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Newsletter – Winter 2004

Open House and Student Research Forum (14 September 2004)

The fifth annual UBC MD/PhD Student Research Forum and Open House was held on Tuesday, 14 September 2004 at the Brain Research Centre, UBC. The forum had an excellent turnout, with about 60 faculty members, students, guests, and potential applicants in attendance (excluding the MD/PhD Program staff and students). Opening remarks by **Dean Gavin Stuart**, Faculty of Medicine, set off the exciting half-day event.

Above: Dean Stuart (standing) at the UBC MD/PhD Open House and Student Research Forum 2004

Two distinguished guest speakers delivered talks on "Issues in the training of clinician-scientists": (1) **Dr. John Mancini**, Professor and former Head, UBC Department of Medicine, spoke on "Training and career opportunities for clinician scientists/ investigators – a personal perspective", (2) **Dr. Jan Friedman**, Professor and former Head, UBC Department of Medical Genetics, gave a talk entitled: "Academic medicine: many paths, many turns". The audience was inspired by the speakers. Two of the MD/PhD students, **Michael Rauh** (Year 6) and **Inna Sekirov** (Year 2) presented talks on "Macrophages, mice, and medical school: managing the MD/PhD maze" and "To MD or to PhD – the why's and how's", respectively. The student presentations were well received, especially by the potential MD/PhD applicants. [See abstracts of talks in this newsletter.] The forum ended with a welcoming dinner enjoyed by invited faculty, staff, students and guests.

1st Annual Medical Undergraduate Society Medical Student Research Forum (MUSMSRF)

Reported by **Aaron Joe** (Year 2 MD/PhD Student, Assistant VP Academic Affairs of the UBC Medical Undergraduate Society)

The first annual MUS Medical Student Research forum was held on Thursday, 25 November 2004, at 7:00 pm, at the Medical Student Alumni Centre (MSAC), and was hosted by the MD/PhD Students. The event was the first in recent history to showcase the research talent found in all four medical classes, whether the research

arose from a summer research project, through the MD/PhD Program, or during research prior to entering medical school. With 18 top-notch research posters, plentiful wine and cheese, and wonderful talks given by Dr. Stephen Yip (UBC MD/PhD Class of 1999, PGY-4 Neuropathology), Dr. Stephen Chung (Professor and Head, UBC Division of General Surgery) and our very own Michael Rauh (Year 6 MD/PhD Student), the event provided a rare opportunity for research-loving medical students and active clinician-scientists to share ideas and to speak candidly about the role research can play in the clinical setting. Most surprising was the diversity of research projects that were undertaken — from the effects of violent video games, to the study of medical ethics, to the examination of anoxia on intracellular pH and Na concentrations. The poster abstracts are available at http://www.med.ubc.ca/mdphd/seminars/musabstract.pdf.

Liam Brunham, our MD/PhD Student Representative, set the scene with his opening comments. Dr. Yip gave a very interesting talk about the opportunities for translational research in neuro-oncology, highlighting several techniques that are beginning to make their way from the bench-side to the bedside. Dr. Chung gave a motivating talk that spoke to the paths that clinician-scientists could take to reach their goals, highlighting the importance of mentorship and collaboration, while using historical references as well as his own research as examples. Michael Rauh provided insight towards the paradigm shift in medicine, speaking to the use of new techniques and discoveries that may change the way that medicine may be delivered in the future. Our posters were judged by Dr. Yip, Dr. Chung, and Dr. Andrew MacNab (Professor and Director of Residency Program, UBC Department of Paediatrics), all of whom provided invaluable comments to the poster presenters. Dr. Bruce Fleming (Associate Dean of Student Affairs) ended the evening with his awards presentations and closing remarks. Congratulations to Kevin Harris (Med-IV) and Andrew Morgan (Med-II), winners of the MD category. Congratulations to Claire Sheldon (MD/PhD-VI) and Trina MacIlhargey (Med-II), winners of the Open category. Honourable mentions were given to May Tee (Med-I) and Suze Berkhout (MD/PhD-I).

Above: Aaron Joe and Clara Tan

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The evening successfully accomplished all it's goals:

1) *to highlight medical students' research;*
2) *to provide a forum for interaction between medical student-researchers, and*
3) *to provide an opportunity to show how research can fit into our future careers.*

It was especially rewarding for Clara Tan and I, who worked feverishly to bring this brainchild to life! The event left geeky-medical students like us invigorated by the exciting opportunities in translational medicine. Many thanks to all the attendees, participants, Dr. Yip, Dr. Chung, Dr. MacNab, Dr. Fleming, Michael Rauh, the UBC Medical Undergraduate Society, the UBC MD/PhD Program, and the MSAC. This event would not have been a success without your support!

Great job! Aaron & Clara. Congratulations!

Clara Tan – VCHRI Outstanding Trainee Award

Above: Clara Tan

Congratulations to **Clara Tan** for winning one of the Outstanding Trainee Awards by the Vancouver Coastal Health Research Institute (VCHRI) at a ceremony held on 29 October 2004. This award is to recognize VCHRI trainees who made an outstanding contribution to their research fields as well as to the scientific community.

Clara is a Year 5 MD/PhD student and is completing the PhD portion of her degree within the Department of Biochemistry & Molecular Biology, under the supervision of Dr. Shoukat Dedhar. Clara has authored seven peer-reviewed publications, three as first author. Her publications have appeared in very high impact journals, including *Cancer Cell, Journal of Biological Chemistry, Oncogene, and Proceedings of the National Academy of Sciences*. Clara's first-authored publication in *Cancer Cell* was featured prominently in the lay media. This work may have significant impact on the treatment of some cancers. As well, Clara won the Best Oral Presentation Award for her research at the Western Student Medical Research Forum, Carmel, CA in 2003.

In addition to her accomplishments as a research scientist, Clara has shown leadership in the scientific community in a variety of ways. As the student representative for the MD/PhD Program, she organized the annual Open House & Student Research Forum in 2003. More impressively however, she initiated a new seminar series entitled "Building Bridges", which is aimed at illustrating the relationship that exists between clinical practice and medical research. Clara developed this idea on her own, and was the chief organizer of the event. She petitioned for funding through the Faculty of Medicine Undergraduate Society at UBC and was successful in obtaining monetary support for the seminar series. Since its inception last year, this series has been well attended and very successful. Clara was also the Co-organizer of the 1st Annual Medical Undergraduate Society Medical Student Research Forum in 2004. This event was a huge success. Clara's high level of energy and volunteerism in the research and scientific community includes her service as a Student Representative to the Medical School Admissions Committee, as the Youth Representative to the Board of Governors for the Canadian Cancer Society, as Co-leader of the Programming Committee, and as Clinic Supervisor for the Community Health Initiative by University Students (CHIUS), in addition to many other volunteer positions that contribute substantially to different health care and scientific communities in Vancouver. Way to go, Clara!!

Michael Rauh – CSCI Best Basic Science Presentation Award

Above: Michael Rauh

Congratulations to **Michael Rauh**,Year 6 MD/PhD student, who won the Best Basic Science Presentation Award at the Canadian Society for Clinical Investigation (CSCI) Young Investigators Forum in Ottawa, Ontario (30 September 2004). Michael did an excellent job on his slide presentation entitled, "SHIP is a Negative Regulator of M2 (Alternative) Macrophage Programming: Implication for Cancer and Chronic Inflammation". All UBC students who attended (Michael Rauh, Liam Brunham, Bryan Coburn, Heather Heine and Aaron Joe) gave excellent poster presentations and represented the UBC MD/PhD Program well.

Michael is completing the PhD portion of his MD/PhD degree within the Experimental Medicine Graduate Program, under the supervision of Dr. Gerald Krystal.

Academic Medicine: Many Paths, Many Turns – Dr. Jan Friedman, MD, PhD, Professor of Medical Genetics, UBC

Among the joys of a career in medicine, and especially a career in academic medicine, are its frequently changing nature and the enormous opportunities for learning it provides. There is always something new to learn and always the opportunity to do something different. Patients pose (and ask) the damnedest questions.

A career in academic medicine offers many choices: one can pursue patient care, teaching, research, administration or various kinds of public service. Patient care can be at the primary, specialty, subspecialty, or sub-subspecialty level and based in a hospital or in the community. Teaching can focus on medical practice at the medical undergraduate, intern, resident, or subspecialty fellow level or on undergraduate, graduate or postdoctoral science students. Teaching may also involve continuing medical education, the development of text books or other learning resources, public education, or interactions with the media. Medical research may be clinical, laboratory-based, translational, population-based or of other kinds.

Some academic physicians lead divisions, departments or faculties or pursue careers in university or hospital administration. Many serve as members of committees or officers of scientific and professional organizations and on various boards and councils. Academic physicians often serve as advisors to universities or hospitals in other provinces or countries and as consultants to governments, lay organizations, lawyers, judges, and industry.

Academic medicine offers many choices, but it also requires many choices. Fortunately, an academic physician can make different choices at different points in her or his career. Only a few choices are irreversible, but all choices have consequences – good or bad (and often both). Choosing to focus in one or a few areas is necessary but always means doing less somewhere else – in your career, with your other interests, or in your personal life.

Dr. Jan Friedman was the former Head of the Department of Medical Genetics, UBC, and he served on the MD/PhD Advisory Committee during 1999-2002. Dr. Friedman's research involves the development and use of clinical databases to study the pathogenesis of congenital anomalies and genetic diseases. His lab has employed numerical and statistical methods to study the basis for the extensive clinical variability that occurs in neurofibromatosis and familial cancer. Another area of focus is the evaluation of risks associated with a variety of human teratogens.

Michael Rauh, Year 6 MD/PhD Student – Macrophages, Mice, and Medical School: Managing the MD/PhD Maze

P(ppp)aradigm shift to prospective, predictive, preventive and personalized medicine: an MD/PhD student's perspective

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 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 (Snyderman, 2004; JCI 114:169). 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 (Snyderman, 2004). While "genomic medicine" may seem far off to many (perhaps rightly so) and "conjure up

space-age images of micro array chips, bioinformatics and designer drugs", current and proven genomic tools, such as the family history "will remain highly relevant for years to come", giving "new meaning and power" to such traditional tools (Guffmacher, Collins and Carmona, 2004; NEJM 351:2333). Those with combined MD/PhD training will be well-poised to participate in this medical revolution. A shining example has been Dr. Brian Druker who, as a Clinician, knew that a BCR/ABL chromosomal translocation was present and causative in greater than 95% of chronic myeloid leukemia (CML) in patients, and as a Scientist, knew that this kinase target was unique to leukemic cells and had insight into the design of a kinase inhibitor. He managed to convince Novartis of the clinical utility of targeting BCR/ABL and this partnership resulted in the creation of Gleevec - one of the first oral, cancer-specific pills, with minimal side effects (as compared to more traditional and toxic chemo- and radio-therapy). As an MD/PhD student at UBC, I had the pleasure to meet Dr. Druker and hear him discuss his revolutionary idea before it came to fruition. I feel that MD/PhD students (and those who perform research at some point during medical training) are provided with a very holistic training experience, whereby the medical and research components complement each other, with the convergence being greater than the sum of the parts. Of course, before these goals can be realized, we will continue to need highly skilled practitioners who can provide patients with the very best current medicine can offer. However, 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.

Inna Sekirov, Year 2 MD/PhD Student
To MD or to PhD – the Why's and How's

While my interest in becoming a physician developed by the end of my third undergraduate year, the decision of pursue a career of a clinician-scientist was a late bloomer that only formed completely during my first year at medical school. It was a long process that has been quietly brewing and maturing for quite a long time. One of the biggest factors that influenced me in this decision was probably the fact that I have had some quite enjoyable exposure to research during my undergraduate years.

My first research experience was in the laboratory of Dr. John McNeill, Pharmaceutical Sciences, UBC. It was a very positive start to what turned out to be a very long journey. As a summer student in Dr. McNeill's lab I was part of a project that allowed me to get to know lab rats quite intimately and most importantly yielded some interesting results that were later included in a paper in which I was a co-author. I can still remember my enthusiasm, first when the results were shaping out to be worth-while, and then when the publication was coming out.

Later I've had a particularly exciting experience as a Co-op student in the laboratory of Dr. B.B. Finlay at the Biotechnology Laboratory of UBC. I started working with one of the post-doctoral fellows, Samantha Gruenheid, on an EHEC project. We investigated the role a newly discovered EHEC effector had in EHEC pathogenesis. The project was very productive, yielding many great results in quite a short time and also resulting in a publication. One of the by-products of our work was the fact that I got completely addicted to getting new and interesting data. I guess I achieved sort of a data high that lasted for a very long time. At least long enough to be the last drop in my decision to pursue an MD/PhD, instead of just an MD degree.

However, as I was very much hooked up on my project as I was applying to medical school, I did not have time to apply to the MD/PhD degree at the same time. Mostly it was because I knew that I'd still get another chance during my first year of medicine. This way has both its pros and cons. On the one hand you need to find time during the first year of medicine to write yet another autobiography, start pestering people yet again with requests for reference letters and worry about the interviews when they come. On the other hand the process is maybe a bit less stressful, since you already are in the medical school, and at least to me it was somewhat reassuring. The bottom line is that it is definitely doable and possible. There is an extension of application deadline for first year medical students, and when the interview time comes, the MD/PhD Program is great at accommodating the schedule of medical school curriculum. One more thing that was worrying me as I was applying to MD/PhD during my first year of medicine was about getting myself funding in the event that I will be accepted. But this task was definitely very quick and painless – the MD/PhD Program took care of pretty much all of it, and everything was organized very efficiently. Now that my data intoxication is long gone, I've had an entirely disastrous summer in terms of research results, and can look back at my decision with a sober eye, I'd like to say that I am still happy with my decision to go into the MD/PhD Program. And I would like to strongly encourage anyone out there who is still sitting on the fence to get down on the MD/PhD side of it.

Claire Sheldon

Congratulations to **Claire Sheldon**, who successfully defended and passed her PhD thesis defense on Friday, 24 September 2004, with flying colors! Claire made a beautiful presentation and answered all questions well; her written thesis was outstanding and overall received a category "1". Nice job, Claire!

Claire is one of our senior students; she has always been an excellent role model for the more junior students in the Program. Claire joined the MD/PhD Program in 1999. Her PhD research supervisor is Dr. John Church, in the Department of Physiology. During academic year 2002-2003, Claire served as the MD/PhD Student Representative on the MD/PhD Advisory Committee, and co-authored the "UBC MD/PhD Survival Manual". Her unfailing effort in supporting the Program and the students is highly appreciated.

Claire is in the sixth year of the Program. She is finishing medical school and will be entering her final year before receiving her MD/PhD dual degree in the spring of 2006.

We are delighted to share Claire's research interest with everyone.

Above: Claire Sheldon

Claire Sheldon – PhD Thesis
"Anoxia and Na^+/H^+ Exchange Activity in Rat Hippocampal Neurons"

In the present study, the effects of anoxia on intracellular pH (pH_i) and intracellular free sodium concentration ($[Na^+]_i$) were examined in isolated rat hippocampal neurons loaded with H^+- and/or Na^+-sensitive fluorophores, and the contribution of changes in Na^+/H^+ exchange activity to the changes in pH_i and $[Na^+]_i$ observed during and after anoxia were assessed. This assessment was aided by the development of a microspectrofluorimetric technique which permitted concurrent measurements of pH_i and $[Na^+]_i$ in the same neuron. It was found that, in rat hippocampal neurons, Na^+/H^+ exchange activity was reduced shortly following the onset of anoxia, possibly as a result of declining internal ATP levels, and did not contribute to the increases in pH_i or $[Na^+]_i$ observed at this time. In contrast, Na^+/H^+ exchange activity was stimulated immediately after anoxia and contributed to acid extrusion and Na^+ influx during this particularly vulnerable period. As a result, the reported neuroprotective actions of Na^+/H^+ exchange inhibitors are likely mediated in the immediate post-anoxic period, consequent upon reductions in acid extrusion and/or internal Na^+ loading. A Zn^{2+}-sensitive H^+ efflux pathway, possibly a voltage-activated H^+ conductance activated by membrane depolarization, also contributed to acid extrusion during and immediately after anoxia and may act to limit the potentially detrimental activation of Na^+/H^+ exchange activity observed after anoxia. The final series of experiments identified additional mechanisms that contribute to the changes in $[Na^+]_i$ evoked by anoxia in cultured postnatal rat hippocampal neurons. Na^+ influx occurred through multiple pathways, the relative contributions of which differed not only during and after anoxia but also in neurons maintained in culture for different durations of time. Understanding the fundamental cellular mechanisms that contribute to anoxia-evoked changes in pH_i and $[Na^+]_i$ in mammalian central neurons may uncover novel therapeutic strategies for the treatment of stroke.

Liam Brunham – MD/PhD Student Representative (2004-2005)

Liam Brunham (Year 4) is the MD/PhD Student Representative for 2004-2005. One of the responsibilities of the student representative is to organize the MD/PhD monthly student meetings. Another major duty of the student representative is to sit on the MD/PhD Advisory and Admissions Committee.

~ ~ Message from Liam ~ ~

My research is focused on identifying the sites of production of high density lipoproteins (HDL) in the body. HDL is a lipid molecule that transports cholesterol through the blood, and high levels of HDL are associated with a decreased risk for cardiovascular disease. However, there are currently no therapies that effectively raise HDL levels.

One hypothesis to explain how HDL protects against atherosclerosis is its ability to transport excess cholesterol from peripheral cells to the liver for excretion, thereby reversing the deposition of cholesterol in arteries. Since the identification of the inverse relationship between HDL and risk for heart disease over 50 years ago, the biogenesis of HDL has been a subject of intense interest. However, it has not been until recently that we have had the tools to adequately address this question.

We are using conditional gene targeting to selectively delete a gene that we have identified as essential for HDL production, called *ABCA1*, in different tissue types. By assessing the effect of selective deletion of *ABCA1* in different tissue we are able to determine the specific contribution of each tissue to HDL production.

By understanding how *ABCA1* acts in different parts of the body and responds to different environmental and genetic signals, we will be in a better position to design ways of raising HDL levels. If we had an effective treatment that raised HDL levels in the general population we could conceivably eliminate the vast majority of heart disease.

Liam won the American Society of Human Genetics 2004 MD/PhD Student Travel Grant to attend the Annual Meeting in Toronto in October 2004. Congratulations!!

When not in the lab I spend time working with a non-governmental organization called Physicians for Global Survival http://www.pgs.ca, the Canadian affiliate to Nobel-laureate organization International Physicians for the Prevention of Nuclear War http://www.ippnw.org. PGS is a physician-led group that attempts to re-frame issues surrounding war, violence, poverty and environmental destruction in terms of the consequences to the health of individuals and communities. By using a medical perspective we believe that we can contribute to the broader movement towards peace and social justice. Currently I am the national student representative for PGS as well as the North American regional representative for IPPNW – which basically means that I get to meet a lot of interesting people, such as at the recent IPPNW World Congress in Beijing http://www.ippnw-students.org/Photos/Beijing.html.

I am very grateful to Dr. Andrew Seal, UBC Medicine's former Dean of Student Affairs, for having pioneered the Faculty of Medicine Spring Gala, because of which I get to play my guitar in the Chan Centre for the Performing Arts. Right now I am working on Francisco Tarrega's Recuerdos de la Alhambra. You can hear Pepe Romero play this here: http://www.peperomero.com. Hopefully one day I will sound like that.

I am looking forward to working with our students and Program Directors over the next year to continue to improve the MD/PhD Program at UBC.

Autumn Gala 10

Above: Dr. Ted Steiner (centre) and students sang in the UBC Medical/Dental Choir.

MD/PhD students and faculty performed at the 10th Anniversary of the Gala 18 September 2004, at the UBC Chan Centre. Dr. Ted Steiner, one of our MD/PhD Advisory Committee members, sang tenor with the UBC Medical/Dental Choir. **Clara Tan**, MD/PhD student was the Choirmaster, she sang alto in the choir and played cello in the Black and Blues band. **Jimmy Lee**, another MD/PhD student, played the trumpet with the band.

The Gala is a fund raising event and a night of performance arts by the UBC Medical and Dental students. Our MD/PhD students have been actively participating in the Spring Gala and the Autumn Gala. Bravo!!

PhD Candidacy

Two of our MD/PhD students, **Liam Brunham** and **Bryan Coburn**, have been admitted to PhD candidacy. Congratulations!!

The basic requirements for a doctoral student to be admitted to candidacy are:

- all required course work has been successfully completed
- the comprehensive examination has been passed
- the research supervisory committee has certified that the thesis proposal has been approved.

MD/PhD Student Conference

Four MD/PhD students (**Liam Brunham, Bryan Coburn, Heather Heine and Aaron Joe**) presented at the National MD/PhD Student Conference at Keystone, Colorado in July 2004.

"New Blood" in the Program

Both first year students (**Susan Berkhout** and **Claire Heslop**) have identified their research area. Susan's research focuses on the interdisciplinary analysis of the social determinants of HIV/AIDS and women's health. Claire's research focuses on the biomarkers of oxidative stress – an evaluation of nutrient-gene interactions in coronary artery disease.

MD/PhD Admissions 2005

From January to March 2005, members of the MD/PhD Program Advisory and Admissions Committee will be interviewing and adjudicating an impressive cadre of short listed candidates. All through the years, exceptional individuals from across the country are recruited to the UBC MD/PhD Program.

Although there are no specific under-graduate course requirements other than the medical and graduate school prerequisites, substantive prior research is essential for consideration of admission.

With the expansion of the UBC Undergraduate Medical Program, the UBC MD/PhD Program is expecting growth in student numbers in the coming academic years.

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