Eighth Western Canadian Medicinal Chemistry Workshop
September 25-27, 2026
Saskatoon, Saskatchewan

Chair: Ed S. Krol
Vice-chair: David R. J. Palmer

Contents

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Message from the Organizers.

We would like to welcome you to Saskatoon and the University of Saskatchewan for the eighth Western Canadian Medicinal Chemistry Workshop. We established the WCMCW in 2008 to be an accessible, regional meeting that connects researchers from a variety of disciplines who are interested in different aspects of pharmaceutical sciences. The major goals of the WCMCW are:

- To foster research connections between researchers who would otherwise never meet at more traditional discipline-specific meetings.
- To make research at Western Canadian institutions the focal point.
- To provide exposure for students and postdoctoral researchers to faculty from other institutions and the pharmaceutical industry.

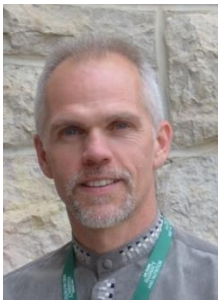
It is our hope that we have been successful in achieving these goals.

Anyone who has organized a scientific meeting knows that these events would be impossible without financial support and we are grateful to our sponsors for helping with this initiative. We have listed our sponsors on our website, in this program book and throughout the workshop, please join us in thanking these generous donors.

We hope that our efforts to put together the seventh WCMCW meeting will be both stimulating and productive. We are fortunate to have seven excellent invited speakers, each coming from different disciplinary backgrounds, but having common goals of improving the quality, efficacy and safety of pharmaceuticals, which ultimately gets to the heart of this meeting.

Finally, we would like to thank you for attending and helping to make this meeting a success.

Sincerely,



Ed S. Krol
Chair
WCMCW

David R. J. Palmer
Vice-Chair
WCMCW

WCMCW Schedule of Events

FRIDAY SEPTEMBER 25, 2026

Time	Event	Location
6:30 pm to 8:30 pm	Registration Opening reception and mixer	Faculty lounge Rm 3050 Education building

SATURDAY SEPTEMBER 26, 2026

Registration and oral presentations to be held in Education Building Room 1004.

Poster presentations to be held in the student lounge of the Education Building.

Time		
8:00 am	Registration and poster set up	Education room 1004
8:50 am	Opening remarks	

***Session 1**. Chair: Ed Krol*

9:00 am	Caterina Ramogida (Simon Fraser University) *Next generation (radio)metals for theranostic radiopharmaceuticals.*
9:40 am	Dominique X. Rwizinkindi (University of Saskatchewan) *Influence of Permanent Zwitterionic Linkers on the Pharmacokinetics of Peptide-Based Radiopharmaceuticals*
10:00 am	Nathan J. Dyck (University of Saskatchewan) *Optimizing the therapeutic index of [177Lu]Lu-DOTATATE using albumin-binding and zwitterionic functionalized linkers.*
10:20 am	Coffee break and poster viewing

***Session 2.** Chair: Radwa Mahmoud*

10:50 am	Michael Meanwell (University of Alberta) *Rethinking Nucleoside Synthesis for Drug Discovery.*
11:30 am	Julio Adam Lopez (Lakehead University) *Development of Novel LPA1 Antagonists for Therapeutic and Diagnostic Applications.*
11:50 am	Alayna Jones (University of Saskatchewan) *Chronic voluntary consumption of cannabinoids in C57BL/6 mice.*
12:10 pm	End of morning session.

WCMCW lunch in Education Building

Session 3. *Chair: Dave Palmer*

1:20 pm	Kalindi Morgan (University of Northern British Columbia) *Integrating genomics and Nitrogen-15 NMR for natural product discovery from Northern Canadian Bark Beetle-associated bacteria.*
2:00 pm	Wrynan Munabirul (University of Saskatchewan) *From molecular dynamics to in vivo analysis: How the cerebrovasculature rewires when VEGFA signaling is blocked in zebrafish.*
2:20 pm	Radwa Mahmoud (University of Saskatchewan) *A Universal Tandem Mass Spectrometric Fragmentation Pattern for the Development of Cannabinoid Screening and Quantification Methods in Animal Model of Pain.*
2:40 pm	Coffee break and poster viewing

Session 4. *Chair: Melissa Mejia Gutierrez*

3:10 pm	Vincent Ziffle (First Nations University of Canada) *On Indigenous Food, Medicine, and Allyship: Working with Indigenous Knowledges and Knowledge Keepers Towards Healing.*
3:50 pm	Speaker Roundtable *Challenges and opportunities at the chemistry-biology interface*
4:30 pm	End of afternoon session

Poster viewing and judging.

6:00 pm	Poster session ends	
7:00 pm	WCMCW Banquet	Location: St. Tropez Bistro

Sunday September 27, 2026

Education Building Room 1004

Time

8:00 am	Breakfast workshop for trainees Tara Smith, Med-Life Discoveries, Saskatoon, SK
9:05 am	Introductory remarks

Session 5. *Chair: Dave Palmer*

9:10 am	Krista Gill (Agriculture and Agrifoods Canada, Saskatoon) *Exploring the natural product diversity of wild Solanum species using LC-MS/MS metabolomics.*
9:50 am	Emma Finch (University of Saskatchewan) *LC-MS Data Normalization, A Key Factor in the Creation of a Clinically Relevant Urinary Metabolite Model for Respiratory Disease.*
10:10 am	Alaa K. Mahmoud (University of Saskatchewan) *Intracellular Distribution of Novel Gemini Lipid-Based Nanoparticles for Astrocytes Reprogramming.*
10:30 am	Coffee break

Session 6. *Chair: Ed Krol*

10:50 am	Michael Wozny (University of Saskatchewan) *From Molecules to Cells: Cryo-EM in Pathogen Research*
11:30 am	Michelle Fernández-Schmitz (University of Saskatchewan) *Gemini-surfactant coated gold nanoparticles as enhancers for radiofrequency ablation in HEPG2 tumor spheroids.*
11:50 am	Melissa Mejia Gutierrez (University of Saskatchewan) *Development of a 4-phenylbutyric acid (4-PBA) diazirine probe to study α-synuclein aggregation.*
12:10 pm	Closing remarks

WCMCW lunch

List of Abstracts

Oral presentations

Session 1 (Saturday am)

9:00 am

Next generation (radio)metals for theranostic radiopharmaceuticals.

Caterina Ramogida
Caterina Ramogida*[1,2] 1. Chemistry, Department of Chemistry, Simon Fraser University, Burnaby, BC; 2. Department of Life Sciences, TRIUMF, Vancouver, BC

Radiopharmaceutical therapy is emerging as a powerful approach for treating advanced and hard-to-treat cancers by delivering radiation directly to cancer cells. Advances in molecular biology have enabled the identification of biomarkers selectively overexpressed on cancer cells, providing opportunities to target radioactive payloads with high affinity ligands (aka targeting vectors). Pairing therapeutic and diagnostic radionuclides with the same targeting molecule enables disease imaging, staging, treatment planning, and targeted therapy, a concept known as theranostics. Radiometal-based radiopharmaceuticals typically rely on bifunctional chelators that act as molecular cages, forming stable and inert complexes with the radiometal while providing a functional handle for attachment to a targeting vector. The availability and diversity of radiometals with optimal physical decay properties for theranostic applications has seen rapid growth in recent years, and realizing the full potential of these next-generation radionuclides requires new tailor-made chelators for their efficient incorporation into a radiopharmaceutical. This talk will introduce the fundamental principles of radiometal-based radiopharmaceuticals, highlighting recent efforts in our group to develop theranostic radiopharmaceuticals incorporating next-generation radiometals, including lead-212/203 (Pb-212/203), mercury-197m/g (Hg-197m/g), and actinium-225/lanthanum-133 (Ac-225/La-133). A particular emphasis will be placed on how bifunctional chelator design can ultimately determine the success of these emerging radiopharmaceuticals.

9:40 am

Influence of Permanent Zwitterionic Linkers on the Pharmacokinetics of Peptide-Based Radiopharmaceuticals.

Dominique X. Rwizinkindi[1], Nathan J. Dyck[1], Morshed A. Chowdhury[1], Venkata K. Garapati[1], Kris Barreto[2], Wendy Bernhard[2], Ronald C. Geyer[2], and Eric W. Price[1]*
1 Department of Chemistry, University of Saskatchewan, Saskatoon, SK
2 Department of Pathology and Laboratory Medicine, University of Saskatchewan, Saskatoon, SK

Peptide-based radiopharmaceuticals have emerged as important tools for targeted molecular imaging and radionuclide therapy due to their high receptor specificity and quite favorable pharmacokinetic properties. However, some unwanted radiation due to non-targeted accumulation in healthy organs like kidney and pancreas remains a huge challenge. In this study, we synthesized GRPR-targeting RM2 and SSTR2-targeting TATE as controls and their zwitterionic (ZW) derivatives, radiolabeled them with 68Ga, 177Lu, or 161Tb, and evaluated the linker effect by PET/CT or SPECT/CT imaging and ex vivo biodistribution. In healthy mice, [68Ga]Ga-DOTA-ZW-RM2 reduced unwanted pancreas uptake by 43% compared to the control [68Ga]Ga-DOTA-RM2 (2.43 vs 4.25 %ID/g). In PC-3 xenograft mice, all compounds retained similar kidney uptake but [177Lu]Lu-DOTA-RM2 showed a higher tumor uptake (21.52% ID/g) vs [177Lu]Lu-DOTA-ZW-RM2 (7.68% ID/g) and [177Lu]Lu-DOTA-3ZW-RM2 (5.00% ID/g) at

24h. For SSTR2-targeting compounds, [177Lu]Lu-DOTA-3ZW-TATE exhibited high renal uptake than [177Lu]Lu-DOTA-TATE at 24h (1.64 vs 0.37 %ID/g), however, in AR42J xenograft mice, [161Tb]Tb-DOTA-ZW-Gly-TATE exhibited the highest tumor uptake at 48h (5.92 % ID/g) with kidney uptake of 2.01 % ID/g. Overall, permanent ZW linkers showed their ability to modulate radiopharmaceutical biodistribution, but their effects might depend on number and position. These results will inspire future optimization of new ZW-modified peptide radiopharmaceutical.

10:00 am

Optimizing the therapeutic index of [177Lu]Lu-DOTATATE using albumin-binding and zwitterionic functionalized linkers.

Nathan J. Dyck[1], Dominique X Rwizinkindi[1], Venkata K. Garapati[1], Jorge Luis Costa Carvalho[2], Andres X. Medina[2], Kris M. Barreto[2], Wendy Bernhard[2], C. Ronald Geyer[2], Eric W. Price[1]*
1: Department of Chemistry, University of Saskatchewan
2: Department of Pathology and Laboratory Medicine, University of Saskatchewan

[177Lu]Lu-DOTATATE is a clinically approved theranostic agent used for radionuclide therapy and SPECT imaging of neuroendocrine tumours. The tendency of the drug to accumulate in the kidneys causes radiation damage to healthy tissues, limiting the maximum safe dose. By utilizing amino acids bearing albumin-binding (AB) or zwitterionic functionalities, this study aims to optimize the therapeutic index of peptide-based radiopharmaceuticals by increasing blood residence time and renal clearance rates through the development of functionalized linker structures and iterative design. To study a possible synergistic effect between AB/zwitterionic functionalities, four novel DOTATATE compounds bearing AB and zwitterionic functionalized linkers were prepared via ultrasonic SPPS protocols. The four linker sequences contain either an AB or zwitterionic moiety, both, or neither, retaining a consistent linker length and backbone structure across each derivative. Peptides were then radiolabelled with 177Lu or 161Tb and subjected to in vivo trials in AR42J-xenografted immunodeficient murine models. Biodistribution was studied via SPECT/CT imaging and ex vivo necropsy, with tissue-specific uptake quantified via gamma counter measurement of collected tissue samples. Preliminary biodistribution results indicate the derivative containing only AB functionality as the lead contender for future generations of linker sequences, displaying lower kidney uptake with no significant difference in tumour activity.

Session 2 (Saturday am)

10:50

Rethinking Nucleoside Synthesis for Drug Discovery.

Michael Meanwell
Department of Chemistry, University of Alberta, Edmonton, AB

Nucleoside analogues (NAs) continue to be a central focus of drug discovery efforts worldwide due to their well-established impact on human health. With more than six decades of intensive research in this area, and a renewed surge of activity in recent years, the accessible chemical space of NAs has become increasingly saturated, making the identification of novel NA-based therapeutics progressively more challenging. Classical approaches to nucleoside analogue (NA) synthesis often suffer from poor modularity and lengthy synthetic routes, thus limiting rapid library generation. As a result, improved chemical methods are needed to streamline the synthesis of “hard-to-make” NAs, thereby increasing the efficiency with which NA chemical space can be explored to enable the discovery of new NA chemotypes. This seminar will

highlight our laboratory's efforts to develop de novo synthesis and molecular editing platforms that reduce step counts by up to 80% while providing access to previously untapped, yet pharmacologically relevant, NA chemical space.

11:30 am

Development of Novel LPA1 Antagonists for Therapeutic and Diagnostic Applications.

Julio Adam Lopez[1,2], Yang Mao[1,2], Jinqiang Hou[1,2]*
1. Department of Chemistry, Lakehead University, 955 Oliver Road, Thunder Bay, ON
2. Thunder Bay Regional Health Research Institute, 980 Oliver Road, Thunder Bay, ON

Lysophosphatidic acid receptor 1 (LPA1) is a crucial part of the wound healing pathway and is present at varying levels of expression throughout the body. However, the dysregulation and aberrant expression of LPA1 have been implicated in the development and progression of a number of diseases, including cancer metastasis and lung fibrosis. LPA1 antagonists have emerged as promising therapeutic and diagnostic agents with multiple candidates progressing to clinical trials, including the biphenyl acid BMS-986020 and the cyclohexyl acid Admiparant, but none have yet progressed into clinical practice. Radiolabeled LPA1 antagonists have also been evaluated for imaging Lung Fibrosis with Positron Emission Tomography. The present work describes our recent efforts on both the therapeutic and diagnostic development of fluorine-containing LPA_1 antagonists based on a novel triazolopyrimidine scaffold identified through scaffold hopping. The goal of this work is to expand the structural diversity of LPA_1 antagonists and establish new candidate chemotypes for the development of both therapeutic agents and diagnostic imaging probes.

11:50 am

Chronic voluntary consumption of cannabinoids in C57BL/6 mice.

Alayna M Jones, Robert B Laprairie
College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, SK

Introduction: The majority of pre-clinical cannabinoid work to date has focused on injection or oral gavage of cannabinoids. However, in humans, cannabis is primarily consumed by inhalation or oral ingestion. Recently, English et al. (2024) developed a voluntary oral consumption model that used Δ9-tetrahydrocannabinol (THC) dissolved in Ensure chocolate gelatin to monitor the acute effects of a cannabinoid in mice. The long-term, or chronic, pharmacodynamic and pharmacokinetic effects of cannabinoids in pre-clinical models remain understudied. Therefore, advancement of the model proposed by English et al. into a chronic treatment is needed to assess behavioural and physiological effects, drug tolerance, and bioaccumulation. The purpose of these experiments is to assess the chronic effects of voluntary oral cannabis use.
Methods: Mice were individually housed and given Ensure chocolate pudding that contained 10 mg/15 mL of cannabinoids [THC or cannabidiol (CBD)] daily for 14 days. There were 6 groups of 12 mice, split between sex and drug that received [control (olive oil), THC or CBD]. Each Ensure cup was weighed before and after placement in the cage to measure voluntary consumption. Mice underwent behavioural and physiological testing and blood collection on alternating days (every 48 hours). Behavioural and physiological tests included the bar holding test for catalepsy; body temperature by rectal thermometer; warm water tail-flick test for nociception; and open field test for locomotion (in that order). Mice also underwent saphenous vein blood collection every 48 hours and cardiac puncture (at the end of the experiment) for final blood and tissue (liver and brain) collection. Data were analyzed using repeated measures 2-way ANOVA (treatment x sex), followed by Tukey's post-hoc for multiple comparisons.

Results: Male and female mice voluntarily consuming CBD or THC gained significantly less weight than their control counterparts ($F_{treatment}(5,65)=4.465$, $p=0.0015$). However, mice in the THC group consumed significantly less Ensure than either control or CBD groups ($F_{treatment}(5,64)=161.6$, $p<0.0001$). Among the physiological measurements made, reduced body temperature ($F_{treatment}(5,65)=33.67$, $p<0.0001$) and nociception ($F_{treatment}(5,65)=9.017$, $p<0.0001$) were observed in THC-consuming males and females compared to control. Analyses of blood CBD and THC levels from these mice are ongoing.
Conclusions: Establishing this animal model will allow our group to explore the long-term harms and benefits of cannabis using an approach that more closely resembles real-world cannabis use. Planned future work will utilize this model to assess changes in metabolism and sleep.

Session 3 (Saturday pm)

1:20 pm

Integrating Genomics and Nitrogen-15 NMR for Natural Product Discovery from Northern Canadian Bark Beetle-Associated Bacteria.

Nirasha Atapattu[1], Nicolas Justus[1], Hariniha Selvarajan[1,2], River Nelson[1], Mitzchilouise Baylosis[1], Daniel Evangelista[1], Marc Schieven[1] and **Kalindi D. Morgan**[1]

1 Department of Chemistry and Biochemistry, University of Northern British Columbia, Prince George, BC
2 Current affiliation: Bakker Lab, University of Manitoba, 66 Chancellor's Circle, Winnipeg, Manitoba

Bacterial natural products remain a rich source of undiscovered bioactive chemistry, particularly in insect-associated microbiomes where ecological pressures may drive secondary metabolite evolution. Bark beetle-associated bacteria from northern Canadian forests are a promising yet largely untapped reservoir of genetically-encoded chemical diversity. We present an integrated strategy combining genome mining, bioactivity screening, and nitrogen-15 NMR spectroscopy to direct discovery toward high-value nitrogen-containing natural products.

Isolates from multiple bark beetle species were prioritized through antifungal and antimicrobial challenge and disc-diffusion assays. Whole-genome sequencing of bioactive strains, with antiSMASH and BiG-SCAPE analysis, revealed over 200 biosynthetic gene clusters (BGCs) — numerous NRPS, NRPS–PKS hybrids, and RiPP pathways — many encoding nitrogen-rich scaffolds with low homology to characterized pathways, indicating strong novelty potential.

To bridge genomic prediction and chemical access, we applied natural-abundance $^{1}H–^{15}N$ HSQC NMR as a rapid, non-destructive prioritization tool that reports directly on amides, amines, and heterocycles in crude extracts. Coupled with OSMAC cultivation, related clusters and altered conditions yield families of structurally related metabolites — natural analogue series differing by small, biosynthetically encoded changes. This positions the workflow for structure–activity exploration of nitrogen scaffolds relevant to antifungal and agrochemical development, within an underexplored microbial niche.

2:00 pm

From molecular dynamics to *in vivo* analysis: How the cerebrovasculature rewires when VEGFA signaling is blocked in zebrafish.

Wrynan Munabirul, Liubov Lobanov, Zyna Hernandez, Gauvrit Sebastien*
Department of Anatomy, Physiology, and Pharmacology, College of Medicine, University of Saskatchewan

Vascular Endothelial Growth Factor A (VEGFA) is a secreted homodimer protein and the principal driver of angiogenesis (blood vessel formation). Excessive VEGFA-driven angiogenesis underlies cerebrovascular pathologies, including brain cancer and stroke. Anti-VEGFA antibodies are clinically established, yet around 40% of patients with neovascular age-related macular degeneration retain pathological angiogenesis. Two mechanisms are proposed: uncharacterized vascular compensatory mechanisms, and intracrine VEGFA signaling occurring inside the cell, beyond the reach of antibodies. Dominant-negative (dn) proteins offer a potential alternative approach, allowing for downregulated VEGFA intracrine signaling. Here, we investigate how VEGFA signaling rewires in the brain when VEGFA activity is inhibited, pairing in silico design with in vivo validation using the zebrafish model. First, structural models of the VEGFA-VEGF receptor 2 complex are generated using AlphaFold Multimer and simulated through 200 nanoseconds molecular dynamics run in GROMACS. Simulation data are used to identify changes in protein-protein interactions and predict differences in binding activity. Leading candidates will be then validated in zebrafish, first by mRNA injection for transient expression, then in stable transgenic lines expressing dn-Vegfaa (zebrafish orthologue) under pan-neuronal and cerebrovascular promoters. Altogether, this project will provide mechanistic insight into VEGFA-dependent resistance in the cerebrovasculature relevant to clinical settings.

2:20 pm

A Universal Tandem Mass Spectrometric Fragmentation Pattern for the Development of Cannabinoid Screening and Quantification Methods in Animal Model of Pain.

Radwa Mahmoud, Amir Khajavinia, Fatma Elessawy, Alayna M Jones, Sedigheh Barzegar, Randy W Purves, Robert B. Laprairie, Anas El-Aneed*

College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon SK

Background: Phytocannabinoids are produced by the cannabis plant. Due to their potential medicinal applications, such as pain management, bioanalytical methods are required for their analysis. We pioneered the establishment of a universal tandem mass spectrometric (MS/MS) fragmentation pattern for phytocannabinoids, enabling development of MS-based strategies for their analysis.
Materials and Methods: Eight phytocannabinoids, including tetrahydrocannabinol (THC), and cannabichromene (CBC), were studied. A Quadrupole Orbitrap and a triple quadrupole linear ion trap mass spectrometers were utilized complementary to establish universal fragmentation pattern. Subsequently, a precursor ion scan (PIS) based mass spectrometry method was developed for screening phytocannabinoids in plant extracts. Animal model of pain was utilized to study pharmacological effects of chemically characterized cannabis extracts.
Results: All cannabinoids shared similar characteristic product ions, enabling the development of a universal MS/MS fragmentation pattern. Furthermore, a PIS based mass spectrometry method was employed successfully for screening method. In the animal study, mice treated with cannabis extracts exhibited reduced antinociceptive responses, and fewer cannabinoid-related side effects compared with those receiving an equivalent dose of pure THC. These findings suggest that non-THC constituents may modulate the pharmacological effects of THC.

Session 4 (Saturday pm)

3:10 pm

On Indigenous Food, Medicine, and Allyship: Working with Indigenous Knowledges and Knowledge Keepers Towards Healing.

Vincent E. Ziffle
First Nations University of Canada

Solutions to the effective treatment of Methicillin-resistant *Staphylococcus aureus* (MRSA) and advanced *Candida albicans* infections have been sought with the assistance of Indigenous Traditional Knowledge Keepers collaborating with chemists and biochemists across western Canada. MRSA wound biofilm infections and, currently, candidiasis fungal infections are now being thwarted thanks to treatments stemming from Indigenous Medicinal Plant Healing Traditions, changing attitudes about medicinal chemistry and who truly understands how to effectively fight disease. To arrive at this point, wayfinding with the help of many Indigenous Elders, Knowledge Keepers and Traditional Healers was imperative, and part of a decade-long unlearning and learning process for a conventional-trained synthetic organic chemist. His journey, beginning with unconventional classrooms, Land-based Learning, Protocol and Ceremony, Truth and Reconciliation, re-evaluation of research conventions and goals (and plenty of hard-won lessons), will be shared. Efforts toward development of successfully Indigenized chemistry courses (i.e., Chemistry of Food and Cooking), interdisciplinarity, and increased systems thinking in lab and field helped shift paradigms to usher in better ways of conducting research and working in a good way with a growing number of Elders, Indigenous Scientists and team members. We will ask if this is part of achieving “allyship” with Indigenous Peoples, or just the start of an ongoing process toward ethical research, teaching, and reciprocity through chemistry.

Session 5 (Sunday am)

9:10 am

Exploring the natural product diversity of wild Solanum species using LC-MS/MS metabolomics.

Krista A. Gill[1], Wan Anastasia Chan[1], Kyle Gardner[2] and Lana Nolan[2].
1. Agriculture and Agri-Food Canada, Saskatoon SK
2. Agriculture and Agri-Food Canada, Fredericton, NB

Potato (Solanum tuberosum L.) is one of Canada’s most economically important crops, yet it remains susceptible to a range of phytopathogens that can significantly impact yield and quality. Wild Solanum species have evolved under diverse environmental pressures and often retain a broader more diverse repertoire of natural products than domesticated potato, representing a valuable resource to improve understanding of plant defense chemistry while expanding our understanding of the natural product variation with the genus. In this study, a non-targeted metabolomics approach was employed to compare the metabolite profiles of three wild Solanum species with domestic S. tuberosum. Plant tissue samples were collected, extracted, and analyzed by LC-MS/MS. Multivariate statistical analyses revealed clear separation between wild and domestic species, indicating substantial differences in secondary metabolite composition. Putative annotation identified several metabolite classes enriched in the wild species. These findings highlight the chemo-diversity among wild Solanum species and demonstrate the utility of LC-MS/MS based metabolomics for the characterization and prioritization of natural products associated with plant defense and disease resistance. Collectively, this work provides a

foundation for future chemical and functional studies of wild Solanum species and contributes to a broader understanding of natural product diversity in this genus.

9:50 am

LC-MS Data Normalization, A Key Factor in the Creation of a Clinically Relevant Urinary Metabolite Model for Respiratory Disease.

Emma Finch[1], Maryam Alyari[2], Darryl Adamko[1], *Anas El-Aneed [2]
1 College of Medicine, University of Saskatchewan
2 College of Pharmacy and Nutrition, University of Saskatchewan

Respiratory diseases are one of the most common reasons for emergency room visits for both adults and children. Diagnosis of respiratory diseases, like asthma and chronic obstructive pulmonary disease (COPD), is primarily dependent on visits to specialists to perform breathing tests, such as spirometry, which may not be accessible in many primary care settings. Diagnosis of children presents a further challenge as spirometry is inconclusive in children under 5 years of age. There is a need for new methods of diagnosis. We have established liquid chromatography-mass spectrometry (LC-MS) methods to quantify 39 potentially diagnostic metabolites in urine (i.e., biomarkers). The challenge with urinary metabolomics is the effect of hydration on metabolite concentrations. Normalization is needed to account for variations in the hydration status of study subjects; however, our research shows that conventional creatinine (CRN) normalization is insufficient for creating models applicable at the population level. Here we present two alternative forms of normalization (creatinine-to-height (CRN/HT) and total metabolome (TM)) that improve urinary metabolomic diagnostic models. CRN/HT and TM both show improved accuracy of diagnosis compared to when biomarkers are normalized to CRN alone in adult and pediatric patients.

10:10 am

Intracellular Distribution of Novel Gemini Lipid-Based Nanoparticles for Astrocytes Reprogramming.

Alaa K. Mahmoud[1], Scot Leary[2], Ildiko Badea[1]* and Anas El-Aneed[1]*
1 College of Pharmacy and Nutrition, University of Saskatchewan
2 College of Medicine, University of Saskatchewan

Purpose: Neurodegenerative diseases, such as Alzheimer's and Parkinson's disease, are characterized by progressive neuronal loss, leading to cognitive, motor, and functional decline. A promising therapeutic strategy involves reprogramming astrocytes into induced neurons. They are abundant glial cells in the central nervous system. In this study, we investigate novel gemini lipid nanoparticles, conjugated with amino acids, to encapsulate nucleic acids coding for transcription factors. However, the complete safety profile of these novel gemini lipids remains unknown. Therefore, determining their intracellular distribution in astrocytes is essential to understand their structure-activity relationship and therapeutic potential.
Methods: Mass spectrometry was employed to detect and relatively quantify three amino-acid conjugated gemini lipid formulations. Flow injection analysis-mass spectrometry (FIA-MS) methods were developed and optimized for each formulation. Detergent based fractionation was used to isolate the cytosolic, mitochondrial, and nucleic fractions of astrocytes to evaluate intracellular distribution patterns.
Results: FIA-MS methods were successfully established for all three gemini lipids. Distinct intracellular distribution profiles among the three formulations were observed. Variations in formulations localization among different organelles suggest differences in safety and potential efficacy, highlighting the importance of the lipid structure in determining the biological behavior and the therapeutic performance as a delivery system.

Conclusion: A sensitive analytical platform was established to evaluate the intracellular distribution of novel gemini lipid-based nanoparticles in astrocytes. The findings will support rational optimization of lipid structure to enhance safety and gene delivery performance.

Session 6

10:50 am

From Molecules to Cells: Cryo-EM in Pathogen Research.

Michael Wozny
Department of Biochemistry, Microbiology & Immunology, University of Saskatchewan, Saskatoon, SK

Cryogenic electron microscopy (cryo-EM) is transforming structural biology and microbiology by enabling visualization of pathogens and their interactions with host cells across multiple spatial scales, from atomic-resolution protein structures to cellular ultrastructure. This talk will introduce the principles and workflows of modern cryo-EM and cryo-electron tomography (cryo-ET) through examples including structure determination of a cross-species anti-enterovirus neutralizing antibody by single-particle analysis (Wozny *et al*., 2024, Microscopy and Microanalysis, DOI:10.1093/mam/ozae044.349), *in situ* visualization of the ER-mitochondria encounter structure using cryo-focused ion beam milling and cryo-correlative light and electron microscopy (Wozny *et al*., 2023, Nature, DOI:10.1038/s41586-023-06050-3), and recent advances in high-throughput cryo-ET and subtomogram averaging workflows (unpublished, presented American Society of Virology, 2025).
These case studies highlight how cryo-EM and cryo-ET can reveal the structures of dynamic, heterogeneous, and membrane-associated complexes in their native environments, complementing and extending traditional structural biology approaches. The presentation will also provide an update on efforts to establish cryo-EM capability at the University of Saskatchewan. Finally, a preview of Dr. Wozny's research program at USask will showcase multimodal imaging approaches to investigate mitochondrial antiviral signaling (MAVS) protein organization at mitochondria-associated ER contact sites during viral infection.

11:30 am

Gemini-surfactant coated gold nanoparticles as enhancers for radiofrequency ablation in HELPG2 tumor spheroids.

Michelle Fernández-Schmitz[1], Dayana Fausto[2], Eiko Kawamura[3], Michael A. J. Moser[4], Wenjun Zhang[1], Ildiko Badea*[2]
1 College of Engineering, University of Saskatchewan
2 College of Pharmacy and Nutrition, University of Saskatchewan
3 CVM Imaging Centre, Western College of Veterinary Medicine, University of Saskatchewan
4 College of Medicine, University of Saskatchewan

Liver cancer is the third leading cause of cancer-related deaths worldwide and a silent cancer often detected in advanced stages. Radiofrequency ablation (RFA) is promising as a minimally invasive technique for small malignancies < 3cm. Improved multidisciplinary approaches are needed to induce more uniform cell death and avoid relapses. This study aimed to enhance RFA therapy using gold nanoparticles (AuNPs) due to their outstanding conductivity. To enhance their cellular internalization, AuNPs were coated with gemini surfactants and were tested with RFA in a 3D tumour model to evaluate cellular uptake. Coated and uncoated AuNPs were characterized. Cytotoxicity and radiofrequency ablation were assessed in HepG2 spheroids using a Live/Dead assay and image-based quantitative analysis. Nanoparticle

localization was evaluated by transmission electron microscopy (TEM). Gemini surfactant-coated AuNPs demonstrated a shift in zeta potential relative to uncoated AuNPs. Live/Dead assay showed that treatments alone did not affect spheroid viability. Post hoc analysis of quantitative image analysis identified a significant increase in cell death between RFA and non-RFA conditions within the AuNPs-GS12 group ($p=0.0118$). TEM images confirmed nanoparticle presence through endocytic vesicles. These findings indicate that gemini surfactant coatings improved AuNPs distribution within the spheroid model, supporting their potential for future cancer therapeutic applications.

11:50 am

Development of a 4-phanylbutyric acid (4-PBA) diazirine probe to study α-synuclein aggregation.

Melissa Mejia Gutierrez[2], David R.J. Palmer[2]*, Ed S. Krol[1]*

1. Pharmaceutical and Nutrition Sciences Research Group, College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, SK.
2. Department of Chemistry, University of Saskatchewan, Saskatoon, SK

4-Phenylbutyric acid (4-PBA) is an FDA-approved drug that is used primarily for the treatment of urea cycle disorders. 4-PBA has been reported to modulate α-synuclein aggregation *in vitro* which is associated with Parkinson's disease. At high concentrations of 4-PBA, α-synuclein was observed to accelerate the fibrillation stage of α-synuclein which reduced the lag time and promoted an early elongation phase. Ultimately 4-PBA led to the formation of longer and larger fibrils that were subsequently more susceptible to proteolytic cleavage. We previously used photoaffinity labelling to probe the α-synuclein binding regions for caffeine and nicotine, compounds which inhibit α-synuclein aggregation. Caffeine and nicotine were both found to bind in the N-terminal region at tyrosine 39. Since 4-PBA accelerates aggregation we are interested in studying the 4-PBA binding region with α-synuclein using photoaffinity labeling to determine whether 4-PBA interacts in the same region as caffeine and nicotine or in a different region. For this purpose, 4-PBA was synthesized with a trifluoromethyl diazirine tag (4-PBA-Dz) and was allowed to react in a photoaffinity model system. 4-PBA-Dz model photolabeling experiments were monitored by HPLC-UV and mass spectrometry. Our results indicated that 4-PBA-Dz required 1 h of UV-A irradiation to photodegrade its diazirine moiety and yields photoinserted products within the solvent system.

Poster Presentations (Saturday 4:30 – 6:00 pm)

1. Pharmacological study of allosteric mechanisms at the Type 1 Cannabinoid receptor and their application in a mouse model of pain.

Theodor S. Zaharia*[1], Harvens Beauzile[2], Ganesh A. Thakur[2], Robert B. Laprairie[1]
1 College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, Canada
2 Bouvé College of Health Sciences, Northeastern University, Boston, United States.

Introduction: Positive allosteric modulators (PAM) of the type 1 cannabinoid receptor (CB1R) can reduce pain without the psychoactivity effects of phytocannabinoids. GAT211 has shown dual agonist-PAM properties in vitro alongside anti-nociceptive effects in vivo. While GAT211 showed promise, it suffers poor pharmacokinetics (PK). This project investigated the GAT2500 series of compounds, structural derivatives of GAT211 designed to resolve and optimize CB1R PAM pharmacodynamics (PD) and PK. The goal of the present research was to determine the PD of these novel CB1R ago-PAMs and their physiological effects in mice.

Methods: Chinese hamster ovary (CHO-K1) cells expressing CB1R were treated with increasing concentrations of CP55,940 (positive control CB1R agonist), GAT2500 compounds (agonism), or combinations therein (allosterism). C57BL/6 mice were treated with a subset of compounds ± CP55,940 then assessed for nociception, as well as movement and body temperature.

Results: Two compounds - GAT2513 and GAT2515 - were efficacious ago-PAMs that shifted the potency of concentration-response curves to sub-nanomolar levels when tested in vitro. When tested in mice, these compounds displayed anti-nociceptive properties.

Conclusions: The GAT2500 series of compounds show strong preclinical potential based on their high potency and efficacy as CB1R AMs with minimal psychoactivity.

2. Linking PROTAC Uptake to FOXM1 Protein Degradation in Lung Cancer Cells

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Purpose: Proteolysis Targeting Chimeras (PROTACs) are a promising strategy for targeting oncogenic proteins such as FOXM1, which is highly expressed in non-small cell lung cancer (NSCLC) and associated with tumor progression and poor prognosis. This study investigated how PROTAC linker length influences cellular uptake and FOXM1 degradation.

Methods: Three FOXM1-targeting PROTACs containing different linker lengths (C5, C7, and C9) were evaluated. FOXM1 degradation was assessed by Western blotting following 24 h treatment in NSCLC cells (H1299). Cellular uptake of the leading PROTAC was quantified in H1299 cells by liquid chromatography-mass spectrometry (LC-MS) following 24 h dose-dependent treatment.

Results: Western blot analysis demonstrated dose-dependent FOXM1 degradation after 24 h. The C9 PROTAC exhibited the highest degradation potency, with a DC50 value of 2.8 μM, while C5 showed the lowest. Preliminary LC-MS analysis indicated that approximately 15-20% of the C9 PROTAC was taken up by H1299 cells, suggesting that limited cellular uptake may constrain its observed degradation potency.

Conclusion: These findings highlight linker length as an important design parameter for FOXM1-PROTACs. Establishing the relationship between cellular uptake and protein degradation will guide us in the development of optimized PROTACs and delivery strategies to enhance their intracellular exposure.

3. Pharmacodynamics of Nine Synthetic Cannabinoid Receptor Agonists at CB1R and CB2R.

Erica Andres[1], Roberta Costi[2], Davide Ialongo[2], Valentina Noemi Madia[2], Robert B. Laprairie[1]*.
1. College of Pharmacy and Nutrition University of Saskatchewan
2. Department of Chemistry and Technology of Drug Design Sapienza University of Rome

Synthetic cannabinoid receptor agonists (SCRAs) are a novel class of psychoactive substances showing high prevalence in illegal markets. Unlike THC, a partial agonist of the type one and type two cannabinoid receptors (CB1R and CB2R), SCRAs can be full agonists of these receptors. This likely accounts for the increased instances of adverse effects from SCRA usage including tachycardia, vomiting, and psychosis. In order to better inform regulations made by Health Canada regarding these drugs, these compounds and their activity at CB1R and CB2R needs to be characterized. Nine different SCRA compounds are to be tested in vitro for their pharmacodynamics at CB1R and CB2R.

4. Bioactive and Nutritional Composition and Antioxidant Activity of Saskatchewan-Grown Haskap (Lonicera caerulea L.) Berries.

Kanchana Madanayake[1], Leilei Sun[1], Anze Svara[2], Bob Bors[2], Haixia Zhang[1]*
1 Department of Food and Bioproduct Sciences, University of Saskatchewan
2 Department of Plant Sciences, University of Saskatchewan

Haskap (Lonicera caerulea L.) is an early-season berry adapted to the Canadian Prairies and is recognized for its rich phenolic composition and antioxidant potential. This study evaluated the compositional and bioactive properties of Saskatchewan-grown haskap berries harvested in 2025. Freeze-dried berry powders from 32 varieties representing six genetic origins were screened for total phenolic content (TPC), and 14 cultivars were selected for further characterization. TPC ranged from 27.3-54.5 mg GAE/g DW, while total flavonoid content (TFC), total anthocyanin content (TAC), and vitamin C ranged from 11.7-22.8 mg CE/g DW, 12.5-22.1 mg C3G/g DW, and 1.07-3.83 mg/g DW, respectively. Antioxidant activities measured by DPPH, FRAP, and ABTS assays ranged from 28.64-47.00 µmol TE/g DW, 74.80-130.57 mg TE/g DW, and 145.67-213.71 µmol TE/g DW, respectively. GC-MS analysis identified 126 unique putative volatile compounds. GC-FID fatty-acid analysis showed a predominance of unsaturated fatty acids, particularly linoleic acid, with clear cultivar-dependent differences in lipid composition. Overall, the results demonstrate substantial varietal variation and highlight Saskatchewan-grown haskap as a promising source of bioactive and nutritional compounds for functional food applications.

5. Stability of injectable drugs in Alberta hospitals when exposed to hydrogen peroxide disinfection conditions.

Erika Loredo Calderon[1], Khaled Ibrahim[1], Blaine Colton [2], Jamie Burkett [2], Jenn Bean [2], Kristina Haagsma [2], Margaret Gray [2], Tania Mysak [2], Jason Pepper [2], Carlos A. Velázquez-Martínez [1]*.
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Background: Vaporized hydrogen peroxide (VHP) is increasingly used for environmental decontamination in healthcare facilities, yet the impact of residual H_2O_2 on compounded sterile preparations remains largely unexplored.

Methods: The oxidative stability of injectable drugs compounded in Alberta hospital pharmacies was evaluated following H_2O_2, exposure representing accelerated oxidative stress (10-1000 ppm) and residual levels (10-1000 ppb). Drug concentrations were measured using validated stability-indicating chromatographic methods at beyond-use date (BUD) time points; stability was defined as ≥95% of the initial concentration.

Results: Most drugs remained stable after ppm- and ppb-level H_2O_2 exposure. However, β-lactam antibiotics, catechol-containing drugs, and sulfur-containing compounds showed progressive degradation, particularly at 100-1000 ppm. Although ppb-level exposure minimally affected most drugs, selected compounds were susceptible at 10 ppb. Levocarnitine was most sensitive, retaining only 78.8% after 10 ppb H_2O_2 exposure and 2 days of storage. Ceftobiprole, famotidine, and isoproterenol also showed measurable degradation during prolonged storage. Susceptibility was associated with peroxide-reactive functional groups.

Conclusions: Residual H_2O_2 is unlikely to compromise most compounded injectable drugs; however, oxidation-sensitive compounds may undergo clinically relevant degradation even at 10 ppb. These findings support incorporating oxidative stability assessments when implementing VHP-based decontamination programs to ensure pharmaceutical quality and patient safety in hospitals.

6. Evaluation of F7-derived PROTACS as potential FOXA1 degraders in HPV-positive cervical cancer cells.

Milena Gonçalves[1], Gazia Buzaakuk[2], Sara Alrawashdeh[2], **Erika Loredo-Calderon**[2], Carlos Velazquez-Martinez[2*].
1 Faculdade de Medicina da Universidade de São Paulo – FMUSP.
2 Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta.

Introduction: The FOXA1 transcription factor promotes human papillomavirus (HPV) activation and represents a potential therapeutic target in HPV-associated cervical cancer. This study evaluated five F7-derived proteolysis-targeting chimeras (PROTACs), originally designed to target a similar oncogenic protein FOXM1, as potential FOXA1 degraders in HPV16-positive SiHa cervical cancer cells.

Methods: FOXA1 and FOXM1 expression was characterized by RT-qPCR, and FOXA1 protein levels were assessed by Western blot. SiHa (cervical cancer cells) and H1299 (lung cancer cells) were treated with F7 or PROTAC F7-$PEG_{(1–5)}$-thalidomide PROTACs, followed by analysis of FOXA1 expression and cell viability.

Results: FOXA1 mRNA increased significantly at 16, 48, and 72 h in SiHa cells, whereas FOXM1 expression remained comparatively low and stable. FOXA1 protein was consistently detectable over 72 h, supporting SiHa cells for degradation studies. F7-PEG_4-T reduced FOXA1 protein, identifying it as the leading candidate for further validation. The parent drug and FOXM1 inhibitor, F7, showed the strongest effect on SiHa viability (IC_{50} = 25.19 μM), whereas F7-PEG_{1-4}-T did not reach 50% inhibition (IC_{50} > 40 μM). F7-PEG_5-T reduced cell viability yielding an (extrapolated) IC_{50} = 49.96 μM. SiHa cells were more responsive than H1299 cells to F7 and thiostrepton. Nonetheless, precipitation observed for several PROTACs in cell culture media may have limited their activity. These findings support FOXA1 as an investigational target in HPV-positive cervical cancer and identify F7-PEG_4-T as a preliminary degrader candidate. Further studies will assess proteasome dependence, ubiquitination and the use lipid nanoparticles to increase cancer cellular uptake.

7. Increased Mitochondrial Biogenesis by Curcumin and Analog NC2603 in Human Colorectal Cancer (Caco-2) Cells.

Felipe Garcia Nishimura[1,2], **Katayoon Karimzadeh***[1], Jonathan R. Dimmock[1], Brian Bandy[1]
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Curcumin possesses antioxidant and anticancer properties but is limited by poor bioavailability and moderate potency. Synthetic analogs containing electrophilic α,β-unsaturated keto groups, such as NC2603, have been developed to improve therapeutic efficacy. This study investigated the oxidative stress-associated antitumor and mitochondrial effects of NC2603 compared with curcumin in human colorectal adenocarcinoma (Caco-2) cells. Caco-2 cells were treated with curcumin or NC2603 for 12 or 24 h. Mitochondrial membrane potential was assessed using TMRE and JC-1 fluorescence assays, while mitochondrial content was evaluated using MitoTracker Green. Intracellular and mitochondrial reactive oxygen species (ROS) were quantified using DCFH-DA and MitoSOX, respectively. Expression of genes involved in mitochondrial function, oxidative stress, and apoptosis was analyzed by quantitative real-time PCR. At concentrations that moderately inhibited cell growth, NC2603 markedly increased mitochondrial membrane potential and content, indicating enhanced mitochondrial activity. Unlike curcumin, NC2603 also increased intracellular ROS and mitochondrial superoxide production. Transcriptional analysis demonstrated increased expression of NRF1, PGC-1α TFAM, and NRF2, consistent with activation of mitochondrial biogenesis and oxidative stress-response pathways. Overall, NC2603 exhibited greater antitumor activity than curcumin and promoted oxidative stress-associated mitochondrial adaptations that may contribute to reduced Caco-2 cell proliferation.

8. Investigating the effects of ionizing radiation on neural brain organoids at the Canadian Light Source.

Jaiden Jocelyn[1], Mackenzie Malo[1], Kevin Allen[1], Wojciech Dawicki[2], Darrell Mousseau[2], Ibi Bondici[3], Amanda Quirk[3], Ekaterina Dadachova[1] *
1. College of Pharmacy and Nutrition, University of Saskatchewan
2. College of Medicine, University of Saskatchewan
3. Canadian Light Source

As we age, we accumulate cellular damage over time which can lead to neurodegeneration. This neurodegeneration is associated with various imbalances in proteostasis and metal

distribution. In this study, we aimed to observe the effects of ionizing radiation on 3D neural organoid models. Neural organoids were generated from WA09, human embryonic stem cells and induced with aftin-5 to mimic aging brains in-vitro. These mini-brains were analyzed utilizing mid wavelength infrared (mid-IR) and biological x-ray absorption spectroscopy (bio-XAS) imaging techniques. Mid-IR utilizes characteristic bond energies to distinguish the distribution of the biomolecular landscape of neural organoids, specifically, alpha helices and beta-sheets. Bio-XAS utilizes x-rays and the photoelectric effect to determine the metal distribution of biological samples. Our results demonstrate that ionizing radiation produces very different effects on aftin-5 induced organoids versus non-induced brain organoids in terms of metal distribution and protein make-up.

9. Biocatalytic Hydrogenation of Unsaturated α-Keto Acids

Alina Uribe, David A.R. Sanders and David R. J. Palmer*.
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Abstract: A quinone oxidoreductase (QOR) from Escherichia coli was recently reported to exhibit an unexpected ene-reductase activity, catalyzing the reduction of the carbon-carbon double bond of α,β-unsaturated benzylidenepyruvates in addition to its native quinone-reducing activity. We have developed a one-pot enzymatic cascade incorporating an aldolase (NahE), QOR, and a dehydrogenase for cofactor regeneration. Using readily available substrates, substituted benzaldehydes and pyruvic acid, this cascade facilitates the synthesis of phenyl keto acids under mild reaction conditions. The process offers several advantages, including environmental sustainability, high chemoselectivity, and efficient hydrogenation. Furthermore, production costs are reduced through the regeneration of NADH from NAD+, providing the cofactor required by QOR. The resulting keto acids serve as valuable synthons for the synthesis of high-value compounds, including aromatic aldehydes, non -canonical amino acids, chiral amines, and hydroxy lactones. Moreover, this versatile platform is suitable for coupling with suitable downstream biocatalysts, highlighting the potential of this cascade for the production of diverse fine chemicals.

10. Isolation and Mass Spectrometric Characterization of NX-2 and NX-3 Trichothecene Mycotoxins for Targeted Detection in Western Canadian Wheat.

Savanna Spendiff[1], Jada Mirosovsky[2] , Maria Alejandra Oviedo-Ludena[1], Ed Krol[2], Lipu Wang[1], Randy Kutcher[1], Anas El-Aneed[2]*
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2. College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, SK

Fusarium head blight (FHB) is a major fungal disease of cereal crops that leads to the contamination of grain with trichothecene mycotoxins, posing risks to food safety, animal health, and agricultural economies. While deoxynivalenol (DON) and related trichothecenes are well-established targets in mycotoxin analysis, NX-2 and NX-3 (NX toxins) are not typically included in current detection methods. Limited data exist on the occurrence of NX toxins in Western Canada, and their presence may be underestimated due to limitations in current detection approaches. Additionally, analytical standards are not commercially available, creating a barrier to their inclusion in targeted detection methods. This research aims to isolate and purify NX toxins from infected rice for inclusion in a targeted multi-mycotoxin liquid chromatography-tandem mass spectrometry (LC-MS/MS) method. NX toxins are produced in rice infected with

NX-producing Fusarium graminearum (Schwabe) and isolated using solid-liquid extraction and solid-phase clean-up, and normal- and reversed-phase liquid chromatography. Purified NX-2 and NX-3 will be characterized by nuclear magnetic resonance (NMR) and tandem mass spectrometry to assess purity, confirm identity, and support LC-MS/MS method development. Ultimately, the developed method will be applied to Saskatchewan wheat samples to investigate NX toxin occurrence.

11. Design and Synthesis of a Bioorthogonal Probe for the Salmonid Toxicant 6PPD-Q.

Jada Mirosovsky[1], Markus Brinkmann[2], Ed Krol[1]*.
1. College of Pharmacy and Nutrition, University of Saskatchewan.
2. Toxicology Centre, University of Saskatchewan

N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine quinone (6PPD-Q) is a known salmonid toxicant which enacts variable toxicity across salmonid species. 6PPD-Q toxicity has been linked to metabolic and mitochondrial effects, but the precise biological target and subsequent mechanism of action remain unknown. To better understand this, we will utilize a biorthogonal approach and synthesize a 6PPD-Q analogue containing both a diazirine photoaffinity label and an alkyne substituent. Our synthetic strategy couples the diazirine-alkyne alkyl group with the quinone-aniline functionality and we have carried out pilot reactions to confirm the feasibility of our strategy. We have prepared model diazirines, the quinone-aniline fragment and confirmed conditions for regioselective addition of an alkyl amine. We are currently optimizing coupling of the alkyne group to the alkyl amine diazirine precursor. Once the analogue is complete it will include the diazirine and alkyne tags on the alkyl portion of the probe to optimize the structure-activity relationship and allow for targeted trapping, isolation, and identification of 6PPD-Q's biological target(s) via mass spectrometric proteomics. Identified target(s) will serve as a hypothesis generator for 6PPD-Q's toxicological mechanism of action and its further investigation.

12. Discovery of Antimicrobial Resistance Determinants in a One Health Framework.

Taslimun Jannat, Antonio Ruzzini*
Department of Veterinary Microbiology, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, SK, Canada.

Antimicrobial resistance (AMR) threatens the effectiveness of antibiotics. This is increasingly tracked in human medicine: in 2019 alone, bacterial AMR was linked to an estimated 1.3 million deaths worldwide. Unified efforts in veterinary medicine lag behind those focused on human health and the determinants that challenge animal health and food production can be related or different from those that impact people. Antimicrobial usage (AMU) provides significant selective pressure on bacterial populations in agrifood systems, which constitute a crucial interface of environmental, animal, and human health. Despite the fact that thousands of antibiotic resistance genes (ARGs) have been identified, unidentified or genetically divergent determinants go unnoticed by conventional surveillance algorithms that rely heavily on high levels of sequence similarity to known AMR genes. Alternatives to conventional pipelines include investigating clusters of resistance genes, assessing the activities of distant ARG homologs and or focusing on discordance between AMR genotypes and phenotypes. Although specific hypotheses can be formulated in the latter cases, the investigation of ARG clusters, which are replete with known determinants of AMR, and include uncharacterized genes with unknown functions relies on a ”guilt-by-association” hypothesis and high-throughput screening. Genes located to near known ARGs in pathogens were prioritized for study via heterologous

expression in Escherichia coli DH5α and Bacillus subtilis to evaluate their functional contribution to resistance. A broad antibiotic screen of approximately 800 compounds, including a customized drug panel based on the list of veterinary-important antimicrobials from the World Organisation for Animal Health was performed. In parallel, plasmid sequences are being analyzed to identify additional uncharacterized genes located near known ARGs for future functional testing. This combined computational and experimental approach may facilitate the identification of resistance determinants overlooked by conventional sequence-based AMR surveillance.

13. Development Of Conduritol Aziridine-Based Chemical Tools for Selective Targeting and Activity-Based Profiling of GBA1/GCase And GBA2.

Enock Obeng, David Palmer and Christopher Phenix
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Glycosidases play important roles in carbohydrate metabolism, with β-glucocerebrosidase (GBA1/GCase) and non-lysosomal GBA2 being key enzymes involved in glucosylceramide metabolism in humans. Malfunction of GBA1 is associated with Gaucher disease and Parkinson's disease, highlighting the need for chemical tools that can selectively inhibit or profile activity levels of these enzymes in biological systems. Conduritol Aziridines (CAz's) are mechanism-based inhibitors that exploit glycosidase catalytic machinery to achieve irreversible enzyme inhibition. Previous studies have established *N*-alkylated CAz derivatives as effective GCase inactivators, while recent work identified a highly potent and selective CAz-based GCase inhibitor with activity in cellular and vivo models.
Building on these findings, my research aims to develop CAz-based probes that combine selective enzyme targeting with bioorthogonal fluorescent labeling. CAz derivatives containing an *N*-linked TCO (trans-cyclooctene) or tetrazine group, as well as GCase-selective analogs will be synthesized and evaluated for GCase inhibition and selectivity over GBA2. A pretargeting strategy will be investigated in which the CAz probe first enters cells and covalently targets active GCase, followed by administration of a complementary fluorescent TCO or tetrazine compound to enable enzyme detection and quantification. Rapid labeling, compatible with biological samples, will occur through the TCO-tetrazine Inverse Electron Demand Diels-Alder reaction (IEDDA).
Overall, this work aims to expand the utility of CAz chemistry identifying novel and versatile tools for selective GCase/GBA2 inhibition, activity-based profiling, and cellular visualization.

14. Analyzing the effects of Cannabinol as an Individual Compound in Mice.

Alayna Jones, Robert Laprairie *
College of Pharmacy and Nutrition, University of Saskatchewan.

Δ^9-tetrahydrocannabinol (THC) is the compound in cannabis that produces the “high” associated with cannabis use. When THC degrades from air, heat, or light, it produces cannabinol (CBN). The intoxication levels and psychoactive effects of CBN are still unknown. The primary objective of this project was to determine whether CBN is intoxicating and therefore should be regulated similar to THC and cannabidiol content that are currently regulated in Canadian cannabis products. There were two parts to this project. First was a battery of tests known as the “tetrad” to study the behavioral effects of 0.1-10 mg/kg CBN in C57BL/6 mice. Second was a pharmacokinetic time course to quantify the amount of CBN in mouse blood 10 min - 8 h following administration. The data collected shows that CBN produced effects in the behavioral tetrad, with some sex differences observed. Dose-dependent effects were observed with lower potency but similar efficacy to THC. Blood levels of CBN suggest a Tmax for CBN of approximately 6 h. The data collected to date indicate CBN is an intoxicating cannabinoid that should likely be regulated in cannabis products.

15. Evaluating CB1R C-Terminal Decoy peptides in their ability to attenuate β-Arrestin2-Mediated desensitization and downregulation of Cannabinoid 1 Receptor.

Diya Patel[1], Haley Anderson[1], Robert B. Laprairie,[1]* Vivek Kuma[2], Bobak Shadpoor[2]
1. University of Saskatchewan
2. University of Houston

The type 1 cannabinoid receptor (CB1R) is widely expressed throughout the central nervous system, where it regulates processes including pain perception and neuronal excitability. Chronic CB1R activation promotes β-arrestin2-mediated receptor desensitization and internalization, contributing to tolerance. This research investigated whether CB1R C-terminal decoy peptides could preserve receptor surface expression by interfering with β-arrestin2 recruitment. Immortalized mouse pituitary gland cells stably expressing human CB1R fused to super-ecliptic pHluorin (AtT20-SEPCB1) were used to monitor CB1R surface expression through fluorescence imaging. Cells were treated with CB1R decoy peptides following baseline fluorescence measurements, and measurements every 5 minutes for 30 minutes. Images were analyzed using Gen5 and ImageJ. Fluorescence was normalized to baseline and vehicle controls. Statistical significance was assessed using two-way ANOVA with Tukey‘s post hoc test. 1 mg/ml CB1C, 0.1mg/ml CB1C and 0.1 mg/ml CB1Palm maintained CB1R surface expression; while 10 mg/mL CB1C increased receptor surface expression independent of pH. However, these effects were not statistically significant. These findings support further investigation of CB1R decoy peptides as a strategy to limit CB1R internalization associated with tolerance.

16. Investigating the role of an active-site asparagine residue in catalysis by the aldolase NahE.

Farah Mustafa, David Palmer*
Department of Chemistry, University of Saskatchewan

trans-o-Hydroxybenzylidenepyruvate hydratase aldolase (NahE) is found in some bacteria in their naphthalene degradation pathway. NahE catalyzes an aldol-condensation reaction of both directions. The crystal structure of NahE showed conserved residues among type 1 aldolases, including Lys 183 and Tyr 155 which are responsible for Shiff base formation. The study also showed another residue, Asn 157 within a H-bonding distance of Tyr 155, suggesting that Asn might have an important role in the dehydration step and the condensation product formation. Here, we are investigating the role of Asn 157 by two different mutations, trying to favor the aldol product formation and making a new chiral center. We performed a series of synthetic reactions using a variety of substrates. Substrates bearing an EDG didn't affect the dehydration step leading to the expected benzylidenpyruvate product. On the other hand, substrates with EWG hindered the dehydration step, leading to the aldol product formation. Interestingly, non-conjugated substrates showed the formation of the aldol product with the WT NahE as well. The isolated yields were lower with the mutants compared to the WT, and the reaction rate was significantly slower. The catalyzed reaction was also monitored using HPLC, and the aldol product formation was detected in some substrates.

17. Inhibition of fatty acid amide hydrolase alters fluid balance but does not change weight or food consumption in C57BL/6Crl mice.

Abby Peace, Erica Andres, Riley Brown, Radwa Mahmoud, **Robert B Laprairie***
College of Pharmacy and Nutrition, University of Saskatchewan

Fatty acid amide hydrolase (FAAH) is an intracellular enzyme present in high amounts in the brain, liver, and small intestine. FAAH catabolizes 3 fatty acid amides: anandamide (AEA), oleoylethanolamide (OEA), and palmitoylethanolamide (PEA). AEA is partial agonist of the type 1 cannabinoid receptor (CB1R) and has been implicated in the regulation appetite and metabolism; however, its precise contributions have not been fully elucidated. The goal of the present study was to determine the effects of chronic FAAH inhibition in mice. Because CB1R activation increases body weight and food intake, we hypothesized chronic FAAH inhibition would increase AEA resulting in elevated food intake and body weight. Male and female C57BL/6Crl mice were treated with the FAAH inhibitor URB597 for 14 days (3mg/kg/day i.p.) and weight, food and water consumption, urination, and defecation were recorded daily. To our surprise, weight and food intake were unchanged; however, water intake was increased whereas urination and defecation were decreased by FAAH inhibition. Therefore, our emerging interpretation is that FAAH inhibition alters fluid balance rather than weight or appetite directly. We are now assessing tissues collected from these mice to determine whether regulators of fluid balance (e.g., renin, angiotensin) were altered by chronic FAAH inhibition.

18. Pharmacological study of cannabichromene and cannabigerol at the serotonin 1A (5-HT1A) and adenosine 2A (A2A) receptors.

Riley Brown[1], Kyle Boniface[2], Robert Laprairie[1]*.
1. College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, SK.
2. Decibel Cannabis Company, Calgary, AB

Minor cannabinoids cannabichromene (CBC) and cannabigerol (CBG) exhibit antinociceptive and anxiolytic effects not fully explained by cannabinoid receptor signaling. Prior research suggests other G protein-coupled receptors (GPCRs), such as 5-hydroxytryptamine 1A (5-HT1A) and adenosine A2A receptors, may contribute to these effects. This study characterizes CBC and CBG activity at these non-cannabinoid GPCRs. Radioligand competition binding was conducted at human 5-HT1A and A2A receptors. Functional signaling at 5-HT1A was evaluated in Chinese hamster ovary (CHO) cells using a luminescence-based calcium assay. In vivo behavioral assays were conducted in wild-type and 5-HT1A knockout C57Bl/6 mice. CBC and CBG displaced radioligand at 5-HT1A receptors (Ki = 11.5 nM and 151 nM, respectively). CBC displayed binding at A2A (Ki = 28.8 nM), while CBG binding did not converge. At 5-HT1A, CBC was a partial agonist (EC50 = 3.84 μM; Emax = 80.8% vs 8-OH-DPAT), while CBG elicited activation (EC50 = 40.8 nM; Emax = 66.7%) and attenuated 8-OH-DPAT responses, consistent with protean agonism. In vivo, CBG reduced nociception in WT mice, whereas this effect was not significant in 5-HT1A knockout mice. These data support direct modulation of 5-HT1A by CBC and CBG with distinct efficacy profiles and suggest 5-HT1A may contribute to CBG-mediated antinociception.

19. Structural Studies of a Hydratase-Aldolase in Naphthalene Degradation Pathway of Pseudomonas putida.

Methni M. Samarasinghe, David A. R. Sanders*
Department of Chemistry, University of Saskatchewan

NahE is a hydratase-aldolase that belongs to the N-acetylneuraminate lyase subgroup of Class I aldolase. NahE is involved in the naphthalene degradation pathway of Pseudomonas putida by catalyzing the conversion of trans-o-hydroxybenzylidenepyruvate to salicylaldehyde and pyruvate. This study focused on structural analysis of NahE, with the aim of obtaining X-ray diffraction quality crystals to determine the three-dimensional structures of enzyme-substrate complexes. Moreover, to expand the current understanding of substrate recognition and the interactions related to the molecular mechanism of the aldolase. For crystallization trials, hexahistidine-tagged NahE was purified by affinity chromatography, and the purity of the enzyme was assessed by SDS-PAGE. Initial screening was performed at room temperature using the microbatch method, followed by hanging-drop vapor diffusion for further optimization. Multiple crystallization grids were explored by systematically varying the buffer pH and precipitant concentration around promising conditions. In addition, the effects of buffer-to-protein ratio, protein concentration, buffer concentration and temperature on crystal formation were analyzed. To confirm the proteinaceous nature, the resulting crystals were evaluated using IZIT dye test and crystal crush test. A buffer system supporting the crystal formation was identified and ongoing work focuses on improving reproducibility and optimizing cryoprotectant conditions for X-ray diffraction studies.

20. An Untargeted Metabolomics and Antioxidant Assay Study to Evaluate the Bioactive Potential of Mutant Faba Bean Seed Coats

Avantika Chougule[1], Hamid Khazaei[2], Anas El-Aneed[1], Randy Purves[1,3]*
1 College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, Canada
2 Department of Agricultural Sciences, University of Helsinki, Helsinki, Finland
3 Canadian Food Inspection Agency, Saskatoon, Canada

Introduction:
Faba bean seed coats are rich in polyphenols and exhibit strong antioxidant activities, features often associated with their color variation[1,2]. Jan Sjödin developed a large faba bean seed mutant collection over 60 years ago that has still not been characterized for polyphenol composition. While typical seed coats (wild type) are buff, this collection contains several colors including purple, red, yellow, black, green, and brown phenotypes that have been largely unexplored in previous biochemical studies of faba bean[2,3]. Here, we applied untargeted UPLC-HRMS (Ultra Performance Liquid Chromatography-High Resolution Mass Spectrometry) metabolomics to investigate these color-dependent polyphenolic profiles, and we also employ antioxidant assays to determine the effect of the changing polyphenol classes on antioxidant capacity.
Methods:
Polyphenolic profiling was performed using an **untargeted UPLC-HRMS workflow** combined with **multivariate statistical analyses**. Color groups were evaluated to determine how seed coat color profiles correlate with metabolite composition. Key genotypes identified through chemometric clustering were assessed for antioxidant activity using biochemical assays including 2,2-diphenyl-1-1picrylhydrazy (DPPH) and 4-dimethylaminocinnamaldehyde (DMAC) assays.
Results and Conclusion:
The UPLC-HRMS analysis of 13 different color groups resulted in the putative identification of metabolites belonging to several classes of polyphenols, including flavonoids and phenolic acids. Multivariate analysis showed differences between colored J. Sjödin mutants and conventional genotypes. The key identified metabolites differentiating the colors were upregulated flavonols and their glucoside conjugates. In contrast, nitrogen containing compounds (likely amino acids) were downregulated in mutant colors. Antioxidant assays showed that select mutants, including several Sjödin lines, had higher antiradical power and procyanidin content than conventional colors. These findings suggest seed coat color can serve as a visual marker for antioxidant potential, highlighting promising genotypes for breeding faba beans with enhanced nutritional value and therapeutic benefits.

21. A Custom 3D-Printed Transwell Platform for In Vitro Screening of Intranasal Vaccine Delivery Systems.

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Purpose: Physiologically relevant nasal epithelial models are essential for evaluating intranasal drug and vaccine nanoparticle delivery; however, conventional transwell systems lack flexibility and are cost-intensive. This study aimed to develop a customizable 3D-printed transwell platform along with integrated transepithelial electrical resistance (TEER) monitoring and to validate its ability to support functional human nasal epithelial barriers through optimization of cell seeding density and biological characterization.

Methods: A transwell-compatible platform was designed and fabricated using high-resolution stereolithographic 3D printing to accommodate 6.5 mm porous membranes and custom TEER electrodes. Immortalized human nasal epithelial cells were seeded at densities ranging from 2×10^4 to 2×10^5 cells/insert. Barrier formation was monitored via TEER over 7 days. Cell viability was assessed using MTT and live/dead staining. Barrier permeability was evaluated using fluorescein transport assays at multiple time points. Cytoskeletal organization was examined via phalloidin staining of F-actin using fluorescence microscopy.
Results: Seeding density critically influenced epithelial barrier formation. Cells seeded at 3×10^4 cells/insert formed a uniform and stable monolayer, whereas higher densities ($\geq5\times10^5$ cells) resulted in aggregation, dome-like structures, and uneven surfaces prone to detachment. TEER values increased over time across all groups, with optimized conditions reaching 377±76 Ω·cm² by Day 7, indicating robust barrier formation. MTT analysis demonstrated time-dependent increases in metabolic activity, with significantly higher absorbance at 48 h compared to 24 h, confirming active cell proliferation and viability. Permeability assays showed a time-dependent increase in fluorescein transport in cell-free controls, while epithelial models exhibited markedly reduced permeability, indicating effective barrier function. Phalloidin staining revealed well-organized cortical F-actin structures, consistent with tight junction formation.
Conclusion: The 3D-printed transwell platform successfully supports the formation of functional human nasal epithelial barriers with integrated, reproducible TEER monitoring. Optimization of seeding density was essential to achieve structural and functional integrity. This validated, cost-effective platform provides a robust tool for future intranasal drug and vaccine nanoparticle delivery studies, with potential to reduce reliance on early-stage animal models for formulation screening.
Keywords: 3D-Model; Nasal Epithelial; 3D—Printing; Vaccine

22. Design and Characterization of a Multi-Adjuvant Lipid Nanoparticle Platform for Dendritic Cell Targeting.

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Purpose: Co-delivery of antigen and immunostimulatory agents within a single nanocarrier remains a critical design challenge in subunit vaccine development. Efficient intracellular delivery to dendritic cells requires controlled lipid composition, reproducible encapsulation, and sustained cellular interaction. This study aimed to characterize a microfluidically assembled lipid nanoparticle (LNP) platform capable of co-encapsulating structurally distinct immunostimulatory agents and to evaluate formulation performance, cytocompatibility, and time-dependent dendritic cell uptake.
Methods: LNPs composed of cationic and neutral lipids were prepared using controlled microfluidic mixing (FRR 9:1; TFR 260 µL/min). Hydrophobic immunostimulatory agent was incorporated in the organic phase, while nucleic acid-based agents were introduced in the aqueous phase to enable electrostatic complexation. Multi-adjuvant configurations and a blank LNP control were generated. Particle size, PDI, and zeta potential were assessed by dynamic light scattering. Lipid recovery was measured qualitatively using a phosphorus assay. Encapsulation efficiencies were determined via UV-Vis and nucleic acid absorbance. Cytocompatibility was evaluated using MTT and Live/Dead assays in JAWS II dendritic cells. Intracellular uptake was assessed by confocal microscopy at different time points.
Results: All formulations produced particles with physicochemical characteristics suitable for dendritic cell interaction (size: 140 nm, PDI: 0.2, zeta: 38 mV). Lipid recovery ranges were demonstrating reproducible nanoparticle assembly. Recovery of hydrophobic agent and nucleic acid encapsulation efficiencies were consistent with electrostatic association within a cationic lipid environment. MTT analysis demonstrated preserved cellular metabolic activity at all evaluated

timepoints, with transient increases observed at intermediate timepoints. Live/Dead staining confirmed the absence of progressive cytotoxicity. Confocal imaging revealed time-dependent intracellular accumulation of LNPs, with minimal signal at 1 h, increased cytoplasmic localization at 3-5 h, and intracellular retention at 24 h.
Conclusion: This study demonstrates a reproducible microfluidic strategy for co-encapsulation of immunostimulatory agents within lipid nanoparticle systems. The produced formulations exhibit favorable recovery, controlled incorporation, preserved cytocompatibility, and enhanced time-dependent cell uptake. These findings support further immunological evaluation of this modular LNP platform for vaccine delivery applications.
Keywords: Lipid Nanoparticle; Adjuvant; Vaccine; Immunogenicity

23. Characterizing an Overlooked Family of α/β-Hydrolases Involved in Antimicrobial Resistance.

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Current antimicrobial resistance (AMR) surveillance systems remain incomplete and may overlook important antimicrobial resistance genes (ARGs), particularly those present in environmental and animal reservoirs. Identifying these hidden resistance determinants is essential to improve AMR surveillance and understand the impact of antimicrobial use in agriculture. During AMR surveillance efforts, we functionally characterized a member of the α/β-hydrolase superfamily as a macrolide esterase. Named EstTSf, this enzyme inactivates tylosin and related macrolide antibiotics and represents the founding member of a previously unrecognized family of macrolide resistance determinants. EstTSf has numerous homologs within the α/β-hydrolase superfamily, suggesting that additional members of this diverse enzyme family may contribute to macrolide resistance.
To investigate this overlooked group of esterases, we selected four EstTSf homologs – EstTAi, EstTSt, EstTBc, and EstTEc based on their sequence identity to EstTSf and their identification in distinct environmental contexts. This approach enabled us to examine the functional and structural diversity of these macrolide esterases and determine their potential contribution to macrolide resistance. We have now determined the three-dimensional structures of EstTSf, EstTBc, EstTEc, and EstTSt, providing insight into the structural features underlying substrate recognition and hydrolysis. Biochemical and structural characterization of these enzymes reveals differences in their macrolide substrate specificities and catalytic activities despite their membership in the same α/β-hydrolase superfamily and the presence of a conserved Ser-His-Asp catalytic triad.
Together, these findings reveal the structural and functional diversity of an overlooked group of macrolide esterases within the α/β-hydrolase superfamily and provide insights that may inform the design of next-generation macrolides resistant to esterase-mediated inactivation, helping address AMR.

Friday night mixer, Education Faculty Lounge 3050
Saturday and Sunday lunches–1004 Education
Scientific sessions - 1004 Education
Saturday banquet - St. Tropez **Parking in Lot F**