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Newsletter – 2021 Summer

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

MD/PhD Program Director - Dr. Torsten Nielsen

We are pleased to announce that Dr. Torsten Nielsen will continue as Director of the MD/PhD Program. After a directorship review at the end of his first three-year term, Dr. Nielsen's appointment has been renewed for another three years.

Dr. Nielsen has accomplished incredible work during his first term as the Program Director, and will continue to provide leadership to the program for it to grow and develop, and support the training of clinician-scientists. In his role, Dr. Nielsen plans to continue to build capacity through attracting top-notch students to the program, making the application and interview process more accessible to a diverse group of candidates, and strategically raising stipend funding for the trainees.

Since its inception, UBC's MD/PhD Program has grown tremendously. In the last 10 years, the program has increased enrollment from 19



Dr. Torsten Nielsen

to 31 students, and has achieved record sizes for both our graduating and incoming classes. Our mandate is to provide openings and mentorship for a new generation of bright young people to pursue their dreams to become clinician-scientists in any of the many areas of medical need and scientific opportunity available in this emerging age of big data that is affecting all fields.

Dr. Nielsen is Professor in Anatomical Pathology, Department of Pathology & Laboratory Medicine. He is a clinician-scientist based at Vancouver General Hospital and the BC Cancer Agency, who specialized in sarcomas and breast cancer, working to translate molecular research findings into clinical care for cancer.

We look forward to the continued growth and development of the MD/PhD Program under Dr. Nielsen's leadership. Please join us in congratulating Dr. Nielsen on his reappointment.

UBC MD/PhD PROGRAM

MD/PhD Award Winners

We are pleased that the current group of UBC MD/PhD students have been very successful in 2021 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.

Shayda Swann and Maryam Vaseghi-Shanjani were winners of the prestigious Canadian Institutes of Health Research (CIHR) Vanier Canada Graduate Scholarship. 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. Shayda's co-supervisors are **Dr. Hélène Côté** and **Dr. Melanie Murray**; the title of her research project is "Investigating the role of reproductive hormones in healthy aging for women living with HIV: A community-collaborative cohort study". Maryam's supervisor is **Dr. Stuart Turvey**; her research project is entitled "Discovery and characterization of novel monogenic causes of allergic diseases in humans". Shayda and Maryam are both hosted by the Experimental Medicine Graduate Program.

Andy An won a CIHR Frederick Banting and Charles Best Canada Graduate Scholarship Doctoral Award (CGS-D). His research project title is "Temporal transcriptomic and epigenetic analysis of leukocytes in sepsis and COVID-19 patients". Andy was also an awardee for the <u>Killam Doctoral Scholarships</u>, provided annually from the Izaak Walton Killam Memorial Fund for Advanced Studies. These are the most prestigious graduate awards administered by UBC, and are awarded to the top doctoral candidates in the annual Tri-Agency Canada Graduate Scholarships - Doctoral and UBC Affiliated Fellowship competition. Also, Andy was one of the <u>finalists</u> in the 2021 UBC Three-Minute Thesis competition, for his talk on "Identifying mechanisms of persistent immune dysfunction in sepsis survivors". Andy's supervisor is **Dr. Robert Hancock**, in the Department of Microbiology & Immunology.

Luke MacLean won a Natural Sciences and Engineering Research Council of Canada (NSERC) Alexander Graham Bell Canada Graduate Scholarship. The title of his research project is "The design of an ultrasound-augmented spinal surgery drill for freehand navigation of pedicle screws". Luke was also a recipient of the UBC Friedman Award for Scholars in Health, receiving funding for six or more months of study outside western Canada. Luke plans to travel to John Hopkins University to work with a laboratory research collaborator on a direct extension of his thesis. His project is entitled "Deformable guidance of spinal surgery bone cutting using ultrasound-augmented tools". Luke's co-supervisors are **Dr. Antony Hodgson** and **Dr. John Street**, in the School of Biomedical Engineering.

Lianne Cho and Li Qing Wang won CIHR Frederick Banting and Charles Best Canada Graduate Scholarship Master's Awards (CGS-M). Lianne's supervisor is **Dr. William Honer**; her hosting department is the Graduate Program in Neuroscience, and the title of her research project is "Studying depression in a homeless and precariously housed sample". Li Qing's co-supervisors are **Dr. Wendy Robinson** and **Dr. Sarka Lisonkova**; her hosting department is the Graduate Program in Reproductive and Developmental Sciences. The title of Li Qing's research project is "Genetic and non-genetic factors of pre-eclampsia".

Congratulations!

All the students in the program were awarded the President's Academic Excellence Initiative PhD Award (PAEIPA) in the winter and summer terms.

Class of 2021

We had a bumper crop of six graduates this spring – Amanda Dancsok, Parker Jobin, Adam Ramzy, David Twa, Cynthia Ye and Allen Zhang.

On 25 May, graduates in MD Program gathered to celebrate their achievements during the Faculty of Medicine's virtual <u>Hooding Ceremony</u>. UBC's interactive virtual graduation ceremony for the Class of 2021 was held on 2 June. Due to the pandemic lockdown, we have made the difficult decision to move our annual May social to the fall. We congratulate our Class of 2021 and wish them all the best!!

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Amanda Dancsok investigated the immune response to aggressive cancers of the bone or soft tissues known as sarcomas. Her findings were used to help design clinical trials for sarcoma patients receiving a new type of cancer treatment called immune therapy, which works by igniting an immune system attack on cancer cells.

Amanda has joined the Pediatrics Residency Program, University of Saskatchewan.

Message from Amanda Dancsok

It is difficult to put into words the closing of this monumental chapter of my education and my life. My journey from hopeful applicant through struggling scientist to budding physician has presented me with challenges that I never anticipated or quite knew how to tackle. I have grown not only as a researcher and clinician, but as a person, in some of the most unexpected ways. Times of stress, exhaustion, and defeat have taught me a sense of empathy for others going through difficult times, on a level of understanding that I couldn't have learned without those experiences. This tenacious empathy serves me as both a clinician and a person, as I seek to see, hear, and understand others with grace, kindness, and humanity. I am incredibly grateful for the supports, mentors, peers, and people who helped me find my way to success through it all, while also fiercely proud of my perseverance and growth.

First, I would like to thank my supervisor and MD/PhD Program Director, **Dr. Torsten Nielsen**, for his wisdom, guidance, encouragement, and unwavering empathy throughout all of the successes and numerous challenges I have faced. His support has been above-and-beyond, and I am truly grateful to have worked with such an inspiring and kindhearted leader. I am thankful to the other program directors, **Dr. Lynn Raymond** and **Dr. Liam Brunham**, as well as **Jane Lee**, our kindhearted administrator and advocate. Thank-you to my PhD supervisory committee – **Dr. Peter Watson**, **Dr. Tony Ng**, **Dr. Michael Underhill**, and **Dr. Haydn Pritchard**, for your practical and administrative support, but also for your strong encouragement and personal and professional mentorship. To the Nielsen lab group, for your practical assistance, encouragement, and collaboration. Particular thanks to **Dr. Jamie Lim** for your dear friendship and unwavering encouragement – I wouldn't have made it without you.

Thank-you to my incredible support base of my family and friends, without whom I would not be able to work as hard as I do. To my fellow MD/PhD peers, especially **Dr. Andrea Jones**, for your endless support and commiseration. To my medical school friends, especially **Dr. Leah Kosyakovsky**, **Dr. Khue Tu Nguyen**, **Dr. John Peel**, **Dr. Jen Clune**, **Dr. Julia Zazoulina**, **Dr. Nitai Gelber**, and **Dr. Dianne Semeniuk**. All of you inspire me every single day. To my lifelong friends, **Lucas Popowich**, **McKeely Borger**, **Keira Lorenzen**, **Taylor Buchko**, **Susie Kasteel**, **Rebekah Leaver**, and **Kayla Gardner**, for your love and understanding and deep emotional support. Thank-you for sticking with me through the harder times, it did not go unnoticed. Thank-you to my sisters **Amy Pusch** and **Alissa Stewart** and their families, who are the whole reason behind the work I do. Most importantly, thank-you to my parents, who always believe in me, especially when I don't.

My time in the UBC MD/PhD family was 8 years long, but all at once it seems short. I am incredibly lucky to have had the opportunity to complete this stage of my training in such a renowned program, among my very inspiring and talented peers, in the most beautiful city in the world. Best of luck to current and future members of this powerful family. I am here for you now and always for support, laughs, or tears. The journey is worth it.



Many proteins secreted outside of cells are regulated by enzymes called matrix metalloproteinases. **Parker Jobin**'s research revealed new extracellular roles for intracellular enzymes and how matrix metalloproteinases modulate these roles, and exposed novel biology by tapping into an unknown well of molecules that react with matrix metalloproteinases.

Message from Parker Jobin

Eight years is a long time. I count myself fortunate enough to have spent the last eight years, nearly a third of my lifetime, with such great company amongst the faculty, staff, and students of the UBC MD/PhD Program. It is hard to express in words everything that's happened over the course of nearly a decade earning both a medical degree and a PhD at UBC. It was a nothing less than a roller coaster ride of emotion. UBC is privileged with world class researchers and clinicians and it was my honour to work with them and learn from them, to have them as mentors. I would like to thank our Program Directors during my time with the program, Drs. Lynn Raymond and Torsten Nielsen, their hard work and simple faith in the success of their students has led us all towards our accomplishments. I remember the first time I met Dr. Nielsen at the annual open house for the program in 2011, I'd never heard of the program before that showcase but after speaking to him then I knew pursuing a career as a clinician scientist was what I should strive for. I also remember when I first ran into Dr. Raymond after my successful PhD defense; she was so happy for me after all of our meetings over the years reviewing my progress through my research. She really cares for her students in her program and it shows. I would also like to thank our associate program director Dr. Liam Brunham for his leadership and Jane Lee for her management especially now with the new challenges the pandemic has placed on us all. As I prepare for the next adventure after UBC, I can't help but feel my time here was some of the best years of life. I wish the best of luck to the current and future students of the MD/PhD program, their training is in excellent hands.

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Adam Ramzy studied the role that the hormone insulin plays in the development of insulinproducing beta-cells. He examined a gene therapy approach to treat diabetes and subsequently developed a new theory on how beta-cells produce mature insulin. This work revises a decades old dogma and provides insight into new treatment avenues for diabetes.

Adam has started his new career as a Research Analytical Consultant, at the Boston Consulting Group, USA.

Message from Adam Ramzy

After eight years it is with a bittersweet taste that my MD/PhD journey at UBC comes to an end. My sincerest thank you to all of those who contributed to my success in science and medicine both directly and indirectly. Though I could reflect upon the many exciting and challenging experiences I've had in the lab and in the hospital, I would prefer to take a moment to recognize the incredible group of people that have made my MD/PhD at UBC one of productivity, growth, friendship, and contribution.

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First and foremost, I owe particular thanks to my supervisor **Dr. Timothy J Kieffer** for his inspirational and supportive guidance. Whether in the form of a hallway chat, a 4-hour lab meeting, or a comment-peppered manuscript, I am grateful for your time to teach, challenge, and push me. Your mentorship has yielded lessons I will use for my entire career ahead.

I thank my supervisory committee members, **Drs. Susanne Clee, Scott Covey, Jim Johnson, Bruce Verchere**, and **Garth Warnock** for their support through challenging me, sharing their expertise, and guidance along the winding road to a PhD. A special thank you to **Dr. Garth Warnock** for sharing his guidance not only in committee meetings, but also for his generosity by taking the time to teach in the operating room. My gratitude to **Dr. Jim Johnson** for his consistent attention to detail and teaching the highest standards of scientific rigor. Thank you to **Dr. Scott Covey** for always making the time to help and sharing his substantial experimental knowledge. My appreciation to **Dr. Bruce Verchere** for his expert guidance and consistent willingness to share resources, time, and support. Thank you to the late **Dr. Susanne Clee** for thinking outside the box and helping find unexpected solutions.

Thank you to all the members of the Kieffer lab for always asking the tough questions. I have been fortunate to work with many talented and kind graduate students, fellows, and technicians. To my fellow office-mates **Chiara Toselli, Nelly Saber, Ursula Neumann, Anna D'Souza,** and **Blair Gage**, thanks for always making time spent in the lab more fun and always taking the time to help. To **Travis Webber, Ali Asadi, Robert Baker, Majid Mojibian, Maria Glavas, Cara Ellis, Sandra Pereira,** and **Shannon O'Dwyer**, thanks for your teaching, guidance, assistance, and comradery. Thanks to **Nazde Edeer** for her hard work and thanks to the many others for their contributions to these studies.

Thank you to the UBC MD/PhD Program for their professional and financial support, including the Vancouver Fraser Medical Program MD/PhD Scholarship. My gratitude to the Canadian Institutes of Health Research for funding support (Vanier Canada Graduate Scholarship) and the other research agencies including Diabetes Canada that made doing this work possible. My appreciation to my MD/PhD colleagues for their support and friendship along the way. It has been a pleasure working with you in the lab and in the hospital, and I hope our paths continue to cross for many years to come. I hope that we all go forward and continue to dream big, work hard, be kind, and ask the tough questions. It is my privilege to graduate as one name among so many incredible young scientists and physicians.

To my parents, thank you for teaching me how to work hard and be happy along the way. I am not sure where I'd be without your example on how to make priorities and live life with moderation, but I am thankful for where it has taken me. I also must give a special thanks to Uncle Rehim for being my friend and teacher. You have always been a source of laughter and been there anywhere, and anytime. Thank you to Matt for being the truest friend one could hope to have and thank you to my sister Miriam for always being someone I can count on. I have been so fortunate to be surrounded by friends and family that have supported me throughout this journey. Finally, a thank you that could never be put into words – thank you to my wife Jessie. No matter the circumstance, you have been the unwavering piece of my life that is kind, positive, and generous. It is because of you that these past five years have been both productive and a sincerely happy phase of life. As I wrote in my dissertation, "[this] is dedicated to Jessie, for maximizing all that is good in life."



David Twa characterized the pathobiology and sequelae, or consequences, of chromosomal rearrangements in lymphoid neoplasia, which arise from cancerous lymphoid cells.

David has joined the Anatomical Pathology Residency Program at the University of Calgary.

Message from David Twa

I am very grateful to be graduating this year. This would not have been possible without the support of my many medical school peers and mentors (including George Chang, Edward Fang, Jack Kooy, Verena Langheimer), VGH colleagues (including Tony Ng, Peter Schutz, Basile Tessier-Cloutier, Douglas Webber, Stephen Yip), BC Children's Hospital colleagues (Nick Au, Kate Chipperfield, Douglas Morrison, Audi Setiadi, Suzanne Vercauteren), BC Centre for Disease Control colleagues (Agatha Jassem, Mel Krajden, Kevin Kuchinski, Aidan Nikiforuk, Natalie Prystajecky), UBC MD/PhD program colleagues (Rozlyn Boutin, Jennifer Ji, Michael Skinnider, Jordan Squair), or members of the BC Cancer Research Centre (including Susana Ben-Neriah, Fong Chun Chan, Liz Chavez, Joseph Connors, Daisuke Ennishi, Pedro Farinah, Randy Gascoyne, Robert Kridel, David Scott, Laurie Sehn, Graham Slack, King Tang, Adele Telenius, Bruce Woolcock).

I am also indebted to my thesis committee for their patience and guidance: **Pamela Hoodless, David Huntsman, Kerry Savage**; the UBC MD/PhD Program Directors: **Liam Brunham, Torsten Nielsen**, and **Lynn Raymond**; and our program coordinator, **Jane Lee**.

I am especially thankful for the support of my supervisors **Christian Steidl** (for the work pertaining to my thesis) and **Inna Sekirov** (for work at the BCCDC). Most critically has been the enduring support of my late aunt **Carol Wishart**, my parents **Dan Twa** and **Brenda Wishart** and their late French bulldog Bella, my wife **Christine Lukac**, and our Boston terrier Sadie.



Cynthia Ye studied the genetic architecture of strabismus, more commonly known as crossed eyes. She identified the likely causal gene in a large family with a history of strabismus, multiple biological pathways, and the involvement of the central nervous system. This research advanced the understanding of strabismus pathology and may improve patient care.

Cynthia has joined the Internal Medicine Residency Program at UBC.

Message from Cynthia Ye

It is with deep gratitude that I am graduating from the MD/PhD Program. I want to take this opportunity to give thanks to the supportive community. There are ups and downs to this journey, and it won't be possible without all the help I received.

I am thankful for the support and guidance I received from **Dr. Lynn Raymond, Dr. Torsten Nielsen,** and **Jane Lee** through the challenges over the years. A heartfelt thank you to my fellow MD/PhD students for your companionship and support and the MD/PhD alumni for your wisdom and encouragement over the years.

The MD/PhD training has helped me gain insight into medicine, research, and myself and grow professionally and personally. I had the opportunity to pursue my interests in clinical medicine and genomics. My dissertation investigated the genetics of different forms of strabismus with genomic approaches, allowing me to interact with participants, clinicians, and researchers. I am grateful to my supervisor **Dr. Wyeth Wasserman** for his mentorship. Thank you for always being supportive through my very long journey and showing me how to be a scientist, mentor, and leader. Thank you to **Dora Pak** and **Cheryl Bishop** for your organizational skills and help.

A thank you to all the lab alumni for being part of my journey and giving me feedback to grow. Last but not least, my fellow medical genetics graduate students, thank you for helping my transition and sharing all the tears and laughs.

I am grateful to be graduating from the UBC MD/PhD Program and excited to join the UBC Internal Medicine residency program in July. Despite all the challenges and limits brought by the COVID-19 pandemic, I hope future MD/PhD students can fully explore their interests. All the best!



Allen Zhang studied how cancer cells resist treatment in ovarian cancer, one of the deadliest cancers. He showed that although the immune system helps keep this cancer at bay, some cancer cells evade immune cells and cause patient relapse. His research highlights current challenges for immune-based therapies for this cancer and how to overcome them.

Allen has joined the Pathology Residency Program at UBC.

Message from Allen Zhang

When I first entered the program eight years ago, I never imagined how much I would enjoy the MD/PhD. Throughout my degree, the quality of mentorship I experienced was what truly made this experience special and convinced me to do an extra year. I am deeply grateful to everyone that has been a part of my journey and helped make it possible. I would recommend the UBC MD/PhD program without reservation to anyone who has an interest in working at the forefront of medical research among world-leading, talented colleagues.

During my time at BC Cancer, I had the incredible fortune of working with a devoted group of clinicians and researchers. I am indebted to my co-supervisors **Dr. Sohrab Shah** and **Dr. Wyeth Wasserman**, who have been unwavering sources of support, given me opportunities I could have never imagined having, and served as role models for exceptional PIs in and out of the lab. None of this would have been possible if they hadn't helped set me on this journey and elevating me to where I am today. I'd also like to thank **Dr. Brad Nelson** for his close mentorship on all things immunology – sometimes it felt like I had a third cosupervisor! I'd also like to thank all the other researchers and clinicians I worked with, especially **Dr. Samuel Aparicio, Dr. David Huntsman, Dr. Jessica McAlpine, Dr. Blake Gilks,** and **Dr. Anthony Mathelier**. And a huge thank you to all the postdocs, graduate students, and lab staff that made it all possible, namely **Dr. Kieran Campbell, Dr. Andrew McPherson, Dr. Tyler Funnell, Dr. Andrew Roth, Dr. Phineas Hamilton, Dr. Alex Miranda, Jamie Lim,** and many others.

Unexpectedly, I got to spend the last year of my PhD with **Dr. Sohrab Shah** at Memorial Sloan Kettering Cancer Center, one of the world's leading cancer research institutions. The clinicians I worked with there, including **Dr. Dmitriy Zamarin, Dr. Claire Friedman, Dr. Carol Aghajanian,** and **Dr. Nadeem Abu-Rustum** were truly inspirational and embodied the clinician-scientist mindset. On the research side, I'd like to thank **Dr. Britta Wiegelt, Dr. Nick Ceglia, Cynthia Berry, Kevin Boehm, Dr. Ignacio Vazquez-Garcia** and our entire MSKCC lab that is too long to list here.

Lastly, I'd like to express immense gratitude towards the UBC MD/PhD Program directors and staff, **Dr. Torsten Nielsen, Dr. Lynn Raymond, Dr. Liam Brunham,** and **Jane Lee**, who have guided me along this journey through the ups and downs. They have supported me closely through my own personal challenges, and advocated for us professionally during uncertain times. I'd like to extend my thanks to some of my closest colleagues in the program and my graduating class, including **Cynthia, Parker, Jennifer, Victor, David, Amanda,** and **Adam.**

I am truly excited to be starting the next chapter of my journey in Anatomical Pathology at UBC. So many faculty and residents, including **Dr. Torsten Nielsen**, have helped guide me to the fascinating world of pathology. Looking to the future, I hope to continue pushing the boundary of cancer genomics throughout residency and beyond.

Alumni News - Suze Berkhout (Class of 2012)

A Road Less Travelled: Pathways to a Clinician-Scientist Career

It's a real pleasure to share some of my experiences over the years, as I have moved from being an MD/PhD trainee to a clinician scientist stream resident (in my case, in psychiatry) and now, as an early career clinician investigator. When I started out in the MD/PhD program at UBC in 2004, I don't think I truly anticipated what the path to independent clinician scientist would be like: it's certainly a journey and not a destination. In many ways I'm still very early on in it. And because my program of research—ethnography, science and technology studies, and arts-based methods—is quite different from what clinicianinvestigators typically do, the path I've taken is also not one that was not wellforged ahead of me. This has made the journey both interesting and complex.

When I started out as an MD/PhD trainee, it was a time when the range and diversity of trainee research interests was not as wide as it is now. I was often the only trainee at meetings who was carrying out qualitative research and applying that research to topics in philosophy of medicine. I'm incredibly grateful that while I was carrying out the MD/PhD program at UBC, there was a strong emphasis on finding peers and mentors doing similar work, and I was supported to find this in Canada and further afield in the US, in addition to having my somewhat different approach embraced by the UBC MD/PhD community. Like many trainees, the



Dr. Suze Berkhout

project I started out thinking I would do ultimately was not what I ended up working on. But a lot of times these alterations in your pathway are serendipitous. It was through my doctoral work shifting in focus, to the area of science and technology studies/philosophy of medicine, that I was able to find a welcoming interdisciplinary home and community of like-minded researchers for the methods and questions I am most interested in. I have been able to find amazing collaborators through this, which is crucial in today's competitive research environment.

Like most people working on their doctoral research, there's almost an incredulousness that goes along with finishing it up: it often feels like training will never end. I finished my field work, wrote my dissertation and defended (2010), and I still remember how the transition back to medicine felt abrupt: shifting from being at the top of your research game to the most junior learner is humbling. And it's easy to become ensconced in the clinical realm. But I had many threads of research that hadn't been mobilized into publications or presentations by the time I had finished my PhD, and I didn't want to lose the momentum that had been building as my doctoral research came to a close. One of the most important skills I developed in my clerkship years and in the first years of residency was the ability to shift between my clinical and research worlds, which was very much a process of learning to shift between ways of thinking and working. Learning how to make the most out of small snippets of time has come to be so important for the way I work now as a clinician investigator. During my PhD I had what felt to be almost endless hours for my research—today, my research work has to fit in with patient care, administrative tasks, supervision and teaching, and my family life. It's a delicate juggling act that has taken time to develop and the more you can find strategies that work for you (e.g. how to task shift quickly, how to pick up paper writing without needing a lot of lead-in time), the more effective you'll be.

Like my PhD research, my clinical work didn't end up where I thought it would. I had expected to go into Ob/Gyn or internal medicine, and instead fell in love with the field of psychiatry. Here, there were so many grey areas, so little that was definitively known, and so much overlap between biological and sociocultural issues – perfect for the kind of research I do. At CaRMS, I took a leap and moved to Toronto to start as a psychiatry resident. I count myself as extremely fortunate to have found a program incredibly supportive of my research interests and right from the start I was connected with a mentor and residency research supervisor who believed in the value of social science and humanities research (even though my supervisor

Alumni News - Suze Berkhout (Class of 2012) con't

himself was a translational scientist). We developed an incredibly rich collaboration that generated my first big project post-PhD, which I ran myself, through my last three years of residency. It's been work that has set me up with a grant and publication track record that is compelling to granting agencies and has generated great spin-off questions and projects. It wasn't easy to run it through residency, with somewhat limited protected time, but I had joined our clinician scientist stream in residency (our department had a pathway for those who had already completed an advanced degree) and the community and research momentum formed around me. My program of research continues to grow, but the thread that runs through it are the same over-arching questions from my PhD. I'm interested in how identities are shaped within medical practices, how these loop back to informing knowledge in/about medicine itself, and the unintended consequences of these relationships. I've moved from working through this in the field of HIV/AIDS, to looking at these questions in first episode psychosis, treatment resistant depression and schizophrenia, transplant medicine, and in the burgeoning field of placebo studies.

Having mentors and supporters who believe in your vision for a program of research is critical throughout your training, but especially in making the next shift to the job market. It's important to be flexible with what you are able to do clinically, where you will work, and not have all your eggs in one basket, as clinicianinvestigator positions with salary support for your research time are highly competitive. I've come out of residency into a clinician-investigator role at the University Health Network in Toronto, where I work clinically as an inpatient psychiatrist (about 40% of my time is clinical) and I'm supported for approximately 60% of my time for my research program. I'm tasked with building our capacity for social science and humanities research within the UHN Centre for Mental Health and count myself as incredibly fortunate to have secured federal and university funding in my first year as staff. My clinical work is rewarding, and it's also organized so that when I'm off-service from our inpatient unit I can be completely focused on my research. This is one way I manage the balance-I try very hard to protect my research time and make the most of it. At this stage, this also means being selective about what else I do. If you're like me, you probably find lots of opportunities, committees, organizations interesting to work with and learn from, but there is a season for everything and the early career stage for clinician-investigators is the season in which you need to really focus on launching a generative program of research that can be sustained in the long term. That means, in plain speak, focusing on publications, grants, growing your research team with solid skills and developing good working relationships as well as finding mentorship to help you navigate life as faculty.

I would be remiss if I didn't talk about my family life, because this of course is also central to who I am. My partner and I had our first two children while I was a resident, and we have just welcomed our third baby a few months ago. Life is hectic. Kids take a village, so to speak, and having kids and a fulfilling, busy career in academic medicine takes a bigger village! And in my case, it takes a partner who jumps into being the lead parent depending on the pace of my work, with the understanding that we take turns with that role. Life as a clinician-investigator is a zoo most days, COVID has made it harder in many ways, but it's also incredibly rich and full of meaning. I would do it all over again, in a heartbeat.

Suze Berkhout, May 2021.



Suze and her three lovely children.

Alumni News - David McVea (Class of 2014)



Dr. David McVea and his daughter, Lula-Rose.

Thank you for inviting me to give an update on what I've been up to since finishing the MD/PhD program in 2014. It has been a bit of a winding path but I'm very happy with where I have ended up.

My PhD research was in neuroscience, and I studied the basic organization of the cerebral cortex and its development during the neonatal period. I had also studied systems neuroscience during my MSc degree before medical school, so a neurology residency seemed like an obvious choice. With this in mind, I entered the UBC Neurology Residency in 2014. It is a wonderful program but I realized after a year that it wasn't a good fit for me, and I transferred into the UBC Public Health and Preventative Medicine residency. This was an excellent match for my clinical interests and at the same time gave me the chance to use the research and analytical skills I used in my PhD.

In 2019, at the tail end of residency, I was accepted into the Canadian Field Epidemiology Program, a program within the Public Health Agency of Canada (PHAC) that supports outbreak responses across the country by rapidly deploying epidemiologists into the field to manage outbreaks. Little did I know that I was joining a few months away from the beginning of a once-in-a-century global pandemic! Early in the pandemic, I was deployed to PHAC's Emergency Operations Centre where I was the epidemiologist responsible for domestic cases. At the time I arrived, I was manually entering some of the first cases into our database – the world had changed by the time I left, about a month later. This will always be one of the most dramatic and intense work-related experiences of my life.

As I was approaching the end of my two year tenure at PHAC, I was hired into a permanent role at the BC Centre for Disease Control, as a Public Health physician in Environmental Health. This is a sub-field of Public Health I have been interested in for a long-time, and I am thrilled to be in this role. I study and respond to exposures to toxins, radiation, and other environmental hazards. I also help health authorities and the province understand and minimize the health effects of climate change – be they fire smoke, heat, or shifting patterns of zoonotic illness.

Though the subject matter is a long way from cortical development, I use my research skills every day and am certain I would not be where I am now if not for the unique training of the MD/PhD program. I'm happy to say all those long hours in the lab, and on the wards, do pay off!

Recently, **Dr. David McVea** contributed to an article on wastewater genomic testing to track COVID-19 variants of concern within a region. https://www.medrxiv.org/content/10.1101/2021.05.26.21257861v1

The news article was reported by UBC News. Congratulations! https://news.ubc.ca/2021/07/12/ubc-research-shows-wastewater-genomic-testing-caneffectively-track-covid-19-variants-of-concern-within-a-region/

Alumni News - Inna Sekirov (Class of 2011) & David Twa (Class of 2021)

Dr. Inna Sekirov, Medical Microbiologist at the British Columbia Centre for Disease Control (BCCDC), is a leader of a project which investigates ACE2. ACE2 is a molecule on the surface of human cells that is used by SARS-CoV-2 to attach itself. **Dr. David Twa**, our recent graduate, is part of the research team. With support from Genome BC and the UBC Faculty of Medicine, the BCCDC research team measured ACE2 expression in British Columbians tested for COVID-19. The study finds individuals with higher ACE2 expression facilitate higher viral replication, and that ACE2 has potential as a COVID-19 biomarker. The findings were published in the Lancet's EBioMedicine. Congratulations!

Class of 2028



Class of 2028: Maggie Chopra, Saif Dababneh, Elizabeth Gregory, Christopher Lee, Erica McDonald, Kira Tosefsky, Amy Wang and Peipei Wang. Welcome!

From January to March 2021, members of the MD/PhD Program Advisory & Admissions Committee interviewed and adjudicated an impressive cadre of short-listed applicants for admission in 2021. We are fortunate to have recruited a record size of eight incoming students to the MD/PhD Class of 2028. On 6 April 2021 we organized a welcome session for the new crop of clinician-scientists. Through the years, exceptional individuals from across the country have been recruited to the UBC MD/PhD Program. Details about our eight incoming students will be reported in the next newsletter.

Based on student input, the program has set up more formalized peer mentor relationships for the incoming students. Starting with the Class of 2028, we are pairing each of the new students with a mentor who is \sim 2-4 years ahead of them in the program. The specific duty for the mentors is to initiate a running conversation and make themselves available to help their matched junior student.

Welcome Aboard

PhD Oral Defence

Four of our students successfully defended their PhD dissertations this spring, all passing with flying colours! We are very proud to share their dissertation abstracts with everyone. Full theses are deposited at UBC <u>cIRcle</u>. These students returned to MD Year 3 Clinical Rotations in the summer of 2021.



Mark Trinder

ABSTRACT

* * *

Mark Trinder Research supervisor: Dr. Liam Brunham Hosting department: Experimental Medicine Graduate Program Defense date: 12 May 2021

Dissertation title: Plasma lipoproteins: Genetic influences and relevance to atherosclerotic and infectious diseases

Plasma lipoproteins, such as low-density lipoprotein (LDL), high-density lipoprotein (HDL), and lipoprotein(a) are highly heritable traits and important biomarkers for atherosclerotic cardiovascular disease (ASCVD). LDL and lipoprotein(a) are atherogenic plasma lipoproteins that are often both elevated among individuals with familial hypercholesterolemia; a common, autosomal co-dominant disorder characterized by pathogenic variants in the *LDLR*, *APOB*, and *PCSK9* genes. These pathogenic variants impair the removal of LDL from the blood and lead to severe hypercholesterolemia and increased risk of ASCVD. Despite the ability to identify individuals with a genetic cause for familial hypercholesterolemia or elevated lipoprotein(a), one of the most challenging aspects in the clinical management of this patient population is the remarkable diversity of ASCVD risk.

Alternatively, HDL has been thought to protect against atherosclerosis because low levels of HDL are strongly associated with increased risk of ASCVD. Several recent clinical trials have unsuccessfully attempted to raise HDL cholesterol to reduce the risk of ASCVD. These results have left unanswered questions about the primordial function(s) of HDL. Plasma lipoproteins undergo extensive changes in structure, function and metabolism during severe infections such as sepsis. However, the implications and causality of these changes to clinical outcomes is poorly understood.

The central objective was to explore the contribution of genetic variation in plasma lipoprotein traits and metabolism on lipid disorders such as familial hypercholesterolemia, elevated lipoprotein(a), and serious infections such as sepsis. Here, we used genetic epidemiology and mouse models of disease to assess how common and rare germline genetic variation affects the risk of atherosclerotic cardiovascular diseases and infectious diseases. Specifically, 1) can background genetic variation related to LDL and lipoprotein(a) modify the risk of ASCVD for individuals with familial hypercholesterolemia? and 2) are associations between HDL and risk of infectious disease causal?

Several broad conclusions can be made. First, background polygenic factors influencing LDL-C and lipoprotein(a) levels modify the penetrance and expressivity of familial hypercholesterolemia. Second, the primordial function of HDL may be related to immunoregulation and resolution of infection. Third, cholesteryl ester protein is an important regulator of HDL levels during sepsis and may be a therapeutic target.

PhD Oral Defence (con't)



Michael Skinnider

Michael Skinnider

Research supervisor: **Dr. Leonard Foster** Hosting department: Genome Science & Technology Graduate Program Defense date: 14 May 2021

Dissertation title: Understanding mammalian biology and disease through tissue-specific protein-protein interaction networks

ABSTRACT

Biological functions are mediated by the dynamic organization of DNA, RNA, proteins, and other biomolecules in complex networks of interactions. Efforts to chart the network of biologically relevant macromolecular interactions—the "interactome"—therefore occupy a central position in the endeavour to understand the biochemical basis of human physiology, and its perturbation in disease. However, existing interactome maps are incomplete, even for well-studied organisms. Moreover, the dynamics of the interactome in response to cellular stimuli and across normal physiological contexts remain incompletely understood.

This thesis considers the application of a quantitative proteomic approach, protein correlation profiling (PCP), to map the interactome in its native physiological context. I explore computational methods for the analysis of PCP data, and describe their application to infer a dataset of protein-protein interactions from seven mouse tissues.

In Chapter 2, I studied the dominant paradigm used to analyze PCP data, which entails the use of supervised machine-learning methods to infer interaction networks from these complex datasets. I found that one widely used strategy needlessly biases network inference towards highly studied proteins and away from novel interactions between functionally un-connected proteins.

In Chapter 3, I applied the methods studied in Chapter 2 to a newly collected, *in vivo* PCP dataset. I used the same machine-learning approach to infer tissue-specific protein-protein interaction networks for seven mouse tissues. I then analyzed these tissue interactome networks to uncover insights about protein function, network evolution, and human disease.

Collectively, the work described in this thesis provides a framework to understand the rewiring of the protein-protein interaction network across physiological conditions using PCP.

PhD Oral Defence (con't)



Jennifer Ji

Jennifer Ji

Research supervisor: **Dr. David Huntsman** Hosting department: Pathology & Laboratory Medicine Graduate Program Defense date: 4 June 2021

Dissertation title: The proteomic and metabolomic characterization of clear cell ovarian cancer: Towards better management strategies

ABSTRACT

Clear cell ovarian cancer (CCOC) is a molecularly unique subtype of epithelial ovarian cancer for which treatment options are still limited. Patients with late stage CCOC do not respond to gold-standard platinum and taxane based chemotherapeutics, and effective targeted therapies for this cancer are still lacking. Due to its relative rarity, the molecular landscape of this ovarian cancer subtype has not been fully deciphered. In this thesis, I used global screening techniques to elucidate the proteomic and metabolomic landscapes of CCOC, compared to other common epithelial ovarian cancer subtypes. I found that CCOC is a unique entity compared to its other epithelial ovarian cancer counterparts in both its proteomic and metabolomic landscapes. I reported proteomic diversity within CCOC cases presented as subgroups of distinct molecular signatures. Moreover, through integrated proteometabolomic analysis, I identified aberrancies in purine metabolism, cysteine/glutathione metabolism, as well as glucose metabolism. I further demonstrated that available CCOC cell lines reflect the proteomic and metabolomic signatures in CCOC clinical samples. The heterogenous biology seen in clinical samples and cell lines suggests that the comprehensive understanding of this cancer require appropriate in-vitro models to represent its diverse molecular phenotypes.

Lastly, our proteomic understanding led to the identification of the lack of an arginine synthesizing enzyme, arginosuccinate synthase, in CCOC and other rare ovarian cancer subtypes including small cell ovarian carcinomas hypercalcemic type. Cancers lacking this enzyme has been shown to be sensitive to a molecular agent depriving extracellular arginine. I show that this therapeutic agent was effective in curbing the growth of arginosuccinate synthase-negative rare ovarian cancers in-vitro and in in-vivo murine models, thus identifying a potential therapy for these very aggressive subtypes.

My research provides the largest reported proteomic landscape of CCOC cases, in addition, I report the first metabolic landscape of CCOC and other ovarian cancer subtypes. Both will serve as valuable resources for further research into CCOC biology and therapeutic development. Furthermore, I demonstrate of how proteomic and metabolomic understanding can accelerate therapeutic development in rare ovarian cancers by using arginosuccinate synthase deficiency as an example.

PhD Oral Defence (con't)



Daniel Kwon

Daniel Kwon

Research supervisor: **Dr. François Bénard** Hosting department: Interdisciplinary Oncology Program Defense date: 14 June 2021

Dissertation title: Radiotheranostic agents targeting the tumor microenvironment

ABSTRACT

The genesis and evolution of the tumor microenvironment is a key determinant in the proliferation and dissemination of cancer and ultimately, patient outcomes. The C-X-C chemokine receptor 4 (CXCR4) is a key player in shaping the tumor microenvironment, attracting stromal and immune cells, and propagating metastasis of expressing cells to distant organ sites. As such, its expression is associated with a poor prognosis and therefore, this protein is a promising therapeutic target. An emerging approach involves the design of molecular probes for non-invasive imaging and radionuclide therapy, through vectors that target the desired protein and carry a radioisotope with imaging or treatment properties. We use this approach to design positron emission tomography (PET) imaging and radionuclide therapeutic pharmaceuticals by modifying a known potent antagonist of CXCR4 called LY2510924.

Through careful design of the linker and radioprosthetic group necessary to confer favorable properties for a pharmacological agent to be used as a molecular probe, I developed a series of radiopharmaceutical ligands that showed high-contrast imaging properties and high accumulation in cancers expressing CXCR4. These radiopharmaceuticals have the capacity to carry a variety of radioisotopes, including ⁶⁸Ga, ¹⁸F and ¹⁷⁷Lu, for imaging and therapeutic purposes. Furthermore, by modifying the LY2510924 pharmacophore, which has been previously optimized as a clinical candidate, I was able to further enhance its affinity to CXCR4, developing one of the most potent pharmacophores of CXCR4 to date. By adapting this new pharmacophore as a radiopharmaceutical, I disclose a lead compound, BL34, which showed excellent accumulation in CXCR4-expressing tissue, while clearing rapidly from non-target organs. The PET images and biodistribution data of BL34 show significant promise as a clinically viable radiopharmaceutical.

Due to the global COVID19 pandemic, I led an effort to develop the first specific inhibitor of transmembrane protease serine 2 (TMPRSS2), a serine protease implicated in SARS-CoV-2 viral entry which has also been documented to be overexpressed in prostate cancer. By leveraging the substrate specificity and catalytic mechanism of TMPRSS2, I designed and evaluated an electrophilic inhibitor with nanomolar potency and high specificity. While this inhibitor showed broad inhibition of wild-type and mutant spike protein processing by TMPRSS2, this compound was not effective in inhibiting live SARS-CoV-2 viral entry, raising questions as to the viability to treat SARS-CoV-2 infection. This work further delineated a novel diazomethane-free route in the synthesis of an irreversible inhibitor of TMPRSS2, enabling further proteomic and structural studies of TMPRSS2 and setting the stage for other groups to design their own irreversible covalent chemical probes without the dangers associated with the use of diazomethane.

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

Our seminar series (currently held virtually) 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 clinicianscientists, and give their opinions on career development options for clinician-scientists. All faculty, clinical investigator trainees of all stripes in our nation, students in the Faculty of Medicine and prospective applicants to our program are invited.



8 February 2021 – Invited speaker: Dr. Subodh Verma Cardiac Surgeon, St Michael's Hospital, Unity Health Toronto Scientist, Keenan Research Centre for Biomedical Science and Li Ka Shing Knowledge Institute of Unity Health Toronto Professor of Surgery and Pharmacology & Toxicology, University of Toronto Canada Research Chair in Cardiovascular Surgery

Dr. Verma leads a dynamic pre-clinical and translational research team that leverages pre-clinical disease models and clinical trial-derived data

to identify novel mediators of cardiovascular and cardiometabolic disease as well as answer timely and relevant healthcare questions. He spoke about aspects of his career and research, which has been incredibly productive, taking lots of questions from our students.



8 March 2021 - Invited speaker: Dr. Poul Sorensen

Professor, Department of Pathology & Laboratory Medicine, UBC Director, Academy of Translational Medicine, Faculty of Medicine, UBC

The Sorensen group is well known internationally in cancer biology; they hypothesize that stress adaptation confers therapy resistance to childhood cancer cells, and increases their capacity for metastatic dissemination. Dr. Sorensen talked about his training and career as a clinician-scientist, including his work leading to the development of the breakthrough anticancer drug larotrectinib, as well as his new role in the Academy of Translational Medicine.

10 May 2021 – Invited speaker: **Dr. Michael Hayden** Killam Professor, University of British Columbia Senior Scientist, Centre for Molecular Medicine and Therapeutics

Dr. Hayden's research focuses on genetic diseases, including gene therapy, Huntington disease, predictive and personalized medicine and drug development. He is the most cited author in the world on ABCA1 and Huntington disease. He shared with us his research and what he would recommend for clinician-scientist trainees. Among Dr. Hayden's successful graduate trainees is our current Associate Director, **Dr. Liam Brunham**!

Thanks to **Alvin Qiu** for capturing the great screenshots, and to all three of these excellent speakers, world leaders in their fields who took time out to speak to our MD/PhD students.

Transition into Medical Education & Transition into Research

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 into 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. Last year, Dr. Liam Brunham, MD/PhD Associate Program Director, facilitated a virtual "re-entry" session for students returning to MD Year 3, and received positive feedback from the participants. This year, a further session was held on Wednesday, 28 April. Prior to the session, everyone read an assigned journal article in preparation. Discussions were 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. Students in the final year were invited to the session for input. 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 peerto-peer mentoring regarding managing this transition; and to highlight program and faculty support for students.

Switching from clinical medicine to research would also require a different set of skills and ways of thinking. MD/PhD students have also asked for support in this transition. This year **Rohit Singla**, Year 3 MD/PhD student, helped to organize a mentorship session, "Transition from MD training into Research (MD to PhD)", which was held virtually on Wednesday, 19 May. This session was for the benefit of the students who completed the first two years of medical curriculum and are starting research in the summer. Prior to the event, a journal article was distributed for discussion. The students had a faculty-free discussion led by senior students (including a couple of alumni) talking about how to succeed in the PhD phase of the program. Thanks to **Dr. Andrea Jones, Dr. Eric Zhao, Daniel Kwon** and **Mark Trinder** for making time to speak to the group and providing open, practical and frank advice. The discussion was especially helpful for the junior students and they took away lots of pearls to help them on their journey.

Overall, the two sessions were assessed as extremely valuable to be continued yearly for future participants. Great job, everyone.

MD/PhD Student Research Presentations

MD/PhD students are offered the opportunity to attend and present their research annually at national and international research forums. Research conference expenses are supported by the program.

The 34th Annual Canadian Student Health Research Forum (CSHRF) was held virtually, June 14-18, 2021. The aim of the CSHRF is to provide a venue for the networking, research exposure and recognition of Canada's most promising research trainees in the health sciences. Four MD/PhD students were nominated as top PhD students in health sciences at UBC and presented their posters at the forum.

Andy An presented "Effects of S100A9 on macrophage cellular reprogramming in the context of sepsis".

Alvin Qiu presented "Subgrouping primary synovial sarcoma based on epigenomic landscape".

Maryam Vaseghi-Shanjani presented "Clinical red flags that warrant workup for monogenic allergic diseases".

Joyce Zhang presented "Low-grade serous ovarian cancers modelled with human fallopian tube organoids and single cell sequencing".

The 36th Annual National MD-PhD Student Conference was held virtually, July 9-11, 2021. This is a great event to meet colleagues and mentors, learn about opportunities available to MD-PhDs, and discuss exciting science. Three MD/PhD students were selected to present at this conference.

Wissam Nassrallah presented "Calcium handling in striatal neurons in Huntington disease".

Shayda Swann presented "The role of cortisol levels in the health and well-being of people living with HIV: A scoping review".

Joyce Zhang presented "Modelling low-grade serous ovarian cancers with human fallopian tube organoids and single cell sequencing".

Kudos

- In June 2021, <u>Dr. Maureen Ashe</u> in the Department of Family Practice, MD/PhD Advisory/Admissions Committee member, was appointed as renewed Tier 2 Canada Research Chair in Community Mobility.
- This spring, two MD/PhD students, **Alvin Qiu** and **Shayda Swann** were interviewed by the Faculty of Medicine Trainee Wellbeing Engagement Group lead. Their input contributed to a report on ways to best support graduate student health.
- <u>Dr. Liam Brunham</u>, MD/PhD Associate Director and Associate Professor in the Department of Medicine, was a winner of the 2021 Innovation and Translational Research Award, Vancouver Coastal Health Research Institute. His study is on performing rapid assessment to diagnose a cardiac condition.
- A number of MD/PhD students served as medical student vaccinators at the COVID19 Vaccination Campaign. On top of immunization, they also assess and counsel patients on vaccination, provide after care for patients post-vaccination and input vaccination data into the provincial system. Bravo!

Spring Gala 2021

UBC Medicine Spring Gala is an annual show featuring performances and visual artwork that celebrate the artistic talents of UBC medical students and faculty! Spring Gala 2021 was held virtually on 15 May - a pre-recorded online show of amazing performances as well as the highly anticipated Grad Skit presented by the graduating Class of 2021. All proceeds from the performance went towards Aunt Leah's Place.

A huge round of applause to our MD/PhD students for their time, effort, and dedication to their talents.

Katie Baillie - Black and Blues Jazz Band (alto sax), Highlights from Moana (singer)

Amanda Dancsok – Grad Skit (director. actor and singer), FIFEsney: A Disney Acapella Medley (singer), UBC Medicine Choir

Shayda Swann - Terpsichore: Where's My Love (dancer)

Maryam Vaseghi-Shanjani – UBC Medicine Choir

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 Email: <u>md.phd@ubc.ca</u> Website: <u>http://www.med.ubc.ca/mdphd</u>

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