



Room D452, Heather Pavilion East, 2733 Heather Street, Vancouver, BC V5Z 3J5

Newsletter – Winter 2003



THANK YOU!

The UBC MD/PhD Program staff and students express their sincere thanks to the Vancouver Hospital & Health Sciences Centre and the St. Paul's Hospital for their continued funding support to the Program.

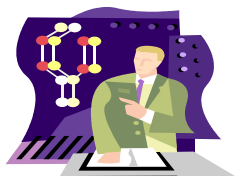
Both the Vancouver Hospital & Health Sciences Centre and the St. Paul's Hospital provided an annual donation of \$5,000.00 to support the operational requirements of the UBC MD/PhD Program. The donation received was also used to sponsor research presentations by MD/PhD trainees at national and international research meetings. The staff and students are deeply indebted to the two organizations for their unfailing support of the MD/PhD Program over the past few years, particularly since the MD/PhD Program does not receive budgeted operational funding from any other sources.

MD/PhD Student Research Forum and Open House: 19 August 2002

The third annual UBC MD/PhD Student Research Forum and Open House was held on Monday, 19 August 2002 at the Peter Wall Institute for Advanced Studies, University Centre, UBC Campus. The forum turned out very well, about 30 faculty members, staff, students, guests, potential applicants and others attended this event (excluding the MD/PhD Program staff and students). Big welcome by Dr. John Cairns, Dean of the Faculty of Medicine, and Dr. Lynn Raymond, Co-Director of MD/PhD Program, set off the exciting half-day event.

Seven MD/PhD students presented at the forum. Two hours of student presentation was concluded with past UBC Clinical Investigator Program Trainee, Dr. John Gill's innovative and entertaining presentation.

Discussion on issues in training of clinician-scientist was led by Dr. Bruce McManus, Scientific Director of the CIHR Institute of Circulatory and Respiratory Health, and Co-Director of the iCAPTURE Centre at UBC, Dr. Anthony Chow, UBC MD/PhD Program Director, and Dr. Peter Paré, Director of UBC Clinical Investigator Program, and Co-Director of the iCAPTURE Centre at UBC.



MD/PhD Student Research Forum and Open House: 19 August 2002 (con't)

| Student Presentation | Hosting Department | Research Supervisor |
|---|----------------------------------|---------------------|
| Jimmy Lee (Year 6) | Pathology & Laboratory Medicine | Dr. Neil Reiner |
| ◀ Distinct PI3-kinase Isoform Regulates Phagocytosis | | |
| Ryan Hung (Year 5) | Experimental Medicine | Dr. Anthony Chow |
| ◀ The G31R Mutant of Toxic Shock Syndrome Toxin-1: Intrinsic and Extrinsic Pathways for Apoptosis | | |
| Michael Rauh (Year 4) | Experimental Medicine | Dr. Gerry Krystal |
| ◀ Resting SHIP-deficient Murine Peritoneal Macrophages Display an Anti-inflammatory Phenotype | | |
| Claire Sheldon (Year 4) | Physiology | Dr. John Church |
| ◀ Intracellular Ph Regulation During Anoxia in Acutely Isolated Rat Hippocampal CA1 Neurons | | |
| Paul Yong (Year 4) | Experimental Medicine | Dr. Wendy Robinson |
| ◀ Preeclampsia and Confined Placental Mosaicism | | |
| Clara Tan (Year 3) | Biochemistry & Molecular Biology | Dr. Shoukat Dedhar |
| ◀ The Role of Integrin-linked Kinase in Angiogenesis | | |
| Liam Brunham (Year 2) | Medical Genetics | Dr. Michael Hayden |
| ◀ Functional Analysis of Mutations and cSNPs in the <i>ABCA1</i> Gene | | |

A highlight of the MD/PhD student year is the annual Student Research Forum and Open House. This annual function provides a valuable opportunity for the MD/PhD students to showcase their research. It also provides an occasion to promote the training of clinician-scientists to the University community and the public. At the forum, MD/PhD students have the opportunity to talk to various graduate advisors, supervisors, students, and potential applicants. MD/PhD students also provide valuable information and serve as a resource for potential applicants to the MD/PhD Program.

The forum ended with a welcoming dinner enjoyed by invited faculty, staff, students and guests, including Ms. Rashmita Salvi and Ms. Judy Finch, Program Managers at the Michael Smith Foundation for Health Research.

Photo below:

Dr. Bruce McManus (left) and Dr. Peter Paré (right) at the forum.



Photo on left:
Dr. John Gill (left) and Michael Rauh, Year 4 student (right) at the poster session.



Dinner photo on right.

UBC MD/PhD Monthly Meetings



Photo above:

Enticing students to come to the MD/PhD monthly meetings with food and drinks.

Standing (from left): Michael Rauh (Year 4), Paul Yong (Year 4), Bryan Coburn (Year 2), Ryan Hung (Year 5).

Seated: (from left) Claire Sheldon (Year 4), Clara Tan (Year 3), Suvendrini Lena (Year 3), Liam Brunham (Year 2).

In 2001-2002, the first series of MD/PhD Monthly Meetings was implemented. This is a developing initiative and desire to respond to the needs of the MD/PhD students. Over the past year, these meetings have provided a casual forum in which the Program Director, Program Co-Director and MD/PhD students have had the opportunity to bring up important issues (e.g. tuition fees, upcoming conferences etc.). The meetings have also served as practice sessions for student conference presentations. 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. So far, we are very honoured to have met with the following topnotch UBC clinician-scientists at the meetings: Dr. Peter von Dadelszen (Obstetrics & Gynaecology), Dr. Lynn Raymond (Psychiatry), Dr. John Mancini (Medicine) and Dr. Ted Steiner (Infectious Diseases).

The second series of the student monthly meetings continues in 2002-2003. For more information on the MD/PhD Monthly Meeting, please contact Clara Tan at htan@interchange.ubc.ca.

MD/PhD Student Representative and Alternate Student Representative

2002-2003

* * *

MD/PhD Student Representative – **Claire Sheldon**.
MD/PhD Alternate Student Representative – **Clara Tan**.

One of the major jobs for the student representative is to assist with the MD/PhD Monthly Meetings. Another major duty of the student representative is to sit on the MD/PhD Advisory Committee and the MD/PhD Admissions Committee.

We would also like to take this opportunity to thank Claire Sheldon and Cheng-han Lee (past student representative) for their outstanding effort in editing the UBC MD/PhD Survival Manual for the current and future MD/PhD students.

Photo on right:

Claire Sheldon thanked the audience after she received the “gavel” from Jimmy Lee, past student representative, at the Open House Welcoming Dinner (19 August 2002).



Claire Sheldon - MD/PhD Student Representative

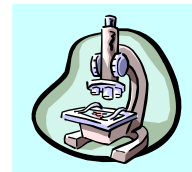
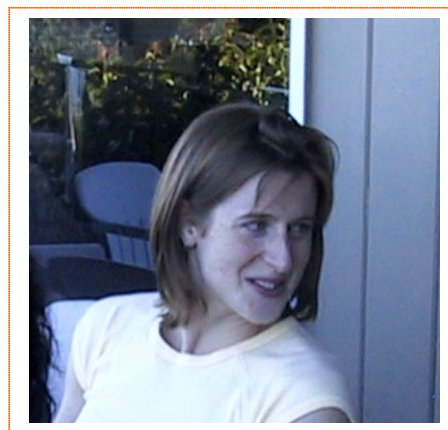
Claire is a fourth year MD/PhD student and is completing the PhD portion of her degree within the Department of Physiology, under the supervision of Dr. John Church. There are two major themes to Claire's research: firstly, she is interested in examining the mechanisms that regulate intracellular pH in hippocampal neurons. It is well established that there are three major pH regulatory mechanisms in neurons in the central nervous system. There are two HCO_3^- -dependent mechanisms and at least one HCO_3^- -independent mechanism, the Na^+/H^+ exchanger. Claire's data suggests that the Na^+/H^+ exchanger in the hippocampus is a novel isoform, as well as suggesting that another, as yet, uncharacterized mechanism (possibly a proton channel) also acts to regulate pH_i . These data are exciting because changes in pH_i are observed during neuronal activity and, in turn, feedback and influence neuronal excitability. Thus, changes in pH_i may be linked to disorders such as epilepsy.

Secondly, Claire is interested in understanding how neurons react to a period of energy deprivation, as would be seen during a stroke. She uses various fluorescent dyes to directly measure changes in pH_i , $[\text{Na}^+]_i$ and $[\text{Ca}^{2+}]_i$ during and following periods of anoxia (oxygen deprivation). Because changes in the intracellular concentrations of each of these cations are central determinants of neuronal death after stroke, Claire would like to understand how the observed ionic changes are produced. She has

been examining the possible contributions of plasma membrane transporters and ion channels to the observed ionic changes and has shown that the activities of plasma membrane transporters, such as the Na^+/H^+ exchanger, are influenced significantly by periods of anoxia. However, other transport mechanisms also contribute to the complex ionic response to anoxia, including the $\text{Na}^+/\text{Ca}^{2+}$ exchanger and non-selective cation channels. Beyond simply understanding what mechanisms are involved, Claire is interested in understanding how these various membrane transporters are regulated to change their activities during anoxia. Anoxia induces dramatic changes in intracellular second messenger systems which may then influence the activities of various transporters and channels. Claire believes that it is important to understand the mechanisms which lead to the dramatic changes in pH, sodium and calcium inside neurons during a stroke-like event because these ionic changes begin a cascade of complex and interlinking events which eventually determine the survival of the neurons.

In the future, Claire wishes to combine her enthusiasm for research with her dedication to patient treatment and, hopefully make an impact on the field of neurological studies. Claire volunteers casually at the Community Health Initiative University Students (CHIUS) medical clinic and, in the future, she wishes to continue to serve underprivileged communities in any capacity as she is able.

Claire Sheldon



See Claire's publication in the [Journal of Clinical and Investigative Medicine](#):
C. Sheldon, J. Church Na^+/H^+ exchange: molecular regulation to therapeutic development.
Clin Invest Med, Vol 25, no 6, December 2002, 229-232.

CSCI/CIHR Joint Program: Young Investigators Forum, Ottawa

Eight MD/PhD students presented at the Canadian Society for Clinical Investigation (CSCI) Young Investigator's Forum, 26-28 September 2002, Ottawa, Ontario. Claire Sheldon was the only student from UBC to do an oral presentation (that comes with being a finalist in the poster competition).

Good job everyone!

- ◆ **Jimmy Lee** (Year 6), Pathology & Laboratory Medicine (Dr. Neil Reiner)
 - Distinct PI3-kinase isoform regulates phagocytosis
- ◆ **Ryan Hung** (Year 5), Experimental Medicine (Dr. Anthony Chow)
 - The G31R mutant of toxic shock syndrome toxin-1: intrinsic and extrinsic pathways for apoptosis
- ◆ **Michael Rauh** (Year 4), Experimental Medicine (Dr. Gerry Krystal)
 - Resting SHIP-deficient murine peritoneal macrophages display an anti-inflammatory phenotype
- ◆ **Claire Sheldon** (Year 4), Physiology (Dr. John Church)
 - Intracellular pH regulation during anoxia in acutely isolated rat hippocampal CA1 neurons
- ◆ **Paul Yong** (Year 4), Experimental Medicine (Dr. Wendy Robinson)
 - Training clinician-scientists: a survey of MD/PhD students in Canadian medical schools
- ◆ **Clara Tan** (Year 3), Biochemistry & Molecular Biology (Dr. Shoukat Dedhar)
 - The role of integrin-linked kinase in angiogenesis
- ◆ **Liam Brunham** (Year 2), Medical Genetics (Dr. Michael Hayden)
 - Identification and validation of genes modulating LDL cholesterol in humans
- ◆ **Bryan Coburn** (Year 2), Microbiology & Immunology (Dr. Brett Finlay)
 - Pathogenomics of *Salmonella* infection

Partial List of Publications by Current MD/PhD Students in the Past Year

Lee CH, Poburko D, Kuo KH, Seow CY, van Breemen C. Ca^{2+} oscillations, gradients and homeostasis in vascular smooth muscle. *Am J Physiol Heart Circ Physiol* 2002;282:H1571-83.

Crowley CM, **Lee CH**, Gin SA, Keep AM, Cook RC, Van Breemen C. The mechanism of excitation-contraction coupling in phenylephrine-stimulated human saphenous vein. *Am J Physiol Heart Circ Physiol* 2002;283:H1271-81.

Lee CH, Rahimian R, Szado T, Sandhu J, Behara T, van Breemen C. Requirement for the opening of IP_3 -sensitive Ca^{2+} channels and SOC in α_1 -adrenoceptor mediated constriction of the rabbit inferior vena cava. *Am J Physiol Heart Circ Physiol* 2002;282:H1768-77.

Lee CH, Poburko D, Kuo KH, Seow CY, van Breemen C. Relationship between the sarcoplasmic reticulum and the plasma membrane. *Novartis Foundation Symposium* 2002; 246:26-41; discussion 41-7:48-51.

Takeshita S, Namba N, Zhao JJ, Jiang Y, Genant HK, Silva MJ, Brodt MD, Helgason CD, Kalesnikoff J, **Rauh MJ**, Humphries RK, Krystal G, Teitelbaum SL, Ross FP. SHIP-deficient mice are severely osteoporotic due to increased numbers of hyper-resorptive osteoclasts. *Nat Med* 2002;8:943-9.

Rauh MJ, Krystal G. Of mice and men: elucidating the role of SH2-containing inositol 5-phosphatase (SHIP) in human disease. *Clin Invest Med* 2002;25:68-70.

Rauh MJ. The forecast is bright for budding clinician-scientists on Canada's west coast. *Clin Invest Med* 2002;25:66-7.

Rauh MJ. An inspiring model for translational research: nuclear factor-kappaB (NF-kappaB), bench to bedside. *Clin Invest Med* 2002;25:65-6.

Sheldon C, Church J. Na^+/H^+ exchange: molecular regulation to therapeutic development. *Clin Invest Med*, 2002;25:229-32.

Partial List of Research Conferences Attended/Presented by Current MD/PhD Students during the Past Year

| Student | Supervisor and Hosting Department | Research Conference Attended/Presented | Title of Presentation |
|---------------------------------|---|--|---|
| Ryan Hung Year 5 | Dr. Anthony Chow Experimental Medicine | Experimental Biology Meeting, New Orleans, Louisiana, USA 20 – 24 April 2002 | Paper presented: Regulation of Apoptosis by Toxic Shock Syndrome Toxin- 1 and the Mutant G31R |
| Michael Rauh Year 4 | Dr. Gerry Krystal Experimental Medicine | Keystone Symposium B8: NF- kappaB: bench to bedside. Keystone, CO, USA 25 February – 3 March 2002 | Paper presented: The SH2-Containing Inositol 5-phosphatase (SHIP) is a Negative Regulator of Macrophage Development and Activation |
| Michael Rauh Year 4 | Dr. Gerry Krystal Experimental Medicine | 31st Annual Meeting of the International Society for Experimental Hematology (ISEH), Montreal, Quebec, Canada 5 – 9 July 2002 | Paper presented: SHIP Deficient Murine Peritoneal Macrophages are Impaired in LPS/IFNg- induced NO Secretion because of a Dramatic Overproduction of L-arginase |
| Michael Rauh Year 4 | Dr. Gerry Krystal Experimental Medicine | 44th Annual Meeting of the American Society for Hematology (ASH), Philadelphia, PA, USA 6 – 10 December 2002 | Paper presented: SHIP-deficiency Leads to Anti-inflammatory Macrophage Programming and Endotoxin Tolerance |
| Claire Sheldon Year 4 | Dr. John Church Physiology | Satellite Symposium of IUPHAR, Advances in Na-H Exchange Research: From Molecular Regulation to Therapeutic Development, London, Ontario, Canada July 2002 | Poster presented: Intracellular pH Regulation during Anoxia in Acutely Isolated Rat Hippocampal CA1 Neurons |
| Paul Yong Year 4 | Dr. Wendy Robinson Experimental Medicine | American Society of Human Genetics, Baltimore, MD, USA 15 – 19 October 2002 | Paper presented: Preeclampsia and Confined Placental Mosaicism |
| Paul Yong Year 4 | Dr. Wendy Robinson Experimental Medicine | International Federation of Placenta Associations, Melbourne, Australia 6 – 10 October 2002 | Paper presented: Preeclampsia and Confined Placental Mosaicism: A Possible Association |
| Liam Brunham Year 2 | Dr. Michael Hayden Medical Genetics | Genomics and Public Policy Symposium, Toronto, Ontario, Canada 7 – 8 June 2002 | Paper presented: From Darwin to Celera: Challenges to the integrity of the Scientific Enterprise |



MD/PhD Barbecue

The MD/PhD students, Dr. Lynn Raymond and Jane Lee, enjoyed a pleasant evening at Dr. Anthony Chow's residence on 19 July 2002. The barbecue was so much fun and Dr. Chow's chicken wings and salmon were yummy! After the food, we exercised ourselves in the field and took some wonderful pictures.

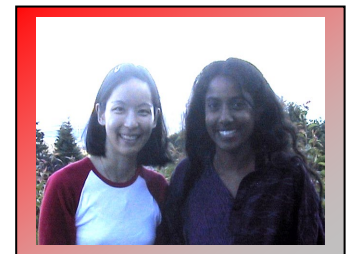
Thanks Dr. Chow!

See our group picture below:

Top row from left: Michael Rauh (Year 4), Jimmy Lee (Year 6), Bryan Coburn (Year 2), Liam Brunham (Year 2), Claire Sheldon (Year 4), Ryan Hung (Year 5), Cheng-han Lee (Year 6). Bottom row from left: Paul Yong (Year 4), Dr. Anthony Chow (Program Director), Dr. Lynn Raymond (Program Co-Director), Jane Lee (Program Co-ordinator). Missing: Amy Weber (Year 1)



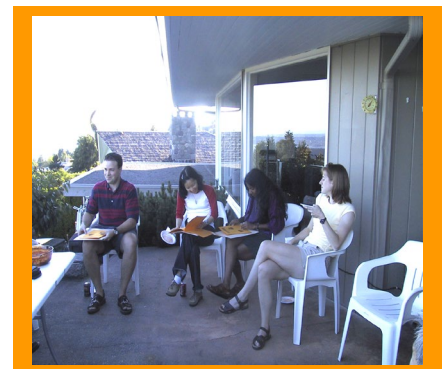
Clara Tan (left) and Suvendrini Lena(right) (both Year 3): ↓





← From left:
Paul, Michael, Cheng-han
- playing basketball
in the field.

From left: →
Michael, Clara, Suvendrini
and Claire - enjoying
sunset on the deck.



Dr. Anthony Chow is on Sabbatical

Dr. Anthony Chow is currently on sabbatical at the University of California, San Diego (October 2002 – September 2003). Any issues related to the MD/PhD Program should be addressed to Dr. Lynn Raymond, Co-Director of the UBC MD/PhD Program, email at lynnr@interchange.ubc.ca.

Congratulations!



Ryan Hung

won a \$800 US Travel Award from the American Federal for Medical Research for presenting at the Experimental Biology Meeting 20-24 April 2002, New Orleans.



Ryan Hung



Liam Brunham

won a GREAT Award at the Science Council of British Columbia (September 2002 - August 2003). Amount value \$20,000.



Liam Brunham



Upcoming Events

*MD/PhD Program Advisory Committee

Dr. Lynn Raymond, Co-Director of the MD/PhD Program, is in the process of revising the MD/PhD Program Advisory Committee. It is expected that there will be 10 new members joining the Committee in 2003. We would like to take this opportunity to thank the following members who have served on the Committee in the last three years. Dr. Jan Friedman (Medical Genetics), Dr. Ismail Laher (Pharmacology & Therapeutics), Dr. Raymond Pederson (Physiology) and Dr. Sam Sheps (Health Care & Epidemiology).

The Committee will be working on applicant selection in the next three months. Shortlisted candidates will be interviewed separately and independently by the MD/PhD Committee following initial screening in conjunction with the Faculty of Medicine Admissions Committee. There will be a committee meeting towards the end of March to finalize the ranking of applicants selected for interview.

*Western Student Medical Research Forum

Eight MD/PhD students will be presenting at the Western Student Medical Research Forum in Carmel, California (28 January 2003 – 1 February 2003). More details to follow in the next newsletter.

Comments and Suggestions!

We welcome comments and suggestions to the UBC MD/PhD Program and to this Newsletter. Please send comments to the MD/PhD Program office, D452 - 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>.



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