



UBC MD PhD

UBC MD/PhD Program

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

UBC MD/PhD Student Research Forum & Open House - 14 September 2009

The tenth annual UBC MD/PhD Student Research Forum and Open House was held on Monday, 14 September 2009, 1:00-4:00 pm, at the Michael Smith Laboratories. Opening remarks by **Dr. Torsten Nielsen**, Associate Director of the MD/PhD Program, set off the exciting half-day event.

Our special thanks go to our invited guest speakers:

- ▶ **Dr. Stephen Yip**, MD/PhD Alumnus, and Consultant Pathologist, BC Cancer Agency, recently recruited back to BC following completion of fellowship training in Boston.
He presented “MSH6 somatic mutations in mediating temozolomide resistance in glioblastomas”.
- ▶ **Dr. Stuart Turvey**, Assistant Professor, Division of Infectious and Immunological Diseases, Department of Pediatrics, UBC and Clinician Scientist, BC Child & Family Research Institute.
The title of his talk was “Combining basic immunology with clinical care”.

Suze Berkhout, Year 6 MD/PhD student, presented “Exploring the possibilities of an MD/PhD degree”.

Michael Kozoriz, Year 4 MD/PhD student, also presented “Research, Classes and Family: an MD/PhD student's perspective”. Thank you!



From left to right: **Dr. Stuart Turvey**, **Dr. Stephen Yip**, **Michael Kozoriz**, **Suze Berkhout** and **Dr. Torsten Nielsen**.

UBC MD/PhD Student Research Forum & Open House (con't)

The following MD/PhD students presented their outstanding research posters:

- **Kate Potter**, Year 5 (supervisor: Dr. Bruce Verchere)
“Heparin induces amyloid formation in cultured human islets”
- **Michael Kozoriz**, Year 4 (supervisor: Dr. Chris Naus)
“The C-terminal region of connexin43 is protective during stroke”
- **Will Guest**, Year 3 (supervisor: Dr. Neil Cashman)
“An estimate of prion beta sheet disassociation gibbs free energy”
“Unfolding energy landscapes of the cellular prion protein”
- **Michael Copley**, Year 2 (supervisor: Dr. Connie Eaves)
“Committed adipogenic progenitors are responsible for novel adipocyte generation in response to dietary stimuli”



The forum had an excellent turnout, with faculty members, students, guests, and potential applicants in attendance. Potential applicants had excellent questions and good discussions with the speakers and current MD/PhD students. There was a welcome reception for the students, their supervisors, our committee members, and invited members from the Dean's office of the Faculty of Medicine and the Faculty of Graduate Studies after the event. We had a good opportunity to give advice on the challenges faced by those taking on the unique experience of PhD research training and supervision within the combined MD/PhD Program. The MD/PhD students were also invited to an informal “pub night” and dinner with the Program Directors. Thanks go to **David McVea**, **Clara Westwell-Roper** and **Michael Copley** for organizing the Open House.

PhD Oral Defense

Congratulations go to **Claire Heslop** and **Aaron Joe**, Year 5 & Year 6 MD/PhD students, for successfully defending their PhD theses. They made beautiful presentations and answered all questions well. We are very proud to share their research interests with everyone. Great work!!

* * *

Claire Heslop, PhD research supervisor **Dr. John Hill**, Department of Pathology and Laboratory Medicine, defended her thesis on 6 July 2009. “Emerging environmental, molecular, and genetic risk factors in stable coronary artery disease”.

ABSTRACT

Both environmental and inherited risk factors make significant contributions to coronary artery disease, however susceptibility and age of disease onset for individuals with similar risk profiles varies widely. Novel biomarkers may yet be found which could improve detection of high-risk individuals, and highlight new areas of research for treatment discovery.

This thesis explores risk factors for coronary artery disease and cardiovascular mortality. The first study investigates one specific environmental variable—neighbourhood socioeconomic status—in a cohort of patients who underwent selective coronary angiography. In patients with coronary artery disease, neighbourhood-level disparities contribute to risk of non-cardiovascular mortality, particularly to deaths from cancer, but did not influence cardiovascular mortality risk. Although disparities in health and access to care may persist, these findings suggest other risk factors should be explored to improve cardiovascular patient risk assessment.

Inflammation and oxidative stress contribute to all stages of atherosclerosis, and subsequent chapters focus on contributions of these pathways to cardiovascular risk. Interleukin-6 and C-reactive protein haplotypes were compared to plasma concentrations for prediction of coronary artery disease and cardiovascular mortality. Significant relationships observed between haplotypes,



plasma concentrations, angiographic disease, and cardiovascular mortality did not demonstrate causality, which underscores the challenge of distinguishing causal from confounding pathways.

Plasma oxidative stress biomarkers were measured to evaluate their utility for risk prediction, compared to conventional cardiovascular risk factors. Elevated plasma myeloperoxidase predicted coronary artery disease and cardiovascular mortality risk, independent of conventional risk factors and disease severity. Polymorphisms in candidate oxidative stress genes were also explored for associations with coronary artery disease, and effects on plasma biomarkers. A compound genotype of five polymorphisms predicted angiographic coronary artery disease and elevations in plasma myeloperoxidase. Following validation, this compound genotype may be a useful marker of lifetime oxidative stress burden and cardiovascular disease risk.

Novel cardiovascular risk markers are explored in this thesis, and tested for association with angiographic coronary artery disease, intermediate disease phenotypes, and risk of mortality. New questions are raised regarding how disease susceptibility is influenced by environmental and inherited factors, and ideas for future research are discussed.

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Aaron Joe, PhD research supervisor **Dr. Fabio Rossi**, Experimental Medicine Graduate Program, defended his thesis on 21 July 2009. "Identification, isolation and characterization of adult adipogenic progenitor cells".



Aaron Joe

ABSTRACT

White adipose tissue, or fat, is a complex endocrine tissue important for energy storage and metabolism, and has significant effects on various physiological phenomena, including growth, behaviour, reproduction and immune-modulation. It has been proposed that fat cells, or adipocytes, arise from connective tissue cells that fill with lipid; however, mounting evidence suggests that adipocytes represent a distinct lineage with its own cellular origins. Yet very little is known about the cells that give rise to new adipocytes.

Here, my colleagues and I developed a strategy to isolate purified populations of adipogenic progenitor (AP) cells from subcutaneous fat, visceral fat and skeletal muscle, using fluorescence-activated cell sorting.

These cells are capable of robust adipogenic differentiation, even at the single cell level. We confirmed their commitment to the adipogenic lineage using a variety of assays, and reveal that they are lineage-restricted cells, incapable of osteogenic, chondrogenic or myogenic differentiation. Thus, we have developed an enabling technology to allow interrogation of the adipocyte lineage among different tissues and fat depots, during different physiological, pathological or developmental stages.

Recent evidence suggests that fat depots with a greater ability to generate new adipocytes are associated with lower metabolic risk. Using our isolation strategy, we confirmed that metabolically healthier depots are associated with greater AP abundance and activity, uncovering a link between stem cell biology and metabolic disease. However, adipocyte production in non-adipose tissues, such as skeletal muscle and bone marrow, is associated with chronic disease and aging. To explore possible reasons for this dichotomy, we examined the role of APs in a model of skeletal muscle injury. Our results suggest that APs expand after damage to assist in muscle regeneration by establishing a pro-myogenic niche, ascribing to them a novel function that is independent of adipogenesis.

Together, our strategy to interrogate the adipogenic lineage has allowed us to formulate new hypotheses to explain adipose and skeletal muscle physiology. This technology forms the basis for future work that will allow us to understand how new adipocytes are formed, and perhaps permit the manipulation of adipogenic progenitors for therapeutic benefit.



Faculty of Medicine Research Council

Will Guest, a third year student in the MD/PhD Program, serves as our student representative on the Faculty of Medicine Research Council beginning 2009-2010, for a term of 3 years. He will replace **Aaron Joe** from our Program.

Thanks, Aaron and Will.

Student Representative - David McVea



David McVea, Year 3 MD/PhD student, is the 2009-2010 student representative along with alternate student representative, **Clara Westwell-Roper**, Year 2 MD/PhD student. Clara will succeed David as the student representative next year. The major responsibility of the student representative is to sit on the MD/PhD Advisory and Admissions Committee. One of the duties of the student representative is to help organize the MD/PhD monthly student meetings.

Congratulations!

David is currently holding three major studentship awards –

- Vanier Canada Graduate Scholarship (2009-2012)
- Michael Smith Foundation for Health Research (MSFHR) Senior Graduate Studentship Award (2009-2012)
- UBC Faculty of Graduate Studies Four Year Fellowship (FYF) for PhD Students (2009-2013)

David's research supervisor is **Dr. Tim Murphy**, Department of Psychiatry.

Message from David:

I am very pleased to be this year's student representative for UBC's MD/PhD program. I entered the program in January of my first year of medicine, a little under two years ago. I am now entering the third year of the program, with all of second year FMED under my belt, and am looking forward to the things yet to come.

I started out on the path towards medical school when, after a year in the University of Alberta's Faculty of Engineering, I switched to their Honours Neuroscience program. After finishing my Undergraduate degree, I spent three years in a Master's program studying the neurobiology of locomotion. I was most interested in the ways that the systems that generate the basic pattern of walking movements could adapt to changes, such as new injuries to the musculoskeletal system or new environments.

This interest in plasticity of the nervous system has carried over into my PhD research. I am working on three fairly different projects, but all relate to the ways that the nervous system is changed by experience. The first project aims to help understand the signals that prompt the brain to reorganize after injury. Specifically, I'll be testing the hypothesis that muscle spindles, which signal length and velocity changes in muscle, act as 'error-detectors' to prompt the motor cortex of the brain to change after an injury such as a stroke. To do this, I'm going to study the ability of the motor cortex to change shape in mice genetically engineered to be lacking muscle spindles. The second project involves the ways that activity early in life helps to guide the development of the cerebral cortex. I'll study how sensory feedback generated by spontaneous muscle twitches early in an animal's life allows the motor system of the brain to be calibrated to effectively control movements as an animal grows. Finally, I am examining how patterns of spontaneous brain activity, which consume much of the brain's energy but are poorly understood, change in response to previous sensory experiences.

It is fun research, and it is exciting to help explain how the nervous system adapts to best interact with the environment. At the same time, I am happy to have this fundamental research balanced out by the medical part of the curriculum. Eventually, I hope to use to combine both forms of training to develop rehabilitation strategies and therapies to help people recovering from injury or trauma. Until then, I feel very lucky to be part of a group of such interesting people, doing fun things and learning everyday.

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 offer a casual and relaxed atmosphere in which to profile individuals who have successfully combined both clinical and research aspects into their medical careers. In addition to talking about their active research, the invited speakers also share their experiences, discuss their training backgrounds, offer advices for prospective clinician-scientists, and provide their opinions on career development options for clinician-scientists.

All faculty, clinical investigator trainees and students in the Faculty of Medicine are invited. Presentations are video-conferenced and broadcast to the Island Medical Program and the Northern Medical Program. The event is being held at the Medical Student Alumni Centre, 12th Avenue & Heather Street, at 6:00 - 7:00 pm.

Our sincere thanks go out to our two invited speakers:

- **Dr. Jane Buxton**, Physician Epidemiologist, BC Centre for Disease Control, and Associate Professor, School of Population & Public Health, UBC, presented on 5 October 2009.
- **Dr. Sam Wiseman**, Surgeon-Scientist and Assistant Professor, Department of Surgery, UBC, presented on 7 December 2009.

For information on upcoming seminars, please visit our webpage at http://www.med.ubc.ca/education/md_ugrad/mdphd/seminars.htm












Drs. Jane Buxton & Sam Wiseman

Award Recipients

- **Kate Potter** is a recipient of the Canadian Diabetes Association (CDC) Doctoral Student Research Award. Kate was ranked #1 out of 43 applications. The CDC doctoral award is intended to provide special recognition and support to students who are pursuing a doctoral degree in the field of diabetes in Canada. Beginning 1 July 2009, Kate will receive \$21,000 per year for up to three years to support her graduate studies at UBC. Her research project title is "Role of islet amyloid in long-term dysfunction and failure of transplanted islets".
- **Michael Kozoriz** won the UBC Faculty of Medicine Dorothy May Ladner Memorial Fellowship, 2009-2010. This fellowship is for a graduate student doing research which could lead to the effective treatment of traumatic brain injury. Michael's thesis topic is "Mechanisms of connexin 43 mediated protection".
- **Will Guest** won the UBC Faculty of Medicine Millie and Ralph Drabinsky Graduate Scholarship in Medicine, 2009-2010. This award is for a graduate student undertaking research into the etiology or treatment of Alzheimer's or related neurodegenerative diseases of the central nervous system.
- **Clara Westwell-Roper** is a recipient of the Michael Smith Foundation for Health Research (MSFHR) Junior Graduate Studentship Award (2009-2011). The MSFHR Research Trainee Program Awards support highly-qualified graduate trainees to prepare for careers as independent health researchers. Her research project title is "Role of beta-cell toll-like receptor signalling in type 2 diabetes".
- **Megan Burns** has been granted a Canadian Institutes of Health Research (CIHR) Frederick Banting and Charles Best Canada Graduate Scholarship (Doctoral Award). This award is for doctoral students pursuing a PhD in a health-related field and it is valued at \$35,000 per year for 3 years (2010-2013).
- **Alexis Crabtree** and **Gareth Mercer** have been awarded a Graduate Entrance Scholarship (GES) for the first year of their MD/PhD studies. They also received a CIHR MD/PhD Studentship award at \$21000 per year beginning March 2010.
- **Farzad Jamshidi** has been awarded a CIHR MD/PhD Studentship award at \$21000 per year starting March 2010.
- **Long Nguyen** is a recipient of UBC's new premier Graduate Entrance Scholarship (GES*). From 2010 to 2013, Long receives an annual stipend of \$16,000 plus full tuition coverage.

Congratulations!

								
Kate Potter Year 5	Michael Kozoriz Year 4	Will Guest Year 3	Clara Westwell-Roper Year 2	Megan Burns Year 1	Alexis Crabtree Year 1	Farzad Jamshidi Year 1	Gareth Mercer Year 1	Long Nguyen Year 1

Incoming Students 2009

Welcome to the Program!

Megan Burns

I am honoured to become a part of UBC's MD/PhD program. Born in Kentville, Nova Scotia, I spent most of my childhood on Prince Edward Island. After completing an honours degree in physics and mathematics at Acadia University in 2006, I came to UBC to pursue a Master's degree in medical physics under the guidance of Dr. Stefan Reinsberg. My Master's research focused on the development and implementation of a pilot study to test the feasibility of various imaging modalities as predictors of vestibular schwannoma (a benign brain tumour) response to radiotherapy. The study included functional magnetic resonance imaging (MRI) techniques as well as 11-C methionine positron emission tomography (MET-PET).

Continuing on with Dr. Reinsberg as an MD/PhD student, my research will investigate the use of functional MRI for lung imaging. This work ultimately aims to implement a new treatment paradigm for reducing the morbidity and treatment failure associated with lung cancer radiotherapy. It is hoped that by applying polarized Xe-MRI techniques enhanced spatial information about the lungs can be used to ameliorate radiotherapy outcome by informing radiotherapy treatment planning methods. By improving the accuracy of the target volume to which radiation is delivered, treatment morbidities can be alleviated and doses can be escalated – providing better treatment outcomes. This research has potentially very high clinical importance as more patients die from lung cancer than from any other cancer.

During my spare time, I enjoy playing the piano, running, soccer, and spending time with my young son, Cyrus. I also try to find time to volunteer in various ways in my local community. So far I am immensely enjoying getting to know my talented classmates at UBC!

Alexis Crabtree

I am very excited to join the MD/PhD Program. I graduated with a BA in Development Studies from the University of Calgary and an MPH from the University of Alberta. In the UBC MD/PhD Program, I work with Dr. Jane Buxton, in the School of Population & Public Health and a Physician Epidemiologist at the BC Centre for Disease Control. Dr. Buxton's areas of interest include: communicable disease control, outbreak investigation, breast cancer risk, hepatitis A, B and C, transfusion transmissible diseases, illicit drug use epidemiology and harm reduction, and social context of health behaviour. My project is to investigate the health and quality of life of illicit drug users in the province's vast rural areas, since little is known about this group in spite of the fact that their peers in Vancouver, BC, have been extensively studied. This study will use epidemiological and qualitative methods to investigate health service utilization and unmet health needs of illicit drug users in several rural communities. The study will incorporate elements of participatory action research (PAR), particularly involving drug users in data collection in order to improve access to this often hidden and marginalized population. I believe medicine and epidemiology make an excellent pair: the first suggests the right questions, and the second helps find the right answers.

Besides studying, I am interested in textile crafts and kayaking.

Farzad Jamshidi

I find myself very fortunate to join the MD/PhD program. It has been a few months since I started medicine here at UBC, and I am already in awe of the vastness of information we have about the human body and disease yet also the vastness of unanswered questions that still exist!

My first exposure to biomedical research started through the career preparation program during the senior years of high school when I was able to get involved with imaging and computer analysis studies on fracture healing at the division of orthopaedics engineering at VGH. Later on, during the summer of my sophomore year as a biology student at UBC, I worked at Dr. Robert Hancock's laboratory in the department of microbiology and immunology under a summer studentship award from the Canadian Cystic Fibrosis Foundation. This project focused on studies of swarming motility in *Pseudomonas aeruginosa*, a unique pattern of behavior associated with increased virulence in the bacteria. Having developed a great interest in medicine, I applied to the MD program in my fourth year and also during the same year I returned to Dr. Hancock's laboratory to do directed studies focusing this time on cytotoxic aspects of *P. aeruginosa*. I really enjoyed my experience during this study and came to the realization that I want to pursue research seriously in my future career. Thus I applied to the MD/PhD program as a MED I student and very recently received admissions.

The area of research to which I am greatly attracted is the study of sarcomas and more specifically bone tumors. During my undergraduate years, I traveled to Iran on two occasions where I was able to shadow an orthopaedic team that partly focused on limb salvage and treatment of patients suffering from bone sarcomas. What struck me most was that most of these patients were so young, many of them in their twenties. Even though they are rare, sarcomas are very diverse and their prognosis very poor. On the other hand, current medical treatment of sarcomas is much less effective when compared to treatment of cancers of similar molecular features such as hematopoietic neoplasms. For my PhD project, I will be joining Dr. Torsten Nielsen's laboratory, which is one of the few groups in BC with a focus on the study of sarcomas.

Aside from my research, I am very enthusiastic about music and enjoy playing the piano. I also love the outdoors and try to spend as much of my weekends as I can outside even when it rains!

Gareth Mercer

It is with great excitement, if an excitement veined with trepidation, that I enter the MD/PhD program at UBC. Thank you all for your warm and generous welcome over the summer. I much look forward to getting to know you over the course the upcoming years.

Having grown up in South Africa, I immigrated with my family to Vancouver eight years ago. Shortly after arriving, I threw myself gleefully into snowboarding and began a B.Sc. in biotechnology at UBC and BCIT from which I graduated in 2008. My research experience during undergrad took me in a loop from medical genetics through biophysics and medicinal chemistry back to genetics, this time as part of an honours thesis in environmental microbiology. I've truly enjoyed laboratory research and, in particular, being a part of interdisciplinary research teams. However, in the year between graduating and commencing medical studies I was fortunate enough to take part in a project aimed at increasing community support for HIV patients at a primary care clinic near Cape Town, South Africa. This experience has helped direct my research interests away from the bench and into the field where I hope to complete my PhD in epidemiology. In particular I am interested in how scientific discoveries can be effectively translated into medical interventions that will allow developing countries to combat infectious diseases using resources that are readily available to them.

Under the supervision of Dr. David Patrick at the BC Centre for Disease Control I hope to be performing operational research relating to the transfer of Canadian surgical training techniques to Rwanda. Development of this training capacity will contribute to the Rwandan Ministry of Health's strategy to incorporate neonatal circumcision services into their national HIV prevention efforts.

This summer I began to learn how to row so I hope that I will also have some time to continue to pursue that, as well as snowboarding, enjoying Vancouver's local music scene, reading, and cooking.

Long Nguyen

These first few months in the MD/PhD program have been very exciting. It has been an adjustment for me moving to the west coast, but once I started in the lab and started classes, I knew that my time at UBC would be unique, enjoyable, yet challenging.

I grew up in Mississauga, Ontario, which is where I call home. I spent the past four years in Montreal, Quebec, attending McGill University where I graduated with a BSc Honours in Biochemistry. The mentors I had at McGill really helped me clarify what my goals and aspirations were for the future. I worked with Dr. Kalle Gehring (Biochemistry, McGill) in the field of structural biology, using x-ray crystallography and nuclear magnetic resonance spectroscopy to determine protein structures and characterize protein-protein interactions. With Dr. Pnina Brodt (Medicine, Surgery & Oncology, McGill), I helped develop and evaluate a

potential in vivo therapy for inhibition of liver metastasis, and with Dr. Peter Metrakos (Hepatopancreatobiliary and Multi-Organ Transplant Teams, McGill), I worked on a transplantation database to monitor post-transplant complications in patients. To gain perspective into different areas of research, I spent short periods of time researching the development of the urogenital system, axon guidance in the development of *C. elegans*, conformational changes of glutamate receptors, the role of Protein Kinase B in breast cancer, and sex-reversal in mice.

I am very excited to be joining the lab of Dr. Connie Eaves in the Terry Fox Laboratory, BCCA Cancer Research Centre. The Eaves lab recently deciphered the mammary epithelial cell hierarchy whereby undifferentiated stem cells generate distinct subpopulations of progenitors, which then generate terminally differentiated cells within the mammary gland. My research will expand upon the techniques already established in the lab, in order to study breast tumors. I hope to provide evidence of how uncommitted stem cells, residing in the mammary gland, give rise to certain types of breast cancer due to deregulation of genes important for intrinsic self-renewal potential and/or differentiation pathways.

Outside the lab, I love to spend time playing piano and violin, and have been enjoying the first few Med/Dent Choir rehearsals. I like to take advantage of beautiful British Columbia, by going hiking, canoeing and swimming outdoors.



Student Interest Group in Neurology

The student interest group in Neurology started in one North American medical school and has now grown to a network of over 150 chapters in the U.S. and Canada. At UBC, the SIGN chapter is involved in promoting an interest in all things neuro. This academic year we are hosting 2 major events, including a neuro career night where a neurologist, neurosurgeon, neuroradiologist and several residents will talk about their careers. In the spring we are also hosting a clinical skills event where students can learn and practice the SIGN also offers mentorship opportunities and, in association with the American Academy of Neurology, student members have access to neurology related publications and scholarship opportunities. For more information please contact myself at kozoriz*at*interchange.ubc.ca

SIGN, UBC Chapter President,
Michael Kozoriz, Year 3, MD/PhD Student

Clinician Investigator Trainee Association of Canada (CITAC-ACCFC)

The mission of the CITAC-ACCFC is to organize and promote activities that support clinician investigator trainees in Canada. The 2009 Annual General Meeting was held from September 21 - September 23, 2009 in Ottawa. We are pleased to announce that students in the UBC MD/PhD Program are performing leading executive roles and participating in the Executive Committee:

President - **Suze Berkhout**
Vice President External - **Aaron Joe**
Treasurer - **Will Guest**
Secretary - **Kate Potter**
Election Officer - **Fiona Young**



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 Email: ubcmdphd@interchange.ubc.ca Website: <http://www.med.ubc.ca/mdphd>

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