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Newsletter – 2020 Summer

http://mdprogram.med.ubc.ca/mdphd/news/

MD/PhD Students - Making a Difference

During the pandemic outbreak, remote work and primarily working from home became a reality for many of the UBC MD/PhD students. Over the past few months, many of our students got together and generously provided random acts of kindness and support to the community. We are very proud to share stories about how the MD/PhD students stepped up to help during this crisis. They proved that their skills as clinician-scientists are widely useful, even if they were doing their PhD work in a different field.

- Rozlyn Boutin volunteered with the Medical School Response Team to support front-line healthcare workers on their life tasks. In her role as Director of Volunteers with the Reading Bear Society, she also initiated and helped to promote and organize a physical distancing-friendly "Bear Hunt" for children in the UBC community to help them stay connected and entertained.
- Amanda Dancsok coordinated a team of PhDs, which also included Eric Zhao. They performed rapid reviews of the latest evidence of SARS-CoV-2 for the Infection Prevention and Control team of Vancouver Coastal Health. They summarized and critically appraised scientific literature surrounding mechanisms of infectious spread, disinfection protocols, biochemical prognostic factors, testing methods, and other topics. These evidence reviews went on to inform clinical guidelines in various departments of VCH hospitals.
- Philip Edgcumbe co-founded the Collective Open Source Medical Innovations for COVID-19 (COSMIC) with Dr. Christopher Nguan and Alex Waslen. The organization developed open-source respiratory support equipment for treating patients with COVID-19. They are working with doctors and design teams in Brazil, India, Bangladesh and Pakistan that are planning to use their products to treat COVID-19 patients. Victoria Baronas and Eric Zhao also contributed to the work.
- Andrea Jones volunteered with the BC Centre for Disease Control's Harm Reduction Team to support the
 rapid development and dissemination of recommendations to reduce SARS-CoV-2 transmission among
 vulnerable populations accessing harm reduction services across the province. She also amended the soonto-be released provincial opioid overdose response guidelines in light of the COVID-19 pandemic, to
 reduce transmission risk between first responders and clients. Andrea is also a co-investigator on a CIHR
 operating grant proposal investigating the rapid detection, prevention, and neurological and psychiatric
 consequences of COVID-19 among adults who are homeless or underhoused in Vancouver.
- **Daniel Kwon** developed new preclinical probes targeting proteases implicated in SARS-CoV-2 entry in collaboration with the Structural Genomics Consortium (<u>SGC</u>) at the University of Toronto.
- **Rohit Singla** delivered Personal Protective Equipment (PPE) on the Vancouver Island ... and otherwise did his part by working from home!
- Shayda Swann wrote a successful research grant with the Simon Fraser University Community Engagement Initiative and received funding to support her COVID-19 related research and knowledge translation events with the community. Shayda also volunteered with the Medical Student Response Team to support family physicians in the local community with daily tasks (i.e. childcare, housework).

MD/PhD Students - Making a Difference (con't)

- David Twa co-wrote two COVID-19 rapid response Genome BC grants with Aidan Nikiforuk (UBC PhD candidate), Dr. Natalie Prystajecky, and Dr. Inna Sekirov (UBC MD/PhD alumna). Both were funded for a total of \$165,000. The first grant supported a collaboration between the BC Centre for Disease Control and the Genome Sciences Centre and concerned the development of automated, non-proprietary extraction protocols to improve SARS-CoV-2 testing throughput for the province. The second grant looks at gene expression profiling for prognosticating COVID-19 disease burden and is in collaboration with Illumina. David Twa and Kevin Kuchinski (UBC PhD candidate) presented at the BC Centre for Disease Control Grand Rounds on June 30, "Angiotensinconverting enzyme 2 (ACE2) expression in the nasopharyngeal epithelium of SARS-CoV-2 patients."
- Maryam Vaseghi-Shanjani volunteered with BC Centre for Disease Control's tuberculosis (TB) services team to enter TB test results into patients' Electronic Medical Record (EMR) charts, as the majority of the employees in this sector have been transferred over to do COVID work.
- Eric Zhao was the project lead for the 8-11 initiative with HealthLinkBC. He helped to coordinate the recruitment and training of students to take calls at 8-11 call centres.

Thank you everyone for your generous support during the COVID-19 outbreak.

MD/PhD Award Winners







Katrina Besler



Katherine Baillie



Dhiraj Mannar

We are pleased that the current group of UBC MD/PhD students have been very successful in 2020 external award competitions. Congratulations to all the recipients and their supervisors for this year's outstanding results!

Rohit Singla won a prestigious Natural Science and Engineering Research Council (NSERC) Vanier Canada Graduate Scholarship. Rohit's application was ranked #1 out of 172 reviewed by the NSERC Vanier CGS Selection Committee. He received full points (9) in all assessed criteria (Academic Excellence, Research Potential, Leadership). Rohit's research co-supervisors are **Drs. Robert Rohling** and **Christopher Nguan**; his hosting department is Graduate Biomedical Engineering Program. Title of Rohit's research project: Intelligent renal ultrasound: Development of ultrasound-based measures using machine learning to prevent renal disease progression.

Katrina Besler is a winner of a prestigious Canadian Institutes of Health Research (CIHR) Vanier Canada Graduate Scholarship. Katrina's supervisor is Dr. Gordon Francis; her hosting department is Experimental Medicine Graduate Program. Title of Katrina's research project: Smooth muscle cell lysosomal acid lipase in atherosclerosis.

Katherine Baillie and Dhiraj Mannar won CIHR Frederick Banting and Charles Best Canada Graduate Scholarship Master's Awards (CGS-M) in their first year of eligibility.

Katie's supervisor is **Dr. Peter Stirling**; her hosting department is the Interdisciplinary Oncology Program. Title of Katie's research project: Identifying conditional synthetic lethal partners of the BAF complex enhanced by PARP or ATR inhibition.

Dij's research supervisor is Dr. Sriram Subramaniam; his hosting department is Biochemistry and Molecular Biology Graduate Program. Title of Dij's research project: The path to next generation cancer therapeutics: A structure guided approach.

More MD/PhD Award Winners!

We take pride in the ongoing achievements of our outstanding students. Congratulations!

Andy An

- Gwynne-Vaughan Memorial Award in Medicine
- Janet Louise Berryman Scholarship in Medicine
- UBC Four Year Doctoral Fellowship

Katrina Besler

- Janet Louise Berryman Scholarship in Medicine
- UBC Four Year Doctoral Fellowship

Daniel Kwon

- IODE War memorial scholarship

Dhiraj Mannar

- Faculty of Medicine Friedman MD/PhD Studentship Award

Rohit Singla

- UBC Four Year Doctoral Fellowship

Michael Skinnider

- Borealis AI Fellowship
- ThinkSwiss Research Scholarship

Shayda Swann

- Faculty of Medicine Clinician Investigator Scholarship

Mark Trinder

- Friedman Award for Scholars in Health
- Centre for Heart Lung Innovation Trainee Travel Award

Maryam Vaseghi-Shanjani

- UBC Four Year Doctoral Fellowship

Li Qing Wang

- UBC Four Year Doctoral Fellowship

All the students in the program have been awarded the President's Academic Excellence Initiative PhD Award in the summer term.

Congratulations!

Transitions in Medical Education

Transitions in medical education are recognized as potential points of difficulty for some students. For MD/PhD students these transitions can be particularly challenging because of the longer duration within each stage of training, the smaller number of peers within a given cohort with whom to share the experience, and the more abrupt transition in modes of thinking between medical research and clinical practice. At UBC, the Transition to Clinical Education (TICE) session prepares medical students to transition from classroom-based to clinical learning environments, but there is currently no structured curriculum for clinical re-entry specifically designed for MD/PhD students. Anecdotally, MD/PhD students have expressed a desire for more support in navigating this transition.

On Wednesday, 8 April, Dr. Liam Brunham, MD/PhD Associate Program Director, facilitated a "re-entry" session for MD/PhD students entering MD Year 3 this summer. MD/PhD students in MD Years 3 and 4 were also invited to the session. Prior to the session, everyone read an assigned journal article in preparation. The session reached its goals: to recognize and identify the potential challenges of the research-to-clinical transition point in MD/PhD training; to discuss strategies for managing this transition; to facilitate peer-to-peer mentoring regarding managing this transition; and to highlight program and faculty support for students. Discussions were also held on learning from the assigned reading; exploring perspectives, priorities and concerns and transitioning to clinical training; and sharing tips from students who have recently completed this transition. Overall, the session was assessed as most valuable to be continued yearly for future participants. Great job, everyone.

Class of 2020

We had five graduates this spring – Victoria Baronas, Philip Edgcumbe, Andrea Jones, Cynthia Min and Eric Zhao. Due to the pandemic lockdown, our annual social in the summer had to be postponed. The MD/PhD Program Directors and students celebrated the graduates at a virtual social on 25 May. UBC's very first interactive virtual graduation ceremony for the Class of 2020 was held on 17 June. Congratulations!



From left: Eric Zhao, Victoria Baronas, Cynthia Min, Andrea Jones, Philip Edgcumbe

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Messages from Victoria Baronas

It is with immense gratitude that I am graduating from the MD/PhD Program. It has truly been a privilege to be a part of this vibrant community at UBC. This journey has been bumpy at times with an unexpected move to Edmonton, but **Lynn Raymond, Torsten Nielsen** and **Jane Lee** have been there for me during the hard times and the good times and for that I am truly thankful.



This all started with a small idea that electrophysiology is a great tool to help us put a magnifying glass to neurons and examine them in detail. I started by trying to find the identity of a powerful regulator of a potassium channel, and ended up discovering that many other proteins (even the redox environment!) can drastically modify function. I feel very fortunate that **Harley Kurata** and **Filip Van Petegem** were my PhD mentors – it is because of them that I have learned what it takes to be a scientist and produce meaningful work.

Finally a heartfelt thank you to my classmates, **Andrea Jones**, **Cynthia Min**, **Philip Edgcumbe**, and **Eric Zhao** for their support through our transition back into clerkship and throughout the CaRMS process. The strength of its program is in the amazing individuals, and I am lucky to have walked this journey with all of you!

As I move on to my residency in General Surgery at UBC, I am excited to carry forward everything that I've learned these past seven years. All the best to the future graduates of the MD/PhD Program!

Message from Philip Edgcumbe

One of my favourite expressions is that "it takes a village to raise a child". As I reflect on my MDPhD journey I feel it also takes a village to create a clinician-scientist. As such, I'd like to the village that has supported me.

Thank you to the UBC MD/PhD Program faculty, staff and students

I am grateful to Jane Lee, Dr. Anthony Chow, Dr. Lynn Raymond, Dr. Torsten Nielsen and Dr. Liam Brunham. They celebrated the highs and supported me through the challenges of my MDPhD journey. Jane Lee provided continuity and support which helped me to stay on top of important applications and deadlines. She has an

incredible institutional memory. Additionally, I'd like to offer special thanks to Lynn. I first met Lynn in 2007 when I was a first year undergraduate student. Lynn kindly made the time to meet with me and during that meeting planted the idea that I could do my undergraduate degree in Engineering Physics and then go on to become a clinician-scientist. Over the next few years I discovered that I loved interdisciplinary research and I became convinced that training as both a physician and scientist was the right path for me. After I joined the MD/PhD Program, Lynn continued to support me through research mentorship and our annual research progress meetings, by giving me permission to take time off to attend the Global Solutions Program at Singularity University and to lead the development of the Alzheimer's XPRIZE and by giving me great advice as I transitioned back to clerkship. Lynn's unwavering support has meant the world to me.

I've formed deep and lasting friendships with many of my classmates. We all share a special bond because we are all in the same academic program. Cynthia Min, Eric Zhao, Andrea Jones and Victoria Baronas became particularly close friends as we went through clerkship and are now graduating together. Cynthia had the foresight to set up a WhatsApp group for us before we started clerkship. That WhatsApp group has been active ever since. I was also fortunate to visit alumni in Halifax, Montreal and Toronto. Will Guest, Clara Westwell-Roper and Victor Li are three alumni who have all been role models and offered great career advice.

Thank you to my research supervisors and collaborators

As I've honed my research skills as an MD/PhD student I've had opportunities to collaborate with researchers from around the world and present my research on four different continents. Thank you to **Dr. Kurt Haas** for welcoming me into his UBC Brain Research Lab when I was a high school student, introducing me to the joy of scientific discovery and for continuing to be a friend and mentor to this day. Thank you to **Dr. Robert Rohling** and **Dr. Christopher Nguan** for co-supervising my PhD and for creating a research lab and environment that brings together biomedical engineers and physicians to solve pressing clinical problems in innovative ways. I am honoured to be a co-inventor on a patent with them and proud to continue to collaborate today. I was always impressed when Chris would show up to our weekly research meetings after doing an emergency overnight kidney transplant. True dedication! Thank you to **Mr. Rohit Singla, Dr. Philip Pratt, Dr. Caitlin Schneider, Mr. Julio Lobo, Dr. Jeff Abeysekera, Dr. Omid Mohareri, Dr. Simon DiMaio** and **Dr. Andrew Wiles** for working with me as research collaborators.

Thank you to my clinical mentors

Over the last two years of clerkship, I have worked with hundreds of physicians. The vast majority of them have been kind and supportive teachers. I asked each clinician I worked with to share a "clinical pearl" that I defined as "something they wish they'd known as a medical student". I have collected over 80 of those "clinical pearls" and I plan to continue to do so during my residency. Some pearls are philosophical ("For procedures, don't let your brain get overly impressed when they go well, and don't let your heart get heavy when they don't") and others very practical ("Never turn your back on twins or triplets because they can shoot out like rockets!").

Some of the clinical mentors that have been particularly generous with their time and have helped me to become the doctor I am today are: **Dr. Chris Nguan**, my research co-supervisor and a kidney transplant surgeon; **Dr. Alex Poole**, general surgeon in Whitehorse; **Dr. Ivan Scrooby**, my rural family practice preceptor in Williams Lake; **Dr. Steven Schendel**, co-founder of our digital eye health start-up and an ophthalmologist; **Dr. Claire Sheldon**, neuro-ophthalmologist and UBC MD/PhD alumna at the Vancouver Eye Care center; **Dr. Brian Brodie**, family doctor and the former Chair of the Canadian Medical Association; **Dr. Michael Smith**, pediatrician; **Dr. Callen Sor**, pediatrician; **Dr. Bruce Forster**, radiologist, **Dr. Axel Rohr**, neuro-interventional

radiologist; **Dr. Sarah Baker**, radiation oncologist; **Dr. Fred Hsu**, radiation oncologist; and **Dr. Karen Joughin**, plastic surgeon and running group mentor. I hope to emulate many of their personal and professional qualities as I move into my own career as a doctor. I will also strive to bring the same willingness to mentor and teach to my own practice.

Thank you to my family

By the time I showed up for kindergarten, my Dad had me convinced that math was my favourite subject and I haven't looked back since. My Mom instilled a true love of learning and curiosity within me. My brother taught me how to find joy in the small victories in life. My sister helped me to develop a positive and resilient attitude. My deepest gratitude to all of them. One sadness is that my dear grandfather, **Marc Soule**, passed away in early 2020 and was so close to seeing me graduate.

Looking to the future – pushing interventional radiology to new frontiers

In response to the recent COVID-19 pandemic and ensuing medical equipment scarcity I co-founded the <u>Collective Open Source Medical Innovations for COVID-19</u> (COSMIC) organization. Our 100+ volunteers at COSMIC are developing open-source respiratory support equipment for treating patients with COVID-19. While creating and coleading COSMIC, I drew on the clinical, research, engineering and leadership skills I developed as an MD/PhD student. COSMIC is a truly interdisciplinary endeavor.

My career mission and massively transformative purpose is to create healthcare abundance and practice deep medicine. I define "healthcare abundance" as universal high-quality and effective healthcare. I define "deep medicine" as medicine in which we digitize relevant patient data, apply the best of deep learning to diagnose and manage the patient's health and have a deep empathetic connection with our patient. I am working towards that goal by building a digital eye health start-up that enables virtual eye exams and teleconsultations and by pursuing a career in interventional radiology. Within radiology, I look forward to both pioneering new advances in image-guided treatments and to help the field of radiology move towards a more patient-facing specialty.

In conclusion, I am grateful and proud to be graduating from the UBC MD/PhD Program and joining the ranks of our accomplished alumni. I look forward to staying in touch with all of you. Please do not hesitate to reach out.

Tuum Est – It's up to you

Message from Andrea Jones



It is with deep gratitude that I reflect on these past seven years, and take this opportunity to give thanks to my incredibly supportive community.

The MD/PhD training experience has been formative to my growth, personally and professionally. Through this program, I had the opportunity to pursue my interests in clinical medicine, social determinants of mental health, neuropsychopharmacology, epidemiology, and biostatistics. My dissertation examined the risk factors, consequences, and dynamics of psychotic symptoms, as part of a longitudinal community-based study of adults living in precarious housing or homelessness in Vancouver. Learning with the community and with the study team has led to some of the most meaningful experiences of my journey.

The numerous brilliant and kind researchers and clinicians that I have had the privilege of working with were instrumental in my development as a clinician scientist. In particular, I have had the great fortune of pursuing this joint program with my supervisor, **Dr. Bill Honer**, an exceptional mentor, scientist, and leader. He challenged me, opened doors, stoked the flames when I was excited about new ideas or directions. Of many, we share the trait of integrating vastly different fields of research to try to make sense of the world. I hope to continue to interface, integrate, and innovate across boundaries, as he has taught me.

My journey would not have been possible without the endless support of the MD/PhD Program. Thank you **Dr. Lynn Raymond** for inspiring me to pursue this path when I was a Masters student in your neuroscience lecture. You have provided invaluable support, wisdom, and leadership over these years, and I am thrilled to be training with you and the neurology community. Thank you **Dr. Torsten Nielsen**, for your unabated enthusiasm and diligence in advocating for the next generation of clinician scientists. **Dr. Liam Brunham**, thank you for your helpful "11th-hour" advice in the days before the CaRMS rank list was due! **Jane**, thank you for your warm encouragement and exceptional organization that has made this journey as smooth as possible.

To my cohort who started in 2013 – we are done, or just about! I am so grateful for our friendship! Victoria, Eric, Philip and Cynthia, it has been so wonderful to ride the throws of grad school and clerkship with you! I am so excited to see where this next chapter takes you all – I am sure to exceptional heights! Amanda, you are a star, and your passion and determination will continue to guide you to achieve greatness. Parker, Frank, Allen, and Adam – I am always impressed by your intellect, talent, and kindness – I can't wait to see all that you will achieve as you round the bend on this chapter! Thank you deeply to the MD/PhD students who have graduated before me, who provided such timely wisdom and inspiration over the years – Clara, Alexis, Victor, Sandy, Gareth, Dan, Long – thank you! To Lianne, Cynthia, Sam, Alvin, Mark, Roz, Paulina, Jennifer, Daniel, and the current MD/PhD students – your enthusiasm and commitment to your work and your communities continue to inspire me. Keep it up and do continue to support one another!

A heartfelt thanks goes to my parents for their continual love, optimism and support to pursue my passions. Thanks to my family and my dear friends, from med school and beyond, who have been so loving and encouraging over the years. Finally, thank you to **Jeremy**, for his steady love, support, and understanding and for challenging us to keep pushing the limits of what we can achieve together.

It is with incredible hope and excitement that I join the UBC Neurology residency program in July. Amidst the challenging and uncertain time of the COVID-19 pandemic, I am grateful for the love and support of this community evermore, and feel privileged to continue on the clinician scientist path.

Message from Cynthia Min

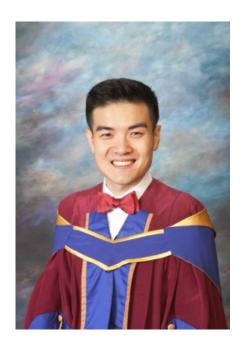


It's hard to believe that I'm graduating! Being in the MD/PhD Program has given me the time and opportunities to explore my true interests and understand what I value in life. I look forward to further exploring how I can integrate academic and clinical medicine to make meaningful change in residency and beyond.

Special thanks to **Dr. Lynn Raymond** and **Jane Lee** for their constant support throughout my training!

Message from Eric Zhao

It is an honour to graduate from the UBC MD/PhD Program standing upon the shoulders of a community of mentors, colleagues, and friends. I could not have anticipated that this time would come during a global pandemic, but the current situation only emphasizes the need for clinician-scientists, prepared to overcome pressing clinical challenges through research. I am proud to see many of my fellow MD/PhD colleagues applying their biomedical research skills to the urgent clinical and biological questions underlying SARS-CoV-2 and its societal impacts.



The MD/PhD Program has been the pinnacle formative experience of my life. It has challenged and supported me through seven rewarding years of non-stop personal and professional development. I wholeheartedly recommend the UBC MD/PhD Program to anyone passionate about pursuing an impactful career as a clinician-scientist. Given the opportunity, I would choose to do it all again. To future UBC MD/PhD students and applicants, do not hesitate to contact me. I would be delighted to learn your career aspirations and answer any questions or concerns. We are strongest as a cohesive and supportive community, and your success is my success.

Through my research, I am thoroughly convinced that open, deep, and comprehensive analysis of the cancer genome is at the core of precision oncology. The Personalized Oncogenomics (POG) Program at BC Cancer and Canada's Michael Smith Genome Sciences Centre has established itself as a world leader in research leveraging the whole genome and transcriptome for treatment selection. I am honoured to have been a part of POG from its early days to its recent publication of the first 570 cases in Nature Cancer. POG is extraordinarily supportive of its trainees, as manifested through its project design, publication policy, and allocation of funding. POG's structure makes trainees feel welcomed, empowered, and valued, and serves as an unparalleled career launchpad for anyone interested in precision oncology research. I an infinitely grateful to my supervisor Dr. Steven Jones for his research/career mentorship and for always challenging me to expand my vision and tap into the resources and opportunities available to me. I would also like to thank Dr. Marco Marra, who was my earliest research supervisor back in 2010 and has been a constant source of mentorship and inspiration since. A big thank you to my fellow graduate students and research colleagues (who are too many to list but are acknowledged in my PhD thesis). Lastly, thank you to all the uniquely visionary cancer physicians I have met through POG, especially Drs. Janessa Laskin, Daniel Renouf, Sophie Sun, Kasmintan Schrader, Howard Lim, Karen Gelmon, Xiaolan Feng, Stephen Chia, Diego Villa, David Schaeffer, Jonn Wu, Christian Steidl, and Stephen Yip.

Thank you to my fellow MD/PhD students, past and present, for your companionship along this journey. The past seven years would not be the same without eye-opening conversations on life and purpose with **Philip**, warm and galvanizing "thesis reality checks" with **Andrea**, commiserating on data science bottlenecks with **Allen**, or sharing in the med student community and the arts with **Amanda**. It has been a privilege to witness your early careers as you become rising stars your fields. I am also grateful for the friendships formed with individuals in the **MD classes of 2016-2020**, the staff of the **Medical Student and Alumni Centre**, as well as fellow representatives of the **Medical Undergraduate Society**, **Canadian Federation of Medical Students**, and the **Clinician-Scientist Trainee Association of Canada**.

I could not have asked for better MD/PhD Program directors and staff, who have supported me in more ways than I can count. The guidance of **Dr. Lynn Raymond** and **Dr. Torsten Nielsen** through the early years helped me navigate the unsteady waters of award applications, committee meetings, and the formation of my professional identity. Their every decision has been rooted in kindness and compassion, with the best interests of students at heart. I appreciate their willingness to "rattle spears" for our benefit. Whether it's arranging a stellar line-up of clinicianscientist mentors to speak at the Building Bridges seminars or offering to rally Faculty support for an unconventional but valuable clinical elective, their willingness to go above and beyond to fight on our behalf has been unparalleled. Congratulations to Dr. Raymond on her illustrious term as MD/PhD Program Director, and for her directorship of the Djavad Mowafaghian Centre for Brain Health. I am excited to see **Dr. Liam Brunham** step in as Associate Director. Last but not least, I am deeply grateful to **Jane Lee**, the heartbeat of the MD/PhD Program, who has been ever responsive, infinitely patient, and always knowledgeable.

My sincerest thanks also go out to the MD/PhD Program Committee, as well as the various institutional partners who make the program what it is. In particular, I'd like to acknowledge **Dr. Cheryl Holmes** and **Dr. Roger Wong** for their support of the program and for being personal mentors throughout my time in the Faculty of Medicine. Lastly, a warm thank you to **Student Affairs**, especially **Dr. Janette McMillan**, for being there for myself and my peers during challenging times.

After 11 years at UBC, it is with excitement and a full heart that I join the Department of Radiation Oncology at The University of Toronto for my residency training. I chose this program for its record of rigorous clinical training and support for research. I am delighted to continue pursuing my research endeavours in Toronto under the supervision of **Dr. Scott Bratman** and **Dr. Trevor Pugh**. I look forward to using all that I have learned at UBC to tackle new challenges in an ever more collaborative national cancer research landscape. I look forward to keeping in touch and working closely with my BC-based colleagues in the future.

Meet Incoming Students - Shayda Swann and Li Qing Wang

Shayda Swann and **Li Qing Wang** were admitted into the MD/PhD Program in May 2020, applying and entering during their Med I year. Welcome aboard!



Shayda Swann grew up in Montana and moved to Canada in 2007. She completed her BSc in Health Sciences at Simon Fraser University and during this time became interested in infectious disease research. Prior to medical school, Shayda worked on HIV cure research with Dr. Mark Brockman at SFU and Dr. Zabrina Brumme at the BC Centre for Excellence in HIV/AIDS. During this time, she also developed an interest in community engagement and participatory health research. Shayda will continue to follow her passion for HIV research during her doctoral studies. She will work at Oak Tree Clinic with Drs. Helene Cote and Melanie Murray to study healthy aging and endocrine changes in women living with HIV. In the age of antiretroviral medication, people living with HIV can reach life expectancies approaching that of the general population. While this is major accomplishment of medical science, it also brings about a new problem – the need to understand the longterm effects of HIV infection and antiretroviral use on healthy aging. Currently, more than half of people living with HIV are women, yet little is known about how HIV infection and antiretroviral treatments affect women's reproductive, endocrine, and social health. Her project will compare the prevalence of hormonal dysregulation, associations of hormonal dysregulation and comorbidities, and longitudinal changes in markers of aging between women living with HIV and their HIV-negative counterparts. Shayda is excited to be part of this multidisciplinary, community-engaged project, which will include biological, clinical, and socio-structural dimensions. She hopes that her research will help to improve the care of women living with HIV and encourage providers to see their patients from a more holistic lens. Outside of research, Shavda enjoys dancing, baking, and spending time with loved ones.



Li Qing Wang completed her BSc. Honours in Cellular, Anatomical and Physiological Sciences at UBC. She is passionate about maternal-fetal health in both the research and the clinical aspects. During her undergraduate studies, Li Qing studied CCR5 polymorphisms and pre-eclampsia with **Dr.** Wendy Robinson. For her PhD research project, Li Qing will work in the Robinson Lab. Her research focus is studying immune-related methylation quantitative trait loci (mQTLs), which are SNPs associated with differential DNA methylation, in the context of placental insufficiency and pregnancy complications. Li Qing hopes to better understand the role of immune imbalance in the pathophysiology of pregnancy complications and develop predictive models for adverse pregnancy outcomes. Outside of research and medical school, Li Oing plays the piano and earned her Licentiate Diploma in Piano Performance (LRCM) in 2015. She also loves travelling, going to concerts, baking, cats and learning new things!

UBC Medical Journal

The UBC Medical Journal (UBCMJ) is a student-driven academic journal with a goal to engage students in dialogue in medicine. MD/PhD students serve as executive members and editors to oversee the day-to-day management and editoral contact of the journal. Daniel Kwon, Alvin Qiu, Mark Trinder and Maryam Vaseghi-Shanjani appeared in the interviews representing the MD/PhD Program. Keep up the good work!

PhD Oral Defense

Three of our students successfully defended their PhD dissertations this spring with flying colours. We are very proud to share their research abstracts with everyone. Full theses are deposited at UBC <u>cIRcle</u>.



Rozlyn Boutin

Rozlyn Boutin

Research supervisor: Dr. Brett Finlay

Hosting department: Microbiology & Immunology

Defense date: 15 May 2020

Dissertation title: Infant gut fungal dysbiosis drives asthma onset and severity

ABSTRACT

Global asthma prevalence has reached epidemic proportions, emphasizing an urgent need for research into the causes of this burdensome and incurable early-onset disease. A growing body of evidence implicates the early life gut microbiota in immunomodulation relevant to asthma, and suggests that an imbalanced (dysbiotic) gut microbiota may precede disease onset. Notably, fungal communities of the infant gut microbiota (the mycobiota) are understudied, but have recently been shown in two birth cohorts to differ strikingly according to atopy/asthma risk in association with bacterial dysbiosis. I hypothesized that fungal dysbiosis in the infant gut contributes to asthma development through interactions with the host and immunomodulatory bacteria to alter key early-life immune mechanisms involved in this disease. To address this hypothesis, I first generated additional evidence supporting associations between bacterial dysbiosis at three months of age with atopic outcomes in Canadian children from the CHILD Cohort Study. I then examined the fungal communities of the gut microbiota in these infants at three months and one year of age and characterized features of early life gut fungal dysbiosis associated with atopic disease outcomes at age five years. Replicating our lab's findings in Ecuadorian infants, these analyses revealed that overgrowth of the yeast Pichia kudriavzevii in the infant gut was associated with atopic outcomes at age five years. Using a mouse model of allergic airway disease, I then established a causal role for overgrowth of P. kudriavzevii within the infant gut in increasing allergic airway disease severity later in life. Finally, I used in vitro microbiology techniques to determine how bacterial-fungal interactions shape asthma-associated gut microbiota community structures. I found that bacterial-derived short-chain fatty acids (SCFAs), which we found to be reduced in abundance in stool from infants at risk of atopic disease, inhibit the growth of P. kudriavzevii and the ability of this yeast to adhere to gut epithelial cells. Using biologically relevant experimental systems that broadly address the role of early life fungal dysbiosis in asthma, I provide mechanistic insights into gut microbiota bacterial fungal interactions, mycobiota-immune interactions, and the gut-lung axis. This work may ultimately inform the development of novel microbiota-based therapeutics.



Frank Lee

Frank Lee

Research supervisor: Dr. Edward Pryzdial

Hosting department: Pathology & Laboratory Medicine

Defense date: 2 June 2020

Dissertation title: Functional regulation of anticoagulant protein C and clotting

factor Va by fibrinolytic plasmin

ABSTRACT

Thrombosis is the leading cause of death and disability. Clots (i.e. thrombi) that obstruct blood flow from delivering oxygen and nutrients to tissues require rapid removal. The main treatment is with tissue plasminogen activator (tPA), which activates the enzyme plasmin from its circulating precursor plasminogen. Plasmin works by

degrading fibrin, a meshwork of fibers that form the structural scaffold of the clot. Although these thrombolytic drugs have saved countless lives, their use is associated with life-threatening complications including increased bleeding risk and cellular toxicity. By greatly elevating plasmin concentrations with intravenous tPA, the effect of plasmin on its other substrates apart from fibrin may play an important role in dysregulating hemostasis, giving insight into physiological mechanisms that are impacted by thrombolysis. This thesis focuses on the modulatory effects of plasmin on protein C (PC) and activated clotting factor (F) V (FVa). Fragmentation of PC by plasmin assessed in conjunction with activated PC (APC)-specific chromogenic substrate cleavage showed increased amidolytic activity correlating with proteolysis of the PC heavy chain (PC-Hc). Plasmin-cleaved PC inhibited inactivation of FVa and had no appreciable effect on prolonging plasma clotting times in PC-deficient plasma compared with APC. N-terminal sequencing showed that plasmin cleaves PC-Hc within the autolysis loop and at the canonical thrombin activation site. Our findings so far are consistent with natural and engineered APC variants, affected within or adjacent to the autolysis loop, that have reduced anticoagulant function. Interestingly, these mutants still signal through protease-activated receptor 1, suggesting a novel role for plasmin-modulated (A)PC in conferring cytoprotection. For FVa, plasmin-specific cleavage of chromogenic substrate and protein staining were used to confirm the requirement for proteolysis by plasmin in converting FVa into an accelerator of tPA. Free and lipid-binding fragments both enhanced tPA activity. 125I-radiolabeled plasminogen binding indicated an interaction with an unbound fragment derived from FVa-Hc that is C-terminal lysine dependent. The tPA-accelerating fragment of FVa-Lc is derived from the C1 and C2 lipid-binding domains and could nonenzymatically enhance fibrinolysis specifically at the site of vascular injury. Understanding the functional regulation of PC and FVa by plasmin offers novel insights toward improving thrombolysis therapy.



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Defense date: 26 May 2020

Dissertation title: Characterization of programmed death ligands in B-cell non-

Hodgkin lymphomas

ABSTRACT

Non-Hodgkin lymphomas constitute a conglomerate of malignancies that originate from a population of white blood cells termed lymphocytes. Lymphoid cancers are a significant health burden in Canada, with over 9,200 new diagnoses in 2018. Of those newly diagnosed, roughly 40% will die within five years. Studying a subpopulation of aggressive B-cell derived non-Hodgkin lymphomas with both high-throughput sequencing and conventional research techniques, we identified recurrent, somatic aberrations in two genes that are contributors to lymphoma pathogenesis: programmed death ligands 1 (CD274) and 2 (PDCD1LG2). In healthy individuals, programmed death ligands are central to maintaining peripheral tolerance and preventing autoimmune disease. However, we establish that malignant B-cells hijack this axis to suppress the antitumor immune response.

Within this dissertation, we report on the frequency of programmed death ligand structural genomic rearrangements in seven different B-cell lymphoma entities and demonstrate the effects of structural genomic rearrangements on gene expression. Additionally, we evaluate ectopic cytokine stimulation, copy number variations, DNA methylation, and micro RNA regulation as additional mechanisms of deregulating programmed death ligand expression. Using novel capture-based high-throughput techniques, we characterize, at base-pair resolution, the subtypes, cluster locations, and partners of programmed death ligand structural genomic rearrangements. We go on to demonstrate the effects of protein expression and characterize the functional impairment resulting from deregulated programmed death ligand binding in both B and T-cell populations using retroviral cell line models. Finally, in evaluating flanking breakpoint sequences of programmed death ligand structural genomic rearrangements, we propose the molecular mechanisms involved in producing these aberrations. Taken together, our work informs on relevant components of B-cell non-Hodgkin lymphoma pathogenesis and substantiates the effectiveness of molecularly precise therapies targeting the programmed death ligand axis, as they become mainstays of lymphoma treatment.

UBC Medicine Spring Gala

The 26th UBC Medicine Spring Gala happened pre-COVID, on Saturday, 7 March 2020, at the UBC Chan Centre. The Spring Gala is a non-profit production, organized completely by the UBC medical and MD/PhD students. Profits from ticket sales were donated to a local BC charity. From dazzling dance displays to moving vocal performances, the students put together an unforgettable night. Many of the M.D/PhD students performed at the event. Here are some memories to share with our readers: https://www.facebook.com/ubcmedgala.

- * Choir: Katrina Besler (conductor), Amanda Dancsok, Eric Zhao, Maryam Vaseghi-Shanjani
- * Terpsichore: Amanda Dancsok, Lianne Cho
- * Murmur & Trill (with Santa Ono): Eric Zhao
- * FIFE Girls: Amanda Dancsok
- * Medical Undergraduate Student Ensemble: Paulina Piesik
- * Karotid Chop: Wissam Nassrallah
- * Class of 2020 Skit "Mamma Mia!": Philip Edgcumbe, Andrea Jones, Eric Zhao

MD/PhD "Building Bridges Seminar Series" - ALL ARE WELCOME

Our seminar series aims to illuminate the relationship that exists between clinical practice and medical research, allowing MD/PhD and other interested students to hear about different career tracks and various ways to combine clinical and research work. In addition to speaking about their active research, the invited speakers discuss their experiences and training backgrounds, share their advice with prospective clinician-scientists, and give their opinions on career development options for clinician-scientists. All faculty, clinical investigator trainees of all stripes, students in the Faculty of Medicine and prospective applicants to our program are invited. Our usual venue is at the Medical Student Alumni Centre, 6:00-7:00 pm, web linked at https://meet.vc.ubc.ca/webapp.

• Date: 27 January 2020

Invited speaker: Dr. Thalia Field

Associate Professor, Department of Medicine (Neurology), UBC

Postgraduate Fellowship Program Director and Co-director of Research, Vancouver Stroke Program

• Date: 20 April 2020

Invited speaker: Dr. Zachary Laksman

Clinical Assistant Professor, Department of Medicine (Cardiology), UBC

Director, Atrial Fibrillation Clinic and Inherited Arrhythmia Clinic, St. Paul's Hospital

Thanks to **Dr. Field** and **Dr. Laksman** for sharing their clinical and research experiences with us.

For information on **upcoming seminars**, please visit our webpage at http://mdprogram.med.ubc.ca/mdphd/seminars/

Comments and Suggestions

We welcome questions, comments and suggestions about our newsletters and our program. Please send comments to the MD/PhD Program office, 2894 Detwiller Pavilion, 2255 Wesbrook Mall, UBC, Vancouver, BC, Canada V6T 2A1. Phone: 1-604-822-7198 Fax: 1-604-822-7917

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