



UBC MD PhD

UBC MD/PhD Program

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Newsletter – Winter 2012

http://www.med.ubc.ca/education/md_ugrad/mdphd/news.htm

MD/PhD Student Research Forum & Open House - 9 September 2011



The 12th annual UBC MD/PhD Student Research Forum and Open House was held on Friday, 9 September 2011, 2:00-4:00 pm, at the Michael Smith Laboratories, UBC.

Opening remarks by **Dr. Torsten Nielsen**, Associate Director of the MD/PhD Program, set off the exciting event.

Our special thanks go to our invited guest speaker, **Dr. Brian Kwon**, Department of Orthopaedics, UBC Orthopaedic Surgeon, specialist in the surgical management of adult spinal disorders.

Potential applicants had some excellent questions and discussions with the speakers and the current MD/PhD students.

➤ Student presentation:

David McVea, Year 5, presented “My MD/PhD Journey”

➤ Poster presentations:

Matt Mayer, Year 5, “Attenuation of inflammatory responses from cystic fibrosis leukocytes by an innate defence regulator (IDR) peptide”

David McVea, Year 5, “Interactions between the developing cortical and peripheral sensorimotor system examined with VSD imaging in vivo”

Michael Copley, Year 4, “High expression of *Hmga2* during fetal and neonatal life is cell-autonomously required for the robust generation of the hematopoietic stem cell compartment”

Clara Westwell-Roper, Year 4, “Blockade of interleukin-1 signalling improves human islet amyloid polypeptide-induced pancreatic islet graft dysfunction”

Alexis Crabtree, Year 3, “Involving illicit drinkers in drug user activism”

Gareth Mercer, Year 3, “Perspectives of intravenous drug users on the harms caused by installing blue lights in public washrooms”

Long Nguyen, Year 3, “Development of a lentiviral-based cellular barcoding strategy to examine the spectrum of in vivo growth and differentiation potential of normal human mammary stem cells”

Thanks to
Michael Copley and
Long Nguyen for
organizing the event.

Program Admissions & Advisory Committee (PAAC) 2011-2012

The MD/PhD Advisory/Admissions Committee consists of clinician-scientists, basic scientists, graduate program advisors, student research supervisors, and a senior student representative. Members of the Committee also serve on the student Thesis Research Supervisory Committees, the PhD Comprehensive Examination Committees, and the PhD Final Oral Examination Committees.

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|  | Lynn Raymond, MD, PhD Director, MD/PhD Program, UBC Professor, Neurosciences, Department of Psychiatry, UBC |
|  | Torsten Nielsen, MD/PhD Associate Director, MD/PhD Program, UBC Associate Professor, Anatomical Pathology, Department of Pathology & Laboratory Medicine, UBC |
|  | Jane Buxton, MBBS, MHSc Physician Epidemiologist, BC Centre for Disease Control Associate Professor, School of Population & Public Health, UBC |
|  | Robert Holt, PhD Associate Professor, Department of Psychiatry, UBC Head of Sequencing, Michael Smith Genome Sciences Centre, BC Cancer Agency |
|  | Claudia Krebs, MD, PhD Senior Instructor, Department of Cellular & Physiological Sciences, UBC UBC MD Curriculum Committee Member |
|  | Haydn Pritchard, PhD Professor, Department of Pathology & Laboratory Medicine, UBC Graduate Advisor, Pathology & Laboratory Medicine Graduate Program, UBC |
|  | Patrick Tang, MD/PhD Medical Microbiologist, Laboratory Services, BC Centre for Disease Control Clinical Assistant Professor, Pathology & Laboratory Medicine, UBC Alumnus, UBC MD/PhD Program |
|  | Stuart Turvey, MBBS, DPhil Associate Professor, Division of Infectious & Immunological Diseases, Department of Pediatrics, UBC Co-Director, Immunity in Health & Disease research cluster and Senior Clinician Scientist, CFRI |
|  | Stephen Yip, MD/PhD Neuropathologist, BC Cancer Agency Clinical Assistant Professor, Department of Pathology & Laboratory Medicine, UBC Alumnus, UBC MD/PhD Program |
|  | Youwen Zhou, MD, PhD Associate Professor, Department of Dermatology and Skin Science, UBC Director, Cheng Genomics Centre & Laboratory of Predictive Medicine & Therapeutics, VCHRI |
|  | Michael Copley MD/PhD Student (Year 4), UBC |

Our sincere thanks go to **Drs. Christian Naus, Fabio Rossi, Alan So, and Rusung Tan** for their contribution to the MD/PhD Committee in the past three years. We welcome four new members to the MD/PhD Committee: **Drs. Jane Buxton, Robert Holt, Patrick Tang, and Stuart Turvey**. Thank you for supporting the MD/PhD Program.

Student Representative - Michael Copley

Michael Copley, Year 4 MD/PhD student, is the 2011-2012 student representative, along with alternate student representative, Long Nguyen, Year 3 MD/PhD student. Long will succeed Mike as the student representative next year. The major responsibility of the student representative is to sit on the MD/PhD Advisory and Admissions Committee. Other duties include helping to organize the MD/PhD monthly student meetings/seminars and presenting at student events to promote the MD/PhD Program.

Message from Mike

It is truly an honour to be representing the amazingly talented and ridiculously good-looking UBC MD/PhD class for 2011/2012. During my term as MD/PhD student representative I hope to work on strengthening ties between our group and other local clinician-scientist trainees (i.e. CIP trainees and MD-only students with a research focus), advocating for MD/PhD student-specific needs and increasing the awareness of the MD/PhD training path.

After graduating from the University of Victoria in 2006 with a B.Sc. in Biochemistry I was keen to further investigate the process of cellular fate choice specifically in relation to cellular differentiation. Although principally interested in this question as it relates to embryology I thought this too complicated and unsolvable an area and therefore turned to the differentiation of blood cells (hematopoiesis) as a simpler more tractable system to study this process. Six years later I have learned that although elegant in its complexity, the process of blood formation and the regulation of the hematopoietic stem cells (HSCs) that supply it are anything but simple.

My PhD research has proven a perfect marriage of my interests in embryology and HSC biology and is aimed at understanding how developmentally distinct HSC populations differ in their behaviour. This work follows from initial studies performed by a previous student in our lab (Michelle Bowie) who demonstrated that fetal and adult HSCs have different properties that appear to be coordinately regulated. After an initial comparison of these fetal and adult HSC populations I have been able to identify and characterize novel molecules responsible for at least some of these developmental differences in HSC behaviour. I hope that this work will help inform ways to improve the efficacy and utility of hematopoietic stem cell transplantation as well as provide clues about the distinct processes underlying leukemogenesis in children and adults.

When I am not studying or in the lab I spend most of my time with my best friend and wife Jenn. I also sing with Chor Leoni (www.chorleoni.org) and make the occasional appearance in the UBC Medicine Spring Gala with my other group Toxic Megacolon. In hopeful anticipation of retirement I have also recently taken up fishing and golf.

My experience so far in the UBC MD/PhD Program has been both challenging and rewarding. The guidance and support provided by our Program Directors (Dr. Lynn Raymond and Dr. Torsten Nielsen) and our Program Coordinator Jane Lee has made the seemingly impossible task of balancing clinical and scientific training not only possible but truly enjoyable. I can't thank them enough for their tireless commitment not only to my training but to that of my peers as well.



PhD Oral Defense

Congratulations go to **Will Guest**, Year 5 MD/PhD student, for successfully defending his PhD dissertation on 2 September 2011. Will's research work was highly recognized by the Examination Committee. The external examiner commented that "the dissertation presents a substantial body of work on the molecular mechanisms underlying protein misfolding processes, believed to be associated with various neurodegenerative diseases and other pathologies. Its originality lies in the fact that it integrates closely experimental approaches on the molecular and cellular levels with computational methods that model thermodynamic and energetic properties of the protein systems involved".

Will made a superb presentation of his research work and answered all questions well. We are very proud to share Will's research interests with everyone. Great work!!

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Will Guest, PhD research supervisors:

Dr. Neil Cashman, Brain Research Centre

Dr. Steven Plotkin, Department of Physics & Astronomy

Dissertation title "Template Directed Protein Misfolding in Neurodegenerative Disease"



Will Guest

ABSTRACT


Protein misfolding diseases represent a large burden to human health for which only symptomatic treatment is generally available. These diseases, such as Creutzfeldt-Jakob disease, amyotrophic lateral sclerosis, and the systemic amyloidoses, are characterized by conversion of globular, natively-folded proteins into pathologic betasheet rich protein aggregates deposited in affected tissues. Understanding the thermodynamic and kinetic details of protein misfolding on a molecular level depends on accurately appraising the free energies of the folded, partially unfolded intermediate, and misfolded protein conformers. There are multiple energetic and entropic contributions to the total free energy, including nonpolar, electrostatic, solvation, and configurational terms. To accurately assess the electrostatic contribution, a method to calculate the spatially-varying dielectric constant in a protein/water system was developed using a generalization of Kirkwood Frohlich theory along with brief all-atom molecular dynamics simulations. This method was combined with previously validated models for nonpolar solvation and configurational entropy in an algorithm to calculate the free energy change on partial unfolding of contiguous protein subsequences. Results were compared with those from a minimal, topologically-based Go model and direct calculation of free energies by steered all-atom molecular dynamics simulations. This algorithm was applied to understand the early steps in the misfolding mechanism for beta-2-microglobulin, prion protein, and superoxide dismutase 1 (SOD1). It was hypothesized that SOD1 misfolding may follow a template-directed mechanism like that discovered previously for prion protein, so misfolding of SOD1 was induced in cell culture by transfection with mutant SOD1 constructs and observed to stably propagate intracellularly and intercellularly much like an infectious prion. A defined minimal assay with recombinant SOD protein demonstrated the sufficiency of mutant SOD1 alone to trigger wtSOD1 misfolding, reminiscent of the "protein-only" hypothesis of prion spread. Finally, protein misfolding as a feature of disease may extend beyond neurodegeneration and amyloid formation to cancer, in which derangement of protein folding quality control may lead to antibody-recognizable misfolded protein present selectively on cancer cell surfaces. The evidence for this hypothesis and possible therapeutic targets are discussed as a future direction.

Congratulations!

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

This well-established seminar series aims to illustrate the relationship that exists between clinical practice and medical research. The seminars are organized for budding clinician-scientists of the MD/PhD and Clinician Investigator Programs, which allow the trainees 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, and students in the Faculty of Medicine are invited. Our usual venue is at the Medical Student Alumni Centre, 6:00-7:00 pm, video-conferenced to Victoria, Prince George and Kelowna. Refreshments are provided! For information on upcoming seminars, please visit our webpage at http://www.med.ubc.ca/education/md_ugrad/mdphd/seminars.htm

Our sincere thanks go to our guest speakers:

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|  | <p>Dr. Stephen Yip presented on 24 October 2011. Dr. Yip is Clinical Assistant Professor, Department of Pathology & Laboratory Medicine, UBC, and BC Cancer Agency, Centre for Translational and Applied Genomics, Vancouver Cancer Centre, BCCA.</p> |
|  | <p>Dr. Steven Miller presented on 12 December 2011. Dr. Miller is Canada Research Chair in Neonatal Neuroscience; Scholar, Michael Smith Foundation for Health Research; Senior Clinician Scientist, Child & Family Research Institute; and Associate Professor, Division of Neurology, Department of Pediatrics, UBC.</p> |

Alumni News

Dr. Paul Yong (Class of 2006) - Paul completed residency in Obstetrics & Gynaecology, UBC in June 2011, and is now a Clinical Fellow in Endometriosis/Advanced Laparoscopy at UBC. Paul is continuing to do post-doctoral research, and recently completed projects on laparoscopic inguinal canal decompression and on ultrasound assisted physical examination in chronic pelvic pain. In addition, Paul and **Cheng-Han Lee** (our alumnus in the Class of 2004) are about to embark on a collaboration investigating nerve fibre immunohistochemistry in endometriosis. Paul and his wife have three children.



Paul and his son



Claire and her son

Dr. Claire Sheldon (Class of 2006) - Claire has recently completed her Ophthalmology residency at UBC. During her residency, she marvelled at the beauty and intricacy of the eye. Claire has maintained her interest in basic neuroscience research, having recently initiated a research project examining alterations in mitochondrial structure and function in cultured human fibroblasts obtained from patients with Lebers Hereditary Optic Neuropathy, the most common mitochondrially-inherited optic neuropathy. She is currently arranging a combined post-doctoral research and clinical fellowship in Neuro-ophthalmology. All the while, she enjoys spending time with her rambunctious 2 year-old son.

Meet Our Incoming Students - September 2011

Philip Edgcumbe, Victor Li, Dmitry Mebel and Cynthia Min were accepted in the MD/PhD Program in September 2011. They each come from different places, graduated from different programs, and are taking on projects in different fields. We welcome them into this first phase of training as future clinician-scientists!

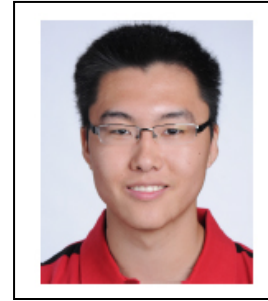
Welcome to the Program!



Philip Edgcumbe

I am a Year 1 student in the Program. In April, 2011 I graduated from the UBC Engineering Physics program with a specialization in electrical engineering. In 2009-2010 I designed and built an ultra-fast two-photon microscope at the UBC Brain Research Center. It is capable of imaging the synaptic activity of a single neuron in the brain of a living tadpole. For my PhD project I plan to continue to do research at the interface of the fields of engineering and life science research.

I have been active in science education, student government, varsity sports and I have benefited from international educational experiences. As a Greater Vancouver Regional Science Fair committee member I worked with the Science Dean's office to organize UBC lab tours for 300 high school students. I have volunteered as a Let's Talk Science teacher and I organized the first ever BC Society for Neuroscience Brain Awareness Week in 2007. I have served as the Science One Survivors President, Applied Science Student Senator and Engineering Physics Board of Studies rep and I played on the UBC men varsity field hockey team for five years. Starting in 2009 I studied for one semester at the Indian Institute of Technology in Delhi, India followed by teaching at Joybells School and Orphanage in a village 300km north of Delhi. I have also lived in Berlin, Germany where I completed a summer research project in computational biophysics research at the Freie Universitat in Berlin.



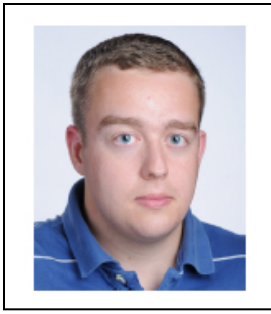
Victor Li

I am very happy to be joining the MD/PhD Program at UBC and look forward to the exciting journey ahead! In the years ahead, I anticipate I will learn much through experiences with my peers and mentors.

I was born and raised in Saskatoon, Saskatchewan, but then moved to Winnipeg, Manitoba where I finished high school and a B.Sc. in General Science at the University of Manitoba. During my undergrad, I worked on two research projects: one where I investigated the anti-cancer applications of hypericin as a photodynamic cytotoxic agent and its mechanism for inducing tumor cell death, and another where I worked on a review book chapter on the current understanding of the molecular events following ischemic cerebral ischemia and potential approaches for intervention and therapy. These experiences were very enjoyable and rewarding for me and were part of what convinced me to aim to become a clinician scientist.

As an MD/PhD student, I will be working with Dr. Yu-Tian Wang in the Brain Research Center to continue exploring ischemia of the brain. My project will focus on means for mitigating neuronal death in stroke and the associated behavioral changes of neuron loss. Hopefully, a better understanding of how neuronal damage following an ischemic episode can be minimized will be useful for developing new stroke therapies as well as for other applications such as minimizing post-perfusion syndrome resulting from cardiac surgery.

Outside of scholastic pursuits, I enjoy playing the piano and spending time with friends and family. Additionally, I am very much enjoying the great skiing and seafood that Vancouver offers, especially since I have spent all my life in the prairies.



Dmitry Mebel

I am very excited to join the MD/PhD program at UBC. Born and raised in Moscow, Russia, I moved with my family to Vancouver around seven years ago. I graduated from UBC with an honours degree in pharmacology, which nurtured my interest in science and research and at the same time prepared me well for the study of medicine. During my degree I spent a year in California working for Roche Palo Alto for my co-op. During that year, I studied hepatic metabolism of drugs, took several road trips to LA, and enjoyed the sunny California beaches. On my return to Vancouver, faced with the rainy weather and the lack of In-N-Out Burger restaurants, I took refuge in science and started working in the lab of Dr. Stephanie Borgland who ironically studied why people get addicted to the kind of food they have at In-N-Out! I ended up completing my undergraduate honours thesis with Dr. Borgland exploring the roles of neuropeptides in the regulation of feeding. I always wanted to study the mysteries of human brain and, having enjoyed the research I've done at Dr. Borgland's lab, I decided pursue my PhD studies at this lab as well.

My current research focuses on the role of neuropeptides in maladaptive motivated behaviours such as addiction and obesity. Drug addiction, as well as certain types of obesity, is thought to result from habits that augment with repetition of the behaviour and thus become increasingly harder for an individual to control despite the potentially adverse consequences. Consumption of food, other than eating from hunger, and certain drug use are often driven by their rewarding properties, which in both cases involves the activation of mesolimbic dopamine circuitry. My research aims to understand the neurobiological mechanisms responsible for the homeostatic regulation of brain reward circuits.

Outside the lab, I also enjoy spending time outdoors skiing, playing soccer or golf. I've recently picked up ping-pong, which seems to be a lot of fun!



Cynthia Min

As I end my first term of medical school, it is still surreal at times that I have been given this amazing opportunity to be in the MD/PhD program. This time a year ago, it would have been hard to believe that I would be making the move from Ontario (where I completed a Bachelors in Health Sciences at McMaster University) to Vancouver.

I am completing my doctoral work With Dr. Kevin Eva from the Faculty of Medicine and Dr. Dan Pratt from the Faculty of Education through the Centre for Health Education Scholarship. My field of research is in medical education which basically encompasses any scholarly work targeted at improving the training of physicians with the ultimate goal of improving patient safety and outcomes. In my undergrad, one of my research interests was looking whether different methods of teaching could help improve the transfer of knowledge from one context to another. The motivation behind this study came from the challenges that medical students experience when they try to take knowledge they learned from a textbook and apply it to clinical cases. The initial results of this project have been promising as it was found that a simple intervention such as providing an analogy for abstract concepts greatly improved the student's understanding of how concepts could apply in multiple clinical contexts.

The focus of my doctoral research will be on better understanding the strengths and limitations inherent in judgment-based assessments. With the creation of the CanMEDS competence framework, it has led undergraduate and postgraduate medical training programs alike to re-direct their attention towards the training and assessment of skills that include good communication, collaborative ability, and patient advocacy. This breadth of focus leads to 50-70 percent of health professional students' grades being determined by faculty ratings. Despite this emphasis, there lacks evidence in the literature that suggests that these competencies are assessed effectively by those charged with documenting student progress.

Ultimately, I hope research I conduct can move beyond application to the local context to influence the advancement of the field as whole and I look forward to the challenges ahead in the upcoming years!

UBC MD/PhD Award Winners

Philip Edgcumbe, Year 1, was awarded a Four Year Doctor Fellowship (4YF) beginning September 2011. The 4YF Program is to ensure UBC's best PhD students are provided with financial support plus full tuition coverage for the first four years of their PhD studies.

Will Guest, Year 5, won the PrioNet Canada Student and Postdoctoral Fellow Oral Presentation Award. Will presented "Misfolding of wild-type superoxide dismutase 1 induced by contact with aggregated mutant superoxide dismutase 1 in a defined *in vitro* system: generalization of the Prion "Protein-Only" hypothesis to Amyotrophic Lateral Sclerosis" at the International Prion Research Conference, PRION 2011, in Montreal, Quebec, 16-19 May 2011.

Farzad Jamshidi, Year 3, and **Daniel Woodsworth**, Year 2, earned the UBC College for Interdisciplinary Studies Graduate Awards for 2011-2012. These are scholarship top-up awards.

Gareth Mercer, Year 3, and **Clara Westwell-Roper**, Year 4, were both Poster Prize winners at the CSCI Young Investigators Forum (12-14 September 2011). Gareth presented, "Perspectives of intravenous drug users on the harms caused by installing blue lights in public washrooms", and the talk Clara gave was titled "Interleukin-1 blockade improves human islet amyloid polypeptide-induced pancreatic islet graft dysfunction".



Long Nguyen, Year 3, won the Dr. Axel Ullrich Scholar-in-Training Award, American Association for Cancer Research Special Conference (Stem Cells, Development and Cancer) Vancouver, BC, 3-6 March 2011. He presented, "Lentiviral tracking of normal and malignant human mammary epithelial cell growth in an *in vivo* xenotransplant model". As well, Long was the Oral Presentation, Runner-up, at the Student Research Day, UBC Experimental Medicine Graduate Program, 21 November 2011. His title of presentation is "Development of a lentiviral-based cellular barcoding strategy to examine the spectrum of *in vivo* growth and differentiation potential of normal human mammary stem cells".

Clinician Investigator Trainee Association of Canada (CITAC-ACCFC)

The mission of the CITAC-ACCFC <http://citac-accfc.org/> is to identify and represent the unique interests of MS/MSc, MD/PhD, and CIP trainees across Canada, to endorse action to improve the academic and postgraduate career opportunities of its members, and to organize and promote other activities that will enable clinician trainees to reach their highest potential. We are pleased to announce that two students in the UBC MD/PhD Program are performing leading executive roles and participating in the committees:

Farzad Jamshidi, Chair, Annual Meeting Planning Committee

Gareth Mercer, Chair, Policy Committee

Comments and Suggestions

We welcome comments and suggestions to the UBC MD/PhD Program and to our newsletters. Please send comments to the MD/PhD Program office, 2N6 - 2818 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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