Undergraduate Student Research Award

Andy Jiang - BC Children's Hospital Research Summer Studentship

Ellen Jopling - The M.I.N.D Summer Studentship

Derin Karacabeyli - BC Children's Hospital Research Summer Studentship

Kushal Khera - Community Health Summer Studentship

Sophia Kim - Centre for International Child Health Summer Studentship

Laveniya Kugathasan - BC Children's Hospital Research Summer Studentship

Austin Lam - Mental Health Summer Studentship

Marc Levin - BC Children's Hospital Research Summer Studentship

Yuchen Li - CIHR Health Professional Student Research Award

Hong Li - Healthy Starts Summer Studentship

Armaan Malhotra - Evidence to Innovations Summer Studentship

Arshdeep Marwaha - BC Children's Hospital Research Summer Studentship

Sarah Mohn - NSERC Undergraduate Student Research Award

Rotem Moshkovitz - NSERC Undergraduate Student Research Award

Carlie Penner - Childhood Diseases Summer Studentship

Craig Stewart - UBC Summer Student Research Program Award

Luckshika Rajendran - BC Children's Hospital Research Summer Studentship

Ishmeet Singh - The M.I.N.D Summer Studentship

Imelda Suen - Childhood Diseases Summer Studentship

Kendra Underhill - The M.I.N.D Summer Studentship

Avani Varshney - BCCA Translational Research Award

Heidi Vieira - NSERC Undergraduate Student Research Award

Qi Wen - Healthy Starts Summer Studentship

Alexander Wong - BC Children's Hospital Research Summer Studentship

Michael Xu - BC Children's Hospital Research Summer Studentship

Paul Yen - UBC Faculty of Medicine Summer Studentship

Annie Yu - BC Children's Hospital Research Summer Studentship

Lynn Zhang - Canucks for Kids Fund Childhood Diabetes Laboratories Summer Studentship

The BC Children's Hospital research community would like to acknowledge all the above organizations for supporting summer student research opportunities on the Oak Street Campus

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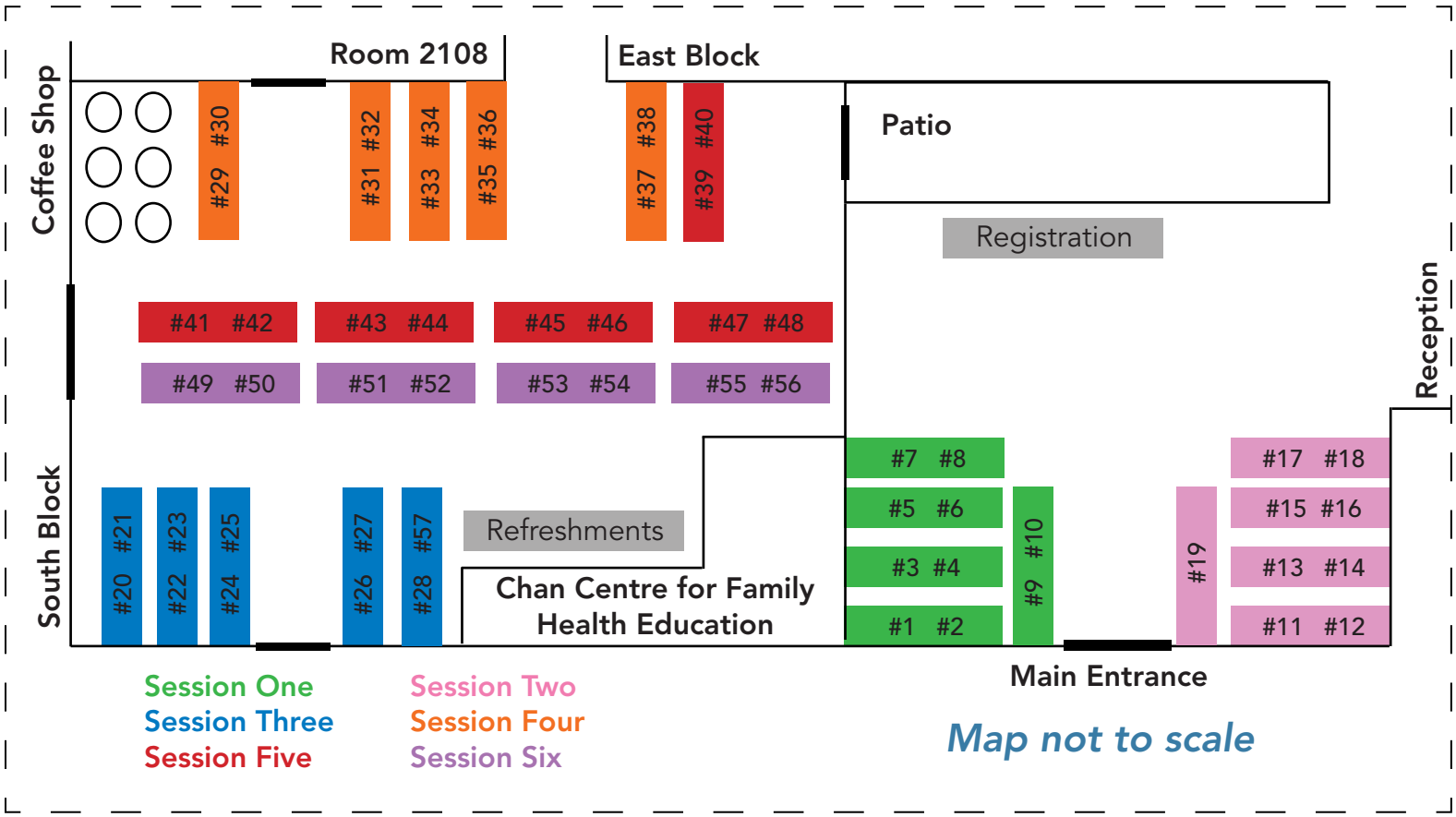

Poster Session One

Basic Science

Moderator:
Folefac Aminkeng

Participants:
Elianne Abramovich
Rumbidzai Chiwaya
Nicole Janusz
Yuchen Li
Arshdeep Marwaha
Andrew Sharon
Imelda Suen
Chin-Vern Tan
Adam Wade-Vallance
Li Qing Wang

Elianne Abramovich, Undergraduate Student, Quest University
Supervisor: Angela Devlin

The effect of maternal obesity and exercise on skeletal muscle gene expression in male offspring

Elianne Abramovich, Nicha Boonpattrawong, Daven Tai, Rika Aleliunas, Ismail Laher, Angela Devlin

Background: The developmental origins of health and disease hypothesis suggests that prenatal and early postnatal environmental factors influence the risk for chronic diseases in offspring, such as cardiovascular disease, later in life. In Canada, approximately 50% of women of childbearing age are overweight or obese. Several studies report increased adiposity and cardiovascular disease risk factors in children born from obese mothers. Accumulating evidence has shown beneficial effects of maternal exercise on the offspring, but the underlying mechanism is not known. Preliminary results from the Devlin Lab showed that exercise intervention in pregnant mice was able to improve glucose tolerance in offspring fed the western diet.

We hypothesized that maternal exercise during pregnancy mitigates the adverse effects of maternal obesity on glucose homeostasis through changes in gene expression in the offspring.

Methods: Female (C57BL/6) mice were weaned onto a control (10% kcal fat) or western diet (45% kcal fat) to induce excess adiposity. At 13 weeks, they were bred and maintained on the diets, with or without access to an exercise wheel. Offspring were weaned onto either the control or western diet and fed for 13 weeks; male offspring were studied. Glucose homeostasis was assessed by intraperitoneal glucose tolerance test (IPGTT). After 13 weeks on diet, skeletal muscle was harvested from the offspring. RNA was extracted from skeletal muscle using the Qiagen RNeasy Mini Kit.

Results: After 13 weeks on diet, control-diet fed offspring from control-diet fed dams that exercised had significantly lower ($p<0.05$) retroperitoneal fat, mesenteric fat, and subcutaneous fat than those from sedentary dams. In western diet-fed offspring, those that were from control diet-fed dams had lower ($p=0.029$) subcutaneous fat than those from western diet-fed dams. Western diet-fed offspring from western-diet fed dams without exercise had greater glucose intolerance (IPGTT area under the curve; $p=0.011$) than those from exercised dams.

Future directions: Maternal exercise during pregnancy improved glucose tolerance in western diet-fed offspring. To determine whether maternal exercise alters gene expression, the extracted RNA will be used to characterize the relative expression of two exercise-regulated genes with roles in glucose homeostasis (Slc2a4 and Pparg1ca) by real-time PCR.

Rumbidzai Chiwaya, Undergraduate Student, University of British Columbia
Supervisor: Suzanne Vercauteren

Exploring the strengths and weaknesses of ATiM database to determine the flow path of its use in the BC Children's Hospital Biobank

Rumbidzai Chiwaya, Suzanne Vercauteren, Tamsin Tarling

Background: The Organization for Economic Co-operation and Development defines a biobank as a "collection of biological material and the associated data and information stored in an organised system, for a population or a large subset of a population." These collections are then made available to researchers. With increase in sample size and number of participants, sample tracking, inventory and annotation play an increased role in biobanking. The BC Children's Hospital BioBank (BCCHB) utilizes the Advanced Tissue Management (ATiM) database to effectively store information on samples from participants consented to the BioBank or specific PI driven studies. The objective of this study is to determine the strengths and weaknesses of ATiM as well as determine the flow path to use ATiM on a daily basis for the BCCHB.

Results: The ATiM database fulfills these tasks: a) supports the BCCHB's daily operations of biospecimen, demographic and clinical data collection b) data repository and biospecimen inventory management system for BCCHB and c) manages research requests for the BCCHB's inventory. Upon arrival of a sample to the BCCHB the collection date, collection site, supplier department, volume of sample and type of collection tube are recorded. The details of the technician who drops, receives and processes the samples are also recorded. ATiM automatically generates codes for each specimen allowing us to print barcoded labels for aliquots.

Future goals: Linking between ATiM and other databases such as Redcap would allow researchers to access their study specimen inventory and annotated clinical data; currently ATiM can only be accessed by BioBank staff. We also aim to include sample volumes and/or cell counts on each printed label for researchers to see before distributing specimen tubes. Monthly updates showing specimen and participant demographics would be useful for documenting the progress of the BioBank. Lastly improving the long term inventory procedure to increase efficiency of storage and decrease the amount of time specimens are kept on dry ice is ongoing.

Conclusion: The BCCHB database efficiently allows data entry and storage efficiency for biobanking purposes and is easily implemented in the daily routine of biobanking. We would like to further the database capabilities in order to continue to meet the growing demands of the BioBank.

Nicole Janusz, Undergraduate Student, University of British Columbia
Supervisor: Michael Kobor

Understanding the effects of truncating Swc4 on yeast's ability to recruit SWR1-C and Nua4

Nicole Janusz, Michael Kobor

The eukaryotic genome is packaged into chromatin, where modifications of this structure by various chromatin-remodelling complexes plays a crucial role in the regulation of many nuclear processes including DNA replication, repair, and transcription. One such complex found in Saccharomyces cerevisiae is SWR1-C, a multi-subunit complex involved in the incorporation of the histone variant H2A.Z into nucleosomes. Swc4, a subunit of SWR1-C, associates with the complex through its C terminus by interacting with Yaf9, another SWR1-C subunit. Previous work has shown that deletion of YAF9 alone leads to a dramatic decrease in Swc4's ability to bind to the SWR1 complex. To date, there are no other known interactions mediating Swc4's association with the complex. Due the fact that Swc4 is an essential gene in yeast, its role in SWR1-C has not been well characterized. In order to gain a more complete understanding of the specific interactions that mediate Swc4's association with the SWR1 complex, we have generated a series of mutant strains harboring increasingly shorter truncations of the Swc4 protein's C terminus. Although truncating the C terminus is a viable mutation, we have shown through phenotypic tests that growth of these truncated strains is compromised when subject to the DNA damage inducing agent - methyl methanesulfanate (MMS) and an inhibitor of DNA synthesis - hydroxyurea (HU). We next performed an immunoprecipitation of Swc4 to determine in which truncations the interaction with either Yaf9 or the SWR1 complex is disturbed. The immunoprecipitation showed that Swc4's association with the SWR1 complex was maintained in all tested Swc4 C terminus truncation mutants. However, we observed a loss of Yaf9 when as few as 24 out of 476 amino acids were removed from the C terminus of Swc4. This suggests that there may be another interaction between Swc4 and SWR1-C maintaining its incorporation in the complex even when the interaction with Yaf9 is lost. Using this set of mutant strains, we will explore the role of Swc4 in SWR1-C biology.

Yuchen Li, Undergraduate Student, University of British Columbia
Supervisor: Wyeth Wasserman

iTFdb: A database of human, manually curated, inducible transcription factors

Yuchen Li, Oriol Fornes, Michael M Gottlieb, Wyeth Wasserman

Gene therapy has re-emerged as a viable treatment for genetic disorders and human diseases. Key is non-insertional gene delivery using adeno-associated virus (AAV) vectors, which persist as episomes in non-dividing cells. Designing minimal promoters that regulate when, where, and to what extent AAV vectors express is an important research goal in gene therapy.

Most AAV-based gene therapies use ubiquitous promoters, resulting in off-target expression and potentially undesired side-effects. In this context, the research community emphasizes the need for selective promoter sequences. The Wasserman lab has designed compact, selective regulatory sequences in three projects: the Pleiades Promoter Project based on transgenic mouse generation, the CanEuCre project featuring AAV-directed gene delivery, and a focused project on aniridia-related expression of the Pax6 gene. The followed approach led to enticing successes, which demonstrate the impact of a robust bioinformatics pipeline for strategic regulatory promoter design. However, the fact that the process is low-throughput and involves hand-design limits its scalability. For this reason, the lab is developing software for the automated selection, design and refinement of cis-regulatory sequences, towards the ultimate goal of advances in gene therapy. The software will incorporate various capabilities, including the modification of cis-regulatory regions to modulate the amount of delivered expression.

One way to modulate AAV vector activity is to design promoter sequences that contain binding sites for transcription factors (TFs) inducible by certain chemicals (iTFs). In this project, we present iTFdb, a database containing all human iTFs and their inducible chemicals.

iTFdb accommodates 4 different types of inducibility: upregulation, downregulation, activation and inhibition. Manual curation of the literature was performed for a total of 1,300 sequence-specific TFs. For each of them, any evidence of inducibility was kept. Evidence included the iTF paper's PubMed ID, link to the PDF file and image of summarized experimental results, annotations on the modelled organism, and the interpreted mechanism of induction. To date, iTFdb contains ~300 manually-curated iTFs.

Future plans to expand iTFdb include using text-mining tools to automate the annotation of iTFs relying on the manually curated iTFs as gold standard to benchmark the approach.

Arshdeep Marwaha, Undergraduate Student, University of British Columbia
Supervisor: Catherine Pallen

The role of PTPα in oligodendrocyte differentiation and remyelination

Arshdeep S Marwaha, Philip T T Ly, Jing Wang, Jie Liu, Wolfram Tetzlaff, Catherine J Pallen

Myelination is the process by which a fatty substance called myelin ensheathes axons to facilitate nerve impulse transmission. Inadequate myelination as occurs in multiple sclerosis (MS) and various pediatric leukodystrophies can result in severe neurological impairment. Promoting endogenous myelin repair (remyelination) is a novel therapeutic strategy to treat MS and related demyelinating diseases.

Our lab has previously shown that receptor-like protein tyrosine phosphatase alpha (PTPα) is important for differentiation/maturation of oligodendrocyte precursor cells (OPCs) into mature oligodendrocytes (OLs), the myelinating cells of the central nervous system. Many molecular events orchestrating OPC differentiation during development and myelin repair are conserved. Therefore, we hypothesize that PTPα regulates OPC differentiation to promote myelin repair after demyelination injury.

To investigate the role of PTPα in OPC differentiation/remyelination, 8-10 week old wild type (WT) and PTPα null (KO) mice were subjected to focal demyelination via intracerebral injection of lysolecithin into the corpus callosum. Brains of these mice were harvested at 7, 14, and 28 days post-injection (dpl) for histological analyses. Luxol Fast Blue stain was performed on stereological coronal brain sections (7 and 14 dpl) to identify myelinated structures in the CNS and confirm the presence of the demyelinated lesion. Furthermore, counterstaining with haematoxylin revealed extensive cell infiltration into the lesioned area. No obvious differences were observed in demyelination and number of infiltrated cells between WT and KO mice. To examine OPC differentiation after injury, we immunostained the brain sections for olig2 (OL lineage marker), CC1 (differentiating OLs), and myelin basic protein (myelin marker). Within the 7 dpl lesion site, the number of olig2+ cells per area was not different between WT and KO brains. However, the number of differentiated OLs (CC1+olig2+) per area was significantly lower in KO brains, indicating defective differentiation/maturation but not impaired cell migration into the lesion site.

Future studies will examine whether differences exist in OPC differentiation and remyelination abilities between WT and KO mice at 14 and 28 dpl. Findings from this study will contribute to the existing knowledge of PTPα's role in OL development and myelination and may provide insights to developing molecularly targeted therapies to treat demyelinating and dysmyelinating diseases.

Andrew Sharon, Undergraduate Student, University of British Columbia
Supervisor: Francis Lynn

The cell cycle regulates the expression of neurogenin 3 in human pancreatic progenitors

Andrew J Sharon, Nicole A J Krentz, Francis C Lynn

Diabetes mellitus is a disease characterized by elevated blood sugar due to the loss of functional insulin-producing beta cells. Transplanting human embryonic stem cell (hESC) derived beta cells reverses diabetes, but these cells are difficult to generate and a greater understanding of human beta cell development is required. As beta cells are formed from NEUROG3+ progenitor cells, we aimed to understand how Neurogenin-3 (NEUROG3) is regulated during hESC differentiation with the goal of improving NEUROG3 expression to produce functional beta cells in culture.

Previously, our lab used CDK inhibitor overexpression in embryonic mouse models to show that CDK inhibition in pancreatic progenitors promotes beta cell differentiation by positively regulating the expression of NEUROG3. Furthermore, rapidly cycling cells with high expression of cyclin-dependent kinases (CDKs) prevent beta cell differentiation by phosphorylating NEUROG3, resulting in its degradation. Because CDKs have been shown to regulate NEUROG3 expression in mice, we hypothesized that human NEUROG3 is regulated in a similar cell cycle dependent manner.

To determine NEUROG3 expression levels at different stages of the cell cycle, a FUCCI hESC transgenic cell line was used to isolate pancreatic progenitors by cell cycle phase. These experiments revealed that NEUROG3 transcription is upregulated 1000-fold in G1 compared to S/G2/M, suggesting that the cell cycle is important for the regulation of NEUROG3 expression. Because CDK inhibition in mice promoted expression of NEUROG3, the effects of inhibiting CDKs on NEUROG3 expression in hESC-derived pancreatic progenitors were investigated. Treatment with CDK inhibitors resulted in a 1.1-fold increase the proportion of cells in G1, leading to a 3-fold increase in NEUROG3 transcription during G1. To investigate the effects of this increase on the number of cells expressing NEUROG3, a reporter hESC line co-expressing NEUROG3 and GFP was used. Treatment with CDK inhibitors resulted in a 1.5-fold increase in the number of NEUROG3 expressing cells, suggesting that NEUROG3 expression is negatively regulated by CDKs.

Together, these results show that human NEUROG3 expression is regulated by CDK activity, and suggests that CDK inhibitors could be used to drive beta cell differentiation of hESC-derived pancreatic progenitors.

Imelda Suen, Undergraduate Student, University of British Columbia
Supervisor: Bruce Verchere

The role of islet amyloid polypeptide aggregation in autoimmune diabetes and islet allograft rejection

Imelda W Suen, Heather C Denroche, Kiana Yau, Galina Soukhatcheva, Derek Dai, C Bruce Verchere

Background: Type 1 diabetes results from autoimmune destruction of insulin-producing beta cells. Replacing beta cells by islet transplantation is a potential cure for diabetes, but most transplants fail within several years. Failure is due to multiple factors, including the host immune response to the foreign graft (alloimmunity) and recurring beta cell autoimmunity. Islet amyloid polypeptide (IAPP) can aggregate to form amyloid, a pathological feature of transplanted islets associated with poor graft function. IAPP aggregates recruit and activate macrophages in transplanted and endogenous islets, inducing pro-inflammatory cytokine production.

Hypothesis: By inducing inflammation, IAPP aggregates accelerate the auto- and alloimmune attack of beta cells, thus contributing to the progression of diabetes and islet transplant rejection.

Methods: Mice transgenically expressing human IAPP (hIAPP) were used, as rodent IAPP does not aggregate. The transgene was backcrossed onto the NOD genetic background (a model of autoimmune diabetes) using speed congenics, generating hIAPP transgenic and non-transgenic littermates. Mice were tracked up to 30 weeks of age for the spontaneous development of diabetes (two consecutive measures of blood glucose > 20 mmol/L). To test allograft rejection, islets from wildtype or hIAPP transgenic donors were transplanted into genetically mismatched recipients made diabetic with streptozotocin. Blood glucose was tracked to monitor islet graft rejection, and grafts were harvested for histological analysis.

Results: In mice that are 97 ± 1% on the NOD background (backcrossed five times), there is no difference in time of diabetes development between hIAPP transgenic and non-transgenic controls (P=0.94), and only 40% developed diabetes. However, preliminary data from mice backcrossed six times suggest greater diabetes incidence earlier in the hIAPP transgenic mice. In the allogeneic transplant experiments, hIAPP transgenic islet allografts show a trend towards faster rejection (26.5 days, versus over 80 days for wildtype islets; P=0.06), and increased immune infiltration in grafts..

Conclusions: While currently unclear whether IAPP aggregation accelerates autoimmune destruction of beta cells in NOD mice, our preliminary data suggest IAPP aggregation promotes islet allograft rejection, implicating IAPP as a possible contributor to islet transplant failure.

Chin-Vern Tan, Undergraduate Student, University of British Columbia
Supervisor: Elizabeth Simpson

Single-copy site-specific cre-driver mouse strains for advancing eye and brain research

Chin-Vern Tan, Andrea J Korecki, Siu Ling Lam , Jack W Hickmott, Oliver Baker, Russell J Bonaguro, Michelle Zhou, A Francis Stewart, Daniel Goldowitz, Wyeth W Wasserman, Elizabeth M Simpson

Background: Cre recombinase is an enzyme that catalyzes specific DNA modifications, allowing for genomic manipulation. By recognizing loxP sites, the cre/loxP system allows investigators to generate knockout mice, deleting a specific gene of interest in a particular tissue or cell type. Researchers can pair cre resources with loxP flanked mice available through public repositories to determine the function of specific genes. Large-scale efforts such as the International Knockout Mouse Consortium, which aims to develop mutations in all protein-coding genes, depend upon inactivation of their conditional alleles by cre-recombinase.

Purpose: This project seeks to expand the number of cre resources available to the research community, specifically cre-drivers that target the central nervous system (CNS). Further development of cre resources targeting the CNS will allow researchers to study specific areas and their involvement in brain and eye disease. We have used single-copy site-specific knock-ins to generate a large number of mouse strains. The constructs feature a MiniPromoter driving first an inducible, then a constitutive, improved cre (icre) allele.

Methods: MiniPromoters driving an inducible icre/ERT2 fusion protein were cloned into Hprt homologous-recombination targeting vectors. Using mouse embryonic stem cells, chimeras were generated and bred to produce germline offspring. A subset of both inducible and constitutive strains were bred to a reporter mouse which requires cre activity to allow tdTomato (a red fluorophore) expression. Adult offspring were processed from both strains, with the inducible strain first being fed a diet of tamoxifen food for 4 weeks. Animals were perfused and the tissues were examined for tdTomato epifluorescence.

Results: In total, 17 MiniPromoter icre/ERT2 strains were established and histological examination of four strains, both inducible and constitutive alleles, was performed. Both the inducible and constitutive cre alleles showed expression in various parts of the eye including subsets of retinal and corneal cell types.

Conclusions: This resource of mouse strains demonstrates the feasibility of single-copy site-specific knock-ins for the generation of a large number of cre-driver strains. As both constitutive and inducible cre alleles were developed, it provides a set of important tools for basic and preclinical eye and brain research.

Adam Wade-Vallance, Undergraduate Student, McMaster University
Supervisor: William Gibson

Ep300/Crebbp deletion within the Islets of Langerhans impairs glucose homeostasis and upregulates Npy

Adam Wade-Vallance, Chi Kin Wong, William Gibson

Introduction: We previously encountered a patient with monogenic diabetes and a heterozygous inactivating Ep300 mutation causal for their Rubinstein-Taybi Syndrome (RTS). This project explores potential causality for Ep300 defects in monogenic diabetes. Ep300 encodes p300, a master regulator that makes up the p300/CBP coactivator family along with its highly homologous paralog CREB binding protein (CBP). Both proteins are lysine-acetyltransferases (LATs) which function as coactivators of transcription. Previously, we demonstrated that Ngn3-Cre Ep300fl/fl mice were glucose intolerant due to hypoinsulinemia and that Ngn3-Cre Ep300fl/flCrebbpfl/WT mice displayed a ubiquitously more severe phenotype. Sequencing of islet mRNA from Ep300fl/fl mice revealed an extreme upregulation of a paracrine transmitter known to impair insulin secretion, Npy. This investigation examines the differences between Ngn3-Cre Ep300fl/fl, Ngn3-Cre Ep300fl/flCrebbpfl/WT mice and their wildtype counterparts with regards to Npy gene and protein expression.

Results: Ep300 deletion was verified by reverse transcription quantitative real-time PCR (RT-qPCR) in both Ep300fl/fl and Ep300fl/flCrebbpfl/WT mice and by immunofluorescence staining in Ep300fl/flCrebbpfl/WT mice. Islet-derived mRNA from both knockout models was ~15-fold Npy enriched compared to wild type islet mRNA as revealed by RT-qPCR. Contrary to Ep300fl/fl RT-qPCR results, results from Ep300fl/flCrebbpfl/WT mice exhibited ~70% reduced Ins1 and Ins2 mRNA. Immunofluorescence staining of Ep300fl/fl pancreata revealed an increased proportion of NPY+ positive β-cells compared to wildtype mice.

Conclusion: NeuroD-null mice exhibit glucose homeostasis defects and upregulated Npy, phenotypes reminiscent of our knockout mice. As Npy is known to impair glucose-stimulated insulin secretion, it could be culpable for the impaired glucose homeostasis of the knockout models. Importantly, NeuroD is an insulin transcription factor whose activity is modulated by p300/CBP-dependent acetylation. Therefore coactivator deletion could abolish acetylated NeuroD, resulting in not only upregulated Npy and impaired glucose homeostasis but also the downregulation of Ins1 and Ins2 mRNA in Ep300fl/flCrebbpfl/WT mice.

Li Qing Wang, Undergraduate Student, University of British Columbia
Supervisor: Wendy Robinson

Assessing the correlation between CCR5Δ32 and A/G (rs1799987) polymorphisms and preeclampsia

Li Qing Wang, Samatha L Wilson, Maria S Peñaherrera, Wendy P Robinson

Background: Preeclampsia (PE) is a serious pregnancy complication that occurs in ~5% of pregnancies and is characterized by hypertension (high blood pressure) and proteinuria (high amounts of protein in the mother's urine). These symptoms can result in impairment of major body systems of the pregnant mother and preterm delivery of the baby, rendering PE a major contributor to maternal and fetal morbidity and mortality. The underlying cause of PE is unclear but both genetic and physiological factors are thought to contribute. The CCR5 gene codes for a pro-inflammatory protein receptor. The binding of chemokines to this receptor promotes inflammation and may influence preeclamptic symptoms. A 32 base pair deletion in this receptor gene (Δ32), which encodes for a dysfunctional receptor, has been associated with a lower risk of PE in several studies. The allele frequency of this mutation differs across ethnicities, indicating a possible relationship between parental ethnicities and PE. Similarly, the CCR5 A/G promoter point mutation (rs1799987) has also been observed to associate with PE susceptibility; however, opposing evidence has been found in different populations. The objective of our study is to determine whether either the CCR5Δ32 mutation or the A/G promoter point mutation is correlated with a lower risk of PE in our Vancouver population.

Methods: Gel electrophoresis and pyrosequencing will be used to detect the Δ32 and A/G polymorphisms in extracted DNA from 115 maternal blood samples and 164 placental villi samples. Analysis: We will first determine if the genotypic frequencies of these two mutations differ amongst ethnicities in a Canadian population. If positive, ethnicity will be corrected for in subsequent analyses. It will also be determined whether this correlation is stronger in maternal or fetal genotype. Additionally, if both Δ32 and rs1799987 confer reduced susceptibility to PE, we will investigate whether the effects of the two mutations are independent of each other.

Significance: Correctly identifying genetic contributors to PE enable better prediction of PE during pregnancy. The results of this research provide a testable genetic variant that may enable early identification of women who are prone to develop PE and would benefit from increased monitoring and preventative treatment.

Poster Session Two

Basic Science

Moderator:
Philip Ly

Participants:
Arshia Beigi
Saelin Bjornson
Anna Black
Christina Botros
Aishwi Roshan
Kendra Underhill
Heidi Vieira
Paul Yen
Lynn Zhang

Arshia Beigi, Undergraduate Student, University of British Columbia
Supervisor: Stefan Taubert

Relationship between vitamin B12 and mediator MDT-15 in caenorhabditis elegans

Arshia Beigi, Grace YS Goh, Stefan Taubert

It has long been known that diet affects gene regulation and organismal phenotypes, but a significant number of the genetic components allowing this adaptation are still unknown. For example, feeding the nematode worm Caenorhabditis elegans, a powerful genetic model organism, a bacterial diet of Comamonas aquatica (CA) instead of the standard Escherichia coli (EC) lab diet causes dramatic changes in gene expression and life-history traits including developmental rate, reproduction and lifespan. The key metabolic compound in the CA diet is vitamin B12, which in mammals is required for embryonic development and cardio-metabolic health.

We have recently found that worms lacking mdt-15, a conserved transcriptional co-regulator, show near-complete embryonic lethality on EC, whereas a CA diet almost completely rescues this phenotype. Therefore, we hypothesized that the same compound (vitamin B12) is responsible for the observed rescue in mdt-15 reduction-of-function (rf) worms. To this end, we grew mdt-15(rf) worms on B12-supplemented EC diets, and compared embryonic lethality with mutants fed non-supplemented EC. Interestingly, we found that B12 partially restored the hatching success rate of mdt-15 worms. In addition to embryonic lethality, mdt-15 (rf) worms show shortened lifespan, reduced brood size and slower pharyngeal pumping rate among other phenotypes. Current work is underway to determine the effects of introducing CA (and B12) on these phenotypes. Further experiments will focus on determining the main pathway by which B12 exerts its effects on the mdt-15(rf) worms. Collectively, this work will determine the role of a conserved transcriptional co-regulator as a genetic buffer for developmental events against adverse environmental effects.

Saelin Bjornson, Undergraduate Student, University of British Columbia
Supervisor: Laura Sly

The role of MALT1 in macrophages

Saelin Bjornson, Mahdis Monajemi, Susan Menzies, Laura Sly

MALT1 is a signaling molecule that plays a role in immune homeostasis. A key role for MALT1 in inflammation was recently demonstrated when a patient deficient in MALT1 developed severe combined immunodeficiency. MALT1 has both a scaffolding role and protease activity, and acts downstream of lymphoid and myeloid cell receptors. Through its scaffolding role it helps to form the CBM (CARD9-BCL10-MALT1) complex, which relays signaling events that increase inflammatory responses through activation of Nuclear Factor kappa B (NF-kB). As a protease it is responsible for the cleavage of substrates (BCL10, A20, CYLD and RelB) which can increase or decrease inflammatory responses.

Previous studies on the role of MALT1 in inflammation have focused on lymphocytes, but its role in macrophage-mediated inflammation has not been investigated. Based on this, we hypothesize that MALT1 deficiency causes inflammation by increasing the macrophage inflammatory responses. To test our hypothesis, we activated murine macrophages through dectin1, dectin-2, and toll-like receptor 4 (TLR-4) and examined both MALT1 expression and proteolytic activity. We also compared pro-inflammatory cytokine production in Malt1 deficient and Malt1 protease-inhibited macrophages to wild-type cells.

Our results show that macrophage activation increases MALT1 expression and decreases MALT1 activity. We have also found that Malt1 deficient macrophages produced lower levels of inflammatory cytokine than wild-type cells, whereas pharmacological inhibition of MALT1 activity produced higher levels of inflammatory cytokines. Taken together, our studies are consistent with a model in which MALT1 activity reduces pro-inflammatory macrophage responses but its scaffolding function increases macrophage inflammatory responses. This directs us to future studies where we will examine MALT1 expression and activity in vivo in mice. These studies will provide critical information about the cell specific role of MALT1 and possible side effects of MALT1 inhibitors currently used for lymphoma treatment.

Anna Black, Undergraduate Student, University of British Columbia
Supervisor: Christopher Maxwell

Cell division and genome integrity require the cytoskeletal protein RHAMM

Anna Black, Helen Chen, Christopher Maxwell

Chromosome movement during mitosis requires precise control of microtubule dynamics by motor proteins. Specifically, chromosome segregation is restricted by the spindle assembly checkpoint until all chromosomes are attached at their kinetochores to the mitotic spindle. Balanced forces exerted by antagonistic motors regulate chromosome attachment to the mitotic spindle and mitotic progression from metaphase to anaphase. Outward forces generated by plus-end directed motors, Eg5 and Kif15, are opposed by inward forces generated by dynein. Motor activities are regulated by non-motor adaptor proteins such as TPX2, and dysregulated activities induce aberrant spindle architecture and mitosis arrest. We showed that silencing the spindle assembly factor RHAMM delayed the progression to anaphase due to sustained activation of the spindle assembly checkpoint. Analysis of fixed cells showed reduced tension at kinetochores, suggesting stable kinetochore-microtubule attachments are absent with RHAMM loss. Re-expression of GFP-RHAMM recovered mitotic kinetics and kinetochore tension while the re-expression of GFP-RHAMM mutants indicated the requirement of a known TPX2- and dynein-interaction domain. Co-precipitation identified complexes between RHAMM and TPX2, dynein, or Kif15, but not Eg5; TPX2-Eg5 complexes attenuate Eg5 motor activity and we found that the depletion of RHAMM reduced the reciprocal co-precipitation of TPX2-Eg5 complexes suggestive of augmented Eg5 activity. Small-molecule inhibition of Eg5, but not the co-depletion of dynein light chain 1, recovered mitotic kinetics and kinetochore tension in RHAMM-depleted cells. These data indicate a requirement for RHAMM to promote the formation of inhibitory TPX2-Eg5 complexes, which balance molecular motor activities necessary to establish tension at kinetochores and promote the completion of the spindle assembly checkpoint prior to the initiation of anaphase.

Christina Botros, Undergraduate Student, University of British Columbia
Supervisor: Soren Gantt

Correlates of aquisition and immune control of primary human herpesvirus infections in Ugandan infants

Christina Botros, Jessi Tuengel, Soren Gantt

Human herpesviruses are ubiquitous viruses that typically cause asymptomatic infections in most patients but are nonetheless associated with substantial disease burden worldwide. Because these viruses are so common, infection with one or more of them usually occurs early in life. As a result, it's difficult to capture and analyze primary infections of these viruses due to their asymptomatic nature in children.

In order to learn more about primary herpesvirus infections in children, our lab established a prospective cohort in Kampala, Uganda consisting of mothers and newborn infants, as well as the siblings in the family. The purpose of this cohort was to capture the time points in which infection by these viruses was occurring, in order to analyze primary infection and the related immune responses in infants. Saliva and blood samples were collected at regular intervals for a median follow-up time of 57 weeks. In total, there were 113 participants.

Our objective is to determine what immune responses are being used at different stages of the infection cycle, thus correlating immune responses with viral loads. The viral loads have already been determined via qPCR reactions. This information will help to inform further vaccine studies and treatment techniques.

Using flow cytometry, we are able to analyze the various populations of immune cells via surface markers. One specific marker that we're interested in is CD21, which is a complement receptor on B cells; it's also the receptor for one of the human herpesviruses – Epstein Barr Virus (EBV).

It's known that CD21 expression is age-dependent, increasing with age. By using flow cytometry with the various time points for each patient, we can look at CD21 expression over time, and whether the degree of expression differs between HIV-exposed infants and HIV-unexposed infants. We hypothesize that HIV exposure accelerates the expression of CD21 in infants, thus resulting in earlier infection with Epstein Barr virus.

Aishwi Roshan, Undergraduate Student, University of British Columbia
Supervisor: Tobias Kollmann

Exploring G-CSF production as a potential mechanism behind granulocyte expansion in the non-specific effects of BCG vaccination

Aishwi Roshan, Nelly Amenyogbe, Byron Brook, Cai Bing, Daniel He, Tobias Kollmann

Background: Sepsis is one of the leading causes of neonatal deaths every year, claiming more than one neonatal life per minute around the world. It was determined in humans that the Bacillus Calmette-Guerin (BCG) vaccine, given at birth to protect against Tuberculosis, reduces mortality from all deaths, particularly infections, by more than 50%. This form of protection is coined as a non-specific effect (NSE). Given the powerful potential to save millions of lives, the World Health Organization (WHO) has declared elucidating a mechanism behind BCG's NSE an urgent priority before repurposing of the vaccine will be considered.

Overview: From experimentation using a C57Bl/6 mouse model, it was determined that BCG vaccinated mice had a significant increase of protective granulocytes than that of the control group. The aim of this project is to determine the biological mechanisms behind the protection against mortality. Given that an expansion of granulocyte precursors in bone marrow and spleen were also detected, we hypothesize that BCG vaccination triggers an increase in granulocyte colony-stimulating factory (G-CSF), and subsequently induces emergency granulopoiesis (EG). Our secondary hypothesis is that G-CSF production is completely mediated by the MyD88 signalling pathway.

Methods/Results: Mice were vaccinated at day of life 4-5, and sacrificed 24 hours after. Luminex bead-based multiplex assay was employed to determine the concentrations of G-CSF, Il-6, and GM-CSF in the plasma of vaccinated and unvaccinated mice. Our data indicates that concentrations of G-CSF are significantly higher in BCG vaccinated wild type mice. MyD88 knockout mice underwent the same protocol to inquire of its contribution as a signalling pathway in G-CSF production. The G-CSF concentrations from BCG vaccinated MyD88 knockout mice is significantly different than unvaccinated mice. Thus we can conclude that the MyD88 pathway is not required to induce G-CSF signalling.

Significance: Despite its success in reducing neonatal mortality, BCG is not administered for its non-specific protection against sepsis. Costing only a mere 9 cents per dose, BCG has the potential in being the world's most cost-effective intervention against newborn deaths yet.

Kendra Underhill, Undergraduate Student, University of British Columbia
Supervisor: Christine Tipper

Brain processes underlying action understanding

Kendra Underhill, Christine Tipper

How does the brain understand actions? This fMRI study investigated action understanding as a step toward elucidating the brain basis of social and cognitive deficits associated with developmental disorders such as autism spectrum disorder and ADHD. In particular, we tested whether a hypothesized system of sensorimotor neurons that fire both when actions are seen and performed, known as the "mirror neuron system", plays a direct role in the neural coding of the physical means of an action and/or its outcome. Mirror neurons have been postulated to support action understanding by generating a neural simulation of observed actions. To date, however, there is little direct evidence that mirror neurons actually exist in humans, and if present, what specific elements of actions they encode to support social understanding.

To identify brain regions that exhibit mirror neuron response properties, we recorded fMRI while participants performed a virtual reality task in which action sequences were either observed or executed. A vetted fMRI technique known as repetition suppression (RS) enabled the identification of cortical networks that contained neural populations that coded for either the physical means of an action or the specific outcome of an action, responding identically regardless of whether that action was seen or performed. Observing this "agent-independent" RS for action coding would reveal brain regions with the dual "see-do" functionality of mirror neurons.

Using an fMRI analysis technique known as constrained principal component analysis (CPCA) we identified two functional networks that exhibited agent-independent RS for coding action means. The first network linked medial frontal, inferior frontal gyrus, premotor, and superior temporal sulcus regions, showing significant RS ($p < 0.05$) for executing a previously observed action. The second network linked superior and inferior parietal and temporal parietal junction regions, showing significant RS ($p < 0.05$) for observing a previously executed action.

These early results provide evidence for a human mirror neuron system that is directly involved in coding the physical means by which an action is performed.

Heidi Vieira, Undergraduate Student, University of British Columbia
Supervisor: James Lim

Characterization of Integrin α6 (CD49f) isoforms in triple negative breast cancer

Heidi Vieira, Karen Jung, Pascal Leclair, Chinten James Lim

Integrin α6 (CD49f) is a cell surface receptor protein with roles in cell signalling and adhesion. Increased expression of integrin α6 in breast cancer cells has been associated with more rapid disease progression as well as reduced survival time (Brooks et al., 2016).

There are two splice isoforms of this integrin, α6A and □6B, which differ in both the length and composition of their cytoplasmic tail (Hogervorst et al., 1991). As the cytoplasmic domains determine the specificity of integrin-mediated signaling, we hypothesized that the two integrin α6 isoforms may have distinct roles in breast cancer cell tumourigenicity.

To examine whether tumourigenic potential is correlated with differential integrin α6 isoform expression, we profiled the mammosphere forming efficiency across a panel of 12 breast cancer cell lines and compared it to their α6A and α6B expression. The mammosphere assay has been shown to enrich for a stem-like, tumourigenic population of cells (Lombardo et al., 2015). We found a correlation between increased mammosphere-forming ability of breast cancer cell lines and high integrin α6B isoform expression, indicating a correlation between α6B and tumourigenic phenotype. Furthermore, the stem-like population of cells harvested from the mammosphere assay had upregulated α6B isoform levels compared to tissue-cultured cells of the same cell line. The upregulation was consistent across cell lines, and was sustained through mammosphere passaging. This finding is suggestive of a cytoplasmic tail-specific role of the integrin α6 isoforms in tumourigenicity.

To assess the functional role of integrin α6, we then used CRISPR-Cas9 silencing to generate an α6 knockout in the MDA-MB-231 cell line; the knockout was confirmed via flow cytometry analysis. Preliminary results show that α6 knockout cells exhibit reduced mammosphere-forming ability. Further work is ongoing to explore isoform-specific changes in tumourigenesis through selective re-expression of α6A or α6B isoform in these knockout cells.

Characterizing the role of integrin α6 isoforms in tumourigenesis will lead to an advance in the understanding of their functional roles across breast tumour subtypes and intratumour cell subpopulations, offering potential drug targets for breast cancer treatment.

Paul Yen, Undergraduate Student, University of British Columbia
Supervisor: Bruce Verchere

Preservation of pancreatic beta cells via inhibition of islet amyloid formation

Paul P H Yen, Jaques A Courtade, Yi-Chun Chen, Derek L Dai, Paul C Orban, C Bruce Verchere

Background: Islet amyloid polypeptide (IAPP), a hormone co-secreted with insulin from pancreatic beta cells, aggregates to form insoluble amyloid plaques, pathological markers of beta cell death and dysfunction. A specific inhibitor (identity is confidential) has been demonstrated to reduce amyloid plaque deposition in a mouse model of Alzheimer's disease. We hypothesize that this inhibitor may similarly reduce islet amyloid formation, based on the common beta sheet-rich structure of all amyloid-forming proteins.

Aim: We aim to determine whether the inhibitor has the ability to reduce the degree of amyloid deposition and beta cell apoptosis in cultured islets.

Methods: To assess the inhibitor's ability to obstruct IAPP aggregation in vitro, we utilized a thioflavin T assay to track aggregation of human IAPP over time, with or without the inhibitor. To translate these results to an ex vivo setting, wild type mouse or human IAPP transgenic mouse islets were isolated, and incubated with or without inhibitor for 7 days in 22.2 mM glucose media. Thioflavin S was used to stain amyloid fibrils. Two parameters were used to quantify the degree of amyloid deposition: amyloid severity (% amyloid-positive area) and amyloid prevalence (% amyloid-positive islets). TUNEL staining was used to identify and quantify apoptotic beta cells.

Results: In vitro, the inhibitor strikingly blocks IAPP aggregation in a concentration-dependent manner. Cultured human IAPP-expressing islets treated with inhibitor had similar amyloid severity and amyloid prevalence compared to untreated controls. Despite there being no observable differences in amyloid deposition, islets treated with the inhibitor developed a trend toward decreased beta cell apoptosis. It is unknown whether this is a result of reduced IAPP aggregation or off-target effects, yet it suggests that the inhibitor may promote improved beta cell health.

Summary and Future Directions: These findings suggest that the inhibitor is very efficacious when it comes to obstructing IAPP aggregation in a concentration-dependent manner in vitro. However, ex vivo, the inhibitor does not seem to induce significant changes in amyloid deposition, but potentially reduces beta cell apoptosis. Future work should be focused on performing more biological replicates, investigating the stability of the inhibitor, and characterizing its mechanism of action.

Lynn Zhang, Undergraduate Student, University of British Columbia
Supervisor: Jan Dutz

Methotrexate as a JAK inhibitor to treat and prevent Type 1 Diabetes

Lynn Zhang, Carol Dou, Yiqun Zhang, Jan Dutz

Hypothesis: Methotrexate, an affordable oral medication, is currently used to treat inflammatory diseases such as Crohn's disease and rheumatoid arthritis. Recent studies suggest that the suppression of the JAK/STAT pathway is the primary anti-inflammatory mechanism-of-action of low-dose methotrexate. A novel application of methotrexate is as a potential treatment for Type 1 diabetes: we hypothesized that when administered to non-obese diabetic (NOD) mice, methotrexate would act as a JAK inhibitor to inhibit insulitis and diabetogenic immune responses, ultimately delaying the onset of Type 1 diabetes.

Method: Female NOD mice were injected intraperitoneally with either methotrexate (1 mg/kg) or PBS as a control for 10 consecutive days. The mice's pancreases were harvested to assess insulitis by immunohistochemistry, and pancreatic lymph node (PLN) cells were obtained to detect immune cell function by flow cytometry.

Results: Insulitis scores were significantly lower in methotrexate-treated NOD pancreas than in control NOD pancreas ($p < 0.001$). Enumeration of PLN cells revealed that there were 25% less cells in methotrexate-treated PLNs ($p < 0.02$). Flow cytometric analysis revealed that CD69 expression on CD4 and CD8 T cells decreased in methotrexate-treated PLNs compared to control PLNs, indicating that methotrexate treatment does inhibit T cell activation. Furthermore, the expression of pSTAT3 and pSTAT5 in CD4 T cells were highly inhibited in methotrexate-treated PLNs compared to the control, indicating that one possible mode of action of methotrexate is through the inhibition of the JAK/STAT pathway.

Conclusions: Methotrexate inhibits insulitis and T cell activation in an NOD mouse model. Future studies on methotrexate include investigating whether its immunosuppressive effect delays the onset of Type 1 diabetes.

Poster Session Three

Basic Science

Moderator:
Laura Cook

Participants:
Ruky Agbahovbe
Hong Li
Amy Poon
Aria Shokoohi
Craig Stewart
Avani Varshney
Tariq Vira
Michael Xu
Kiana Yau

Ruky Agbahovbe, Medical Student, University College Dublin
Supervisor: William Gibson

Utilizing detailed phenotyping to interpret variants in patients with rare overgrowth syndromes

Ruky Agbahovbe, Ana SA Cohen, William T Gibson

Although individually uncommon, approximately 1 in 12 Canadians, two-thirds of them children, are affected by a rare disorder. These disorders are usually sporadic, which means family studies are not appropriate. Many patients with these genetic disorders spend years pursuing a definitive diagnosis, a process referred to as "diagnostic odyssey". With the advancement of sequencing technologies and decrease in costs, we can now examine all of an individual's genes using whole-exome sequencing (WES). The exome refers to the protein coding portion of the genome and contains approximately 85% of known disease-related variants. Every individual (healthy or diseased) has hundreds of unique variants in their exome. Most of these are benign and reflect normal variation, making results difficult to interpret. To address this, our study utilizes detailed phenotyping of patients with undiagnosed rare overgrowth syndromes to better interpret the coding variants that may cause disease.

We performed WES in undiagnosed patients from our overgrowth cohort. For most patients, there was no obvious causative variant and thus we analyzed the participants' clinical records to look for phenotypic traits that may lead us to novel candidate genes. After further mining of the WES data, we prioritized possible disease causing variants. This selection was made based on their biological function, the frequency of the variant in the general population and the likelihood of the variant producing a protein with altered function. Once the candidate variants were chosen, these were validated in the proband using Sanger sequencing. Subsequently, because we are looking for de novo variants, the same technique was used in the parents to determine the inheritance of the variants. Rare de novo variants in our candidate genes may be able to explain the etiology of undiagnosed overgrowth cases.

Hong Li, Undergraduate Student, University of British Columbia
Supervisor: Pascal Lavoie

Unique phenotype and functional characteristics of neonatal naive CD4 T cells

Hong Li, Elizabeth Marchant, Hamid Reza Razzaghian, John Priatel, Pascal M Lavoie

Background: Neonates are highly susceptible to infections due to vulnerabilities of their immune system. Previous studies have shown that neonatal naïve CD4 T cells exhibit rapid production of a non-glycosylated intracellular form of IL-4 (ngIL-4, a Th2 archetypal cytokine), and IL-8 (a powerful neutrophil chemoattractant chemokine) upon stimulation. However, not much is known about the phenotype of these innate-like neonatal T cells and their specific role in responses to infection.

Methods: Naïve CD4 T cells were isolated from neonatal cord blood and adult peripheral blood and stimulated with different strengths of anti-CD3/CD28 in vitro for 0, 24, and 48 hours. NgIL-4 and IL-8 secretion were measured by ELISA, and intracellular cytokine staining (flow cytometry). We also assessed the function of IL-8 via migration assays using neonatal and adult neutrophils. Finally, we performed a screening for developmental characteristic surface markers expression only on neonatal cells using a novel differential gene expression dataset (arrays).

Results: Neonatal naïve CD4 T cells produced high levels of IL-8 rapidly, within <24 hours and required strong anti-CD3/CD28 stimulation, whereas adult naïve CD4 T cells produced this chemokine at much lower level only later (>24-48h). Neonatal neutrophils were attracted by IL-8 (recombinant). IL-8 producing cells in both neonates and adults expressed high levels of the surface markers CD31, CD38, and CD127, and neonatal IL-8 producing cells seemed to distinctly express CD93, CD96, and IL-27Rα, which was not detected in adult cells.

Conclusions: Our findings suggest that naïve neonatal CD4 T cells are phenotypically distinct from their adult counterpart, and that IL-8 production occurs rapidly upon strong antigenic stimulation. The innate-like features of neonatal T cells and the biological attractive effect on neutrophils (an important cell type in responses to infection) may be indicative of an important role of these cells in neonatal immune defense. Future experiments are underway to understand the phenotypic and functional relationships of IL-8 and ngIL-4-producing neonatal CD4 T cells.

Amy Poon, Undergraduate Student, University of British Columbia
Supervisor: Stefan Taubert

Adaptation to environmental stress via the transcriptional coregulator MDT-15

Amy Poon, Naomi Shomer, Stefan Taubert

Early development of an organism may be impaired by environmental and nutritional stresses. Specific gene expression programs are activated in order to adapt to chemical or dietary stresses and to protect against damage by detoxifying the stressor. MDT-15 is a transcriptional coregulator that coordinates protective gene programs in response to multiple stressors, including environmental contaminants (organic carcinogens, heavy metals), dietary changes (vitamin B12 deficiency) and temperature changes. Therefore, we hypothesized that environmental stresses would cause an increase in MDT-15 protein abundance as an adaptive response to aforementioned stresses (feedback regulation).

Experiments were carried out in the powerful model organism Caenorhabditis elegans (a nematode worm), in which MDT-15 and its regulatory pathways are conserved. Based on preliminary data, MDT-15 transcription (mRNA level) is not altered by stress. To measure MDT-15 protein abundance, we used a worm strain harbouring an epitope tag fused to MDT-15 protein (3xFlag-MDT-15). Synchronized worms were exposed to an organic carcinogen (vs. solvent), a vitamin B12 deficient diet (vs. standard laboratory diet), or different temperatures (vs. growth at standard 20°C). We then performed Western blots to compare MDT-15 protein levels in all these conditions (compared to actin or GAPDH control). We found that MDT-15 protein abundance was increased substantially in several conditions where mdt-15 is required for adaptive responses. These results confirm strong induction of MDT-15 as an adaptive response to stress. Collectively, this project has provided new insights into the interplay between metabolic gene expression and changing environmental conditions.

Aria Shokoohi, Undergraduate Student, University of British Columbia
Supervisor: Daniel Goldowitz

Investigating the genes that modulate the effects of prenatal alcohol exposure on the developing mouse brain

Aria Shokoohi, Emilie Théberge, Mike Xu, Kristen M Hamre, Daniel Goldowitz

Fetal Alcohol Spectrum Disorder (FASD) is the most prevalent developmental disability among children in Canada, and encompasses a range of birth defects caused by prenatal alcohol exposure. Previous research has shown a strong correlation between alcohol consumed by the mother during pregnancy and the effects on fetal development. The brain is a specific and vulnerable target of alcohol's impact. It has been demonstrated that cells of the developing brain can undergo death following alcohol exposure. However, the underlying pathways by which alcohol acts remain largely unknown. The purpose of our research is to identify genes responsible for mediating the extent of alcohol's effect on brain development. Mouse embryos were orally gavaged with alcohol on embryonic day 9.0 (E9.0) and examined the amount of ethanol-induced cell death within the forebrain and the brainstem. Cell death was determind by labelling apoptotic cells through terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL) staining and then calculating the density of dying cells witin the different regiosn using ImageJ. GeneNetwork, an open-access mouse genome database, was used to evaluate potential genes of interest. Our results thus far have shown likely candidate genes on Chromosomes 10 and 19 that mediate alcohol's effect in the forebrain. In addition, we were able to narrow the QTL on Chromosome 14, which mediates cell death in the brain stem, from 178 candidates down to 12. One of these candidates is bone morphogenic protein 4 (BMP4), which has previously been shown to induce apoptosis in neural crest cells. Ultimately, our research has important preventative therapeutic implications by furthering our understanding of developmental processes in the brain impacted by alcohol.

Craig Stewart, Undergraduate Student, University of British Columbia
Supervisor: Catherine Pallen

PTP Alpha (PTPα) relays laminin-induced signals to promote NDRG1 phosphorylation and oligodendrocyte maturation/ differentiation

Craig Stewart, Philip T T Ly, Catherine J Pallen

Myelination in the central nervous system (CNS) ensures efficient transmission of nerve impulses necessary for normal cognitive and motor functions. Prior to CNS myelination, immature oligodendrocyte precursor cells (OPCs) must differentiate through a series of steps, involving changes in morphology and gene expression, to form mature myelinating oligodendrocytes (OLs) that can ensheathe axons. Inadequate myelination or myelin damage occurs in diseases such as multiple sclerosis and pediatric leukodystrophies, and often results in debilitating cognitive and motor impairments.

PTP alpha (PTPα) is a brain-enriched receptor-like protein tyrosine phosphatase. PTPα-mediated cell signaling is important for CNS myelination as indicated by impaired myelination in the brains of PTPα-deficient (αKO) mice. Our previous work has revealed an essential role for PTPα in transmitting signals mediated by the extracellular matrix factor laminin to promote OPC differentiation; as in contrast to laminin-stimulated wild-type (WT) OPCs, OPCs lacking PTPα (αKO) have reduced expression of the mature OL marker myelin basic protein (MBP). These αKO OPCs also fail to elaborate cellular processes. Laminin stimulation in other cell types has been shown to induce phosphorylation of the tumor suppressor protein NDRG1. Although NDRG1 is expressed in OLs, its function in these cells, and how this is influenced by its post-translational modification, is unknown. We investigated if NDRG1 was altered upon laminin-induced OPC differentiation using the mouse OPC cell line, Oli-neu. We observed increased NDRG1 expression in Oli-neu cells that were differentiated in the presence of laminin. Increased phosphorylation of NDRG1 also correlated with laminin-induced differentiation, which was PTPα−dependent. Furthermore, siRNA-mediated depletion of NDRG1 prevented morphological differentiation, as these cells were unable to form complex cell branching morphology.

Altogether, our findings reveal a novel role for NDRG1 in regulating OPC differentiation, and demonstrate that NDRG1 acts as an effector of laminin/PTPα-mediated pro-differentiation signaling. By improving the understanding of the molecular pathways that orchestrate OL maturation, we may enable the development of novel and effective treatments to promote myelin repair in demyelinating and dysmyelinating diseases.

Avani Varshney, Undergraduate Student, University of British Columbia
Supervisor: Kirk Schultz

Phenotypical characterization of the CD56bright NK regulatory cells in G-CSF mobilized peripheral and marrow stem cell

Avani Varshney, Amina Kariminia, Kirk R Schultz

Allogeneic blood and marrow transplantation (BMT) is the only successful, well-established form of immune therapy for refractory and high-risk hematopoietic cell malignancy. One of the major long term complications of BMT is chronic graft-versus-host disease (cGvHD), a condition in which immune cells from the transplanted donor immune system recognizes the recipient tissues as foreign. Chronic GVHD usually occurs after 3 months and up to 3 years after transplantation and can cause chronic disease in any organ of the body with the most common organs being the skin, hair, tendons, mouth, eyes, vagina, and lungs. These patients have a high mortality as well as a very high life long morbidity including cardiovascular disease, infections, mobility issues, and diabetes mellitus. Thus, identifying biomarkers that can predict the development of cGVHD are to allow for early preemptive therapies to prevent cGVHD. Our lab has previously found that lower percentages of donor CD56bright NK cells were significantly associated with a higher frequency of cGvHD. To date we know these cells are CD3-, NKp46+, CD16, and non-cytolytic. We hypothesized that ex vivo isolation and expansion of this cell population followed by adoptive transfer may be used to decrease or treat cGvHD. In the present study, we proposed to better characterize the CD56bright populations as a first step in understanding how this population can be isolated and utilized to prevent cGvHD in recipients following BMT. We attempted to comprehensively characterize the NKreg cell subpopulation phenotypically using approximately 65 BMT donor samples. We utilized multi-colour cytometry to investigate the expression of surface markers: CD3, CD56, CD27, CXCR3, CD158b, CD94, CD69, CD314, CD122, CD11b, NKB1, CD117, CD226, CD16, CD45RA, CCR6, CD25, CCR7, and CD127. Using comprehensive subpopulation characterization, we evaluated which subset within the donor regulatory CD56bright cells correlated most closely with development of cGvHD. We also evaluated whether the same CD56bright NK cell subpopulation in the donors persisted in patients who did not develop cGvHD and may be considered immunologically tolerant 3 months after transplantation. The results of these experiments will be a critical building block toward developing NKreg therapy to minimize or prevent cGvHD in BMT.

Tariq Vira, Undergraduate Student, University of British Columbia
Supervisor: Laura Sly

MAPK dependent IL-10 production in pooled Immunoglobulin G-activated human macrophages

Tariq Vira, Lisa Kozicky, Sue Menzies, Laura Sly

Inflammatory bowel disease (IBD) is an immune-mediated disease characterized by chronic inflammation of the gastrointestinal tract. 40% of patients are expected to become treatment resistant; the development of new therapeutics to treat patients with IBD is urgently needed. Macrophages initiate the immune response, promoting the inflammation that characterizes IBD, as well as terminate the immune response. The Sly lab has shown that macrophages treated with pooled Immunoglobulin G (IgG) can be skewed into an anti-inflammatory phenotype in response to an inflammatory stimulus, bacterial lipopolysaccharide (LPS). IgG and LPS treated macrophages show increased production of the anti-inflammatory cytokine IL-10 and decreased production of pro-inflammatory cytokines. Production of IL-10 can be attributed to activation of Mitogen-Activated Protein Kinases (MAPKs) Erk1/2, Erk5, and p38, when mouse macrophages are treated with IgG and LPS. Based on these findings, we ask whether MAPKs are required for the production of anti-inflammatory IL-10 and reduction of pro-inflammatory cytokines in IgG treated human macrophages. Blood was collected from healthy control volunteers and their peripheral blood monocyte-derived macrophages were stimulated with LPS, pooled IgGs, or both, in the presence or absence of MAPK inhibitors: Erk1/2 inhibitors (SCH772894 and PD98059), p38 inhibitors (SB203580 and BIRB796), and Erk5 inhibitors (BIX02189 and XMD8-92). The production of cytokines IL-10, IL-12/23p40, IL-6, and TNF, were assessed using an Enzyme Linked Immunosorbent Assay (ELISA). Our results show the MAPKs Erk1/2, Erk5, and p38 are involved in both the production of IL-10 and the reduction of pro-inflammatory cytokines in IgG and LPS stimulated macrophages. Our results are consistent with mechanistic findings in mouse macrophages. These findings provide improved understanding of the IL-10 production mechanisms, which can be use to develop more effective macrophage targeted therapeutics. In the future, we will examine whether gene variants in the IgG receptor correlate with MAPK induced IL-10 production.

Michael Xu, Undergraduate Student, University of Toronto
Supervisor: Glen Tibbits

Cytosolic Ca2+ regulation in atrial specific Sodium Calcium Exchanger (NCX) Knockout (KO) mouse

Michael H Xu, Grace C Renfrew, Helen Sheng, Glen F Tibbits, Leif Hove-Madsen

Atrial fibrillation (AF) is a supraventricular tachycardia and has been associated with increased intracellular calcium in atrial cardiomyocytes. In our previous studies involving the characterization of sodium-calcium exchanger (NCX) knockout (KO) mice, we observed shared features between NCX KO mice and human AF patients, including dilated atrial chamber and dysfunctional atrial contraction. Due to the importance of NCX in calcium efflux, we suspected that the absence of the protein NCX greatly affects calcium homeostasis in atrial cardiomyocytes, contributing to arrhythmogenesis, and that the presence of β-adrenergic receptor agonists might exacerbate this effect.

Single atrial cells were isolated from either NCX KO or wild type (WT) mice hearts through retrograde perfusion of a collagenase containing solution via Langendorff preparation. These cells were loaded with Fluo-4-AM, a Ca2+ indicator that exhibited increased fluorescence upon calcium binding. Ca2+ transients were then recorded via a 16 MHz resonance scanning confocal microscope with and without electrical stimulation for 30 seconds each. Selective (i.e. fenoterol) or non-selective (i.e. isoproternol) agonists with selective β1 (betaxolol) or β2 (ICI-118,551) antagonists were administered to the perfusate at specific concentrations between recordings and the resultant calcium transients were recorded. A custom-written program was used to analyze the calcium transient and quantify the amplitude (change in fluorescence), full duration half-maximum (duration of transient at half-maximum amplitude), and calcium events (spontaneous waves, mini-waves, and sparks).

Our results thus far indicate significantly elevated baseline levels of cytosolic calcium at rest (0.5 ΔF/F0 vs 0.06 ΔF/F0, $p<0.05$), decreased full duration half-maximum time (287 ms vs 449 ms, $p<0.05$), and increased time spent above 90% amplitude threshold (19.5s vs 12.3s, $p<0.05$) in NCX KO mice compared to WT. Isoproterenol elevated baseline levels at rest (0.49 ΔF/F0 vs 0.059 ΔF/F0, $p<0.05$) and caused increasing baseline and amplitude levels during stimulation in KO mice while WT mice maintained constant levels in both.

Our next step is to perform more trials with different stimulation challenges along with the application of other β-agonists to further understand the mechanism of arrhythmogenesis. We will also continue to analyze existing data for calcium events for use as a marker of arrhythmia.

Kiana Yau, Undergraduate Student, University of British Columbia
Supervisor: Bruce Verchere

The role of islet amyloid polypeptide (IAPP) aggregates in the activation of the Nlrp3 inflammasome

Kiana W Yau, Heather C Denroche, Imelda Suen, C Bruce Verchere

Background: Islet-amyloid formed by aggregates of the beta-cell derived hormone, IAPP, is thought to contribute to beta-cell dysfunction in type 2 diabetes, but the mechanism is unclear. We previously found that IAPP aggregates recruit macrophages to pancreatic islets and induce secretion of interleukin-1β which impairs beta-cell function. The Nlrp3 inflammasome plays a central role in the inflammation by processing mature interleukin-1β. Previous in vitro studies have shown that this process is dependent on the activation of the Nlrp3 inflammasome by soluble IAPP aggregates and mature fibrils.

Aim: We aimed to determine whether Nlrp3 deficiency attenuates islet inflammation and beta-cell dysfunction in a mouse model of islet amyloid induced diabetes.

Methods: We crossed hIAPP transgenic (hIAPPTg/0) mice (rodent IAPP cannot aggregate) with global Nlrp3 knockout mice to generate hIAPPTg/0 mice and hIAPP0/0 controls with (Nlpr3+/-) and without (Nlrp3-/-) functional Nlrp3. Mice were fed chow diet (6% fat) and blood glucose and body weight monitored from 8 to 31 weeks of age. A glucose tolerance and insulin tolerance test were performed at 14 and 30 weeks of age respectively.

Results: ANOVA analysis of blood glucose data collected up to 19 weeks of age shows that genotype has a significant effect on glycemia (p=0.0031). Expectedly, hIAPPTg/0 mice displayed a trend toward hyperglycemia relative to hIAPP0/0 mice. While Nlrp3 deficiency lowered blood glucose in hIAPP0/0 mice, interestingly, there was a trend toward exacerbated hyperglycemia in hIAPPTg/0;Nlrp3-/- mice relative to hIAPPTg/0;Nlrp3+/- controls. Presence of hIAPPTg/0 significantly impaired glucose tolerance (p=0.0381). However, there was no difference between hIAPPTg/0;Nlrp3+/- and hIAPPTg/0;Nlrp3-/- mice. Insulin sensitivity appears to be similar between hIAPPTg/0;Nlrp3+/- and hIAPPTg/0;Nlrp3-/- mice based on preliminary data.

Conclusions: Despite its known contribution to hIAPP-induced inflammation in vitro, our data indicate that the Nlrp3 inflammasome acts to limit hIAPP-induced hyperglycemia in vivo. This appears to be an amyloid specific response, as Nlrp3 deficiency lowers blood glucose in mice lacking hIAPP. We will continue to monitor the mice up to 31 weeks of age. Plasma insulin, pro-insulin, and cytokines will be quantified, and pancreas histology performed to assess islet inflammation, islet amyloid formation, and beta-cell mass.

Poster Session Four

Clinical, Population Health & Health Services

Moderator:
Kathryn Duff

Participants:
Maria Bleier
Ingrid Blydt-Hansen
Ross Gardner
Jazzmin Grose
Ellen Jopling
Laveniya Kugathasan
Marc Levin
Sarah Mohn
Qi Wen
Alexander Wong

Maria Bleier, Undergraduate Student, University of British Columbia
Supervisor: Sylvia Stockler

Patient/caregiver online surveys on the natural history of very rare diseases: MPS IV B/late-onset GM1 (LO-GM1) as an example

Maria B Bleier, Nataliya Yuskiva, Maria Bolduta, Tina Priest, Sylvia Stockler-Ipsiroglu

Objectives: Knowledge on the natural history and presentation of MPS IV B (Morquio B) and late-onset GM1 gangliosidosis (LO-GM1) is currently limited. This study investigates the long-term outcomes of medical interventions and their effects on the quality of living and on healthcare interactions for patients and families who have this rare inborn error of metabolism.

Design and Methods: This study utilizes a qualitative online survey to collect cross-sectional data from patients and families where these rare diseases are present. The survey contains 72 questions organized in 7 sections as follows: patients' demographics, their health, quality of life, access to healthcare, diagnostic history, lifestyle, and participation in research and clinical trials. Patient advocates reviewed the survey questions and provided valuable feed-back for each of the 7 sections. REDCAP is the secure platform used to create the survey and also to collect and store data. The study link is hosted by a parent support group website (morquiob.com), by the National Organization for Rare Diseases (NORD at rarediseases.org) page, and supported by patients and families on social media groups on Facebook.

Results: There is evidence available within REDCAP and on social media that the survey is well received, with 15 completed submissions (out of 25 hits) between March and July, 2016. The survey will be available for a year and data analysis will be completed after closing, in March 2017. We expect the outcomes reported by patients and their families to give us an insight on the variety of unique and overlapping manifestations of Morquio B and LO-GM1 from childhood to adulthood. The relationships between the number and degree of medical interventions and the self-reported quality of life will provide valuable information on ways to improve clinical approaches to symptom management, as well as current treatment methods.

Conclusions: We expect the study results to improve and create new tools for counseling newly diagnosed patients with regards to health issues, opportunities, and limitations in their everyday lives. The natural history data collected will also contribute to the establishment of clinically meaningful outcomes for trials which observe the effects of newly developed therapies.

Ingrid Blydt-Hansen, Undergraduate Student, Queen's University
Supervisor: Kathryn Selby

A Cross-Canada perspective on the impact of steroids on the need for surgical correction for scoliosis in males with Duchenne Muscular Dystrophy

Ingrid Blydt-Hansen, Christopher Reilly, Kathryn Selby

Introduction: It is widely accepted that the use of steroids in Duchenne Muscular Dystrophy (DMD) help to prolong ambulation, delay the onset of cardiomyopathy, improve lung function and reduce the need for scoliosis surgery. To date, there have been multiple single-centre investigations on the impact that steroids have on the need for surgical intervention, though none has been performed on a national scale in Canada. The aim of this observational review is to investigate the impact that steroids have on the need for scoliosis surgery in Canadian males with DMD.

Hypothesis: Steroids significantly reduce the need for scoliosis surgery in boys with DMD.

Methods: The Canadian Neuromuscular Disease Registry (CNDR) was utilized to extract the necessary data. The CNDR is a nation-wide registry comprised of patients with neuromuscular disease that provides access to de-identified data, enabling clinical research and facilitating access to novel neuromuscular therapies for Canadians affected by neuromuscular disease. Patient data is updated to the CNDR following routine clinic visits and chart review of registered neuromuscular patients. Variables including steroid use, presence of scoliosis and surgery for scoliosis, ambulatory status and age were collected from the CNDR for male DMD patients. Patients were separated into specific age groups to correlate stage of disease and scoliosis progression; subsequent analysis of these groups will provide insight into the impact of steroids on scoliosis progression and the need for surgery. Data will also be analyzed by province to account for differences in practice at centres across the country.

Discussion and Significance: Investigating the impact of steroids on scoliosis surgery through the CNDR will help to determine this relationship in Canada. Documenting the introduction of steroids and the need for surgical correction of scoliosis will also inform us of the prevalence of steroid utilization in males with DMD registered with the CNDR. These results will prove invaluable in standardizing best practices across the country, and provide insight into the progression of DMD.

Ross Gardner, Undergraduate Student, University of British Columbia
Supervisor: Kevin Harris

Validation of the FitBit Charge Heart Rate™ device to monitor physical activity in children with congenital heart disease

Ross Gardner, Christine Voss, Paige Dean, Kevin Harris

Background: Commercial wearable activity trackers, like the FitBit™, may be useful to monitor and promote activity in children. However, these trackers are designed for adults and it is unclear whether they are valid for use in children. The aim of this study was to determine whether the FitBit Charge HR™ accurately estimates daily step counts in a pediatric population.

Methods: Eligible participants (10-18yrs) were recruited from the Children's Heart Centre at BC Children's Hospital and partnership clinics across the province of British Columbia. Participants were fitted with an accelerometer positioned over the right hip (Actigraph LLC; 'criterion') and a wrist-worn FitBit Charge HR™ ('measure'). Participants were asked to wear both devices simultaneously for 7 consecutive days. We retrieved daily sums of step counts from valid accelerometry days, which was defined as monitor wear time of ≥600 minutes/day (Actilife LLC). We paired these days with corresponding daily step counts from the FitBit™ for analyses. A subset of participants underwent exercise tolerance testing while wearing the FitBit™ to validate its heart rate tracking feature. We calculated intra-class correlation coefficients (ICC) and mean bias (criterion-measure) with 95% limits of agreement (95%LoA) to estimate agreement between devices.

Results: Twenty-eight participants (13.6±2.2yrs, 57%female) provided 127 person-days of data. Overall, there was a strong association between the two devices for daily step counts across person-days (ICC=0.868, $p<0.001$). However, FitBit™ devices systematically recorded more steps than accelerometers (10,489±5,333 vs. 8,104±4,147 steps/day) with a mean bias of -2,386 steps/day (95%LoA= -7,420-2,649). We were unable to assess the validity of the FitBit™ heart rate tracking feature during exercise tolerance testing because of electromagnetic interference from clinical equipment, which temporarily impacted the data recording ability of the FitBit™.

Conclusion: FitBit Charge HR™ devices are a valid tool to assess patterns in daily step count in a pediatric population; however, caution is required when comparing FitBit Charge HR™ step counts to physical activity studies that are based on the more conservative criterion measure.

Jazzmin Grose, Undergraduate Student, University of Guelph
Supervisor: Amrit Dhariwal

Clinical outcomes following the mind-body connection group-based family intervention

Amrit Dhariwal, Theresa Newlove, Marilyn Ransby, Andrea Chapman

Pediatric somatization creates a significant burden on the medical system, and children and families can suffer for prolonged periods if they do not receive appropriate treatment. When considering the full spectrum of somatization disorders (e.g., somatic symptom disorders, medical disorders with a component of somatization, and conversation disorders), there are no high-level empirically-validated treatments for children and adolescents. Existing treatments using a randomized-control trial (RCT) approach pertain to single symptom pediatric disorders (e.g., recurrent abdominal pain) and rely heavily on cognitive behaviour therapy (CBT). Thus, our research looks to the adult literature for treating multiple disorders of somatization within one treatment paradigm. In particular, an RCT approach has shown therapeutic benefits of integrating elements of client-centered and emotion-focused therapy (EFT) in with CBT to alleviate somatic distress. Promising new studies are suggesting these treatment components may also be of help to children, adolescents, and their families in areas such as somatic symptoms, emotional well-being, and parent-child relationships. Emerging research further suggests that the treatment of somatization can be successful when implemented within a group setting. As such, the MBC group treatment was designed to be administered in groups of youth and the content to be in line with client-centered, EFT, and CBT perspectives. Specific treatment elements include involving parents as significant others in the program, listening to and validating families' medical journeys, providing information on the perplexing mind-body connection, and emphasizing emotional processing and responsiveness.

The objective of the current research is to evaluate whether MBC is linked with changes in participants' functioning post-intervention compared with baseline on variables including level of somatic symptoms, emotion regulation, and parent-child attachment. Fifty-two families of youth (11-17 years) participated in MBC. Parent and youth report questionnaires were administered at baseline and post-intervention. Data will be analyzed to identify any significant changes over time. Findings from this study may have profound implications for the pediatric somatizing population. In particular, it may provide a juncture to turn towards psychological services, in addition to medical services, for care and monitoring.

Ellen Jopling, Undergraduate Student, Queen's University
Supervisor: Ali Eslami

Suicide attempts in pediatric emergency psychiatry: Demographic and clinical correlates of the lethality of suicide attempt

Ellen Jopling, Sinéad Nugent, Ali Eslami

We aim to develop a stronger understanding of the clinical presentation and demographic characteristics of youth admitted to the Child and Adolescent Psychiatric Emergency (CAPE) inpatient unit at BC Children's Hospital between 2009 and 2014 due to suicide attempt. Additionally, we endeavor to investigate the prognostic value of various demographic and clinical features in predicting the medical and potential lethality of suicide attempts in youth.

In this retrospective chart review, patients presenting due to suicide attempt were identified using the Discharge Abstract Database. Our sample (N=112) includes patients 10-17 years of age (75% female). Information collected includes sex, age, season of admission, type of attempt, actual medical lethality and potential lethality of attempt (with ratings based on the Columbia Suicide Severity Rating Scale (C-SSRS)), primary diagnosis on both admission and discharge, and psychiatric comorbidities. Data was analyzed using SPSS v24. Patient demographics and clinical factors were examined using descriptive statistics and linear regression.

Descriptive statistics indicated: a bi-modal pattern of seasonality with 12.5% of presentations each in April and October, an over-representation of suicide attempts via self-poisoning (78.4% of admissions) and of Major Depressive Disorder diagnoses (36.4% of patients). Further, linear regression analyses demonstrated that our predictors (sex, age, type of attempt, season of admission, discharge diagnosis, number of comorbidities, length of stay) accounted for over a third of the variability in medical lethality R2 0.34, $F(18, 91)=2.25$, $p=.008$. In addition, summer admission, suicide attempt via jumping, and a discharge diagnosis of Borderline Personality Disorder significantly predicted medical lethality. A second linear regression demonstrated that predictors including sex, age, season of admission, discharge diagnosis, number of comorbidities, and length of stay accounted for over a quarter of the variability in potential lethality R2 .256, $F(15, 105)=2.07$, $p=.019$. In addition, male sex and summer admission predicted the potential lethality of suicide attempt.

These findings have direct implications both for the strategic care of adolescents admitted due to suicide attempt (reactive), as well as for all adolescents presenting with suicidal ideation (proactive). Ultimately, these findings may guide the design and implementation of future suicide prevention measures.

Laveniya Kugathasan, Undergraduate Student, University of British Columbia
Supervisor: Deborah Giaschi

Reading ability of children treated for amblyopia

Laveniya Kugathasan, Marita Partanen, Deborah Giaschi

Amblyopia is a developmental visual disorder affecting approximately 4% of the population. It is characterized by decreased visual acuity in an otherwise healthy eye and cannot be fixed with the use of corrective lenses. Amblyopia also impairs other aspects of visual perception, including motion and depth perception, and possibly reading ability. Previous studies have examined the effect of amblyopia on reading ability, but the findings have been mixed due to a lack of consistency in documenting treatment status, as well as to the failure to use standardized tests to evaluate reading ability. It is important to use standardized tests to determine if a child is eligible for reading support at school. Currently, it is unknown if reading ability is impaired in children who have been successfully treated for amblyopia. Thus, the goal of this study is to administer standardized reading tests to evaluate reading in children treated for amblyopia. We will use two control groups and one experimental group. The first control group will consist of children with healthy vision and the second control group will consist of children with strabismus without amblyopia. The experimental group will consist of children treated for amblyopia. We hypothesize that children with amblyopia will show deficits in reading rate, accuracy, and fluency relative to both groups of children without amblyopia, but not relative to the normative sample used to standardize the reading tests. If our hypothesis is not supported and the children with amblyopia show deficits relative to the normative sample, these children may require adjustments and additional reading support in school to accommodate their educational needs. Furthermore, it is important to know if current treatment for amblyopia fails to correct an important life skill like reading.

Marc Levin, Undergraduate Student, Queen's University
Supervisor: Caron Strahlendorf

The use of ward-based dopamine therapy to treat septic shock in pediatric oncology patients at British Columbia Children's Hospital

M. Levin, C Strahlendorf, J Potts

Introduction: The prognosis for children with cancer has improved considerably in the past decade, mostly due to increases in the specificity of treatments. Unfortunately, these treatments can result in patients becoming immuno-compromised, increasing their susceptibility towards complications such as infection, sepsis and septic shock. Multiple organ failure and death may ensue. Fluids and first line therapy with pressor agents like dopamine are often used as first-line therapy, with escalation of drug therapy and more complex treatment necessitating transfer to the Intensive Care Unit (ICU). Dopamine is an attractive therapeutic agent to use in cases of septic shock and heart failure because it is easily titratable, provides protection to organs like the brain and kidneys during periods of low perfusion and hypoxia, and is relatively inexpensive to use. Therapeutic interventions which can delay or prevent ICU admissions are very cost-effective from a health care economics perspective. The purpose of this study was to review the medical records of pediatric oncology patients who were treated for septic shock with dopamine at British Columbia Children's Hospital (BCCH) with a specific aim to: (1) determine the incidence of ICU admissions for septic shock in patients treated with dopamine; and (2) perform an economic analysis to determine whether or not treatment with dopamine results in reduced hospital-related costs for these patients.

Methods: This is a retrospective cohort study involving pediatric oncology patients with septic shock who were treated as in-patients with dopamine at our hospital between January 1, 2000 and December 31, 2015. A review of the available clinical records has been completed, with further interrogation of ICU databases and hospital medical records pending. Data was entered into a database using REDCap software and hosted by the Research Institute at BCCH. The data was analyzed using SAS v9.4 Statistical Software (SAS Institute, Cary, NC).

Results: Preliminary data have been retrieved and analyzed for 90 patients. Notable findings include: ICU admission was prevented in 45% of patients with septic shock who were administered dopamine; all of the patients had at least one dopamine infusion, 57% required two infusions and 29% required three or more infusions; 7% of patients died. No results from the economic evaluation of dopamine use are currently available.

Conclusions: Compared with the adult literature, a higher incidence of patients were admitted to the ICU. Despite this, 45% of patients remained on the ward, indicating that treatment with dopamine on hospital wards may result in considerable health care savings. We hope that our study will provide pilot data to support current ward-based clinical practice guidelines for treating septic shock with dopamine and guide future cost-benefit studies and clinical trials.

Sarah Mohn, Undergraduate Student, University of British Columbia
Supervisor: Guy Dumont

Removing motion artifacts from pulse oximetry signals

Sarah Mohn, Roberto Pagano, Erin Cooke, Guy A Dumont, J Mark Ansermino

Background: Pulse oximetry evaluates the cardio-respiratory function of patients by non-invasively measuring blood-oxygen arterial saturation (SpO2) and heart rate (HR). Pulse oximetry nowadays is considered a standard of care in the operating room and intensive care unit, helping to prevent permanent brain damage or death caused by low SpO2. However, in many developing countries there is a lack of pulse oximeters available due to their high cost. In the last four years, the collaboration between the UBC Electrical and Computer Engineering in Medicine (ECEM), LionsGate Technologies Inc., and the Pediatric Anesthesia Research Team (PART), has led to the development of a smartphone-based Pulse-Oximeter. External hardware is minimal and inexpensive, with a sensor that connects to smartphones through the audio port. The electrical signals produced by the sensor are photoplethysmographs (PPG), which can be used to measure HR and SpO2.

Problem: ECEM and PART are now developing a neonatal and pediatric versions of the phone oximeter; however, the PPG signals are very sensitive to external motion. Motion causes PPG signal distortions, which calculate incorrect SpO2 and HR calculations, causing false alarms to go off. As false alarms become common, medical staff responding to the alarms become desensitized and more likely to respond slowly to real alarms.

Solution: We are currently developing an algorithm using advanced signal processing to identify and remove motion artifacts from the phone oximeter's PPG signals using concurrent accelerometer-based movement recordings. Our method involves removing the PPG signal's direct current component, a high pass filter removing frequencies below 0.25Hz, and a motion detection algorithm that compares each pulse in the PPG signal to a mean pulse. We are currently working on a Least Mean Square Adaptive Filter to filter out the motion recorded by the accelerometer. The elimination of motion artifacts will result in a high quality PPG signal that can be used for in-depth and goal directed analyses, with robust results than can be relied on for clinical purposes.

Qi Wen, Undergraduate Student, Langara College
Supervisor: Sarka Lisonkova

Temporal trends in the rates of severe birth trauma by mode of delivery

Qi Wen, Sarka Lisonkova, Giulia M Muraca

Background: Birth trauma is an injury sustained by the neonate during the process of labor and delivery, especially during instrumental vaginal delivery (forceps and vacuum). In industrialized countries, the rate of instrumental vaginal delivery declined over time. We hypothesized that the rate of birth trauma also declined.

Objective: To examine temporal trends in severe birth trauma.

Methods: We included singleton, live births in Washington State, USA, from 2004 to 2013. Breech deliveries were excluded. Severe birth trauma (brain injury, fractures, nerve injury and other birth trauma) was identified by ICD-9-CA codes recorded in the hospitalization database. Mode of delivery, maternal and birth characteristics were obtained from birth certificates.

The Cochran-Armitage test was used to assess statistical significance of temporal trends. Logistic regression was used to estimate odds ratios (OR) and adjusted odds ratios (AOR) of birth trauma and 95% confidence intervals (CI). Adjustment was made for potential confounders including maternal and infant characteristics (maternal age, body-mass-index, birth weight, etc.).

Results: We included 732,818 infants. The rate of birth trauma declined from 52.7 per 10,000 deliveries in 2004 to 45.2 per 10,000 in 2013 (P-value <0.0001). A significant decline was observed in the rate of fractures (P-value <0.0001) and other birth trauma (P-value 0.0085), but not for brain and nerve injury.

Significant trends were observed only among infants delivered by spontaneous (non-instrumental) vaginal delivery; overall birth trauma declined on average by 3% per year (OR 0.97; 95% CI 0.95 - 0.98), the rates of fractures and other birth trauma both declined by 4% per year (OR 0.96; 95% CI 0.94 - 0.98 and OR 0.96; 95% CI 0.93 - 0.99, respectively). Adjustment for potential confounders did not alter these results.

We also observed a marginally statistically significant increase in nerve injury among infants delivered by forceps (OR 1.12; 95% CI 1.00 - 1.24), which was not significant after adjustment for potential confounders (AOR 1.10; 95% CI 0.98 - 1.23).

Conclusion: The rate of birth trauma declined between 2004 and 2013, mainly due to the decline in fractures and other birth trauma among infants delivered by spontaneous vaginal delivery.

Alexander Wong, Undergraduate Student, University of British Columbia
Supervisor: Tom Blydt-Hansen

Tryptophan pathway activity specific to acute kidney graft rejection in children

Alexander Wong, Li Wang, Atul Sharma, Tom Blydt-Hansen

Pediatric kidney transplants save lives of children with end-stage of kidney disease. Rejection is a major concern of transplants, which requires kidney biopsy for diagnosis. Urinary metabolite testing is a promising alternative to biopsy for non-invasive diagnosis. We hypothesize that the urinary metabolites tryptophan (Trp), kynurenine (Kyn), and serotonin (Ser) of the Trp pathway are perturbed during rejection and may be effective predictive biomarkers.

Urine samples (n=383) from 59 patients <19 years at transplant with concurrent surveillance or indication biopsies were assayed for the 3 Trp pathway metabolites by direct-injection mass spectrometry and normalized to urine creatinine (Cr). Samples were grouped according to Banff scoring: T cell-mediated rejection (TCMR) (n=33), borderline rejection (BRD) (n=115), and NoTCMR (n=235). Candidate metabolite ratios were selected by univariate testing for association with TCMR (vs. BRD, NoTCMR). Multivariable analysis was used to adjust for repeated measures, determine test characteristics and assess independence from relevant covariates.

Fifty-nine patients with a mean age of 11.4±4.4 years contributed 383 urine samples with a median of 6 (IQR 4-8) samples per patient. Candidates identified were Ser:Trp, which was reduced in TCMR (0.009±0.006) compared to BRD (0.013±0.012; p=0.007) and NoTCMR (0.013±0.010; p=0.003), and Kyn:Cr was increased in TCMR (1.74±1.67) relative to BRD (1.13±1.22; p=0.057) and NoTCMR (0.95±1.08; p=0.011). Adjustment for repeated measures confirmed the associations (TCMR vs. BRD+NoTCMR) for Ser:Trp (OR=0.476; p=0.034) and Kyn:Cr (OR=1.353; p=0.02). Both were highly accurate at identifying TCMR (Ser:Trp AUC=0.89; 95%CI 0.84-0.94 and Kyn:Cr AUC=0.91; 95%CI 0.88-0.95). Significant correlation between Kyn:Cr and Ser:Trp (r=-0.28, p<0.01), suggesting co-linearity of association with TCMR. Kyn:Cr association with TCMR was independent of renal function and antibody-mediated rejection (ABMR). Ser:Trp association was independent of renal function but confounded by AMR (OR 0.55; p=0.086).

The discriminatory power of these two metabolite ratios for TCMR and independence from confounding variables shows potential of the three principal metabolites of the tryptophan pathway in the development of urinary metabolomics-based non-invasive diagnostics for pediatric acute kidney rejection.

Poster Session Five

Clinical, Population Health & Health Services

Moderator:
Jim Potts

Participants:
Mackenzie Campbell
Humaam Hamado & Iris Liu
Farnaz Javadian
Andy Jiang
Austin Lam
Rotem Moshkovitz
Karimah Naguib
Carlie Penner
Sylvia Wei
Annie Yu

Mackenzie Campbell, Undergraduate Student, Queen's University
Supervisor: Osman Ipsiroglu

Sleep and challenging behaviours in individuals with down syndrome - An explorative study using a participatory research concept

Mackenzie Campbell, Melvin Chan, Susan Fawcett, Patricia Hanbury, Dawn McKenna, Amy Salmon, Sylvia Stockler, Osman Ipsiroglu

Background: Children and adolescents with Down syndrome are at high-risk for disturbed, non-restorative sleep and often exhibit a variety of challenging/disruptive daytime behaviours. Such behaviours are usually attributed to underlying global developmental delay and/or intellectual disability. We are applying a novel, observation-based approach to explore the relationship between overall sleep quality (i.e., the degree of restorative sleep) and the nature of challenging/disruptive behaviours in individuals with Down syndrome.

Research Questions: (1) How does sleep affect the frequency of daytime challenging behaviours (e.g., frustrations) in individuals with Down syndrome? (2) How do families define 'wellbeing' and 'challenging behaviours' in their children with Down syndrome? (3) How can we catalogue challenging behaviours in individuals with Down syndrome and monitor them in the most convenient way?

Methods: Ethics Application ID: H16-01280. Study subjects include students (ages 10 to 25) attending the Summer School program at the Down Syndrome Research Foundation (Burnaby, BC) over a two-week period. Data collection is occurring by two means: (1) a sleep diary/log and survey completed by families; (2) in-class recording of the nature of challenging/disruptive behaviours using an adapted 'Functional Assessment Observation Form'©. The sleep diary/log and survey provide a comprehensive overview of sleep/wake behaviours, including sleep patterns, daytime challenging/disruptive behaviours and mood. Intake interviews are conducted with parents to tailor in-class behavioural observations for each student. Observational data will be analyzed using descriptive statistics.

Next Steps: This study will provide direction for future projects on sleep-related causes of challenging/disruptive behaviours in individuals with Down syndrome. By refining our understanding of the relationship between sleep quality and daytime behaviours, we hope to improve the quality of life of individuals with Down syndrome, as behaviours affect overall wellbeing and predict ability to participate in everyday life.

Humaam Hamado & Iris Liu, Undergraduate Students, University of British Columbia
Supervisor: Damian Duffy

BC Children's Hospital operating room turnover time analysis

Humaam Hamado, Iris Liu, Damian Duffy

Introduction: Turnover (TO) time in the operating room (OR) is crucial in delivering promised patient care and subsequently avoiding overtime work and additional expenses. This analysis was conducted in order to identify the factors causing delays and areas of improvement as well as what is being done correctly.

Methods: Observations in BC Children's Hospital OR over the course of January and February, divisions of primary focus being Ophthalmology and Otolaryngology. These divisions have higher amounts of TO than the rest and thus were selected for that matter. In total, 60 procedures were observed. The data collected from the OR was combined with the Operating Room Scheduling Office System (ORSOS) data to compose a master list for analyzing the four main factors: housekeeping arrival, housekeeping cleaning, nurse setup and hand over times. Excel and R were used to compute numerical summaries including the median time it takes to complete the four factors above.

Results: Housekeeping arrival times and cleaning times were consistent with the median values. Set up times were significantly longer on Wednesdays and Thursdays – up to 8 minutes longer. Additionally, setup times were longer from 7 am to 9 am – a spike of up to 19 minutes. Handover times were longer between 11 am and 12 pm – up to 9 minutes.

Conclusion: Implementation of key strategies targetting the spikes observed can greatly reduce TO time and could possibly make way for another short elective surgery to be scheduled in the time saved. For example, if components of the TO timeline were adjusted to the median values, the Otolaryngology patient waitlist could have been reduced by 31.3% in the 2015/16 fiscal year.

Farnaz Javadian, Undergraduate Student, University of British Columbia
Supervisor: Deborah Giaschi

Motion perception in children

Farnaz Javadian, Kim Meier, Deborah Giaschi

Introduction: Global motion perception is the ability to combine the motion of individual dots moving in different directions to perceive a global pattern moving in a single direction. Global motion perception is immature in children compared to adults for slower dot speeds. This may be due to immature motion processing mechanisms in the brain, or due to spatial integration limitations at earlier stages of visual processing before the visual input reaches motion-processing regions of the brain. To test this hypothesis, we will determine the effect of the area of the moving dots on motion perception.

Methods: We aim to recruit 12 adults and 12 young children (aged 4-6), and assess their global motion perception. The stimulus consists of an array of dots, where a proportion of signal dots move in the same direction (left or right), and the others (noise dots) move randomly. The task is to determine which way the whole pattern appears to move. A coherence threshold is the lowest proportion of signal dots needed to accurately determine the global motion direction. We are measuring thresholds for 9 conditions: 3 area sizes (small, medium, large) and 3 speeds (slow, moderate, fast). We will compare the effect of area on thresholds in each age group.

Results: Preliminary results show that adults only show an effect of area for fast speeds, such that a smaller area leads to elevated coherence thresholds. We will assess whether children show a similar pattern, or if they show an additional effect of area at slow and moderate speeds. If an effect is shown at these conditions, then their immature performance in previous studies might be due to a smaller integration area, rather than immature motion mechanisms. If they do show the same effect as adults, then we can confirm that the immaturity in motion perception is not due to integration area and may be due to deficits in motion processing.

Andy Jiang, Undergraduate Student, University of British Columbia
Supervisor: Ian Pike

Patterns in poisoning hospitalizations in British Columbia, 2007/08 – 2013/14

Andy Jiang, Fahra Rajabali, Roy Purssell, Ian Pike

Background: In BC, recent increases in prescription and illicit drug overdoses have sparked a public health emergency. While previous research has primarily focused on fatalities, an understanding of non-fatal poisonings can also be valuable in the development of prevention initiatives and policies to address the issue. Notably, hospital admissions data provides insight into many of the most clinically severe poisoning cases in BC.

Aim: To identify patterns in poisoning hospitalizations occurring in BC for the fiscal periods 2007/08 – 2013/14 by age, sex, intent, geography, and substance(s).

Methods: Data from all hospitalizations in BC for the fiscal periods 2007/08 – 2013/14 was acquired from the BC Discharge Abstracts Database. Cases with poisoning as the primary cause of hospitalization were identified by ICD-10 codes X40 – X49 (unintentional poisoning), X60 – X69 (self-harm poisoning), X85 – X90 (assault by poisoning), and Y10 – Y19 (poisoning of undetermined intent). Hospitalization rates per 100,000 population were analyzed by age-group, sex, intent, health service delivery area, and the causative substance(s).

Results: A total of 16,278 poisoning hospitalizations occurred during the study period. The rate of self-harm poisoning hospitalizations was greater than that of unintentional poisonings (29.3 vs. 16.5 per 100,000). Unintentional poisoning hospitalization rates were highest among young children (0 – 4 years) and older adults (75+ years), whereas rates for self-harm poisoning hospitalizations were highest among female youth (15 – 19 years). Opioids and benzodiazepines were involved in a large proportion of unintentional poisonings, while 4-aminophenol derivatives and antidepressants were most often implicated in self-harm poisonings. Geographic hotspots for unintentional and self-harm poisoning hospitalizations tended to be associated with less urban areas of the province.

Conclusions: Distinct patterns associated with poisoning hospitalizations have been identified in BC. These patterns can inform the development of targeted prevention initiatives and policies across the province, as well as aid clinicians to identify and counsel high-risk patients to prevent poisonings from occurring.

Austin Lam, Undergraduate Student, McGill University
Supervisor: Tonia Nicholls

The relationship between childhood maltreatment and risk outcomes in adult forensic psychiatric patients

Austin Lam, Hanie Edalati, Ilvy Goossens, Tonia Nicholls

Background: Child maltreatment is common and has wide-ranging, long-lasting detrimental effects for mental health and well-being. It is especially prevalent among marginalized populations (e.g., psychiatric patients, inmates, and offenders). However, we know little about the experience of child maltreatment in forensic populations (mentally ill individuals with criminal justice involvement) and how it is relevant to patient risks (e.g., violence, suicide) and treatment needs (e.g., substance abuse).

Objectives: The present study investigated the relationship between childhood maltreatment and multiple risk outcomes in an adult forensic psychiatric sample. We addressed three objectives:

1) Assess the prevalence and nature of childhood maltreatment including neglect (emotional and physical), and abuse (emotional, physical, and sexual) among forensic psychiatric patients;

2) Examine the prevalence, frequency, and severity of risk outcomes highly relevant to the forensic psychiatric context: internalizing outcomes (e.g., self-harm, suicide ideation and behaviours), victimization, and externalizing outcomes (e.g., verbal, physical, and sexual aggression); and

3) Evaluate the relationship between childhood maltreatment and multiple risk outcomes, specifically, internalizing outcomes (e.g., suicide, self-harm), victimization, and externalizing outcomes (e.g., crime, violence).

Hypothesis: We hypothesized that participants with histories of childhood maltreatment have more incidents of adverse outcomes compared with participants without histories of child maltreatment.

Methods: Participants are recruited from a forensic psychiatric hospital in Canada. To be included in this study participants have to be (1) found Not Criminally Responsible on Account of Mental Disorder (NCRMD), and (2) under treatment in the hospital for at least three months at the time of recruitment. Participants are interviewed to complete the Adverse Childhood Experiences (ACE) measure to identify childhood experiences of abuse and neglect. Multiple risk outcomes are assessed in file reviews that consist of completing the Short-Term Assessment of Risk and Treatability Outcome Scale (START Outcome Scale or SOS).

Outcomes: This study is ongoing. Nevertheless, we anticipate that the results of this study can increase the understanding of how experience of childhood maltreatment and multiple risk outcomes in adulthood interact among individuals struggling with mental illness and criminal justice involvement, and support a transition to trauma-informed practice for forensic psychiatric patients.

Rotem Moshkovitz, Undergraduate Student, University of British Columbia
Supervisor: Matthias Görges

Cardio-respiratory coherence monitor for use in the operating room

Rotem Moshkovitz, Klaske van Heusden, Mark Ansermino, Guy Dumont, Matthias Görges

Background: During general anesthesia, a combination of drugs is used to control depth of hypnosis, analgesia, and if necessary paralysis. The patient's inability to report pain requires the use of indirect indicators for an accurate assessment of the presence of a noxious stimulus, such as an increased heart rate or blood pressure, movement, or sweating. These stress responses are undesirable during anesthesia as they are associated with adverse outcomes. This project aims to develop a nociception index (NI), which provides the anesthesiologist with direct feedback on the stress response exhibited by the body in response to a noxious stimulus. A novel cardio-respiratory coherence algorithm, developed by the Pediatric Anesthesia Research Team, integrates data from electrocardiogram and exhaled carbon dioxide waveforms into a single feedback variable indicating the patient's nociceptive state.

Motivation: Currently, artifacts in heart rate (HR) or respiratory rate (RR) waveforms invalidate the NI value for over one minute. This is caused by the filter used during the NI calculation, which propagates HR and RR errors and distorts the NI for an unacceptably long period for real-time clinical use in the operating room.

Methods: To reduce the impact of artifacts in real time, a prediction function, based on an auto-regressive model, has been developed to interpolate missing or incorrect heart rate data. This artifact removal method is currently being tested and optimized, using previously recorded anesthetic cases, with the goal of clinical testing by the end of the summer.

Results: Prediction errors for both HR and NI have been evaluated and compared to their respective original signals. A representative case shows that a prediction of two seconds of HR data results in a median absolute NI error of 0.9386 (IQR 0.4475-2.2028), relative to a scale of 100. The threshold for the length of predicted HR segments is yet to be determined, pending on the analysis of more data as it becomes available.

Future work: Future directions for this project include developing a similar respiratory waveform interpolator to address respiratory artifacts, as well as establishing an SQI to provide a measure of the NI's reliability.

Karimah Naguib, Undergraduate Student, University of British Columbia
Supervisor: Crystal Karakochuck

The prevalence of G6PD deficiency, anemia, and malaria infection in Congolese children ages 6-59 months

Karimah G Naguib, Mikaela K Barker, Rika Aleliunas, Angela M Devlin, Tim Green, Crystal D Karakochuk

Background: Glucose-6-Phosphate Dehydrogenase (G6PD) is an enzyme that protects red blood cells from oxidative damage. G6PD deficiency is a X-linked recessive hereditary disorder, which arises from mutations in the G6PD gene. In central Africa, G6PD A- variant is thought to be most prevalent and is characterized by two substitution mutations in the G6PD gene (A376G [rs1050829] and G202A [rs1050828]). Previous studies have found that G6PD deficiency is associated with malaria and acute hemolytic anemia. Our aim was to determine the prevalence of G6PD deficiency, anemia and malaria infection in Congolese children 6-59 months.

Methods: Venous blood was collected from 744 children in South Kivu (SK) and Kongo Central (KC) provinces and analyzed for hemoglobin and malaria infection. DNA was extracted from blood and real time quantitative PCR was used to detect two mutations in the G6PD gene (A376G [rs1050829] and G202A [rs1050828]).

Preliminary Results: The proportion of children with anemia (Hb <110 g/L) was 35% (n=105/300) in SK and 44%(n=195/444) in KC. The prevalence of malaria was 3% (n=9/300) in SK and 38% (n=168/444) in KC. In SK, 42% of children had the A376G mutation, 18% had the G202A mutation, and 6% had both the A376G & G202A mutations. In KC, 48% of children had the A376G mutation, 24% had the G202A mutation, and 11% had both the A376G & G202A mutations.

Interpretations: Overall, children in KC had a higher prevalence of G6PD deficiency, anemia, and malaria infection, as compared to children in SK. In the next steps of analysis, we will use linear regression models to investigate associations among G6PD deficiency, hemoglobin concentration, and malaria infection.

Carlie Penner, Undergraduate Student, Simon Fraser University
Supervisor: Kevan Jacobson

Inflammatory bowel disease in the South Asian pediatric population of British Columbia: Dietary and environmental factors

Carlie Penner, Alam Lakhani, Azita Hekmatdoost, Kevan Jacobson

Background: Inflammatory bowel disease (IBD) is a chronic relapsing immune mediated inflammatory condition that affects the gastrointestinal tract. There are two main subtypes of IBD: Crohn's disease (CD) and ulcerative colitis (UC). Although the etiology of IBD is unknown, it is hypothesized to be precipitated by interactions between the genetically susceptible host, the mucosal immune system, and the environment. Epidemiological studies of the diseases suggest that extrinsic environmental factors play an important role in the initiation, modulation, and phenotypic expression of the diseases.

Studies have shown that individuals who migrate from low prevalent areas (e.g., South Asia) to high prevalent countries (e.g., Canada and England) are at increased risk for developing IBD, particularly among first- and second-generation immigrants, highlighting the importance of environmental influences. A previous study at BC Children's Hospital suggested that South Asian children living in BC are approximately 3 times more likely than non-South Asian children to develop IBD.

Objectives: The primary aim of this study is to obtain a cross sectional picture of the diet and dietary determinants in the South Asian pediatric IBD population as well as in the healthy family members.

The secondary aim is to evaluate environmental risk factors that are associated with the development of IBD in the South Asian pediatric IBD population.

Methods: IBD patients of South Asian heritage are invited to participate. Patients and at least one other immediate family member (sibling, parent, or grandparent) are asked to complete a 7-day food record and an environmental risk assessment questionnaire. The environmental risk questionnaire includes information such as education level of parents, socio-economic status, dietary determinants, religious affiliation, ethnic background, medical history, smoking history, and family history. Our goal is to recruit 62 patients and 124 family members.

Future Directions: Recruitment of families, collection of questionnaires, and data analysis is ongoing. The next steps will be to analyze trends in the data and begin understanding why BC's South Asian pediatric population seems to be at a higher risk for developing IBD.

Sylvia Wei, Undergraduate Student, University of British Columbia
Supervisor: Rajavel Elango

Evaluation of a liquid human milk fortifier for growth and feeding tolerance in preterm neonates

Sylvia Wei, Julie Matheson, Vikki Lalari, Susan Albershiem, Sheila Innis, Rajavel Elango

Studies over the past thirty years have reported the benefits of maternal milk versus contemporary formula (Kramer et al., 2001), with maternal milk diets being ideal for all infants particularly those of very low birth weight (Colaizy, 2015). However, human milk meets the nutritional needs of term infants born after term gestation (Hawthorne et al., 2015), and may be insufficient for preterm infants. To address this, liquid or powdered fortifiers are used to increase the nutritional content of milk. These fortifiers contain nutrients such as protein, carbohydrate, fat, linoleic acid, as well as essential vitamins and minerals. Additional research is still required to understand the best medium (powder vs. liquid form) to fortify human milk in order to achieve optimal growth, development, and health outcomes in the long term. Our study will investigate this using the medical records of 40 preterm neonates, who were admitted to the Neonatal Intensive Care Unit at BC Children's Hospital from Jan-Dec 2015, and prescribed SSC30, the liquid human milk fortifier. The primary objective is to retrospectively analyze weight gain (g/d), growth rate (g/kg/d), and z-scores with SSC30 feeding. In addition, we will determine history of feeding intolerance, defined with number of days NPO duration of >24 hours. Feeding intolerance will also be considered based on the frequency of any two of the following: vomiting, irregular stool pattern, and abdominal distension. Our expected outcome is that the liquid human milk fortifier SSC30 will be an effective human milk fortifier and will not have an adverse effect on the feeding tolerance of preterm infants in the NICU. This study will be the first to collect Canadian NICU data on the effectiveness of SSC30, and provide data on whether preterm babies benefit from a liquid fortifier.

Annie Yu, Undergraduate Student, McMaster University
Supervisor: Suzanne Lewis

Deep phenotype and genetic subgrouping for Autism Spectrum Disorder (ASD)

Annie Yu, Kristina Calli, Franz-Edward Kurtzke, Boris Kuzeljevic, Ben Callaghan, Ying Qiao, Xudong Liu, Guy Rouleau, Yingrui Li, Evica Rajcan-Separovic, Paul Pavlidis, Suzanne Lewis

Background: Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder affecting 1 in 68 individuals in North America. Although twin and family studies have shown that ASD has a strong genetic basis, the diverse range of ASD-associated phenotypes likely reflects a heterogeneous etiology. The identity of ASD pathogenic genes and their pathways remain largely unknown.

Objective: To help delineate the clinical and genetic heterogeneity of ASD by defining phenotypic biomarkers correlating to the developmental origins of the disorder.

Methods: Subjects enrolled in the ASPIRE (Autism SPectrum Interdisciplinary REsearch) cohort have a confirmed ASD diagnosis (DSM IV; ADOS/ADI-R) and underwent a detailed standardized assessment protocol through the Provincial Medical Genetics Programme. K-means and canonical discriminant clustering analyses were applied to the phenotype data, which stratified subjects into 3 distinct subgroups. We then selected 120 subjects from the 2 most stable subgroups for individual analyses. To characterize their genetic variation, we used both copy number variant (CNV) microarray and whole genome sequencing (WGS). Variants within the WGS data were called using the Genome Analysis Toolkit against the human reference genome and filtered for quality and rarity in the population data. To further prioritize these variants, bioinformatics tools incorporating both gene-level and variant-level metrics were used. We will then validate the association of genetic variation findings to individual and cluster phenotypes, which include extensive data from birth and medical histories, craniofacial anthropometric measurements, physical exams, ASD diagnostic assessments, and demographics questionnaires. Prevalence of phenotypic traits in our cohort will be compared to control population reported in literature.

Results: In total, 66 candidate missense gene mutations were prioritized as potentially pathogenic. These include 12 affecting literature-associated ASD genes and 8 affecting genes associated with other neurodevelopmental disorders.

Future Directions: Validation and inheritance testing of these variants are currently underway. The result of this testing will be used to identify phenotypic susceptibility criteria for genetic risk factors of ASD.

Poster Session Six

Clinical, Population Health & Health Services

Moderator:
Mary Dunbar

Participants:
Sandra Botros
Rayleigh Chan
Anita Dahiya
Vivien Hu
Xiaoning Guan
Derin Karacabeyli
Kushal Khera
Armaan Malhotra
Eric Zhao

Sandra Botros, Medical Student, University of Western Ontario
Supervisor: Brenden Hursh

Initiation of insulin pump therapy at a pediatric tertiary care centre - An introduction

Sandra Botros, Brenden E Hursh

Background: Intensive glycemic management using insulin pump therapy is has become an established form of pediatric type 1 diabetes treatment, and its use has been increasing over time. It has been shown to have modest advantages over insulin injections on glycemic control. However, this technology can also improve quality of life of children and their parents and increase perceived control over their illness. The prevalence of IPT varies widely between countries and between specific centres, and there is variation in eligibility criteria and prescribing recommendations. There is no recommended age or time after diagnosis for starting pump therapy; the decision is often based on individualized patient factors and preferences, as a joint decision between physician and patient.

Hypothesis: We hypothesize that as IPT in continuing to evolve and patients and physicians are becoming more familiar with it, we will see a trend initiating IPT at younger ages and earlier in the disease course. Additionally, we hypothesize that certain characteristics will predict greater success, such as the home environment, younger age, and previous insulin regimen.

Methods: We will identify patients in the clinical database started on IPT between 2011 and 2016. Charts will be reviewed for baseline characteristics such as gender, age at diagnosis, age at pump initiation, and family structure, and this will describe the population of children receiving IPT. To look for changing trends in IPT, children started in the first and last 12 months of this 5-year period will be compared using appropriate statistical tests. To look at factors associated with improved outcomes on IPT, post-pump glycemic management will be measured by using HbA1c values taken between 9-18 months after pump initiation. We will determine change pre- to post-pump HbA1c change in each patient, and analyze whether pre-determined variables are associated with a more desirable change in HbA1c over this time period.

Future Directions: This study is currently in process; up-to-date data will be presented. This study will provide a summary of current practices, trends, and predictors of success to our diabetes centre, and help inform guidelines for optimal judgement when choosing children to start on insulin pumps.

Rayleigh Chan, Medical Student, University of British Columbia
Supervisor: Cynthia Verchere

Outpatient burn care at BC Children's Hospital burn treatment room: A 3-year review

Cynthia Verchere, Aaron Van Slyke, Rayleigh Chan

Background/Purpose: The Burn Treatment Room (BTR) at BC Children's Hospital (BCCH) is run by a multi-disciplinary team, providing sedation to burn patients undergoing dressing changes in a monitored setting. The purpose of this study is to review the safety and efficacy of the BCCH BTR in conjunction with a qualitative analysis of staff experience.

Methodology: A retrospective chart review of all patients treated in the BTR from 2013 to 2015 was conducted as well as qualitative interviews with BTR staff.

Results: 59 patients (average age 4.0 years old) with a total of 216 BTR visits (average visit time 64.75 minutes) were included. Scald burns were the most common mechanism of injury (76%), followed by flame (14%) and contact burns (7%). Most burns were superficial dermal (54%) and initially estimated at 5-10% TBSA (57%). A total of 38% of patients received surgical intervention. The majority of patients required intravenous sedation during dressing changes (72%), with the most common medication used for intravenous sedation being propofol (83%). Nine patients were converted from oral to IV sedation, 2 had short apnea periods that recovered spontaneously and 2 had prolonged sedation. Overall, there were no major sedation related complications. Interviews with 6 staff members revealed an overall positive experience and few safety concerns.

Conclusion: Our findings are consistent with current reports from other burn facilities. The BTR at BCCH is a safe and effective way to treat burn patients, preventing what would historically require inpatient management.

Anita Dahiya, Medical Student, University of British Columbia
Supervisor: Douglas J Courtemanche

Multidisciplinary cleft palate program at BC Children's Hospital: Are we meeting the standards of care?

Anita Dahiya, Rebecca Courtemanche, Douglas J Courtemanche

Introduction/Background: Orofacial clefting is one of the most common congenital anomalies in North America. Multidisciplinary clinics create treatment plans for patients based on team expertise and recommendations from the American Cleft Palate-Craniofacial Association (ACPA). The cleft palate program (CPP) at BC Children's Hospital is composed of the craniofacial (CF), cleft palate (CP), and jaw clinics. To date, no evaluation has been conducted of the CPP to determine if we are meeting the standards of care.

Objective: Characterize current CPP practices and evaluate appointments with respect to timeliness according to CPP recommendations and ACPA standards of care.

Methods: A retrospective review of CPP patient appointments from November 6th, 2012 to March 31st, 2015 was done. Descriptive data analysis was conducted. Results: 1214 appointments were considered in the analysis, including syndromic and non-syndromic patients of 0 to 27 years of age. Our results show patients five years and younger or non-syndromic were more likely to be seen on time ($p < 0.001$). No relationship between the timeliness of an appointment and specific patient diagnoses or distance to clinic was found. With the exception of nursing (97% of appointments were on time), all disciplines had less than 45% of appointments on time. Only 32% of appointments met CPP recommendations for timeliness, while 51% of appointments met ACPA standards of care.

Conclusion: Timely care for certain cleft/craniofacial patient populations represents a challenge for the CPP. Adjustments may be needed in resource allotment and program support to provide better patient care.

Vivien Hu, Medical Student, University of British Columbia
Supervisor: Erika Henkelman

Post-operative intravenous fluid ordering practices in children among plastic surgery trainees

Vivien Hu, Sean Bristol, Erika Henkelman

Background: Hypotonic fluids have been traditionally ordered post-operatively in children. However, there is increasing evidence in favour of isotonic fluids and reports of hyponatremia and adverse events associated with hypotonic fluids. Hospital restrictions for using isotonic fluids in Europe since 2011 has led to improved safety of children. However, in the United States (US) and Canada, there is no standardization and hospitals have varied practices. We hypothesize that hypotonic fluids continue to be ordered post-operatively.

Objectives: To determine the current IV fluid ordering practices of plastic surgery trainees post-operatively in children, and the hospital policies that influence their choices in the US and Canada.

Methods: An ad-hoc online survey was distributed via email to plastic surgery trainees for a 4-week period. The survey asked for the preferred IV fluid based on a brief clinical scenario, as well as hospital restrictions and factors contributing to their decision. Analysis was conducted using descriptive statistics.

Results: There were 51 responses, of which 36 were complete and used for analysis. The most frequently chosen fluid was hypotonic, Dextrose 5% + 0.45% NaCl (38.9%). Overall, hypotonic fluids were preferred by 41.7%, isotonic by 44.6%, and 13.9% of respondents indicated that they did not know the best choice. Regardless of level of training, pediatric clinical experience, hospital type, province/state, there was no significant difference in the type of fluid ordered. The main factor that influenced the trainees' decision was their belief that it was the best choice (77.8%), followed by staff preference (27.8%). There were no hospital restrictions in 69.4% cases. Several respondents commented favourably for evidenced based post-op fluid recommendations and guidelines to improve patient safety.

Conclusions: A significant proportion of plastic surgery trainees in US and Canada would order hypotonic IV fluids post-operatively, despite safety concerns in children. The majority of respondents were not aware of any hospital restrictions. Hospital guidelines may help improve post-operative fluid ordering practices among medical trainees.

Xiaoning Guan, Medical Student, University of British Columbia
Supervisor: Jennifer Hutcheon

Pregnancy weight gain and adverse perinatal health outcomes in twin pregnancies

Xiaoning Guan, Jennifer Hutcheon, Lisa Bodnar

Background: Current guidelines for pregnancy weight gain in women carrying twin pregnancies are based on an extremely limited evidence base. Research establishing the association between gestational weight gain and adverse perinatal outcomes in twin pregnancies in large, well-designed studies is needed to identify the optimal gestational weight ranges for twin pregnancies.

Objective: To determine the association between total gestational weight gain and 4 short term adverse health outcomes for mothers and offspring in twin pregnancies.

Methods: The study population included 2934 women with twin pregnancies who delivered at Magee-Women's Hospital in Pittsburgh, Pennsylvania, 1998-2013. Information were taken from an electronic database and supplemented with manual chart abstraction. Gestational weight gain was standardized for gestational duration using gestational age-specific z-scores. Logistic regression was used to establish the association between gestational weight gain z-scores and four outcomes (gestational diabetes, pre-eclampsia, early spontaneous preterm birth and birthweight discordance), controlling for potential confounders.

Results: The risk of pre-eclampsia increased significantly by 153% among women with the highest gestational weight gain compared to women with average weight gain (Adjusted OR: 2.53; CI 1.39-4.61). A similar trend was observed for gestational diabetes with an increase of 50%, however, this increase was not statistically significant (Adjusted OR: 1.51; CI 0.49-4.63). The relative risk of spontaneous preterm birth <32 weeks was significantly higher in the smallest (Adjusted OR: 2.47; CI 1.38-4.42) and largest (Adjusted OR: 4.88; CI 2.76-8.61) gestational weight gain categories. A similar trend was observed for birth weight discordance. In the highest z-score category, the risk of birth weight discordance increased by 89% (Adjusted OR: 1.89; CI 1.06-3.36).

Conclusions: Extremely low or high gestational weight gain increases the risk of both early spontaneous preterm birth and birth weight discordance in twin pregnancies. Non-significant trends showing increased risks of gestational diabetes and pre-eclampsia associated with high weight gain should be confirmed in cohort with larger sample sizes.

Derin Karacabeyli, Medical Student, University of British Columbia
Supervisor: Garth Meckler

An analysis of pediatric emergency department outcomes after care in the clinical decision unit: A retrospective cohort study

Derin Karacabeyli, Garth Meckler, Quynh Doan

Introduction: A clinical decision unit (CDU) is an area within the emergency department (ED) that allows for protocolized treatment and observation (up to 24 hours) of patients who may not need to be admitted to hospital, but who also may not be ready for discharge. It can therefore serve as an alternative to inpatient admission, decreasing hospital resource utilization, freeing up inpatient beds, and allowing families to go home sooner following recovery. A CDU was established at BC Children's Hospital in October 2014.

Objectives: To determine: 1) Outcomes of CDU stay (e.g. the number of admissions avoided); 2) The number of preventable return visits, and the root causes of return.

Methods: Retrospective administrative database and chart review of CDU visits (and their associated ED return visits within seven days) at BC Children's Hospital from Jan 1, 2015 to Dec 31, 2015.

Preliminary Results & Interpretation: Of the 1696 index CDU visits in 2015, 1342 (79.1%) were successfully treated and discharged without ED return, representing 1342 instances where inpatient admission may have been avoided. Of the remaining visits, 193 (11.4% of all CDU visits) were admitted from the CDU to an inpatient ward, denoting potential CDU failures and raising flags as to whether these patients were appropriate CDU candidates. 158 CDU cases (10.5%) returned to the ED within seven days, representing another set of potential CDU failures. Among these, 40 (25.3%) were admitted upon return within one week of their initial CDU stay, signifying additional CDU patients who may have needed a longer observation and hospitalization period. Of the remaining 118 return visits, 99 (62.7% of all CDU returns) did not require care beyond standard ED treatment. Some only required reassurance, highlighting an opportunity to potentially prevent ED return visits following CDU care with comprehensive education and discharge instructions.

Next Steps: Two clinical investigators will review the return visits to determine the root causes of return, as well as whether the return visits were preventable. Further analyses around clinical conditions associated with admission to an inpatient ward following CDU treatment will be conducted.

Kushal Khera, Medical Student, Royal College of Surgeons in Ireland
Supervisor: Kevin Harris

Cardiovascular health and physical activity in adolescents

Kushal Khera, Christine Voss, Paige Dean, Ross Gardner, Kevin Harris

Background: Fewer than 1 in 10 Canadian adults (age 20+) and fewer than 1 in 5 Canadian youth (age 12-19) are in ideal cardiovascular health as per the CANHEART Health Index. Increasing physical activity is key to improving cardiovascular health. This is especially relevant in the pediatric cardiology patient population as a child's medical condition may impact their ability to engage in physical activity.

Objectives: The primary objective was to assess the association between cardiovascular health and physical activity levels in adolescents. The secondary objective was to explore medical, environmental, and socio-cultural correlates of physical activity.

Methods: Adolescents aged 13-19 attending cardiology outpatient clinics at BC Children's Hospital and partnership clinics across BC were invited to participate. Cardiac diagnosis was categorized as heart disease (congenital and acquired) or no heart disease (e.g. syncope). Adolescents and their parent/guardian completed a questionnaire regarding their health and health-behaviours. Responses were categorised into ideal/not ideal according to CANHEART criteria, a composite score of cardiovascular health (scored 0-4 in adolescents, 0=poor, 4=ideal). Physical activity was estimated using a validated questionnaire (PAQ-A; scored 1-5, 1=low, 5=high). Neighbourhood walkability of participants' homes was obtained from WalkScore® (score 0-100, 0=car-dependent, 100=walkers' paradise).

Results: As of July 2016, 48 adolescents (16.0 years(IQR=14.9-17.5) 39.6% female; 91% consent rate) and 44 parents/legal guardians (44.0 years (IQR=41.2-48.0), 88.6% female) participated. 62% had heart disease. Adolescent CANHEART score was 3.0 (IQR=2-4), and PAQ-A score was 2.0 (IQR=1.6-2.9). There was a significantly positive correlation between adolescent CANHEART and PAQ-A scores (rho=0.376, p=0.015). Younger adolescents had higher PAQ-A scores (rho=-0.402, p=0.009). Adolescents with heart disease had lower PAQ-A scores than those without heart disease; in multi-level regression analyses however this effect was entirely attributed to the significant age-difference between groups rather than heart disease. PAQ-A scores were significantly related to parent-reported encouragement (rho= 0.515, p=0.001) and parents watching them play sports (rho=0.471, p=0.004). There was no association between PAQ-A scores and parental physical activity or neighbourhood walkability.

Conclusions: Physical activity is a key factor in improving the cardiovascular health of adolescents. Parental support and encouragement play a major role in increasing levels of physical activity.

Armaan Malhotra, Medical Student, University of British Columbia
Supervisor: Jugpal Arneja

Evaluation of outcomes: A 6-Year retrospective review of surgical gynecomastia management at BCCH

Armaan Malhotra, Shazhan Amed, Jugpal Arneja

Background: Gynecomastia is a benign proliferation of glandular breast tissue in males. This proliferation typically manifests as concentric swelling of the retro-areolar tissue, resulting in unilateral, bilateral or asymmetric presentation. The prevalence of gynecomastia in pubertal males is between 45-65%, with peak incidence between the ages of 13-15. By age 17, up to 90% of cases resolve spontaneously. Pubertal gynecomastia may be either physiologic – due to transiently unbalanced estrogens and androgens - or pathologic. In adolescents, gynecomastia may be detrimental to psychosocial health; it has been shown to have a significant negative impact on social functioning and self-esteem. Surgical management is a treatment option for patients with persistent pubertal gynecomastia.

Objective: The objective of this study is to review the complications and outcomes of the surgically managed gynecomastia patients at BC Children's Hospital over the past 6 years.

Methods: A 6-year retrospective chart review was conducted. Data collection included all patients with gynecomastia <19 managed surgically at BC Children's Hospital between August 2009- July 2015. Anthropometrics, gynecomastia stage, surgical technique, complications and revisions were reviewed and summarized.

Results: The review was comprised of 47 patients undergoing 48 primary gynecomastia reconstruction procedures (91 total breasts). Techniques included periareolar, extended periareolar and free nipple graft subcutaneous mastectomies. The overall complication rate was 32% (18 complications in 15 patients) with the most common complication being post-operative hematoma (n=11); 2 complications were classified as major, requiring surgical evacuation. The revision rate following primary reconstruction was 25% (n=12), of which 83% (n=10) were graded 2B or worse. Of the 48 pre-operative endocrinology assessments performed, 1 yielded an important clinical finding in a patient with known ambiguous genitalia and exogenous estrogen supplementation. No risk factor associations with post-operative complications were found from our analysis.

Implications: The reported complication rate is on the high end those published in the literature, which warrants a more detailed investigation into complication aetiology. 75% percent of patients had a good outcome after the first procedure. Our study raises questions about the utility of ordering routine endocrine investigations for evaluation of gynecomastia in adolescents prior to surgery, which is current protocol.

Eric Zhao, Medical Student, University of British Columbia
Supervisor: Theresa Newlove

Evaluation of a biofeedback tool to minimize procedural pain and anxiety in children

Eric Zhao, Evgenia Torodova, Chris Petersen, Theresa Newlove

Introduction: Decreasing children's anxiety towards medical procedures is associated with decreased distress, decreased pain and less negative attitudes towards future medical procedures. Belly breathing, or deep diaphragmatic breathing, is a popular behavioural intervention and coping strategy used to reduce anxiety in children undergoing medical procedures. However, the effectiveness of belly breathing in reducing stress is limited to the availability of trained healthcare professionals to coach patients through pain- and stress-management techniques.

Objectives: The primary objective of this study is to evaluate the effectiveness of using a smartphone-based biofeedback game to teach belly breathing in order to reduce procedural anxiety and pain in children (age 5-17) having their blood drawn using traditional venipuncture. Methods Study subjects were recruited from children undergoing blood tests at the blood collection lab of BC Children's Hospital. Participants were randomized to one of the following groups: 1) the standard of care control group, 2) the belly breathing using traditional teaching techniques group, or 3) the belly breathing using the biofeedback app. In all groups, the participants' anticipated anxiety and pain were assessed at two time points (T1 and T2) before venipuncture, and procedural anxiety and pain were assessed after venipuncture (T3). Anxiety and pain are quantified using the Visual Analogue Scale for Anxiety (VAS-A) and the Colour Analogue Scale for Pain (CAS). Between T1 and T2, participants in groups 2 and 3 are taught to belly breathe using traditional teaching techniques or by playing the biofeedback app, respectively. The changes in VAS-A scores and CAS scores between T1-T2 and T1-T3 will be compared between groups using a one-way analysis of variance.

Results: Interim analysis shows that patients employing belly breathing, either with traditional teaching techniques or with the novel biofeedback app, experience a significant decrease in anticipated procedural pain between T1 and T2 compared to standard of care controls ($p = 0.01$, $F = 4.87$, $n = 62$). Conclusion Belly breathing is an effective intervention in decreasing anticipatory procedural pain. The effectiveness of the biofeedback app in decreasing procedural anxiety and pain compared to traditional teaching methods and standard of care requires additional data.