University of British Columbia M.D./Ph.D. Program

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Newsletter – Summer 2007

MD/PhD Associate Director – Dr. Torsten Nielsen

We are delighted that Dr. Torsten Nielsen has agreed to take on the responsibility as Associate Director of the MD/PhD Program as of 1 May 2007.

Dr. Nielsen is an Assistant Professor in the Department of Pathology and Laboratory Medicine. As a shining role model for our students, Dr. Nielsen will bring a fresh perspective to our Program. Welcome!

Message from Dr. Nielsen

I am both happy and honoured to have been chosen as the new Associate Director of the UBC MD/PhD Program. I myself graduated from the combined program at McGill back in 1997, so what it was like to be a student in both programs remains very fresh in my mind. As a clinician-scientist pathologist, my everyday experience still takes me back and forth between patient care and research, and I wouldn't have it any other way!

On the research side, I run a wet lab as a PI, doing microarray-based translational research on sarcomas and supervising graduate students and fellows. I am also one of the directors of the Genetic Pathology Evaluation Centre, the most active tissue microarray facility in the country, where we have a particular focus on developing new tests for breast cancer that can guide individualized therapy. On the clinical side, I specialize in musculoskeletal tumor pathology, and hold associate member appointments in Orthopaedics and in the new Department of Urological Sciences. My clinical office is in VGH one floor above the emergency room, and my research office is in the Jack Bell Pavilion. I am also cross-appointed at the BC Cancer Agency.

We now live in an age where generating data and accessing information is easy, but figuring out what is valid scientifically, relevant clinically and important and useful for patient care has become a bigger challenge than ever before. MD/PhD clinician-scientists, though few in number, are arguably better placed than anyone to combine critical insight into science with a real world perspective on health care delivery. These vital skills will ensure that all our graduates will have opportunities for careers that are not only busy and productive, but also a wonderfully interesting and fulfilling.

Having been on the MD/PhD Admissions & Advisory Committee for the past three years, many of the current students will already know me, and I look forward to getting to know you all even better. As Associate Director, I intend to do my best to be a strong advocate for those of you already in the Program, those about to graduate and wondering what comes next, and those of you reading this newsletter as you consider applying to our Program. You have chosen a great career that will keep you interested, excited, and, yes, working hard for many years to come. My door is always open to you … if you can somehow get past the security-card controlled perimeter access, of course! Do feel free to drop in on me at VGH or the Jack Bell Research Pavilion, or contact me at VGH 604-875-5555 extension 66768, email: torsten@interchange.ubc.ca

UBC MD/PhD PROGRAM

Michael Rauh, MD, PhD

Our most recent MD/PhD graduate, **Michael Rauh**, received his MD/PhD dual degree in May 2007. Michael's PhD research supervisor is Dr. Gerald Krystal. Michael defended his PhD thesis on 17 January 2007. He presented his synopsis very well and responded to all questions in a thoughtful manner and overall received a category "1". The examination committee was unanimous that the performance was at the level of excellence expected of a doctoral student at UBC. The external examiner from Oxford reflects the feelings of the committee, "It is rare for the expert to learn from the thesis, as in this case". Michael is a stellar example for the MD/PhD Program. Congratulations, Michael.

Michael was the winner of the Hematology Award and the Advanced Therapeutics Award for his graduating class.

Michael Rauh – PhD Thesis
"The Role of SHIP in Macrophage Differentiation and Function"

Congratulations!

ABSTRACT

The SH2 containing inositol 5'-phosphatase (SHIP) is a hemopoietic-specific protein that catalyzes the hydrolysis of the phosphatidylinositol 3-kinase (PI3K)-generated second messenger PI-3,4,5-P_3 (PIP_3) to PI-3,4-P_2 (PIP_2) and thereby negatively regulates hemopoietic cell survival, proliferation, differentiation and activation. Herein, macrophage development and function were compared in SHIP+/+ and -/- mice. SHIP was found to restrain *in vitro* bone marrow-derived macrophages (BMMϕ) survival (or proliferation) and differentiation, consistent with the increased number of macrophages observed in SHIP-/- mice. We also compared the function of J2 virus-transformed SHIP+/+ and -/- BMMϕ cell lines and found that SHIP-/- J2M BMMϕ cell lines (-/-J2Ms) were functionally impaired in inducible nitric oxide (NO) synthase (iNOS) induction and high-output NO production, an important, classical (M1) macrophage activation strategy to combat the growth of tumours and microorganisms. This was ascribed to deficient nuclear localization of IRF1 and inhibition of iNOS transcription in these transformed Mϕs. In contrast, primary SHIP-/- BMMϕs routinely demonstrated enhanced LPS-stimulated iNOS/NO induction, likely as a result of PI3K-mediated enhancement of the p70S6K/IFNβ/Stat1/iNOS pathway. Differential impacts upon this axis also provided an explanation for the opposite effects of the PI3K inhibitors, LY294002 and wortmannin, on iNOS/NO. We also found that SHIP-/- BMMϕs failed to tolerize to a second dose of LPS, likely because SHIP protein levels were upregulated in wild-type BMMϕs in an autocrine-acting, TGFβ-mediated tolerance loop.

Analysis of *in vivo*-differentiated, resident peritoneal and alveolar macrophages (PMϕs, AMϕs) from SHIP-/- mice revealed impaired NO generation, despite sufficient iNOS induction, due to constitutive arginase I-mediated L-arginine substrate competition, which redirected L-arginine metabolism away from cytotoxic NO and towards the production of healing/inflammation-resolving intermediates. These and other features were recognized as alternative (M2) Mϕ activation. Consistent with pathological M2-skewing in SHIP-/- mice, their lungs were fibrotic and contained macrophage-associated Ym1 crystals. Moreover, implanted tumours grew more rapidly in the M2-skewed environment of SHIP-/- mice. Interestingly, BMMϕs from SHIP-/- mice did not display this M2 phenotype unless exposed to TGFβ-containing mouse plasma early during *in vitro* differentiation, suggesting that an environment of elevated PIP_3 and TGFβ arising during *in vivo* macrophage differentiation may contribute to M2-skewing.

Parting Words from Michael Rauh

Thanks to my experience with the UBC MD/PhD Program, I've recently matched to the Hematological Pathology Residency Program at the University of Toronto. There, and perhaps also through elective research opportunities at Cambridge, I hope to pursue further Clinician-Scientist training, with an emphasis on the molecular biology of leukemia, stem cells, and cancer immunotherapy. As I approach my MD/PhD graduation day, I've been reflecting on my journey to this point, the many wonderful people I've met, the incredible privileges and opportunities that have come my way, and the many doors that have been opened for my future career.

As with many others, my life was influenced and touched by witnessing the struggles and eventual loss of loved ones in their battles with cancer. As a child growing up in Sudbury, Ontario, I also vividly remember a young man named Terry Fox running through our community. His story touched my heart and, coupled with experiences closer to home, had a definite impact on my life. Encouraged and supported by loving parents, these experiences helped to harness my general fascination with science into curiosity for this entity called cancer.

An Honours Bachelor of Science degree and thesis in Biochemistry at Laurentian University provided me with the background necessary to pursue cancer research and medical education. My hard work and dedication allowed me to excel academically and to be competitive for scholarships and research funding.

Masters level research at McMaster University, under the guidance of Dr. William Muller, involved signal transduction in normal and neoplastic mammary gland development. During this time I was introduced to the first Pathologist I was to meet, a collaborator from the University of California Davis, named Dr. Robert Cardiff. Sessions with Dr. Cardiff at the microscope examining mammary gland and lung histopathology sparked my interest in Pathology and my pursuit of combined research and medical training. Moreover, I distinctly recall a breast cancer patient advocate, who had been invited to a research conference I attended, challenge the research crowd at the conclusion of the session with the question: "If tomorrow you had the answers to the questions you seek today, do you know what you'd do with them?". It struck me that out of my group of peers I was most affected by her comments. This was a defining moment that helped to affirm my interest and the importance of bridging research with medicine.

The possibility of combining MD/PhD studies drew me to the University of British Columbia and the guidance of Dr. Krystal of the Terry Fox Laboratory/BC Cancer Agency. My PhD research encompassed signal transduction in myelopoiesis and innate immunity, and involved characterizing the role of SHIP in cells of the monocyte/macrophage lineage in a knockout mouse model. SHIP is a lipid phosphatase, restricted in expression to hematopoietic cells, which plays important negative regulatory roles in these cells. While my research focused on macrophages, I was also fascinated by the work of others in the lab and of collaborators who studied the role of SHIP in other hematopoietic lineages. Moreover, at the Terry Fox Laboratory and BC Cancer Agency, I was immersed in a rich environment of normal and malignant, basic and clinical hematopoiesis research.

Throughout my undergraduate medical education, regardless of the field of study, I found myself drawn toward a greater understanding of pathophysiology. Moreover, throughout my clerkship experience, whenever possible, I sought to maximize my exposure to Hematology/Oncology. For example, in third year, during my Pediatric rotation, I requested and was granted the opportunity to conduct my in-patient rotation on the Hematology/Oncology ward. During Surgery, my in-patient experience was with the Surgical Oncology service, and elective rotations included Thoracic Surgery and Radiation Oncology. While on my Internal Medicine rotation, I made a point of following as many Hematology patients as possible. During a two-week elective period, I chose to conduct a rotation in General Pathology, including my first exposure to Hematopathology, at the Royal Columbian Hospital.

My fourth-year senior clerkship was designed to maximize my educational opportunities and exposure to aspects of Laboratory Medicine and Hematology, in an effort to best prepare myself for a future in a Hematological Pathology Residency Program. Specifically, I conducted rotations in Hematopathology at VGH, the Lymphoma Pathology group at the BC Cancer Agency, the Hospital for Sick Children in Toronto, the University of Ottawa and Dalhousie University. Moreover, I spent four weeks of combined ward/research with the Bone Marrow Transplant Service at Vancouver General Hospital/Terry Fox Laboratory. Finally, my pre-residency elective was conducted in Anatomical Pathology with Drs. David Huntsman, Blake Gilks and Torsten Nielsen at the Genomic Pathology Evaluation Centre (GPEC).

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Before my decision to apply to Hematological Pathology, I had also considered Internal Medicine/Hematology. Ultimately, I am interested in utilizing my research experience and knowledge to further the understanding and characterization of disease at the molecular level, to improve diagnostic and prognostic capabilities and to identify novel targets and strategies for therapeutics. I feel this can best be achieved through a career as a Clinician-Scientist in Hematopathology. While most have been supportive of my decision, some have been slightly disappointed, citing how they feel I interact well with patients and their families. While I do enjoy this aspect of medicine very much, I disagree with those who believe Pathology and Laboratory Medicine are devoid of such interactions. On the contrary, I feel there are many opportunities to interact with others, including staff, students, colleagues, patients and their families, through laboratory, clinical and academic settings.

We are in the midst of an unprecedented medical paradigm shift. The wealth of information ushered in by the emergence of "omics" (i.e. genomics, proteomics, metabolomics, etc.), combined with advances in medical technologies and bioinformatics will soon enable the practice of medicine to shift its focus from the reactive to the prospective. Traditional medicine is generally dominated by patients presenting with symptoms at late stages of disease. It is the hope of those who champion this new ideology (including myself) that medical practitioners may be able to intervene at earlier stages and employ personalized, preventive strategies that may ultimately be more cost effective and translate into better outcomes for patients. However, this goal will only be achieved if "omics" technologies are combined with more traditional basic discovery, translational research, clinical trials, outcomes research, classical epidemiology, health policy and ethics. Those with combined MD/PhD training will be well poised to participate in this medical revolution.

I am grateful that the UBC MD/PhD Program has provided me with a very holistic training experience, whereby the medical and research components have compliment each other and the convergence has been greater than the sum of the parts. I encourage you to challenge yourself, and take up a position at the front line of this medical revolution, as this paradigm shift will only be realized by the concerted effort of Scientists, Clinicians, and Clinician-Scientists alike.

Acknowledgements

I wish to thank my MD/PhD Directors, Dr. Anthony Chow and Dr. Lynn Raymond, and my PhD supervisor, Dr. Gerald Krystal, for their mentorship, guidance encouragement, support, and friendship. They have all been very inspirational people to work with. Words cannot sufficiently express my gratitude.

Thank you to members of my MD/PhD Supervisory Committee, Dr. Alice Mui and Dr. Urs Steinbrecher, for their input, suggestions, and support throughout my PhD studies and during the process of presenting my findings in thesis format. Many thanks also to Dr. Charles Snelling for excellent mentorship over eight years, and to members of the UBC Medicine Dean's Office.

I wish also to thank my fellow MD, PhD, and MD/PhD students, including Paul Yong, Claire Sheldon, Ryan Hung, Cheng-Han Lee, Jimmy Lee, and more current students for their support and advice in combining research and medical school. I wish you all the best in your future studies and careers. Importantly, I must also thank the MD/PhD Coordinator, Ms. Jane Lee, for all of her amazing work and support, often behind the scenes.

A sincere thank you is also in order to my lab mates, past and present, including Vivian Lam, Michael Hughes, Janet Kalesnikoff, Jackie Damen, Mark Ware, Michael Huber, Laura Sly, Frann Antignano, Jens Ruschmann, Tom Buchse, Daisy Chow, Sandie Yew, Victor Ho, Carla Pereira, Anita Sham, Michael Lane, Nicole Baur, Shir Minnes, Melisa Hamilton, and Jessica Palmer, for all their help and friendship in and out of the lab.

I next wish to thank Drs. Norman Wong, Vincent Duronio, Jackie Damen, Cheryl Helgason, Pamela Correll, Michael Huber, William J. Murphy, Manuel Modolell, and Zhou Zhu for helpful discussions.

I also acknowledge financial support from the Canadian Institutes of Health Research and the Michael Smith Foundation for Health Research that, among many things, enabled me to network with the international community.

Lastly, I would like to thank my family: parents John and Jackie, sisters Mary Catherine and Stephanie, and extended family for their love, support and encouragement. Finally, thank you to Jennifer for being with me every step of the way. Together we've moved mountains!

Liam Brunham – PhD Thesis Defense

Liam Brunham, Year 7 MD/PhD student, successfully defended his thesis on 13 March 2007. Liam's study suggested that problems with cholesterol regulation in the insulin-producing cells of the pancreas may be responsible for the development of Type 2 diabetes. Liam's work has been published in highly-cited journals such as Nature, Circulation Research and Journal of Clinical Investigation. His PhD research supervisor is Dr. Michael Hayden in the Department of Medical Genetics. Congratulations, Liam.

Liam Brunham – PhD Thesis
"The Impact of Genetic Variation in *ABCA1* on Cholesterol Metabolism, Atherosclerosis and Diabetes"

ABSTRACT

The ATP-binding cassette transporter, sub-family A, member 1 (ABCA1) mediates the major pathway for cholesterol exit from non-hepatic cells and thereby controls the rate-limiting step in the biogenesis of high density lipoprotein (HDL) particles. In humans, ABCA1 deficiency results in Tangier disease, characterized by low levels of HDL cholesterol, cellular cholesterol accumulation and increased risk for atherosclerosis. More than 100 coding variants have been described in the ABCA1 gene. We attempted to understand how both naturally occurring and engineered mutations in ABCA1 impact its role in cholesterol transport in a variety of in vitro and in vivo systems. We attempted to correlate specific genetic variants in ABCA1 with phenotypes in patients carrying these variants, and used an evolutionary approach to predict which specific variants in ABCA1 would impact its function. We then turned to the study of tissue-specific genetic deletion of ABCA1 in mice to study its role in HDL biogenesis, atherosclerosis and glucose metabolism. We found that intestinal ABCA1 is an important site of HDL biogenesis and that activation of intestinal ABCA1 raises HDL levels in vivo. Hepatic ABCA1, which is a major site of HDL biogenesis, was shown to significantly contribute to susceptibility to atherosclerosis. Finally, we show that ABCA1 plays an unsuspected role in ß-cell function and insulin secretion. These studies have contributed to our understanding of the impact of genetic variation in ABCA1 on diverse biological and pathological processes, and have identified novel aspects of ABCA1 function in specific cell types.

Annual MD/PhD Party

The MD/PhD group enjoyed a very pleasant evening at Dr. Torsten Nielsen's residence on Friday, 8 June 2007. The food was yummy and everyone had an enjoyable time. After dinner, we exercised ourselves in the pool and took some nice pictures. The party was a great success! Thanks go to Fiona Young for organizing the set up and clean up of the party, and for taking photos for everyone.

Thanks Dr. Nielsen!

MD/PhD Student Meeting

MD/PhD students meet monthly to bring up important issues (e.g. upcoming conferences, curriculum planning etc). As well, the students have used this monthly meeting to invite UBC clinician-scientists to speak informally about their experiences and provide advice for how to combine research with clinical practice. Dr. Sian Spacey, Director of the UBC Clinical Investigator Program (CIP), met with the students on Wednesday, 31 January. 2007. She expressed her enthusiasm for research, and she outlined the goals of the CIP program to provide interested clinicians with an opportunity and training to conduct research. She also stressed the fact that MD/PhD students have a chance to benefit from the CIP program by integrating research into their residency training, thus bridging their clinical training with their overall research career goals. Students learned about the requirement of the CIP program, as well as the many different ways that students can fit research time into their residency.

Research Conferences Attended/Presented by Current MD/PhD Students in January – June 2007 (Partial List)

Students	Research Conference Attended/Presented	Titles of Presentation
Arezoo Astanehe	American Physician Scientists Association (APSA) 3rd Annual Meeting, Chicago, IL (13 – 15 April)	Profiling YB-1 Responsive Genes in Basal-like Breast Cancer Cells by ChIP-on-chip Reveals Direct Binding to *PIK3CA*
Suze Berkhout	American Philosophical Association, Pacific Division Meeting, San Francisco, CA (3 – 8 April)	Relational Autonomy and Human Capabilities
	Social Sciences and Medical humanities Conference, Chicago, IL (20 – 22 April)	Risky Measures: Objectivity and Interpretation in the Methods and Science of Public Health
	Canadian Association of HIV/AIDS Researchers (CAHR) Annual Meeting, Toronto, Ontario (26 – 29April)	Risky Measures: Objectivity, Interpretation and HIV-Related Stigma as Emerging Issues for an Ethic of Public Health
	18th Canadian Bioethics Society Conference, Toronto, Ontario (30 May – 1 June)	Risky Measures: Objectivity and Interpretation in the Methods and Science of Public Health
Liam Brunham	Canadian Student Health Research Forum (CSHRF), Winnipeg, Manitoba (5 – 7 June)	✓ Critical Role of ATP-binding Cassette Transporter A1 (ABCA1) in Beta Cell Function, Glucose Homeostasis and Response to Thiazolidinedione Treatment
Bryan Coburn	American Physician Scientists Association (APSA) 3rd Annual Meeting, Chicago, IL (13 – 15 April)	Novel Overlapping Roles of *Salmonella* Pathogenicity Islands 1 and 2 in Intestinal Salmonellosis
Brennan Eadie	American Physician Scientists Association (APSA) 3rd Annual Meeting, Chicago, IL (13 – 15 April)	Decreased Neurogenesis in a Mouse Model of Fragile X Syndrome
Heather Heine	International Society for Stem Cell Research (ISSCR) 5th Annual Meeting, Cairns, Australia (17 – 20 June)	The Endothelial Progenitor Cell: Characterization and Contribution to Vascularization
Claire Heslop	The 2nd World Congress on Gender-Specific Medicine and Ageing, Rome, Italy (8–11 March)	Sex Difference in Outcome of Cardiac Syndrome X: Identifying Biomarkers to Accurately Assess Risk and Improve Care
	American Physician Scientists Association (APSA) 3rd Annual Meeting, Chicago, IL (13 – 15 April)	Characterizing Sex Differences in Cardiac Syndrome X to Accurately Assess Risk and Improve Care
	Canadian Student Health Research Forum (CSHRF), Winnipeg, Manitoba (5–7 June)	CRP Gene Polymorphism Predicts Mortality in Patients with Coronary Artery Disease
Aaron Joe	Western Student Medical Research Forum (WSMRF), Carmel, CA (31 Jan – 3 Feb)	Prospective Isolation of Adipogenic Progenitors from Skeletal Muscle
	UBC CIP Research Day, Vancouver, BC (26 April)	Prospective Isolation of Committed Adipogenic Progenitor Cells from Murine Adult Skeletal Muscle
	International Society for Stem Cell Research (ISSCR) 5th Annual Meeting, Cairns, Australia (17 – 20 June)	Segregation of Adipogenic and Myogenic Activities in Skeletal Muscle: A Paradigm for Unipotent Progenitor Cell Crosstalk during Muscle Homeostasis
Michael Rauh	Keystone Symposia Conference (D2): The Macrophage: Homeostasis, Immunoregulation and Disease, Copper Mountain, CO (11 – 16 April)	The Effect of SHIP and the P13K Pathway on Macrophage Activation and Polarization
Inna Sekirov	American Physician Scientists Association (APSA) 3rd Annual Meeting, Chicago, IL (13 – 15 April)	The Not-so-silent Partner: Intestinal Microbiota Modulates Virulence and Pathology of Enteric Pathogens
	UBC CIP Research Day, Vancouver, BC (26 April)	Intestinal Microbiota Modulates Host Susceptibility to Enteric Pathogens
Patrick Yang	Western Student Medical Research Forum (WSMRF), Carmel, CA (31 Jan – 3 Feb)	✓ Distribution and Expression of Transgene Green Fluorescent Protein in Mice Survived Up to Four Weeks Following *in Utero* Gene Therapy

✓ **Liam Brunham** won the gold medal from the CIHR Institute of Nutrition, Metabolism and Diabetes for the best poster in the CIHR National Research Poster Competition. Congratulations!

✓ **Patrick Yang** won the Subspecialty Award in Genetics for the WSMRF presentation. Congratulations!

Kudos


Arezoo Astanehe
Year 3


Suze Berkhout
Year 4


Liam Brunham
Year 7


Bryan Coburn
Year 7


Brennan Eadie
Year 3


Heather Heine
Year 5


Claire Heslop
Year 4


Aaron Joe
Year 5

Congratulations go to **Inna Sekirov** and **Fiona Young** for winning the Michael Smith Foundation for Health Research (MSFHR) Doctoral Trainee Incentive Award 2007. These awards provide top-up funding for our students who also hold concurrent CIHR MD/PhD Studentship Awards. Inna is currently receiving a CIHR-UBC Training Program for Translational Research in Infectious Diseases (TRID) MD/PhD Studentship Award. Fiona is currently receiving a CIHR Walter and Jessie Boyd & Charles Scriver MD/PhD Studentship Award. Inna's research project is entitled, "The Role of the Intestinal Microbiota in Host Response to Enteric Pathogens", her research supervisor is Dr. Brett Finlay, Microbiology & Immunology. Fiona's research project is entitled, "Palmitoylation in the Pathogenesis of Huntington Disease", her research supervisor is Dr. Michael Hayden, Medical Genetics.

Mike Kozoriz and **Patrick Yang** both received a CIHR MD/PhD Studentship Award for six years beginning 2006-2007. Mike's research project is entitled "The Neuroprotective Mechanism of Connexin-43", his research supervisor is Dr. Christian Naus, Cellular & Physiological Sciences. Patrick's research project is entitled "*In Utero* Gene Transfer in Mice: A Model of Fetal Gene Therapy for Cystic Fibrosis", his research co-supervisors are Drs. Erik Skarsgard and William Jia, Experimental Medicine Graduate Program. Congratulations!

Heather Heine passed her PhD Comprehensive Examination on 17 April 2007. Her research project is entitled, "Vascular Endothelial Growth Factor in Cardiac Allograft Vasculopathy". Heather's research supervisor is Dr. Bruce McManus, Pathology & Laboratory Medicine. Congratulations!

Suze Berkhout passed her PhD Comprehensive Examination on 7 May 2007. Her research project is entitled "Relational Autonomy and Human Capabilities: Reconceiving Risks and Resources in HIV/AIDS and Women's Health". Suze's research co-supervisor are Drs. Mark Tyndall and Scott Anderson, Experimental Medicine Graduate Program. Congratulations!

Kate Potter, **Fiona Young** and two other MD-09 students worked on a Doctor, Patient and Society (DPAS) self-directed project entitled "Development of Medical Skills in Second Languages to Facilitate Patient Care" during this past year. They use French as an archetype to establish resources, workshops, shadowing contacts, a website, and opportunities in the UBC medical curriculum for students wishing to gain clinical vocabulary and comfort in practicing medicine in their second languages. This project was successful and has been passed on to the next group of students for continuation next year. Workshops in other languages have been held for other students. One of their objectives was to introduce a "language matching" pilot project for the Family Practice (FMPR) course of year II. Dr. Gurdeep Parhar, who teaches the FMPR courses, was very supportive of the initiative and supported setting up this pilot project. Congratulations!

Fiona Young and **Inna Sekirov** participated in the "Get into Graduate School" event for UBC undergraduate students, organized by the UBC SciTeam and the Faculty of Graduate Studies on 14 March 2007. They attended a booth at this event to try to increase applications to our program from UBC undergrads. Thanks.

Claire Heslop and Dr. Andrew Seal, Department of Surgery, together with students and members of the Faculties of Arts and Medicine, launched the Arts and Humanity in Medicine initiative. Their effort has been supported by many faculty members, BC physicians and students. They all agree that creative and artistic pursuits are essential to their well-being and enhance their vocation. Congratualtions!


Michael Kozoriz
Year 2


Kate Potter
Year 3


Inna Sekirov
Year 5


Patrick Yang
Year 3


Fiona Young
Year 3

Meet Our Incoming Students


Patrick Yang


William Guest


Matthew Mayer


Jeremy Daniels

Patrick Yang

My name is Patrick Yang. I was born and raised in Vancouver and attended UBC where I studied Microbiology and Immunology as an undergraduate science major. I was accepted into the UBC MD Program in September 2005. In the summer of 2006, I participated in the competitively salaried summer research programs sponsored by the UBC Faculty of Medicine and the Child and Family Research Institute (CFRI), project entitled "Distribution and Durability of Transgene Expression in Survived Mice Following in utero Gene Therapy". I was awarded a basic science research prize at the CFRI Research Day held in August 2006.

I am happy to accept the offer of admission to begin retroactively in the MD/PhD Program in September 2006. I am completing my PhD research in gene therapy with Drs. Erik Skarsgard (BC Children's Hospital) and William Jia (UBC Brain Research Centre). My research focuses on fetal gene therapy for cystic fibrosis. Using viral vectors and non-viral nanoparticles, my research involves delivering working copies of a gene into the fetus, in hopes of replacing the defective copies. I am working on methods to sustain transgene expression in specific tissues. So far, therapy for cystic fibrosis has all been palliative in nature. If my research is successful, fetal gene therapy could lead to a cure for those born with cystic fibrosis. In addition to tweaking viruses and genes, I am an avid snowboarder in the winter, a rough-necked camper in the summer and a basket ball player all year round. On my spare time, I enjoy karaoke, lifting weights and video gaming, as well as helping out with soup kitchens and volunteering with adults living with special needs.

William Guest

My name is Will Guest, and I am delighted to be joining the community of MD/PhD students at UBC. I was born and raised in Winnipeg, and this June I graduated from the University of Manitoba with a bachelor's degree in physics and biochemistry. For three years I have worked in Dr. Ken Standing's mass spectrometry lab, implementing a new ion fragmentation technique called electron capture dissociation in a time-of-flight mass spectrometer. Although my work has focused on overcoming problems with the physics of this new technology, the resulting device has applications in proteomics for protein sequencing.

My primary research interest is the application of physical methods to the understanding of biological systems. I have not yet picked a research supervisor: it is a difficult choice, as there are so many professors doing work of first-rate quality at UBC. I am considering supervisors in a range of fields, from prion diseases to signalling pathways in breast cancer to bioinformatics-based drug design.

In my spare time, I enjoy reading, cooking and cycling (which I hope to do more of in bike-friendlier, topographically-varied Vancouver). I'm looking forward to the start of the program with much excitement and a little trepidation, knowing that it will be a tremendously fulfilling experience.

WELCOME!

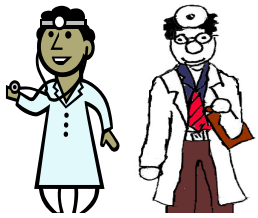
Matthew Mayer

My name is Matt Mayer, and I am thrilled to be joining the student body at UBC as a new MD/PhD trainee. Originally hailing from Winnipeg, Manitoba, where I completed a BSc Honours (Biochemistry), I have spent the last two years living on Canada's other coast while completing a MSc degree in Microbiology and Immunology at Dalhousie University in Halifax.

My background in research has so far been focused on the discovery and use of experimental vaccines and therapeutics for the treatment and prophylaxis of infectious disease. I've had the opportunity to isolate new antimicrobial compounds from nature, study the relationship between the pharmacology of antibiotics and the emergence of bacterial resistance, and most recently, worked on the development of an injection-free platform for vaccine delivery.

The burden of infectious disease on humanity continues to be enormous; the World Health Organization reports that between 25 and 30% of human deaths each year are caused by infectious agents. Granted, these figures are heavily skewed by regions in the world that lack the education, sanitation, finances, and health care infrastructure present in developed countries such as our own. However, even in first world countries, the abilities of modern medicine and science to combat infectious disease are constantly being stretched to their limits by rapidly emerging antibiotic resistance, the spread of germs in a global world, and the threat of bioterrorism.

During the course of my studies at UBC, I plan to continue working on these themes. My PhD research will be supervised by Dr. Bob Hancock, and will investigate the use of anti-infective compounds that fight disease by modulating key components of the host's immune system, rather than attacking the invading pathogen directly. The immune system is highly specialized and generally effective at keeping us pathogen free, despite the millions of organisms we encounter daily in our environment. The development of therapeutics that can combat infectious agents by safely influencing the immune system to correct dysfunctions or selectively enhance key components would allow for sidestepping a central problem we face, i.e. the acquisition of resistance to therapeutics by pathogens to escape selective pressure. I believe that the interplay between medicine and science lies at the very core of this type of work, which has a huge benefit to the health and well being of Canadians and people around the world. As I study medicine, I will have the chance to develop my clinical skills as a doctor and to prepare myself to best address this research from the point of both medical practice and science.



Jeremy Daniels

My name is Jeremy Daniels, and I am very pleased to be an MD/PhD student in our program here at UBC. Medicine has held a special place in my heart. When I was four months old, I contracted Kawasaki's disease (which causes cardiovascular degeneration from an as-yet-unidentified virus[1]), and subsequently grew up making regular visits to cardiologists, which I sustain today. This perspective on medicine and surgery informs my current research agenda, which seeks to improve healthcare effectiveness through human factors engineering of clinical practice. My aim in carrying out this research is to improve patient safety. My dream is a world where patients and families can receive medical treatment without fear of unintentional injury, which is currently not the reality[2]. My belief is that by providing solid evidence on the measurable benefit that human factors-based interventions can have on improving clinical practice, that these new procedures will be adopted and put into practice.

On a personal side, I maintain broad interests in life and the world around me. I regularly bike, do yoga and meditation, read, write, listen to music, and watch more movies than some small countries do. Ever since I was a child I have relished in science and questioning the world. Posing questions and wondering about things around me are basically my way of life, and I am very pleased to work with a supervisor (Mark Ansermino) who supports this, and to be admitted to a program where this is valued. My premedical degree was in mechanical engineering, and I am a registered engineer-in-training in the most beautiful place on earth, British Columbia. I look forward to working with the other students and faculty involved with the program.

[1] N. Engl. J. Med. 2007 Feb 15;356(7):659-61.
[2] CMAJ. 2004 May 25;170(11):1678-86.

Alumni News

Dr. Patrick Tang (Class of 1999)

Patrick completed his MD/PhD in Dr. Brett Finlay's lab in 1999. His research focused on the interaction of *Listeria monocytogenes* with host eukaryotic cell signaling pathways. He went on to do a residency in Medical Microbiology at the University of Toronto where he was involved in many clinical microbiology research projects. During the SARS outbreak in Toronto, he was able to take advantage of all aspects of his medical and research training to aid in the efforts to contain the outbreak – including providing clinical care to SARS patients, screening suspect cases, maintaining the Toronto SARS database and conducting molecular testing for the virus. Following his residency, he spent two years as a post-doctoral research fellow in the laboratories of Drs. Don Ganem and Joseph DeRisi at the University of California San Francisco. He worked on the implementation and optimization of the Virochip, a microarray with oligonucleotides representing all known viruses, to detect novel viruses in various human diseases.

Patrick joined the B.C. Centre for Disease Control as a Medical Microbiologist in November 2006. He is also a Clinical Assistant Professor with the Department of Pathology and Laboratory Medicine at UBC. He brings expertise in molecular diagnostics, microarrays and bioinformatics and he hopes to apply these skills in the clinical microbiology setting. At the BCCDC, Patrick is the head of the Mycobacteriology/TB Program as well as the Advanced Technology Program which provides core molecular services at the BCCDC. He will continue searching for novel pathogens in infectious diseases and infectious etiologies in chronic diseases and cancer.

Selected Publications:

1) **Tang P**, Walsh S, Murray C, Alterman C, Varia M, et al. Acupuncture-associated cutaneous *Mycobacterium abscessus* infections. J Cutan Med Surg 10(4):166-9, 2006.
2) **Tang P**, Roscoe M, and Richardson SE. Limited clinical utility of *Clostridium difficile* toxin testing in infants in a pediatric hospital. Diagn Microbiol Infect Dis 52(2):91-4, 2005.
3) **Tang P**, Louie M, Richardson SE, Smieja M, Simor AE, et al. Interpretation of diagnostic laboratory tests for severe acute respiratory syndrome: the Toronto experience. CMAJ 170(1):47-54, 2004.
4) Brumell JH, **Tang P**, Zaharik ML, and Finlay BB. Disruption of the *Salmonella*-containing vacuole leads to increased replication of *Salmonella enterica* serovar typhimurium in the cytosol of epithelial cells. Infect Immun 70(6):3264-70, 2002.

Dr. Stephen Yip (Class of 1999)

Stephen obtained his combined MD/PhD degree in 1999 and completed his PhD in Dr. Julia Levy's laboratory at the Department of Microbiology & Immunology. He studied the use of photodynamic therapy (PDT) to purge contaminating leukemic cells in hematopoietic stem cell grafts used for autologous bone marrow transplantation. He also studied the use of drug combinations in different sequences to achieve improved therapeutic ratio in the elimination of neoplastic cells while preserving enough of the stem cells to effect hematopoietic engraftment using in vitro and in vivo models. He also looked at other aspects of molecular oncology by studying the role of retinoblastoma (Rb) and p53 proteins in modulating leukemic cell susceptibility to PDT. Stephen was a member of a team that was successful in obtaining a US patent on using PDT to improve the immunological acceptance of xenogeneic tissue grafts.

After graduation, Stephen joined the Neurosurgery Residency Program at the Vancouver General Hospital. During the four years with the division he participated in approximately 500 neurosurgical operations, of which 150 were tumor resection surgeries and biopsies. Stephen then switched to Neuropathology, his subsequent training in Neuropathology helped to consolidate knowledge gained from exposure during his neurosurgical training.

Stephen received his FRCPC in Neuropathology in 2006 and has since been at the Massachusetts General Hospital in Boston, doing his fellowship with Dr David Louis. This fellowship is funded by the Clinician Investigator Program (CIP) of the Royal College which he won in 2006. The award lasts for two years and will end July 2008. His work primarily concerns the study of mismatch repair defects in untreated gliomas and also in gliomas treated with chemotherapy. Stephen is also engaged in some clinical molecular pathology research on brain tumors-looking at epigenetic changes. He spends another portion of his time keeping up his clinical neuropathology skill by attending the regular neuropath signout sessions and rounds at MGH. Stephen plans to combine his interests in the molecular diagnostics of brain tumors, with clinical neuropathology, and bench-top research into the molecular underpinnings of gliomas.

Stephen loves Boston – runs along the Charles River regularly. He might stay in Boston a bit longer than the original period to complete his project or to pursue a MPH degree.

Selected Publications:

1) **Yip S**, Sabetrasekh, R, Sidman R. and Snyder EY. Neural stem cells as novel cancer therapeutic delivery vehicles. Euro J of Cancer 42:1298-1308, 2006.
2) Heran NS, Yong RL, Heran MS, **Yip S**, and Fairholm D. Primary intradural extra archnoid Hodgkin lymphoma of the cervical spine. Case Report. J of Neurosurgery: Spine 5:61-4, 2006.
3) **Yip S**, Aboody KS, Burns M, Imitola J, Boockvar JA, Allport J, Park KI, Teng YD, Lachyankar M, McIntosh T, O'Rourke DM, Khoury S, Weissleder R, Black PM, Weiss W, and Snyder EY. Neural stem cell biology may be well suited for improving brain tumor therapies. Cancer J 9:189-204, 2003.
4) Honey CR, Obochi MOK, Shen H, Margaron P, **Yip S**, and Levy JG. Reduced xenograft rejection in rat striatum after pretransplant photodynamic therapy of murine neural xenografts. J of Neurosurg 92:127-31, 2000.

Dr. Jimmy Lee (Class of 2006)

After graduating last year, Jimmy began working as a post-doctoral fellow with the MS/MRI Research Group at UBC Hospital. Under the supervision of his preceptors Drs. David Li, Tony Traboulsee, and Alex Mackay, Jimmy investigated the role of hydration status on quantitative MRI measurements of brain water content and volume. Going from making buffers to crunching batch files on a MATLAB workstation was definitely a drastic change. It was a rewarding experience of Jimmy and really got him prepared for imaging research.

Participating in the residency match in two different countries was at the same time an exciting, expensive, stressful yet memorable experience. In the end, Jimmy was matched into his first choice. Starting this July 2007, he will be doing his PGY-1 internship at Hospital of St. Raphael, a community hospital affiliated with Yale School of Medicine at New Haven, Connecticut. Next summer, Jimmy will move again to Philadelphia for diagnostic radiology residency at the Hospital of the University of Pennsylvania (PGY-2 to 5). Jimmy plans to do research as a resident, likely in MRI or molecular imaging, and then do a research-intensive fellowship.

From: Jimmy. I want to thank everyone at the UBC MD/PhD Program and the Faculty of Medicine for all the support I received. It is nice to see how the MD/PhD Program has grown and prospered over the years, and continues to attract students with a passion and talent for clinical investigation. Best wishes to the current students!

Selected Publications:

1) **Lee JS**, Nauseef WM, Moeenrezakhanlou A, Sly LM, Noubir S, Leidal KG, Schlomann JM, Krystal G, and Reiner NE. Monocyte p110α phosphatidylinositol 3-kinase regulates phagocytosis, the phagocyte oxidase and cytokine production. J of Leukocyte Biol 81(6):1548-61, 2007.
2) Forster BB, **Lee JS**, Kelly S, O'Dowd M, Munk PL, Andrews G, and Marchinkow L. The proximal tibiofibular joint: An often forgotten cause of lateral knee pain — Pictorial Essay. Am J of Roentgenology 188(4):W359-66, 2007.
3) **Lee JS** and Reiner NE. Stable lentiviral vector-mediated gene silencing in human monocytic cell lines. In Macrophage: Methods in Molecular Medicine. Humana Press Inc. [In press].
4) **Lee JS**, Aldrich JE, Arash Eftekhari, Nicolaou S, and Müller NL. Implementation of a new undergraduate radiology curriculum: Experience at the University of British Columbia. Can Assoc Radiologists J [In press].

CSCI Meeting

Eight MD/PhD students will be presenting their outstanding research projects at the Canadian Society for Clinical Investigation (CSCI) Young Investigator's Forum, 27 September 2007, Winnipeg, Manitoba.

- **Inna Sekirov** (Year 5), Microbiology & Immunology (Dr. Brett Finlay)
  - Intestinal microbiota balance modulates host susceptibility to infection with enteric pathogens
- **Suze Berkhout** (Year 4), Experimental Medicine (Drs. Mark Tyndall & Scott Anderson)
  - Through the looking-glass: Objectivity, interpretation, and the construction of social kinds as emerging issues in research ethics
- **Claire Heslop** (Year 4), Pathology & Laboratory Medicine (Dr. John Hill)
  - Relative value of plasma nitrotyrosine for predicting mortality in patients with coronary artery disease
- **Arezoo Astanehe** (Year 3), Experimental Medicine (Dr. Sandra Dunn)
  - Profiling YB-1 responsive genes in basal-like breast cancer cells by ChIP-on-chip reveals direct binding to *PIK3CA*
- **Brennan Eadie** (Year 3), Neuroscience (Drs. Brian Christie & Y.T. Wang)
  - Abnormal neurogensis in the hippocampus of a mouse model of fragile X syndrome
- **Kate Potter** (Year 3), Pathology & Laboratory Medicine (Dr. Bruce Verchere)
  - Heparin induces amyloid formation in cultured human islets
- **Patrick Yang** (Year 3), Experimental Medicine (Drs. Erik Skarsgard & William Jia)
  - Distribution and expression of transgene green fluorescent protein in mice survived up to four weeks following *in utero* gene therapy
- **Fiona Young** (Year 3), Medical Genetics (Dr. Michael Hayden)
  - Regulation of huntingtin palmitoylation and its role in Huntington Disease

Over the summer of 2006, a group of MD/PhD students from across Canada developed a plan to create a nation-wide network for MD/PhD and other clinician-scientist trainees. The goal was to enhance communication across the different Canadian clinician-scientist training programs, as well as to centralize information resources and address common challenges. In September of 2006, the fledgling association held a very successful planning meeting where many MD/PhD trainees were present, with the goal to have an established network by September 2007. On 4 December 2006, **Fiona Young,** Year 3 MD/PhD student, presented the goals and plan of the association to the CIHR Institute of Genetics (IG) Annual meeting, held in Vancouver, BC. The planning committee members have been meeting regularly via teleconference since then, again with the support of the CIHR IG. The Clinician-Investigator Trainee Association of Canada (CITAC) is now on track to hold its first annual meeting in conjunction with the CSCI meeting in September of 2007, in Winnipeg, Manitoba.

Thank you, Fiona!

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, D25 - Heather Pavilion East, 2733 Heather Street, VHHSC, Vancouver, BC Canada V5Z 3J5. Phone: 1-604-875-5063. Fax: 1-604-875-4013.
Email: ubcmdphd@interchange.ubc.ca Website: http://www.med.ubc.ca/mdphd

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