THE UNIVERSITY OF BRITISH COLUMBIA

Faculty of Pharmaceutical Sciences

2025 Faculty of Pharmaceutical Sciences Graduate and Postdoctoral Research Symposium

May 1, 2025, 8:00 am–4:30 pm

University Golf Club, 5185 University Blvd., Vancouver

Sponsored by fisher scientific part of Thermo Fisher Scientific & BONG PANG YEE FAMILY

Table of Contents

Organizing Committee Members

Vignesh Krishnamoorthy
PhD student
Co-chair

Chloe White
PhD student
Co-chair

Anne Meyer-Miner
Manager, Graduate and
Postdoctoral Affairs

Noah Brittain
PhD student
Abstract and Program Co-lead

Natalie Stewart
PhD student
Abstract and Program Co-lead

April St Pierre
PhD student
Abstract and Program Co-lead

Dan Everton
PhD student
Abstract and Program Co-lead

Jacob Melamed
PhD student
Judging Co-lead

Aashiq Ahamed Schukkor
MSc student
Judging Co-lead

Angeline Wu
PhD student
Judging Co-lead

Organizing Committee Members – continued

Vanessa Chan
PhD student
Judging Co-lead

Jonas Olsen
PhD student
Venue and Logistics Co-lead

Jimmy Kim
MSc student
Venue and Logistics Co-lead

Conall McCutcheon
PhD student
Venue and Logistics Co-lead

Sarah Ng
MSc student
Event Support Co-Lead

Priya Samuel
MSc student
Event Support Co-Lead

Ramin Rezaeianzadeh
PhD student
Event Support Co-Lead

Khanh Nguyen
MSc student
Event Support Co-Lead

Brenda Ma
MSc student
Event Support Co-Lead

Nazafarin Esfandiari
MSc student
Event Support Co-Lead

Acknowledgements

Land Acknowledgement

The 2025 Graduate and Postdoctoral Research Symposium is being held on the traditional, ancestral, and unceded lands of the xʷməθkʷəy̓əm (Musqueam) people. This area has always been a place of learning for the xʷməθkʷəy̓əm, and we feel privileged to have the opportunity to learn from our graduate and postdoctoral trainees and celebrate their research on this land during today's event. We hope you will take some time today to learn about the history of this land and to honour its original inhabitants. The resources at musqueam.bc.ca or indigenous.ubc.ca can help you get started. Acknowledging the land that we are situated on, and recognizing our role in the redress process, is an important part of our responsibilities as uninvited visitors on xʷməθkʷəy̓əm territory, and of the ongoing work required for reconciliation. We also invite you to identify, acknowledge and research the history of the lands you have come from, or are currently living and working on, by visiting the website native-land.ca.

Judges

Thank you to all our judges—this event wouldn't be possible without you!

Dr. Alex Smith
Dr. Brian Rodrigues
Dr. Wei Zhang
Dr. Jen Brown
Dr. Joel Finbloom
Dr. Peter Loewen
Dr. Tom Velenosi
Dr. John Daly
Dr. Mark Harrison
Dr. Karla Williams
Dr. Brodie Thomson
Dr. Ramya Kannan
Dr. Mary De Vera
Dr. Nicole Krentz
Dr. Nikki Salmond
Dr. Po-Han Chao
Dr. Petar Iliev
Dr. Anil Maharaj
Dr. Gilciane Ceolin
Dr. Michael Coughtrie
Dr. Dwayne Tucker

Invited Speaker

Dr. Matthew Wright, UBC Pharm Sci BSc (Pharm), MSc, PhD
Vice-President, DMPK at Arcus Biosciences

Website and Advertising

Faculty of Pharmaceutical Sciences Office of Communications and Marketing

Engagement and Support

Faculty of Pharmaceutical Sciences
Office of Development and Alumni Engagement

&

Faculty of Pharmaceutical Sciences
Office of Associate Dean, Graduate and Postdoctoral Studies

Thank you to all our presenters and attendees!

Schedule

08:00–08:45 **CHECK-IN, POSTER SET UP, CONTINENTAL BREAKFAST**

08:45–08:55 **LAND ACKNOWLEDGEMENT**
Vignesh Krishnamoorthy and Chloe White, GPRS Organizing Committee Chairs

WELCOME
Dean Lalitha Raman-Wilms, Faculty of Pharmaceutical Sciences

OPENING REMARKS
Vignesh Krishnamoorthy and Chloe White, GPRS Organizing Committee Chairs

08:55–09:55 **PODIUM SESSION 1: MSC STUDENT PRESENTATIONS**
Session Chair: *Jonas Olsen*

08:55–09:05
Elucidating the role of *RREB1* in beta-cell and diabetes
Presenter: *Woojung Kim*

09:05–09:15
Development of SP1 Knockout Cell Lines for Characterization of SP1 Mediated Regulation of SAT1 Induction in Response to Doxorubicin Treatment
Presenter: *Janice Wu*

09:15–09:25
Experiences of Partners of Patients Diagnosed with Cancer: A Systematic Review and Thematic Synthesis of Qualitative Literature
Presenter: *Preet Kang*

09:25–09:35
Implications of Circulatory Protein Adhesion on Lipid Nanoparticle Pharmacokinetics
Presenter: *Kevin Fox*

09:35–09:45
Targeted Synthetic Disease-Modifying Antirheumatic Drugs in Pregnancy: Patterns of Use Among Females with Autoimmune Diseases and Maternal-Neonatal Outcomes
Presenter: *Vienna Cheng*

09:45–09:55
Effect of Ischemic Stroke on Subsequent Oral Anticoagulant Adherence in Patients with Atrial Fibrillation: A Scoping Review
Presenter: *Aashiq Ahamed Shukkoor*

09:55–10:20 **COFFEE BREAK AND NETWORKING**

Schedule – continued

10:20–11:00 **PODIUM SESSION 2: JUNIOR PHD STUDENT PRESENTATIONS**
Session Chair: *Noah Brittain*

10:20–10:30
Taking nanomedicine down a PEG: mRNA-LNP formulations using PEG alternatives
Presenter: *April St Pierre*

10:30–10:40
What's in a Choice? A Study of the Medication Preferences of People with Heart Failure
Presenter: *Blair MacDonald*

10:40–10:50
The Small Molecule Aggregation Rescue of Target Assay: A *SMART* Approach to Drug Discovery
Presenter: *Dan Everton*

10:50–11:00
Population-based Case-Control Study of Antidepressants and Early-Age Onset and Average-Age Onset Colorectal Cancer: The Impact of Exposure Window, Class, Dose, and Intensity
Presenter: *Vicki Cheng*

11:00–11:20 **COFFEE BREAK AND NETWORKING**

11:20–12:00 **PODIUM SESSION 3: SENIOR PHD STUDENT PRESENTATIONS**
Session Chair: *Vignesh Krishnamoorthy*

11:20–11:30
Investigating the Biological Effects of G4 Destabilization on Telomere Maintenance in ALT Cancers
Presenter: *Chad Hou*

11:30–11:40
Applying an Intersectionality Lens to Characterizing Chronic Disease and Patient Outcomes: A Latent Class Analysis Using a Nationally Representative Sample of Adults with Arthritis in Canada
Presenter: *Megan M. Thomas*

11:40–11:50
Daily Fentanyl Usage Patterns Among People Using Unregulated Fentanyl and Utilizing Drug Checking Services
Presenter: *Sahithi Thotakura*

Schedule – continued

12:00–13:00 **LUNCH AND NETWORKING**

13:00–14:00 **KEYNOTE SPEAKER**
Dr. Matt Wright, Vice-President, DMPK at Arcus Biosciences
Opening and Closing Remarks: *Vignesh Krishnamoorthy and Chloe White*

14:00–14:05 **TRANSITION BREAK**

14:05–14:45 **PODIUM SESSION 4: POSTDOCTORAL FELLOW PRESENTATIONS**
Session Chair: *April St Pierre*

14:05–14:18
Transitions in Social Isolation and Diverse Participation and Effects on Cardiovascular Risk Factors (CVRFs): A Prospective Investigation of in Aging Women and Men in Canada
Presenter: *Gilciane Ceolin*

14:18–14:31
CRISPR Activation Screens Map the Genomic Landscape of Cancer-Associated Hypersialylation
Presenter: *John Daly*

14:31–14:44
Lung-Optimized Gene Editing in Human Cystic Fibrosis Models Following Topical Application of Lipid Nanoparticles
Presenter: *Tiffany Carlaw*

14:45–15:00 **COFFEE BREAK AND NETWORKING, TRANSITION TO POSTERS**

15:00–15:35 **POSTER SESSION 1 (ODDS)**
Junior MSc Student Poster Presentations

1. Auto-Fluorescent and Colorimetric Properties of G-Quadruplex Ligands Prompt Exploration of Alternative High-Throughput Assays for Cancer Cell Cytotoxicity Studies
Presenter: *Ilnigar Namat*

3. CRISPR Activation Screens Map the Genomic Landscape of Cancer-associated Hypersialylation
Presenter: *Lidia Piatnitca*

5. PRMT2 Influence on PRMT1 Methylation of Phosphorylated Nucleosomes
Presenter: *Maia Davey*

Schedule – continued

Senior MSc Student Poster Presentations

7. Rural–Urban Inequities In Oral Anticoagulant Prescribing Patterns In Atrial Fibrillation: A Scoping Review
Presenter: *Mahsa Eslami*

9. Effectiveness of Different Dosing Schedules for Pneumococcal Conjugate Vaccines on Invasive Pneumococcal Disease in Children: A Systematic Review and Meta-analysis
Presenter: *Jenny Cheng*

11. Plasma Oxylipins as Potential Biomarkers for Indomethacin Treatment Response in Preterm Infants with Patent Ductus Arteriosus
Presenter: *Khanh Nguyen*

Junior PhD Student Poster Presentations

13. Developing a Chemical-Genetic Screening Platform To Identify Receptors for Tumor-Associated Carbohydrate Antigens
Presenter: *Angeline Wu*

15. Potentiating the Multi-Kinase Activity of Trk-Selective Inhibitors for the Management of Chronic Pain in Osteoarthritis
Presenter: *Conall McCutcheon*

17. Bioinspired Peptide Amphiphile Nanofibre (PANF) Microgels for the Encapsulation of Bacteria
Presenter: *Noah Brittain*

Senior PhD Student Poster Presentations

19. The Impacts of Perinatal Loss on Work and Work Productivity
Presenter: *Jacynthe L'Heureux*

21. Rational Design of a Novel Adenosine Base Editor For Clinical Applications
Presenter: *Tessa Morin*

Postdoctoral Fellow Poster Presentations

23. Needle-free intranasal delivery of a protein-based vaccine for enhanced immune responses
Presenter: *Po-Yu Chou*

Schedule – continued

15:40–16:15

POSTER SESSION 2 (EVENS)

Junior MSc Student Poster Presentations

2. Impact of mRNA Size and Structure on Lipid Nanoparticle Morphology, Stability, and Potency
Presenter: *Janell Ko*

4. A Scoping Review of the Healthcare Impacts of Extreme Weather Events
Presenter: *Nazafarin Esfandiari*

6. Scoping Review: Strategies Utilized by Pharmacists and Pharmacy Students in Prescribing-Related Decision-Making
Presenter: *Priya Samuel*

Senior MSc Student Poster Presentations

8. Development of an *in-silico* Pharmacokinetic Platform for the Prediction of Monoclonal Antibody Distribution in the Brain
Presenter: *Andy Kim*

10. Ultra-Rapid Genetic Screening Reveals GCN2 as a Potential Regulator of Cancer-Associated Hypersialylation
Presenter: *Jimmy Kim*

12. The Impact of *RREB1* Overexpression and Knockdown on β-Cell Viability and Function in Type 1 Diabetes
Presenter: *Milda Kiravaityte*

Junior PhD Student Poster Presentations

14. Stimuli-Responsive Nanocomplexes for Targeted Antibiotic and Enzyme Codelivery to Treat Chronic Biofilm Infections
Presenter: *Chinekwu Nwagwu*

16. Investigating the Role of Endothelial Cell-Released Heparanase in Physiological Cardiac Hypertrophy
Presenter: *Gala Araujo*

Schedule – continued

Senior PhD Student Poster Presentations

18. GABA-Induced Invadopodia Formation Drives Metastasis in Triple Negative Breast Cancer
Presenter: *Esther Afolayan*

20. Bad to the Bone: Unmasking the Osteopontin Receptor in Metastatic Breast Cancer
Presenter: *Kendal Ruzicki*

22. The Glycosyltransferase ST3GAL4 drives Immune Evasion in Acute Myeloid Leukemia by synthesizing ligands for the glycol-immune checkpoint receptor Siglec-9
Presenter: *Vignesh Krishnamoorthy*

16:15–16:30

DOOR PRIZES
Jonas Olsen, PhD student, Venue and Logistics Co-lead

AWARDS CEREMONY
Ian Richmond, Senior Regional Manager, BC/Manitoba, Fisher Scientific

CLOSING REMARKS
Tom Chang, Professor and Associate Dean, Graduate and Postdoctoral Studies

Invited Speaker

Dr. Matthew Wright
UBC Pharm Sci BSc(Pharm), MSc, PhD
Vice-President, DMPK at Arcus Biosciences

Opening & Closing Remarks: *Chloe White and Vignesh Krishnamoorthy*

Matthew Wright started at UBC in his BSc, and continued to do his MSc and PhD in the Faculty of Pharmaceutical Sciences under the supervision of Dr. Jim Axelson. Upon graduating, he took a postdoc position at the University of Alberta and became an assistant professor at Dalhousie University. It was then that he made the jump into industry, first as a scientist at Dupont-Merck. He has spent the last 30 years in the pharmaceutical industry and has been a director at several different companies including Gilead, Tularik Inc., and most recently Genentech. Matt recently started at Arcus Biosciences where he is the Vice President of DMPK.

ARCUS BIOSCIENCES

Presentations

MSc Student Podium Presentations

Elucidating the Role of *RREB1* in Beta-cell and Diabetes

Presenter: *Woojung Kim*

Woojung Kim[1], Søs Skovsø[2], Luan Sambati[1], Niki Duan[1], Xiaoke Hu[3], Anna Tamakhina[3], Frank Han[1], Dorsa Sadeghi[1], James D. Johnson[3], & Nicole A. J. Krentz[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, Canada*
[2]*Valkyrie Life Sciences, Vancouver, Canada*
[3]*Department of Cellular and Physiological Sciences, Vancouver, Canada*

BACKGROUND
Variants in the Ras-responsive element binding protein1 (*RREB1*) locus have been associated with altered type 2 diabetes (T2D) risk and other traits, including fasting blood glucose. *RREB1* encodes for a zinc finger transcription factor, downstream of the Ras signaling pathway and is important for cell proliferation and differentiation. Loss of *RREB1* in human β-cell models reduces insulin content and impairs β-cell function *in vitro*. However, whether *RREB1* is similarly required for β-cell function and glucose homeostasis *in vivo* remains unknown.

METHODS
In this study, we used a constitutive $Ins1^{Cre}$ knock-in allele to specifically delete *RREB1* in β-cells of male and female mice. Over the experiment period, body weight was measured from 4 weeks of age to 15 weeks of age. Experiments including the measurement of random blood glucose, fasting blood glucose, and glucose tolerance tests were conducted.

RESULTS
Female homozygous *RREB1* knockout mice ($Ins1^{cre/wt}$; $RREB1^{fl/fl}$) weighed significantly more at 4 and 5 weeks of age compared to littermate controls ($Ins1^{cre/wt}$; $RREB1^{wt/wt}$). There were significant differences in fasting blood glucose levels at week 10 between male *RREB1* knockout mice and controls, as well as, female *RREB1* knockout mice had reduced random blood glucose levels at 8 weeks of age compared to controls. Both male and female *RREB1* homozygous knockout mice showed an improved glucose tolerance compared to littermate controls at 10 and 14 weeks of age. Lastly, female *RREB1* knockout mice showed improved c-peptide content over the controls.

CONCLUSION
Our preliminary results suggest, that contrary to previous data in human cellular β-cell models, loss of *RREB1* improves glucose homeostasis *in vivo* in mice. Our current study will determine the β-cell-specific role of *RREB1* in glucose homeostasis *in vivo* and will further clarify the mechanism by which variants in *RREB1* influence T2D risk.

MSc Student Podium Presentations

Development of SP1 Knockout Cell Lines for Characterization of SP1 Mediated Regulation of SAT1 Induction in Response to Doxorubicin Treatment

Presenter: *Janice Wu*

Janice Wu[1], Caroline Liang[1], & Thomas Velenosi[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND

Triple-negative breast cancer (TNBC) is a highly proliferative disease that is accompanied by challenges in drug resistance. Therefore, early identification of chemotherapy effectiveness is important for TNBC prognosis. Doxorubicin (DOX) treatment has been found to induce the expression of Spermidine/spermine N^1-acetyltransferase (SAT1), a metabolic enzyme involved in the production of diacetylspermine, a polyamine metabolite that acts as a urinary biomarker of DOX effectiveness. However, the mechanism behind this induction is still unknown. Two recent publications have proposed contrasting theories on this mechanism regarding the role of specificity protein 1 (SP1), a transcription factor known to bind the SAT1 promoter region. One theory supports SP1 as an SAT1 inducer, whereas another theory supports SP1 as a SAT1 repressor. The goal of this project is to characterize the role of SP1 in SAT1 induction upon DOX treatment in TNBC.

METHODS

Plasmid constructs containing CRISPR/Cas9 and a SP1-targeting single guide RNA were packaged into lentivirus for lentiviral transduction of the Hs578T and MDA-MB-231 TNBC cell lines. Single transduced cells were isolated through flow cytometry and cultured for growth. Sanger sequencing and western blot were used to identify and validate potential SP1 knockout (KO) clones.

RESULTS

Multiple SP1 KO clones in the Hs578T and MDA-MB-231 cell lines were successfully developed and validated through sanger sequencing and western blot. Hs578T clones with -1 and -17 nucleotide deletions and MDA-MB-231 clones with -1, -4, and -19 nucleotide deletions were identified. Western blot analysis confirmed the absence of the SP1 protein in all tested KO clones.

CONCLUSIONS

The development of SP1 KO cell lines provides the foundation to explore various theories regarding the role of SP1 on SAT1 induction. Investigating this mechanism may lead to a deeper understanding of urinary diacetylspermine as a biomarker of DOX effectiveness, with potential applications to other cancers and chemotherapies.

MSc Student Podium Presentations

Experiences of Partners of Patients Diagnosed with Cancer: A Systematic Review and Thematic Synthesis of Qualitative Literature

Presenter: *Preet Kang*

Preet Kang[1], Ursula Willis[2], & Mary A. De Vera[2]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*
[2]*Woodward Library, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
Cancer is a complex diagnosis, which impacts the patient as well as the patient's community. Partners of cancer patients often experience emotional and lifestyle changes, demonstrating the profound indirect impact of the disease. Our objective was to conduct a systematic review and thematic synthesis of qualitative studies on experiences of partners of cancer patients.

METHODS
We searched online databases for English-language, qualitative studies capturing the experiences of partners of cancer patients. We extracted findings from included studies and applied thematic synthesis to develop descriptive and higher-order analytical themes.

RESULTS
Our search identified 9,212 records. Of 9 included studies, our analysis identified themes of 1) emotional burden on the relationship 2) changes in sexuality of partners 3) need for support from health care providers 4) partners' experience of the diagnosis and 5) benefits of partners' support to the patient. Cancer significantly impacted relationship dynamics, often adding strain. The strain was mitigated by couples through coping strategies, such as extensive communication and counselling. Partners expressed the need for support to equip both themselves and patients with strategies to navigate the cancer diagnosis.

CONCLUSIONS
This study identified the challenges faced by partners of cancer patients, highlighting the need to recognize the impact of cancer on them as well. These findings emphasize the importance of raising awareness and advocating for support and resources not only for patients but also for their partners.

MSc Student Podium Presentations

Implications of Circulatory Protein Adhesion on Lipid Nanoparticle Pharmacokinetics

Presenter: *Kevin Fox*

Kevin Fox[1,2], Suiyang Liao[1,3], Miffy Cheng[2], Colin Ross[2], & Pieter Cullis[1]

[1]Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, British Columbia, Canada
[2]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia, Canada
[3]Michael Smith Laboratories, University of British Columbia, Vancouver, British Columbia, Canada

BACKGROUND

Lipid nanoparticles (LNPs) have revolutionized the field of drug delivery by enabling the encapsulation of ribonucleic acid (RNA). Initial development of LNPs has produced a pharmacokinetic profile which targets the liver with rapid blood clearance following IV injection, earning LNP-RNA its first clinical approval in 2018 for hereditary amyloidosis. To address the need for extra-hepatic delivery and extended circulation times, this work aims to investigate the role of circulatory protein adhesion on the pharmacokinetics of long circulating LNP systems. Data from *in-vivo* radiolabeling and *in-vitro* mass spectrophotometry proteomics shows that formulations which bind the least protein circulate the longest and target the most extra-hepatic tissues. We anticipate this discovery will allow for targeting of LNP delivered gene therapies beyond the liver.

METHODS

1. LNP Formulations and Characterization: LNP-RNA were formulated as previously described, with fluorescent dye for *in-vitro* work, and tritium for *in-vivo*.
2. *In-Vitro* Proteomics: LNP-RNA were incubated in mouse plasma for 1hr. Incubations were passed through a column prior to analyzing lipid:protein ratios by fluorescent assays, and protein identity by mass spectrophotometry by UBC's Proteomics Core.
3. *In-Vivo* Radiolabeling: Mice were injected with 0.5mg/kg of RNA and 1 uCi tritium by BC Cancer's Pharmacore.

RESULTS

LNPs showed consistent particle size, polydispersity, and RNA encapsulation. *In-Vitro* plasma Incubations produced a unique proteomics profile for each formulation. Formulations which bound less protein *in-vitro*, particularly clotting, coagulation, and complement factors, showed increased circulation and biodistribution *in-vivo*.

CONCLUSIONS

Confirming the impact of circulatory protein adhesion on LNP pharmacokinetics, this work validates the potential for extra-hepatic delivery of LNP-RNA. As LNP circulation half-life is extended beyond the 50 minutes of clinically approved formulations, active targeting strategies will foreseeably have a greater chance of success.

MSc Student Podium Presentations

Targeted Synthetic Disease-Modifying Antirheumatic Drugs in Pregnancy: Patterns of Use Among Females with Autoimmune Diseases and Maternal-Neonatal Outcomes

Presenter: *Vienna Cheng*

Vienna Cheng[1], Neda Amiri[2], Jacquelyn J. Cragg[1], Mark Harrison[1], & Mary A. De Vera[1]

[1]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada
[2]Division of Rheumatology, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada

BACKGROUND
Targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs) have significantly expanded treatment of autoimmune diseases in the recent decades. However, these diseases often strike during the childbearing years and many disproportionately affect females more than males. As the use of these drugs grows, there is a critical need to characterize the utilization of tsDMARDs and evaluate maternal-neonatal outcomes in order to generate evidence on their safety during pregnancy.

METHODS
Using population-based administrative data linkages from Population Data British Columbia (BC), BC PharmaNet and BC Perinatal Data Registry, we generated summary statistics of the demographics of 29,749 females with autoimmune diseases who filled ≥1 tsDMARD prescription in BC between January 1, 2002, to December 31, 2022. We characterized 19 pregnancies that filled ≥1 tsDMARD prescription during the perinatal period (1 year before, during and 1 year after pregnancy), and described their patterns of drug utilization and maternal-neonatal outcomes.

RESULTS
Among our study cohort of 49,220 pregnancies and 50,111 babies in 29,749 females diagnosed with autoimmune diseases, the most common conditions were psoriasis/psoriatic arthritis (n = 10,541, 35.4%), rheumatoid arthritis (n = 7,818, 11.3%) and inflammatory bowel disease (n = 4,731, 15.9%). A total of 17,084 tsDMARD prescriptions were filled by 2,423 females, with an increasing trend over the 20 years. Of 19 pregnancies that filled ≥1 tsDMARD prescription during the perinatal period, 26% discontinued their tsDMARD within the first trimester. In terms of outcomes, 58% of pregnancies were delivered via Caesarean section, 58% of pregnancies experienced preterm membrane rupture and 26% delivered a preterm baby.

CONCLUSION
To our knowledge, our study is the first to describe the patterns of tsDMARD utilization in BC and their related maternal-neonatal outcomes. Our findings have important implications for facilitating future evidence synthesis and thus informing clinical decision-making during pregnancy for physicians and patients with autoimmune diseases.

MSc Student Podium Presentations

Effect of Ischemic Stroke on Subsequent Oral Anticoagulant Adherence in Patients with Atrial Fibrillation: A Scoping Review

Presenter: *Aashiq Ahamed Shukkoor*

Aashiq Ahamed Shukkoor[1], Peter Loewen[1], Mary De Vera[1], Mark Harrison[1], Ricky Turgeon[1], & Nimmy Elizabeth George[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
Atrial fibrillation (AF) increases ischemic stroke risk, and while oral anticoagulant (OAC) therapy is essential for prevention, post-stroke adherence remains a challenge. This study aimed to investigate the association, potential causal relationship and factors influencing OAC adherence following ischemic stroke in AF patients.

METHODS
In February 2023, we conducted a scoping review of observational studies from PubMed/Medline, Embase, and Web of Science (from inception) to explore the association and causality between ischemic stroke and subsequent OAC adherence in AF patients. Bradford Hill's (BH) criteria were used to assess the causal relationship between ischemic stroke and subsequent OAC adherence in these patients.

RESULTS
The analysis included 42 studies on OAC adherence across different phases: initiation (n=1), implementation (n=14), implementation and discontinuation (n=7), and persistence (n=20). Of these, 25 studies showed a positive association between ischemic stroke history and OAC adherence, while one showed a negative association. The evaluation of the body of evidence suggests a strong association between ischemic stroke and subsequent OAC adherence. While causality isn't definitively established, BH's criteria (temporality, consistency, biological gradient, coherence, plausibility) support a potential causal link between ischemic stroke and subsequent OAC adherence in AF patients. Patients experiencing first ever stroke was positively associated with OAC adherence, while factors like age, COPD, cancer, heart failure, hypertension, myocardial infarction, anemia, dementia, smoking, prior warfarin use, education level, and stroke severity and recurrence were negatively associated.

CONCLUSIONS
While a strong association exists between ischemic stroke and OAC adherence in AF patients, causality remains inconclusive. Given the ethical constraints of randomized trials, further observational studies using causality methods are needed to definitively confirm this causal effect.

Junior PhD Student Podium Presentations

Taking nanomedicine down a PEG: mRNA-LNP formulations using PEG alternatives

Presenter: *April St Pierre*

April St Pierre[1] & Shyh-Dar Li[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
mRNA therapeutics are a Nobel-prize-winning development that promises to give scientists the ability to easily and effectively dose patients with virtually any protein-based therapeutic, by giving the body's cells the mRNA instructions to make it themselves. To make this concept a reality, mRNA is encapsulated in lipid nanoparticles (LNP) to protect it from degradation and help it enter cells.

Current LNP technologies for mRNA delivery incorporate a poly-ethylene glycol (PEG) lipid, which can help avoid aggregation and increase circulation time, but can also induce anti-PEG antibodies. In cases of repeated LNP administration, these may lead to accelerated clearance (decreasing drug efficacy), and also cause undesirable reactions[1]. Thus, we propose new LNP formulations containing a simple PEG alternative molecule.

METHODS
mRNA-LNP were formulated using PEG-alternatives and tested to determine the effect of substituting PEG on LNP uptake into cells, and mRNA expression. LNP were also characterized for size, surface charge and encapsulation efficiency.

RESULTS
Our PEG-free LNP show promising results as an alternative to typical PEG-containing LNP. PEG-free LNP can be successfully formulated, and show favourable mRNA expression in cell culture compared to PEG-containing LNP.

CONCLUSIONS
Our results indicate that PEG-free LNP are an interesting alternative to currently approved mRNA-LNP formulations, particularly for applications that may require repeat dosing and thus particular concern about anti-PEG antibodies. Further experiments will seek to continue to elucidate the differences between PEG-free and typical LNP formulations, including the mechanisms of their uptake into cells and their pharmacokinetics.

REFERENCES
1. Gergely Tibor Kozma, Taro Shimizu, Tatsuhiro Ishida, Janos Szebeni. Anti-PEG antibodies: Properties, formation, testing and role in adverse immune reactions to PEGylated nano-biopharmaceuticals. *Advanced Drug Delivery Reviews* 154–155, 163–175 (2020).

Junior PhD Student Podium Presentations

What's in a Choice? A Study of the Medication Preferences of People with Heart Failure

Presenter: *Blair MacDonald*

Blair MacDonald[1], Logan Trenaman[2], Nick Bansback[3,4], Mark Harrison[1,4], & Ricky Turgeon[1,4]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia*
[2]*School of Public Health, University of Washington*
[3]*School of Population and Public Health, Faculty of Medicine, University of British Columbia*
[4]*Centre for Advancing Health Outcomes, St. Paul's Hospital*

BACKGROUND
Heart failure affects approximately 800,000 Canadians, impairing their quality of life, lowering their chances of survival, and increasing their risk of hospitalization. Heart failure medications have the potential to substantially improve these outcomes but at the expense of increased pill burden, risk of side effects, and cost. Research into the preferences of people with heart failure is necessary to support the navigation of these potentially difficult trade-offs.

METHODS
We conducted a discrete choice experiment in people with heart failure from across Canada. Participants were presented with a series of 12 choices, each involving a decision between one of two drug regimens or no additional medication. These choices were described according to six key heart failure medication attributes (quality of life, survival, hospitalization, side effects, cost, and pill burden). The results were analyzed using conditional logistic regression to estimate aggregate preferences and latent class analysis to identify subgroups with distinct preferences.

RESULTS
Among the 202 participants, the mean age was 63 years old and 43% were female. Of the assessed attributes, cost, survival, and quality of life were of high relative importance, hospitalization was of moderate importance, and adverse effects and pill burden were of lower importance. Latent class analysis revealed three preference subgroups: those who were primarily concerned with maximizing medication efficacy (53%), those who tended to avoid the most expensive options but still wanted to take some medication (38%), and those who focused primarily on minimizing costs, pill burden, and side effects (9%).

CONCLUSIONS
In the context of heart failure medication choices, people are primarily concerned about the trade-off between efficacy and cost. However, this is not universal as some people are primarily concerned with minimizing medication downsides. These nuances indicate a need for the development of a heart failure medication decision aid that can support personalized decision-making.

Junior PhD Student Podium Presentations

The Small Molecule Aggregation Rescue of Target Assay: A *SMART* Approach to Drug Discovery

Presenter: *Dan Everton*

Daniel K. Everton[1], Adam Frankel[1], & Brent D. G. Page[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND

Target engagement assays are essential drug discovery tools, enabling the detection and quantification of physical interactions between experimental compounds and their protein target(s) in cellular settings. Ligand binding can protect proteins from unfolding caused by exogenous stressors; demonstrating ligand-induced target rescue can validate experimental compound-target interactions. Conventional target engagement assays use heat to disrupt protein folding; however, heat-based assays have intrinsic limitations concerning analyte compatibility, undesired reactivity, and physiological pertinence. We developed an innovative heat-free target engagement technique—the *Small Molecule Aggregation Rescue of Target* (SMART) assay—that employs small molecule destabilizers (SMDs) to induce protein instability, from which ligand binding can be characterized via rescue of protein stability.

METHODS

This project employs dihydrofolate reductase (DHFR), Nudix-type hydrolase 5 (NUDT5), and signal transducers and activators of transcription 1 and 3 (STAT1 and STAT3) as protein targets. SMD-1, recombinant proteins, and breast cancer cells are used for assay validation investigations, wherein centrifugation and Western blotting facilitate the detection of changes in soluble target protein levels. SMD-1 and its analogues were synthesized chemically.

RESULTS

SMD-1 destabilized all protein targets in biochemical and cellular settings. Using established inhibitors, ligand-induced rescue of target stability was demonstrated in biochemical settings for all targets, and in cellular lysate for DHFR and NUDT5. SMD-1 reacts with end-protected cysteine in a biochemical environment at physiological conditions, but two SMD-1 analogues—each with the suspected reactive group modified—did not react. When tested in the SMART assay instead of SMD-1, both analogues produced a slight target destabilization effect; however, they were significantly weaker than SMD-1.

CONCLUSIONS

The SMART assay successfully facilitates target engagement characterization for diverse protein targets, without heat. SMD-1 has detergent-like molecular properties and may covalently modify cysteine residues; likely, the combination of these factors disrupts protein folding to promote aggregation.

Junior PhD Student Podium Presentations

Population-based Case-Control Study of Antidepressants and Early-Age Onset and Average-Age Onset Colorectal Cancer: The Impact of Exposure Window, Class, Dose, and Intensity

Presenter: *Vicki Cheng*

Vicki Cheng[1,2], Eric C. Sayre[3], Vienna Cheng[1,2], Jonathan M. Loree[4,5], Sharlene Gill[5], Rachel A. Murphy[4,6], & Mary A. De Vera[1,2,7]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*
[2]*Collaboration for Outcomes Research and Evaluation, Vancouver, BC, Canada*
[3]*British Columbia Centre on Substance Use, Vancouver, BC, Canada*
[4]*BC Cancer, Vancouver, BC, Canada*
[5]*University of British Columbia, Faculty of Medicine, Division of Medical Oncology, Vancouver, BC, Canada*
[6]*University of British Columbia, School of Population and Public Health, Vancouver, BC, Canada*
[7]*Centre for Health Evaluation and Outcome Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
Previous epidemiologic studies have yielded inconsistent findings on the association between antidepressants and colorectal cancer (CRC). We sought to conduct a rigorous and comprehensive investigation to clarify the relationship between antidepressant use and CRC, including consideration of early age onset (EAO; diagnosed <50 years) and average age onset (AAO; diagnosed ≥50 years) CRC.

METHODS
We conducted a population-based case-control study using administrative health databases from British Columbia, Canada. We included CRC cases and controls, matched (1:10) on age, sex, and index date (i.e., CRC diagnosis date/matched date). Exposure to antidepressants was ascertained according to duration (e.g., varying windows from 15 to 1 year before CRC diagnosis), class, dose, and intensity. We used multivariable conditional logistic regression models and interpreted odds ratios as relative risks.

RESULTS
We included 10,171 cases with CRC (688 EAO-CRC; 9,483 AAO-CRC) and 90,928 controls. The use of antidepressants in the 15-year window before diagnosis was associated with a reduced risk of CRC overall (adjusted relative risk [aRR] 0.84; 95% CI 0.80, 0.89), as well as for both EAO-CRC (aRR 0.54; 95% CI 0.44, 0.66) and AAO-CRC (aRR 0.87; 95% CI 0.83, 0.92). An apparent trend was observed across narrowing exposure windows, with the association remaining evident and significant up to the 7-year window before diagnosis, then weakening in shorter exposure windows. We also observed inverse associations between the use of non-selective monoamine reuptake inhibitors (aRR 0.83; 95% CI 0.77, 0.89) and selective serotonin reuptake inhibitors (aRR 0.86; 95% CI 0.81, 0.91) and the risk of CRC.

CONCLUSIONS
Our large, population-based study identified an inverse association between antidepressant use and CRC across all age groups, with the strongest effect observed at the 15-year exposure window, particularly in EAO-CRC. Findings offer insights into how drug-related factors, particularly antidepressant use, may potentially influence the etiology of CRC.

Senior PhD Student Podium Presentations

Investigating the Biological Effects of G4 Destabilization on Telomere Maintenance in ALT Cancers

Presenter: *Chadwick Hou*

Chadwick Hou[1], Robert Hudson[2], David Monchaud[3], & Judy Wong[4]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*
[2]*Department of Chemistry, University of Western Ontario, London, ON, Canada*
[3]*Institut de Chimie Moléculaire, 'Université de Bourgogne, Burgandy, France*

BACKGROUND
To achieve replicative immortality, ~15% of cancers maintain their telomeres using a recombination-based telomere maintenance mechanism called alternative lengthening of telomeres (ALT). ALT telomere elongation is initiated by telomeric DNA damage, which is repaired with break-induced telomere synthesis (BITS). G-quadruplexes (G4s) are enriched in the G-rich telomere strand of ALT+ cancers and facilitate the binding of telomere repeat-containing RNA (TERRA) to the C-rich strand, forming an R-loop. G4s and R-loops mediate telomeric DNA damage. As such, G4 destabilization using molecular ligands could decrease ALT-initiating DNA damage and BITS, making it a potential ALT-specific therapeutic mechanism. We tested the first-in-class G4-destabilizing molecule phenylpyrrolocytosine-based G-clamp (PhpC) for its utility as an ALT inhibitor. PhpC transiently captures base-flipped guanines in G4s, destabilizing the columnar structure. To further develop PhpC as an anti-ALT therapeutic agent, we used cellular assays to characterize its *in vitro* DNA-G4 interactions and biological effects.

METHODS
Immunocytochemistry (ICC) and chromatin immunoprecipitation (ChIP) were used to quantify G4 and R-loop abundance after PhpC treatment in the ALT+ osteosarcoma cell line U2OS. ICC and ChIP were also used to quantify telomeric DNA damage. Cell death assays were used to track PhpC's toxicity in U2OS after 5 days of PhpC treatment, while real-time PCR was used to measure telomere length over 2 weeks of continuous PhpC exposure.

RESULTS
PhpC reduces telomeric G4 abundance in ALT+ cancers. G4 destabilization causes the reduction of TERRA-mediated R-loops, suppressing ALT-initiating telomeric DNA damage. PhpC treatment induces ALT+ cancer-specific toxicity 5 days following single dose PhpC treatment, while continuous PhpC exposure causes telomere attrition over 2 weeks of treatment.

CONCLUSIONS
Treatment with the G4-destabilizing agent PhpC inhibits ALT telomere maintenance and is selectively toxic in ALT+ cancers. Our study highlights the biological relevance of G4s, and implicates G4 destabilization as a promising ALT-specific therapeutic strategy.

Senior PhD Student Podium Presentations

Applying an Intersectionality Lens to Characterizing Chronic Disease and Patient Outcomes: A Latent Class Analysis Using a Nationally Representative Sample of Adults with Arthritis in Canada

Presenter: *Megan M. Thomas*

Megan M. Thomas[1,2], Eric C. Sayre[3], Mark Harrison[1,4], Cheryl Barnabe[5,6], Charlene E. Ronquillo[7], J. Antonio Avina-Zubieta[1,2], Anna Samson[8], Michael Kuluva[9], Natasha Trehan[10], Nikki Bhatti[2], & Mary A. De Vera[1,2]

[1]The University of British Columbia, Vancouver, British Columbia, Canada
[2]Arthritis Research Canada, Vancouver, British Columbia, Canada
[3]British Columbia Centre on Substance Use, Vancouver, British Columbia, Canada
[4]Centre for Advancing Health Outcomes, Vancouver, British Columbia, Canada
[5]University of Calgary, Calgary, Alberta, Canada
[6]McCaig Institute for Bone and Joint Health, Calgary, Alberta, Canada
[7]The University of British Columbia Okanagan, Kelowna, British Columbia, Canada
[8]Canadian Arthritis Patient Alliance, Ottawa, Ontario, Canada
[9]Creaky Joints, Vancouver, British Columbia
[10]University of Ottawa, Ottawa, Ontario, Canada

BACKGROUND
Social determinants of health (SDOH) such as sex, gender, race, and socioeconomic status, are associated with the burden of chronic diseases such as arthritis. However, associations have largely utilized variable-centered approaches to consider independent factor effects, which do not account for relationships between factors.

METHODS
Applying the Campbell and Cochrane Equity Methods Group's PROGRESS-Plus framework on risk factors that lead to inequities in health (Place of residence; Race, ethnicity; Occupation; Gender, sex; Religion; Education; Socioeconomic status; Social capital), our overall aim was to understand how SDOH intersect and impact arthritis burden. Leveraging rich data from the Canadian Community Health Survey (CCHS), we conducted latent class analysis (LCA) to develop distinct profiles of people with arthritis and evaluate the intersection of SDOH. We then conducted logistic regression on the resultant model to consider how these factors impact perceived health, perceived mental health, and satisfaction with life in general for people living with arthritis.

RESULTS
Of 113,290 total respondents to the CCHS, 22,148 respondents had arthritis. After conducting LCA, we identified five distinct class profiles of people living with arthritis in Canada. Those who were White and married had the highest odds of experiencing better perceived health (OR:1.27; 95% CI:1.18-1.37; p-value<0.001), mental health (OR:1.64; 95% CI:1.52-1.76; p-value<0.001) and satisfaction with life (OR:1.68; 95% CI:1.55-1.81; p-value<0.001). Those who were older, female, and living alone had the lowest odds of experiencing better perceived health (OR:0.81; 95% CI:0.75-0.88; p-value<0.001), second-lowest odds of better mental health (OR:1.08; 95% CI:0.99-0.1.17; p-value=0.07) and lowest odds of satisfaction with life (OR:0.79; 95% CI:0.72-0.85; p-value<0.001).

CONCLUSIONS
An intersectional lens is required to consider how SDOH are linked to one's well-being to provide equitable care and improve outcomes. Though this work focuses on arthritis, there are applications to other fields, particularly chronic diseases where SDOH are important to consider.

Senior PhD Student Podium Presentations

Daily Fentanyl Usage Patterns Among People Using Unregulated Fentanyl and Utilizing Drug Checking Services

Presenter: *Sahithi Thotakura*

Sahithi Thotakura[1], Lianping Ti[2], & Anil Maharaj[1]

[1]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver BC, Canada
[2]British Columbia Centre for Substance Use, Vancouver, BC, Canada

BACKGROUND
In Canada, fentanyl, a highly potent opioid is detected in approximately 80% of the opioid-related toxicity deaths since 2016. Over the past decade, exposure to unregulated fentanyl has shifted from accidental to intentional, with many people who use unregulated opioids now preferring fentanyl. However, there is no information on the amount of fentanyl administered by people who use unregulated fentanyl (PWUUF). Quantifying the use of fentanyl in PWUUF is crucial to evaluate their overdose risk and initiate appropriate harm reduction strategies. In this study, we aimed to quantify the daily amount of unregulated fentanyl administered by PWUUF.

METHODS
Participants who answered questions on unregulated fentanyl usage patterns and submitted samples to drug checking services in British Columbia between December 2022 to July 2024 were included. Two datasets were integrated to estimate the daily amount of unregulated fentanyl used by participants: (1) Questionnaire results of self-reported unregulated fentanyl use and (2) Sample analysis results with proportion of fentanyl determined by Fourier-transform infrared analysis. Descriptive analysis was conducted to summarize the unregulated fentanyl usage patterns including the average amount used in a day, frequency and route of administration.

RESULTS
89 participants were included in the study, with a mean age of 41 years. The mean (%CV) daily amount of unregulated fentanyl used is 206.5 mg (181%), with a minimum of 106.2 mg (230%) and a maximum of 418 mg (154%). Majority of the participants (88%) reported inhaling unregulated fentanyl. Additionally, most participants (38%) indicated using it more than six times a day.

CONCLUSIONS
This study is the first to quantify the daily amount of unregulated fentanyl used, providing essential data to evaluate overdose risk and initiate appropriate harm reduction strategies. Additionally, this data will be used to identify patient level factors associated with high and low doses of unregulated fentanyl use.

Postdoctoral Fellow Podium Presentations

Transitions in Social Isolation and Diverse Participation and Effects on Cardiovascular Risk Factors (CVRFs): A Prospective Investigation of in Aging Women and Men in Canada

Presenter: *Gilciane Ceolin*

Gilciane Ceolin[1], Gerry Veenstra[2], Nadia A. Khan[3,4], Rana Madani Civi[1], Sanaz Mehranfar[5], & Annalijn I. Conklin[1,4,5,6]

[1]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada.
[2]Department of Sociology, Faculty of Arts, University of British Columbia, Vancouver, BC, Canada
[3]Division of General Internal Medicine, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada
[4]Centre for Advancing Health Outcomes, Providence Healthcare Research Institute, St. Paul's Hospital, Vancouver, BC, Canada
[5]Faculty of Land and Food Systems, University of British Columbia, Vancouver, BC, Canada.
[6]Edwin S.H. Leong Centre for Healthy Aging, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada

BACKGROUND
Social connections matter for longevity and mortality. However, our social environment changes as we age and current literature does not capture the impact of alterations in different social ties on cardiovascular risk factors in the older population.

METHODS
A population-based, prospective study of adults (45+ years) using 3 waves of Canadian Longitudinal Study on Aging data (2011-2021). Stratified, logistic regression on multiple imputed datasets analyzed transitions in social isolation (≤1 monthly activity) and diverse participation (≥5 monthly activities) in relation to new-onset hypertension (self-reported or 140 mm Hg and/or 90mm/Hg; for diabetes: 130/80mm/Hg) and central obesity (women ≥88 cm and men ≥102 cm) in 13,773 women and 13,086 men.

RESULTS
The final multivariable-adjusted models showed that only women remaining isolated across Wave 1 and 2 were significantly more likely to develop hypertension (OR 1.63 [CI95%: 1.05, 2.53]) compared to those remaining not isolated; and, women remaining less diverse in their social activities were significantly more likely to develop central obesity (1.20 [1.04, 1.39]) compared to those maintaining social diversity. No significant associations were observed among men.

CONCLUSION
Results showed distinct alterations in different social ties have unique impacts on health that are gendered. Older women in Canada were particularly vulnerable to adverse effects of persistent isolation and persistent lack of social diversity on cardiovascular risk factors.

Postdoctoral Fellow Podium Presentations

CRISPR Activation Screens Map the Genomic Landscape of Cancer-Associated Hypersialylation

Presenter: *John Daly*

John Daly[1], Lidia Piatnica[1], Mohammed Al-Seragi[1], Vignesh Krishnamoorthy[1], & Simon Wisnovsky[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
The activity of the human immune system is finely controlled by signaling receptors expressed on the surface of immune cells. Many cancer types have been shown to upregulate the expression of sialic acid-containing glycans on the tumor cell surface. These oligosaccharides subsequently engage inhibitory sialic acid-binding Siglec receptors on immune cells, allowing cancer cells to evade immune surveillance and contributing to metastasis. However, the genetic mechanisms by which this glycome remodeling occurs remain poorly defined.

METHODS
In this study, we performed multiple gain-of-function CRISPR activation (CRISPRa) screens to broadly define genetic pathways that regulate expression of Siglec-binding glycans. We subsequently leverage this dataset to validate numerous important insights into cancer glycome remodeling and to identify specific targets for cancer immunotherapy.

RESULTS
We show that Siglec ligand expression is largely controlled through genetic competition between genes that catalyze α2-3 sialylation and GlcNAcylation of galactose residues. Disturbance of enzyme expression at this key biosynthetic node provides multiple "paths" by which cancers can acquire elevated expression of Siglec ligands. We show that cancer glycome remodeling is aided by overexpression of novel "professional ligands" that facilitate Siglec-glycan binding. Notably, we also find that expression of the CD24 gene is genetically dispensable for cell-surface binding of the inhibitory receptor Siglec-10. Finally, by integrating our functional genetic model with clinical tumor genomic data, we identify the sulfotransferase enzyme GAL3ST4 as a novel driver of immune evasion in glioma cells.

CONCLUSION
Taken together, this study provides a first-in-class genomic atlas to aid understanding of cancer-associated glycosylation and identifies immediately actionable targets for cancer immunotherapy.

Postdoctoral Fellow Podium Presentations

Lung-Optimized Gene Editing in Human Cystic Fibrosis Models Following Topical Application of Lipid Nanoparticles

Presenter: *Tiffany Carlaw*

Tiffany Carlaw[1,2], Belal Tafech[1], Gaurav Sadhnani[3], Tessa Morin[1], Jerry Leung[4], January Weiner[3], Kevin An[5], Anita Balász[6], Colin Ross[1], Dieter Beule[3], Marcus A. Mall[3,6], Hendrik Fuchs[6], Jay Kulkarni[5], Pieter R. Cullis[4,5], & Sarah Hedtrich[1,2,3]

[1]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada
[2]School of Biomedical Engineering, University of British Columbia, Vancouver, BC, Canada
[3]Center for Biological Design, Berlin Institute of Health @ Charité, 13125 Berlin, Germany
[4]Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, British Columbia, Canada
[5]NanoVation Therapeutics, 2405 Wesbrook Mall, Vancouver, BC, Canada
[6]Department of Pediatric Respiratory Medicine, Immunology and Critical Care Medicine and Cystic Fibrosis Center, Charité Universitätsmedizin Berlin, 13353 Berlin, Germany

BACKGROUND
Cystic fibrosis (CF) is a severe monogenic disease characterized by debilitating lung dysfunction caused by loss-of-function mutations in the CFTR gene. While CRISPR-based gene editing holds promise for treating and potentially curing CF, efficient delivery of gene editors to the lung epithelium remains a major challenge. Mucosal surfaces of lung epithelia pose a challenging barrier for the delivery of therapeutics (currently no approved nanoparticles for lung delivery). Formulations must address the complex nature of the mucus gel to reach the underlying epithelium. Mucus gel has dynamic motion due to the continuous secretion, shedding and beating cilia; steric obstruction, owing to the size filtration properties of the mucus; adhesive interactions; and its heterogenic composition and thickness.

METHODS
In this study, we developed a lung-targeted gene editing strategy using lipid nanoparticles (LNPs) and evaluated it in increasingly complex, biomimetic human-based models. We tested LNP delivery strategies in both 2D primary bronchial cell culture and 3D human lung models.

RESULTS
Systematic optimization of helper lipids, genetic cargo and guide RNA modifications achieved ~50% editing efficiency in 2D models. However, editing efficiency dropped to ~5% in 3D CF bronchial epithelial tissue models following topical LNP application. To overcome the mucosal layer, we pretreated with the approved mucolytic agent dornase alpha, which improved editing efficiency nearly two-fold, to a clinically relevant ~10%. Finally, in CF patient-derived cells harboring the $CFTR^{R1162X}$ mutation, our optimized LNP formulation achieved ~12% correction, offering a potential treatment avenue for this untreatable mutation.

CONCLUSION
This study demonstrates that optimizing the genetic cargo as well as the delivery vehicle is key when striving for clinically applicable treatment approaches. It further provides insights into gene editing rates in bronchial tissue models which express all relevant biological barriers and, thus, can pave the way for new treatment options for lung diseases.

Junior MSc Student Poster Presentations

1. Auto-Fluorescent and Colorimetric Properties Of G-Quadruplex Ligands Prompt Exploration of Alternative High-Throughput Assays for Cancer Cell Cytotoxicity Studies

Presenter: *Ilnigar Namat*

Ilnigar Namat[1] & Judy MY Wong[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
G-quadruplexes (G4s) are found enriched in numerous malignancies, including breast cancers. Thus, G4 ligands are potential cancer therapeutics, where their G4-stabilizing effect induces replication fork collapse and eventual cancer cell death. In the case of breast cancer, novel G4 ligands are currently being tested for homologous recombination repair-deficient subtypes. However, studying the cytotoxicity of G4 ligands in a high-throughput manner is challenging, as these small-molecules' auto-fluorescent property precludes the use of existing cell death assays, which rely on fluorescent DNA stains. While cell confluency measurement is an optically unbiased approach, it does not distinguish between viable, dead, and senescent cells. In the present study, we systemically evaluate available dose-response assays that assess cell death and/or viability associated with the cytotoxicity of fluorescent chemotherapeutic compounds. RHPS4—a G4 ligand with significant auto-fluorescent emission across the visible light spectrum—will be used as the prototype G4 ligand.

METHODS
We quantified RHPS4-induced cell death in T47D breast cancer cells in the live-cell imaging platform Incucyte by using either red EthD1 or green YOYO1 dye, both of which fluoresce upon binding to DNA within dead cells' nuclei. Conversely, T47D cell viability at endpoint of RHPS4 treatment was measured by WST-1 colorimetric assay. WST-1 solution absorbance at 450nm, which correlates with viable cell metabolism, was obtained by the Pherastar plate-reader.

RESULTS
RHPS4-treated T47D cells displayed RHPS4 dose-dependent fluorescent signals even in absence of EthD1 and YOYO1 dead-cell dyes. Similar interference was observed in WST-1 analyses, where RHPS4's inherent red hue distorted 450nm absorbance readings.

CONCLUSIONS
RHPS4 shows incompatibility with standard fluorescent and colorimetric readouts such as EthD1/YOYO1 dyes and WST-1. We are experimenting with other cell death and viability assays to generate dose-response curves. Once refined, we will employ our approach to validate existing RHPS4-treated T47D cell confluency data.

Junior MSc Student Poster Presentations

2. Impact of mRNA Size and Structure on Lipid Nanoparticle Morphology, Stability, and Potency

Presenter: *Janell Ko*

Janell Ko[1], Jerry Leung[2], Emma Kang[2], Michelle Tong[2], Hemashree Bommadevara[2], Nicolas Salcedo[2], Yao Zhang[2], Madelaine Robertson[2], Colton Strong[2], Kevin Fox[1,2], Eric Jan[2,] Pieter R Cullis[2], & Miffy HY Cheng[1]

[1]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada
[2]Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, BC, Canada

BACKGROUND
Lipid nanoparticle (LNP) delivery systems have shown immense potential for gene therapy and vaccine applications, enabling efficient delivery of RNA therapeutics. Recent studies have highlighted the impact of LNP morphology on transfection potency, such as the formation of mRNA-rich "bleb" structures, where mRNA is sequestered into the aqueous pocket of the LNP, enhancing mRNA stability and transfection efficacy. However, it is unclear how mRNA characteristics such as length and structure might impact LNP structural features and transfection potency, as induction of bleb structures has been shown to be dependent on formulation conditions. Understanding how different mRNA properties influence bleb formation is critical for enhanced transfection to maximize the therapeutic potential of LNP-mRNA delivery systems.

METHODS
LNPs comprised of KC2, DSPC, cholesterol, and PEG-DMG encapsulating mRNA of various lengths between 2-10 kb, and with different internal ribosome entry sites (IRES) or superfolder structures were formulated in pH 4 25 mM NaOAc or 300 mM Na-citrate buffer to induce bleb formation. LNP stability was analyzed through measurement of size and encapsulation efficiency, while LNP morphology was assessed by Cryo-TEM imaging.

RESULTS
LNPs formulated with varying mRNA lengths and structures were stable over 14 days at 4oC, with no substantial changes in particle size (40–70 nm), PDI (~0.1), and encapsulation efficiency (>90%). Cryo-EM showed that in the presence of 300 mM Na-citrate, most LNP formulations formed bleb structures, including LNPs encapsulating large mRNA, mRNA with structured IRES, and with superfolder structures. While only mRNA with less rigid IRES structures prevented bleb formation.

CONCLUSIONS
The findings of this study demonstrate the influence of mRNA structural differences on LNP morphology. Future studies will investigate the role of mRNA structure on mRNA integrity, mRNA translatability, and transfection potency of LNP-mRNA.

Junior MSc Student Poster Presentations

3. CRISPR Activation Screens Map the Genomic Landscape of Cancer-associated Hypersialylation

Presenter: *Lidia Piatnitca*

John Daly[T,1], Lidia Piatnitca[T,1], Mohammed Al-Seragi[1], Vignesh Krishnamoorthy[1], & Simon Wisnovsky[1]

[1]University of British Columbia, Faculty of Pharmaceutical Sciences, Vancouver, BC

[T]These authors contributed equally to this work

BACKGROUND

Many cancer types upregulate expression of sialic acid-containing glycans. These oligosaccharides subsequently engage inhibitory Siglec receptors on immune cells, allow cancer cells to evade immune surveillance. The genetic mechanisms by which this glycome remodeling occurs remain poorly defined.

METHODS

In this study, we performed multiple gain-of-function CRISPR activation (CRISPRa) screens to broadly define genetic pathways that regulate expression of Siglec-binding glycans.

RESULTS

We show that Siglec ligand expression is largely controlled through genetic competition between genes that catalyze α2-3 sialylation and GlcNAcylation of galactose residues. Perturbation of enzyme expression at this key biosynthetic node provides multiple "paths" by which cancers can acquire elevated expression of Siglec ligands. We show that cancer glycome remodeling is aided by overexpression of novel "professional ligands" that facilitate Siglec-glycan binding. Notably, we also find that expression of the CD24 gene is genetically dispensable for cell-surface binding of the inhibitory receptor Siglec-10. Finally, by integrating our functional genetic model with clinical tumor genomic data, we identify the sulfotransferase enzyme GAL3ST4 as a novel driver of immune evasion in glioma cells.

CONCLUSIONS

Taken together, this study provides a first-in-class genomic atlas to aid understanding of cancer-associated glycosylation and identifies immediately actionable targets for cancer immunotherapy.

Junior MSc Student Poster Presentations

4. A Scoping Review of the Healthcare Impacts of Extreme Weather Events

Presenter: *Nazafarin Esfandiari*

Nazafarin Esfandiari[1], Mark Harrison[1,2], Sarah Batke[1], & Glory Apantaku[1]

[1]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada
[2]Centre for Advancing Health Outcomes, St. Paul's Hospital, Vancouver, BC, Canada

BACKGROUND
Extreme weather events—such as extreme temperatures and floods—have become more frequent and intense. This creates challenges for various sectors, including the healthcare sector, which is uniquely vulnerable. While the health impacts of these events are well-documented, there is perceived to be a gap in comprehensive methodologies for estimating their economic impacts on healthcare systems. This review will explore current approaches to conducting economic assessments of the impacts of extreme weather events on healthcare systems.

METHODS
We searched three electronic databases (MEDLINE, Web of Science, and SCOPUS) for articles published from database inception to May 2024. Our search strategy comprised a combination of terms capturing various types of extreme weather events and their economic impacts on healthcare systems.

RESULTS
Our review of the literature is ongoing, but to date, the titles and abstracts of 9,526 studies have been screened, and data has been extracted from 26 studies. All studies were published since 2011, with 73% published between 2019 and 2024. Most studies (58%) focused on regions of Australia and the US. The studies covered heatwaves, extremes of heat and/or cold, floods, wildfires, typhoons, and multiple events. The breadth of healthcare impacts ranged broadly; the majority of studies considered hospital and emergency department visits but only for specific illnesses like respiratory diseases, some considered effects as narrow as emergency department visits for specific illnesses, and only a few considered the cost of impacts beyond healthcare utilization. The data sources used varied across studies, ranging from self-reported survey data to administrative datasets.

CONCLUSIONS
The body of evidence identified by this review revealed considerable heterogeneity and a lack of consistency, indicating a methodological gap and need for a comprehensive approach that can overcome the potential issues in understating the short- and long-term economic consequences of extreme weather events on health systems.

Junior MSc Student Poster Presentations

5. PRMT2 Influence on PRMT1 Methylation of Phosphorylated Nucleosomes

Presenter: *Maia Davey*

Maia Davey[1] & Adam Frankel[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND

Gene expression in eukaryotes is regulated by many factors including enzymatic modifications to histones, the proteins around which DNA is tightly wrapped to form nucleosomes. Arginine methylation, catalyzed by protein arginine N-methyltransferases (PRMTs), is one such modification within the histone code. PRMT activity on histones is affected by other post-translational modifications and the influence of other PRMTs, as demonstrated recently by our research group. Using the dCypher™ Nucleosome Panel (EpiCypher) to screen for nucleosomes whose modifications enhanced PRMT2's influence on PRMT1 activity, we identified nucleosomes phosphorylated on histones H2AX and H3.3 among top hits. The goal of my research is to explore this synergistic effect, identifying the specific histones and site(s) methylated by the PRMT1/2 complex to aid in elucidating this contribution to the histone code.

METHODS

Nucleosomes with phosphoserine modifications (H2AX S139phos and H3.3 S31phos) were used to assess PRMT1/2 activity toward these designer nucleosomes. Reactions containing a 1-to-10 ratio of PRMT1 to PRMT2 were incubated with radioactive S-adenosyl-L-methionine and nucleosomes for 16 h at 37˚C. Histone methylation reactions were separated via gel electrophoresis, proteins were visualized by Coomassie blue staining, and methylation activity was quantified by phosphor imaging.

RESULTS

Phosphorylated nucleosomes enhance PRMT2-mediated PRMT1 methylation activity. Interestingly, the H2AX S139 and H3.3 S31 nucleosomes demonstrated distinct methylation patterns, indicating specific phosphorylation marks uniquely affect PRMT1/2 activity.

CONCLUSIONS

Site-specific histone phosphorylation enhances PRMT1/2 methylation, suggesting that kinases may play a role in modulating methylation through this modification. Since phosphorylation of H2AX and H3.3 are associated with DNA damage response and cell cycle regulation, respectively, this research demonstrates a potential functional crosstalk between kinases and PRMTs in these pathways. Understanding how phosphorylation affects PRMT activity could identify critical kinase-methyltransferase interactions that might be targeted in diseases like carcinomas, where gene regulation is frequently disrupted.

Junior MSc Student Poster Presentations

6. Scoping Review: Strategies Utilized by Pharmacists and Pharmacy Students in Prescribing-Related Decision-Making

Presenter: *Priya Samuel*

Priya Samuel[1,2], Theresa Charrois[1], Kerry Wilbur[1], & Marion Pearson[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*
[2]*Pharmacy Services, Alberta Health Services, Edmonton, Alberta, Canada*

BACKGROUND
Pharmacists have long been vital members of the healthcare team, but their role has transformed over the past two decades with the expansion of prescribing authority. The act of prescribing requires pharmacists to take increased responsibility for patient care, creating challenges in the clinical decision-making process. Most of the research in this area focuses on other healthcare practitioners, thus, the clinical decision-making challenges pharmacists face, and the strategies they use to address them, are not well delineated. An understanding of how pharmacists address these challenges is imperative in ensuring they have the skills to prescribe with confidence.

METHODS
This scoping review follows the guiding principles of the Joanna Briggs Institute and the PRIMSA Extension for Scoping Reviews. It is restricted to the context of clinical decision-making within pharmacist or pharmacy student prescribing, and therefore, excludes other health prescribers. All modes of therapeutic prescribing—independent, dependent, and collaborative—are included. No geographical restrictions were placed, however, only studies written in the English language were included to minimize misinterpretation of findings during thematic analysis. The search was limited to studies published in 2000 or later, to coincide with the expansion of pharmacist prescribing globally.

RESULTS
Using comprehensive strategy developed collaboratively with a medical librarian, MEDLINE Ovid, Embase Ovid, and CINAHL EBSCO were searched, resulting in 10,388 studies. Two review authors will independently screen studies for inclusion and extract data. A combination of inductive and deductive content analysis will be used, and findings will be presented descriptively.

CONCLUSIONS
The goal of this scoping review is to synthesize findings on the challenges faced and strategies utilized by pharmacists when making prescribing-related decisions and to inform areas for future studies. We plan to publish the scoping review in a peer-reviewed medical education or pharmacy services journal.

Senior MSc Student Poster Presentations

7. Rural–Urban Inequities in Oral Anticoagulant Prescribing Patterns in a Trial Fibrillation: A Scoping Review

Presenter: *Mahsa Eslami*

Mahsa Eslami[1] & Peter Loewen[1]

[1]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada

BACKGROUND
Atrial fibrillation (AF) is a major risk factor for stroke, and oral anticoagulants (OACs) are essential for stroke prevention. However, rural–urban healthcare disparities may affect OAC prescribing patterns, including whether therapy is initiated, which agent is chosen (e.g., warfarin vs direct OACs), when initiation occurs, and whether dosing is appropriate. We conducted a scoping review to map these differences globally.

METHODS
We systematically searched MEDLINE, Embase, CINAHL, Scopus, and Web of Science for studies comparing OAC prescribing in rural versus urban AF populations. All study designs were eligible if they examined OAC prescribing patterns (initiation rates, OAC type, timing, dose appropriateness), patient outcomes, or influencing factors. Data from included studies were extracted and descriptively summarized.

RESULTS
We included 56 studies from North America, Europe, Asia, Africa, and Oceania. Most studies reported that rural AF patients had lower OAC initiation rates and were less likely to receive direct OACs, often leaving them untreated or reliant on warfarin, which requires monitoring that may be less available in rural areas. Several studies noted more frequent inappropriate dosing and suboptimal anticoagulation management in rural settings, associated with higher stroke or mortality rates. Contributing factors included limited healthcare access, socioeconomic and sociodemographic barriers, and variations in provider characteristics. Notably, even in countries with universal healthcare (e.g., Canada), these disparities largely persisted.

CONCLUSIONS
Our scoping review highlights persistent rural–urban inequities in OAC prescribing patterns and associated outcomes. Possible solutions to address these disparities include targeted system-level interventions, such as improved resources and telemedicine-based access to specialist services in rural areas. Implementing these strategies could improve equity in AF care and help reduce preventable strokes in rural communities. Our findings form a basis for policy action and future research to evaluate these interventions and address remaining gaps, such as long-term rural OAC adherence.

Senior MSc Student Poster Presentations

8. Development of an *in-silico* Pharmacokinetic Platform for the Prediction of Monoclonal Antibody Distribution in the Brain

Presenter: *Andy Kim*

Andy Kim[1], Etienne Lessard[2], Binbing Ling[2], & Anil Maharaj[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*
[2]*National Research Council Canada, Ottawa, ON, Canada*

BACKGROUND
Monoclonal antibodies (mAbs) are revolutionizing the treatment of neurological disorders through high target specificity, but their large size limits brain penetration. Traditionally, preclinical *in-vivo* studies measure cerebrospinal fluid (CSF) concentrations to assess brain penetration, but these require extensive sampling and complex procedures. Physiologically-based pharmacokinetic (PBPK) models offer a promising alternative for predicting mAb brain penetration, but current models lack the ability to generate mAb-specific predictions of CSF concentrations without *in-vivo* data. This study aims to assess the capacity for PBPK models to generate *a priori* estimates of CSF concentrations for mAbs by integrating information from *in-vitro* apparent permeability (Papp) assays.

METHODS
An updated rat brain PBPK model was developed in the open-source software PK-Sim® by incorporating new brain compartments and CSF fluid dynamics informed by the literature. Model simulations for 4 mAbs in rats were then conducted to compare the predictive accuracy of two approaches: (1) the existing approach in literature that assumes fixed brain permeability values for all mAbs, and (2) our mAb-specific approach that incorporates *in-vitro* Papp data into model parameterization to account for mAb-specific brain permeability.

RESULTS
The updated PBPK model incorporated 8 additional brain compartments (4 CSF, 2 endosomal, 2 perivascular) and 19 new transport mechanisms, significantly expanding upon the original 4-compartment framework in PK-Sim®. The average prediction error of the CSF area under the concentration-time curve (AUC) was reduced by 134% for the model incorporating *in-vitro* Papp data. For example, the average prediction error (range) was 252% (75%–419%) without incorporating *in-vitro* data. In contrast, the average prediction error (range) was 118% (12%–227%) with our approach that incorporates *in-vitro* Papp data.

CONCLUSIONS
This study presents an innovative approach to PBPK modeling that improves mAb CSF concentration predictions using *in-vitro* data. The method enhances *a priori* predictions of mAb brain distribution, potentially accelerating neurological treatment development.

Senior MSc Student Poster Presentations

9. Effectiveness of Different Dosing Schedules for Pneumococcal Conjugate Vaccines on Invasive Pneumococcal Disease in Children: A Systematic Review and Meta-analysis

Presenter: *Jenny Chang*

Chia-Yuan Chang[1], Sharifa Nasreen[2], Manish Sadarangani[3,4], Kenny Aquino[1], Jacquelyn Cragg[1], & Fawziah Marra[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*
[2]*School of Public Health, SUNY Downstate Health Sciences University, New York, USA*
[3]*Department of Pediatrics, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada*
[4]*Vaccine Evaluation Center, BC Children's Hospital Research Institute, Vancouver, British Columbia, Canada*

BACKGROUND
The introduction of PCV7 and PCV13 vaccines has significantly reduced invasive pneumococcal disease (IPD) incidence, though vaccine-type IPD (VT-IPD) persists. This study evaluates vaccine effectiveness (VE) against VT-IPD in children ≤18 years by comparing different dosing schedules.

METHODS
We searched MEDLINE/Embase/Web of Science/CENTRAL databases from January 1, 2000, to Dec 21, 2024, for studies reporting on the VE of PCV7/PCV13 against VT-IPD in children ≤18 years old. VE estimates were recorded for primary + booster group, and 1-, 2-, or 3-primary doses group, then pooled using random-effects models. Studies were excluded if they did not publish outcomes for the primary dose-only groups. Serotype distribution, clinical characteristics, sensitivity analyses, and risk of bias were assessed.

RESULTS
From 1982 studies, we included 25 observational studies reporting 525 primary + booster cases and 821 primary dose-only cases. Pooled VE estimates from 14 studies were 94.42% (95% CI: 87.32–97.55%) for primary + booster doses, 66.75% (95% CI: 56.37–74.66%) for one primary dose, 78.84% (95% CI: 68.58–85.75%) for two, and 82.01% (95% CI: 73.05–87.99%) for three. Meta-regression indicated vaccine effectiveness differed significantly by dose level, accounting for approximately 41.96% of the observed heterogeneity ($p<.0001$). Serotype 19A was most common (27%), followed by 19F and 3. Bacteremia/sepsis was the predominant VT-IPD presentation (68.3%), while meningitis occurred only in partially vaccinated children (12.9%). Sensitivity analyses showed VE of ~95% for the 2+1 and 3+1 schedules, versus 78.94% for the 3+0 schedule when all doses were received.

CONCLUSIONS
VE increases with the number of doses, and while a single primary dose provides notably lower VE, additional primary doses beyond two offer minimal additional benefit. The booster dose is essential for sustained protection against VT-IPD. Ongoing surveillance will be crucial to inform policy decisions, especially with the recent introduction of reduced-dose schedules.

Senior MSc Student Poster Presentations

10. Ultra-Rapid Genetic Screening Reveals GCN2 as a Potential Regulator of Cancer-Associated Hypersialylation

Presenter: *Jimmy Kim*

Jimmy Kim[1] & Simon Wisnovsky[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
In 2018, the Nobel Prize in Medicine recognized the groundbreaking potential of cancer immunotherapies, drugs that allow the immune system to target and eliminate cancer cells. The human immune system utilizes receptors expressed on the surface of immune cells which, upon binding to specific targets (ligands), modulate the immune response. In diseases like cancer, the cell surface may be altered to overexpress certain ligands, leading to suppression of immune cell activity and immune evasion. The signaling pathways and genetic changes that modify the cell surface in cancer cells, however, are not well defined. Identifying and characterizing these regulators could open doors to the development of targeted immunotherapeutics that act by remodeling the cancer cell surface.

METHODS
I developed and optimized a CRISPR screening approach based on magnet-activated cell sorting to rapidly conduct CRISPR screens in epithelial cancer cell lines. I then carried out a CRISPR-knockdown screen targeting known “druggable” genes (i.e., kinases, phosphatases) to map pathways underlying cancer hypersialylation.

RESULTS
The screen revealed a list of “hit genes” whose knockdown reduced surface sialylation, which included two known sialic acid biosynthesis genes: CMAS and GNE. Notably, one gene, EIF2AK4, exhibited a comparative reduction of sialylation as CMAS and GNE. This gene encodes a kinase, GCN2, that plays a key role in activating the cell’s integrated stress response. A targeted knockdown of GCN2 further confirmed reductions in surface sialylation.

CONCLUSIONS
This magnetic screening method would produce a collection of genes for reversing cancer-associated hypersialyation, which I hope to compile into an open-source database to catalyze research in the broader field of tumor glycobiology. I will also characterize the effects of GCN2 knockdown on the cell-surface glycome, giving us a better idea of the broader impact of this gene on cell-surface sialylation and assessing its potential as a target for immunotherapy.

Senior MSc Student Poster Presentations

11. Plasma Oxylipins as Potential Biomarkers for Indomethacin Treatment Response in Preterm Infants with Patent Ductus Arteriosus

Presenter: *Khanh Nguyen*

Khanh Nguyen[1], Cindy Yeung[2], Tamorah Lewis[3,4], & Thomas Velenosi[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*
[2]*College of Pharmacy, Dalhousie University, Halifax, NS, Canada*
[3]*Department of Paediatrics, University of Toronto, Toronto, ON, Canada*
[4]*Division of Clinical Pharmacology & Toxicology, University of Toronto, Toronto, ON, Canada*

BACKGROUND
Preterm infants often experience patent ductus arteriosus (PDA)—a vascular opening between the aorta and pulmonary artery, and indomethacin (IND) is a standard treatment for PDA. IND inhibits the production of prostaglandins and other oxylipins. While some infants respond to IND treatment, others do not and require surgery. Our study aimed to identify oxylipin biomarkers that could predict IND treatment response as no biomarkers are currently available.

METHODS
A prospective cohort study at Children's Mercy Hospital in Missouri included preterm infants (≤32 weeks gestational age) with PDA receiving IND treatment. Infants were categorized based on treatment response: no surgery required, or surgery required. Plasma and urine samples were collected pre- and post-treatment for targeted oxylipin analysis. Multilevel Partial Least Squares Discriminant Analysis identified oxylipins differentiating between surgery and non-surgery outcomes. Pearson correlation tests assessed associations between oxylipin levels and clinical characteristics.

RESULTS
Of the 14 infants, 10 infants did not require surgery while 4 did. Targeted oxylipin metabolomics revealed significantly higher baseline plasma concentrations of the oxylipins 12,13-DiHOME, 9,10-DiHOME, 15,16-DiHODE, and 9,10-DiHODE in the “no surgery required” group ($P < 0.05$). Following IND treatment, these oxylipin levels decreased in the "no surgery required" group but remained stable in the "surgery required" group. No associations were found between baseline oxylipin concentrations and clinical characteristics of infants. Urinary 12,13-DiHOME levels showed an opposite trend, with higher baseline concentrations in the "surgery required" group. However, this finding requires further investigation with a larger sample size to establish statistical significance.

CONCLUSIONS
Plasma levels of four oxylipins at baseline were found to be associated with IND treatment outcome. This finding has the potential to contribute to the identification of biomarkers and guide PDA management in preterm infants.

Senior MSc Student Poster Presentations

12. The Impact of RREB1 Overexpression and Knockdown on β-Cell Viability and Function in Type 1 Diabetes

Presenter: *Milda Kirvaityte*

Milda Kirvaityte[1], Zeynep Sugle[1], James D. Johnson[2], & Nicole A. J. Krentz[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, Canada*
[2]*Life Sciences Institute, Departments of Cellular and Physiological Sciences and Surgery, University of British Columbia, Vancouver, Canada*

BACKGROUND
Currently 300,000 Canadian adults have been diagnosed with type 1 diabetes (T1D), with an estimated 4.4% increase annually. Autoimmune-mediated destruction of β-cells is central to T1D progression, resulting in loss of up to 80% of β-cell mass before T1D diagnosis. The progression of β-cell death is driven by immune cell infiltration into the pancreatic islets, where insulin-producing ß-cells are located. Within the islets, immune cells release pro-inflammatory cytokines that trigger downstream pro-apoptotic pathways, leading β-cell death. We have previously shown that knockdown and knockout of Ras Responsive Element Binding Protein 1 (RREB1) in human β-cells reduces expression of pro-apoptotic genes, suggesting that RREB1 is required for cytokine-induced β-cell apoptosis. Therefore, the aim of this study is to investigate whether altering the expression of RREB1 can protect β cells from cytokine-mediated death, with potential implications for T1D therapy.

METHODS
RREB1 will be overexpressed and silenced in a mouse β cell line before treatment with cytokines to induce apoptosis. We will then assess β-cell death through propidium iodide incorporation and cleaved caspase 3 protein expression. Additionally, the effects of RREB1 perturbation on transcription will be analyzed by measuring gene expression of key β-cell markers (Ins1, Ins2, and Pdx1) and genes involved in cytokine signaling (Stat1, Stat2, Nfkb1, and Mapk10). Finally, glucose-stimulated insulin secretion will be performed to determine how RREB1 modulation influences β-cell function.

RESULTS
The results will provide insights into the potential of targeting RREB1 as a therapeutic strategy for protecting β cells in T1D.

Junior PhD Student Poster Presentations

13. Developing a Chemical-Genetic Screening Platform to Identify Receptors for Tumor-Associated Carbohydrate Antigens

Presenter: *Angeline Wu*

Angeline Wu[1], Paolo Giuliana[2], Landon Edgar[2,3,4], & Simon Wisnovsky[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*
[2]*Department of Pharmacology & Toxicology, University of Toronto, Ontario, Canada*
[3]*Department of Chemistry, University of Toronto, Ontario, Canada*
[4]*Department of Immunology, University of Toronto, Ontario, Canada*

BACKGROUND
All living cells are coated with oligosaccharides called glycans. Glycan interactions with cognate receptors are vital for many biological processes including immune regulation. In cancer, alterations in glycan presentation can lead to structures termed tumor-associated carbohydrate antigens (TACAs), which have been linked to tumorigenesis, such as the Tn antigen and the T antigen. Many TACAs lack annotated binding partners, and thus their roles remain unclear. Uncovering TACA receptors could therefore provide invaluable information on mechanisms behind cancer progression, but current methods for probing protein-glycan interactions are extremely resource-intensive. An alternative approach, where binding interactions between natively-expressed receptors and synthetic glycan-presenting biomolecules can be screened in a cell-based assay, would be highly impactful.

METHODS
Fluorescent lipid nanoparticles (LNPs) were conjugated with various TACAs (referred to as TACA-LNPs). Formulation chemistry of TACA-LNPs was optimized through flow cytometry, followed by two pilot screens using Tn antigen LNPs (Tn-LNPs) with a lectin-only as well as a genome-wide library of CRISPR activation cells. Afterwards, further genome-wide screens using Tn-LNPs and T antigen LNPs (T-LNPs) were done. Using casTLE analysis, several inhibitory immune receptors were identified as potential therapeutic targets for downstream validation.

RESULTS
Analysis of Tn-LNP screens found known binder MGL, as well as CD72, as hits. AXL, Siglec-6, and CXCL16 were found across Tn-LNP and T-LNP genome-wide screens. These are all genes naturally expressed by human immune cells, and have been reported to exhibit inhibitory effects on immune function.

CONCLUSIONS
This research demonstrated the application of a novel genetic screening methodology that can broadly catalyze research in the field of glycobiology. Previously known and novel immune-inhibiting receptors for TACAs were found as screening hits. Future directions will involve generating overexpression cell lines to confirm binding with the TACA-LNPs, as well as immune functional assays to validate screening findings as potential cancer immunotherapy candidates.

Junior PhD Student Poster Presentations

14. Stimuli-Responsive Nanocomplexes for Targeted Antibiotic and Enzyme Codelivery to Treat Chronic Biofilm Infections

Presenter: *Chinekwu Nwagwu*

Chinekwu Nwagwu[1], Alaleh Yourdkhani[1], & Joel A. Finbloom[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
Biofilms contribute to antibiotic resistance by creating complex barriers that protect bacteria from the action of antibiotics and the host immune system, making infections harder to treat. The negatively charged extracellular polymeric substances (EPS) within biofilms trap positive-charged antibiotics like tobramycin (TOB), reducing their efficacy. This study aims to create pH-responsive nanocomplexes (NCs) to co-deliver TOB and deoxyribonuclease (DNase), an EPS-degrading enzyme, to overcome biofilm barriers and improve therapeutic outcomes. Since many bacterial infections are associated with acidic environments, the study focuses on developing pH-responsive NCs to release their cargo at lower pH levels. We hypothesize that this method of co-delivering antibiotics and biofilm-disrupting enzymes, DNase, will significantly enhance treatment outcomes by improving drug localization, disrupting the biofilm barrier, and minimizing adverse effects.

METHODS
The NCs were formulated by combining the TOB and DNase with polycationic and polyanionic polymers in varying ratios. The effect of buffer compositions, pH, and incubation time on the NCs was evaluated. In addition, other physicochemical parameters of the NCs, such as size, PDI, surface charge, encapsulation efficiency, and *in vitro* drug release, were also evaluated.

RESULTS
The formulated NCs exhibited a particle size of ~340 nm with low PDI (~0.2), and encapsulation efficiencies of TOB and DNase exceeding 80% and 30%, respectively. Upon exposure to acidic conditions mimicking biofilm environments, the NCs displayed significant swelling, increasing to >2 µm.

CONCLUSIONS
This data suggests that the NCs possess promising features that could be explored in designing more effective delivery systems for antibiotics. However, further studies will involve utilizing *in vitro* biofilm models to evaluate the dynamics of NCs within biofilm structures and their antibiofilm activity.

Junior PhD Student Poster Presentations

15. Potentiating the Multi-Kinase Activity of Trk-Selective Inhibitors for the Management of Chronic Pain in Osteoarthritis

Presenter: *Conall McCutcheon*

Conall McCutcheon[1], Petar Iliev[1], & Brent D. G. Page[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND

Osteoarthritis is a leading cause of disability, severely impacting the quality of life of affected individuals. Chronic pain is the most common and debilitating symptom; despite this, current treatment approaches fail to address the molecular actors responsible for driving disease-associated chronic pain. To address this gap, our team has identified chemically-novel small molecule multi-kinase inhibitors that are potent against TrkA, Src, and JAK2 – three kinases that contribute to and amplify osteoarthritis-associated chronic pain. Our inhibitors have demonstrated the selective inhibition of TrkA at nanomolar concentrations in biochemical and cell-based settings. Given the progress achieved thus far, this study seeks to further optimize the pharmacodynamic properties of our compounds.

METHODS

Lead compound BP347 is a potent inhibitor of TrkA, JAK2, and Src (IC_{50} = 17.3 nM, 177 nM, and 502 nM, respectively), and has demonstrated *in vitro* pharmacokinetic properties sufficient to warrant *in vivo* testing. While BP347 progresses onto pharmacokinetic studies *in vivo*, ongoing efforts are focused on further potentiating the selectivity of the BP347 scaffold for JAK2 and Src. This is being accomplished through the use of parallel docking experiments to predict how structural changes affect compound selectivity across the three kinases, while the inclusion of novel BP347 derivatives in subsequent structure-activity relationship studies will better characterize their activity against JAK2 and Src in both biochemical and cell-based settings (CETSA, cell viability assay, etc.).

RESULTS

Parallel docking experiments have identified novel BP347 analogues exhibiting predicted improvements in activity against all three kinases. This series of analogues will be synthesized and undergo testing *in vitro* to better characterize their pharmacodynamic properties.

CONCLUSIONS

In further potentiating the multi-kinase activity of the BP347 scaffold, we can procure analogues with optimized pharmacodynamic activity; with further evaluation and optimization, these analogues have the potential to serve as tools through which novel analgesic pathways may be explored in osteoarthritic contexts.

Junior PhD Student Poster Presentations

16. Investigating the Role of Endothelial Cell-Released Heparanase in Physiological Cardiac Hypertrophy

Presenter: *Gala Araujo*

Gala Araujo[1], Chae-Syng Lee[1], Bahira Hussein[1], & Brian Rodrigues[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
There are eleven different major cell types within the heart. Of these various cells, cardiomyocytes which are the contractile unit of the heart, and endothelial cells which line the blood vessels and relay signals to the heart are dominant. However, these two cell types do not work in isolation. Endothelial cells through their proximity to the underlying cardiomyocytes can release signaling mediators that affect their function. One of these mediators is the endoglycosidase heparanase (Hpa). Our lab has previously described roles of Hpa in regulating cardiomyocyte function through angiogenesis, metabolism, and cell survival. Serendipitously, we discovered that transgenic mice with global overexpression of human Hpa (Hpa-Tg) have significantly larger hearts compared to control animals. Echocardiography of these animals confirmed that this cardiac hypertrophy does not adversely alter the function of the heart and thus is considered physiological. However, how the ECs communicate with the cardiomyocytes to induce their growth using signals generated by Hpa is unknown.

METHODS
Cardiomyocytes were isolated from 7–9-week-old male Wistar rats and seeded on 6-cm culture dishes. Following a 24-hour attachment period, cardiomyocytes were treated with perfusate containing Hpa for 24 hours to induce physiological hypertrophy. The length and width of individual cardiomyocytes were then quantified using ImageJ software. Cell lysates were collected for Western blot determination of hypertrophic signaling. Cardiomyocyte conditioned media was collected and used for a cytokine array to determine proteins released in response to Hpa.

RESULTS
Treatment of cardiomyocytes with concentrated perfusate containing Hpa for 24-hours resulted in significant increases in their length-width ratios. Western blot analysis confirmed the downstream activation of ERK and PI3K-AKT signals associated with hypertrophy.

CONCLUSIONS
Hpa overexpression *in vivo* has been shown to cause physiological cardiac hypertrophy. In this study we showed for the first time that Hpa has similar effects *in vitro* on individual cardiomyocytes.

Junior PhD Student Poster Presentations

17. Bioinspired Peptide Amphiphile Nanofibre (PANF) Microgels for the Encapsulation of Bacteria

Presenter: *Noah Brittain*

Noah Y. Brittain[1] & Joel A. Finbloom[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
Most bacteria live in fibrous matrices called biofilms. Biofilms comprise biological polymers that provide nanoscale structural support and regulate beneficial bacterial behaviour. We will take inspiration from the protein fibres found within natural biofilms to develop self-assembling peptide amphiphile nanofibres (PANF) as a scaffold for bacterial encapsulation. In this study, we aim to investigate how altering PANF material properties influences hydrogel and microgel (microparticle format of hydrogels) formation and how subsequent interactions alter bacterial behaviour (growth, metabolism, gene expression), allowing us to understand better how to encapsulate bacteria in nanostructured systems.

METHODS
Peptide amphiphiles were synthesized using solid-phase peptide synthesis and then self-assembled into nanofibres, which was confirmed using electron microscopy, circular dichroism, the fluorescent β-sheet indicator thioflavin T, and zeta potential charge measurements. PANFs were then incubated with the model bacteria *Escherichia coli*, and biocompatibility was assessed using a fluorescent metabolic assay. A water-in-oil emulsion was used to form microgels with Ca^{2+}-based ion-bridges. Mechanical properties were assessed through dynamic light scattering microrheology, and bacterial distribution and survival were assessed through confocal microscopy.

RESULTS
We demonstrated that we can form PANFs with different physicochemical properties, which altered PANF biocompatibility with *E. coli*. We then showed that we can encapsulate *E. coli* within PANF hydrogels, and by altering nanofibre density, we can modulate hydrogel rheological properties. We then showed that we can form these gels into micron-sized particles that enable long-term encapsulation and survival.

CONCLUSIONS
We have shown that bacteria can be encapsulated within peptide amphiphile nanofibre microgels and that changes in PANF chemistry can change bacterial behaviour. These findings will help inform how biomaterial properties can influence the encapsulation and behaviour of bacteria. Future directions will investigate how we can use these materials for the therapeutic delivery of bacteria to the gut microbiome.

Senior PhD Student Poster Presentations

18. GABA-Induced Invadopodia Formation Drives Metastasis in Triple Negative Breast Cancer

Presenter: *Esther Afolayan*

Esther Afolayan[1] & Karla Williams[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
Metastasis, a process describing the movement of cancer cells from primary tumors to distant sites within the body, is the leading cause of cancer-related deaths. Metastasis is in-part mediated by tiny finger-like, actin-rich membrane protrusions called invadopodia. Invadopodia facilitate the degradation of the extracellular matrix, allowing cancer cells to invade surrounding tissues and blood vessels. Gamma-aminobutyric acid (GABA), a prominent neurotransmitter in the brain, is expressed by cancer cells, particularly in triple negative breast cancers (TNBC). GABA expression in TNBC is associated with tumor progression and poor prognosis, therefore, understanding how GABA facilitates tumor cell invasion and migration through invadopodia will help identify key molecular targets for the development of effective therapeutic agents.

METHODS
We assessed invadopodia formation *in vitro* in response to GABA using a standard invadopodia formation assay in TNBC cell lines (BT-549, MDA-MB-231 and its brain-homing derivative MDA-MB-231BR).

RESULTS
Our investigation into the role of GABA in promoting tumor cell extravasation and metastasis into GABA-rich microenvironments has found that GABA stimulates invadopodia formation and promotes brain metastasis in TNBC cells. All three cell lines were responsive to exogenous GABA and this response could be blocked using the specific and selective GABA-A receptor agonist, gabazine but not the GABA-B receptor agonist 2-OH-saclofen. This work also identified endogenous GABA expression in TNBC cell lines.

CONCLUSIONS
These findings underscore the importance of GABA in promoting invadopodia formation and function. Targeting GABAergic signaling may offer a therapeutic strategy to disrupt invadopodia formation and lessen the metastatic potential of TNBC.

Senior PhD Student Poster Presentations

19. The Impacts of Perinatal Loss on Work and Work Productivity

Presenter: *Jacynthe L'Heureux*

Jacynthe L'Heureux[1], Abigail Stites[1], Jack Smith[1], Alexander Tam[2], Gary Johns[3,4], & Wei Zhang[2,5]

[1]*School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada*
[2]*Centre for Advancing Health Outcomes, Vancouver, BC, Canada*
[3]*Sauder School of Business, University of British Columbia, Vancouver, BC, Canada*
[4]*John Molson School of Business, Concordia University, Montreal, QC, Canada*
[5]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
Perinatal loss encompasses loss prior, during and after pregnancy. This loss is often profoundly traumatic, multi-faceted, highly consequential on daily living, such as the ability to maintain employment. Testimonies point to lasting impacts on health and work because of inadequate policies, health care services and workplace supports.

While previous studies have reported changes in labour force participation following perinatal loss, no estimates of reduced labour productivity were measured. In fact, there is a lack of methods to measure work productivity loss following perinatal loss, creating a knowledge gap for decision-makers to evaluate policy options. The objectives of this research are to 1) perform a scoping literature review about the impacts of perinatal loss on work and work productivity loss; 2) adapt a work productivity loss instrument to encompass the experiences of perinatal loss.

METHODS
Objective 1) Our search included publications from 2014 to 2025, available on MEDLINE, CINAHL, EconLit, Psycinfo, or EMBASE. We examined evidence from qualitative, quantitative, and mixed methods studies. Objective 2) Our semi-structured interviews explored each participant's experience of perinatal loss within their work; along with their views on how to adapt the Valuation of Lost Productivity. Cognitive interviewing methods were used in an interactive process until data saturation was reached.

RESULTS
Our work-in-progress screened 8,390 records, found 50 studies that were assessed for eligibility. 19 studies were retained for data extraction. We conducted 26 one-on-one interviews until saturation was reached. Participants guided the instrument adaptation by suggesting how to: attribute work productivity loss to perinatal loss; align the instrument to present a logic consistent with perinatal loss; and situate the questionnaire to elicit purposeful responses.

CONCLUSIONS
Measuring and designing policies, services and supports for individuals experiencing perinatal loss will help support the health and well-being of all employees in Canada.

Senior PhD Student Poster Presentations

20. Bad to the Bone: Unmasking the Osteopontin Receptor in Metastatic Breast Cancer

Presenter: *Kendal Ruzicki*

Kendal Ruzicki[1] & Karla C. Williams[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
Invadopodia are F-actin cellular protrusions involved in motility, invasion and ECM remodelling. Cancer cells utilize invadopodia during the metastatic cascade, and their formation can be stimulated by extrinsic factors. Osteopontin (OPN), a bone matrix protein secreted by osteoblasts, is thought to promote homing and invasion of BCa cells in the bone microenvironment. OPN contains functional domains that interact with receptors and activate signaling; the RGD domain binds several integrins, while CD44 binds the C-terminal. BCa cells are responsive to exogenous OPN, and OPN may induce tks5 expression and increase invadopodia formation. Therefore, BCa cells may interact with OPN through an integrin/CD44 receptor to signal invadopodia formation in the bone.

METHODS
MDA231 and the bone-homing cell-line derivative MDA231BO were used for experiments. OPN mutants unable to bind specific integrins/CD44 were generated to determine their effect on invadopodia formation and tks5 expression. To assess invadopodia formation, cells were seeded on a fluorescent gelatin-OPN matrix, and gelatin degradation was quantified with fluorescence microscopy. Tks5 protein expression was assessed with western blot when cells were treated with OPN/mutant proteins.

RESULTS
Full length OPN increased invadopodia formation and tks5 expression in both cell lines. TC OPN showed no significant differences to full-length OPN when assessing invadopodia formation. However, RAA OPN showed decreased invadopodia formation and tks5 expression in MDA231BO cells.

CONCLUSIONS
Results demonstrate that invadopodia formation is stimulated by OPN; as the metastatic-bone derived cells form invadopodia at elevated rates, invadopodia may be important for promoting tumor growth at the bone. Further, the RGD domain may be central to OPN binding in MDA231BO cells. In BCa, ~70% of metastatic lesions present in the bone. Improving our understanding of the molecular mechanisms regulating BCa metastasis at the bone could lead to the identification of new therapeutic treatment options to prevent or reduce metastatic disease.

Senior PhD Student Poster Presentations

21. Rational Design of a Novel Adenosine Base Editor For Clinical Applications

Presenter: *Tessa Morin*

Tessa Morin[1], Sarah Ng[1], Michael Rowley[2], Tiffany Carlaw[1], Lane Messier[2], Liam O'Keeffe[1], Sarah Hedtrich[1], Sriram Subramaniam[2], Pieter Cullis[2], & Colin Ross[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, Canada*
[2]*Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of British Columbia, Vancouver, Canada*

BACKGROUND
Gene editing can potentially treat genetic diseases, but current technologies, like CRISPR/Cas9, face challenges with safety and precision. Base editors, derived from CRISPR/Cas9, offer improved on-target editing with fewer double-stranded breaks[1] but still suffer from off-target mutations, which can lead to unwanted edits and potential tumourgenesis. Efforts to improve adenine base editors have had limited success in enhancing efficacy and safety[2].

In this study, we explored whether novel combinations of mutations or *de novo* mutations in the deaminase of the base editor ABE8e could enhance editing precision. We hypothesized that a rationally mutated TadA deaminase could improve on-target editing and reduce off-target edits.

METHODS
We developed a cloning strategy to screen different deaminases and protein linkers for our base editor. New base editors were then tested in HEK293 cells on the *EMX1* site to assess editing efficacy and off-target effects. Genomic DNA was sequenced to analyze editing levels.

RESULTS
Results showed that three novel mutations paired with Y123H, increased editing while narrowing the editing window compared to ABE8e. Removing the protein linker shifted the editing window closer to the 5' end of the target sequence, and combining these mutations without a linker produced a novel ABE with a unique editing window at positions 3–5.

CONCLUSIONS
We successfully generated a new ABE with an editing window of 3–5, with comparable on-target editing rates to ABE8e. This novel ABE allows for editing at previously untreatable sites, addressing an unmet need in the gene editing field and has the potential for therapeutic applications.

REFERENCES
1. Richter, M. et al. Phage-assisted evolution of an adenine base editor with improved Cas domain compatibility and activity. *Nature Biotechnology* 38, 883–891 (2020).
2. Chen L. et al. Engineering a precise adenine base editor with minimal bystander editing. *Nat Chem Biol.* 19, 101–110 (2023).

Senior PhD Student Poster Presentations

22. The Glycosyltransferase ST3GAL4 drives Immune Evasion in Acute Myeloid Leukemia by synthesizing ligands for the glycol-immune checkpoint receptor Siglec-9

Presenter: *Vignesh Krishnamoorthy*

Vignesh Krishnamoorthy[1], John Daly[1], Jimmy Kim[1], Lidia Piatnica[1], Katie Yuen[2], Bhoj Kumar[3], Mehmoush Taherzadeh Ghahfarrokhi[3], Tom Q. T. Bui1[2], Parastoo Azadi[3], Ly Vu[1,2], & Simon Wisnovsky[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*
[2]*BC cancer agency, Vancouver, BC, Canada*
[3]*Complex Carbohydrate Research Center, University of Georgia, USA*

BACKGROUND
Cancer cells often express aberrant levels of molecules containing sialic acid resides (sialoglycans) on their cell surface. These sialoglycans can bind to Siglec receptors expressed by immune cells and quench their cytotoxic activity. Studies have shown that blocking the interaction between cancer associated sialoglycans and the Siglec receptors can unleash the activity of immune cells against cancer cells and eliminate them. Siglec-9 is one such receptor expressed on the surface of myeloid cells. Demystifying the identify of Siglec-9 binding glycan ligands would allow to develop enhanced immunotherapeutic approaches against cancer cells.

METHODS
A CRISPR-Cas9 screen performed on a myeloid leukemia cell line identified the glycosyltransferase ST3GAL4 as a topic hit gene controlling the synthesis of Siglec-9 binding ligands. ST3GAL4 expression levels was analyzed in multiple cancer models. Acute myeloid leukemia (AML) cell lines were evaluated for the expression levels of Siglec-9 binding ligands through flow cytometry. ST3GAL4 was knocked out in multiple AML cell lines through CRISPR-Cas9 based approach. The WT/ ST3GAL4 KO cells were co-cultured with primary macrophages and the phagocytic index was calculated.

RESULTS
The mRNA expression levels of ST3GAL4 was high in AML cells compared to healthy blood cells. Flow cytometry analysis revealed that AML cells express high levels of Siglec-9 binding ligands. Loss of ST3GAL4 significantly reduced the expression levels of Siglec-9 binding ligands compared to the WT cells. Co-culture of WT/ST3GAL4 KO cells with primary macrophages revealed that the ST3GAL4 KO cells are more sensitive to phagocytosis compared to the WT.

CONCLUSIONS
Our studies indicate that the expression of Siglec-9 binding ligands on AML cells are controlled by ST3GAL4. Loss of ST3GAL4 in AML cells makes them more prone to phagocytic attack by macrophages. These results illustrate a novel checkpoint inhibitory pathway utilized by AML cells that could be exploited for developing effective immunotherapies.

Postdoctoral Fellow Poster Presentations

23. Needle-free Intranasal Delivery of a Protein-based Vaccine for Enhanced Immune Responses

Presenter: *Po-Yu Chou*

Po-Yu Chou[1] & Shyh-Dar Li[1]

[1]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

BACKGROUND
Intranasal vaccination provides an effective, non-invasive alternative to subcutaneous immunization by eliciting both mucosal and systemic immune responses. However, efficient nasal absorption of protein antigens remains a challenge due to mucociliary clearance and epithelial barriers. This study employed a machine learning approach for virtual screening and design of novel cell-penetrating peptides (CPPs) derived from protamine to enhance intranasal delivery of a model antigen, OVA.

METHODS
The machine learning model integrated key molecular descriptors, including charge distribution, hydrophobicity, and amino acid sequence variability, derived from previously tested CPPs to predict their effectiveness in facilitating intranasal antigen delivery.

In vivo, six-week-old C57BL/6 mice were randomized into nine groups and immunized intranasally with 30 µg of OVA alone or co-formulated with various delivery enhancers, including protamine, Dendri-P, Nano-P, P9 or P13. Immunization was administered three times at one-week intervals. Seven days after the final dose, blood, nasal tissues, lungs, tracheas and spleens were collected for analysis. OVA-specific IgA levels in nasal homogenates and OVA-specific IgG, IgG1, and IgG2a levels in plasma and spleen were quantified via ELISA. Additionally, a separate study utilized confocal microscopy to assess the penetration and localization of Alexa647-labeled OVA in the nasal epithelium, providing insights into antigen uptake efficiency.

RESULTS
OVA-specific IgA and systemic IgG levels were significantly elevated in groups receiving OVA co-administered with protamine, P9 or P13 compared to OVA alone. Confocal imaging revealed greater fluorescence intensity in the nasal epithelium and lamina propria in the presence of CPP-based formulations, indicating improved antigen penetration and uptake.

CONCLUSIONS
CPP-based delivery strategies significantly enhance the immunogenicity of intranasal OVA vaccines, highlighting their potential for broader applications in mucosal vaccine development.

University of British Columbia
Faculty of Pharmaceutical Sciences
2405 Wesbrook Mall, Vancouver, BC V6T 1Z3
pharmsci.ubc.ca