

UB C MD PhD

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NEWSLETTER - 2023 SUMMER https://mdprogram.med.ubc.ca/mdphd/news/

The last couple of months have been really eventful for all of us in UBC'S MD/PhD program. Pictured above is a selfie shot by our outgoing Student Liaison Maryam Vaseghi-Shanjani, showing our June MD/PhD Building Bridges Social. This event, held at the rooftop patio of the BC Cancer Research Centre, capped off the spring term and gave the students a chance to meet and chat before some went separate ways over summer. Now, let's see more about what has been happening in the program over the last few months!



MD/PhD Award Winners:



Elizabeth Gregory

Maggie Chopra Peipei Wang

Joyce Zhang

Kira Tosefsky T

CONGRATULATIONS

Torin Halvorson Chloe Gao

Reid Vassallo

We are pleased that the current group of UBC MD/PhD students have been very successful in 2023 external and internal award competitions. Congratulations to all the recipients and their supervisors for this year's outstanding results! We take pride in the ongoing achievements of our outstanding students.

Elizabeth Gregory and **Maggie Chopra** were winners of prestigious Canadian Institutes of Health Research (CIHR) Vanier Canada Graduate Scholarships. The mandate of the Vanier awards program is to strengthen Canada's ability to attract and retain world-class doctoral students and establish Canada as a global centre of excellence in research and higher learning. Elizabeth's supervisor is Dr. Fidel Vila-Rodriguez and she is hosted by the Experimental Medicine Graduate Program. The title of her research project is "Individualized Functional Targeting for Repetitive Transcranial Magnetic Stimulation". Maggie's supervisor is Dr. Kelly McNagny and she is also hosted by Experimental Medicine. The title of Maggie's research project is "a proteomic approach to understand determinants of lung disease throughout development and aging".

Peipei Wang and Joyce Zhang won a CIHR Frederick Banting and Charles Best Canada Graduate Scholarship Doctoral Awards (CGS-D). Peipei's research project title is "Investigating the biological effects of environmental air pollution on lung cancer in never smokers using an integrated genomics approach" and is hosted by the Interdisciplinary Oncology Graduate Program, with her supervisor being Dr. William Lockwood. Peipei was also an awardee of a Killam Doctoral Scholarship, provided annually from the Izaak Walton Killam Memorial Fund for Advanced Studies. Joyce is hosted by the Pathology and Laboratory Medicine Graduate Program and is supervised by Dr. David Huntsman. Joyce's research project is "Dicing the tumorigenesis trajectory of DICER1 syndrome with novel murine model". Joyce also won the BC Cancer Rising Stars Award; these awards are dedicated to the advancement of the next generation of women and BIPOC leaders in research at BC Cancer.

Kira Tosefsky and Torin Halvorson are winners of 2023 Canada Canada Graduate Scholarship Master's Awards (CGS-M). Kira is hosted by the Experimental Medicine Graduate Program and her supervisor is Dr. Silke Cresswell for her research project entitled "Ketogenic Diet Interventions in Parkinson's Disease: Safeguarding the Gut Microbiome". Torin's research project title is "Engineering immune tolerance in transplantation through chimeric antigen receptor regulatory T cells (CAR-Tregs) targeting MHC Class II," hosted by Experimental Medicine under the supervision of Dr. Megan Levings.

We would also like to give a shout-out to **Chloe Gao** and **Reid Vassallo** for winning Friedman Awards for Scholars in Health. Friedman Scholars are given the opportunity to travel to other areas of the world to seek new perspectives, initiate new collaborations with experts in their fields and be exposed to different cultures. Chloe will be heading to New York, and Reid to California, to start new collaborations that will end up being incorporated into their PhD work – another opportunity we are happy to give our trainees!



Class of 2023

We had five graduates this spring - Jennifer Ji, Daniel Kwon, Michael Skinnider, Jordan Squair, and Mark Trinder. The MD/PhD Associate Program Director, Dr. Liam Brunham - Mark's supervisor - attended and celebrated with our students at the graduation ceremony for the Class of 2023 on 24th May. Congratulations! Pictured below: Daniel Kwon, Jennifer Ji and Mark Trinder. Our other graduate, Jordan Squair, could not attend as he had already headed off to start his new position in Switzerland (where he is running a lab while training in neurosurgery!). Jordan did however describe his research in a prize-winning essay entitled **"Invisible consequences of paralysis"** that was published by Science in April 2023: https://www.science.org/doi/10.1126/science.adg7669



CLASS of 2023

MESSAGE FROM JENNIFER JI

As I reflect upon the last 8 years, I am grateful for those who have supported me in my MD/PhD journey. Those were some of the best and most challenging years of my life, as I learned the ropes of becoming a physician, a scientist, and a mom. The MD/PhD program team has been an unwavering support, I thank Dr. Torsten Nielsen, Dr. Lynn Raymond, Dr. Liam Brunham for their guidance. In addition, I want to thank Jane Lee and Naureen Khan for their help.

I would like to thank my PhD mentor Dr. David Huntsman for his wisdom and kindness. Dr. Huntsman has always provided invaluable opportunities and a nurturing environment for my growth not only as a clinician scientist, but also as an individual. I am truly privileged to have the chance to work with OVCARE's world class research group and am grateful for my peers and mentors who have all been so supportive.

Finally, I am thankful for the long-lasting friendships I've built from the MD/PhD program. I look forward to taking on the next adventures with all of you!









MESSAGE FROM MICHAEL SKINNIDER

Who knew an MD/PhD would take so long?

It's been a pleasure to spend the better part of a decade in Vancouver, exploring the frontiers of computational biology. I am very grateful for the mentorship of Leonard Foster, who gave me a huge amount of freedom to develop and pursue my own ideas - I wouldn't have enjoyed my time as a graduate student nearly as much without his patient and generous support. Lynn and Torsten also provided a great deal of support in a number of different regards. I also feel very lucky to have entered the program in the year I did and to have had the chance to spend this time with some great peers.

After graduation, I will be moving to Princeton to take up a position as assistant professor. My laboratory will focus on developing machine-learning tools to decode chemical structures from mass spectrometry data. Our ability to measure small molecules in the world around us is astonishingly limited compared to more mature technologies for measuring DNA, RNA, or protein, so I see this as an opportunity to tackle a fundamental biological challenge using computation.

This was not the path I foresaw for myself when I first entered the MD/PhD program in 2015, but by the end of the pre-clinical years of medical school, I already had questions about how residency training would align with my research goals. These doubts deepened during clerkship and I ultimately made the decision not to pursue further clinical training. I spent several months exploring options in industry and academia before ultimately opting to go on the faculty job market. It was challenging to balance this with even a light elective schedule - my research stalled for most of fourth year - but in the end it proved possible and even successful. I am indebted to many people to who took time to share their experiences with me - too many to list here - especially since there is relatively little information for MD/PhDs considering careers outside of medicine. I am happy to share what I learned through this experience with anyone who is contemplating a similar path.

MESSAGE FROM MARK TRINDER

7 years is a long time. However, I have no regrets on my MD/PhD journey. I learned a lot and had a fun time doing it. My time in the MD/PhD was full of scientific discovery, transferable skill development, academic productivity, and some well-intentioned shenanigans with my friends/fellow colleagues.

There are several people that I must thank for helping me complete my MD/PhD training in one piece. I give a special thank you to Liam for his mentorship as my thesis supervisor and also providing guidance as the MD/PhD program Associate Director. My success in the program is a large testament to our strong working relationship and his encouragement of sharing our academic accomplishments. I also owe a big thank you to Torsten, Lynn, Jane, and Naureen for their help making the 7-year journey as smooth as possible. Lastly, I would not have made it through without the support of my fellow MD/PhD classmates and colleagues that have become my close friends. I give a special mention to Daniel, Alvin, Sam, Allen, and Jen.



Although we did not get any wise words of wisdom from them, in time for our Newsletter, the MD/PhD Program congratulates Jordan Squair and Daniel Kwon on their graduation!



PhD Oral Defense

Three of our students successfully defended their PhD dissertations this spring (and one more will be defending later in the term), all passing with flying colors! We are very proud to share their dissertation abstracts with everyone. Full theses are deposited at UBC cIRcle. These students returned to MD Year 3 Clinical Rotations in the summer of 2023.



Lay Summary:

Rohit Singla

Research Supervisors: Dr. Robert Rohling and Dr. Christopher Nguan Hosting Department: School of Biomedical Engineering Defense date: April 26, 2023 Dissertation title: Quantitative Kidney Ultrasound from Macroscale to Microscale

Chronic kidney disease is a common health problem that affects 1 in 10 adults. This disease can be serious, with an increased risk of adverse events and death. The standard treatment for advanced kidney disease is renal replacement therapy, which can be invasive and costly. This thesis presents ways to use ultrasound imaging and machine learning to study the kidneys non-invasively. It shows that these methods can accurately predict the health of transplanted kidneys. These results suggest that ultrasound imaging is useful for detecting, measuring, and understanding kidney disease.

ABSTRACT

Chronic kidney disease impacts 1 in 10 adults globally, with exponential increases in hospitalization, adverse cardiovascular events and mortality risk. Those who reach end-stage kidney disease require renal replacement therapy, a significant burden on a patient's quality of life and on healthcare budget. Serum and urine biomarkers of kidney disease are insensitive, potentially producing false negative results, whereas tissue biopsy is an invasive procedure that is not routinely performed and comes with complications such as bleeding and infection. There is a need for non-invasive characterization of the kidney. This thesis investigates several methods of kidney tissue characterization, ranging from the macro whole-organ scale to microstructural scale, using ultrasound imaging methods and machine learning. It presents an open detailed high-quality data set for kidney segmentation, with a demonstration of how automatic morphological measurements can be obtained in clinical ultrasound settings using machine learning. This automated measurement is comparable to human experts. It contributes how physics-based data augmentation techniques can improve the robustness of such algorithms, showing that a time-gain compensation augmentation reduces algorithmic uncertainty. It then investigates the speckle properties of transplanted kidneys, showing such properties are patient- and machine-agnostic. This study also identifies the Nakagami distribution as the best model of speckle in the kidney. Subsequent work demonstrates that ultrasound images alone can be used to predict kidney decline in transplant recipients, with speckle parameters being amongst the most prognostic. Finally, quantitative ultrasound parameters are measured in a murine study. The results show the versatility and accuracy of quantitative ultrasound to characterize the kidney, and enabling a non-invasive method for quantifying kidney disease.



Dhiraj Mannar

<u>Research Supervisors</u>: Dr. Sriram Subramaniam <u>Hosting Department</u>: Biochemistry and Molecular Biology <u>Defense date</u>: May 26, 2023 <u>Dissertation title</u>: Structure, Function, and Neutralization of SARS-CoV-2 Spike Glycoproteins

ABSTRACT

The COVID-19 pandemic erupted in 2019 and went on to have devastating impacts on global health and economies. The causative agent of COVID-19 is a novel coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was found to cause respiratory illness in humans, with symptoms ranging from mild to life threatening (pneumonia, multi-system organ failure). Like previous disease-causing coronaviruses, SARS-CoV-2 relies on a spike glycoprotein to recognize and infect human cells; and antibodies that target the spike protein can prevent viral entry from occurring, effectively neutralizing the virus. However, viruses possess the ability to evolve, and previous experience with other coronaviruses has set the precedence for spike proteins evolving altered antigenic properties and epitopes, permitting escape from neutralizing antibodies. This thesis represents efforts to respond to the COVID-19 pandemic in real time, as we sought to first define the antigenic properties and vulnerabilities of the SARS-CoV-2 spike protein, and then proceed to characterize emerging spike protein mutations and variants, with an emphasis on spike protein structure, receptor binding, and antibody neutralization. We identified antigenic and vulnerable regions in the spike protein amino terminal domain and receptor binding domain and describe heterogenous ways in which antibodies can bind epitopes within these regions. Over the course of the pandemic, significant mutational drift was observed within these regions. We found that mutations within the receptor binding domain were modular in nature, and when combined to represent variant strains of SARS-CoV-2, served to simultaneously prevent recognition of neutralizing antibodies, and enhance or preserve receptor binding affinity. Analysis of variant spike proteins showed that there was high architectural conservation across most variants, with one glaring exception revealing a novel dimers-of-trimers assembly. All variant spike proteins were antibody evasive, with some exhibiting concerning escape from immunized iv and convalescent sera. Structural analyses on the amino terminal and receptor binding domains of these variants revealed mutational mechanisms underpinning antigenic drift and rationalizing antibody escape. Finally, we structurally defined an epitope on the spike protein that enables broad neutralization of several variants, offering hope for the development of broadly effective therapies to combat variants of SARS-CoV-2.



Andy An

<u>Research Supervisors</u>: Dr. Robert Hancock <u>Hosting Department</u>: Microbiology and Immunology <u>Defense date</u>: May 19, 2023 <u>Dissertation title</u>: Dynamic analysis of gene expression trajectories in Sepsis and severe COVID-19

ABSTRACT

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection, which kills 11 million people each year. Sepsis affects the most vulnerable patients, including neonates, the elderly, and the immunosuppressed. Sepsis also has mechanistic parallels to severe COVID-19, which has killed up to 18 million people since the start of the pandemic. Furthermore, survivors of these diseases suffer long-term consequences such as post-sepsis syndrome and "Long COVID". Therapeutics for sepsis and severe COVID-19 are critically needed but designing them requires understanding of their immune dysfunction, which is highly complex due to its dynamic nature. Longitudinal analyses must be performed to fully comprehend pathophysiological trajectories. In this thesis, I analyzed whole blood gene expression trajectories in three populations: adult sepsis, adult COVID-19, and neonatal sepsis patients. Severe COVID-19 was shown to be a form of viral sepsis, since COVID-19 patients and non-COVID-19 sepsis patients converged into the same pathophysiological mechanisms after a week in the ICU, while the main initial difference was elevated antiviral response in COVID-19. Persistent immune dysfunction, consisting of both inflammatory processes and suppression of adaptive immunity, was identified to be associated with eventual mortality in both severe COVID-19 and non-COVID-19 sepsis patients, and potential immunomodulatory treatments that might reverse this persistence were predicted. These findings were recapitulated in another population of COVID-19 patients, where disease phase-specific mechanisms were analyzed and drugs targeting phase-specific mechanisms were identified to enable personalized treatment. In addition, gene expression trajectories were found to differ between discharged patients with and without "long COVID", with those without post-COVID symptoms showing resolution of immune and hemostatic processes post-discharge. Gene signatures were developed that could stratify patients into different underlying mechanisms/endotypes of long COVID. Lastly, in neonates, sepsis disrupted immune and metabolic developmental trajectories in the first week of life and predictive biomarkers for neonatal sepsis were identified. By analyzing trajectories of adult sepsis, neonatal sepsis, and severe COVID-19 disease, I was able to identify the time-dependent pathophysiological mechanisms occurring, leading to the identification of potential therapeutic and diagnostic/prognostic tools, ultimately contributing to improving management of these diseases.

MD/PhD Program and Student Highlights:

The UBC MD/PhD program made a very successful day-long tour and presentation at the University of Victoria on June 23, 2023, to promote and spread awareness about our students, their projects, and the overall program and to update ourselves on the many exciting research opportunities at the Island Medical Program in the University of Victoria.



Pictured to the right: (from left to right) Program Director, Dr. Torsten Nielsen; Program Coordinator, Naureen Khan; and Program Associate Director, Dr. Liam Brunham at the University of Victoria campus.



In April 2022, one of our current MD/PhD students, **Lianne Cho**, was contacted by a local newspaper, "The Source", to do an interview with one of their staff writers. They saw Lianne's profile on the UBC page and wanted to write an article about her and the Public Scholars Initiative she is working on.

Lianne completed her undergraduate degree at Brown University (Providence, RI), where she studied affective processing in the Clinical and Affective Neuroscience Lab. She also did internships in Toronto and the Bronx (New York, NY), which led her to appreciate how the distinct characteristics of a population inform what is needed to build an effective healthcare system for a particular community.

At UBC, Lianne is studying the relationships between early life experiences, trauma, substance use, and mental illness as part of the Hotel Study, which examines multimorbidity in those who are precariously housed. Lianne is interested in exploring different ways of knowing, and in investigating how life experiences, social environments, and cultural elements interact to inform well-being. Her objective is to contribute to the advancement of personalized mental healthcare. She is entering her 6th year in the combined MD/PhD program and is planning to defend her PhD thesis, titled "Characterization of depression among homeless and precariously housed adults", next year within the Neuroscience Graduate Program.

See full article here: <u>https://thelasource.com/en/2023/04/24/community-brain-art-understanding-and-engaging-with-research-findings/</u>

TOP GRADUATING DOCTORAL STUDENT AWARD & RISING STAR AWARD 2023



Rohit Singla Award: Top Graduating Doctoral Student Supervisors: Drs. Christopher Nguan and Robert Rohling Area of research: Chronic kidney disease

Vancouver

CoastalHealth Research Institute

Congratulations to our current MD/PhD student, **Rohit Singla**, on winning a Vancouver Coastal Health 2023 Top Doctoral Student Awards!

Vancouver Coastal Health Research Institute (VCHRI) is proud to support the future leaders of research with the Top Graduating Doctoral Student Awards and the Rising Star Awards. These awards (only two are awarded) recognize the outstanding efforts by VCHRI trainees in the realm of research excellence, serving as role models and making significant contributions to the Vancouver Coastal Health research community.

See full announcement and the 2023 Top Doctoral Student and Rising Star Award recipients here:

https://www.vchri.ca/announcement/2023/06/27/top-graduating-doctoral-student-award-and-rising-staraward-2023-recipients Our Student Liaison, **Maryam Vaseghi-Shanjani** (who ended her student liaison term this July), was nominated by Vanier -- and won -- an award to attend the 72nd Lindau Nobel Laureate Meeting in Germany. Daniel Kwon from our program was also given the opportunity to attend after his previous invitation was deferred by the COVID-19 pandemic.

Since their foundation in 1951, the Lindau Nobel Laureate Meetings have developed into a unique international scientific forum. The annual Lindau Meetings provide an opportunity for an exchange between different generations, cultures and disciplines. Once every year, around 30-40 Nobel Laureates convene in Lindau to meet the next generation of leading scientists: 600 undergraduates, PhD students, and post-doc researchers from all over the world. Maryam and **Daniel Kwon** (one of our 2023 MD/PhD graduates!) attended this year's Lindau Nobel Laureate Meeting; they were 2 out of just 4 Canadian attendees that earned the opportunity to connect and exchange ideas with Nobel Laureates and other selected young scientists from across the globe.



Daniel Kwon, recent MD/PhD graduate, and Maryam Vaseghi-Shanjani, current MD/PhD student at the 72nd Lindau Nobel Laureate Meeting in Germany.

Our newly appointed Student Liasion, **Shayda Swann** (who took over the role in July 2023 and will be supported by Saif Dababneh as alternative student liasion), attended the inaugural International Congress on Academic Medicine (ICAM) in Quebec City from April 11-15th.

ICAM is the first international gathering dedicated to academic medicine, acting as a place for the academic medicine community to meet, network, and develop new relationships and collaborations with colleagues from around the world. ICAM showcases innovation and scholarship in medical education and health research. Medical students, residents and graduate students have the opportunity to present their work, network and connect with medical education and research mentors as well as prospective employers.



At ICAM, Shayda presented a poster about her knowledge translation work titled "An artistic approach to knowledge translation: using art to connect women living with HIV to research findings". She also had a great time meeting trainees from across the country, attending workshops on writing and data visualization, and exploring Quebec City!







From January to March 2023, members of the MD/PhD Program Advisory & Admissions Committee interviewed and adjudicated an impressive cadre of short-listed applicants for admission in 2023. We are fortunate to have recruited four new students to the MD/PhD program. Details about our four incoming students will be reported in the next newsletter but for now please welcome:

Andrew Dissanayake, Catie Futhey, Curtis Leclerc and Kiera Lee. Welcome to the MD/PhD Program!



The UBC MD/PhD Program Twitter is now Live! Follow us on: https://twitter.com/UBC MDPhD

Comments and Suggestions

We welcome questions, comments and suggestions about our newsletters and our program. Please send comments to the MD/PhD Program office at: md.phd@ubc.ca

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