**CONFERENCE ABSTRACT BOOK OPEN ACCESS** The 2025 Canadian Undergraduate Conference on Check for updates Healthcare Abstract Book Andrew R. Lacelle, BScH Student [1]\*, Tima Al Shamma, BScH Student [1], Angela Liu, BHScH Student [2] [1] Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada K7L 3N6 [2] Faculty of Health Sciences, Queen's University, Kingston, Ontario, Canada K7L 3N6 URNCST Journal

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"Research in Earnest"

#### Abstract:

The following abstracts highlight research by undergraduate students on a diverse array of healthcare topics presented during the 2025 Canadian Undergraduate Conference on Healthcare Research Competition at Queen's University. This year's theme of "Honoring the Past, Exploring the Future: Two Decades of Discovery and the Two to Come" explores advances in medical sciences from the past, as well as potential future discoveries, that enhance patient care in a rapidly changing world. Abstracts are grouped into oral presentations, followed by those for poster presentations. For more information, please visit: https://www.cucoh.com/.

Keywords: cucoh; research; cucoh 2025; undergraduate

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#### **Conference Abstracts**

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#### **Oral Presentations**

## The Fitness Cost of Metallo-β-Lactamase Expression is a Potential Target for New Therapeutic Approaches to Carbapenem Resistance.

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**Introduction:** The rise in multidrug-resistant bacteria is causing a growing public health crisis. Carbapenem antibiotics represent the most reliable last-resort treatment for bacterial infections. The widespread acquisition of metallo- $\beta$ -lactamases (MBLs), such as VIM-2, is a significant contributor to the emergence of carbapenem-resistant pathogens. We demonstrate that Enterobacteriaceae expressing VIM-2 have impaired growth in clinically relevant zinc-deprived environments, including human serum and in murine infection models.

**Methods:** Using RNA-sequencing, genomic, and chemical approaches, we identify pathways critical for VIM-2 expression in *Escherichia coli* under zinc limitation, including envelope stress responses. Disruption of these pathways reduced the growth of VIM-2-expressing bacteria in vitro and in vivo. VIM-2 expression increases antibiotic accumulation, rendering these bacteria more susceptible to antibiotics like azithromycin. We highlight azithromycin's potential to treat VIM-2-expressing *Klebsiella pneumoniae* in a murine infection model.

**Results:** We demonstrated that VIM-2 expression disrupts the integrity of the outer membrane, rendering VIM-2-expressing bacteria more susceptible to antibiotics that are typically ineffective against Gram-negative bacteria, such as azithromycin. We underscored the therapeutic promise of azithromycin against a clinical isolate naturally expressing VIM-2 in a murine infection model, showing that a dose (50 mg/kg) 8 times lower than the human equivalent reduced the bacterial load below the limit of detection in 75% of the mice; concurrent treatment with zinc every 4 hours reduced the efficacy of azithromycin by 3-logs. Additionally, we showed that higher levels of VIM-2 expression in clinical isolates correlated with increased sensitivity to azithromycin.

**Conclusion:** These findings encourage further investigation into the combination of azithromycin and meropenem against VIM-2-expressing bacteria in vivo. In all, our findings provide a framework to uncover and exploit the fitness trade-offs of resistance, potentially accelerating the discovery of novel treatments for multi-drug resistant bacteria.

### Evaluating the Effectiveness of Machine Learning Models for Predicting Outcomes in Lung Transplants Using Ex Vivo Lung Perfusion

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**Introduction:** Lung transplantation is a critical lifesaving intervention for patients with end-stage lung disease, where the quality of donor lungs significantly impacts outcomes. Ex Vivo Lung Perfusion (EVLP) is a key technique that enhances the assessment and usability of donor lungs. This paper evaluates the impact of machine learning (ML) models on predicting outcomes in lung transplants using EVLP data, aiming to refine the decision-making process in donor lung suitability and improve patient outcomes.

**Methods:** Following PRISMA guidelines for systematic reviews, we searched databases including Medline, Embase, and IEEE Xplore up to June 2024. We identified 11 studies (2 randomized controlled trials, 5 cohort studies, and 4 retrospective analyses) that utilized ML models to predict the viability of donor lungs and patient outcomes post-transplant. Data extraction focused on model accuracy, types of ML algorithms used, and their predictive performance in terms of AUROC.

**Results:** ML models, particularly ensemble methods like Random Forest and XGBoost, demonstrated robust predictive capabilities. The average AUROC across studies was 0.85, indicating high predictive accuracy. These models effectively utilized clinical, radiographic, and physiological data from EVLP assessments to predict transplantation outcomes. Significant improvements were noted in anticipating post-transplant recovery metrics including time to extubation and primary graft function.

**Conclusion:** Machine learning models significantly enhance the predictive accuracy of donor lung suitability and posttransplant outcomes when integrated with EVLP. This integration promises to optimize lung transplant outcomes by supporting personalized clinical decisions. Future research should focus on exploring real-time predictive modeling of EVLP in clinical settings.

# Hayden's Hub: An Evidence-Based Community Hub to Support Social Prescribing for Youth With Neurodevelopmental Disabilities

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**Introduction:** Social prescribing (SP) is an innovative healthcare approach that connects individuals with local, non-clinical services addressing social determinants of health, bridging gaps between primary care and community resources. While evidence demonstrates that SP enhances mental and physical health, its accessibility for youth with neurodevelopmental disabilities (NDDs) remains underexplored. This gap underscores the need for SP models tailored to the needs of this population.

**Methods:** A rapid review was conducted to explore Ontario's SP landscape and identify strategies for improving accessibility for youth with NDDs. Following Cochrane Review Methods Group guidelines, searches were performed across Medline EBSCOhost, PsychInfo, Wiley, and Sage databases. The search, covering publications from January 2010 to September 2024, included both peer-reviewed and grey literature. Findings were summarized using content analysis for descriptive synthesis.

**Results:** The review identified a significant gap in SP research for youth with NDDs, particularly challenges faced when accessing services through primary healthcare pathways. These insights guided the development of Hayden's Hub, a pilot project in Ottawa designed to bridge this gap by offering social prescribing tools tailored to youth with special needs.

**Conclusion:** By promoting SP, the project adopts an upstream approach to social determinants of health, emphasizing the need to understand how youth with NDDs experience SP pathways and identifying necessary adaptations. Hayden's Hub aims to improve access to community resources and enhance mental health outcomes for this population.

Funding: This project was funded by Canada Service Corps (CSC) at Employment and Social Development Canada and GLOCAL Canada.

#### Next Generation of Nanomedicine for Novel Cancer Therapies: Functionalized Folate Amphiphilic Alternating Copolymer Immobilizes Folate Receptor Functionality in Disabling Key Survival Pathways Critical for Pancreatic Tumor Progression and Metastases

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**Introduction:** Nanopolymers offer targeted cancer treatments by using tumor-specific receptors to kill cancer cells while sparing normal ones. This study introduces an empty functionalized folic acid (FA) polymer with poly (styrene-alt-maleic anhydride) (SMA) linked by 2,4-diaminobutyric acid (DABA) (FA-DABA-SMA) to penetrate three-dimensional pancreatic and breast tumor spheroids.

**Methods:** The FA-DABA-SMA copolymer was tested for its penetration into cancer spheroids. In a mouse model of pancreatic cancer, we assessed its impact on tumor growth and metastasis in comparison with untreated and curcumin-treated groups. Immunocytochemistry staining evaluated pathways essential for tumor survival, including Agrin/YAP/TAZ oncoproteins, Ki-67, Casp3, PhoH3, hypoxia markers, and vasculogenesis indicators.

**Results:** FA-DABA-SMA penetrated deep into tumor spheroids and reduced primary tumor growth and metastasis in the mouse model. Immunostaining showed that binding to FR $\alpha$  immobilized oncoproteins in the cytoplasm, blocking their nuclear translocation, and disrupting pathways involved in growth, apoptosis, and hypoxia.

**Conclusion:** FA-DABA-SMA's unique mechanism—binding to  $FR\alpha$  to immobilize intracellular oncoproteins—affects pathways critical for cancer progression. These findings suggest that FA-DABA-SMA may offer a novel therapeutic approach by disrupting intracellular signaling in tumor cells, highlighting FR $\alpha$  as a potential target for cancer treatment.

#### Testing the Inhibition of Activins via Receptor-Ligand Traps to Reduce Kidney Fibrosis

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**Introduction:** This study assesses the efficacy of activin type IIA and type IIB receptor-ligand traps as potential therapeutics for chronic kidney disease (CKD). Activins A and B, members of the TGF- $\beta$  superfamily, contribute to kidney disease by promoting inflammation and fibrotic changes. Receptor-ligand traps, engineered to bind specific ligands, block these activins from interacting with their native receptors, reducing downstream pro-fibrotic signaling. Testing these traps provides a baseline for evaluating future receptor-ligand trap designs. The objective was to determine the effects of activin type IIA and IIB receptor-ligand traps on kidney fibrosis by measuring three markers: fibronectin, phosphorylated (activated) Smad3 (pSmad3), and alpha smooth muscle actin (SMA) in a mouse model.

**Methods:** C57BL/6 male mice underwent unilateral ureteral obstruction (UUO) (n=5/group) in three groups: two treatment groups (type IIA and IIB receptor-ligand traps) and one control (vehicle). Treatment identity was blinded. Fibronectin, pSmad3, and SMA expression were assessed via immunohistochemistry, with analysis performed in a blinded manner.

**Results:** Both activin type IIA and IIB receptor-ligand traps significantly decreased fibrotic marker expression in treatment groups relative to control. Fibronectin, pSmad3, and SMA levels were reduced in both treated groups, with no significant difference observed between the treatments.

**Conclusion:** The reduction in fibrotic markers supports the effectiveness of activin receptor- ligand traps in mitigating kidney fibrosis. These findings establish a foundational understanding of receptor-ligand traps' role in kidney disease, providing a valuable baseline for comparing future novel traps and advancing targeted treatments, contributing to improved healthcare outcomes in fibrosis management.

#### Targeting Escherichia Coli With a Novel Boron Compound Library

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**Introduction:** The rise in antibiotic-resistant gram-negative bacterial infections gives urgency to finding new antibacterial drugs. Boron-drug design is a compelling option for next-generation pharmaceuticals. Elemental boron (B) imparts unique structural and bonding properties. B-compounds may form high-affinity covalent bonds with cellular molecules that might be optimized to treat cancer or microbial infections. However, the use of boron compounds is limited. Our aim is to find new B-compounds that inhibit bacterial growth. We hypothesize that B-compounds with cytostatic or cytotoxic effects in vitro may be promising targets for drug design and discovery.

**Methods:** Escherichia coli (E. coli) cultures were grown overnight in Luria Broth (LB) media and diluted to an OD600 value of 0.1. Nineteen B-compounds were serially diluted and mixed with cells to allow treatment over 16 hrs. Each compound's half-maximal inhibitory concentration (IC50) was calculated. The IC50 value is a dose that characterizes a compound's inhibitory strength against E. coli and can be used to compare potency of B-compounds.

**Results:** Out of 19 compounds screened, a benzoxazole with NO2 and BPh2 R-groups generated the lowest IC50 value  $(32.4 \ \mu M)$  and caused cell death.

**Conclusion:** K-NO2-BPh2 exerts potent antibacterial effects. Our structural assessment suggests synergy between phenolic R-groups and the benzoxazole core. Future work will test the mechanisms of action which kill E. coli.

#### Niacin Acid and Nad+ Maintenance: Salvage Pathway and Extension of Cell Lifespan

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**Introduction:** This study investigates niacin acid's role in extending cell lifespan by enhancing NAD+ levels through the salvage pathway. Aging is linked to cellular inefficiency and DNA damage, driven partly by declining NAD+, a coenzyme crucial for energy production and DNA repair. Boosting NAD+ via niacin acid may slow cellular aging.

**Methods:** Yeast strains, including a wild-type (BY1474) and mutants ( $\Delta$ Tna1,  $\Delta$ Npt1,  $\Delta$ Nma1) with altered NAD+ synthesis, were grown in media with varying niacin concentrations. Serial dilution assays and light intensity measurements quantified growth, while a synthetic dropout medium without tryptophan ensured that NAD+ was primarily synthesized through niacin.

**Results:** Niacin supplementation increased NAD+ levels and cell growth in the wild-type strain, with diminishing returns at higher concentrations. Mutant strains, lacking key enzymes in the NAD+ pathway, showed reduced growth, underscoring the salvage pathway's role in NAD+ synthesis.

**Significance:** The findings suggest that niacin acid supplementation could be a viable strategy for maintaining NAD+ levels, potentially delaying cellular aging. By supporting NAD+ synthesis, niacin aids crucial processes like energy production and DNA repair, which are essential for cell longevity.

**Conclusion:** Niacin acid effectively boosts NAD+ levels, supporting cell growth and lifespan, although the effect plateaus with increasing concentrations. This study highlights the NAD+ salvage pathway's significance in aging prevention and points to further research on alternative pathways and supplements for broader anti-aging applications.

# Understanding the Role of Mast Cells and Microbiota in Irritable Bowel Syndrome Pathogenesis: Characterization of the "Hello Kitty" Mouse Model

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**Introduction:** Irritable Bowel Syndrome (IBS) is a gut-brain disorder marked by abdominal pain, altered motility, and visceral hypersensitivity. This condition is linked to increased mast cell numbers and altered gut microbiota. Mast cells are also implicated in psychiatric conditions often associated with IBS. Bacterial histamine promotes visceral hypersensitivity by recruiting and activating mast cells through histamine receptor 4, though the specific microbiota-mast cell mechanisms remain unclear. This study examines mast cell roles using specific pathogen-free (SPF) mast cell-deficient (Cpa3-Cre;Mcl-1fl/fl, Hello Kitty (HK)) mice at steady state and after colonization with high histamine-producing IBS microbiota.

**Methods:** Visceral motor responses (VMRs) to colorectal distension (CRD), proxy for visceral pain sensitivity, were evaluated alongside light/dark, open-field, and tail suspension tests for anxiety- and despair-like behaviours. 40 SPF HK mice (20 heterozygous, mast cell-sufficient; 20 homozygous, mast cell-deficient) were tested. Additional antibiotic-treated HK mice were colonized with high histamine-producing IBS microbiota, and VMRs to CRD assessed three weeks post-colonization. Mast cell presence was confirmed using tryptase staining.

**Results:** Preliminary data show no significant differences in VMR responses to CRD in heterozygous and homozygous mice, suggesting activation—not presence—of mast cells drives hypersensitivity. Anxiety, despair, and exploratory behaviours were similar. Colonization of antibiotic-treated HK mice is on-going.

**Conclusion:** Homozygous mice exhibit similar VMRs and behaviour to heterozygous mice at steady state, supporting mast cell activation likely drives hypersensitivity. Experiments with mice colonized with histamine producing microbiota will help establish the role of mast cells and microbiota in hypersensitivity and psychiatric comorbidities in IBS.

#### Behavioural Profiling of Fungal Secondary Metabolites for Neuroactive Compound Discovery

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**Introduction:** Neurodegenerative diseases are the leading cause of illness and disability worldwide. The overall amount of disability-adjusted life years (DALYs) has increased 18% since 1990, and in 2021 more than 3 billion people were living with a neurological condition. This upward trend reflects a failure to capture the complexities of human neurobiology in the discovery of new neurological drugs through the commonly used reductionist, target-based screening approaches.

**Methods:** We utilize the nematode Caehnorhabditis elegans as a whole-animal model to study behaviour-altering molecules, offering a high-throughput alternative to rodent models. The nervous systems of humans and C. elegans are highly conserved and serves as a model for neurodegenerative disease where motor behaviour is a proxy for nervous system function. The Kastl-HighRes imaging system is a platform for high-throughput worm screening that captures high-resolution videos of C. elegans in a standard 96-well microwell plate format. Tierpsy Tracker, an open-source software, identifies behavioural changes in over 1000 distinct behavioural features and summarizes them as fingerprints. Altogether, this phenotypic screening platform will identify neuroactive chemical matter that would otherwise be overlooked in target-based screening.

**Results:** Our platform has been validated using Emamectin Benzoate, Pirimicarb, and Mianzerin Hydrochloride, as control compounds and behavioural changes were confirmed using our system. Next, we identified behavioral features, specifically related to speed, that were altered by certain fungal metabolites.

**Conclusion:** These findings support use of this platform to identify natural product and synthetic small molecules that exhibit neuroactivity in neurodegenerative whole animal models in high- throughput using robotic automation and library screening.

#### **Poster Presentations**

#### Pbmc Rnaseq Profiling of Als Reveals Male-Specific Dysregulation in the Peripheral Immune System

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**Introduction:** ALS prevalence, severity, and progression differ between the sexes, with males being more susceptible. The underlying molecular mechanisms, including differences in inflammatory response, are not well understood.

**Methods:** We conducted RNAseq profiling of Peripheral Blood Mononuclear Cells (PBMC) from ALS patients and sex-matched controls. After identifying differentially expressed (DE) genes, we performed pathway enrichment analysis and cell-type deconvolution to estimate proportions of immune cell types.

**Results:** The ALS male vs healthy male comparison revealed the most DE genes, primarily related to immune response and inflammation. Pro-inflammatory cytokines, such as IL-8, were highly enriched in Male ALS, while showing no changes in females. We also observed that anti- inflammatory pathways, such as IL-10, PPAR, and LXR/RXR, were inhibited in Male ALS. Comparing healthy females with healthy males showed higher immune activity in females. Cell- type deconvolution also showed that healthy females have higher immune activity than healthy males. A potential explanation could be that females have more active baseline immune activity, as observed in previous studies, while male immune cells over-activate in ALS leading to more severe inflammatory response.

**Conclusion:** We have identified DE genes, involved in inflammation and related pathways, in male ALS patients, and didn't see much dysregulated pathways in female ALS patients. To increase the statistical power and confirm findings, we are planning to sequence more ALS samples.

#### **Exploring Determinants of Homecare Use in Older Adults**

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**Introduction:** Homecare services play a critical role in enabling older adults to age in place. However, access to these services is inconsistent, with disparities influenced by socioeconomic, cultural, and geographic factors. Understanding the social determinants driving homecare demand is essential to address these gaps and ensure services reach those in need. This study aims to identify and analyze the primary factors influencing homecare use among older adults through a systematic review.

**Methods:** A systematic review was conducted following PRISMA guidelines to capture quantitative, peer-reviewed studies published from 2000 to 2024 that examine determinants of homecare use among adults aged 65 and older. Next steps include a meta-analysis to measure the impact of identified factors and an analysis of the Canadian Longitudinal Study on Aging (CLSA) to further explore how socioeconomic, physical, and contextual elements intersect in shaping homecare utilization patterns across diverse older populations in Canada.

**Results:** Preliminary findings reveal significant disparities across various populations in homecare access and utilization. Factors such as limited social networks, ethnicity, rural versus urban residency, and underlying health conditions contribute to varied usage patterns. Those facing economic disadvantages, social isolation, or managing chronic health conditions tend to have higher homecare needs, underscoring areas for targeted intervention.

**Conclusion:** The insights gained from this research will support policymakers and healthcare providers in creating more equitable homecare policies, fostering targeted strategies for aging populations, and informing future research to improve care delivery, ultimately contributing to enhanced well-being for older adults in Canada and aging in place.

## Survey of Radiation Therapists' Current Practices and Perceptions of Psychosocial and Supportive Care in Canada and Norway

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**Introduction:** Many cancer patients undergoing radiation therapy report unmet psychosocial needs, which can negatively impact their treatment outcomes and quality of life. This study explored the current practices and perceptions of radiation therapists (RTs) practicing in Canada and Norway with respect to addressing the psychosocial and supportive care (PSSC) needs of their patients.

**Methods:** An international cross-sectional study was conducted using an online evidence- informed survey of RTs practicing in Canada and Norway. The survey focused on: (1) demographics, (2) RTs' confidence level and perceptions related to PSSC, and (3) RTs' current practices related to PSSC. Descriptive statistics were used to summarize the study sample, and Chi-square tests and Mann-Whitney U tests compared differences between countries.

**Results:** A total of 79 Canadian and 131 Norwegian RTs completed the survey. Although RTs practicing in both countries identified PSSC as an important aspect of quality care, Canadian RTs expressed a greater desire to expand their scope of practice. Norwegian RTs were satisfied with delivering PSSC at their current capacity despite spending more time providing such care. Barriers common to both countries included a lack of training and resources, and time constraints.

**Conclusion:** There is variation in the current practices and perceptions of RTs in Canada and Norway with respect to PSSC delivery. However, Canadian and Norwegian RTs agree that engaging in PSSC ensures the best care for patients undergoing radiation therapy. With enhanced training, greater knowledge translation of resources, and institutional support, RTs can better address the PSSC needs of their patients.

Factors Affecting Access to Neurosurgical Care in Diverse Communities in Canada: A Scoping Review

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**Introduction:** Access to neurosurgical care is crucial for individuals with conditions such as traumatic brain injuries and brain tumours. However, equitable healthcare distribution, particularly in neurosurgery, remains a significant challenge in Canada. Disparities persist among populations defined by socioeconomic, geographic, racial, gender, and cultural factors, affecting their ability to access neurosurgical services. This scoping review aims to explore these disparities and identify key barriers to accessing neurosurgical care across diverse communities in Canada.

**Methods:** We conducted a comprehensive review of academic and gray literature from January 2000 to August 2024. Articles were identified through five databases: MEDLINE, EMBASE, Cochrane Library, PsycINFO, and Scopus. Gray literature from government reports and NGOs was also included. A total of 1345 records were screened, and 7 studies met the inclusion criteria. Thematic analysis was applied to qualitative studies to identify barriers and facilitators to neurosurgical care.

**Results:** The analysis revealed five primary barriers: geographic distance, socioeconomic status, racial and cultural influences, gender-related challenges, and health literacy. Rural populations faced difficulties accessing care due to distance, while lower-income groups encountered financial constraints. Racialized and Indigenous communities experienced systemic

discrimination, and gender-specific issues affected access to sensitive care. Health literacy also emerged as a barrier across diverse groups. However, the intersectionality of these barriers was rarely considered.

**Conclusion:** The findings emphasize the need for targeted policy interventions, improved healthcare infrastructure in underserved areas, and culturally competent care to ensure equitable access to neurosurgical services. Addressing these barriers is vital to advancing healthcare equity in Canada.

#### **Rats Anticipate Damaged Rungs on the Elevated Ladder: Applications for Rodent Models of Parkinson's Disease** *Maira Chaudhry, BScH* [1,2]

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**Introduction:** The study emphasizes the importance of flexible motor behaviors for object avoidance, particularly in the context of Parkinson's disease, which often leads to slow and rigid movements. The rats were tested on their ability to adapt to gaps in a ladder apparatus, and the results showed that encountering a breakaway rung following a step-up led to decreased velocity and stepping proportions. These findings have implications for understanding motor behavior differences and potential treatments for Parkinson's disease.

**Methods:** In this experimental setup, the ladder's incline was adjusted daily as needed. Two feeding cages were used to place the rats before and after each trial, with one placed on the counter next to the ladder and the other at the ladder's end. Trials were recorded using a GoPro HERO3+ camera, positioned on a tripod to capture the ladder, and lighting was provided by two 12V lamps. Rats were motivated to walk the ladder with Cheerios placed in the feeding cages.

**Results:** To analyze velocity data, the ladder was divided into four zones with distinct rung configurations. The study examined changes in 14th rung stepping proportions between baseline and breakaway conditions, considering the impact of incline. While a significant phase group interaction was found, there was no significant Phasegroup Incline effect. In the second experiment, a PhaseZone interaction was observed, with significant velocity changes in the third zone but no overall phase group incline zone interaction.

**Conclusion:** The study anticipated velocity slowdown near environmental breaks, especially in the second ladder zone, but found decreases primarily in the third zone, varying by incline and step direction.

# Towards Novel Phosphonate Natural Products: The Phosphoglycerate Kinase Homolog in a Putative Phosphonofructose Pathway

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**Introduction:** Phosphonates are a niche class of natural products but are dramatically over- represented as commercialized pharmaceuticals and agrochemicals. For example, the antibiotic fosfomycin and the herbicide phosphinothricin are both commercially successful natural products originating from bacterial sources. Because many phosphonate biosynthetic pathways are analagous to primary metabolic pathways, there are opportunities to discover new phosphonates by examining variations of standard primary metabolic pathways. We developed the branch point inventory strategy for efficiently discovering novel phosphonates by identifying potentially novel pathways from genomic data. My research focuses on one such pathway that we hypothesize makes phosphonofructose, which is a novel compound. The pathway involves seven genes, the first two of which we have verified. The third enzyme in the proposed pathway is a homolog of phosphoglycerate kinase, PGK. However, PGK presents a challenge in being characterized because it is insoluble.

**Methods:** My project aims to: (i) solublize PGK through varying protein expression and purification conditions, and (ii) test enzyme activity. Buffer screening of varying salt concentrations, pH, detergents, and stabilizers is used to test for solubility. Once solubility is achieved upon SDS-PAGE analysis, the catalytic activity of PGK will be tested to demonstrate its existence in the pathway.

**Conclusion:** Based on sulfofructose, the only known natural analog to phosphonofructose, phosphonofructose has the potential to provide a novel metabolic framework or serve as a basis for new therapeutic approaches.

#### Beyond the Surface: Evaluating Surgical Performance in Deeper Sites - Virtual Reality Simulation

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**Introduction:** Virtual reality surgical simulators provide qualitative and quantitative insights into surgical proficiency, offering an understanding of psychomotor performance. It is essential to understand expert-level surgical skills at varying depths, as deeper surgical sites often present challenges in accessibility and precision. In this study, we evaluated expert and trainee performance on realistically simulated brain tumor resections at varying depths. Our hypotheses were: (1) Performance scores of expert neurosurgeons remain consistent at varying depths, while (2) trainees' performance scores decline as they navigate into deeper, more challenging areas.

**Methods:** The performance of 45 participants during a simulated resection was analyzed. The Intelligent-Continuous-Expertise-Monitoring-System (ICEMS) measured surgical performances at 0.2-s intervals, including metrics like performance score, instrument tip separation, bleeding risk, tissue damage, aspirator force, and bipolar force. An average score for each metric for each depth interval was calculated across four expertise levels including neurosurgeons, senior trainees, junior trainees, and medical students. 3D modeling was performed using MATLAB, and regression analysis was carried out with IBM-SPSS.

**Results:** The analysis revealed variations in trainee performance by depth. Notably, neurosurgeons were an exception to this trend, consistently maintaining their scores irrespective of depth and showcasing their expertise. Interestingly, while medical students and junior trainees increased their scores as depth increased, senior trainees' scores declined. Among the metrics, instrument tip separation was particularly revealing, with neurosurgeons maintaining the smallest separation and medical students the largest.

**Conclusion:** The use of virtual reality surgical simulators in this study provided invaluable insights into surgical proficiency across varying depths. The study's findings emphasize the critical role depth plays in surgical performance, with distinct variations observed across different expertise levels. This highlights the importance of depth in surgical skills, ensuring that upcoming surgeons master the complexities of performing deeper surgical sites.

#### Characterizing Alternatively Activated M2d Macrophages

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**Introduction:** Macrophages are immune cells that are categorized into types based on activation by different stimuli. Unactivated M0 can be polarized to classically activated M1 or alternatively activated M2. 1 M1 macrophages, stimulated by LPS and IFN-, produce pro- inflammatory cytokines such as IL-1 $\beta$ , IL-6, IL-12, and TNF- $\alpha$ . 1 M2 macrophages, characterized by the production of anti-inflammatory mediators, include subtypes M2a, M2b, M2c, and M2d. 2 IL-4 stimulation leads to M2a differentiation. 2 Stimulation of M0 macrophages with LPS, a TLR agonist, and NECA, an adenosine receptor agonist, generates the M2d phenotype. 3 Research is ongoing to characterize M2ds gene expression, protein production, and functional properties.

**Methods:** Bone-marrow derived macrophages (BMDMs) and splenic macrophages (SpMs) from mice are used as in vitro models. RT-PCR examines the gene expression profile, enzyme-linked immunosorbent assay (ELISA) measures protein secretion, and flow cytometry measures intracellular and extracellular membrane protein expression. Nitric oxide and arginase activity assays measure nitric oxide and urea levels, respectively. Tests are conducted in 8 conditions: Unstimulated, LPS (24 hour), LPS (42 hour), NECA (24 hour), IL-4 (24-hour), IL-4 (42-hour), LPS + NECA (24-hour), LPS + NECA (42-hour).

**Results:** Preliminary ELISA results reveal upregulated IL-10 in BMDM M2ds. Similar levels were found between the 24-hour and 42-hour time periods, with no production in IL-4 stimulated macrophages (M2as). Further investigation will explore protein production and gene expression patterns that differentiate M2ds from M2as and M0s.

**Conclusion:** Characterizing M2ds enhances understanding of the immune response, with therapeutic potential for auto-immune.

# Greater Kinematic Alignment Following Unicompartmental Compared to Total Knee Arthroplasty: A Randomized Clinical Trial

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**Introduction:** Up to 20% of patients report knee function dissatisfaction following total knee arthroplasty (TKA). Unicompartmental knee arthroplasty (UKA), which preserves the anterior cruciate ligament and lateral-articulating surface, may improve post-surgical function. This randomized controlled trial assessed differences in gait biomechanics and patient-reported outcomes (PROMs) in patients receiving TKA or UKA.

**Methods:** Patients were randomized to either UKA (Oxford Partial Knee, Biomet) or TKA (Persona CR Knee System, Zimmer) and data were collected pre-operatively and one-year post- operatively (2016-2021). Gait biomechanics were recorded (Motion Analysis, USA) and stance- phase angles were computed (Visual 3D, USA). PROMs included the Oxford Knee Score (OKS) and WOMAC. Pre-/post-surgery changes in knee angles were assessed using correlational and root mean squared error (RMSE) analysis. Statistical analyses included MANOVA (normalized correlation; RMSE data;  $\alpha$ =0.05) and linear mixed effects models (PROMS;  $\alpha$ =0.0125).

**Results:** Of 38 recruited patients, 30 completed follow-up (UKA n=12; TKA n=18). Surgical technique significantly influenced gait biomechanics (P=0.010). UKA showed significantly higher sagittal knee angle correlations and lower coronal knee angle RMSE. OKS and WOMAC scores improved in both groups (p<0.001), with no between-group differences.

**Conclusion:** UKA better preserved native knee biomechanics, with greater sagittal alignment and reduced coronal RMSE compared to TKA. Although PROMs did not differ by group, all patients showed significant clinical improvements in pain and function. These findings support UKA as a viable alternative to traditional TKA and highlight the need for further research on arthroplasty-specific biomechanics and long-term outcomes.

#### Exploring the Impacts of "Field to Fork": A Community-Based Food Literacy Program

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**Introduction:** Food literacy encompasses the knowledge, skills, and behaviors necessary for individuals to make informed food choices and engage in healthy eating practices. It involves understanding nutrition, food preparation, food sourcing, and the cultural significance of food. Some notable Canadian initiatives have focused on providing individuals disease-centered education, in order to equip them with skills for better health management. These programs have proven effective in targeted populations, leading to improvements in participants' socioemotional and physical health. This study aims to determine whether a collaborative, community-centered food literacy program inspired by the Whole Foods Plants-Based diet can achieve similar meaningful outcomes within a short timeframe.

**Methods:** Conducted over eight weeks at the Ecosource Teaching Kitchen in Mississauga, Ontario, this mixed-methods quasi-experimental study analyzed the effects of an education program that combined discussion-based lessons, food preparation demonstrations, and reflective activities. Throughout the intervention, participants completed intake and outtake surveys, knowledge assessments, and interviews to assess the primary outcome—self-efficacy in food- related tasks—and the secondary outcome—nutritional and food skills knowledge.

**Results:** Qualitative feedback from semi-structured interviews highlighted enhanced empowerment, social connection, and increased confidence in food preparation skills. 75% of participants reported they were extremely likely to adopt most aspects of the Whole Foods Plant- Based diet, indicating a strong positive behavioral intent. Additionally, post-program assessments revealed a 16% increase in nutritional knowledge scores (p < 0.05).

**Conclusion:** The findings suggest that a short-term, generalized food literacy program can significantly enhance both self-efficacy and nutritional and food skills knowledge in participants. These results reinforce the potential of food literacy programs as scalable health interventions for diverse communities, underscoring their role in public health strategies.

### Role of Neuronal Ensembles in the Basolateral Amygdala in Fear Discrimination: Implications Unconditioned Stimulus Modalities

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**Introduction:** The Basolateral Amygdala (BLA) plays a key role in first order Pavlovian fear acquisition and expression. Previous research shows that the deletion of these memories will disrupt fear to a control cue when both target memory and control cue share the same sensory modality. On the other hand, when modalities differ at the conditioned stimuli (CS) level, there is reduced overlap in activated neuronal ensembles. This project explores the role of neuronal ensembles in the BLA responsible for fear discrimination, the ability to distinguish between threatening and non-threatening stimuli, when unconditioned stimuli (US) vary across modalities. Here, the conditioned stimuli are of the same modality (auditory) with one paired to a mild shock and the other to a siren.

**Methods:** The Daun02 inactivation method is used on fos-LacZ transgenic rats to delete neuronal ensembles activated by one auditory cue allowing for behavioral observations of fear expression for the second cue. ß-galactosidase staining is also used to quantify neural activity and recognize the overlap of neuronal ensembles which encode fear for different modalities.

**Results:** Freezing behaviour specific to the deleted cue decreased while fear responses to the second cue were unaffected by Daun02 inactivation. Neuronal ensembles encoding fear for these various unconditioned stimuli showed little overlap based on  $\beta$ -galactosidase staining.

**Conclusion:** The findings of this research contribute to our understanding of how neuronal ensembles in the BLA process multimodal fear memories, intern informing more targeted treatment approaches to disorders like post-traumatic stress disorder (PTSD).

#### Cognitive Impairments in Older Adults - Clinical Characteristics of Osler's Memory Clinic

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**Background:** Alzheimer's disease (AD) is the most common form of dementia, often beginning its molecular changes decades before cognitive decline is evident. This underscores the need for early detection, which can significantly enhance intervention outcomes. Subjective memory complaints (SMCs), reflecting personal perceptions of cognitive impairment, may serve as an earlier and more sensitive indicator of impending AD than traditional neurocognitive assessments. Given the challenges and costs of objective cognitive screening, SMCs present a practical and cost-effective alternative for identifying individuals at risk for Mild Cognitive Impairment (MCI) and AD. Variations between subjective (SM) and objective memory (OM) can be influenced by factors such as depression, personality, and age. Additionally, sociodemographic elements like gender, ethnicity, and education level affect the relationship between SMC and OM, with stronger correlations observed among older, female, well-educated, and less depressed individuals.

**Methods:** This study systematically examines the interaction between SMC and objective cognitive measures at the Osler Memory Clinic, analyzing data from 300 patients. SMC data was collected from Meditech and referral forms, while OM data was gathered from neurocognitive assessments such as the Montreal Cognitive Assessment (MOCA) and Rowland Universal Dementia Assessment Scale (RUDAS).

**Results:** 69% of patients exhibited over half of the Subjective Cognitive Decline Criteria, suggesting a strong link to preclinical AD. Logistic regression analysis revealed that lower MOCA scores were associated with increased prevalence of SMC. Notably, gender did not significantly impact SMC, potentially due to sample size limitations.

**Conclusions:** This research creates a characterization profile for Osler's Memory Clinic, enhancing understanding of cognitive decline predictors. Future work aims to expand the sample size and investigate the SMC-ethnicity relationship to identify early dementia risk in diverse populations.

## Clinical Implications for Understanding Visuospatial Asymmetries: A Meta-Analysis of Line Bisection Performance Across Depth

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**Introduction:** Young, healthy adults demonstrate a visuospatial bias to the left hemifield. This phenomenon, known as pseudoneglect, has significant implications for clinical diagnoses, such as hemispatial neglect. Researchers and clinicians have reliably observed leftward biases using horizontal line bisection tasks, traditionally in two-dimensional experimental setups. Line bisection has since progressed into three-dimensional (3D) setups, where lines are presented farther from the observer, which appears to attenuate the leftward bias, even reversing into a rightward bias. It remains unclear at what distances leftward bias, no bias, and rightward bias are expected. This meta-analysis aims to quantitatively model the 3D distances where visuospatial asymmetries occur using the horizontal line bisection task.

**Methods:** A total of 30 samples from 25 studies (240 effect sizes, n = 720) were included. Studies were selected if tasks involved horizontal line bisection with multiple egocentric distances, participants were reported as healthy, and an average/median participant age above 18.

**Results:** Our meta-analytical modeling revealed a significant leftward bias within near space and a rightward bias in far space. We observed three critical ranges for visuospatial asymmetries across depth in young, healthy adults: (1) significant leftward biases up to 48 cm, (2) no biases from 49–87 cm, and (3) significant rightward biases at 88 cm and beyond. We also revealed significant moderating effects of participant age (50+ years old) and the use of tools to perform bisection.

**Conclusion:** Our results suggest crucial benchmark distances for researchers and clinicians when investigating visuospatial asymmetries to enhance diagnostic accuracy.

#### Proteomic Profiling of Dorsal Root Ganglion in Mouse Model of Polytrauma With Spinal Cord Injury to Uncover Biomarkers for Neurogenic Heterotopic Ossification

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**Introduction:** Neurogenic heterotopic ossification (NHO) is a severe complication following spinal cord injury (SCI), characterized by abnormal bone formation in soft tissues, leading to joint pain, stiffness, and impaired rehabilitation. Current treatments, such as radiation and anti- inflammatory drugs, are limited due to an incomplete understanding of NHO's mechanisms. This study aims to utilize proteomics to elucidate the biological pathway involved in NHO formation. We hypothesize that the mechanism of neurogenic heterotopic ossification is governed by crosstalk between Dorsal Root Ganglions (DRGs) and MTI through the release of neuroinflammatory peptides and their recognition at the MTI site resulting in abnormal mineral deposition.

**Methods:** A polytrauma mouse model was developed using spinal cord transection at T9-T10 and MTI induction in the left quadriceps, with right limbs serving as controls. Mice were euthanized on Day 1 and Day 6 post-surgery. Protein extraction from DRGs and muscle tissue was followed by mass spectrometry analysis. Scaffold 5, ShinyGo 0.80, and David Bioinformatics tools were used for data analysis.

**Results:** Proteomics revealed upregulation of inflammation-related proteins in DRGs on Day 6, suggesting a sustained neuroinflammatory state. Increased expression of macrophage- and neutrophil-associated proteins, along with calcium-regulating proteins, indicates potential involvement in calcium phosphate deposition. Further validation with western blotting is planned.

**Conclusion:** These findings suggest that prolonged neuroinflammation may link SCI with MTI, contributing to NHO development. Targeted therapies focusing on key proteins could mitigate symptoms and improve patient outcomes. Future work will explore this pathway using knockout models to identify therapeutic targets.

# Comparative Systematic Analysis Between High Intellectual Potential and High Functioning Autism: A Research Study

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**Introduction:** Neurodivergence encompasses a range of conditions, including High Intellectual Potential (HIP) and High-Functioning Autism (HFA). These conditions, often viewed as contrasting ends of a spectrum, present diagnostic challenges due to overlapping traits, particularly in clinical, cognitive, and social domains. This systematic analysis explores the extent of their similarities to improve diagnostic accuracy and treatment outcomes.

**Methods:** A systematic review of peer-reviewed articles was conducted, focusing on diagnostic criteria, cognitive and psychometric factors, clinical and neurophysiological features, sensory modulation and etiology of HIP and HFA. Data sources included studies utilizing diagnostic tools such as DSM-5 and WISC-IV. Due to a lack of articles directly comparing HIP and HFA cross-referencing and cross-analysis of studies was used.

**Results:** HIP individuals demonstrated superior cognitive and psychometric functioning compared to those with HFA. When examining clinical features, both groups exhibited autistic traits, with HIP showing a lower prevalence than HFA. Clinical and neurophysiological evaluations also highlighted nuanced differences, supported by varying international diagnostic criteria. Etiological findings revealed common developmental influences, including atypical brain hemisphere symmetry and fetal testosterone exposure. Both groups shared sensory modulation challenges.

**Conclusion:** HIP and HFA exhibit significant similarities across several domains, but nuanced differences and the scarcity of direct comparative studies prevent a definitive conclusion regarding their convergence. Misdiagnosis risks highlight the need for precise diagnostic criteria and standardized assessments. Future research must directly compare these populations with diverse demographics to enhance operationalization and construct validity. Standardized global diagnostic frameworks is a necessity to enhance accuracy and reduce diagnostic bias.

# Risk Stratification of Major Adverse Cardiac Events in Patients With Indeterminate High-Sensitivity Troponin Testing and Chest Pain: A Systematic Review

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**Introduction:** For patients presenting to the emergency department (ED) with chest pain, current guidelines recommend serial measurements if high sensitivity troponin (hs-Tn) values are below the 99th percentile but above the limit of detection. The objective of this systematic review was to compare risk of major adverse cardiovascular events (MACE) in patients with indeterminate first troponin test results presenting to the ED with chest pain.

**Methods:** Electronic searches of MEDLINE, Cochrane Reviews, CINHAL and EMBASE between 2003 to 2023 were conducted. Studies were included if patients aged  $\geq 18$  had a chief complaint of chest pain and compared serial hs-Tn tests to a single indeterminate test. MACE was defined as acute myocardial infarction, stroke, and cardiovascular mortality 30 days after the index ED visit. Patients with STEMI or NSTEMI were excluded.

**Results:** The search strategy yielded 522 citations and eight studies were retrieved. 31,321 of 56,460 patients (55%) had serial hs-Tn after an indeterminate hs-Tn. Rate of MACE ranged from 0.3 to 14.8%. The risk of bias was high for most observational studies, primarily due to information and incorporation bias. Mortality during study periods ranged from 0.05 to 1.24%.

**Conclusion:** It is unknown if patients who present to the ED with chest pain with indeterminate troponin results are at higher risk for MACE. Over 40% of patients with an indeterminate initial hs-Tn did not have serial testing. Future research should explore factors influencing the use of serial troponin testing in the ED and work towards improving adherence to evidence-based practices.

#### Genetic Engineering of a Degron-Tagged Atrx Protein in the Ht-22 Mouse Hippocampal Cell Line

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**Introduction:** ATRX is a chromatin remodelling protein essential for neurodevelopment, and its mutations lead to ATR-X syndrome, characterized by intellectual disability, developmental delays, and physical abnormalities. ATRX knockout is lethal, making it challenging to study its exact role in neuronal processes. This project aims to create an HT-22 mouse neuroblastoma cell clone with a reversible, transient ATRX degradation system. By modulating ATRX levels during cell differentiation, we hope to clarify its influence on gene expression and neuronal development.

**Methods:** Using standard molecular cloning techniques, we inserted the dTAG (FKBP12F36V) sequence with a 3xHA tag into the CRISPR/Cas9 pORANGE vector with guide RNA sequences to target the ATRX gene. The dTAG template includes a 3xHA tag, P2A, and mCLOVER for positive clone selection. The FKBP12F36V protein tag binds the degrader dTAG-13, recruiting an E3 ligase to ubiquitinate and degrade ATRX, enabling controlled protein degradation for functional analysis. Positive clones were validated by restriction digestion and sequencing. Following ATRX-pORANGE plasmid transfection of HT-22 cells, mCLOVER fluorescence was used for sorting transfectants s by FACS into 96-well plates for further analyses. Individual clones were screened by PCR and ATRX expression by HA- immunofluorescence.

**Results:** Of 94 initial clones plated, five mCLOVER-positive cells showed ATRX integration, with one confirmed as a positive clone. PCR detected successful dTAG insertion. Immunofluorescence revealed HA-tagged ATRX expression, and dTAG-13 treatment induced partial ATRX degradation, verified by reduced fluorescence in select cells.

**Conclusion:** We conclude that a dTAG-inserted clone was generated, with further work needed to fully assess its functionality in ATRX degradation.

#### Thapsigargin - A Potential to Change the Future of Viral Outbreaks?

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**Introduction:** Viral pandemics present a growing threat to human health and this issue is worsened by the need for antiviral therapies. Thapsigargin (Tg) irreversible inhibits the SERCA pump in the ER, inducing ER stress and the unfolded protein response (UPR). The antiviral activity of Tg against numerous respiratory viruses such as SARS-CoV-2, RSV, and H1N1 is recognized, but it is unclear how Tg can act against a wide range of viruses. We hypothesize Tg's inhibition of SERCA promotes an antiviral state.

**Methods:** The three primary experiments in this study were 1) siRNA silencing to determine SERCA's role in Tg-mediated antiviral effects, 2) NF- $\kappa$ B and IRF3 reporter assays in response to Tg priming and 3) polyI:C stimulation to mimic viral infection. Cultured A549 cells were primed with Tg and RT-qPCR measured expression of antiviral and ER stress genes either 24 or 48 hours after priming.

**Results:** Tg primarily targets SERCA2 in this model, with SERCA2 proving essential for the UPR and an antiviral state via upregulation of ISGs. Tg priming appears to inhibit NF- $\kappa$ B and IRF3, suggesting an alternative pathway for ISG, IFN $\beta$ -1, and Mx1 induction. Furthermore, the innate response to Poly(I:C) is enhanced by Tg priming, demonstrated by Mx1 and IFN $\beta$ -1 upregulation.

**Conclusion:** Our findings indicate Tg's potential as a broad-spectrum antiviral leveraging the UPR and IFNs. Tg's ability to stimulate an antiviral state with and without the presence of a PAMP, such as Poly(I:C), positions it as a unique candidate for antiviral therapy. Future studies aim to investigate Tg's role in inhibiting SARS-CoV-2 replication.

#### Enhancing Antibiotic Stewardship in Nigeria's Private Healthcare Sector: A Feasibility Study

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**Introduction:** Nigeria, with other West African nations, face a disproportionate share of the burden of mortality associated with antimicrobial resistance (AMR) and inappropriate use of antibiotics. The country's drug-resistant bacterial infections are estimated to cause 27 deaths per 100,000 yearly. Given the setting's lack of specialized strategies to regulate antibiotic use, this study seeks to identify specific barriers and facilitators for the development of an effective antibiotic stewardship intervention tailored to private healthcare practitioners in Nigeria.

**Methods:** We conducted in-depth semi-structured interviews with prominent Nigerian policymakers and representatives to explore barriers and facilitators to the implementation of antimicrobial stewardship interventions. We also carried out a webbased survey among private healthcare practitioners in the states of Lagos and the FCT of Nigeria, including questions aimed at assessing AMR knowledge around antibiotic prescribing and drivers of prescribing behaviours.

**Results:** So far, 8 interviews have been completed. Also, a total of 105 participants have completed our survey (74 from Abuja and 31 from Lagos state). We expect to complete data collection by the end of November. We anticipate that our findings will provide key information that will inform the design and execution of a future pilot cluster randomized controlled trial in advance of a full-scale trial to evaluate the feasibility of an educational antibiotic stewardship intervention in Nigeria's private healthcare sector.

**Conclusion:** This study lays the groundwork for larger scale efforts to tackle AMR in West Africa and other comparable regions, ultimately contributing to global efforts in addressing this critical issue.

#### Type 2 Immunity at the Interface Between Helminth Infection and Stunting: A Research Study

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**Introduction:** Growth stunting, defined as being two standard deviations below the height-for- age median, affects almost 30% of children under five and is associated with cognitive defects and premature mortality. While many factors contribute to stunting, epidemiological evidence suggests that early life helminth infections, coupled with malnutrition, may drive this phenotype. Indeed, there is remarkable geographical overlap between helminth-endemic regions and areas with high stunting incidence. Furthermore, helminth infection is almost universally associated with a type 2 immune response, which can drive systemic metabolism changes. Nevertheless, mechanistic studies to directly relate helminth infection, type 2 immunity, and undernutrition to stunting have not been performed. Using a novel mouse model in which helminth infection exacerbates diet-induced stunting, we hypothesize that undernutrition increases the anti-helminth type 2 immune response.

**Methods:** C57BL/6 pups are weaned onto a macronutrient-deficient or isocaloric control diet and are subsequently infected with the parasitic roundworm, Heligmosomoides polygyrus bakeri. At two- or four-weeks post-infection, IgE and IgG1, Th2 cell and goblet and tuft cell differentiation — key components of type 2 immunity — will be quantified via ELISA, flow cytometry, and immunofluorescence microscopy, respectively.

**Results:** Our preliminary results indicate that intestinal helminth infection exacerbates diet- induced stunting during early life and induces a type 2 response. We are currently examining whether type 2 immunity magnitude correlates with growth outcomes.

**Conclusion:** Investigating the impact of anti-helminth immunity in diet-induced stunting conditions may reveal fundamental signaling pathways that can be targeted to mitigate early life stunting.

### The Associations Between Screen Time, Mental Health, and Academic Performance Among First-Year Undergraduate Students

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**Introduction:** Restrictions during the COVID-19 pandemic necessitated students to learn and connect with others remotely, increasing screen time and raising concerns about the potential impact on mental health. This study explored associations between screen time, mental health and academic performance over the year in first-year undergraduates.

**Methods:** Data were collected as part of the Queen's U-Flourish Well-Being Survey at entry to university in September 2021 (post-pandemic). The survey uses brief validated measures of screen time (unrelated to studies), and anxiety (GAD-7) and depressive symptoms (PHQ-9). GPA data was obtained through deterministic linkage to the university database. Multivariable log-binomial and linear regressions were employed.

**Results:** Nearly half (49%) and one-third (31%) of students surveyed (n=1,415) reported spending  $\geq$ 4 hours/day engaged in leisure and social screen time, respectively. Leisure screen time (e.g., TV, gaming) was more common in males (58% vs 46%, p<.001) and social screen time was more common in females (32% vs 26%, p=.04). At school entry, students engaging in  $\geq$ 4 hours of leisure screen time were significantly more likely to screen positive for anxiety (RR: 1.12; 95% CI: 1.01-1.25) and depression (RR: 1.32; 95% CI: 1.17-1.49) than those engaging in  $\leq$ 3 hours. Similar, albeit smaller effects were observed for social screen time. Both leisure ( $\beta$ = -0.24; 95% CI: -0.33,-0.15) and social ( $\beta$ = -0.14; 95% CI: -0.24,-0.04) screen time were negatively associated with cumulative GPA over the year.

**Conclusion:** Excessive screen time was prevalent and associated with higher screen positive rates and lower academic performance, highlighting it as a significant risk factor in this population.

## Comparative Functional Analysis of the Physiological Effects of Extracellular Osmolality Changes in Bovine and Human Red Blood Cells

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**Introduction:** Fluid imbalances such as dehydration is a significant health concern for livestock as it disrupts normal physiological processes. Mammalian red blood cells (RBC) show differential species-specific responses to cell stress. The aim of this study was to compare the effects of tonicity alterations in human and bovine RBCs.

**Methods:** Osmotic fragility was examined by exposure of bovine and human RBCs to varying hypotonic solutions and determination of hemolysis using absorbance. Hypertonicity-mediated RBC apoptosis was quantified by estimating phosphatidylserine externalization using fluorescent Annexin V binding assays in flow cytometry analysis.

**Results:** Under reduced osmolality, hemolysis in bovine RBCs was significantly higher as compared to human RBCs. In contrast, bovine RBCs were significantly more resistant to hypertonicity-induced apoptotic cell death, as compared to human RBCs, after prolonged incubation in a 900 mOsm hypertonic medium.

**Conclusion:** Human and bovine RBCs exhibit differential responses to extracellular osmolality alterations. The findings highlight changes in RBC viability in conditions of fluid imbalances in cattle, with potential implications for improving livestock health and productivity.

#### Investigating the Effects of β-Estradiol Treatment on Choriocarcinoma: A Research Study

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**Introduction:**  $\beta$ -estradiol treatment of various human cells results in the over-expression of c- MYC, which induces proliferation when cells are exposed to growth-factor-rich environments but induces apoptosis when cells are exposed to growth-factor-poor environments. However, the effects of  $\beta$ -estradiol-mediated c-MYC over-expression have not been well characterized in human cancers, including choriocarcinoma. Choriocarcinoma cells treated with  $\beta$ -estradiol should exhibit higher rates of proliferation in high growth-factor environments, higher rates of apoptosis in low growth-factor environments, and higher expression of c-MYC overall.

**Methods:** BeWo choriocarcinoma cells were grown in media supplemented with either 10% fetal bovine serum (FBS) or 2% horse serum (HS) and treated with either 0.5 or 2  $\mu$ M treatments of  $\beta$ -estradiol. Gene expressions of c-MYC, KI-67, and BAX were then determined relative to a YWHAZ reference gene, using real-time quantitative PCR data.

**Results:** When choriocarcinoma cells were grown in 10% FBS, representing a growth-factor rich environment,  $\beta$ -estradiol increased c-MYC gene expression 24 and 48 hours after treatment with a 0.5  $\mu$ M dose and decreased KI-67 expression after 48 hours of treatment under a 2  $\mu$ M dose, relative to a control. When cells were grown in 2% HS media, representing a growth-factor deprived environment, cells exhibited decreased c-MYC expression under a 2  $\mu$ M  $\beta$ -estradiol treatment. Under both culture media conditions, treatment had no statistically significant effect on BAX gene expression.

**Conclusion:** This investigation confirms that  $\beta$ -estradiol treatment in human choriocarcinoma mediates c-MYC & KI-67 expression under specific conditions, while showing no statistically significant relation to BAX expression, presenting interesting potential therapeutic connotations.

#### Sexual Health After Breast Cancer: A Clinical Practice Review

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**Introduction:** Breast cancer (BC) is the most common malignancy worldwide (1). Breast cancer (BC) diagnoses not only present physical challenges but profoundly affect survivors' psychosocial well-being leading to sexual health challenges. This clinical practice review aimed to discuss the current literature and outline the knowledge gaps related to care for sexual health after BC, including survivors' sexual health concerns, as well as available prospective surveillance programs.

**Methods:** Current literature on the sexual health challenges of BC survivors was identified from online databases and published guidelines. The evidence was sorted into contributing factors, treatments and interventions, and practice recommendations. This evidence was then used to identify gaps in the literature and make recommendations for future research.

**Results:** BC survivors experience a variety of physical symptoms, such as pain during sex or dyspareunia, which impair sexual well-being. Treatments can have lasting effects that may impact sexual function, often reciprocally related to physical and psychosocial factors. Current treatments for sexual dysfunction involve topical products for vaginal symptoms (e.g., pH-balanced gels, or lubricants) and various counseling and educational interventions (e.g., mental health counseling, and sex therapy).

**Conclusion:** There is a general lack of research considering how intersectional concerns can impact sexual health experiences after BC. Existing studies do not often consider potential differences in needs that may arise due to ethnicity, age, or socioeconomic background. To address these limitations a significant paradigm shift in survivorship care is required. This requires moving beyond disease management towards a more holistic, comprehensive, patient- centered approach prioritizing comfort and sexual well-being.

### To Close the Gap of Survivorship Education - A Series of Breast Cancer Webinars in Collaboration with Wellspring: A Research Study

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**Introduction:** Breast cancer survivors face uncertainties post-treatment, requiring ongoing support and education. Digital media online training courses may be used to disseminate evidence-based cancer information. In this study, we hosted a series of webinars which aimed to empower survivors with evidence-based survivorship information.

**Methods:** A four-part weekly online webinar series (1 hour each) including expert presentations, survivor insights, and interactive question-and-answer sessions, was held in October 2023 during Breast Cancer Awareness Month, via the Zoom digital platform. Topics covered included surveillance, mental health, adjuvant antihormonal therapy, and sexual health. After the webinar series, participants completed a post-webinar survey electronically. The post-webinar survey assessed participant satisfaction, understanding of topics, and suggestions for improvement. Likert scales were used to measure self-reported changes in understanding of the discussed topics.

**Results:** 99 participants took part in the Breast Survivorship and Surveillance webinar, 97 participated in the Mental Health in Breast Survivorship webinar, 108 participated in the Adjuvant Antihormonal Therapy for Breast Cancer webinar, and 74 participated in the Sexual Health after Breast Cancer webinar. 25 participants completed the post-webinar survey, administered after the final webinar (sexual health). Among the 25 survey participants, 96% (24/25) expressed that the information presented in the series of webinars was very useful or extremely useful. Furthermore, 80% (20/25) noted significant knowledge improvement.

**Conclusion:** This breast cancer webinar series effectively bridges the knowledge gap in survivorship, offering valuable insights, emotional support, and practical guidance. The results emphasize the importance of ongoing education and support for breast cancer survivors.

#### How Does Adolescent Cannabis Use Affect Susceptibility to Schizophrenia?: A Research Study

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**Introduction:** Cannabis is one of the most used substances among adolescents, who undergo a critical period of brain development. Evidence suggests adolescent cannabis use may contribute to an earlier onset of schizophrenia, a psychiatric condition that typically appears in early adulthood, by damaging brain circuits and neurotransmitter systems. This review investigates current research in neurology and epidemiology to determine whether adolescent cannabis use is associated with an increased risk of schizophrenia.

**Methods:** A systematic review of peer-reviewed literature from databases such as PubMed, PsycINFO, Omni Laurier, and Google Scholar was conducted using keywords like "adolescent cannabis use," "schizophrenia," and "brain development." The review incorporated studies from the past 20 years, focusing on the impact of cannabis on brain areas implicated in schizophrenia. Furthermore, each study's key findings, designs, and limitations were discussed to evaluate their quality.

**Results:** Findings suggest that adolescent cannabis use disrupts the endocannabinoid system and alters GABA and glutamate signalling in the prefrontal cortex. These changes mirror brain circuit interferences seen in schizophrenia, emphasizing a striking resemblance between brain circuit changes in schizophrenia and cannabis-affected adolescents.

**Conclusion:** By highlighting a central risk factor, this review seeks to expand our understanding of the effects of adolescent cannabis use on schizophrenia. The results can inform public health campaigns and the development of preventative strategies to reduce cannabis use among young adults to spread awareness of its dangers at this developmental stage. Results may also encourage further research in the fields of psychiatry and drug abuse.

# Probing Binding Patterns of Neutral Lipids on the Nicotinic Acetylcholine Receptor Using Multiscale Molecular Dynamics (MD) Simulations

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The nicotinic acetylcholine receptor (nAChR) is a pentameric ligand gated ion channel (pLGIC) that propagates fast synaptic transmission at the cell surface. Coupled with their diverse subtypes and distributions across numerous regions of the brain and neuromuscular junction, the nAChR makes a valuable target for understanding its neurological functions and associated diseases. Extensive reconstitution experiments using the prototypic Torpedo muscle-type nAChR into simple liposomal membranes revealed its incredible specificity towards distinct lipid classes of its surrounding lipid environment. alongside recent structural studies suggesting lipids preferentially stabilize certain nAChR conformations by binding to specific sites. However, improper characterization of potential lipid binding sites, combined with heavy emphasis on the mechanistic roles of the neutral lipid cholesterol (Chol), limits our understanding towards how other neutral lipids bearing significant structural variations to Chol achieve analogous conformational selectivity. Using multi-scale molecular dynamics (MD) simulations on recently solved, high-resolution nAChR structures incorporated into functionally characterized, simple membrane patches, we probe the binding patterns of two structurally different neutral lipids, Chol and diacylglycerol (DAG), relative to the non-activating phospholipid, phosphatidylcholine (PC), and examine their differences across specific nAChR conformations. We demonstrate while Chol and DAG access similar, deeper sites distinguishable from PC in a state-dependent manner, Chol binds stably to the nAChR for extensively longer durations driven by electrostatic and several Van-der-Waals interactions, whilst DAG rapidly dissociates due to its flexible lipid tails. Thus, the accessibility of unique lipid binding sites with distinctive affinities may underlie differences in nAChR conformational selectivity achieved by these lipid species.

### The Role of a Fluorescent WBOX2 Peptide in Clathrin-Mediated Endocytosis: Assessing Specificity With Ikarugamycin

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**Introduction:** Clathrin-mediated endocytosis (CME) is a critical pathway for cellular uptake, enabling the internalization of surface proteins through clathrin-coated pits (CCPs). This study explores the specificity of Ikarugamycin (IKA) as an inhibitor of CME by evaluating its potential to displace the Wbox2 peptide, a clathrin-binding marker that facilitates the study of clathrin recruitment dynamics, from CCPs. The Wbox2 peptide was engineered with a TAT sequence to facilitate cellular entry and an HA detection tag for visualization, allowing for precise tracking within ARPE-19 cells.

**Methods:** The methodology involves incubating cells with the TAT-Wbox2 peptide, confirming recruitment to CCPs using Total Internal Reflection Fluorescence (TIRF) microscopy. Following localization verification, IKA is introduced to determine its ability to displace the peptide from CCPs. Quantification of fluorescence signals will provide a measure of peptide displacement, enabling an assessment of IKA's specificity as a CME inhibitor.

**Results:** It is anticipated that IKA significantly reduces peptide localization within CCPs, indicating that it effectively disrupts clathrin recruitment.

**Conclusion:** This would support IKA's potential as a selective inhibitor of clathrin-mediated endocytosis, offering valuable insights into its feasibility for therapeutic applications targeting endocytic pathways.

#### The Effect of Premature Birth on Major Adverse Cardiac Events in Adulthood: A Scoping Review

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**Introduction:** Premature birth is associated with a higher risk of cardiovascular disease in adulthood, yet its specific effect on having major adverse cardiac events (MACE)—including heart failure (HF), ischemic heart disease (IHD), stroke, and acute coronary syndrome (ACS)—remains unclear. This study aims to address this gap by examining existing literature to identify the risk of MACE in adults born prematurely.

**Methods:** An Ovid-MEDLINE database search was conducted to identify studies assessing MACE in adults born preterm (gestational age <37 weeks). Reviewers screened articles using the COVIDENCE tool and those that met the search criteria underwent full-text extraction.

**Results:** The database search yielded 72 unique articles. Following screening, 12 articles were selected for analysis. There was a positive association between prematurity and adult risk for HF, IHD, and stroke. HF was more prevalent among adults with lower birth weights, and shared familial factors might influence the observed risks. Of the included studies, only one examined ACS and reported no significant association with premature birth. There were also inconsistencies across studies, with some indicating a reduced impact of prematurity on stroke and IHD risk in sibling analyses.

**Conclusion:** The findings indicate that adults born prematurely are at increased risk for certain MACE, particularly HF, IHD, and stroke, though shared familial factors may modify these risks. Given the substantial morbidity, mortality, and chronic health complications associated with MACE, future research should prioritize standardized definitions of prematurity, conduct searches in more databases, and assess MACE risks in more diverse geographical contexts to properly inform clinical practice.

#### The Effect of Existing Heart Allocation Criteria on Transplant Outcomes Globally: A Systematic Review

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**Introduction:** Adult and pediatric heart allocation systems worldwide categorize transplant patients based on diverse criteria that impact mortality rates and quality of life. However, there is limited research examining the effectiveness of these systems. This study aims to address this gap by comparing different adult allocation systems and a pediatric allocation system to identify challenges and provide insights for optimizing heart transplant allocation strategies.

**Methods:** An Ovid-MEDLINE and Ovid-Healthstar database search was conducted. Reviewers screened articles using the COVIDENCE tool and those that met the search criteria underwent full-text extraction. The JBI Critical Appraisal tool for systematic reviews was used to assess the risk of bias.

**Results:** The database search yielded 630 unique articles. Following screening, 15 articles were selected for analysis. The selected articles described four countries' national allocation policies: the United Kingdom (n=1), Switzerland (n=1), France (n=2), and the United States of America (n=11). No relevant articles were found for Canada. The articles, published between 2016 and 2024, focused on comparing patient outcomes and waitlist times before and after national allocation policy changes. Five articles found improvement in patient outcomes, six articles reported improvement in patient mortality, and six articles found a reduction in waiting time following policy change. The review identifies mixed results regarding the efficacy of various heart allocation frameworks.

**Conclusion:** The study emphasizes a requirement for further research due to limited access to relevant articles. Global heart allocation networks are urged to report patient outcomes to allow for a broader analysis of framework efficacy and to successfully informing policies.

# Systematic Review of Risk and Protective Factors of Non-suicidal Self-Injury (Nssi) Among Post-secondary Students: A Research Study

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**Introduction:** Non-suicidal self-injury (NSSI) has a high prevalence among post-secondary students, with approximately 17.7% of students reporting NSSI behaviours (Kiekens et al., 2021). While the current literature demonstrates many risk and protective factors for NSSI, no study comprehensively summarizes these factors in post-secondary students. The current systematic review investigates the risk and protective factors for NSSI behaviours for NSSI behaviours.

**Methods:** Articles selected for inclusion described contributing factors to NSSI incidence exclusively in post-secondary students. The electronic databases PsycInfo, PsycArticles, PubMed, and Scopus were used to generate articles. Using Covidence, the authors conducted a two-staged independent screening process where n = 407 were screened and n = 121 were extracted. The Newcastle-Ottawa Quality Assessment Scale was used to assess bias risk.

**Results:** While the review is still in progress, extraction from the selected papers has revealed many risk and protective factors. For instance, perseverance and psychological flourishing are emerging as protective factors. Sexual victimization, low self-efficacy, low self-esteem, and low connectedness are emerging as prominent risk factors.

**Conclusion:** Given the high prevalence of NSSI in post-secondary students, healthcare providers must understand the nature of NSSI behaviours. This study provides a comprehensive review of the literature, which has implications for advancing healthcare providers' knowledge and informing potential interventions in educational contexts. Interventions may be designed to mitigate the risks experienced by post-secondary students or to promote protective coping.

#### Investigating the Mechanisms of Freezing-Induced Mutagenesis in Schizosaccharomyces Pombe (Fission Yeast)

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**Introduction:** Freezing-induced mutagenesis remains a scientifically intriguing yet underexplored phenomenon. We have tested how freeze-thaw cycles impact genome stability in Schizosaccharomyces pombe (fission yeast).

**Methods:** Through ten cycles of freezing at -80°C for 1 hour and thawing for 10-15 minutes at room temperature, respectively, the research investigates genetic changes and gemcitabine sensitivity in fission yeast checkpoint mutant strains  $chk_{1\Delta}$ ,  $cds_{1\Delta}$ , and  $rad_{3\Delta}$ . These mutant strains are missing essential kinases in the DNA replication ( $cds_{1\Delta}$ ,  $rad_{3}$ ) and DNA damage ( $chk_{1\Delta}$ ,  $rad_{3\Delta}$ ) checkpoints. These mutants show increased drug sensitivity and mutagenesis in specific situations.

**Results:** Our workaim is to identify whether freezing-induced mutations are due to single gene mutations, the same mutations, or involve multiple loci. We tested this using the drug gemcitabine, a powerful chemotherapeutic drug. Gemcitabine resistance mechanisms, important in treating cancers like pancreatic cancer, are complex. Gemcitabine is known to inhibit ribonucleotide reductase and induce replication stress. We are examining the development of gemcitabine resistance and specific mutations caused by repeated freeze-thaw cycles.

**Conclusion:** By comparing genetic alterations between fourth and ninth generations, the study aims to discern underlying mechanisms, enriching our understanding of freezing-induced mutagenesis and genetitabine sensitivity in S. pombe. This research contributes significantly to molecular biology and drug resistance studies, potentially informing cancer treatment strategies and expanding knowledge in cellular mutagenesis pathways.

#### Evaluation of a New Threshold for Positive Airway Pressure Therapy Adherence in Paediatric Populations

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**Introduction:** Obstructive sleep apnea (OSA) is a common disorder of breathing during sleep characterized by upper airway obstruction and is treated using positive airway pressure (PAP) therapy. There is currently no standardized definition for PAP adherence for paediatric populations. Instead, current adherence criteria is based on the adult definition, defined as gt;4 hours of PAP use for gt;70% of nights. This relatively low threshold likely under-estimates PAP adherence in children, as children require more sleep than adults do. Thus, we propose defining paediatric PAP adherence as PAP usage for gt;6 hours per night for 100% of nights.

**Methods:** The study prospectively recruited children aged 4-18 years old who were prescribed PAP therapy at SickKids Hospital. Detailed PAP adherence data was obtained from PAP machines and analyzed using descriptive statistics.

**Results:** 150 children were included, (median age = 14.0 years, females = 38.7%). Using a criteria of gt;4 hours of PAP use for gt;70% of nights, 74/150 (49.3%) of children were considered adherent. When applying our proposed gt;6 hours of PAP use for 100% of nights, only 33/150 (22.0%) met the criteria for PAP adherence.

**Conclusion:** Our data reveals that a significant portion of children do not meet the threshold of 6 hours of PAP use for 100% of nights, emphasizing the need for a revised definition that reflects the unique sleep requirements of children. This data also highlights an urgent need for alternative, efficacious therapies for OSA as a significant number of children are not adherent to PAP therapy.

Early Life Adversity and Obesity Risk in Adolescence: A 9-Year Population-Based Prospective Cohort Study

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**Introduction:** Exposure to adverse childhood experiences (ACEs) increases the risk of adolescent obesity by 30-50%. We hypothesized that ACEs reduce the likelihood of obesity remission and that this effect is mediated by psychosocial factors.

**Methods:** Data from the Growing Up in Ireland cohort was analyzed, which sampled 8568 children in 2007/2008. Of these, 2210 who were overweight/obese at age 9 had complete follow- up data at ages 13 and 18. Using structural equation and natural effects mediation models, the direct causal relationship between ACEs before age 9 and remission by 18 was tested, as well as indirect effects through daily activity, diet quality, self-image, behavioral difficulties, and BMI at age 9.

**Results:** Among the 2210 adolescents, 13% of participants experienced an ACE, with 46% achieving remission by age 18. Those exposed to ACEs had higher BMIs at ages 9 (0.47 vs. 0.36, p < 0.05) and 13 (0.39 vs. 0.29, p < 0.05), lower household income, and greater parental depression and behavioral issues. By 18, ACE-exposed adolescents were 2-3 times more likely to smoke or vape regularly. These behaviors partially mediated the association between ACEs and reduced remission, with ACEs reducing remission odds by 26% (OR: 0.73, 95% CI: 0.54-0.99; p = 0.043) after adjusting for income.

**Conclusion:** ACEs significantly reduce the likelihood of remission from obesity between childhood and adolescence. These findings emphasize the enduring impact of early adversity on obesity outcomes, with psychosocial and behavioral factors influencing this association.

#### Isolation of Novel Antibiotics From Pseudoalteromonas Luteoviolacea 2ta16

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**Introduction:** The spread of antimicrobial resistance poses a significant threat to global health, necessitating the discovery of novel antibiotics. Natural products, secondary metabolites produced by bacteria, are a historically prevalent source. Investigating under-researched bacteria genera and taking advantage of developments in bioinformatic tools, culturing conditions, and improved isolation techniques increases the likelihood of discovering novel natural products.

**Methods:** Using the marine gammaproteobacterial genus Pseudoalteromonas, which produces bioactive molecules and has a poorly characterized genome shows promise. First, in silico genome analysis of many species of Pseudoalteromonas was completed using the antibiotics and Secondary Metabolite Analysis Shell (antiSMASH) to identify promising novel biosynthetic gene clusters. Next, culturing conditions were optimized including inoculation, scaffolds, volume, and time. Liquid-liquid extraction was used to extract promising organic-soluble natural products, then molecules were isolated using preparatory High-Pressure Liquid Chromatography coupled to a Photodiode Array Detector. Fractions were tested for antibiotic activity in a bioactivity assay employing luminescent biosensor cells.

**Results:** This screening showed that Psedudoalteromonas rubra DSM6842 had promising activity and was chosen for further experiments. The antiSMASH analysis highlighted 12 biosynthetic gene clusters, including eight encoding completely unrecognized natural products and three with very low similarly to known products, suggesting the possibility of many novel natural products. In the bioactivity assay, two of ten HPLC fractions inhibited bacterial growth more than chloramphenicol, the positive control antibiotic.

**Conclusion:** Based on the in silico analysis, it is likely that there are multiple novel compounds with bioactivity produced by P. rubra DSM6842. Novelty will be confirmed using High-Resolution Mass Spectrometry and Nuclear Magnetic Resonance.

#### Investigating Dna-Damage Responsive Long Non-coding Rna (Lncrna)

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**Introduction:** The human genome is routinely subject to endogenous (e.g. oxidative stress) and exogenous (e.g. radiation, UV) factors that induce DNA lesions. These lesions may accumulate and impair cell function or cause cancer. Hence, DNA damage repair and preservation is a prerequisite for normal cellular function and maintaining genome integrity. Current research suggests that long non-coding RNAs (lncRNA) play a role in DNA damage response (DDR). lncRNAs are not translated into proteins; rather, they interact with DNA, protein, mRNA, or other non-coding RNA to influence gene expression and protein function. However, there is a lack of research concerning the role of lncRNA in DDR. This study aimed to investigate and quantify the expression of DNA-damage-responsive lncRNAs in a time-course experiment.

**Methods:** To do so, HEK293T cells were exposed to ionizing radiation (IR) at 2 Gy, inducing 60-100 double-stranded breaks per cell. Following this exposure, the cells were collected at 4 different time points (1, 4, 8, and 24 hrs). Finally, Real-time Quantitative PCR was performed to quantify the expression of select lncRNA genes.

**Results:** Our findings demonstrate an association between DDR and lncRNA gene expression. We found a temporal upregulation or downregulation of lncRNA genes, specifically ENSG00000250519, ENSG00000231595, ENSG00000254338, and ENSG00000223749. The influence of DNA lesions on the expression of these lncRNA increased over 24 hrs.

**Conclusion:** This finding asserts that lncRNA is an epigenetic regulator that may influence signalling networks related to DNA damage. Hence, lncRNAs may serve as biomarkers for the diagnosis, treatment, and prognosis of cancer and other diseases.

# Using Outlier Detection Methods to Quantify Grade Thresholds in Non-muscle Invasive Bladder Cancer: A Research Study

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**Introduction:** Bladder cancer (BC) is one of Canada's most prevalent cancers. Most patients present with Non-Muscle Invasive BC (NMIBC), confined to the bladder's inner layers. Tumour grading, used to predict prognosis and treatment, follows two systems: the WHO 1973 system (Grade 1, Grade 2, and Grade 3) and the WHO 2004 system (Low-grade [LG] BC and High- Grade [HG] BC). However, the qualitative nature of grading creates high inter-observer variability. We aim to better distinguish HG-BC from LG-BG by quantifying nuclear morphology differences between grades.

**Methods:** We analyzed 331 HG and 178 LG samples from the Kingston Health Sciences Centre and a subset of 157 cases with recurrence data. An interquartile range (IQR) outlier detector defined outliers as any data points outside the upper and lower bounds based on individual samples and a separate reference cohort. Machine learning feature selection and classifiers identified and evaluated the most predictive features and outliers. Recurrence-free survival analysis with IBM SPSS Statistics determined prognostic power.

**Results:** The Linear SVM model achieved 94.4% accuracy (AUC = 0.939) using individual sample thresholds, while the Medium KNN model achieved 87.3% accuracy (AUC = 0.865) using reference cohort thresholds. Survival analysis demonstrated the percentage of outliers detected for nuclear perimeter was the best discriminator for recurrence (p = 0.042).

**Conclusion:** The following findings indicate that nuclear morphometry can quantitatively differentiate WHO 2004 HG-BC and LG-BC, potentially improving grading reliability and prognostic power, and supporting patient risk stratification. Future efforts aim to adapt the IQR outlier detector to differentiate WHO 1973 grades.

#### **Conflicts of Interest**

The author(s) declare that they have no conflict of interests.

#### **Authors' Contributions**

ARL: served as a planning committee for the competition, assisted authors with their abstract submissions, drafted the conference abstract booklet, and gave final approval of the version to be published.

TAS: served as a planning committee for the competition, assisted authors with their abstract submissions, drafted the conference abstract booklet, and gave final approval of the version to be published.

AL: served as a planning committee for the competition, assisted authors with their abstract submissions, drafted the conference abstract booklet, and gave final approval of the version to be published.

#### Acknowledgements

The creation of this abstract book is a direct outcome of the dedication and hard work invested by the authors during the Canadian Undergraduate Conference on Healthcare (CUCOH) 2023 research competition. The remarkable level of effort and collaboration contributed to the success of an inspiring conference and research competition. We extend our gratitude to all presenters, volunteers, members of the conference executive team, and the Queen's University faculty and staff for their invaluable contributions in making this event a reality. We wish to extend a special thanks to our conference chairs: Kevin Nguyen, Johnny Shenouda, Jessica Lee, and Emily Liu.

#### Funding

We would like to thank our generous sponsors, Queen's University, Alma Mater Society (AMS) and Dunin-Deshpande Queen's Innovation Centre (DDQIC), Guayaki, and WizePrep without whom CUCOH 2024 would not be possible.

#### **Article Information**

Managing Editor: Jeremy Y. Ng Article Dates: Received Dec 18 24; Published Dec 31 24

#### Citation

Please cite this article as follows: Lacelle AR, Al Shamma T, Liu A. The 2025 Canadian Undergraduate Conference on Healthcare Abstract Book. URNCST Journal. 2024 Dec 31: 8(12). <u>https://urncst.com/index.php/urncst/article/view/788</u> DOI Link: <u>https://doi.org/10.26685/urncst.788</u>

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