PhoP/PhoQ TWO-COMPONENT REGULATORY SYSTEM IS REQUIRED FOR OMPTIN PROTEASE ACTIVITY IN *Escherichia coli*

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Hosts control access to their cell surfaces through the production of innate immune factors that exhibit anti-microbial activity. Bacteria that colonize or infect mammalian hosts have evolved complex pathways for resisting host innate immunity, including the degradation of host molecules. One class of proteins encoded by enterobacteriaceae is the omptin protease family, a group of cell surface proteins involved in the cleavage of incoming host defence peptides (HDPs) and complement factors. Although omptins have been linked to HDP or complement resistance, little is known about how these molecules are regulated. Here, we demonstrate that omptin activity is regulated by the PhoPQ activating signal of low Mg^{2+}. Furthermore, we show that deletion of the *phoP* gene from the PhoPQ two-component regulatory system results in complete loss of omptin protease activity and OmpT protein production. We have identified a putative PhoP-binding site to present evidence that mutation of this site results in the loss of low Mg^{2+} mediated regulation, and suggesting that PhoP is a direct transcriptional activator of OmpT. Our understanding of this virulence factor is crucial for a plethora of questions relevant to enterobacterial colonization and virulence.

ORAL PRESENTATION

Group A: Cell, Molecular, & Genetics

THE ROLE OF CLATHRIN IN AKT ACTIVATION IN LEGIONELLA

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Abstract

Legionella pneumophila (Lp) is genus that contains 39 species of gram negative bacteria and causes legionellosis, commonly presented as pneumonia. *Lp* can exist in coccal or filamentous form, and how the filamentous form contributes to infection remains poorly understood. Many studies to date have focused on *Lp* pathogenicity in alveolar macrophages. However, most of the respiratory tract is covered with epithelial cells that may be subject to infection by *Lp*. Consistent with this, recent work demonstrated that filamentous *Lp* is readily able to infect lung epithelial cells (LECs) through unique adhesion and internalization properties. Specifically, the attachment of filamentous *Lp* to LECs requires the formation of actin-driven membrane wraps that surround the *Lp* filament, leading to the activation of host signals, including the serine/threonine kinase Akt. The mechanism by which filamentous *Lp* attachment leads to membrane wrap formation and Akt activation remains poorly understood. We have examined the role of the host cell protein clathrin, which is well-established to facilitate the formation of clathrin coated pits at the plasma membrane that participate in receptor-mediated endocytosis. Specifically, we examined the recruitment and function of clathrin at sites of contact of *Lp* and LECs and what consequences this may have on the infection process of LEC by Legionella. Various cell line models were infected with fluorescent-labelled *Lp*, followed by detection of clathrin localization. Our data suggests that some *Lp* filaments in fact do indeed recruit clathrin at sites of attachment, suggesting that clathrin may be a novel regulation of *Lp* infection.

Oral Presentation

A: Cell, Molecular & Genetics

RIBONUCLEASE INTERACTING PARTNERS AND BEHAVIOUR IN *STREPTOMYCES VENEZUELAE*

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Ribonucleases (RNases) are enzymes that degrade or process RNA. They are involved in a multitude of cellular functions including RNA maturation, RNA metabolism, and ribosome quality control. The extensive role of RNases in cells means that they serve a central regulatory function and, as such, can significantly impact gene expression. The majority of research on the behaviour of RNases in bacteria has been done in model organisms like *Escherichia coli* and *Bacillus subtilis*. This project moves beyond these model organisms to investigate RNase behaviour in the Gram-positive actinobacteria *Streptomyces venezuelae*. *Streptomyces* produces several specialized metabolites, including many antibiotics, and a better understanding of RNases and gene expression in these bacteria will help develop methods for manipulating *Streptomyces* biosynthetic clusters. A bacterial adenylate cyclase two hybrid (BACTH) system was used to screen a library of the *S. venezuelae* genome for proteins that interact with *S. venezuelae* RNases of interest. In particular, screens were independently conducted against RNase J (*sven_5394*), YbeY (*sven_2322*), and the C-terminal scaffold domain of RNase E (*sven_2380*). Preliminary screens against RNase J and RNase E did not result in detection of any significant interactions, but a screen against YbeY showed interactions with fragments of six different *S. venezuelae* proteins. These include proteins involved in siderophore biosynthesis and proteins with as-of-yet unknown functions. Future directions for this project are directed testing of interactions observed in the screens and RNA stability assays investigating the impact of RNase deletions on RNA profiles in *S. venezuelae*.

Oral Presentation

Judging Category: A

PATHOGENESIS OF ENTEROHEMORRHAGIC *ESCHERICHIA COLI* IN THE *GALLERIA MELONELLA* MODEL

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Enterohemorrhagic *Escherichia coli* O157:H7 (EHEC) is a major food-borne pathogens that causes severe illness in humans. EHEC infection symptoms include hemorrhagic colitis and can lead to the sometimes fatal disease hemolytic uremic syndrome (HUS). During passage through the gastrointestinal tract, EHEC encounters various microenvironmental stresses that they must overcome prior to reaching their preferred site of colonization. One major stress encountered during transit through the small intestine is bile and bile salts. EHEC exposed to physiologically relevant levels of bile triggers upregulation of genes encoding the two component system, *pmrAB,* and the *arn* operon, resulting in modification of the lipolysaccharide and increased resistance to host cationic antimicrobial peptides (CAMPs). A second two component system, PhoPQ cooperates with PmrAB through the protein, PmrD, to further mediate resistance to CAMPS was established. What is unclear is the relevance of these systems and of CAMP resistance to EHEC survival and infection in an *in vivo* model. The primary goal studied was to determine the role of bile salt stress in these two component systems to EHEC pathogenesis using the wax moth larvae *Galleria mellonella* as an invertebrate model of infection. Through this *in vivo* model, this study will assess the pathogenesis of EHEC, before and after bile salt treatment, as well as the effect of isogenic mutations of *pmrA*, *pmrB*, *pmrD*, and *phoP* within this model. This study provides important insights into the mechanisms by which this enteric pathogen utilizes this key intestinal environmental signal to modulate virulence and optimize fitness during infection.

Oral Presentation
Cell, Molecular & Genetics

SELECTION OF ANTIMICROBIAL RESISTANT BACTERIA FROM MEDICATED FEEDS

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The spread of antimicrobial resistant (AMR) bacteria is dangerous for human health, resulting in increased morbidity of infections, increased mortality, as well as economic burden. AMR bacteria can be transferred from feeds to the gut of food animals and then to humans through consumption of animal products. Current regulations permit use of specific antimicrobials in animal feeds for prophylaxis, many of which aren't considered important for human medicine. Utilizing PCR screening methods, the study conducted shows that incorporation of antimicrobials not utilized in human medicine in feeds could still permit co-selection for AMR with implications for human health.

Abstract is for an oral presentation

Group selection: A (Cell, Molecular, & Genetics)

DIVERSE HOST INTERACTION PHENOTYPES OBSERVED IN INFLAMMATORY BOWEL DISEASE ASSOCIATED ADHERENT-INVASIVE ESCHERICHIA COLI (AIEC)

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Canada has one of the highest rates of inflammatory bowel disease (IBD) in the world. The cause(s) of IBD are complex and multifactorial but involve host genetics, environmental factors and the microbial composition of the host gastrointestinal tract. Recent studies have linked adherent-invasive *Escherichia coli* (AIEC) presence and IBD status, specifically Crohn's disease. AIEC are characterized to adhere, invade, internalize into macrophages using a clathrin-dependent mechanism, and replicate at low levels without inducing cell death. The mechanism(s) of adherence and invasion into host cells by AIEC is poorly characterized. Published studies with AIEC typically only use the prototypical strain LF82 to characterize phenotypic behaviour; however, it is suggested that they should be evaluated on an individual strain basis due to its genetic diversity. In this project, we characterize the invasiveness of AIEC in Caco-2 cells using an adhesion/invasion assay. Furthermore, we establish the role of host clathrin-coated pits in the endocytosis of AIEC into epithelial cells using the inhibitory drug Pitstop2. An increase in the adhesion/invasion index was observed in select strains after Pitstop2 treatment. Microscopy results illustrate a decrease in recruitment of clathrin-coated pits in the presence of select AIEC strains. Our study demonstrates AIEC isolates to be dynamic and heterogeneous in their adherence and invasiveness to Caco-2 cells.

Oral Presentation

A: Cell, Molecular, & Genetics

ONTOLOGICAL CLASSIFICATION OF RESISTANCE GENE ANNOTATIONS FOR ANTIMICROBIAL SURVEILLANCE

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As the threat of antimicrobial resistance increases, the scientific community is placing heavy emphasis on understanding, detecting, and predicting resistance genes and virulence mechanisms. Advances in Next Generation Sequencing (NGS) have further led to a rapid proliferation of genetic data, proving to be highly useful for antimicrobial surveillance. The Comprehensive Antibiotic Resistance Database (CARD) is developing a Virulence Ontology (VIRO) and Virulence Gene Identifier (VGI), allowing for the extraction and analysis of biologically-relevant information from large datasets. While the VGI utilizes a Protein Homolog Model to identify virulence-associated genes, VGI results fail to provide contextually pertinent information. Functional programming techniques were thus utilized within the Mathematica language to ontologically classify VGI annotations through percent similarity to reference sequences. Ontological classification allows VGI results to be interpreted on the basis of both the definition of the detected gene, and its relationships with curated concepts. The software developed in this project can be generalized to further include CARD's primary goals, the Antibiotic Resistance Ontology (ARO), and the Resistance Gene Identifier (RGI), in addition to including other web-based ontologies. Tools that allow the extraction of contextually pertinent biological information are incredibly useful for antimicrobial surveillance, and will assist us in better understanding virulence determinants and resistance mechanisms.

Oral presentation

A: Cell, Molecular & Genetics

INCORPORATING PHENOTYPIC TESTING INTO ONTOLOGICAL DATA SHARING PARADIGMS

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Ontologies aim to organize scientific information in a standardized manner by formally naming and defining set terms to describe data sets and their relationships. The Genomic Epidemiology Ontology (GenEpiO) project aims to develop a standardized vocabulary for describing and relating data on infectious disease surveillance and outbreaks. A subsection of GenEpiO, termed the Antibiotic Resistance Ontology (ARO), creates a common framework for sharing antimicrobial resistance (AMR) data within the Comprehensive Antibiotic Resistance Database (CARD). Up until now, CARD has functioned largely as a genotypic tool that allows users access to data on AMR gene and mutation sequences. We have since created a standard for organizing and sharing phenotypic terms related to AMR in CARD. 46 existing terms from GenEpiO, CARD and other ontologies (ex. NCIT) were revived and 43 new terms were created in the compilation of the AMR phenotypic terminology branch. Terms were generated for the different tests, reagents and platforms involved in testing for AMR in a laboratory setting, as well as commonly used reference standards for interpretation. In order to properly relate phenotypic terms to each other, four new relationship terms were curated. For example, the relationship term ‘manufactures’ was created to relate ‘automated testing platform vendor’ to ‘automated testing platform’. Ultimately, it was found that the processes involved in determining AMR vary greatly. The AMR phenotypic terminology branch aims to reflect current tests and parameters used in determining microbial susceptibility in order to create standards for data sharing among provincial, national, and international public health agencies.

Oral presentation

A: Cell, Molecular, & Genetics

THE UTILIZATION OF WHOLE-EXOME SEQUENCING IN IDENTIFYING THE GENETIC BASIS OF A RARE DISEASE

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Rare disease represents a significant burden at both the individual and systematic level; affecting 1 in 12 Canadians and accounting for countless hospital visits, tests and consultations. The diagnostic odyssey is a journey many individuals with rare genetic diseases face; as more encompassing diagnostic tests are limited. Whole-exome sequencing offers just this, having previous success in diagnosing rare Mendelian diseases at an affordable price. Ataxia—a disorder affecting balance, coordination, and speech—is one of many rare diseases that has been and can be diagnosed using whole-exome sequencing. Here, we introduce a Canadian family in which three of eight siblings exhibit a novel form of ataxia characterized by the additional features of dystonia and intellectual disability. By conducting whole-exome sequencing and applying bioinformatics analysis, we aim to identify a causative variant underlying the disorder. Identifying the genetic basis may further our understanding of ataxia, allow for genetic counselling in the family, and may contribute to the development of improved treatment options for those with ataxia.

Oral Presentation
A: Cell, Molecular, & Genetics

COMPUTATIONAL TOOLS FOR ANALYZYING MOUSE MICROARRAY DATA

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Large amounts of data created from genotyping has created a demand for new computer programs and programming packages to process the data. More specifically, genotyping data produced from a mouse microarray called the Mouse Diversity Genotyping Array (MDGA) is used to evaluate single nucleotide polymorphisms (SNPs) and copy number variations (CNVs). The large amount data produced from this creates special challenges relating to filtering, parsing, and presenting. As a result, in this research we present tools created in the programming language R that are used to evaluate the SNP and CNV information from the data created by the MDGA.

Oral Presentation; Cell, Molecular, & Genetics

OBSERVATION OF CONJUGATION BETWEEN ESCHERICHIA COLI S17-1 AND BL21(DE3) PLYSS STRAINS USING A MICROFLUIDIC CHEMOSTAT

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The increased prevalence of antibiotic resistance through the transfer of resistance genes between bacterial species by conjugation is a major health concern. The process of conjugation has been studied extensively through plating experiments, with the acquisition of antibiotic resistance serving as the typical indicator of successful conjugative transfer. Although this reveals the overall outcome of conjugation, the dynamics of the process are difficult to ascertain through colony observation and quantification. In this study, a microfluidic chemostat is being developed, which will allow for the controlled manipulation of fluids at the microscale, in order to permit real-time observations of bacterial conjugation dynamics. Greater control of environmental conditions including temperature, nutrient concentrations and cell concentrations within the chemostat are possible, with limited waste and reagent use compared to conventional methods. The chemostat will be used in parallel with traditional culturing techniques in order to compare observations of the conjugative process between two Escherichia coli strains. The design, fabrication, and testing of the microfluidic device will be discussed, along with the preliminary results of these bacterial conjugation experiments.

Oral Presentation, Group A: Cell, Molecular, & Genetics

DEVELOPMENT OF A NOVEL, STIFFNESS-TUNABLE TOOL TO STUDY DUROTAXIS

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Cell migration is a crucial process for many physiological events, such as development, immune system function, wound healing, but it is also implemented in cancer metastasis, a process in which cancer cells migrate from a primary tumour to distal organs and develop deadly secondary tumours. The ability of cancer cells to metastasize makes cancers incredibly difficult to cope with. Thus, finding a targeted treatment that suppresses cancer cell migration is extremely important for health care. Cancer cells migrate directionally following various guidance cues, for instance, gradients of nutrients, soluble growth factors, *etc*. However, these diffusible factors are not the only cues that guide cancer cells. Mechanical cues, such as a gradient of tissue stiffness, were recently shown to be extremely potent in guiding cancer metastasis. The ability of cells to sense tissue stiffness and move up a stiffness gradient is referred to as durotaxis. Despite the well-established clinical significance of the durotaxis, the experimental techniques to screen for durotaxis suppressing drugs are unavailable. Here, I combined my knowledge in chemistry and cell biology to develop a protocol for fabrication of biocompatible matrixes with a gradient of stiffness. I demonstrated that fibroblasts plated on these matrixes undergo durotaxis and that suppression of specific signaling pathways reduce durotaxis response. Moreover, enabling us to perform high-throughput imaging of migrating cells under different treatments, this protocol will also be invaluable for identifying key players involved in mechanotransduction and revealing new pharmaceuticals to suppress cancer metastasis.

Oral and Poster presentation
A: Cell, Molecular, & Genetics

MODELLING DNA SYNTHESIS AND PROTEIN CO-LOCALIZATION USING DNA FIBER ANALYSIS

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Chromatin fiber analysis provides an inexpensive, high-content way to study replication dynamics. Unique to this method, proteins are retained, allowing replication complexes to be detected directly on DNA and relative to specific locations. This fiber assay involves lysing cells, stretching out protein-bound chromatin fibers, and then fluorescent staining to see replicated tracts of DNA and protein locations using fluorescent microscopy. Little is known about DNA replication complexes on DNA in relation to replicated areas, and we use this method to characterize **individual** replication fork complexes under normal and stressed conditions. However, there is a critical gap in modelling replication fork structure: the large amount of data generated in these fibers is difficult to analyze and use for modeling. ODD-BLOBS (One Dimensional Data – Boolean Logic Operations Binning System) is an analysis tool that systematically correlates DNA synthesis with protein location. ODD-BLOBS measures tract lengths to determine replication processivity or instability. We have reproduced ODD-BLOBS to create a graphical application called Tangible Chromatin, in which fibers can be visualized, quantified, and compared on screen. We now use Tangible Chromatin to test replication protein co-localization in different mutant yeast strains, allowing us to model the role of checkpoints on replication fork structure stability. Another use will be to map histone domains relative to proteins or DNA replication. Our goal is to understand whether replication protein location can predict disease or later damage to DNA.

Oral Presentation

A: Cell, Molecular & Genetics

THE ROLE OF CYSTATHIONINE GAMMA-LYASE IN GHRELIN SUPPRESSION

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Twenty years ago it was found that there are cells present in animal stomachs which regulate appetite and metabolism. These endocrine cells called ghrelin-producing-cells secrete the ghrelin hormone which is the endogenous ligand for the growth hormone secretagogue receptor. Studies have shown that protein – specifically the amino acid L-cysteine – induces the longest suppression of ghrelin release. One suggested pathway for the action of L-cysteine is through the desulfhydration of the molecule by the enzyme cystathionine gamma-lyase (CSE) which produces hydrogen sulphide gas (H_2S) as a product. It is believed that this gas has the ability to suppress the release of ghrelin but it is not known in which cells this biochemical reaction is taking place in the stomach. This study investigates the location of the CSE enzyme in the stomach to see if there is co-localization between the enzyme and the ghrelin hormone. Fluorescent immunocytochemistry staining of rat primary stomach cells was preformed. These cells were treated with ghrelin and CSE primary antibodies and associated florescent secondary antibodies. In addition, a Western blot was used to ensure that the CSE antibody was indeed targeting the enzyme and not some other cellular component. These experiments showed that CSE and ghrelin are co-localized, meaning that ghrelin-producing-cells have the ability to endogenously suppress the release of the ghrelin hormone through the CSE-H_2S pathway. The location of this enzyme is important in understanding the regulation of this hormone and could lead to new therapeutic targets for metabolic disorders.

Oral Presentation
Group A: Cell, Molecular, & Genetics

DETERMINING PROTEIN-PROTEIN INTERACTIONS BETWEEN AROGENATE DEHYDRATASE2 AND CHLOROPLAST DIVISION PROTEINS OF *ARABIDOPSIS THALIANA*.

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AROGENATE DEHYDRATASES (ADTs) are important enzymes that catalyze a carboxylation/dehydration reaction converting arogenate into phenylalanine. In *Arabidopsis thaliana,* there are six genes encoding ADT's named *ADT1-ADT6.* All six ADT proteins localize to the stromules of chloroplasts. ADT2 plays a unique role as it also localizes in a ring structure around the equatorial plane of the chloroplast, similar to the Z-ring during chloroplast division. Additionally, mutations in *ADT2* affect chloroplast morphology and Z-ring positioning suggesting ADT2 has a second "moonlighting" function in chloroplast division. I hypothesize that ADT2 plays a role in chloroplast division and will interact with at least one of the chloroplast division proteins. I am using Bimolecular Fluorescent Complementation (BiFC) in *Nicotiana benthamiana* to determine if an interaction between *Arabidopsis* ADT2 and select chloroplast division proteins occurs. BiFC constructs have been designed using a GATEWAY® recombination strategy. The full-length genes are inserted into vectors containing partial Yellow Fluorescent Protein (YFP) sequences for expression of fusion proteins. Constructs are infiltrated, pairwise, by *Agrobacterium tumefaciens* mediated transformation into *N. benthamiana* leaves for transient expression of the fusion proteins. Interaction between the proteins of interest allow the N-terminal and C-terminal portions of YPF to arrange in the beta-barrel conformation and fluoresce yellow which can be visualized with a confocal microscope. Determining an interaction will allow for a better understanding of the molecular mechanisms of chloroplast division. An interaction can further support ADT2's role as a moonlighting protein leading to a better understanding of the evolution of enzymes and diversity of organisms.

Oral Presentation

Cell, Molecular, & Genetics

INVESTIGATING THE CTD CODE IN SCHIZOSACCHAROMYCES POMBE: THE ROLE OF THREONINE-4 PHOSPHORYLATION

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The C-terminus of the largest subunit of the RNA polymerase II holoenzyme is comprised of multiple repeats of the heptad sequence, $Y_1S_2P_3T_4S_5P_6S_7$. These repeats – referred to collectively as the carboxy-terminal domain or CTD – are subject to a variety of complex post-translational modifications that together form a "CTD code". This code recruits various interacting factors involved in the regulation of transcription, mRNA processing, and histone modification. Therefore, understanding the effects of individual CTD modifications (e.g. phosphorylation) may provide insight into transcriptional control and its relationship to eukaryotic developmental complexity. In this study, I began characterizing the phenotypic role of Thr-4 phosphorylation in the model eukaryote, *Schizosaccharomyces pombe*. A dephosphorylated state was mimicked by mutating all threonine-4 residues to alanine in an *S. pombe* strain; likewise, another strain had threonine-4 residues mutated to glutamate to mimic a phosphorylated state. After constructing these strains *in ura4-D18 S. pombe*, I sporulated cells and then assessed whether the two mutants were lethal. T4A strains were viable and resulted in cells that were morphologically similar to *ura4-D18 S. pombe*; in contrast, T4E strains were inviable and resulted in filamentous cells that could no longer divide. Future studies will examine how different patterns of threonine-4 phosphorylation affect S. *pombe* viability. Ultimately, this will illuminate the functional organization of phosphoregulation at this residue in context of the rest of the CTD phosphorylation code.

Oral Presentation

Cell, Molecular, & Genetics

IDENTIFICATION OF A CELL SURFACE RECEPTOR FOR STB ON STC-1 CELLS

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Enterotoxigenic *Escherichia coli* (ETEC) may express several virulence factors during infection. Such factors include three toxins: heat-labile or LT toxin, heat stable or STa toxin, and heat-stable enterotoxin b (STb). Research has shown STb to be involved in infections leading to diarrhea in domestic animals; specifically farm animals. Although the molecular mechanisms on the cellular targets and subsequent intracellular signalling related to LT and STa are well established, they have not been well studied in the case of the STb toxin. The objectives of this study are to use an intestinal cell line, STC-1 cells, and tagged STb toxin to identify the specific cell surface receptor responsible for STb toxicity in STC cell lines. STb toxin was expressed from *E. coli* BL21: pull down, ELISA, dot blot and far western experiments were utilized to see if direct interaction between STb and STC-1 cell line take place during STb secretion. Since previous studies in our lab show that STb can activate the calcium channel in the STC-1 cell line, the receptor on epithelial cells (STC-1 cells) will be identified using mass spectrometry and the N-terminal sequences of the targeted proteins. The expected results were proven correct when a protein of different size than confirmed in previous studies was identified by mass spectrometry, revealing the protein to be approximately 25 kDa. These findings may provide insight on how the intracellular signalling is triggered and how these events lead to the observed experimental and clinical observations upon treatment of intestinal issues with STb.

Oral Presentation

A: Cell, Molecular & Genetics

ABSTRACT: PURIFICATION AND CHARACTERIZATION OF AN ENZYME RESPONSIBLE FOR THE DETOXIFICATON OF FUMONISINS PRODUCED BY ASPERGILLUS WELWITSCHIAE

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The objective of my honors thesis is to purify and characterize an enzyme responsible for the deamination of fumonisin produced by *Aspergillus welwitschiae.* Fumonisin is a mycotoxin relevant to global economic and health issues. Fumonisins pose health risks because they are structurally similar to sphinganine which is a precursor in the pathway for ceramide synthase, an important enzyme in the sphingolipid synthesis pathways. Interruption of this synthesis pathway causes failures in cell regulation and cell membrane processes which will have consequences for the health of the organism. An enzyme with the ability to detoxify fumonisin could be developed into a product that could reduce fumonisin contamination in crops and animal feeds. A protocol was developed to enrich for fumonisin deamination activity from fungal cultures using fast protein liquid chromatography (FPLC). In order to measure deamination activity throughout the purification process reverse–phase liquid chromatography mass spectrometry (LC-MS) was used in a similar method described in Burgess *et al.* 2016. Using LC-MS proteomics analysis of recently purified samples an amine oxidase protein is present in higher abundance in more active samples and absence in samples without activity. This amine oxidase protein is currently the best candidate for the fumonisin detoxification enzyme.

Oral Presentation

A: Cell, Molecular and Genetic

GLOBOTRIAOSYLCERAMIDE METABOLISM IN FIBROBLASTS FROM A FABRY DISEASE PATIENT FOLLOWING NOVEL LENTIVIRAL GENE THERAPY TREATMENT.

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Fabry disease (FD) is an X-linked lysosomal storage disorder caused by mutations in the α-galactosidase (α-gal) encoding gene, *GLA*. Loss of α-gal enzyme activity in FD patients results in lysosomal accumulation of its substrate, globotriaosylceramide (Gb3). Currently, FD is treated by enzyme replacement therapy. This study aims to demonstrate that fibroblasts from a FD patient can take up α-gal produced by gene therapy treated autologous stem cells and metabolize Gb3. It is hypothesized that patient produced α-gal will display Gb3 metabolism levels similar to wild-type α-gal. Synthetic Gb3, tagged with BODIPY-C16 fluorophore, was loaded into fibroblasts, allowing for fluorescent tracking of Gb3 localization in cells. Loaded fibroblasts will be treated with patient plasma extracted before and after gene therapy. Pre-gene therapy plasma has effectively zero α-gal enzyme activity whereas, post-gene therapy plasma has physiological levels of α-gal activity. Gb3 metabolism or lack thereof will be determined by the absence or presence of fluorescence, respectively, in patient fibroblasts after plasma treatment. Furthermore, Gb3 metabolism will be quantified by high-performance liquid chromatography. The metabolism of Gb3 in patient fibroblasts would suggest that gene therapy resulting in α-gal producing autologous stem cells is a corrective treatment for enzyme deficiency caused by FD.

Oral presentation: Cell, Molecular & Genetics

EFFECTS OF CHAGA MUSHROOM (*INONOTUS OBLIQUUS*) EXTRACTS ON THE GROWTH OF B16-BL6 MURINE MELANOMA CELLS AND ALONGSIDE CONVENTIONAL CANCER TREATMENTS

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Chaga mushroom (*Inonotus obliquus*) is a fungus which has been used traditionally because it is believed to possess medicinal properties. Recently, it has been growing in popularity as an anti-cancer therapeutic. But little is known about the mushrooms ability to interfere or interact with chemotherapy and radiation. Nevertheless, several studies have shown that chaga mushroom can affect the cell cycle of cancer cells. The objectives of this study are to: 1) determine the effects of chaga mushroom extract on B16-BL6 melanoma cell growth; 2) identify possible contraindications between chaga mushroom extracts and chemotherapeutic agents and\or radiation, and 3) identify the molecular pathways affected by chaga mushroom. 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) growth viability was used to determine the effects of chaga mushroom extracts on B16-BL6 cell growth, and on the ability of chemotherapeutic agents and\or radiation. Acridine orange and ethidium bromide staining, and flow cytometry were used to help determine the mechanism of chaga mushroom extract. Cell viability is notably reduced in cells treated with ethanol and water extracts. When combined with radiation the effect of the ethanol extract is markedly reduced in comparison to the water extract. A similar relationship is seen with the addition of chemotherapeutic agents; the ethanol extract does not create a synergistic relationship with the agents while the water extract does. Results generated from this project will help to determine the if chaga can act as an anti-cancer therapeutic and whether or not there is cause for concern when combining it with conventional cancer treatment.

Oral presentation

A. Cell, Molecular, & Genetics

A STUDY OF THE RELATIONSHIP BETWEEN CHEMOTHERAPY-INDUCED RIBOSOMAL RNA DEGRADATION AND APOPTOSIS IN THE HUMAN A2780 OVARIAN EPITHELIAL CARCINOMA CELL LINE

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Various cytotoxic effects are associated with chemotherapy treatments and have been well documented in the scientific literature. Ribosomal RNA degradation (RNA disruption) has been characterized in various cancerous cell lines and types in response to various cell stressors including many chemotherapeutic drugs. A temporal correlation between chemotherapy-induced RNA disruption and apoptosis has been observed through the RNA disruption assay (RDA), immunoblotting experiments, and flow cytometric analysis. To assess whether these two phenomena are causally linked, we attempted to inhibit intrinsic and extrinsic apoptotic signalling pathways in A2780 ovarian tumour cells to examine the consequences, if any, on RNA disruption. Treatment with docetaxel, methotrexate or vincristine reproducibly induced RNA disruption, PARP cleavage, and activation of several caspase proteins in A2780 ovarian carcinoma cells. Successful overexpression of anti-apoptotic proteins c-FLIP and Bcl-2 was confirmed through immunoblotting experiments but failed to inhibit apoptosis as measured by PARP and caspase cleavages. It is thought that the lack of apoptotic inhibition upon Bcl-2 upregulation was due to inactivation by the microtubule targeted agent's docetaxel and vincristine. This inhibition is thought to be the result of hyperphosphorylation of Bcl-2 protein at T69, S70 and S87 peptide residues. The inability to inhibit apoptotic signalling by overexpression of Bcl-2 or c-FLIP prevents us from making definitive conclusions on the relationship between apoptosis and RNA disruption in A2780 ovarian tumour cells. Other molecular approaches to inhibit apoptosis should be explored to assess whether the two processes are dependent upon one another *in vitro* and *in vivo*.

Oral Presentation

A: Cell, Molecular, & Genetics
B: Ecology & Evolution
C: Physiology & Toxicology
D: Science Education

ROLE OF MECHANICAL AND STRUCTURAL PROPERTIES OF GLIOBLASTOMA MULTIFORME MICROENVIRONMENT IN TUMOUR AGGRESSIVENESS AND THERAPY RESISTANCE

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Glioblastoma Multiforme (GBM) is the most common and aggressive type of brain cancer, accounting for 15% of intracranial tumours. With a median survival of three to six months for patients with recurrent GBM, there is an urgent need for advancements in the study, diagnosis, and treatment of GBM. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a method of non-invasive tumour analysis that describes fluid stress properties of a tumour. DCE-MRI combines static mechanical descriptions of analyzed tumours to the flow and fluxes of the fluids in the tumour, generating a complete picture of the local stresses and pressures around a tumour. By studying the expression of stress response markers Vinculin and Hyaluronic Acid (HA), this project aims to establish protein signatures correlating with DCE-MRI readings as a tool for improved diagnosis of GBM. Furthermore, to study tumour stress responses to changes in extracellular matrix pressures in a three-dimensional setting, we employed brain tumour organoid (BTO) cultures. BTOs provide an *in-vitro* modeling method that more accurately represents *in vivo* tissue organization. By controlling microenvironmental factors which an organoid is suspended in, solid stresses can be manipulated and responses studied. As a result, the organoid model can reinforce characterization of cellular responses found when studying tumours. Preliminary results suggest that varying extracellular matrix stiffness results in quantifiable and correlated changes in invasion, aggressiveness, and marker protein levels. Defining local stress factor effects on tumour proliferation, aggressiveness marker expression and drug treatment response can create better diagnostic tools and more effective therapy strategies.

Oral Presentation
Group A: Cell, Molecular, and Genetics

ROLE OF $GABA_B$ AND CXCR4 IN MEDULLOBLASTOMA

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Medulloblastoma (MB) is the most common malignant pediatric brain tumor and it occurs in 16-25% of diagnosed cases, with a higher incidence in children aged 1 to 9 years old. The current standard of care consists of multiple stages of therapy including surgery, irradiation, and chemotherapy. However, a subset of tumors with a still devastating prognosis remains. Metabotropic receptors are G-protein coupled receptors (GPCRs) that act as second messengers. C-X-C chemokine receptor type 4 (CXCR4) and its ligand, SDF-1 (CXCL12), are important in cell migration during inflammation. Γ-aminobutyric acid receptor B ($GABA_B$) and its ligand, γ-aminobutyrate (GABA), are responsible for G-protein activation. $GABA_B$ receptors are made of 2 subunits namely, B1 and B2. B2 subunit is coupled to G-proteins regulating activities of the Ca2+ channels, K+ channels, and adenylyl cyclase (AC). Previous studies showed that CXCR4 is highly expressed by glial and neuronal cells in the central nervous system (CNS) and in GABAergic neurons. $GABA_B$ was also found to be highly expressed in MB showing increased Ca^{2+} levels. Also, CXCR4 was shown to be overexpressed in MB and administration of an antagonist decreased the proliferation rate in Type II MB. Current results show that upon administration of the $GABA_B$ agonist; baclofen increased cell proliferation in MB cells and immunofluorescence showed increased levels of $GABA_B$. In conclusion, by administering a $GABA_B$ antagonist; phaclofen would enhance the efficacy of chemotherapeutic treatments on MB patients decreasing the proliferation rate of the aggressive tumors.

Oral Presentation

A: Cell, Molecular, & Genetics

ROLE OF SPY1 IN MAMMARY DEVELOPMENT

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Breast cancer accounts for 25% of all new cancer cases in women. Determining the key mediators that regulate both normal and abnormal development of the breast is crucial to the development of better diagnostics and treatment options. Proper cell cycle regulation guides cellular changes during the stages of mammary development, and misregulation or mutation/deletion of key cell regulatory genes represents an important step in breast cancer initiation and progression. The cyclin-like protein Spy1 is tightly regulated during normal mammary gland development and has been implicated in several cancers, including breast cancer. Spy1 binds and activates cyclin-dependent kinases, promoting progression through the G1/S and G2/M phase of the cell cycle. Elevated levels of Spy1 significantly increases proliferation and overrides the DNA damage response. This study seeks to explore the question - Is Spy1 required for normal and abnormal development of the breast? My thesis work involved using the novel genome-editing tool CRISPR-Cas9 to knockout Spy1 in the mouse mammary epithelial cell line HC11 and the breast cancer cell line, MDA-MB 231. These knockout cells were tested for effects on cell growth and development such as proliferation, differentiation, stem cell expansion and migration. My results support that this unique cell cycle regulator plays a critical role in the differentiation and stem cell maintenance in the mammary gland. This work sheds light on the mechanisms of normal mammary development as well as breast cancer initiation and progression and supports further exploration of this mechanism as a therapeutic direction for breast cancer.

Oral presentation
A: Cell, Molecular, & Genetics

CCN1 AND CCN2 ARE INVERSELY REGULATED TO CCN3 IN HUMAN GINGIVAL FIBROBLASTS

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Fibrosis is the loss of extracellular matrix homeostasis with excessive deposition and remodeling of fibrous connective tissue, often resulting in fibrotic diseases and cancer. There is still no effective antifibrotic therapy. However, members of the CCN family of matricellular proteins are being considered as novel candidates for therapeutic targeting in fibrotic diseases, including gingival overgrowth (GO). Research has shown that CCN2, is positively related to the degree of fibrosis seen in gingival tissues. Increasing evidence suggests that CCN3 is reciprocally expressed to CCN2 in dermal fibroblasts. This implies that CCN3 may be an endogenous antagonist of CCN2 activity, highlighting its potential as an anti-fibrotic target. However, the fibrotic response in the oral cavity is functionally and phenotypically distinct from those observed in dermal fibroblasts. We aim to investigate the molecular mechanisms underlying the reciprocal control of CCN proteins to better understand fibrotic disorders. Real-time polymerase chain reaction was used to detect and quantify CCN mRNA expression in the presence of transforming growth factor beta (TGFβ) and/or small molecule inhibitors of focal adhesion kinase (FAK), yes-associated protein 1 (YAP1) and activin receptor-like kinase-5 (ALK5). Results indicate that CCN1 and CCN2 mRNA levels are TGFβ-induced while CCN3 mRNA levels are TGFβ-suppressed. Furthermore, TGFβ-induction of CCN1 and CCN2 are sensitive to inhibition of ALK5, FAK, and YAP1, whereas; TGFβ1-suppression of CCN3 is sensitive to inhibition of ALK5 and FAK but not YAP1 in human gingival fibroblasts. Therefore, reestablishing the ratio of CCN proteins in fibrotic diseases may be a novel therapeutic approach.

Oral Presentation

A: Cell, Molecular, & Genetics

CCN1 EXPRESSION BY FIBROBLAST IS REQUIRED FOR ANGIOGENESIS IN MICE

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The CCN family of matricellular proteins play a major role in tissue repair and pathogenesis. CCN1, a member of the CCN family, is thought to be important in angiogenesis during tissue repair. CCN1 expression is increased at angiogenic sites during dermal remodeling and wound healing— the loss of CCN1 has been attributed to the inhibition of melanoma metastasis and bleomycin-induced fibrosis. The aim of this study was to investigate the contribution of CCN1 to angiogenesis in melanoma, bleomycin-induced fibrosis, and wound healing in mouse models. C57BL/6 mice with a fibroblast-specific CCN1 knockout were injected with melanoma cells, bleomycin, or were subjected to injury. Tissue samples were then collected and analyzed. As revealed by immunohistochemical staining, there was a decrease in angiogenesis within the melanoma tumor stroma, bleomycin-induced fibrotic tissue, and wound healing tissue. Thus, mice with a fibroblast-specific loss of CCN1 display a decrease in angiogenesis—suggesting that CCN1 expression by fibroblast is required for the formation of new blood vessels.

Oral presentation.
Cell, Molecular, and Genetics.

UNDERSTANDING THE MOLECULAR MECHANISM OF EARLY ATHEROSCLEROSIS BY STUDYING THE EFFECTS OF RAB17 ON ENDOTHELIAL CELL TRANSCYTOSIS

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Atherosclerosis, the leading cause of death in Canada for men and women, is defined as the formation of low-density lipoprotein (LDL)-derived plaques in the artery. This occurs due to elevated levels of LDL, which cross the arterial endothelial layer and trigger an inflammatory response that culminates in narrowing of the vessel, eventually causing a heart attack, heart failure, or death. Since an intact endothelial layer lines early plaques during lipoprotein retention, it follows that LDL has gone *through* the tissue via transcytosis, whereby endocytosis occurs on the apical side of the polar endothelial cells, and exocytosis on the basolateral. The canonical pathway of LDL uptake via the LDL receptor accounts for the recycling of the latter, however, the fate of LDL and effector proteins remains unclear. Rab17, a GTPase protein that helps relay vesicle trafficking was studied in primary human coronary artery endothelial cells (HCAEC) using a novel *in vitro* LDL-uptake assay to image transcytosis. The HCAEC were viewed using total internal reflection fluorescence microscopy complemented by spinning disk confocal microscopy, while LDL vesicles were tracked and quantified using a MATLAB designed machine learning algorithm. Rab17 was shown to have an instrumental role in LDL transcytosis; the number of vesicles significantly dropped under *Rab17* dominant negative (DN)-transfections. Using a dextran-uptake assay, the DN-transfected HCAEC showed no significant difference in viability compared to the GFP-transfected group. Rab17 was therefore shown to be a key protein in the LDL transcytosis mechanism, and could be a novel target for atherosclerosis prevention or therapy.

Oral presentation
A: Cell, Molecular, & Genetics

THE EFFECTS OF E-CADHERIN DEPENDENT ADHESION ON THE INTEGRIN-ACTIVATED MAP KINASE PATHWAY

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The MAP kinase pathway was utilized to study the relationship between E-cadherin and cell-cell contact-dependent inhibition of mitogenic signaling. The MAP kinase pathway mediates cellular proliferation and can be activated by integrin-dependent adhesion. Cell-cell contact inhibition is a fundamental process in non-malignant cells but is not active in cancer cells. Confluent cultures of non-malignant cells arrest growth through cell-cell interactions, while cancer cells can continue growing to form multiple layers. E-cadherin mediates cell-cell adhesion, is not expressed in many cancer cells, and is hypothesized to mediate cell-cell contact inhibition. E-cadherin was up-regulated in MDA-MB-231 breast cancer cells by transfection. MDA-MB-231, MDA-MB-231-E-cadherin, and HBL-100 non-malignant breast cells were adhered to uncoated and fibronectin-coated plates at low and high cell densities for 1 hour. Immunoblot analysis of phosphorylated ERK and Raf-1 proteins was used to monitor adhesion-dependent MAP kinase activation. The HBL-100 cell line showed increased ERK phosphorylation when plated on fibronectin-coated substrates at low density, but at high density ERK phosphorylation was not elevated as expected for cell-cell contact inhibition. Alternately, MDA-MB-231 cancer cells did not show cell-cell contact inhibition and adhesion to fibronectin activated ERK phosphorylation at both low and high density. MDA-MB-231-E-cadherin cells did not activate ERK phosphorylation when adhered to fibronectin at high cell density suggesting they were subject to cell-cell contact inhibition similar to non-malignant cells. This suggests that E-cadherin can mediate cell-cell contact inhibition as measured by inhibition of the MAP kinase pathway.

Oral Presentation
A. Cell, Molecular, & Genetics

PKC-ALPHA ACTIVATION BY SYNDECAN-4 REGULATES EXTRAVILLOUS CYTOTROPHOBLAST CELL MIGRATION

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Extravillous cytotrophoblast (EVT) invasion is essential for remodeling the uterine vasculature during human placentation, as deficiencies in this process can lead to severe obstetrical complications. Although EVT invasion is a highly regulated process, its molecular mechanisms are not well understood. Previous studies in other cell types have shown that syndecan-4 (SDC4), a heparan sulfate proteoglycan, is highly associated with cell invasion and migration by facilitating interactions with extracellular matrix, and coordinating cellular responses such as activation of the protein kinase C-alpha (PKCα) pathway. However, the role of SDC4 in EVT invasion is not well understood. Here, we show that *SDC4*-deficient HTR8 EVTs had significantly reduced PKCα and AKT phosphorylation, which correlated with decreased invasion and migration capacity (60% invasion deficit and 40% migration deficit, $P<0.05$). Concordant with this finding, inhibition of PKCα by Gö6976 mitigated HTR8 EVT invasion and migration (60% invasion deficit and 50% migration deficit, $P<0.05$). Furthermore, we show that *SDC4*-deficient HTR8 EVTs had reduced AKT phosphorylation compared to control cells after treatment with Fibroblast Growth Factor 2, a cytokine known to associate with SDC4. Our findings reveal an essential role of SDC4 as a vital regulator of EVT invasion and migration by coordinating PKCα activation.

Oral presentation – A: Cell, Molecular, and Genetics

FORMINS – A FAMILY OF KEY REGULATORS OF CELL MIGRATION BY TISSUE STIFFNESS

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Directed cell migration is an integral process in animal development and disease. Cell migration is orchestrated by a variety of chemical and biological factors, but is also regulated by mechanical properties of tissue. Tissue mechanics, *e.g.* stiffness, is particularly important for cancer progression and metastasis. Despite the apparent clinical importance of the mechanical cues, the mechanisms that allow cells to sense tissue stiffness are unknown. Recently, by using a mathematical model we have predicted that the dynamics of stress fiber polymerization governs cell mechano-sensing. Here, I confirmed this prediction experimentally. By combining pharmacological perturbations and siRNA-induced gene silencing I have identified formins, a family of actin nucleating proteins, as a key regulators of stress fiber polymerization. I tested how cellular contractile forces regulate the dynamics of stress fiber polymerization and showed that suppression of formin mediated stress fiber polymerization abolishes the cell's ability to mechano-sense. My project, has identified a novel mechano-sensetive structure in mammalian cells and teased apart the role of formin-mediated stress fiber elongation as an integral constituent in mechano-sensing. Since expression of many formins has been reported to be elevated in metastatic tumors, my data has revealed new prominent targets for therapeutics that suppress cancer metastasis.

Oral presentation or Poster presentation.

A: Cell, Molecular & Genetics

SEXUAL SIZE DIMORPHISM IN THE ARCTIC FOX (*ALOPEX LAGOPUS*) POPULATION NEAR ARVIAT, NUNAVUT

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Abstract
Sexual size dimorphism (SSD) is widespread throughout the animal kingdom and sexual selection is considered as one of the main drivers of SSD. This is more prominent in polygamous mammals, where larger males have a greater advantage in obtaining and defending females. Other drivers include ecological factors like gender-specific niche divergence, which reduces intersexual competition for resources or an adaptation driven by differing male and female social or reproductive roles. Most Canids are monogamous, therefore sexual selection and sexual size dimorphism are typically less significant. During the denning season, male arctic foxes hunt and protect the den, whereas females play a reproductive and nurturing role. Therefore, selective pressures may favor larger males. The objective of this research is to determine if sexual size dimorphism is occurring in foxes as a result of their differing roles in a monogamous mating pair. A total of 855 arctic fox carcasses were purchased from Inuit trappers. The foxes were trapped during consecutive hunting seasons (November 1st to April 15th) from 1983 to 1985, near Arviat, Nunavut. The carcasses were frozen until necropsied. Morphometric measurements and age (cementum annuli method) were recorded for each carcass collected. Males were on average 19.2% heavier than females, had a 5.9% longer trunk than females, a 3.4% longer condylo-basal length and a wider zygomatic breadth by 3.5%. Therefore, there is a small but significant male-biased size dimorphism in arctic foxes. This research aims to help increase understanding of how differing roles in a monogamous pairing can drive sexual dimorphism.

Key-words
Arctic fox, *Alopex lagopus*, sexual size dimorphism, reproductive roles, monogamy

Oral presentation
Ecology & Evolution

THE TROPHIC NICHE OF SCULPINS (*COTTUS* SP.) IN FORAGE FISH COMMUNITIES OF NEAR NORTH AND FAR NORTH LAKES IN ONTARIO

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The trophic niche, defined as an organism's functional role as a consumer in an ecosystem, is an important concept in ecological research. It can be used as a framework for studying species interactions and habitat use, and for predicting food web structure in diverse environments. My research project is examining the trophic niche of freshwater sculpins (*Cottus* sp.), a poorly-studied group of forage fishes that live in a diversity of lakes across northern Canada. My main objective is to determine the trophic niche of sculpins relative to other co-habiting forage fishes in two different regions of Ontario, the Near North and Far North, that have different lake environments. Near North lakes are deeper, more oligotrophic, and contain lake trout (*Salvelinus namaycush*) as the main predator. Far North lakes are shallower, more mesotrophic, and contain northern pike (*Esox Lucius*) and/or walleye (*Sander vitreus*) as the primary predators. Because of differences in habitat availability between lakes of these regions, I predict that sculpins will occupy a trophic niche that is very distinct from other species in the Near North, but not in the Far North. Sculpins and other forage fishes were sampled from lakes of both regions and analyzed for stable isotope compositions ($\delta^{13}C$ and $\delta^{15}N$). The dispersion of individual fish in isotope space will be analyzed using recently developed stable isotope trophic niche metrics in order to make inferences about their niche positions, sizes, and shapes. Overall, this research will provide new information on food web structure and sculpin ecology in northern lakes, and improve our understanding of the flexibility of the trophic niche.

Oral Presentation
B: Ecology & Evolution

ISOTOPIC DISCRIMINATION AND TURNOVER IN TISSUES OF THE TRUE ARMYWORM, *MYTHIMNA UNIPUNCTA* HAWORTH: APPLICATIONS TO TRACING LONG-DISTANCE MOVEMENTS

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Tracking migration of insects is logistically challenging due to their small body size. Isotopic values ($\delta^{13}C$ and $\delta^{2}H$) in tissues of insects can be used to infer natal origins, movement, and diet. However, it is necessary to quantify how isotope ratios change between diet and tissues (discrimination) and the elemental turnover rate (in metabolically active tissues) following encounters with isotopically different foodwebs (isoscapes). The $\delta^{2}H$ values of metabolically inactive chitinous tissues (head capsule, legs, wings and thoracic cuticle) of adult true armyworm moth (*Mythimna unipuncta*) raised on a constant diet were used to investigate if all chitinaceous tissues could be used to infer origins. Analyses demonstrated that tissue $\delta^{2}H$ differed among certain tissues types, but not between individuals for any given tissue type. These preliminary results indicate which tissues can be combined together for bulk isotopic analysis and which cannot for tracking purposes. Additionally, adult true armyworm moths were exposed to three different artificial nectar diets in order to establish muscle tissue turnover rates. These results provide fundamental information on the utility of the stable isotope approach to tracking insect origins.

The abstract is for oral presentation.
Group B: Ecology & Evolution

RESIDENCY AND MOVEMENT PATTERNS OF ARCTIC SKATE (*Amblyraja hyperborea*) IN CUMBERLAND SOUND

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Understanding habitat selection and the impact of environmental variability due to climate change is critical for the effective conservation and management of at risk species. In the Arctic, decline in extent and thickness of sea ice is leading to the expansion of both community and commercial fisheries within previously untapped Arctic ecosystems. In one such established fishery, in Cumberland Sound, Southern Baffin Island, Artic skates (*Ablyraja hyperborea*) are a potential species at risk. Low fecundity, slow maturation, and the Arctic skate's status as principle bycatch species within the Cumberland Sound Greenland halibut fishery raises concerns over their long-term population trends within this ecosystem. Through acoustic telemetry monitoring at depths between 400 and 1200 m, this study examined the residency, individual movement patterns, and biotic and abiotic factors driving Arctic skate movement across the fishing grounds. Detection data indicated that the majority of Arctic skates remain concentrated in the northern section of the southern deep-water region, with residency index values ranging from 0.13 in April to 0.73 in August. Throughout the year, Arctic skates exhibited seasonal movements between the southern and northern regions of the Sound with northern shallow water residency peaking at 0.75 in April and skates remaining resident to some degree (0.2-0.4) until the end of October. A total of 40% of detected skates (n=16) were identified in the northern region during the summer and 88% (n=35) were detected in the southern region in the winter. Individual movement patterns were classified based on the number of receivers a fish was detected on and whether they engaged in short-range movements via gates or long-range movements between gates. A total of 60% (n=24) of skates were detected on multiple receivers with each individual exhibiting clear and categorizable patterns of travel. A mixed effects model was then performed to examine the effect of biotic and abiotic factors on the presence and absence of skates in the northern shallower winter fishing area and the southern deep-water region. We present an overview of the results and explore study limitations, in particular the inability of the receiver array to adequately detect and therefore characterize the finer scale movements of Arctic skates. Nonetheless, telemetry shows great promise as a tool for understanding the movement patterns of deep-water skate species and improving our ability to conserve at risk species.

Oral Presentation - Group B (Ecology & Evolution)

IMPACT OF FOREST DERIVED ORGANIC MATTER ON FRESHWATER ZOOPLANKTON ABUNDANCE AND COMPOSITION

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In this study we intend to assess the role of forests in fueling aquatic ecosystems. To test this we used the littoral zone of two lakes as our study sites. Littoral zones are the terrestrial-aquatic interphase were terrestrial organic matter (tOM) is introduced into water bodies. By placing sediment boxes with a range of quantities of tOM in the littoral areas, we expect to find how zooplankton varies in quantity and composition. The two lakes chosen are situated in the Greater Sudbury Area, and represent an acidic and a non-acidic lake. We filled 69 plastic bins of 17.5L volume with different amounts of organic matter and submerged them at a 1 meter depth within the littoral zone. Once per month in the summer of 2017 (June, July and August), zooplankton traps consisting of 0.5L inverted cups and a funnel were deployed individually over the bins. Zooplankton were then counted and classified in two main groups: copepods and cladocerans. We measured the organic matter and carbon being emitted from the bins and on the surface layer (DOC, DOM and LOI%), as we think that the original treatments may had degraded over time. We found a higher productivity of zooplankton in the non-acidic lake. Copepods also seem to outcompete cladocerans with increasing organic matter (LOI%). Further results have yet to be concluded. Once our results are completed we hope to provide valuable information that may aid reforestation efforts around freshwater bodies and maximize their health and resources.

For Oral Presentation, Group B.

PREFERENCE RESPONSE TO PHENYLETHYL ALCOHOL AMONG PREVIOUSLY EXPOSED CHINOOK SALMON *(ONCORHYNCHUS TSHAWYTSCHA)*

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For Chinook salmon, the sense of olfaction is critical to reproductive fitness. Salmon imprint on the odours they experience at early life stages, allowing them to return years later to the natal streams they were hatched in to find suitable nesting sites. This experiment tested whether exposure to an odorant in the larval stage can influence the behaviour of Chinook salmon when exposed again at the juvenile stage. Imprinting to phenylethyl alcohol (PEA) has been well documented among salmonids, and was used in this study. A 2-choice Y-Maze setup was used to test odour preference for PEA among juvenile Chinook salmon raised with or without this odorant during the larval stage. Among salmon exposed to PEA, a preference for PEA treated water was found, and salmon raised without this exposure showed no preference for treated or untreated water. The results show that imprinting during the larval stage was able to affect behaviour, specifically behavioural preferences, within the juvenile stage. This research has applications in conservation efforts for declining Chinook salmon populations, as well as in the management of hatcheries for research and aquaculture.

Oral Presentation
Group B

HOW MUCH DO YOU CHANGE? AN EVALUATION OF THE ANATOMICAL CONSEQUENCES OF MAXILLOMANDIBULAR ADVANCEMENT SURGERY

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Obstructive sleep apnea (OSA) is a chronic sleep disorder characterized by recurrent collapse of the upper airway causing complete or partial blockage during sleep. Maxillomandibular advancement surgery (MMA) is an effective intervention for OSA. However, details regarding which anatomical features are changed by MMA within the pharyngeal airway remain unclear. Previous studies suggest the velopharyngeal region (VPR) has the greatest obstruction potential during OSA. Accordingly, it is hypothesized that MMA surgery will specifically alter VPR, increasing anterior to posterior distance in the velopharynx. Analysis of anterior to posterior distances of the VPR were measured in cephalometric x-rays of OSA patients before and after MMA. Twenty-two patients (11 males and 11 females) with a mean age of 44 $\pm$ 13.9 years were measured. Measurements obtained by cephalometric analysis consisted of two velopharyngeal anteroposterior lengths (VAPL1,2) and a minimal velopharyngeal anteroposterior length (VAPLM). All distances were measured electronically using Osirix, 9.0.1. Mean change in distances among VAPL1, VAPL2, and VAPLM variables, were 1.6 $\pm$ 5.4mm, 3.9 $\pm$ 5.0mm and 4.7 $\pm$ 3.0mm, respectively. Mean VAPLM after MMA surgery increased significantly to 10.6 $\pm$ 3.6mm compared to pre-MMA, 5.9 $\pm$ 2.6mm, (t_{21} = 7.37, $p < 0.001$). Overall, there was a strong correlation between mean VAPL1 and VAPL2 ($r = 0.835$), (t_{20} = 4.55, $p < 0.001$) and between VAPL2 and VAPLM ($r = 0.738$), ($t_{20} = 2.81$, $p < 0.01$). Maxillomandibular advancement surgery does significantly alter the minimal velopharyngeal region and experienced the greatest change in unidimensional airway length.

Oral Presentation
Group C: Physiology & Toxicology

REPRESENTATION OF HAPTIC SIZE IN THE HUMAN BRAIN

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When a person looks at an object while exploring it with their hand, both vision and haptic provide information about the characteristics of the object. Previous results show that a high level visual area, the lateral occipital cortex can be activated by both visual and haptic shape exploration, which suggests that the two modalities may share representation of object shape. It is not clear whether the primary visual cortex (V1) also responds to both modalities. We will address this question by investigating the visual and haptic representation of object size because visual size is a low level feature that is known to be primarily represented in V1. First, we will conduct a behavioural study to examine the extent to which haptic and visual size matches. Then we will conduct a fMRI study to examine if haptic size is represented in the same way as visual size in the primary visual cortex. We hypothesize that those individuals who matched haptic and visual size would share a more common representation in the V1 or anywhere else in the brain than compared to those who did not match haptic and visual size. If the hypothesis holds true, this provides new evidence that the primarily visual cortex, which is thought to respond to only visual information can also respond to other modality cues.

Oral Presentation

C. Physiology & Toxicology

ASSESSING BRAINSTEM SENSITIVITY IN AN ANIMAL MODEL FOR AUTISM

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Altered processing of auditory information is commonly seen in developmental disorders such as autism spectrum disorders (ASD). A novel rodent model for the auditory and behavioral deficits seen in ASD, the *Cntnap2*$^{-/-}$ rat, can be used to study underlying neural alterations in these disorders. The CNTNAP2 gene codes for receptors and cell adhesion molecules, and is highly important in the development of the auditory nervous system. This study aims to compare early auditory processing of *Cntnap2*$^{-/-}$ rats, heterozygous rats (*Cntnap2*$^{+/-}$*),* and wildtype rats during different developmental stages. Auditory processing was evaluated by measuring evoked potentials from the brainstem auditory pathways in rats, called auditory brainstem responses (ABRs). The ABRs were measured for acoustic stimuli of varying intensities (40-90 dB SPL) and across three developmental ages (28 days, 42 days, 70 days). Analysis of ABRs across the ages showed no significant and enduring differences in peak I amplitudes between animal autism models (*Cntnap2*$^{-/-}$ rats) and control wildtype rats, indicating that developmental deficits associated with the CNTNAP2 gene do not stem from the cochlear nerve. *Cntnap2*$^{-/-}$ rats exhibited significantly lower peak IV amplitudes compared to controls, suggesting the CNTNAP2 gene related deficits affect the lateral lemniscus. The peak latencies, which indicate neural conduction speed, for both peaks I and IV were significantly higher in *Cntnap2*$^{-/-}$ rats during the younger ages, but the deficits were ameliorated during the adult ages. The results suggest that early brainstem structures are not implicated in the persisting auditory deficits seen in *Cntnap2*$^{-/-}$ rats.

Oral presentation

Physiology & Toxicology

K^+ TRANSPORT AND ACID-BASE BALANCE IN THE MALPIGHIAN TUBULES OF THE LARVAL CABBAGE LOOPER, AN IMPORTANT AGRICULTURAL PEST OF NORTH AMERICA

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Larval butterflies and moths are well known as crop pests due to their intense feeding habits that damage numerous vegetable crops. This plant-based diet is digested by a midgut whose extreme alkalinity is maintained by secreting K^+ and base. As such, vigorous ionoregulatory mechanisms are employed by the Malpighian tubules and hindgut forming the insect's functional kidney. The fluid secretory portion of the Malpighian tubule secretes ions (with water following osmotically). It is composed of the distal cryptonephridial Malpighian tubules, a short section known as the rectal lead, and a highly convoluted section of tubule adjacent to the ileum termed the ileac plexus. Different tubule regions (similar to different portions of the vertebrate nephron) modify the [K^+] and pH of the fluid passing through them. The distal ileac plexus secretes slightly alkaline fluid high in K^+ content. In this study, the Ramsay assay was used to evaluate the effects of K^+ channel blockage on the rate, K^+ content, and pH of fluid secreted by the distal ileac plexus of the Malpighian tubules in the larva of the cabbage looper moth. Treatment with a non-specific K^+ channel blocker, $BaCl_2$, resulted in significantly decreased fluid secretion due to K^+ flux decrease. As a result of these changes, the pH of secreted fluid decreased significantly. Taken together, these results indicate that decreased K^+ content leads to luminal acidification in the Malpighian tubules, where acid-base balance relies on the transport of K^+.

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C: Physiology & Toxicology

A STUDY ON THE INCIDENCE OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*, ESBL-PRODUCING *ENTEROBACTERIACEAE*, AND AMPICILLIN-RESISTANT *HAEMOPHILUS INFLUENZAE* AND DESCRIPTION OF THE PATIENTS THEY INFECT IN A NORTHERN ONTARIO HOSPITAL

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The increasing prevalence of antibiotic-resistant bacteria poses a large risk for public health such that the World Health Organization (WHO) has published a list of "priority pathogens" in response to the issue. A better understanding of human populations affected by these bacteria is needed in order to better treat and manage the infections they cause. The purpose of our study was to determine the incidence of infections caused by three bacterial species outlined by WHO, as well as describe the patients that succumb to these infections in Northern Ontario. The descriptive study consisted of a secondary analysis of retrospective chart review data. The charts of patients older than 16 years of age who presented to Health Sciences North with an infection caused by either *Enterobacteriaceae* (ESBL-producing), *Staphylococcus aureus* (methicillin-resistant) (MRSA), and *Haemophilus influenzae* (ampicillin-resistant) in 2017 were selected for the study. Patient demographics, health indicators, and infection details were extracted to be analyzed for the study. In total, 88 cases of MRSA infection occurred resulting in an incidence of 3.9/1,000 admissions; which is higher than the 2.2/1,000 admissions National rate of Canada in 2012. For *Enterobacteriaceae*, 73 cases of infection occurred over 2017, with 67.1% of patients being female and 78.1% of cases being urinary tract infections. The incidence rate was found to be 3.3/1,000 admissions. Only 20 cases of *H. influenzae* occurred over the 12 months, 75% were male patients, and 100% of cases were due to pneumonia. The incidence was found to be 0.9/1,000 admissions.

Oral Presentation
C: Physiology & Toxicology

INCREASED SPERM MORTALITY AND MORPHOLOGICAL ABNORMALITIES IN MICE WITH PI-BASED CART *IN UTERO* EXPOSURE

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Abstract: Protease inhibitor (PI)-based combination antiretroviral therapy (cART) is currently the gold standard for inhibition of Human Immunodeficiency Virus (HIV) vertical transmission. However, multiple reports have associated PI-based cART exposure to adverse birth outcomes such as hormonal abnormalities, small-for-gestational-age (SGA) births and preterm delivery. The purpose of this study was to explore the effect of PI-based cART administered *in utero* on future fertility. Two parameters were analyzed; the viability based on motility and the morphology of sperm cells that had been exposed to various PI-based cART regimens via a mouse pregnancy model**.** All 65 mice in the study were either given PI-based regimens, Truvada with Atazanavir or Kivexa with Atazanavir, while control mice were given water by gavage. The data indicated increased sperm mortality in mice exposed to PI-based regimens *in utero*. PI-based cART mice presented no flagellar motility, and sperm morphological abnormalities such as hammerheads, hairpin loops and rough-surfaced tails were observed. The findings suggest that administered PI-based cART during pregnancy is linked to future offspring fertility issues.

Key Words: HIV; cART; combination antiretroviral therapy; protease inhibitor; sperm; fertility

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