CHILD & FAMILY RESEARCH INSTITUTE

2014 | STUDENT POSTER DAY

TABLE OF CONTENTS

Session One – Basic Science

Session Two – Basic Science

Session Three – Basic Science

Session Four – Clinical

Session Five – Clinical

POSTER SESSION ONE

BASIC SCIENCE

MODERATOR: Shane Fung

PARTICIPANTS: Carly Aspden
Sandra Botros

Helen Fu
James Leung
Dhruv Pandey
Erik Venalainen
Marcus Wong
Ellia Zhong
Misha Zarbafian
Allen Zhang

Carly Aspden, Undergraduate Student
Supervisor(s): Bruce Vallance

Board #: 1

Title: Intestinal myeloid MyD88 signalling during Salmonella colitis: A fine balance between minimizing systemic spread of pathogens and limiting collateral damage

Authors: Carly Aspden, Ganive Bhinder, Tina Huang, Bruce A Vallance

Abstract:

Introduction: MyD88, a key adaptor protein in the innate immune response, plays a critical protective role during many models of intestinal inflammation, including chemically- and bacterially-induced colitis. However, MyD88 dependent signalling likely also contributes to maladaptive repair responses, as our lab recently found that mice lacking MyD88 in the Salmonella Typhimurium (St) infection model of intestinal inflammation are protected from developing excessive intestinal inflammation and deposition of extra-cellular matrix (fibrosis). Currently, it is not well understood which cell types contribute to the protective or potentially detrimental effects of MyD88 signalling, though hematopoietic and non-hematopoietic linages are likely involved. This study aims to examine the role of MyD88 signalling in endothelial and myeloid cells during St infection utilizing cell type specific knockout mice. Overall, we aim to determine the role of endothelial and myeloid MyD88 signalling during intestinal inflammation.

Methods: Mice lacking MyD88 specifically in the endothelium (EC-MyD88-/-), myeloid cells and endothelium (MEC-MyD88-/-) or wildtype (WT) were infected with St ΔaroA following streptomycin pretreatment. Cecal samples were collected at day (D) 7 post-infection (pi) to characterize the extent of inflammation via qPCR and immunostaining. Bacterial pathogen burdens were also assessed in cecal, colonic and several extra-intestinal tissues.

Results: Although EC-MyD88-/- and WT mice exhibited similar levels of macroscopic intestinal tissue damage by D7 pi, MEC-MyD88-/- were protected from developing overt inflammation and damage. Upon closer assessment, MEC-MyD88-/- tissues had significantly decreased histological damage scores compared to EC-MyD88-/- and WT mice. Surprisingly, St pathogen burdens were similar between all groups in intestinal tissues; however, MEC-MyD88-/- mice had increased burdens at several extra-intestinal sites. Gene expression analysis revealed significantly impaired induction of several macrophage chemokines in MEC-MyD88-/- mice. Moreover, MEC-MyD88-/- tissue exhibited decreased positive immunostaining for the macrophage marker F4/80.

Conclusion: These findings suggest that although MyD88 signalling within the endothelium and cells of myeloid lineage is likely required for macrophage infiltration to intestinal tissue during St infection, its signalling within these infiltrating cells is likely also contributing to the observed collateral tissue damage. Further, MyD88 signalling within myeloid cells seems to be required for appropriate responses during infection to limit systemic pathogen invasion.

Sandra Botros, Undergraduate Student
Supervisor(s): Rusung Tan

Board #: 2

Title: Correcting a fatal primary immunodeficiency using CRISPR-Cas9 genome editing
Authors: Sandra Botros, Kevin Tsai, John Priatel, Rusung Tan

Abstract:
Primary immunodeficiencies are genetic disorders in which part of the body's immune system is missing or does not function properly with affected individuals being especially prone to infections and inflammatory diseases. Current therapeutic regimens for severe diseases involve hematopoietic stem cell transplantation through bone marrow transplant, but this carries serious risks such as life-threatening infections and graft-versus-host diseases. Recent studies suggest the potential of CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) method of genetic recombination to correct genetic defects in the mammalian genome. The CRISPR-Cas9 system utilizes a designed guide RNA to engineer DNA breaks at a specifically defined locus, and provision of an oligonucleotide template mediates homology-directed repair of the mutated gene. Here, we will test the feasibility of CRISPR-Cas9-mediated recombination as a curative therapy for congenital primary immunodeficiency by experimentation with mice bearing the Scurfy gene, a nonsense mutation (dinucleotide insertion) within the FOXP3 gene. Similar to FOXP3-deficient humans, Scurfy mice lack regulatory T cells and develop a severe, fatal autoimmune disease. Scurfy T cells transfected with plasmid containing CRISPR-Cas9 components and corrective oligonucleotides will be screened for genomic repair by DNA analysis and flow cytometry using a C-terminal FOXP3 antibody, since the mutant protein is truncated and missing this portion. Importantly, successful repair of the Scurfy mutation will hold great promise for the future treatment and study of human primary immunodeficiencies, and potentially other genetic diseases.

Helen Fu, Undergraduate Student
Supervisor(s): Pascal Lavoie

Board #: 4

Title: Characterizing innate immune recognition of Candida albicans in preterm infants
Authors: Helen Fu, Bernard Kan, Pascal Lavoie

Abstract:
Infants born prematurely (<30 weeks gestational age) are at a much greater risk of mortality (up to 40%) from disseminated fungal infections (e.g. Candida species) compared to their full term counterparts. A critical component in the defence against fungal infections is the innate immune system; especially important is the dectin-1 signalling pathway that is active in myeloid phagocytes. Despite data showing equal levels of surface dectin-1 expression when compared to term infants and adults, preterm infants are significantly more susceptible to C. albicans infections. Therefore, we hypothesize that preterm infants do not respond in the same manner to C. albicans due to defects in their downstream dectin-1 signalling pathway.

Mononuclear cells were extracted from peripheral blood (for adults) and cord blood (for term and preterm infants) before stimulated with fixed C. albicans yeast. Two downstream responses were evaluated between the three cohorts. The key inflammatory cytokine IL-1ß is measured via ELISA while the level of phagocytosis is monitored by flow cytometry. To determine the importance of dectin-1 in these responses, cells were incubated with a dectin-1 neutralizing antibody before stimulation and the resulting downstream inhibition compared.

Preliminary results show that IL-1ß secretion peaks when administered with 10^6 yeast/ml to stimulate 500,000 mononuclear cells extracted from adults and term infants. Subsequent tests indicate that this cytokine production can be successfully blocked with the dectin-1 neutralizing antibody using a concentration of 5 µg/ml. When stimulated with a MOI of 10, monocytes from preterm infants have equal proportions of phagocytic cells but lower phagocytic capacity when compared to that of term infants and adults. A significant decrease in levels of phagocytosis can be detected when cells were pre-incubated with dectin-1 neutralizing antibody.

Upon completion of this study, strain differences between different members of Candida spp. will be evaluated in the same context. In addition, the generalizability of these results to live Candida in a clinical setting will need to be determined through the usage of heat-killed C. albicans due to its known altered structure.

James Leung, Undergraduate Student
Supervisor(s): James Zlosnik & David Speert

Board #: 5

Title: Invasion & progression of infection of burkholderia cepacia complex infections in Cystic Fibrosis

Authors: James Leung, James Zlosnik, David Speert

Abstract:

Cystic Fibrosis (CF) is an autosomal recessive genetic disorder caused by a mutation in the CFTR gene. CF affects the permeability of epithelia to chloride and sodium ions in affected carriers. Symptoms of the disease include, but are not limited to, poor digestion and absorption of nutrients, chronic bouts of coughing, and difficulties breathing. Due to the secretion of thick fluid, the lungs of cystic fibrosis (CF) patients often become host to a plethora of different bacterial infections, the most common being Pseudomonas aeruginosa and Staphylococcus aureus. The Burkholderia cepacia complex (including at least 17 species) is another such pathogen, with infections often resulting in pneumonia, rapid decline in lung function, and in many cases, death.

Burkholderia cepacia complex (BCC) infections often progress unpredictably into fatal septicaemia, known as cepacia syndrome. BCC is the only pathogen reliably observed to cause septicaemia in CF patients; however, the mechanism and cause of this phenotypic shift is poorly understood. In order to discover whether or not increased cellular invasion could partially account for this change in behaviour, and in order to elucidate the behaviour of BCC throughout infection, clinical isolates cultured from patients during early infection, late infection, and post-septicaemia were cultured and assayed for invasion. Isolates of interest were allowed to invade 16HBE14o- and CFBE41o- cells for 2 hours, at which point extracellular bacteria were killed with antibiotics. Epithelial cells were lysed, and cell contents were plated. The amount of cellular invasion caused by different isolates was compared. Thus far, findings indicate that BCC clinical isolates are most invasive earlier on during infection.

Dhruv Pandey, Undergraduate Student
Supervisor(s): William Gibson

Board #: 6

Title: Metabolic effects of omega-3 fatty acid supplementation in different types of high-fat diets in mice

Authors: Dhruv Pandey, Chi Kin Wong, Sanjoy Ghosh, William Gibson

Abstract:
Initial studies on the Inuit from Greenland and in Europeans from Mediterranean regions linked low rates of cardiovascular disease (CVD) and diabetes with omega-3 rich fish consumption. However, the Inuit also consume a diet rich in animal blubber with saturated fats (SFA) while the Mediterranean's consume a diet rich in olive oil with monounsaturated fats (MUFA).

Due to the high prevalence of CVD and diabetes in North America, health initiatives promote consuming fish and fish oil rich in omega-3 to reduce the risk of these chronic diseases. However, North Americans consume a diet rich in vegetable oils with omega-6 polyunsaturated fat (PUFA). No previous study has explored this variation in background fat profile to test the metabolic effects of different high fat diets rich in omega-3s. This has prompted us to question whether fish oil interacts with the background high fat diet to cause different metabolic effects. Our preliminary data suggest that a high fat corn oil diet reduces locomotor activity and induces insulin resistance in mice. Therefore, we hypothesize that a high fat corn oil diet supplemented with fish oil could result in a more severe metabolic dysfunction than olive oil or saturated fat diet supplemented with fish oil.

To test this, adult mice will switch from a standard chow diet to one consisting of either high fat corn oil (PUFA), olive oil (MUFA), or anhydrous milk (SFA) for six weeks. Energy expenditure, food /water intake, and physical activity will be measured with a metabolic chamber. Body composition will be assessed with quantitative MRI, and glucose and insulin tolerance tests will be done before and after the diet changes. We expect that mice consuming the high fat corn oil with fish oil diet will be diabetic with glucose resistance and have reduced locomotor activity relative to mice fed the other high fat diets with fish oil. This may indicate that recent trends where consumers supplement fish oil to their diet may not receive the full protective effects due to the omega-3 fatty acid interactions with the background diet.

Erik Venalainen, Undergraduate Student
Supervisor(s): Michael Kobor

Board #: 7

Title: Investigating potential suppressors of RNA polymerase II C-terminal domain truncation mutants

Authors: Erik Venalainen, Maria Aristizabal, Michael Kobor

Abstract:
RNA Polymerase II (RNAPII) is a highly conserved complex that, in eukaryotes, is responsible for the transcription of most protein-coding genes. The catalytic portion of the complex, Rpb1, contains a unique C-terminal domain (CTD) made of 25/26 repeats of the consensus sequence YSPTSPS. This unique domain acts as a binding platform for various RNA processing enzymes, a function dependent on its differential phosphorylation throughout transcription. In an effort to better understand the role of the RNAPII-CTD, we performed a genetic screen, wherein we identified two putative suppressors of a RNAPII-CTD truncation mutant (rpb1-CTD11): chd1 a chromatin remodeler, and mud1 an mRNA splicing factor. The role of loss of CHD1 and MUD1 in suppressing rpb1-CTD11 mutant phenotypes was confirmed and specifically, we observed that loss of CHD1 suppressed the growth defects of RNAPII-CTD truncation mutants at 16℃ or when exposed to formamide, while MUD1 suppressed the growth defects of rpb1-CTD11 when grown in MMS or Inositol deficient conditions. These results indicate that the suppression of rpb1-CTD11 phenotypes by loss of CHD1, or MUD1, are likely a results of functions in different pathways. To better determine the mechanisms involved in the suppression, we checked to see if the loss of CHD1 or MUD1 suppressed previously reporter rpb1-CTD11 defects. In particular, we observed that loss of MUD1, and to a lesser extent CHD1, slightly normalized the decreased Serine 2 phosphorylation levels characteristic of rpb1-CTD11 mutants. These results suggest a possible restoration of altered transcriptional processes including the recruitment of chromatin remodelers and splicing factors. Given a prominent role for Mud1 in splicing, we aimed to establish a splicing assay in hopes of determining if the suppression and normalization of Serine 2 phosphorylation reflect an effect in splicing efficiency. Preliminary results suggested that our assay could detect splicing defects in the rpb1-CTD11, and in future we hope to determine if these can be alleviated upon deletion of CHD1 or MUD1. Ultimately, understanding the roles and regulation of key players involved in the transcription process is ideal when developing therapeutics for conditions like cancer, which are often characterized by altered gene expression.

Marcus Wong, Undergraduate Student
Supervisor(s): Stefan Taubert

Board #: 8

Title: Molecular analysis of nuclear hormone receptor NHR-49 binding to a conserved transcriptional co-regulator

Authors: Marcus Wong, Grace Goh, Ka Young Lee, Stefan Taubert

Abstract:
Transcriptional regulation is critical for maintaining homeostatic processes essential for life. Specificity in transcriptional regulation is accomplished in part through interactions between transcription factors and co-regulators. Nuclear hormone receptors (NHRs) are a large class of metazoan transcription factors involved in energy regulation, xenobiotic stress responses, and many other processes necessary for cell survival. This study focuses on an important transcription factor in Caenorhabditis elegans, NHR-49, which regulates fatty acid desaturation and mitochondrial β-oxidation. NHR-49 interacts with the conserved Mediator subunit MDT-15, a transcriptional co-regulator required for the activation of fatty acid metabolism genes downstream of nhr-49. Previously, we showed that the ligand binding domain of NHR-49 is crucial for this protein-protein interaction. In a forward genetic screen, Svensk et al. (2013) obtained three putative gain-of-function point mutants in the ligand binding domain of NHR-49((nhr-49(et7), (et8), and (et13)). Phenotypic analysis of these mutants revealed unique mRNA profiles of downstream fatty acid desaturation and β-oxidation genes and lifespans for each mutant allele. We therefore addressed whether the protein-protein interaction with MDT-15 is affected by these three nhr-49 point mutations through a yeast two hybrid assay. We found that each of these three alleles affect binding strength to MDT-15 in a distinct fashion, suggesting that these changes in binding strength may cause these mutant phenotypes. In future, we will utilize a GST-pull-down assay to verify our results.

Ellia Zhong, Undergraduate Student
Supervisor(s): Amina Kariminia & Kirk Schultz

Board #: 9

Title: Ruxolitinib induces YB-1/MDR pathway in a subpopulation of cutaneous T cell lymphoma

Authors: Ellia Zhong, Amina Kariminia, Susanna Sung, Jacob Rozmus, Alex Bohm, Waren Baticados, Kirk Schultz

Abstract:
2-3% of non-Hodgkin lymphomas are cutaneous T cell lymphomas (CTCL) which have increased in incidence in recent years to 0.54 in 100,000 people. Survival rates vary from several months to many years. In early stages, 5 year survival can be up to 97%, but in advanced stages of CTCL, the survival rate drops to 41%. YB-1 signaling protein has previously been shown to play a role in cell survival and proliferation and is highly expressed in many cancers which renders it a potential target for specific drug treatment, however it has not yet been investigated in T cell malignancies. The MDR-1 protein, known to cause cells to develop drug resistance leading to poor cancer prognoses, has also been shown to be controlled by pYB-1 expression. We investigated pYB-1 expression and MDR-1 protein expression with and without the presence of the JAK1/JAK2 pathway inhibitory drug Ruxolitinib in the CTCL cell line HUT-78 and in mature T cells isolated from normal adult peripheral blood as controls for comparison. Ruxolitinib is the drug of choice since STAT5 plays a role in the pathogenesis of lymphomas, specifically in HUT-78. Using flow cytometry, YB-1 and MDR-1 expression was shown to be higher in HUT-78 cells compared to normal cells. The ratio of the mean fluorescent intensity of YB-1 protein versus isotype control was 4±0.91 in two normal populations and 19±11 in the HUT-78 population ($p<0.02$ t test). We performed Western blot analyses using the HUT-78 cell line and observed that pYB-1 was induced by Ruxolitinib. The HUT-78 cells treated with Ruxolitinib were also shown to display a 33±16% population of cells that were double positive for pYB-1 and MDR1 which was 16±9.7% in the control HUT-78 cells (vehicle treated, $p<0.02$). Ruxolitinib may therefore induce cytotoxic killing in CTCL cells, but simultaneously activate YB-1/MDR-1 pathway and drug resistance in a subpopulation of the malignant cells. Those results led us to conclude that it is necessary to block the YB-1/MDR-1 pathway for an efficient treatment. Future directions will involve analysing YB-1/MDR-1 pathway induced by other cytotoxic drugs and performing similar experiments on primary leukemic T cells.

Misha Zarbafian, Medical Student
Supervisor(s): Jan Dutz

Board #: 10

Title: Ultraviolet light-mediated induction of systemic lupus erythematosus
Authors: Misha Zarbafian, Mehran Ghoreishi, Jan Dutz

Abstract:
Systemic lupus erythematosus (SLE) is an autoimmune disease with protean clinical manifestations. The most consistent trigger factor for SLE is ultraviolet (UV) light. Repeated UV exposure in non-obese diabetic (NOD) mice, animals that have a genetic predisposition to develop type 1 diabetes, results in a lupus-like disease characterized by high titers of anti-nuclear antibodies (ANA), and glomerulonephritis. These observations suggest that UV induced skin inflammation may be a trigger for SLE in genetically pre-disposed individuals.

Type-1 interferons (IFN) have a central role in SLE development. Using in vivo and in vitro assays, I assisted in determining the cellular source of IFN-alpha. Specifically, I examined the role of plasmacytoid dendritic cells, neutrophils and keratinocytes in the initiation of cutaneous inflammation as a result of UV exposure. Follicular helper T cells (FHT) are a recently identified subset of T cells within lymph nodes that coordinate antibody production.

As SLE is characterized by the presence of autoantibodies, I determined if FHT cells in the skin draining lymph nodes are activated following UV skin injury. The dorsal skin of NOD mice, non-obese diabetes resistant (NOR) mice and Balb/c mice was acutely exposed to UV light. I will expose groups of 5 mice (NOD, NOR, Balb/c) to single doses of UV irradiation. Acute histologic response was evaluated at 24 hours and chronic response at 15-23 days post-UV exposure. Histologic analysis included determination of type and extent of cellular infiltrate using immunohistochemistry. I analyzed skin-draining lymph nodes by flow cytometry and determined the activation status and number of FHT cells. I obtained serum and assay the levels of auto-antibodies following treatment with standard ELISA to confirm induction of auto-immunity.

Our preliminary results have shown that there is up-regulation of CD40 molecules on B cells, as well as up-regulation of CD40L on FTH cells in lymph nodes of NOD mice, in contrast to results obtained using NOR and Balb/c mice, following UV therapy. These results demonstrate that UV light activates B cells that have the potential to produce autoantibodies in mice that are genetically-predisposed to autoimmune disease.

Allen Zhang, Medical Student
Supervisor(s): Wyeth Wasserman

Board #: 11

Title: Platinum resistance and cis-regulatory variations in high-grade serous ovarian cancer

Authors: Allen Zhang, Anthony Mathelier, Yikan Wang, Sohrab Shah, Wyeth Wasserman

Abstract:

Ovarian cancer is a type of malignancy that typically originates in the ovaries or fallopian tubes. Asymptomatic at first, ovarian cancer is often diagnosed at later stages, when the tumour has already metastasized and the survival rates are slim. High-grade serous ovarian cancer constitutes the majority of ovarian cancers (70%) and is the most malignant subtype. High-grade serous ovarian tumours are characterized by widespread genomic instability, which renders them susceptible to DNA damage from platinum-based chemotherapy. As a result, the response to platinum-based chemotherapy in these patients is rapid. However, the DNA repair defects in ovarian cancer also speed up the mutation rate, which can lead to platinum resistance and relapse ("short recurrent" patients). Nevertheless, some patients can survive for prolonged periods of time without relapsing ("long survival" patients). Understanding the genomic signatures of short recurrent and long survival patients may allow for better, targeted therapies for ovarian cancer.

Cis-regulatory variants are mutations that fall within noncoding regions, which comprise 98% of the genome. Mutations that fall within transcription factor binding sites (TFBSs) are potentially disruptive to gene expression, and consequently, an organism's phenotype. Thus far, however, genome analysis techniques have largely been limited to the exome—the "coding" portions of the genome. With the advent of whole-genome sequencing techniques, analyzing the noncoding portion of the genome is now feasible. Analyzing the cis-regulatory changes in ovarian cancer, coupled with protein-coding variants, will give us a more complete picture of the mutational spectrum in high-grade serous ovarian cancer.

In order to find cis-regulatory variants in the tumour genomes of the 30 short recurrent (SR) and 22 long survival (LS) patients, we filtered for variations only present in the tumour samples, but not their matched normals. Of these, we characterized the variations to find those lying within transcription factor binding sites with significant predicted impact on gene expression. We computed empirical p-values for enrichment and showed overrepresentation of cis-regulatory mutations nearby genes involved in growth and apoptosis. We also observed enrichment for genomic rearrangements in long survival patients compared to short recurrent patients. Our next step will be to analyze data for copy number variations, gene expression, and DNA methylation.

POSTER SESSION TWO

BASIC SCIENCE

MODERATOR: Anthony Mathelier

PARTICIPANTS:
Yuliya Badayeva
Alexandra Bohm
Jenny Chen
Jillian Diamond
Patrick Hopkins
Nicole J Leung
Lindsay Richter
Carly Sable
Alishah Saferali
Zheng Yu Zhao

Yuliya Badayeva, Undergraduate Student
Supervisor(s): Bruce Vallance

Board #: 12

Title: Cell shape and motility within mucus as keys to successful Campylobacter Jejuni infection

Authors: Yuliya Badayeva, Martin Stahl, Emilisa Frirdich, Erin C Gaynor, Bruce A Vallance

Abstract:
Campylobacter jejuni is a gram-negative bacterial pathogen commonly associated with the consumption of undercooked poultry. It is one of the most commonly reported causes of foodborne illness and clinical gastroenteritis worldwide. C.jejuni displays a helical shape, which is dependent on the structure of peptidoglycan within the bacterial cell wall. This helical shape is thought to allow the bacteria to traverse the intestinal mucus layer and invade the intestinal epithelium, an important factor in C.jejuni colonization and pathogenesis, leading to intestinal inflammation and diarrhea in humans.

Previous work has indicated that the deletion of the peptidoglycan-modifying enzymes Pgp1 or Pgp2, results in a rod-shaped morphology of C. jejuni. Additionally, we have previously established SIGIRR-deficient (Sigirr-/-) mice as a model of C.jejuni infection and gastroenteritis. We infected Sigirr-/- mice with wild-type, Δpgp1 or Δpgp2 mutant strains of C.jejuni. The pathogen burden of Sigirr-/- mice by the C. jejuni mutants was determined 3 and 7 days post-infection, while histological analysis and immunofluorescent staining was used to determine colonization of the intestinal crypts. We found that the Δpgp1 and Δpgp2 mutant strains were not only unable to cause inflammation, but both mutant strains were also unable to traverse the mucus layer to the epithelium as neither mutant strain was observed within the intestinal crypts.

To quantify this mucus-motility phenotype in vitro, we measured the movement of C. jejuni mutant strains through a mucin column, and tracked the velocity of live bacteria in liquid medium. These approaches continued to indicate a mucus-specific motility defect with the rod-shaped C. jejuni mutants, compared to helical wild-type cells.

Together these data provide strong evidence that the characteristic helical shape of C. jejuni plays an important role in its ability to traverse the intestinal mucus layer and to induce inflammation and gastroenteritis in its human host. Understanding the impact of C. jejuni shape on its pathogenicity and host interactions will aid in further research towards better treatment strategies for Campylobacter infections.

Alexandra Bohm, Undergraduate Student
Supervisor(s): Kirk Schultz

Board #: 13

Title: A novel combined immunodeficiency characterized by a SENP1 mutation
Authors: Alexandra Bohm, Maja Tarailo-Graovac, Kanwaldeep Mallhi, Kyla Hillebrand, Tammie Dewan, John Wu, Clara Van Karnebeek, Kirk R Schultz, Jacob Rozmus

Abstract:

Background: We describe a patient with a novel combined immunodeficiency associated with lissencephaly, developmental delay, failure to thrive, autoimmunity and myelodysplastic syndrome. One of the most striking features of her complex clinical phenotype was a profound arrest in the development of her B cells. Whole exome sequencing revealed a novel mutation in the gene encoding for the SENP1 (SUMO1/sentrin specific protease 1) protein. The addition of SUMO groups is a post-translational modification that alters the function of numerous biological pathways. SUMOylation is a dynamic process with deconjugation by SUMO specific proteases (SENPs) regulating levels.

Signaling through the B cell antigen receptor (BCR) is necessary for the survival and differentiation of transitional B cells into mature B cells. It has previously been shown that SUMO-1 modification inhibits the downstream elements of BCR signaling such as Iκβα degradation, a crucial step in BCR triggered NF-κB activation, and Burton's tyrosine kinase (Btk) activation, which is required for BCR-induced calcium release.

Hypothesis: Absence of SENP1 in our patient leads to an increased level of SUMO-1 modified proteins resulting in an inhibition of BCR signaling. This causes an arrest in B cell development.

Methods: Whole exome sequencing of the patient and both parents was performed in collaboration with the TIDE-BC (Treatable Intellectual Disability Endeavor in BC) research initiative at BC Children's Hospital. Western blotting and qRT-PCR was used to measure SENP1 gene and protein expression. Flow cytometric immunophenotyping was performed on peripheral blood samples. Immunoprecipitation was used to assess SUMO-1 modified Iκβα. We used flow cytometry-based functional assays to measure BCR-triggered calcium release and NF-κB activation.

Results: We demonstrated significantly reduced expression of SENP1 in the patients' peripheral blood lymphocytes. Flow cytometric analysis demonstrated a significant arrest in B cell development at the early transitional stage. There was an increased amount of SUMO-1 modified Iκβα.There was also an absence of BCR-triggered calcium release in the patients primary B cells.

Significance: Our experiments provide novel insights into the role of SUMOylation in B cell development. We are currently in the process of immortalizing primary B lymphocytes in order to further study the effect of SUMO modification on components of B cell signaling pathways.

Jenny Chen, Undergraduate Student
Supervisor(s): Michael Kobor

Board #: 14

Title: Investigating mutations in Eaf1 suppressors in budding yeast
Authors: Jenny Chen, Joshua Brown, Michael Kobor

Abstract:
DNA is tightly condensed to fit into the nucleus. However, it must be stored in a way that can be accessed by transcription proteins. DNA packaging is complex and dynamic in nature, allowing for precise gene expression in response to internal and external stimuli. Chromatin structure is modified by changes such as histone modifications. Histone acetylation disrupts the interaction between DNA and the histone, which promotes accessibility and alters gene expression. NuA4, the only essential histone acetyltransferase complex in Saccharomyces cerevisiae, acetylates the terminal tails of the histone subunits H4, H2A, and H2A.Z. This acetylation plays roles in transcription, DNA damage repair, and cell cycle control. Within NuA4, Eaf1 acts as a scaffold protein that anchors the rest of the subunits and is the only component unique to this complex. Deletion of eaf1 results in the collapse of this 13-subunit complex. NuA4 is conserved in eukaryotes; the human homologue Tip60 has similar functions to NuA4 and is linked to signaling pathways of tumourigenesis. Consequently, investigating Eaf1 can help us gain insight into histone acetylation in budding yeast and higher eukaryotes.

eaf1 knockout suppressors are strains containing mutations that suppress eaf1 knockout phenotypes. These mutations could suppress eaf1 by restoring acetylation, or modifying another mechanism. In this study, we aim to identify mutations that can suppress eaf1 knockout phenotypes via sequencing, with the goal of discovering novel genetic interactions of eaf1. eaf1 knockout suppressors emerged from eaf1 knockout mutants after being stressed under unfavourable conditions. These suppressors had partially restored H4 acetylation levels compared to the knockout strain. Suppressors were also less susceptible to DNA-damaging drugs than the knockout, but more sensitive than the wild type strain. The degree of suppression varied between strains and phenotypes, suggesting that our suppressors had mutations on different genes and affected a range of processes. Using the sequencing data, we aim to directly associate multiple genes to eaf1 and NuA4 complex function.

Jillian Diamond, Undergraduate Student
Supervisor(s): William Gibson

Board #: 15

Title: Determining the genetic cause for familial intracranial aneurysms in a family
Authors: Jillian Diamond, Katelin Townsend, William T Gibson

Abstract:
Intracranial aneurysms are bulging spots found on the walls of arteries caused by endothelial weakness. If enough pressure builds up within this spot, the aneurysm could rupture, allowing blood into the brain space. This bleeding is also known as subarachnoid hemorrhage and can lead to brain damage, or even death. When individuals have two or more close relatives with intracranial aneurysms, we consider the possibility of Familial Intracranial Aneurysms, and hypothesize a genetic component to aneurysm formation. However, no diagnostic genetic tests are yet available to determine whether an individual has, or will have, an intracranial aneurysm in their lifetime.

Our goal is to identify the gene that leads to intracranial aneurysms in a family with three generations of affected individuals. We plan to do this using whole-exome sequencing to identify rare variants that may lead to altered protein function, causing the formation of intracranial aneurysms. Whole-genome single nucleotide polymorphism (SNP) microarray analysis will also be used to exclude genomic regions shared between affected and unaffected family members, limiting the list of candidate genes identified by whole-exome sequencing. This serves to increase the likelihood of identifying the causal genetic variant. Exome sequencing and whole-genome SNP microarray studies are underway to identify any genomic regions containing variants of interest.

This knowledge could be applied to other affected families, and lead to the development of a diagnostic genetic test for familial intracranial aneurysms in the future. Such a test is crucial as it would enable young adults at risk due to family history to know whether they will develop an aneurysm and allows them to make decisions that could potentially be life-saving. Those that are positive for having the disease-causing variant would know to go for regular screening either with Computed Tomography Angiography (CTA) or Magnetic Resonance Angiography (MRA) scans to find any developing aneurysm(s) they may have. Upon identification, the aneurysm(s) can then be treated accordingly to prevent any future complications.

Patrick Hopkins, Undergraduate Student
Supervisor(s): Jan Dutz

Board #: 16

Title: Using CpG oligodeoxynucleotides as an adjuvant for melanoma immunotherapy in a mouse model

Authors: Patrick Hopkins, Jacqueline Lai, Jan Dutz

Abstract:
Melanoma is the deadliest form of skin cancer. While some success has been attained through surgical removal, standard chemotherapy results in poor therapeutic outcomes for malignant melanoma. With malignant melanoma incidence rising, more effective therapies are needed. The recent use of immunomodulation to induce immune responses to melanoma has the potential to revolutionize therapy. However, this no-specific therapy can result in life-threatening auto-immunity. The ability of the immune system to combat the tumor relies on the generation of tumor specific CD8 T-cells. However, as tumor antigens are considered self-antigens, it is difficult to generate CD8 T cells that will recognize the tumor. Secretion of type I interferon by dendritic cells enhances antigen recognition by MHC class I molecules, increasing CD8 T-cell activation. Type I interferon production can be induced by Toll-like receptor 9 signaling; therefore, Toll-like receptor 9 presents a good target for potential adjuvants.

Tumor antigens released by cryotherapy of melanoma tumors may mount a similar CD8 T-cell response to that of immunization with protein antigens. As epicutaneous application of CpG oligodeoxynucleotides is an effective adjuvant when immunizing with peptide antigens, we hypothesize that topical application of CpG oligodeoxynucleotides combined with cryotherapy can induce a strong CD8 T-cell response to tumor antigens.

The objective of this study was to establish a relationship between treatment with epicutaneous CpG in combination with cryotherapy and the generation of an OVA-specific CD8 T-cell response. C57BL/6 wild type mice were injected subcutaneously with a melanoma cell line expressing the OVA peptide and monitored for tumor growth. Melanoma tumors were treat with either cryotherapy alone or cryotherapy with epicutaneous CpG application. Post-treatment tumor growth was monitored over the course of a week. The OVA-specific CD8 T-cell response in the spleen was quantified by interferon-gamma ELISpot and flow cytometry. Preliminary outcome data will be presented.

Nicole J Leung, Undergraduate Student
Supervisor(s): Rusung Tan

Board #: 17

Title: Enhanced Il-17 in peripheral blood of patient with Henoch-Schonlein Purpura, Psoriasis, and Crohn's Disease

Authors: Nicole J Leung, Ashish K Marwaha, Nikhil Sawhney, William Gibson, Kevan Jacobson, Rusung Tan

Abstract:
Interleukin-17 (IL-17) is a cytokine that plays a role in host-defense against candidal infections and autoimmune disease. T helper (Th) cells primarily secrete IL-17 (CD4+ Th17 cells); however, an increasing amount of evidence has shown that macrophages, dendritic cells, and natural killer T cells can also secrete IL-17.

A 17 year old female of Ashkenazi Jewish descent presented to BC Children's Hospital with Henoch-Schonlein Purpura (HSP), psoriasis and steroid-resistant Crohn's disease. She was clinically stable on Infliximab, an anti-tumor necrosis factor therapy. As previous research has shown that elevated proportions of Th17 cells have been implicated in the pathogenesis of HSP, Psoriasis and Crohn's, we hypothesized that this subject may have an altered level of Th17 cells in her peripheral blood. We developed novel flow cytometry and fluorospot assays to assess the circulating Th17 proportion. We confirmed there was a significantly increased amount of Th17 cells in the patient's peripheral blood in comparison to healthy age-matched controls (Th17 percentage: Subject 7.9%±0.74, Controls 1.2% ± 0.06, $p<0.0001$). This observation was maintained over time and repeatedly observed when the subject was clinically stable. The same phenotype was not observed in other subjects with Crohn's before or after Infliximab therapy.

We would like to perform future genetic and immunological studies to assess the causes of this phenotype and test the hypothesis that this subject has an unidentified genetic deficit leading to a higher proportion of peripherally circulating Th17 cells and multiple IL-17 mediated autoimmune pathologies.

Lindsay Richter, Undergraduate Student
Supervisor(s): Daniel Goldowitz

Board #: 18

Title: Impact of unilateral cerebellar haemorrhage combined with early systemic inflammation on the development of the neonatal mouse cerebellum

Authors: Lindsay Richter, Sophie Tremblay, Daniel Goldowitz

Abstract:
Neurological complications in preterm infants are a major health concern, especially in the extremely low birth weight (ELBW, less than 1000g) population. This population is highly vulnerable and is exposed to multiple stressors during their postnatal development. Two major risk factors for neurodevelopmental impairments are perinatal cerebellar haemorrhage (CBH) and post natal infection. How these two risk factors may interact is currently unknown. We aim to understand how CBH and inflammation will alter cerebellar genesis and how neurobehavior will be worsened by this double insult.

To understand how cerebellar development is altered by these risk factors, we have developed a neonatal mouse model of a cerebellar haemorrhagic insult combined with an inflammatory event. We injected bacterial collagenase in the right cerebellar hemisphere at postnatal day 1 in mice pups in combination with an intraperitoneal injection of E. coli lipopolysaccharide to induce a systemic inflammatory state.

We assessed the impact of the combined concomitant insults on cerebellar development by monitoring neonatal and juvenile behavioral changes as well as collecting cerebellar tissues throughout development for histological studies. Unilateral cerebellar haemorrhages induced at P1 delay forelimb grasp acquisition in neonatal mouse pups by 24-48 hours and increase locomotor activity in P15 mice during open-field recording. Early inflammatory state induction also leads to comparable delay in neonatal forelimb grasp acquisition followed by a significant decrease in grip strength and muscular strength measured by the inverted screen task in juvenile mice. Two weeks after the insult, preliminary analysis of cerebellar volume at P15 revealed decreased cerebellar volume mainly related to early inflammatory state in the right cerebellar hemisphere. However, an increased sample size analysis is required to reach significance.

Early insults in the developing neonatal brain alters juvenile motor milestones in a mouse model of cerebellar haemorrhage combined with early systemic inflammatory stress. This new model will allow us to measure short and long-term impact of combined early insults on cerebellar development, their impact on neurobehavior and to test neuroprotective strategies to improve extremely preterm infant neurodevelopmental outcomes.

Carly Sable, Undergraduate Student
Supervisor(s): Angela Devlin & Dina Panagiotopoulos

Board #: 19

Title: Catechol-O-methyl transferase (COMT) and blood pressure in children treated with second-generation antipsychotics

Authors: Carly Sable, Anita T Coté, Constadina Panagiotopoulos, Angela M Devlin

Abstract:
Second-generation antipsychotics (SGA) are increasingly being used to treat children for a wide-range of mental health conditions. In some children, SGA-treatment is associated with cardiometabolic side effects, such as rapid weight gain and elevated blood pressure (BP). Why some children are susceptible to these SGA-related side effects is not fully understood.

The catechol-O-methyl transferase (COMT) Val158Met variant is associated with BP and mental health conditions in adults. We recently reported higher BP in SGA-treated children with the Met allele, but found no relationship in SGA-naïve children. Further, the COMT Val158Met variant is also associated with differential methylation of the COMT promoter. The aim of this study is to investigate the interaction of the COMT Val158Met variant and COMT methylation on BP in children with mental health conditions.

A cross-sectional population of SGA-treated and SGA–naïve children (n=320), ≤18 years of age, were recruited through Psychiatry at BC Children's Hospital and assessed for markers of cardiometabolic health. DNA was extracted from buccal epithelial cells and the COMT Val158Met variant genotyped by real-time PCR. A bisulfite pyrosequencing assay was developed to quantify the methylation status of 13 CpGs in a region of the COMT promoter between -116 and -51 bp relative to the transcriptional start site. Relationships between SGA treatment, COMT Val158Met genotype and COMT promoter methylation on BP were assessed using general linear models and Pearson correlation. Z-scores were calculated for body mass index (zBMI), and systolic and diastolic BP (zSBP, zDBP) to account for age and sex.

To date, 36 SGA-treated and 28 SGA-naïve children have been analyzed. No effect of SGA treatment or mental health diagnosis on COMT promoter methylation was observed. Independent of SGA treatment, a negative relationship between COMT promoter methylation (CpG 6) and zSBP (r= -0.313, p=0.039) was observed in children with the COMT 158 Met allele. A positive relationship was observed between COMT promoter methylation (CpG 5) and zBMI in children with the COMT 158 Val/Val genotype (r= 0.581, p=0.012). These findings suggest an interactive effect of COMT promoter methylation and the COMT Val158Met variant on BP and BMI in children with mental health conditions.

Alishah Saferali, Undergraduate Student
Supervisor(s): Chinten James Lim

Board #: 20

Title: Alpha integrin cytoplasmic tail signalling in cell adhesion mediated drug resistance in pediatric acute lymphoblastic leukemia

Authors: Alishah Saferali, Chi-Chao Liu, Eva Yap, Chinten James Lim

Abstract:
Integrins are heterodimeric transmembrane cell adhesion receptors composed of noncovalently associated α- and β- subunits. The α4-integrins are highly expressed in lymphocytes and are required for lymphocyte recruitment at inflammatory sites and engraftment in the bone marrow stroma. Dysregulated or aberrant α4 integrin function contributes to haematological malignancies including pediatric acute lymphoblastic leukemia (ALL). Acquired chemoresistance is a significant factor in minimal residual disease and treatment relapse. This can arise when a few malignant cells remain in the bone marrow niche, which is protected from initial chemotherapy.

A heterodimeric integrin, α4β1, has been shown to confer enhanced resistance to chemotherapeutic drugs when cells are adhered to extracellular ligands. This phenomenon is known as Cell Adhesion Mediated Drug Resistance (CAM-DR), one of the major contributors of treatment relapse. The cytoplasmic domains of α-integrins share a highly conserved membrane-proximal KxGFFKR motif, which is required to maintain the α-β integrin heterodimer. Previous studies in our lab investigated the requirement of the α4 integrin cytoplasmic domain in the regulation of α4-dependent CAM-DR in Jurkat T-ALL cells. Expression of a tail truncated α4-mutant consisting of the minimal KxGFFKR sequence yielded a chemoresistant phenotype that is independent of cell adhesion. Since the KxGFFKR motif is conserved across all α-integrins, and adhesion of Jurkat cells via other β1-integrins also conferred CAM-DR, we are intrigued by the notion that adhesive engagement via different integrins may confer differing survival signals. To address this, we are engineering a series of T-ALL cell lines expressing chimeric integrins that allow comparative analysis of CAM-DR attributable to the α-integrin cytoplasmic tail. The chimeric α-integrin consists of the extracellular and transmembrane domain of α4 that is fused with the cytoplasmic domain of various α-integrins (α5, α6A, α3, α2, α9, αV, and αL). When expressed in the available α4 null Jurkat cell line, the various chimeras will engage a common α4β1-specific substrate (such as CS1-Fibronectin) but transduce survival signals directly attributable to the unique fusion cytoplasmic tail. A detailed understanding of these mechanisms will help to elucidate the relative contribution of various integrin-ligand pairs in tumour cell survival and chemoresistance of pediatric acute lymphoblastic leukemia.

Zheng Yu Zhao, Undergraduate Student
Supervisor(s): Laura Sly

Board #: 21

Title: Intravenous immunoglobulin skews human macrophages to a regulatory phenotype in vitro

Authors: Zheng Yu Zhao, Lisa Kozicky, Susan Menzies, Laura M Sly

Abstract:
Inflammatory Bowel Disease (IBD) is a chronic, life-long disease characterized by inflammation along the intestinal tract. Current treatments for IBD rely on non-specific immune suppression. Macrophages are key players in the inflammatory response and contribute to the inflammation present in IBD. It has been suggested that antibody-based biological therapies can be used to treat IBD by skewing macrophages to a regulatory phenotype. Regulatory macrophages (Mregs) are anti-inflammatory. In response to inflammatory stimuli, they produce large amounts of the anti-inflammatory cytokine, IL-10, and very low amounts or no pro-inflammatory cytokines such as IL-12 and IL-6. Mice macrophages can be skewed to a regulatory phenotype through co-stimulation with Intravenous Immunoglobulin (IVIG) and lipopolysaccharide (LPS). Mregs have been shown to reduce inflammation in mice both in vitro and in vivo.

My overarching hypothesis is that co-stimulating human macrophages with Intravenous Immunoglobulin (IVIG) and lipopolysaccharide (LPS) can skew them to a Mreg phenotype. To test this hypothesis, I propose the two following objectives:

Objective 1. Measure the cytokines produced by human monocyte derived macrophages (MDMs) co-stimulated with IVIG and LPS

Objective 2. Assess the ability of IVIG to skew MDMs to a Mreg phenotype

Methods: Peripheral mononuclear cells (PBMCs) from donor blood were isolated. Monocytes were cultured overnight in either 10% human autologous serum or 10% human AB serum. The human MDMs were stimulated with various doses of IVIG and LPS for 24 hours. Their supernatants were collected and the cytokine production was measured using enzyme-linked immunosorbent assay (ELISA). Macrophage phenotype was assessed based on cytokine production.

Results: Human MDMs cultured in autologous serum, when co-stimulated with low dose IVIG and LPS, produced high levels of anti-inflammatory IL-10 and low levels of pro-inflammatory IL-12 and IL-6. Human MDMs cultured in human AB serum, when co-stimulated with IVIG and LPS, did not show a change in anti-inflammatory IL-10 production levels but had decreased pro-inflammatory IL-12 and IL-6 production.

POSTER SESSION THREE

BASIC SCIENCE

MODERATOR: Brian Chung

PARTICIPANTS:
Sara Alhowar
Steven Bae
Justin Chan
Anna Jo
Anita Lim
Anik Muhuri
Amandeep Parhar
Robert Ragotte
Julia Schmidt
Clara Van Ommen
Steven Zhao

Sara Alhowar, Undergraduate Student
Supervisor(s): Chinten James Lim

Board #: 22

Title: Effect of chemokines on cell adhesion and chemotherapeutic resistance in acute leukemias

Authors: Sara Alhowar, Daniel He, Eva Yap, Pascal Leclair, Chinten James Lim

Abstract:
Acute Lymphoblastic Leukemia (ALL) is the most common of childhood cancers. While highly amenable to chemotherapy, about 12-15% will relapse and become chemoresistant. This is mostly due to Cell Adhesion Mediated Drug Resistance (CAM-DR) which is an association between acquired drug resistance and increased functional expression of cell adhesion molecules such as integrins. The α4β1 integrins play a vital role in lymphoblast cell adhesion, migration and survival; they facilitate ALL cell retention within the bone marrow microenvironment where their adhesion increases their survival rate against chemotherapy and development of drug resistance. In addition, the interaction between the chemokine SDF-1, with its receptor CXCR4, regulates cell trafficking and migration, and contributes to development of drug resistance in ALL. These findings raise the intriguing question of the specific mechanism of CAM-DR and the interplay between SDF-1/CXCR4 signaling with that of α4β1-integrins and adhesion.

To investigate this mechanism, we generated CXCR4 knockout T-ALL cell lines and the role of CXCR4 on drug resistance was tested without SDF-1 stimulation. First, cell viability was measured against different vincristine concentrations where the cells were stained with Alamar Blue after 48 hrs of exposure to the drug. Data shows no difference in cell viability between wild type and CXCR4 knockout ALL cells. Then, the role of CXCR4 in α4β1 integrin activation was assessed using appropriate antibodies and data collected using flow cytometry. The results show no difference in α4β1 integrin activation between the wild type, CXCR4-knockout, or the CXCR4-rescued cell lines. Furthermore, a cell adhesion assay was conducted to test the effect of CXCR4 in lymphoblast cell adhesion where the cells were stained with a reporter dye and plated on fibronectin, an integrin substrate. Using spectrophotometry, there was no difference found in the percent of adhered cells in the different ALL cell lines. Therefore, the data accumulated thus far suggests little or no role for CXCR4 on adhesion and chemoresistance in the absence of the chemokine receptor stimulation. Finally, the same assays will be conducted to measure the effect of CXCR4 knockout comparing SDF-1 stimulation and non-stimulated cells.

Steven Bae, Undergraduate Student
Supervisor(s): Christopher Maxwell

Board #: 23

Title: Role of RHAMM at the spindle assembly checkpoint and in mosaic variegated aneuploidy syndrome

Authors: Steven Bae, Helen Chen, Chinten J Lim, Christopher Maxwell

Abstract:
Proper functioning of the spindle assembly checkpoint (SAC) is essential for equal segregation of chromosomes during mitosis. The SAC generates a "wait" signal at the kinetochores in the presence of misattached or unattached chromosomes. This delay prevents the onset of anaphase until all chromosomes are attached to the mitotic spindle in a bipolar fashion. Completion of the SAC requires structural cues including kinetochore tension through spindle attachment and stripping of checkpoint proteins from the kinetochore, and biochemical cues from kinases, phosphatases, and the anaphase-promoting complex. A defective SAC can result in a condition known as mosaic variegated aneuploidy syndrome. Affected patients have a high proportion of aneuploid cells, often leading to cancer and growth defects. Our protein of interest, the receptor for hyaluronan-mediated motility (RHAMM), has been shown to regulate kinase activation at the kinetochores and interact with the motor protein, dynein, to maintain spindle integrity and orientation, suggesting a possible role during the SAC. We hypothesize that RHAMM provides structural and biochemical cues during the SAC, and that its silencing, or changes to its expression, induces chromosome nondisjunction and aneuploidy. Analysis of live HeLa cells followed through mitosis revealed that RHAMM-depleted cells took longer to complete the SAC compared to control siRNA and GFP-RHAMMFL rescue groups. Immunostaining of Mad2, a protein expressed only at misattached or unattached kinetochores, showed a higher proportion of Mad2-positive cells in RHAMM-knockdown cells versus control siRNA and GFP-RHAMMFL rescue groups. Anaphase defects were also more frequently observed in RHAMM-knockdown cells. Immunostaining of kinetochore markers and measurement of interkinetochore distance as an indicator of tension revealed that interkinetochore distance was decreased in RHAMM-knockdown HeLa cells when compared to control siRNA and GFP-RHAMMFL rescue groups. Similar experiments for intrakinetochore distance revealed comparable results. These observations will be validated using live HeLa cells expressing fluorescently-tagged kinetochore markers. Lastly, immunostaining and immunoprecipitation experiments with RHAMM and known key checkpoint proteins revealed co-localizations and protein interactions. Further work will examine changes in RHAMM expression related to chromosome non-disjunction both in vivo and in vitro. Kinase and phosphatase activity during the SAC will also be analyzed.

Justin Chan, Undergraduate Student
Supervisor(s): Bruce Vallance

Board #: 24

Title: Impacts of Muc2 Core-1 glycosylation on the intestinal colonization of bacterial pathogens

Authors: Justin Chan, Kirandeep Bhullar, Hyungjun Yang, Lijun Xia, Bruce Vallance

Abstract:
The intestinal mucus is composed primarily of Mucin 2 (Muc2), a highly glycosylated (O-linked) glycoprotein. The addition of Core-1 glycans to Muc2 is mediated by Core 1 β 1,3 –N-galactosyltransferase (C1galt1).

Previous research has shown that C1galt1-/- mice (lacking Core 1-derived O-glycans) develop spontaneous colitis. However, how the changes in the mucus layer composition affect the colonization of pathogenic bacteria is still unknown. Our objective is to investigate how changes in the glycosylation patterns of Muc2 affect colonization of Citrobacter rodentium(mouse-specific enteric pathogen related to the human enterohemorrhagic and enteropathogenic Escherichia coli) in the intestine.

C57BL/6 (B6) and C1galt1-/- mice were infected with C. rodentium and monitored over the course of infection. Stool samples from each mouse were collected. Subsequently, stool samples underwent DAPI fixation and fluorescence microscopy was used to determine the total commensal microbe depletion. These samples were also plated on DifcoTM MacConkey agar to enumerate pathogen shedding in the stool. Mice were euthanized Day 6 PI and systemic tissues (liver, spleen, mesenteric lymph node), colon, caecum and lumen were collected for plating on MacConkey agar. Colonic tissues were also collected for histological analysis.

Our data showed that C. rodentium infected C1galt1-/- mice displayed 15-20% weight loss by Day 6 PI and had significantly higher C. rodentium burdens in the colonic tissues. Stool shedding revealed significantly higher C.rodentium burdens in C1galt1-/- mice. C1galt1-/- mice were impaired in commensal depletion compared to B6 mice. Furthermore, C1galt1-/- mice had higher macroscopic and histological damage in the colon compared to B6 mice. Overall, our data suggest that lacking Core 1 derived O-glycans increase the host susceptibility to enteric pathogens.

Future experiments will be done to determine which specific components in the mucus layer of C1galt1-/- mice allow for increased colonization of C. rodentium. Mass spectrometry analysis and lectin staining will be conducted to identify the changes in mucus oligosaccharide composition during C. rodentium infection. Use of a bioluminescent strain of C. rodentium could provide data on how Muc2 glycosylation affects pathogen interactions with the mucus layer and will allow the comparison of C. rodentium colonization patterns in different glycosylation knockout strains of mice.

Anna Jo, Undergraduate Student
Supervisor(s): Soren Gantt

Board #: 25

Title: Correlation between regulatory T cells and immune control of EBV infection in children

Authors: Anna Jo, Zach Liang, Soren Gantt

Abstract:
Epstein-Barr virus (EBV) is an ubiquitous oncogenic virus which infects more than 95% of the world's population, and it has been known to cause diseases such as infectious mononucleosis and Burkitt's lymphoma, the latter of which is the one of the most common pediatric cancers in Africa. Given its global burden on public health, it is essential and urgent to develop effective vaccines against the virus; currently, however, very little is known about the immune control of the virus in young children, whose need for a vaccine is greater due to their greater suffering from EBV infection. To provide children a better protection from EBV-related malignancies, we are investigating the association between various immune factors of children and immune control of EBV. Especially, we focused on the significance of regulatory T cells (Tregs) in the different immune correlates of virus control between adults and children, given that the disproportionately suppressive action of Tregs has been implicated in the weaker immune responses of children against EBV. Tregs are known to suppress Th1 responses, which are crucial in effectively combatting viral infections. In order to compare the level of T cell activity in the presence and absence of Tregs, blood samples from both children and adults were divided into Treg-depleted and non-depleted groups. Flow cytometry was used to compare the levels of cytokine secretion and proliferation of T cells in response to EBV antigenic stimulation. We found that in both adult and child, there was no significant difference in the level of T cell proliferation between the depleted and non-depleted samples. However, in adults but not children, Treg-depletion led to higher levels of IFN-y upon stimulation. In addition, in children but not adults, higher levels of IL-2 were observed in Treg-depleted groups when compared to non-depleted groups. Although the exact role of Tregs in the different immune responses observed between adults and children are yet to be discovered, further research is likely to give us a better understanding of EBV immune control in children, and contribute to efforts in vaccine development.

Anita Lim, Undergraduate Student
Supervisor(s): Catherine Pallen

Board #: 26

Title: The role of protein tyrosine phosphatase α in oli-neu differentiation
Authors: Author(s): Anita Lim, Philip T. T. Ly, Hoa T. Le, Catherine J. Pallen

Abstract:
Objective: Myelination of the central nervous system is carried out by oligodendrocytes (OLs) and is preceded by the differentiation of oligodendrocyte precursor cells (OPCs) into OLs. Elucidating the molecular mechanisms of this process may provide insights into therapies for demyelinating and dysmyelinating disorders. The receptor protein tyrosine phosphatase PTPα is an important regulator of OPC differentiation, but the signalling pathways underlying PTPα-dependent OL differentiation remains to be explored. In this study, we are investigating the differentiation of the murine OPC cell line, oli-neu, and the role of PTPα in oli-neu differentiation.

Methods: Oli-neu cells are mouse OPCs immortalized by infection with a retroviral vector containing the t-neu oncogene. Previous studies have shown that oli-neu cells can be induced to differentiate by the addition of dibutryl-CAMP into the culture medium. To confirm differentiation, we treated the cells with 1mM dibutryl-cAMP for 0, 3 and 6 days. The extent of differentiation was determined by examining the expression of the mature OL marker CNPase by Western blot analysis. In addition, we examined cell morphology using immunocytochemical staining for CNPase and quantified the extended processes of differentiated and undifferentiated oli-neu cells.

To investigate the dependency of PTPα in oli-neu differentiation, we employed the CRISPR/Cas9 system to generate PTPα-deficient clones by transfecting oli-neu cells with CRISPR/Cas9 plasmids targeting the PTPα gene for deletion. The clones were validated by Western blot analysis for PTPα expression.

Results: CNPase expression increased by 150% in oli-neu cells differentiated for 6 days with dibutryl-cAMP as compared to undifferentiated cells. Moreover, the number and complexity of the extended processes increased in the differentiated cells as compared to undifferentiated cells. The majority of the undifferentiated oli-neu cells have a bipolar morphology, whereas cells differentiated for 6 days developed three or more processes. Additionally, we identified 2 clones deficient in PTPα from a number of selected colonies, thus showing that PTPα expression can be depleted using the CRISPR/Cas9 system. Taken together, these results indicate that the oli-neu cell line is a valid model of OL differentiation and that PTPα expression can be diminished to study the dependency of PTPα in OL development.

Anik Muhuri, Undergraduate Student
Supervisor(s): Stefan Taubert

Board #: 27

Title: The role of Cdk-8 in the cadmium-induced stress response in C. elegans
Authors: Anik Muhuri, Jennifer Grants, Grace Goh, Stefan Taubert

Abstract:
Appropriate gene transcription is necessary for homeostatic and developmental processes and therefore is regulated by transcription factors as well as transcriptional co-regulators. The metazoan Mediator complex is an important transcriptional co-regulator that is capable of general transcriptional activation or gene program-specific regulation. The Mediator subunit CDK-8 is the focus of this study because it regulates gene-specific programs. Microarray data has demonstrated that cdk-8 regulates a subset of genes in Caenorhabditis elegans, some of which overlap with genes which are overexpressed in response to cadmium exposure. In this study, we address whether cdk-8 is involved in the transcriptional regulation of cadmium-responsive genes. We have found that cdk-8 is required for the induction of cadmium detoxification genes mtl-1, mtl-2, and cdr-1 in vivo. In addition, we show that loss of cdk-8 results in enhanced cadmium sensitivity in cdk-8 null worms compared to wild-type worms. Thus, CDK-8 promotes cadmium resistance by regulating cadmium detoxification genes. Furthermore, previous research has demonstrated the presence of several regulatory elements in the cdr-1 promoter. In future, we will determine which transcription factors and regulatory elements are required in conjunction with cdk-8 to up-regulate cdr-1 by mutating the cdr-1 promoter regulatory elements or knocking down transcription factor expression by RNAi.

Amandeep Parhar, Undergraduate Student
Supervisor(s): Elizabeth Conibear

Board #: 28

Title: Investigating the role of endospanin in receptor down-regulation in the yeast model system

Authors: Amandeep Parhar, Lauren Dalton, Elizabeth Conibear

Abstract:
Obesity is a leading risk factor in the development of type 2 diabetes, heart disease and stroke. Activation of the leptin receptor (OB-R) initiates cell signaling pathways responsible for controlling food intake and body weight. The endospanin protein binds directly to OB-R and leads to its down-regulation. Reduced expression of endospanin increases OB-R levels on the cell surface and can prevent died-induced obesity in mice. However, the exact molecular function of endospanin is still unknown. We have previously shown that the yeast endospanin homolog, Vps55, forms a protein complex with Vps68 and has a conserved role in receptor down-regulation at endosomes. We hypothesize that the Vps55/Vps68 complex works as a cargo adaptor to recruit specific receptors into developing transport vesicles. Our preliminary work suggests that Vps55 interacts with Arf1, which is a major regulator of vesicle formation. Thus, our objectives are to identify mutations that specifically disrupt the Vps55/Arf1 interaction and determine their effect on the Vps55/Vps68 complex and receptor sorting.

As Arf1 is a cytosolic protein, we have mutated four conserved residues in the cytosolic domains of Vps55 through targeted alanine mutagenesis. Using a protein-fragment complementation assay we have assessed the binding of two Vps55 mutants to Arf1 and Vps68 and neither appears to have a significant effect on the interactions. We are currently in the process of testing the remaining two mutants.

Once a Vps55 mutant has been identified to disrupt the Arf1 interaction we will be able to determine if this disruption causes trafficking dysfunction or alters the Vps55/Vps68 complex formation, stability of localization. If disrupting the Vps55 and Arf1 interaction does affect the Vps55/Vps68 complex it would strongly agree with our hypothesis that this complex works as a cargo adaptor.

In the future, corresponding mutations could be studied in the mammalian endospanin protein to determine if an interaction with Arf1 is important to regulate cell surface levels of the OB-R. Studying the specific sorting function of the yeast endospanin homolog, Vps55, will therefore help elucidate how endospanin down-regulates the OB-R, which could potentially have clinical applications in the treatment of diet-induced obesity.

Robert Ragotte, Undergraduate Student
Supervisor(s): Stuart Turvey

Board #: 29

Title: Characterization of a germ-line acquired JAK1 gain-of-function mutation
Authors: Robert J Ragotte, Kate L Del Bel, Margaret L McKinnon, Shan-Yu Fung, Stuart E Turvey

Abstract:

Background: Whole exome sequencing technology has permitted the discovery of rare mutations as the cause of immunological disease that is not otherwise specified. Two brothers were identified as carrying a germ-line acquired gain-of-function mutation in JAK1, part of the JAK/STAT signalling pathway. The mutation was inherited from their mother who, we hypothesized, acquired the mutation during embryonic development. The A634D mutation was suspected to be driving the brothers' unique clinical phenotype that included profound peripheral eosinophilia, eosinophil infiltration into the spleen, liver and esophagus, hypothyroidism, whole body dermatitis, failure to thrive and in-utero liver cysts. This investigation aimed to identify how this mutation is driving the observed phenotype.

Methods: Epstein-Barr Virus (EBV) immortalized B cells were made for biochemical studies from peripheral blood mononuclear cells (PBMCs). The phosphorylation state of STAT1 and STAT3, both downstream of JAK1, were assessed through western blotting to determine JAK1 activity with and without IL-6 or IFN-alpha stimulation, relative to a healthy control. Ruxolitinib, an FDA approved JAK1/2 selective inhibitor, was used to determine whether the promiscuous activity of JAK1 could be diminished through inhibition. Results were also demonstrated in whole blood through flow cytometry that utilized intracellular phospho-STAT3 staining to determine the cellular response to stimulus.

Results: The results indicate that A634D JAK1 has little constitutive activity but is hyper responsive to IL-6 stimulation. Through pretreatment with 50nM Ruxolitinib, JAK1 activity in the patient samples was reduced to baseline levels, suggesting that this may be an effective intervention.

Conclusions: The A634D mutation in JAK1 more readily activates the downstream signalling cascade compared to wild type cells. This supports the notion that the JAK1 mutation is a gain-of-function mutation that is driving the observed phenotype in the patients. Based on preliminary data, the possibility of using Ruxolitnib to reduce JAK1 activity will be explored further as a possible treatment.

Julia Schmidt, Undergraduate Student
Supervisor(s): Anthony Bailey

Board #: 30

Title: EEG Analysis of Semantic Language comprehension in Individuals with ASD
Authors: Julia Schmidt, Keith McLarren, Anthony Bailey

Abstract:
Introduction: Approximately 50% of children diagnosed with Autism Spectrum Disorders (ASDs) and IQ in the normal range experience developmental language delay, and about 30% developmental language loss. Very little is known about the neurophysiology of the language loss group. Previous studies from our group suggested a difference in language lateralization in ASD individuals with and without a history of language delay using magnetoencephalography (MEG), but the findings were confounded by mixed handedness within the ASD groups. Thus we will investigate this finding further, including ASD individuals with a history of language loss as a distinct group and controlling for handedness. In an electroencephalogram (EEG), the N400 response can be used as a marker of semantic comprehension of language. The response is a negative brainwave that appears after about 400ms in response to a mismatch between a word and a previously established semantic context. It has already been established that the N400 response is weaker in ASD individuals. We hypothesize that the N400 response in individuals with ASD and a history of language loss will be even less than that of other individuals with ASD or neurotypical people.

Methods: EEG datasets are being generated and then processed for analysis through the EEGlab software suite from UCSD. We are using a 256-channel HydroCel Geodesic Sensor net from EGI sampling at 1000Hz to record event-related potential (ERP) responses from a sentence reading task.

Results: Refinement of our data collection and processing protocols with pilot data sets is ongoing. The raw EEG data recordings contain a number of undesirable artifacts, such as eyeblinks, muscle movements and ambient 60Hz electromagnetic noise. The epochs of time surrounding the trial events need to be reliably identified and aligned before averaging responses to expected and anomalous sentence endings.

Conclusion: The N400 is detectable in this reading paradigm but still requires more refinements in data collection and processing to increase the signal to noise ratio.

Clara Van Ommen, Undergraduate Student
Supervisor(s): Dan Goldowitz

Board #: 31

Title: Examining genetic factors involved in ethanol induced cell death in BXD recombinant embryonic mice

Authors: Clara Van Ommen, Julia Boyle, Scott Lattimer, Kristen Hamre, Dan Goldowitz

Abstract:
Fetal Alcohol Spectrum Disorder (FASD) describes a spectrum of damage caused to developing embryos as a result of maternal alcohol consumption during pregnancy. FASD results in cognitive impairments and sensory- motor deficits, caused by central nervous system (CNS) damage, that can range in severity between individuals exposed to similar levels of ethanol. Previous work has shown that genetics play a role in determining susceptibility to ethanol-induced damage. However, little has been examined regarding the genetic pathways affected that contribute to the differential susceptibility observed, and it has yet to be determined if ethanol affects only a few genetic pathways involved in global brain development or if it affects multiple pathways involved in the development of different brain areas. In this study, the parental strains (C57BL/6J and DBA/2J) and 25 strains of BXD recombinant mice embryos were exposed to ethanol in utero at embryonic day 9 (E9) and examined at E9.5. The level of apoptotic cell death was measured in the developing forebrain, brainstem and otic vesicles, compared between strains, and analyzed via WebQTL. Variation in the level of cell death between the BXD strains in the three areas examined was observed, but there was weak correlation in the level of cell death between different brain areas within the same strain. QTL analysis of data from the otic vesicles identified three suggestive QTL's on chromosomes 2, 8 and 19; data from the brainstem identified three suggestive QTL's on chromosomes 3, 4, and 13; and data from the forebrain identified two suggestive QTL's on chromosome 10 and 19. The lack of overlap between the QTL's identified and the weak correlations suggests that ethanol's affects are mediated through multiple genetic pathways. However, there may be genetic overlap between these pathways that has yet to be identified that could potentially be used as a marker for ethanol's teratogenic effects. These findings should prove to be the basis for further work seeking to identify specific genetic pathways involved in the observed variation in susceptibility to damage in the hopes of ultimately developing interventions for FASD.

Steven Zhao, Undergraduate Student
Supervisor(s): Rajavel Elango

Board #: 32

Title: Determination of urinary sulfate in human pregnancy as a non-invasive marker for protein status

Authors: Steven Zhao, Rajavel Elango

Abstract:

Background: All human proteins are comprised of 20 amino acids. Amino acids are used in protein synthesis and are a source of energy when oxidized. When sulphur containing amino acids (methionine, cysteine) are fully catabolized, sulphur is excreted primarily in the urine as sulfate ions. Because the amount of proteins within our body remains fairly constant, the synthesis of new proteins will equal the amount degraded. Therefore, by measuring the amount of an excreted endpoint, in response to test protein intake, a prediction can be made for protein needs. Human pregnancy increases nutritional needs as progressive changes occur in the body to accommodate the growing fetus. As a result, sufficient protein intake must be reached to ensure proper development of the fetus, although protein needs during this crucial stage are not well defined.

Objectives:

1) To establish a method to test urinary sulfate concentrations from samples collected earlier from a study examining protein requirements during early and late pregnancy.

2) To examine whether urinary sulfate excretion can be used as a non-invasive marker for protein status.

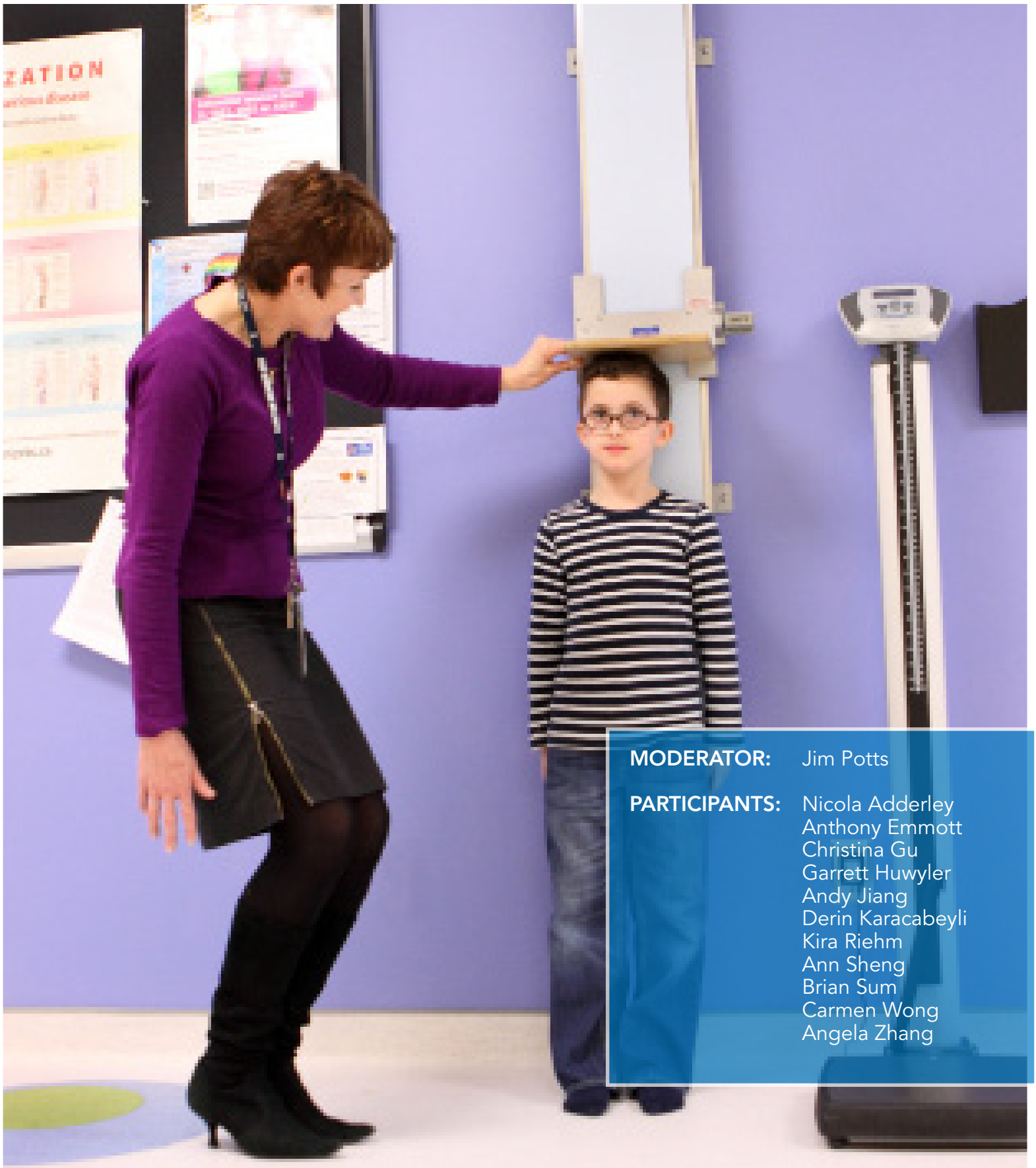
Methods: Urine samples were collected at 16 and 36 weeks of pregnancy (n=37 and n=44, respectively). Subjects were tested with varying amounts of protein (0.22-2.56 g/kg/day). Samples were analysed for sulfate concentration by reacting with a solution containing sodium rhodizonate and barium chloride to produce an orange, pink color. The intensity of color is representative of the sulfate concentration and was measured as absorbance of 520nm using an Ultraspec-3000 spectrophotometer. The absorbance was compared to a standard sulfate curve to determine sulfate concentrations. Sample sulfate concentrations were standardized with urinary creatinine(Cr) concentrations.

Results: Urinary sulfate concentrations were mean (range) of 3.89 (0.53-10.79) μmol SO4/μmol Cr in early pregnancy, and 4.05(0.63-8.72) μmol SO4/μmol Cr in late pregnancy. Urinary sulfate concentrations increased with increasing protein intake in both early and late pregnancy.

Conclusion: Linear, exponential, and polynomial regression models were fit to the data. Although no clear breakpoint was observed in urinary excretion of sulfate in response to protein intake, the linear fit is most likely the best model to define the relationship.

POSTER SESSION FOUR

CLINICAL



MODERATOR: Jim Potts

PARTICIPANTS:
Nicola Adderley
Anthony Emmott
Christina Gu
Garrett Huwyler
Andy Jiang
Derin Karacabeyli
Kira Riehm
Ann Sheng
Brian Sum
Carmen Wong
Angela Zhang

Nicola Adderley, Undergraduate Student
Supervisor(s): Connie Yang

Board #: 33

Title: Risk factors for failing to eradicate Pseudomonas aeruginosa in pediatric patients with cystic fibrosis

Authors: Nicola Adderley, James Zlosnick, Yolanda Lillquist, Connie Yang

Abstract:

Background: Lung damage secondary to chronic Pseudomonas aeruginosa infection leads to increased morbidity and mortality among cystic fibrosis patients. Early antibiotic treatment has been shown to slow or prevent the onset of chronic infection. In spite of these advances, few studies have proposed risk factors for failing to eradicate P. aeruginosa. In addition to factors investigated in previous studies, we evaluated the potential predictive value of anti-pseudomonas antibodies and clonal isolates as risk factors for eradication failure and subsequent P. aeruginosa regrowth.

Objective: To determine factors associated with a) eradication failure, and b) shortened time to regrowth for CF patients infected with P. aeruginosa.

Methods: This study employed retrospective analyses of pediatric cystic fibrosis patients followed by BCCH and admitted for P. aeruginosa eradication therapy between 2008 and 2013. Successful eradication was defined as the absence of Psa in the first respiratory culture following the completion of antibiotic treatment. RAPD (randomly amplified polymorphic DNA) PCR was used to type patient isolates, while anti-pseudomonas antibody levels were quantified using ELISA (enzyme-linked immunosorbent assay).

Results: First growth eradication was successful in 52 of 63 attempts (85.7%). None of the factors investigated increase the risk of P. aeruginosa eradication failure. The same proportion (25%) of patients w ho failed to or successfully eradicated the bacteria grew strains clonal to those they had isolated in previous infections, suggesting no link between bacterial suppression and eradication failure. Positive antibodies did not predict eradication failure.

Conclusions: Preliminary results are not statistically significant with regards to any of the factors followed. Clonal analysis of patient isolates currently stored at BCCH, but not yet typed, is ongoing. The study period may be expanded to include patients who isolated P. aeruginosa prior to 2008, as a larger sample size would allow for more appropriate data analysis. A linear regression on the factors investigated will be performed.

Anthony Emmott, Undergraduate Student
Supervisor(s): Mark Ansermino

Board #: 34

Title: Simplifying self-report measures of pain intensity for preschool-aged children
Authors: Anthony Emmott, Nicholas West, Dustin Dunsmuir, Vincent Ng, Carolyne J Montgomery, Gillian R Lauder, Carl L von Baeyer

Abstract:

Introduction: Self-report is widely accepted as the primary source for assessment of pain intensity. Tools like the Faces Pain Scale – Revised (FPS-R) are suitable for older children, but many children aged 3 to 4 years lack developmental skills needed to use these scales. We are currently evaluating two simplified pain intensity scales using a two-step procedure: a dichotomous "pain-no pain" question followed by a simple 3-point scale scoring mild, moderate and severe pain.

Objective: To characterize the utility, sensitivity, reliability and limitations of these simplified scales in 3- to 6-year-old children.

Methods: 180 children aged 3-6 years undergoing blood collection are to be recruited. Subjects are asked to rate pain intensity at three time-points: T1 (before venipuncture), T2 (immediately after), and T3 (5 minutes later). Each time, the child uses two of the following three self-report pain assessment tools: FPS-R, a simplified two-step faces scale (S-FPS), or a simplified two-step concrete ordinal scale (S-COS) representing magnitude of hurt. At each time-point, the investigator also rates each child's pain intensity according to the Face, Legs, Arms, Cry, Consolability (FLACC) scale.

Results: 118 subjects have been recruited so far (52% male). A greater proportion of 4- and 5/6-year-olds reported a pain score of zero during the expected no-pain scenario T1 when using the simplified scales (88%) over the FPS-R (70%). In 4-year-olds, the median (IQR) T1-to-T2 increase in pain scores were 1 (0-4.5) for FPS-R, 7 (3-10) for S-FPS and 3 (3-10) for S-COS and T2-to-T3 decrease in pain scores were 2 (0-7) for FPS-R, 5 (0-7) for S-FPS and 3 (0-7) for S-COS. These differences between scales are less clear in 3-year-olds and not observed in 5/6-year-olds.

Conclusions: Our preliminary findings suggest the simplified scales, compared to the FPS-R, have improved sensitivity in discriminating between pain and no pain and may offer better options for reporting no pain. The implementation of these simplified scales could improve pain management for preschool-aged children, especially in 4-year-olds. However future studies should evaluate their utility in collecting self-reports of pain in a broad spectrum of clinical scenarios.

Christina Gu, Undergraduate Student
Supervisor(s): Shazhan Amed

Board #: 35

Title: SCOPE: Childhood obesity prevention resources for families
Authors: Christina Gu, Shazhan Amed, Susan Pinkney, Stephanie Shea

Abstract:

Background: Due to rising trends of childhood obesity, many prevention programs have arisen within Canada and globally. Sustainable Childhood Obesity Prevention through Community Engagement (SCOPE) is a community-based, multi-sectoral initiative aimed at promoting healthy weights in children, and is piloted in three communities in British Columbia. Having engaged various sectors at multiple levels, SCOPE communities identified the need to develop family resources and tools to address the challenges that parents might encounter.

Objectives: To identify families' barriers and facilitators of adopting healthy behaviours and to develop resources to support families in overcoming the challenges that prevent them from making healthy choices.

Hypothesis: Healthy lifestyles are not only individual choices, but are also shaped by the built environment that people live in. By understanding parents' perspectives on the barriers and facilitators in their social and community contexts, researchers and communities may be able to tailor comprehensive family resources that can be used to improve parents' awareness and knowledge of healthy lifestyle recommendations and to sustain healthy practices in their home.

Methods: A literature review was conducted to explore the barriers and facilitators that were commonly perceived by parents in childhood obesity prevention interventions. Social cognitive theory was selected as the theoretical framework that guided the research design. A purposeful sampling method is being used to recruit parents with diverse demographics who have children aged 6-12 years. Healthy habits questionnaires will be administered to the participants to collect baseline data about their children's current health behaviours. This will be followed by four semi-structured focus groups in order to understand parents' perspectives related to barriers, facilitators and potential resources in terms of making healthy lifestyle choices. Questionnaire responses will be analyzed using descriptive statistics, while focus group discussion will be coded for thematic analysis. The family-based resources will be created and shared within the pilot communities and other regions in BC to enhance families' capacity to encourage healthy behaviours in children and to facilitate the adoption of health messages within families in the long term.

Garrett Huwyler, Undergraduate Student
Supervisor(s): Ran Goldman

Board #: 36

Title: Patient family perceptions of tattooed physicians in a paediatric hospital setting
Authors: Garrett Huwyler, Ran Goldman, Bruce Phillips

Abstract:

Background: Over the last 2 decades, tattoos have become more commonplace in the mainstream population as is evidenced by the large increase in numbers of tattoo parlours across Canada. With one in five Canadians having at least one tattoo, this increased prevalence is likely resulting in the number of tattooed physicians increasing as well. Extensive evidence from literature has documented the importance of physician attire, but there is little data about parental/guardian attitudes towards the appearance of physicians treating children.

Objective: This study seeks to examine the parental/guardian attitudes towards physicians who have visible tattoos, as well as exploring whether the age of the parent/guardian influences this perception. The information gathered may be useful to doctors and medical students to help guide their decisions about acquiring a visible tattoo. In addition it will also be useful information for hospital administrators in making policy decisions.

Methods: 200 participants will be recruited for this study at BC Children's Hospital. The study participants are the accompanying adult of patients that present to one of the clinical cluster study areas. A cross sectional survey involving a guided self-administered questionnaire will be provided to the individual for them to voluntarily complete and will be collected upon completion by a researcher assistant. Surveyed patient's families data will be analyzed using statistical software to examine the perceptions that visible tattoos are potentially creating. Our findings will contribute towards the development of future studies exploring if location and imagery of tattoos plays an influential role, as well as repeating this survey over time to plot changes (if any) in attitudes towards this societal phenomenon.

Andy Jiang, Undergraduate Student
Supervisor(s): Mariana Brussoni

Board #: 37

Title: Perceptions of injury risk associated with booster seats and seatbelts among injury prevention professionals and researchers

Authors: Andy Jiang, Takuro Ishikawa, Ian Pike, Mariana Brussoni

Abstract:

Importance: Motor vehicle collisions remain one of the leading causes of death and injury for Canadian children. Transport and health authorities around the world recommend children be restrained in rear-facing infant seats, forward-facing toddler seats, booster seats, or a seatbelt alone based on their age, weight, and height. When correctly used, safety restraints greatly reduce the risk of injury by redistributing crash forces across the child's strongest anatomical structures. Despite recommendations from Transport Canada, the rate of booster seat use has been reported as low as 39%. Children are often prematurely transitioned from booster seats to seatbelts, or skip the booster seat stage entirely, which can lead to severe injuries or death.

Aim: To investigate perceptions of injury risk associated with booster seats and seatbelts among injury prevention professionals and researchers.

Hypotheses: We hypothesize that (1) there exists an ejection stereotype around motor vehicle injuries. This ejection stereotype leads people to believe that seatbelts are good enough to protect children riding in cars: "collision injuries are ejection related, seatbelts prevent ejection, therefore seatbelts are good enough." Further, we propose that (2) this stereotype is independent of knowledge such that it may be prevalent even among injury prevention professionals and researchers. Lastly, (3) this stereotype can be countered by reminding people of non-ejection injuries that can occur to children due to improperly used seatbelts (e.g. abdominal, spinal injuries).

Participants: Injury prevention professionals and researchers were selected as they have substantial knowledge about child passenger safety.

Methods: An online questionnaire is in development and will be administered to injury prevention professionals and researchers across Canada. The questionnaire will ask participants to estimate risks of injury associated with seatbelts and booster seats in two formats: one that reminds them of non-ejection injuries and one that does not.

Outcomes & Relevance: Evidence that an ejection stereotype exists even among professionals with knowledge would suggest that (1) current interventions providing information to parents may not be effective enough, and (2) interventions to increase booster seat use should aim to reduce the ejection stereotype.

Derin Karacabeyli, Undergraduate Student
Supervisor(s): Shazhan Amed

Board #: 38

Title: Multi-sectorial community engagement to prevent childhood obesity: Strategies to engage the private business sector

Authors: Derin Karacabeyli, Shazhan Amed, Susan Pinkney, Stephanie Shea

Abstract:

Background: Childhood obesity is a growing problem in Canada. SCOPE is a community-based participatory initiative in BC aimed at preventing childhood obesity by engaging and empowering all sectors within a community. Although SCOPE has successfully engaged and empowered many sectors in its three pilot communities, the private business sector, which has a strong influence over many daily lifestyle choices that children and parents make, has so far been only minimally engaged.

Objective: To develop strategies and resources to further engage the private business sector in community health promotion to support childhood obesity prevention.

Hypotheses: Business perceptions of community engagement and health promotion (i.e. businesses' motivations to engage, the barriers they may face, their expectations, and their ideas for health-promoting action) may vary based on a business's size and sub-sector. With a better understanding of how these perceptions differ, engagement resources and strategies can be created and adapted to address a targeted business's unique situation. By developing and using sector-specific strategies that minimize identified risks, maximize mutual benefit, and provide the necessary support to implement sustainable health-promoting action plans, we may be able to increase business engagement in SCOPE pilot communities.

Methods: First, the existing literature on business engagement with community health promotion initiatives was reviewed in order to discover what has made certain public-private partnerships successful, and what has made community engagement difficult for other businesses. Currently, formative data collection is being conducted through 45-60 minute semi-structured interviews with business owners and managers, exploring their perceptions of community engagement and health promotion. A stratified purposeful sampling methodology is being used to recruit businesses from various sub-sectors and of various sizes. Thematic analysis will be performed to analyze the data. Following data analysis, business engagement strategies and resources will be developed.

Kira Riehm, Undergraduate Student
Supervisor(s): Penny Sneddon

Board #: 39

Title: Perceived executive and socio-emotional functioning in children and adolescents with Supraventricular Tachycardia (SVT): Preliminary results

Authors: Kira Riehm, Penny Sneddon, Carolina Escudero, Shubhayan Sanatani, Elizabeth Sherwin, Saira Mohammed

Abstract:

Background & Purpose: Supraventricular Tachycardia (SVT) is the most common heart arrhythmia in children. Although SVT is rarely life threatening, few studies have investigated developmental outcomes that might be impacted due to recurrent episodes of decreased cerebral blood pressure. Of the existing studies, most have used neuropsychological tests to examine cognitive functioning, whereas few have used self-report measures of perceived abilities. Information about perceived functioning could be used to guide future studies when selecting standardized measures, as well as provide clinicians with a better understanding of any learning, socio-emotional or behavioral challenges associated with SVT. The purpose of this study is to evaluate perceived executive functioning, behavioral and socio-emotional functioning in children and adolescents with SVT using self-report and parent-proxy measures. In addition, the feasibility of a larger, multi-site study using similar methodology will be determined.

Methods: Patients with SVT between the ages of 7 and 17 were recruited from the BC Children's Hospital Heart Centre. After obtaining consent and assent, parent(s) completed a Child Demographic Questionnaire, Child Behavior Checklist (CBCL) and a Behavior Rating Inventory of Executive Function (BRIEF). Children ages 11 and older completed a Youth Self-Report (YSR) and a BRIEF Self-Report. A cardiology fellow completed an SVT Severity Scale for each participant based on information obtained from the patient's medical chart

Results: At present, 3 participants have been gathered. Due to the small sample size, means will be presented in comparison to the normative sample for each questionnaire. In addition, data concerning the severity of SVT in this sample will also be presented.

Future Work: Data collection is ongoing, with the goal of recruiting 30 participants. Future analyses will determine if patients with SVT and their parents perceive more challenges with social, behavioral and executive functioning than children and parents in a normative sample. Future analyses will also determine the extent to which different qualities of SVT attacks (i.e., duration, severity, and frequency of attacks) predict executive, social and behavioural functioning.

Ann Sheng, Undergraduate Student
Supervisor(s): S Evelyn Stewart

Board #: 40

Title: A neuroimaging study of pediatric Obsessive-Compulsive Disorder, at-risk siblings, and healthy controls

Authors: Ann Sheng, Fern Jaspers-Fayer, Elaine Chan, Rhonda Ellwyn, S Evelyn Stewart

Abstract:

Background: Obsessive-Compulsive Disorder (OCD) is a common (1-3%) and debilitating neuropsychiatric illness that frequently begins in childhood. OCD has strong but complex genetic underpinnings, with a 10- to 30-fold increased risk for biological siblings of OCD-affected youths. However, despite intensive efforts via family, linkage, candidate gene and genome-wide association studies, specific genes central to illness onset have not been identified, possibly due to the heterogeneous nature of samples diagnosed with OCD. Since brain structure and function are highly correlated with an individual's genetic makeup, identifying neural correlates associated with increased genetic risk for OCD could potentially help researchers pinpoint the genes contributing to symptom severity and disorder onset.

Objective: This study has multiple aims: to identify potential heritable risk markers of OCD; to increase our knowledge of the neurocircuitry involved in OCD; and to ultimately help guide treatment strategies for affected individuals.

Method: We will perform a cross-sectional study to examine potentially heritable neural correlates of pediatric OCD in three groups of youths aged 8-18 with different levels of genetic risk: OCD-affected youths, their biological siblings at risk for OCD, and age- and sex-matched healthy controls (n=30 per group). Brain structure and white matter tracts implicated in OCD will be analyzed using structural Magnetic Resonance Imaging (MRI) and Diffusion Tensor Imaging (DTI) recorded with a 3.0 Tesla MR scanner. In addition, we will use functional MRI to investigate group differences in brain function during three neuropsychological tasks designed to probe emotional and cognitive processes: the Tower of London (ToL) planning task, the Stop Signal Task (SST) and the Symptom Provocation Task (SPT). Task performance and neural profiles will be examined for correlations with OCD symptom severity, measured using the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS).

Brian Sum, Undergraduate Student
Supervisor(s): Deborah Giaschi

Board #: 41

Title: Global motion perception in children with amblyopia
Authors: Brian Sum, Kim Meier, Deborah Giaschi

Abstract:
Introduction: Global motion perception is the ability to combine motion of individual dots moving in different directions to perceive a dot pattern moving in a single direction. The speed of a global motion pattern can be broken down into a ratio of distance (how far a dot moves between each frame in a motion movie) over time (how long each frame lasts before the next is displayed). Recently, we found that the performance of typically-developing children depends on the distance/time components making up the speed ratio, rather than speed per se. Amblyopia is a developmental visual disorder characterized by reduced vision in one eye that cannot be corrected with glasses. There are conflicting results on whether children with amblyopia have deficits in global motion perception. We hypothesize that differences in the speed ratio components tested in different studies have led to these discrepancies. Our goal is to test this hypothesis by investigating the effect of distance and time components on global motion perception in children with amblyopia.

Methods: We will recruit 12 children with amblyopia and 12 age-matched controls. We first measure their visual acuity and stereoacuity. Next, global motion coherence thresholds are determined. The stimulus consists of an array of dots, where a proportion (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 pattern is moving. A coherence threshold is the lowest proportion of signal dots needed to accurately determine the direction of motion. We measure thresholds at 6 distance/time speed ratios that include 3 distances (small, medium, large) and 2 times (short, long), creating 6 different speeds. Thresholds of children with amblyopia are compared to those of controls.

Results: Preliminary results show that children with amblyopia (n = 6) perform significantly worse than controls (n = 7) when the speed ratio is made with smaller distances, but not larger distances, regardless of time. Therefore, global motion deficits in amblyopia are only detectable with specific combinations of stimulus parameters. This finding has important implications for understanding the mechanisms underlying this disorder and for improving treatment.

Carmen Wong, Undergraduate Student
Supervisor(s): Mariana Brussoni

Board #: 43

Title: Challenging play meets nature play
Authors: Carmen Wong, Sara Brunelle, Tak Ishikawa, Susan Herrington, Mariana Brussoni

Abstract:
Background: Play is essential for social, cognitive and physical development. Evidence suggests that limited access to natural play environments and outdoor challenging play opportunities can have detrimental effects on children. Despite this, the space restrictions and efforts to make play spaces more structured and "safe" result in play spaces that provide inadequate physical or cognitive challenge conducive for healthy development.

Objective: To investigate the impact of play space design on child behavior and social interactions.

Design/Methods: An intervention study was conducted with two Vancouver childcare centres rated as having low quality outdoor play. Longitudinal qualitative and quantitative data were collected at each centre before (Time 1) and after (Time 2) an intervention that introduced natural play elements to promote challenging play in each centre's outdoor play space. A total of 46 children and 12 Early Childhood Educators (ECE) participated in the study. ECEs at each centre completed measures for each child, including sociometric status, relational and overt aggression, emotional symptoms, peer relationship problems, hyperactivity/inattention, conduct problems and prosocial behavior. Accelerometer data were collected from the children to measure physical engagement (energy expenditure, steps taken and intensity level). Based on the ECE assessments of sociometric status, the most and least dominant boy and girl from age groups 2, 3 and 4 (total n=8 at each centre) were selected for video observations and spatial behavior mapping of their outdoor play behaviour before and after the intervention. Both play spaces were re-evaluated on the outdoor play space quality after the playground change. Videotapes were coded to examine social relationships, play behavior, and engagement in challenging play. Time 1 and Time 2 data were compared to determine the impact of the intervention on children's behaviours and social interactions. Focus groups were conducted with ECEs to determine their perceptions of the impact of the intervention on the children.

Results/Future Direction: Preliminary analyses indicate increases in variety of play behaviours and challenging play opportunities. ECEs report positive changes in children's play opportunities and behaviours due to the intervention. A randomized controlled trial to rigorously test the effect of this intervention is recommended.

Angela Zhang, Undergraduate Student
Supervisor(s): Deborah Giaschi

Board #: 44

Title: Effectiveness of reading interventions for children with developmental dyslexia
Authors: Angela Zhang, Marita Partanen, Deborah Giaschi

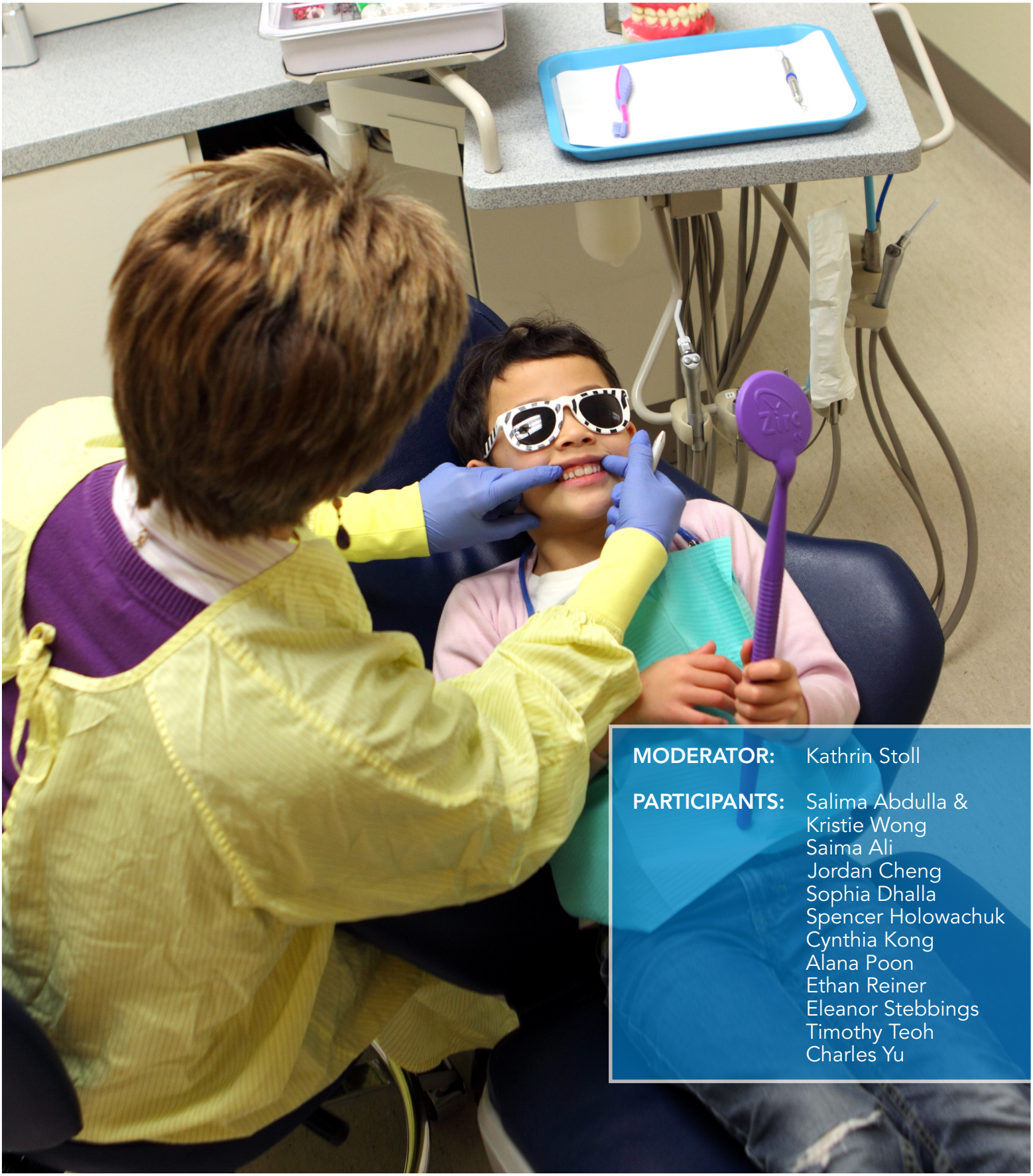
Abstract:
Dyslexia is a reading disability of neurobiological origin that affects approximately 700,000 children and youth in Canada. In addition to poor academic performance, this reading disability is associated with several mental health and economic concerns later in life, but reading interventions may be able to mitigate those consequences. Our study investigates the effectiveness of an intensive reading intervention, called the Literacy Centre program, for Grade 3 students with a diagnosed reading disability. We compared this intervention to a less intensive school-based learning assistance program.

The study is on-going; here we report results for 8 children in the Literacy Centre program, 14 children receiving learning assistance, and 31 children with typical reading ability who did not receive a reading intervention. Tests of reading comprehension, word recognition, nonsense word reading, and timed word reading, as well as listening comprehension, spelling, phonological awareness, short-term memory, and processing speed were administered. To assess improvement, comparisons were made for each group of students, before and after a 3-month intervention period.

The typical reader group showed some improvement in reading skills, but these results were not significant ($p>0.05$). The poor readers receiving learning assistance significantly improved in one reading skill over the 3-month period: timed word reading ($p<0.05$). Poor readers in the Literacy Centre program improved in a broader range of skills with a significant improvement in three areas: timed word reading, timed non-word reading, and reading comprehension ($p<0.05$), and a significant decrease in listening comprehension ($p<0.05$). These preliminary results indicate that intensive reading approaches like the Literacy Centre program may be more effective than less intensive school-based approaches at improving reading skills. The decrease in listening comprehension requires further study. We are also conducting a brain imaging study to determine the structural and functional predictors that are associated with a good response to intervention.

POSTER SESSION FIVE

CLINICAL



MODERATOR: Kathrin Stoll

PARTICIPANTS: Salima Abdulla &
Kristie Wong
Saima Ali
Jordan Cheng
Sophia Dhalla
Spencer Holowachuk
Cynthia Kong
Alana Poon
Ethan Reiner
Eleanor Stebbings
Timothy Teoh
Charles Yu

Salima Abdulla & Kristie Wong, Medical Students **Board #: 45**
Supervisor(s): Ronald G Barr

Title: Relative effects of the duration and frequency of inconsolable crying on frustration levels among female and male adolescents

Authors: Kristie Wong, Salima Abdulla, Ronald Barr, Nichole Fairbrother, Rollin Brant, Alissa Antle, Mandy Chen

Abstract:
Findings from studies over the last 40 years have shown that early infant crying, especially inconsolable crying bouts, can be associated with parental feelings of frustration. This frustration can result in an increase in non-accidental injury to the infant, as in the case of Shaken Baby Syndrome. However, there have been no studies to date assessing frustration responses in adolescents using prolonged cry bouts. Our primary goal is to assess the effect of the duration and frequency of inconsolable crying on frustration levels among female and male adolescents in a two-hour babysitting session.

We will recruit a total of 114 participants to achieve a statistical power of 80%. Eligible participants are nulliparous male and female adolescents ages 15-17 who are fluent in English. The participant is asked to babysit Ethan for two hours while being observed behind a one-way mirror. Ethan is a doll programmed to follow one of three crying schedules: consolable, frequent inconsolable, and long inconsolable. Participants complete 11 frustration ratings on a computer at predetermined time-points during the two hours.

To date, 54 adolescents (43 females, 11 males) have been run. The mean frustration increased over the two hours from the baseline rating of 4.7 to 37.6. Group differences on frustration levels between the three were not statistically significant (all $p > .25$). However, graphically we observed a trend that is consistent with our prediction that longer and more frequent bouts of inconsolable crying result in higher frustration levels than consolable crying bouts. Frustration levels were noted to be higher during crying bouts (mean frustration ratings ranged between 21.6-37.6) as compared to periods of quiet or fussing (mean frustration ratings ranged between 4.7-13.8). Contrary to our expectation, no statistically significant difference in frustration levels between genders has been found (all $p > .28$).

Our data shows a trend towards inconsolable crying eliciting greater frustration than consolable crying and that a model infant may be an effective research tool capable of changing frustration levels depending on its state (quiet, fussing, or crying).

Saima Ali, Medical Student
Supervisor(s): Nichole Fairbrother & Patricia Janssen

Board #: 46

Title: The Mother-Infant Wellness Project: Phase II New mothers' thoughts of harm: Prevalence and relation to OCD and child harm

Authors: Saima Ali, Harmandeep Sidhu, Nichole Fairbrother, John Abramowitz, Sheila Woody, David Wolfe, Patricia Janssen, Dana Thordarson

Abstract:

Background: Unwanted, intrusive thoughts of harm coming to one's infant are experienced universally by new mothers, and close to half of all new mothers experience unwanted, intrusive thoughts of harming their infant. Both accidental and intentional thoughts of harm can be extremely upsetting to the mothers who experience them, and may provoke fears about their mental stability and ability to parent. Perinatal caregivers often worry that these thoughts could lead to child abuse. However, the evidence suggests that the occurrence of these thoughts is normal, and is much more likely to lead to the development and/or worsening of obsessive compulsive disorder (OCD), a potentially debilitating anxiety disorder, than to child harm. Responding appropriately to women who report these kinds of thoughts is critical for mothers and their infants.

Objectives:

1. Document the prevalence of OCD and maternal postpartum thoughts of infant-related harm.
2. Determine if maternal thoughts of intentional harm predict infant harming behaviours.
3. Determine if maternal thoughts of harm predict postpartum OCD among women.
4. Determine if there is an increase in the prevalence of OCD from pregnancy to early postpartum.

Design: This is a prospective cohort study of 1000 pregnant women living in British Columbia.

Procedures: Women who agree to participate in the research will be administered an interview and set of questionnaires at approximately 33 weeks gestation, and at 1- and 3-months postpartum. Prenatal questionnaires assess demographic information, reproductive history, parenting attitudes, beliefs about thoughts, OCD symptoms, social support and current mood. Postpartum questionnaires will additionally assess birth information and maternal sleep. The final questionnaire also includes an anonymous questionnaire pertaining to aggressive parenting and infant harm. Interviews assess postpartum thoughts of harm, OCD and depression.

Outcomes: Recruitment is active since August 2013. This research will determine (a) the prevalence of perinatal OCD (b) the prevalence of postpartum thoughts of harm and postpartum OCD, (c) whether or not there is an association between postpartum intrusive thoughts of infant-related harm, and i) postpartum OCD and ii) maternal harming behaviours. This information will be vital to the development of interventions and educational material for maternity care providers, pregnant and postpartum women.

Jordan Cheng, Medical Student
Supervisor(s): Karen Campbell

Board #: 47

Title: Investigating oral health outcomes in Soroti children and adolescents
Authors: Jordan Cheng and Karen Campbell

Abstract:

Background/Purpose: Evidence in recent literature reports that soft drinks are easily accessible and affordable in sub-Saharan Africa. Children and young adults may purchase soft drinks to supplement their meals despite the lack of nutritional value. We hypothesize that, in addition to their living conditions, limited access to dental care, dietary and oral hygiene practices, consumption of soda along with other sweetened beverages may further increase their risk of negative oral health outcomes. The purpose of this study is to investigate the association between dental health measures and oral health determinants in children and young adults in the Soroti region of Uganda.

Methods: A stratified two-stage cluster sample of children(8-10 yrs) and adolescents(16-19 yrs) were recruited from seven different schools in Soroti, Uganda. Our convenience sample (n= 84) including private, public, and rural schools were first surveyed using pre-tested questions regarding economic status, dental care access, weekly diet/beverage consumption and oral hygiene practices. Following the survey, each subject had a series of retracted intra-oral photographs taken to document dental anomalies, caries, erosion, and hygiene status. Weight and height were also measured in order to calculate body-mass index (BMI).

Analysis: Questionnaire data will be collated and analyzed to investigate the association between socio-economic status, diet, dental care access, and measures of dental disease as assessed by the intra-oral photographs. Dental disease indices will include Decayed, Missing, Filled Teeth (DFMT) and Basic Erosion and Wear Examination (BEWE). BMI will also be calculated as a basic measure of general health.

Results: The evaluation of our intra-oral photographs and questionnaire data is ongoing and is expected to be completed by the end of August 2014. Preliminary analysis suggests that sweetened tea consumption is much more prevalent than soft drinks in this particular region of Soroti. The practice of flossing was also unheard of and may lead to poorer long-term oral health.

Sophia Dhalla, Medical Student
Supervisor(s): Osman Ipsiroglu

Board #: 48

Title: Willis Ekbom Disease (WED) & Sensory Processing Abnormalities (SPAs): Presentations & interconnections in children with Neurodevelopmental Conditions (NDCs)

Authors: Sophia Dhalla, Mai Berger, Nadia Bayzaei, Melvin Chan, Tami Lin, Alexandra Wagner, Osman Ipsiroglu

Abstract:

Introduction: Sleep problems, mainly chronic insomnia—falling asleep and sleep maintenance difficulties—occur in up to 80% of children with NDCs. WED, a neurologic disorder characterized by discomfort (up to pain) of feet, legs, hands, and/or other body parts that is relieved by movements, seems to be the most frequent cause of insomnia. We observed that children with NDCs and sleep problems often experience SPAs, the inability to integrate and respond to sensory information from the body and environment appropriately. We hypothesize that all children/adolescents with WED or a WED-like presentation have significant SPAs. We investigate presentations and interconnections between WED and SPAs in patients with NDCs.

Methods: 28 children/adolescents with NDCs and insomnia due to familial WED (mothers had symptoms of WED and/or iron deficiency during pregnancy) were assessed. Clinical presentations and symptoms were (a) captured in reports that utilized the concept of therapeutic emplotment and (b) recorded retrospectively in a clinical phenotyping database. A case report of a 10-year old representative patient framed and highlighted our hypothesis from a clinical perspective.

Results: Children: 100% presented with WED, insomnia and SPAs. When stratified based on the type of SPA, 89% of patients had tactile sensitivity (including high pain tolerance), 32% auditory, 25% visual, and 18% oral sensitivity. Of the 28 patients in the cohort, 82% and 39% of the children had an NDC and/or psychiatric presentation (diagnosis and/or like-presentation), respectively. The case analysis of the 10-year old male patient supported the database findings; the assessment, including the Suggested Clinical Immobilization Test, confirmed his WED diagnosis, and he scored 135/190 on the Sensory Profile™, experiencing difficulties with touch, textures, loud noises, bright lights, and taste.

Conclusion: We analyzed the clinical presentation of children/adolescents with NDCs who suffer from familial WED. All patients had SPAs; however, their presentation varied due to the different descriptions in the clinical reports. Our current understanding is that sleep problems caused by SPAs have to be investigated further. Therefore, in the next step of our analysis, the Sensory Profile of children assessed by an occupational therapist will be compared with age-matched children seen at our clinic.

Spencer Holowachuk, Medical Student
Supervisor(s): Kevin Harris

Board #: 49

Title: Early extubation in neonates, infants and children undergoing surgery for congenital heart disease

Authors: Kevin C Harris, Spencer Holowachuk, Sandy Pitfield, Shubhayan Sanatani, Norbert Froese, James E Potts, Sanjiv K Gandhi

Abstract:

Objective: We sought to determine the feasibility and assess the clinical outcomes associated with an early extubation strategy for all children undergoing congenital heart surgery, including neonates (<30 days).

Methods: We performed a linked database analysis of all patients undergoing congenital heart surgery between July 1, 2010 and December 31, 2012. We collected data on cardiac diagnoses, preoperative status, procedure, and postoperative course, including duration of invasive and noninvasive ventilation, failure of extubation, hemodynamic data, length of stay, complications, and mortality. A multivariable model was used to assess the independent factors associated with inability to extubate within the operating room and with delayed extubation (>24 hours).

Results: We operated on 613 children, including 97 neonates. Intraoperative extubation was achieved in 71% of cases and early extubation (≤ 24 hours) was achieved in 89% of cases. Overall mortality was 1.5% (9 out of 613). Notably, 63% of neonates were extubated within 24 hours, including 67% of arterial switch operations and 54% of total anomalous pulmonary venous return repairs. Norwood operations were the only procedure in which no patient was extubated within the first 24 hours. A multivariable logistic regression demonstrated that predictors of delayed extubation included preoperative mechanical ventilation, weight <5 kg, longer procedure time, and need for postoperative inotropes. Implementation of an early extubation strategy was associated with low rates of complications (5.1 per 10 procedures), short lengths of intensive care unit (ICU) stay (median, 1 day; interquartile range (IQR), 1-3), and short hospital stays (median, 4 days; IQR, 3-6).

Conclusions: The majority of children undergoing congenital heart surgery can be extubated in the operating room. Most neonates, including many undergoing complex procedures, can be extubated in the first 24 hours after surgery. Early extubation is associated with low morbidity rates and short length of ICU and hospital stays.

Cynthia Kong, Medical Student
Supervisor(s): Suzanne Vercauteren

Board #: 50

Title: Adolescent and parental attitudes towards pediatric biobanking: a school and hospital outpatient survey

Authors: Cynthia Kong, Tamsin Tarling, Caron Strahlendorf, Michelle Dittrick, Ruth Milner, Suzanne Vercauteren

Abstract:

Since September 2011, the Childhood Cancer and Blood Research (CCBR) BioBank has been collecting biospecimens such as blood, bone marrow, DNA and cerebrospinal fluid donated from patients with blood disorders, for research purposes. The success of this program led to the development of the BC Children's Hospital BioBank (BCCHB), a campus-wide initiative to include patients at both BC Children's and Women's Hospitals.

Since samples are taken from the pediatric population, ethical issues such as parent/guardian consent, patient assent, and re-consenting of childhood samples when patients reach adulthood, are major areas of discussion in the biobanking community. To explore these key issues, we conducted a survey with adolescents and their parents across outpatient clinics (Oncology, Cardiology, Orthopedics) at BC Children's Hospital, and in several Vancouver high schools. Participants rated their willingness to donate samples under different hypothetical scenarios, their perceived importance of re-consent, age at which patient assent should be obtained, and provided personal opinions about pediatric biobanking.

Our study found differences between the responses of participants approached in hospital, versus the predominantly healthy high school populations. In particular, youth and parents in the hospital cohort exhibited greater willingness to donate pediatric samples. School participants were more likely to consider parental consent sufficient, and age of assent unnecessary. Finally, re-consent was considered important to the majority of all participants. As an extension of this project, we intend to conduct additional surveys in high schools across the Lower Mainland in the coming school year. The results of this study and our future survey responses will help to assess public perceptions and inform protocol development as the field of biobanking progresses, both at BC Children's Hospital and on an international scale.

Alana Poon, Medical Student
Supervisor(s): Jugpal Arneja

Board #: 51

Title: The surgical management of Pierre Robin Sequence – when and which type of surgery?

Authors: Alana Poon, Marija Bucevska, Douglas Courtemanche, Cindy Verchere, Sandra Robertson, Claudia Malic, Jugpal Arneja

Abstract:

Background: The three clinical features that define Pierre Robin Sequence (PRS) are micrognathia, glossoptosis and airway obstruction. The treatment of patients with PRS is aimed at alleviating the breathing and/or feeding difficulties that exist as a result of the airway obstruction. Although a variety of operative and non-operative management options exist, there is a lack of consensus on the ideal timing and type of management and no clear indications for surgical intervention.

Purpose: The purpose of our study was to determine the ideal timing and type of management for PRS. Our objectives were three-fold: (1) to determine the ratio of non-operatively versus operatively managed PRS patients, (2) to compare the types of surgical treatments in terms of their frequency, indications, timing and outcomes, (3) to stratify the indications for surgical intervention and (4) to develop a classification system for babies with PRS based on their clinical presentation that may serve to guide management.

Methods: We performed a retrospective chart review of patients diagnosed with Pierre Robin sequence who received early management at BC Children's Hospital between 2004 and 2013.

Results: 65 patients were found eligible for the study. 74% of subjects were managed successfully without surgical intervention and had breathing difficulties resolve at a mean age of 6.38 months.

17 subjects received surgical management of the airway. The initial surgical intervention was floor of mouth release (FMR) in 8 subjects, mandibular distraction osteogenesis (MDO) in 5 subjects and tongue-lip adhesion (TLA) in 4 subjects. 12 subjects were successfully managed with a single procedure. Of those who required multiple procedures, 3 ultimately required tracheotomies and 2 were managed successfully with a subsequent MDO.

The proportion of successful cases of each type of surgery performed at any time was 3/8 for FMR, 6/7 for MDO and 3/4 for TLA.

Conclusion: The surgical procedure with the highest success rate in treating patients with PRS who could not be managed by positioning alone was MDO with a success rate of 86%.

Ethan Reiner, Medical Student
Supervisor(s): Quynh Doan

Board #: 52

Title: Pediatric visits to community emergency departments: Outcomes from referrals and unscheduled return visits to a pediatric center

Authors: Ethan Reiner, Eric Grafstein, Quynh Doan

Abstract:

There have been unremitting increases in Emergency Department (ED) usage over the last few decades, throughout North America. A proportion of these ED visits (2-5%) are repeated visits for the same complaint within 72 hours of their original visit. While many occur at the same ED, some occur at a different ED from where they originally consulted. ED revisits have been considered a marker for quality of care and several articles have been written on this subject in both the adult and pediatric literature. However, the focus on single or same site revisit studies potentially misses revisits to regional pediatric centers for care.

The relationship between children attending general/community hospitals and the regional pediatric center, BC Children's Hospital (BCCH), is unknown. The pediatric literature does not describe the relationship between children from general/community EDs who have visits to pediatric hospital EDs. This information is essential in evaluating the quality of pediatric emergency care provided in general EDs and in assessing the unperceived knowledge need of the general ED-based physicians.

The purpose of this retrospective cohort study will be to understand the revisit pattern of pediatric patients seen in a general/community hospital ED. We will look specifically at the proportion of patients who may have been referred to BCCH from general/community hospital EDs as well as revisit rates by those patients who decided to obtain a second opinion or follow up care at the regional pediatric ED. This study will aid in our goal to understand the burden of pediatric ED revisits and the gaps in care we are providing our pediatric population. Using this information we will develop improved educational opportunities for managing common pediatric emergencies in adult oriented hospital EDs.

Eleanor Stebbings, Medical Student
Supervisor(s): Dan Rurak

Board #: 53

Title: Do third trimester middle cerebral artery Doppler blood variables predict neonatal behavioral state regulation of day 6 infants with prenatal SSRI antidepressant exposure?

Authors: Eleanor Stebbings, Gillian Hanley, Ursula Brain, Meisan Brownlum, Ken Lim, Tim Oberlander, Dan Rurak

Abstract:

Background: Approximately 20% of women experience depression during their pregnancy; of these, 1/3 will be treated with a selective serotonin reuptake inhibitor (SSRI) antidepressant. Previously we reported that in utero SSRI exposure reduces fetal middle cerebral artery (MCA) flow, stress regulation and increases the risk for a cluster of postnatal behavioral disturbances (i.e. rapid breathing, respiratory distress, jitteriness and abnormal tone).

Objective: To study whether 3rd trimester fetal cerebral vascular changes predicted neonatal neurobehavior following in utero SSRI

Methods: We recruited mothers in their 2nd trimester of pregnancy [36 SSRI exposed (EXP) and 58 non-exposed (NEXP)]. At 36 weeks, fetal MCA flow parameters were obtained in the morning and afternoon with Doppler ultrasound. On day 6 postpartum, infant neurobehavior was assessed using supplemental items from the Neonatal Behavioral Assessment Scale (NBAS) in response to a standardized neurobehavioral assessment.

The statistical tests used included: t-tests and chi-squared tests to compare MCA flow variables and NBAS scores in EXP and NEXP groups; repeated measures ANOVA to examine time (morning versus afternoon) by group (SSRI exposed or non-exposed) differences in MCA flow measures and crude and adjusted regression models to examine the relationship between average daily MCA flow variables, SSRI exposure and NBAS scores. We adjusted for antenatal maternal mood, use of other psychotropic medicines, infant sex, and delivery by cesarean section.

Results: MCA diameter and morning MCA pulsatility indices (MCA PI) were reduced in EXP compared with NEXP fetuses ($p=0.045$ and $p=0.027$ respectively). EXP infants scored lower in the NBAS for cost of attention ($p=0.035$), examiner persistence ($p=0.042$), robustness and endurance ($p=0.038$) and regulatory capacity ($p=0.008$). Decreased 3rd trimester MCA flow was associated with decreased NBAS scores for cost of attention ($p= 0.021$), examiner persistence (0.032), irritability ($p=0.028$), regulatory capacity ($p=0.018$) and state regulation ($p=0.037$).

Discussion: Our results demonstrate that the antecedents to altered neonatal behaviour following prenatal SSRI exposure may be already evident during gestation as illustrated by 3rd trimester decreased middle cerebral artery blood flow. The implications for neurobehavioral development associated with links between fetal brain blood flow and neonatal behavior following in utero SSRI exposure remain to be determined.

Timothy Teoh, Medical Student
Supervisor(s): Edmond Chan

Board #: 54

Title: What is the ethnic distribution of Eosinophilic Esophagitis (EoE) among children in British Columbia?

Authors: Timothy Teoh, Vishal Avinashi, Preeti Vekaria, Edmond S Chan

Abstract:

Eosinophilic Esophagitis is an allergic condition resulting from esophageal infiltration with white blood cells known as eosinophils, and subsequent inflammation. Symptoms include dysphagia, abdominal pain and vomiting, and a majority of patients have co-morbidities such as food allergy, allergic rhinitis, asthma, and atopic dermatitis. EoE is treated by dietary restriction or medical treatment with corticosteroids. US-based epidemiological studies have shown a predominance of the disease in males and Caucasians, with increasing prevalence in African Americans. EoE's ethnic distribution in Canada remains largely unknown. In light of a previous study showing a higher prevalence of IBD among South Asian children in BC, our primary outcome was to describe EoE's ethnic distribution among children in BC. Secondarily, if EoE exists in non-Caucasians in BC, we sought to describe differences between ethnic groups in terms of symptom presentation, preferred treatment, and medical history.

Sixty-six patients consented to prospective recruitment from the EoE clinic at BC Children's Hospital into a registry created with REDcap software. Demographic, Gastrointestinal, Allergy, and Nutritional data were collected. The data was analyzed with Excel and SPSS.

The proportion of South Asian patients in the registry was significantly larger than the proportion of South Asians in BC (28.6 vs. 18.0%, p=0.029). There was a larger proportion of males in the registry compared to the general population of BC (81.0 vs. 51.6%, p=<.0002). South Asians were significantly younger than Caucasians at the time of diagnosis (4.11±4.93 vs. 6.47±4.15 years, p=0.005). Furthermore, medical treatment choices were less likely to be chosen by South Asians compared to Caucasians (22.2 vs. 51.1%, p=0.036). History of atopic disease, documented food allergy, and symptom presentation did not vary between both ethnic groups.

We identified a relatively large number of South Asian children with EoE, that has not been previously described in the literature. Despite a large variety of ethnicities living in BC, Caucasian and South Asians were disproportionately affected by EoE. Though the clinical presentation of EoE overall did not differ by ethnicity, South Asians were more than two years younger than Caucasians at the time of diagnosis, and chose medical treatment less than dietary management.

Charles Yu, Medical Student
Supervisor(s): Neil K Chadha

Board #: 55

Title: Prevalence and ethnic variation of preauricular sinuses in children
Authors: Charles Yu, Neil K Chadha, Julie Pauwels, Kushal Kherar

Abstract:

Background: A preauricular sinus (PAS) is a congenital ear malformation most often characterized by a small pit or sinus located on the anterior margin of the ascending limb of the helix. While some prevalence data of PAS has been documented in adults, the prevalence in the pediatric population remains unclear. In addition, while anecdotal evidence suggests a potential variation in prevalence amongst different ethnic groups, suggesting higher rates amongst Asians and African Americans, this proposed variation has never been spcefically investigated. There is also a lack of robust evidence surrounding the genetic basis of PAS.

Objective: This study will be the first to investigate the prevalence and ethnic variation of PAS using population level data, and may provide additional support for the genetic basis of this malformation in healthy children. We hypothesized that there does exist an ethnic variation in the prevalence of preauricular sinuses.

Methods: This prospective, cross-sectional study will aim to recruit approximately 1500-2000 participants, with a minimum of 20 children less than 18 years of age who are positive for a PAS. Participants will be recruited BC Children's Hospital's Emergency Department, Orthopedic Clinic, Otolaryngology Clinic, and hospital entranceways. Participants whose reason for admission is for treatment or consultation of a PAS or other malformations of the ear will be excluded. Participants will be visually inspected for the presence of a PAS by an observer (Medical student) and a brief questionnaire will be completed, including demographics, self-identified ethnicity, and family history of PAS.

Results: We are currently in the data collection phase of the study. Data analysis will use Fisher's Exact Test to determine whether or not an ethnic variation exists. Preliminary results show from the 524 participants recruited, 12 PAS were found, giving an overall prevalence of 2.3% in the population, with higher rates in African Americans (11.1%) and Asians (5.1%), compared to Caucasians (1.4%) and mixed races (3%).

Conclusions: As the study is still in progress, no conclusions can be made at this point. We expect, however, that the results of this study will provide valuable population level data on preauricular sinuses and provide further insight to its potential genetic basis.

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