Ryan Hung, MD, PhD

Our most recent MD/PhD Graduate, Ryan Hung, received his MD/PhD dual degree in May 2005. Ryan started in the MD/PhD Program in September 1998. His PhD research supervisor is Dr. Anthony W. Chow, Infectious Diseases, Department of Medicine. Ryan is currently working in Edmonton to undertake a Residency in Diagnostic Radiology. Ryan is our super role model for the students in the MD/PhD Program. Congratulations, Ryan.

If you had asked my impressions of the clinician scientist career when I started the MD/PhD program in 1998, I would have proffered some naïve comments about wanting to combine the best of medicine with the best of research. As a matter of fact, I would guess that many of us used that exact phrase in our interviews. Seven years later, armed with those five letters affixed after my name, I honestly have not a clue how to adequately convey the paradox that is the clinician scientist's career. However, if you yourself are on the MD/PhD track, then explanation becomes unnecessary because through this long process you become inculcated in the clinician scientist paradigm.

But doesn’t that word “long” strike a nerve? Whether it be family and classmates doubting your sanity from the time of enrollment in this very “long” program, or graduating classmates inevitably opening conversations with you to the effect of, “it’s been a long time for you, hasn’t it?”, we seemingly cannot escape being judged for pro-“long”ing the agony of our education. Admittedly, for me, there were times when the days seemed very long, mostly when things weren’t working. I recall spending a year optimizing a DNA extraction protocol for assessing the nuclear fragmentation of apoptosis, using a reagent that turned out to be optimized to remove the same low molecular DNA I sought, despite the company’s assurances! Yet, I would not call any of the time I have spent wasted or worthless. Others may consider their education long because they perceive a time-dependent diminishing of benefit balanced against increasing cost. In my estimation, spending the time to forge through even the most difficult situations—failed experiments, rejected papers, mind-numbing clerkships, and of course thesis writing—has trained me in the
best ways to balance responsibilities and achieve tangible results.

Moreover, I’ve learned not listen to bystanders urging me to give up, until I’m satisfied I really should give up. When I started my research, I was looking to see whether apoptosis, or programmed cell death, was the explanation for the extreme depletion of lymphocytes in patients with toxic shock syndrome (TSS). Now, the primary virulence factor, toxic shock syndrome toxin-1 (TSST-1), produced by \textit{S. aureus}, has traditionally been thought to act by over-stimulating a certain subset of host T lymphocytes. All initial indicators were that TSST-1 didn’t have any appreciable apoptotic activity. Instead, we started looking at mutants that did induce apoptosis, in a broad and non-specific fashion. Years later, I was still unsatisfied with the notion that we had somehow created mutants with an activity that was lacking in the wild-type toxin. So I tried higher concentrations, a log order higher than had previously been used in the literature—and lo and behold, it turned out the native toxin had the same, broad pro-apoptotic effect. As a result, we’ve now proposed a new hypothesis to explain not only the lymphopenia in TSS, but also a possible pathogenic role for this apoptotic activity. In my thesis, I concluded with the suggestion that \textit{S. aureus}, at sites of infection, might produce high enough local concentrations of TSST-1 to dispose of lymphocytes and monocytes doing immune surveillance in the area.

Lest there be new MD/PhD students reading all this with much trepidation, first allow me to congratulate you on undertaking this challenging but worthwhile endeavour. Six to ten years in our society’s estimation constitutes an enormous investment in time. But I promise that provided you choose research that inspires you, the experience will be, on the balance, enjoyable, fulfilling and mutually complementary. Along the way, you may find, as I have, that these are not mere technical degrees. In both clinical and PhD-level research training, we learn not so much how to do tasks, but rather are inducted into a way of thinking. The unique aspect of this is that by intertwining the formative stages of our research and clinical reasoning, those new synaptic connections become intricately linked, and mental cross-bridging is achieved. While you’ll find this process natural, those around you who live in one world or the other will find you becoming increasingly strange. You’ll think more deeply on clinical problems and techniques than your colleagues, seeking to understand rather than just accepting entrenched modes of management. You’ll see a broader perspective in biomedical research, appreciating the potential for clinical application as well as the limitations. In the end, you’ll become that undefinable creature called a clinician scientist, and as a result, our world will become a better place (no, I’m not being facetious or overstating the case!).

Some of you are nearing the final stages, facing agonizing decisions, and perhaps enjoying so many rotations that narrowing the field is nearly impossible. Despite the anxiety this causes, pause to consider that the benefit of such a quandary is the certainty that this career truly suits you well, so that you will very likely be happy in many of these fields. For me, the end is finally here; but it merely heralds a new beginning. I move on to Edmonton to undertake a Residency in Diagnostic Radiology. Among my specific interests is Interventional Radiology, due to the minimal invasiveness of its techniques and to the increasing capabilities. With the National Institute in Nanotechnology being built in Edmonton, I also hope to integrate nanotechnology into everyday clinical medicine. Initially, this may involve designing novel contrast materials; ultimately, these could serve as components of two-way signaling systems for in situ nanorobots. Anyways, I leave you with the following:

\textbf{DR. HUNG’S TOP TEN WAYS TO TELL YOU’RE IN THE UBC MD/PHD PROGRAM}

10. You’ve been mistaken for being just a medical student or a graduate student—until you start talking.
9. You’ve been accused of being difficult because you think too much.
8. You get E-mail from every md-0# and fmd-0# mailing list in existence.
7. You associate “Carmel” with “conference”, rather than “Pebble Beach”.
6. When going to the lab on evenings or weekends, you lie about it so people think you actually have a life.
5. You’ve secretly hoped for more information on molecular mechanisms of disease in medical school lectures.
4. Residents ask you for advice on their research.
3. You’ve gotten an “H” without meaning to.
2. You’ve applied the “stages of change” model toward your studying, research and thesis writing.

…and the number one telltale sign…

1. PubMed is your textbook for PBL.
Aaron Joe, Year 3 MD/PhD student, was successful in the Michael Smith Foundation for Health Research (MSFHR) Doctoral Trainee Incentive Award 2005 competition. This award provides a top-up for Aaron who also holds the CIHR MD/PhD Studentship Award. In 2004, Aaron also won the Victoria Herman Van Dine Scholarship in Medicine, UBC Faculty of Medicine. Aaron has been selected by the MD/PhD Program Directors to serve as the student representative for the Program on the newly formed Faculty of Medicine Research Council, for a 3-year term, beginning 2005-2006. Aaron is completing the PhD portion of his MD/PhD degree within the Experimental Medicine Graduate Program, under the supervision of Dr. Fabio Rossi, at the UBC Biomedical Research Centre.

Aaron has been elected to take the role of VP Academic for the UBC Medical Undergraduate Society (MUS) 2005-2006. Aaron was the Assistant VP Academic for the society last year. Bravo, Aaron!! This past year, the academic wing of the MUS has taken several steps towards raising the profile of research and quality of education in the medical school, and Aaron played a leading role in some of these projects.

The 1st annual MUS Medical Student Research Forum in November 2004 certainly increased research awareness within the MD and MD/PhD student population. The MD/PhD students played an instrumental role as hosts of the event, which was mainly geared towards MD students. The event brought together established and budding clinician-scientists as the guest speakers, highlighting the fact that both MDs and MD/PhDs will play a crucial role in building bridges between science and medicine.

A re-established MUS Learning Resources Committee has worked to improve educational

Michael Rauh, Year 7 MD/PhD student, was one of the two winners of the 2004 BC Cancer Research Centre Lloyd Skarsgard Research Excellence Award for Outstanding Graduate Student. The award was created in honour of Dr. Skarsgard, who, in 1973, established the Medical Biophysics Department (or the Biophysics Department as it was originally named) at the BC Cancer Research Centre. The award was presented to Michael in November 2004. Michael was invited to present his research on 17 January 2005. The title of his talk was “The Jekyll & Hyde Nature of Macrophages in Cancer and Chronic Inflammation”.

Michael has twice won a subspecialty award at the American Foundation for Medical Research (AMFR)/Western Student Medical Research Forum (WSMRF), in Carmel, California, and twice has shared the top prize at the CIHR/ Canadian Society for Clinical Investigation (CSCI) Young Investigators Forum, in Canada. Michael was among the inaugural group of Michael Smith Foundation for Health Research (MSFHR) Trainees and has served as an ambassador between our Program, MSFHR, the media, and the public.

Michael has always been an active participant in the MD/PhD Program, contributing to our annual Open House, mentoring prospective and new MD/PhD students, providing consultation to the Program website, and serving on the MD/PhD Selections Committee. Michael is a personable young man, who is well respected by his colleagues and peers. Michael has demonstrated great devotion to his combined Clinical and Research training and strongly believes in the merits of such training for improving cancer research.

Michael’s research focuses on the molecular pathways that lead to the development of myeloid leukemia and how the innate immune system interacts with cancer cells. Under the guidance of Dr. Gerald Krystal at the Terry Fox Laboratory of the BC Cancer Agency, Michael has helped identify the SHIP phosphatase (Src homology 2–containing inositol 5'-phosphatase) as a key regulator of myeloid-cell development and macrophage innate immunity. Specifically, Michael has helped elucidate how the absence of SHIP predisposes to myeloid leukemia and immune tolerance in cancer and chronic inflammation.

Upon completion of his MD/PhD degree, Michael plans to continue clinician–scientist training in internal
Aaron Joe (con't)

resources throughout UBC Medicine. The Committee helped to purchase shared textbooks for the gross anatomy lab, provided funds for the maintenance of the MSAC computer room, developed new clinical skills videos to be posted on the web, and is developing the MUS website to include resources such as animations, articles, and videos. The most ambitious project is the establishment of a student resource room in the new Academic Ambulatory Care Centre on 12th and Oak to provide space to house charts, anatomical models, pathological specimens, and other innovative resources to augment student learning.

In March 2005, Aaron traveled to Ottawa to represent UBC Medical Students in the Canadian Federation of Medical Students (CFMS) Lobby Day. Aaron met students from across the country, and spoke with MPs and Ministers about accessibility to medical education.

This upcoming year, Aaron’s goals as VP Academic are: 1) to bring the student resource room to fruition, 2) to continue to raise the profile of research, 3) to foster the development of academic events such as suturing workshops, research seminars and career nights, and 4) to encourage communication between students and faculty regarding the curriculum and the quality of education. Aaron will also be a voice for the MD/PhD students on the MUS executive council, on the Faculty of Medicine Research Council, in the CFMS, and as a student institutional representative of the American Physician Scientists Association.

Congratulations, Aaron!! Way to go!! We are indeed blessed with so many bright and capable students who not only excel academically, but also chose to serve their fellow students so well.

Michael Rauh (con't)

medicine (medical/hematological oncology) or hematological pathology. His ultimate goals include learning how to identify cancer at its earliest, most treatable stages, and how to harness the power of the host immune system to enable more effective preventive strategies.

Michael has excelled at research, its integration with clinical medicine, and its promotion in the community. Congratulations again, Michael.

Dr. Victor Ling, Vice President, Research, BCCA presents Michael Rauh with the Lloyd Skarsgard Research Excellence Prize at the November 2004 Annual BC Cancer Agency Conference Banquet.

Important things to consider when choosing a research supervisor for MD/PhD studies:
1) A good match in areas of research interest;
2) The prospective supervisor must have current CIHR or equivalent peer-reviewed research funding for operating grants (this is a CIHR requirement);
3) Compatibility on a personal level, mentorship and supportive of the student;
4) Actively involved in translational research (bench to bedside to population and back);
5) Laboratory has both basic scientists and clinician-scientists;
6) An appointment within the Faculty of Graduate Studies (an absolute requirement in order to be able to supervise UBC graduate students);
7) An appointment within the Faculty of Medicine (this can usually be arranged or facilitated if all the above criteria are met).

The MD/PhD Program will assist you in finalizing your research project and other members of your Thesis Research Supervisory Committee.
Partial List of Publications by Current MD/PhD Students in the Past Year

Brennan Eadie

Meet Our Incoming Students (2005)

I am very excited to have been admitted into the UBC MD/PhD Program. I am interested in conducting my PhD research in Neuroscience, focusing on neurodevelopmental disorders caused by natural mutations to a single gene, such as Fragile-X (FXS) and Rett syndrome (RS). I believe that careful investigation of these learning disorders will lead to an enhanced understanding of how the brain works and to the development of novel, rational therapeutics. My research supervisors are Dr. Brian Christie and Dr. Yu-Tian Wang, two recent recruits to the UBC Brain Research Centre.

It has recently been theorized that loss of the Fragile-X Mental Retardation Protein in brain cells leads to learning impairment in FXS by deleteriously increasing one specific form of neuronal communication (long-term depression; LTD) that is dependent on activation of the metabotropic glutamate receptor 5 receptor (mGluR5). Dr. Wang’s laboratory has developed a peptide that will interfere with the mGluR5 receptor. It is our hope that this peptide will normalize mGluR-LTD. In Dr. Christie’s laboratory we will test the efficacy of this peptide to improve learning and memory ability in a mouse model of FXS.

Rett syndrome research has also seen exciting developments in recent years. Two papers in Science suggest that the protein lost in this disorder (MeCP2) mediates the relationship between electrical activation and expression of brain-derived neurotrophic factor (BDNF). BDNF has been shown to be extremely important for learning and memory. Alterations to BDNF have never been tested in vivo. We are exploring the possibility that neuronal communication dependent on BDNF is altered in RS, by performing electrophysiological and behavioural experiments on a mouse model of RS. If our hypotheses are supported by our research, we will explore the development of novel therapeutics targeting BDNF.

I am excited about the possibility of eventually observing children with neurodevelopmental disorders in the clinic as a Pediatric Neurologist, identifying the most important research goals, conducting the research in the laboratory and, ultimately, bringing these results back to patients in the clinic to improve their well-being.

Kathryn Potter

My name is Kate and unfortunately, I am not related to Harry Potter, though we do share a last name. I am a prairie girl who cannot get enough of the ocean and who despises snow and sub-zero temperatures, thus I moved to Vancouver five years ago and I have loved every minute of my time here. I was extremely pleased to recently be accepted into the UBC MD PhD program, extending my stay here by at least another seven years!

As the daughter of two geologists, my “education” in science began early on. I have yet to meet another pre-schooler who had a drawer full of her mother’s scientific publications and who took coprolites (fossilized dinosaur droppings) for show-and-tell. Yet it was not until I moved to the coast from Calgary for UBC’s Science One program that I became seriously interested in research. I spent my undergraduate summers and co-op terms getting a taste of diverse areas of the biological sciences. I worked on phospholipid bilayers under chemist Dr. D. Cramb (University of Calgary), yeast oxidative-stress signaling under Dr. A. English (Concordia University), and vascular smooth muscle calcium signaling under Drs. C. van Breemen (UBC) and U. Ruegg (Universite de Lausanne, Switzerland). In my third year at UBC, I entered the Honours Pharmacology program, as it touched on many of the clinically-related aspects of science that have always intrigued me, from molecular interactions at the drug-receptor level and the associated cell signaling to the impact of drugs on organ systems, individuals, and populations of people. I became interested in Type 2 diabetes because of its complexity at each of these levels and did my Honours thesis project on a related topic under Dr. C.B. Verchere (UBC). For my PhD, I will be staying on in Dr. Verchere’s laboratory studying the role of amyloid in the dysfunction and eventual loss of β cells in Type 2 diabetes and in transplanted islets.

Outside of school, I love ballet, hiking, and touring around Vancouver on my bike. In the winter, I am a huge fan of snowshoeing and both downhill and cross-country skiing in spite of the snow. I am also a travel nut and I just returned from a trip to England and Germany. For the rest of the summer, I am working as a summer student, going to Bard on the Beach and Symphony of Fire, moving, and spending a few weekends at my family’s cottage at Mabel Lake, BC. And of course, the end of August will arrive in no time and I am very excited about starting the first year of my medical studies!
**Fiona Young**

I am very excited to have been accepted into the UBC MD/PhD program. A bit about myself … a native Montrealer, I completed a Bachelor of Science (Honours Biology) at McGill University before coming to UBC. Throughout my studies, I have had the opportunity to work in multiple labs with diverse research interests. My experience began as a CEGEP student volunteering for Dr. William Foulkes, who studies BRCA 1 & 2 mutations in Ashkenazi Jewish populations. Then working as a laboratory assistant for Dr. Michael Pollak in cancer research and prevention led to my first publication this year. Last summer I worked as an NSERC USRA student with Dr. Wayne Sossin investigating potential protein interactions with a novel splice variant of the protein Synaptotagmin 1. This year, my Honours project was with Dr. Eric Shoubridge investigating the molecular characterization of two mitochondrial metallochaperone assembly factors of cytochrome c oxidase, SCO1 & SCO2. Mutations in either of these proteins invariably result in very early-onset and fatal disease in humans. I have also volunteered in several hospital departments, keeping in mind the ultimate goal of my research. My area of interest for a PhD is in neurology and genetics, and also in psychiatry - in particular, neurodegenerative disease.

Outside of academia, I have had the opportunity to work with a dynamic group of students as President of the McGill Biology Student Union, which involves everything from student representation to social events to promoting student involvement in the department. I am currently trying to resume playing the violin and to learn Hindi. I love photography and I also enjoy cycling, hiking and snowboarding but especially dancing of all types.

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**MD/PhD Studentship Award**

The UBC MD/PhD Program is grateful to the Michael Smith Foundation of Health Research (MSFHR) and the BC Research Institute for Children’s & Women’s Health (BCRICWH) for their partnership to fund an additional MD/PhD Studentship Award to one of the incoming students.

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The deadline for application to the UBC MD/PhD Program for 2006 admission is 3 October 2005.

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### MD/PhD Enrolment History

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The MD/PhD tuition fee is $3937 per year for the first six years, and a continuing fee of $1729.80 per year in each subsequent year.

All UBC MD/PhD trainees receive an annual stipend of $21,000; renewable each year for a maximum of 6 years. They are also funded to attend and present research findings at two research meetings per year.
Upcoming Events

◆ MD/PhD Student Conference, Keystone, Colorado, USA, July 2005

Three MD/PhD students will be presenting at the 20th Annual MD/PhD Student Conference 2005
 navigator

◆ Liam Brunham, Bryan Coburn and Clara Tan.

◆ CSCI/CIHR Joint Program: Young Investigators Forum, Vancouver, September 2005

UBC will be very well represented at this year’s Canadian Society for Clinical Investigation (CSCI) Young Investigators Forum, on Thursday 22 September 2005, in Vancouver, BC. Ten current MD/PhD students have been selected to present their outstanding research projects! The UBC MD/PhD students would be interested to host a student-directed forum for all MD/PhD students in attendance from across the country. Topics for discussion include career pathways and residency choices, different successes and challenges faced by different MD/PhD programs. Please contact the Program office ubcmdphd@interchange.ubc.ca for more information.

◆ Jimmy Lee (Year 9), Pathology & Laboratory Medicine – supervisor: Dr. Neil Reiner
 o STABLE GENE SILENCING IN HUMAN MONOCYTIC CELL LINES USING LENTIVIRAL-DELIVERED SIRNA: SILENCING OF THE PI10α ISOFORM OF PHOSPHOINOSITIDE 3-KINASE REVEALS DIFFERENTIAL REGULATION OF ADHERENCE INDUCED BY 1α, 25-DIHYDROXYCHOLECALCIFEROL AND BACTERIAL LIPOPOLYSACCHARIDE

◆ Paul Yong (Year 7), Experimental Medicine – supervisor: Dr. Wendy Robinson
 o PROTEIN KINASE PROFILING IN TRISOMY 16 AND EUPLOID MISCARRIAGE

◆ Clara Tan (Year 6), Biochemistry & Molecular Biology – supervisor: Dr. Shoukat Dedhar
 o MORBIDITY AND MORTALITY OF PATIENTS WITH METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) INFECTIONS IN A BURN UNIT SETTING

◆ Liam Brunham (Year 5), Medical Genetics – supervisor: Dr. Michael Hayden
 o TARGETED DISRUPTION OF ENTEROCYTE ABCA1 IDENTIFIES THE Intestine AS A CRITICAL SITE OF HDL BIOGENESIS In Vivo

◆ Bryan Coburn (Year 5), Microbiology & Immunology – supervisor: Dr. Brett Finlay
 o DITCHING THE DOGMA: SALMONELLA PATHOGENICITY ISLANDS 1 AND 2 DO NOT PLAY DICHOTOMOUS ROLES IN MURINE ENTEROCOLITIS AND TYPHOID

◆ Aaron Joe (Year 3), Experimental Medicine – supervisor: Dr. Fabio Rossi
 o A CLONAL, HIGH-THROUGHPUT ASSAY FOR THE OPTIMIZATION AND CHARACTERIZATION OF MESENCHYMAL STEM CELLS

◆ Heather Heine (Year 3), Pathology & Laboratory Medicine – co-supervisors: Drs. B McManus & T Podor
 o INTRAVENOUS AND DIRECT MYOCARDIAL INJECTION OF SIDE POPULATION STEM CELLS LABELED WITH GREEN FLUORESCENT PROTEIN INTO A MURINE MODEL OF MYOCARDIAL INFARCTION

◆ Inna Sekirov (Year 3), Microbiology & Immunology – supervisor: Dr. Brett Finlay
 o CHARACTERIZATION OF SECRETED PROTEIN PROFILES OF NON-O157:H7 ENTEROHEMORRHAGIC Escherichia coli SEROTYPES AND PREPARATION OF THEIR SECRETED PROTEINS FOR USE IN BOVINE VACCINE STUDIES

◆ Susan Berkhout (Year 2), Experimental Medicine – supervisor: Dr. Mark Tyndall
 o LIFE AT THE MARGINS: UNDERSTANDING THE SOCIAL DETERMINANTS OF HIV/AIDS AND WOMEN'S HEALTH

◆ Claire Heslop (Year 2), Pathology & Laboratory Medicine – supervisor: Dr. John Hill
 o BIOMARKERS OF OXIDATIVE STRESS: AN EVALUATION OF NUTRIENT-GENE INTERACTIONS IN CORONARY ARTERY DISEASE

Edited by Jane Lee, Program Co-ordinator, MD/PhD Program, UBC.