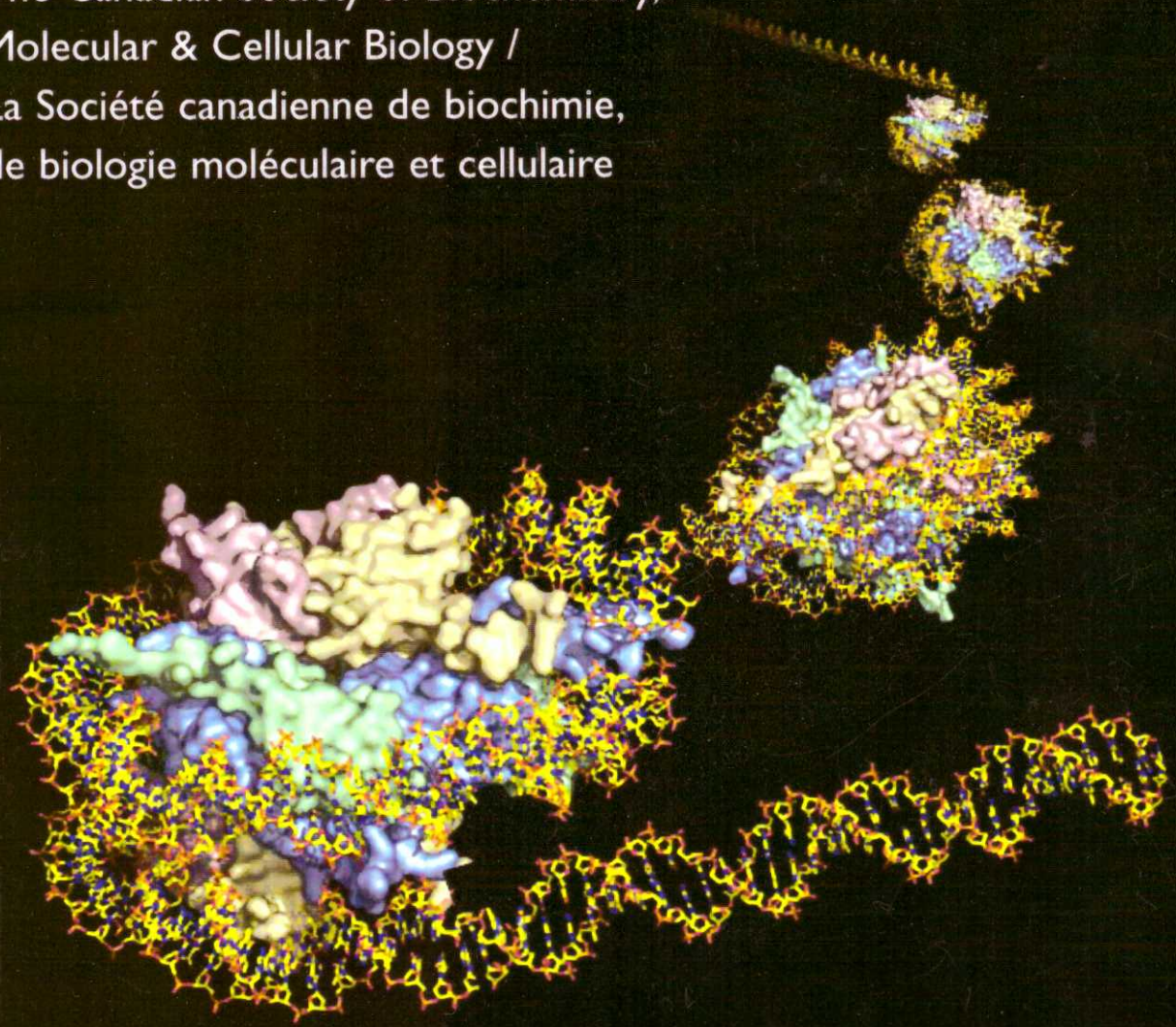
Bulletin

The Canadian Society of Biochemistry,
Molecular & Cellular Biology /
La Société canadienne de biochimie,
de biologie moléculaire et cellulaire



2008

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CSBMCB President's Report

Dr. Laura S. Frost

Introduction

It has been a pleasure being the President of the CSBMCB this past year. By far the most rewarding aspect of this position has been my interactions with other members of the Executive from across the country as well as correspondence with members of the CSBMCB. The goals of my presidency were to improve communications within the society through an improved website and increased communications from the Executive. The demise of the Canadian Federation of Biological Sciences (CFBS) has meant that there is no longer a national organization representing all the life sciences that can effectively lobby governments on behalf of scientists across the country. This means that there is an increased role in advocacy and development of science policy for societies such as the CSBMCB. The past year has been one of economic uncertainty for researchers: on the one hand, there has been an enormous stimulus package from the government through increased funding for graduate student scholarships and for infrastructure within the Canadian Foundation for Innovation (CFI) program. On the other hand, operating budgets, the essential third leg of the funding stool, saw only modest increases that did not cover inflation. CIHR is to be commended for maintaining its commitment to improved success rates in the face of the economic downturn. NSERC has implemented a new mechanism for awarding grants that maintains its commitment to excellence through funding that ensures graduate student training. However, both funding agencies have vowed to make technology transfer a priority. I hope that they do not throw out the baby with the bath water and turn their backs on Canada's long history of excellence in basic research. With that, here are some highlights of the past year.

The Website

It is with great pride that I announce our new website. The Executive decided to spend the money and hire a professional team to re-design the website as well as incorporate features that allow us to register attendees at meetings and also pay annual dues and registration fees on-line. Thanks to Vince Duronio (UBC) for identifying NewGen Technologies Incorporation as the web designers and many thanks to David Williams (Univ. of Toronto) for consulting with NewGen every step of the way to ensure that the website is user friendly and efficient. Also thanks to Rob Reedijk, our website administrator and contact person at CSBMCB, who held the fort during construction of the new website by handling all the society's business manually.

Advocacy

This was a busy year for advocacy as many issues came up that required comment from the CSBMCB Executive. Firstly, there was the demise of CFBS (Canadian Federation of Biological Sciences). CSBMCB had previously decided to cancel its membership in the CFBS, which was yet another reason for CFBS to close shop. The advocacy function that CFBS performed has been assumed by Research Canada that promotes biomedical research in Canada. As yet, no organization that represents all the life sciences has been formed although Gabrielle Adams, the last President of CFBS, is trying to institute a group called Life Sciences Canada. We wish her well and will stay tuned as things progress with this organization. Members of Research Canada (http://www.rc-rc.ca/en/) are academic organizations, hospitals, regional boards, societies, foundations and industries involved in promoting health research and delivery. They have been very active in advocating on behalf of health researchers in Canada and we have forwarded their correspondence to our members as well as posted a link to their website on our home page.

As a member of Research Canada, CSBMCB promoted a letter writing campaign to MPs and responded to the Budget in a letter to Rt. Hon. Stephen Harper dated Feb. 5, 2009. It has also recently written to the President of CIHR, Dr. Alain Beaudet, about the Five-Year Strategic Plan dated May 25, 2009 (see our website at http://www.csbmcb.ca/).

The CSBMCB has also agreed to help sponsor the Canadian Science Policy Conference 2009 in October 28-30, 2009, which is being organized by graduate students across the country. I encourage everyone to attend. I have always felt that it is our students who will have the most impact on politicians and I heartily congratulate these young organizers for taking the bull by the horns and wrangling with the tough issue of science policy in this country.

BCB and the NRC Press

CSBMCB worked to strengthen ties with our official journal BCB (Biochemistry & Cell Biology), published by NRC Press, by inviting its editor, Dr. Jim Davie (Univ. of Manitoba), to sit on the CSBMCB Executive. We appealed to NRC Press to ensure that BCB meets the requirements of many granting agencies to allow free access to articles within 6 months. This has been complicated by the privatization of NRC Press, a process that is still underway. We look forward to working with Dr. Davie to increase Canadian content in this journal. It is important that Canada have its own front-ranking journals rather than regarding journals from Europe or the USA as being the only "worthwhile" ones.

CSBMCB and the IUBMB

The CSBMCB is a member of the International Union of Biochemistry and Molecular Biology through the official Adhering Body, the NRC (National Research Council). As such, we successfully nominated Dr. Michael Walsh (Univ. of Calgary), as the new General Secretary of the IUBMB. Dr. Walsh will be formally voted in in August at the General Assembly of the IUBMB in Shanghai. Dr. Reinhart Reithmeier (Univ. of Toronto) and Dr. Joel Weiner (Univ. of Alberta) will be our official representatives at the meeting. Congratulations Mike!

E.link

CSBMCB has started an E.newsletter called E.link, edited by Dr. John Orlowski (McGill Univ.). The first issue came out in the last week of May 2009. Congratulations to John and his team on putting this together and making it happen.

The CSBMCB New Investigator Award and the Roche Diagnostics Award

The CSBMCB is very proud of these awards that are given to encourage young investigators as well as acknowledge the lifetime achievements of senior Canadian scientists. (See the list at http://www.csbmcb.ca/awards/researchawards.aspx). This year, the society awarded two of its major awards, the New Investigator Award (formerly the Merck Frosst Prize) and the Roche Diagnostics Award. Our other two awards, the Jeanne Manery Fisher Lectureship, given to an outstanding Canadian woman in science, and the Arthur Wynne Gold Medal, a lifetime achievement award that was inaugurated in 2008, will be awarded in 2010.

Perhaps the biggest disappointment this year was the cancellation of support by Merck-Frosst for the travel awards for graduate students and the Merck-Frosst Prize, which has been awarded since 1966. We hope that Merck-Frosst reconsiders funding this award when the economy improves. This year, the award is named the CSBMCB New Investigator Award with Dr. Mick Bhatia, McMaster University, being the first recipient. The Roche Diagnostics Award for a distinguished career in biochemistry, molecular or cell biology was awarded to Dr. Hans Vogel, University of Calgary, who will accept the award at the next annual meeting in Banff.

Membership

The CSBMCB is working towards increasing its membership in the next few months. Thanks to Dr. Linda Penn (OCI) and her team for designing the new ad to be distributed throughout the land. It is very important that our membership increase so that we have the kind of numbers that allow us to lobby governments effectively. Please encourage your

colleagues and students to join the CSBMCB. There is a lot to be done to ensure that the important fields of biochemistry, molecular and cellular biology are supported in Canada. A constant item for discussion has been the nature of our annual meetings that are focused on a particular topic. Many people have said that they would become members if the annual meeting had more than one topic so that their research interests would be showcased on a more regular basis. However, a more inclusive approach might jeopardize the excellence of our meetings with the fracturing of the CFBS, which had an annual meeting composed of many different sessions, being a salutary example. We have gone for depth rather than breadth and will continue with this format for the foreseeable future. We encourage our members to suggest topics for future meetings and get involved in organizing them. Keep in mind that topics and locations are decided 2-3 years in advance. Another topic for discussion is the name of the society. CSBMCB is quite a mouthful but it does have an inclusive quality that encourages members from all the life sciences. Thus, the Executive has decided that, although it is a long name, it is our name for now.

Thanks

I would like to thank Reinhart Reithmeier, Past-President, (Univ. of Toronto) for suggesting that I become involved with the CSBMCB and for nominating me as Vice-President two years ago. It has been wonderful to work with the Executive to promote and improve the CSBMCB by discussing great ideas and grand plans and then helping them become reality. I cannot thank enough our new President (past Vice-President), David Williams (Univ. of Toronto), who not only carried us through the process of redesigning our webpage but who put on a successful meeting in Niagara-on-the-Lake on the subject of Protein Folding: Principles and Diseases in early June, 2009. Our Treasurer, Vince Duronio (UBC), has done such a splendid job that we are unwilling to let him go. Vince has kept a tight rein on our finances and we have weathered the financial crisis rather well because of his stewardship. I would like to thank Albert Clark (Queen's Univ.) for all his help with the nomination process for our awards as well as his help in approaching sponsors for the CSBMCB. Albert is also the society historian and has been a great resource for me on procedures and policies within the CSBMCB constitution. For many years, Frances Sharom (Univ. of Guelph) was the editor of the Bulletin and we all owe her a vote of thanks for making it such a success. John Glover (Univ. of Toronto) has taken over this duty which requires a lot of diligence and powers of persuasion to pull all the articles together. Thanks John. Many thanks to our continuing councillors including John Orlowski, Linda Penn, Frances Sharom and Jim Davie. New councillors include Jean-Pierre Perreault (Univ. de Sherbrooke) and Alba Guarné (McMaster Univ.). Jean-Pierre has agreed to be Vice-President next year and our newest councillor is Josée Lavoie (Univ. Laval). I also want to thank Rob Reedijk once again for all that he does for the society and for his patience in educating this president about the CSBMCB. Rob has an office full to the brim with historical artifacts and mementos from past meetings that are a treasure trove for the society. I enjoyed rummaging in there very much!

I hope I see all of you, and many more new members, at the next meeting in Banff, April 15-18, 2010 on Membrane Proteins in Health and Disease. A satellite meeting on Bicarbonate Transporters and Sodium-proton Exchangers, April 14,15 will also be held. See you then!

Incoming Member of the CSBMCB Executive Board 2008-2009

Alba Guarné, Councillor

I was born in Barcelona (Spain), the oldest daughter of a family with strong artistic influences. Hence, it came as a surprise to most that I wanted to pursue a career in science. However, I have always been driven by curiosity. Curiosity to know how "things" work. My parents fostered my and my brother's interests and so, with the help of a scholarship from the Spanish Government, off I went to study Chemistry at the University of Barcelona. On my senior years, I specialized in Biochemistry and did my undergraduate senior thesis in the laboratory of Joan Antoni Subirana studying crystal structures of short DNA duplexes. That work re-shaped my idea of "things". In fact, I wanted to understand how molecules work inside a cell. In that regard, I found a niche early on in my career as structural biology satisfied my desire to see how "things" look and function.

After graduating in 1993, I continued my graduate studies in protein crystallography at the Institute of Molecular Biology of Barcelona (IBMB, CSIC) under the supervision of two fantastic mentors. Ignasi Fita showed me the rigor of the scientific method and the importance of understanding the basic principles to succeed as a scientist. Josep Tormo, a new investigator at the time, instilled in me the excitement of research in biomedical sciences and shared long-hours, laughs and ups-and-downs of my research project. During my years as graduate student, we did significant contributions towards the understanding of how a viral protease, the leader protease, regulates the viral cycle of Foot-and-Mouth Disease Virus (FMDV). I worked extremely hard, but I specially remember how fun graduate school was. I got to do cool science, visited various synchrotrons in Europe, did exchange visits at the Vienna Biozentrum and the Pasteur Institute to learn new techniques and had the opportunity to present my work at several major International Conferences.

I got my PhD degree *cum laude* in 1999 and I could not picture myself doing anything else in life than research. At that point, Josep mentioned the laboratory of a new and very driven PI at NIH that worked in DNA mismatch repair. I saw that as an opportunity to link both DNA and protein. So my next move took me to the National Institutes of Health in Bethesda (MD, USA) for a post-doc in the laboratory of Wei Yang, where I studied how proteins determined the faith of DNA in replication and repair. Working at NIH was one of the most rewarding experiences of my life. Not only because I had yet another fabulous mentor, but also for the privilege of being exposed to such high-caliber scientific network. I remember fondly the crystallographic meetings with the Davies, Hurley and Dyda laboratories and the recombination meetings with the Gellert, Mizzuchi and Felsenfeld laboratories.

With Wei, we worked hard and play hard. Wei has now gone on to a spectacular career, but back in 2000 she was just starting her own laboratory and lab meetings meant her four post-docs sitting in her office at 5 pm on Fridays discussing ideas while eating cookies. She encouraged collaborative work and I had the opportunity to work closely with a Canadian fellow from London (ON), Murray Junop, for a couple of years. Murray and I

did great science together on proteins of the human non-homologous end-joining and mismatch repair pathways and, as a proud Canadian, he also took upon himself to educate me on the beauty of his country. Murray left Wei's laboratory in 2001, but fortuitously had a great impact on the next step in my career. Early in 2002, he casually mentioned that the Department of Biochemistry at McMaster University was expanding and was particularly interested on strengthening his structural biology group. Indeed, they had an opening for another crystallographer. That was not only good news to me as a crystallographer, but also to my husband who was doing a post-doc at NIH in a renown electron microscopy group at the time. I came to visit McMaster University and found a young and vibrant Department, led by a driven Chair, Gerry Wright. In 2003, my husband and I were both offered faculty positions in the Department of Biochemistry and Biomedical Sciences at McMaster University. Gerry, Murray and other members of the Department have been great mentors and have helped me navigate the system. I continue to study the roles of mismatch repair, replication and segregation proteins on maintaining genome integrity; a work that I could not pursue without the help of excellent graduate students and technicians in my laboratory, as well as, continuous funding from NSERC and CIHR.

Throughout my career, I have been blessed with great scientific opportunities that have defined my path and have molded the way that I do science. My family has been a source of constant support, even when hard choices were made. In the recent years, I have become even more attached to my country of adoption, as I now have a little Canadian of my own that divides the world in artists and scientists, being the former better than the latter because artists can color within the lines and, apparently, scientists cannot quite do the trick. For the record, I will say that I have recently been promoted to "artist".

For the last few years I have been involved with the CSBMCB as a Departmental correspondent for the Bulletin and this year, I joined the CSBMCB council with the intention of reaching out to our younger members, as they are the future of research in Canada.

Minutes of Annual General Meeting

Banff Alberta, March 2008

CHAIR: Reinhart Reithmeier, Board members present: Vincent Duronio, David Williams, Linda Penn, Laura Frost, Albert Clark, Jim Davie, Rob Reedijk, one post-doctoral fellow.

840. Approval of Agenda

The Agenda was approved with the addition of Membership as an item (Motion by Williams, seconded by Penn).

841. Approval of minutes of previous meeting

The minutes of the 50th Annual General Meeting held in Montreal, July 2007 were approved as circulated (Motion by Duronio, seconded by Penn)

842. Business Arising from Minutes

Most items of business arising from the minutes will be discussed under other items later in the agenda. It was noted that our arrangements with CFBS have been severed as of December 31, 2007. The CFBS office will help with the audit for 2007.

843. Treasurer's Report

Dr. Duronio reported that an "up-to-date" balance sheet was not available at this time for several reasons, but in part because of the Society separation from CFBS the website arrangements were not yet complete. Overall the society is in good shape financially. Material is being assembled for the 2007 audit. The statements for the 2007 meeting have been slow coming in from McGill University and so the final financial statement for that meeting cannot be prepared yet. Dr. David Thomas, an organizer for the Montreal meeting will be contacted to facilitate the sending of statements from McGill University.

Because of the technical difficulties with the website the Society is sending out reminder notices to members to renew their memberships and pay their annual dues. It was agreed that extra effort must be made to reconnect with these members and especially PENCE members who had become members of the society.

844. Website update

When ties between CFBS were severed there was an effort to move the server site and possible arrangements with The University of Toronto were explored. This was deemed not to be in the best interests of the Society and continued links with the current server company were being negotiated. Dr. Duronio will request that Mr. Reedijk, the Society administrator be the link with and further develop the arrangements with the company.

845. Advocacy

The Society is active in promoting science and funding to support research. It seizes any potential opportunity to do so. The society is a member of Research Canada which is a very active group; they regularly send out updates. Interest was expressed by the members in having a representative on the Research Canada Board. Dr Reithmeier will check on the nomination process.

846. Meetings

Current (2008) Meeting. Dr. Davie, organizer of the current meeting in Banff reported that the meeting was going well. Approximately 130 people were in attendance. It is too early to predict how the finances for the meeting will turn out.

2009 Meeting. This meeting will be held in Niagara-on-the-Lake at the white Oaks Resort, June 1-5. The theme will be protein folding and disease. The program chairs are Drs. Williams and Chan from the University of Toronto. A program Committee with members form across Canada is being assembled.

2010 Meeting. This meeting will be held in Banff, April 14-18. The theme will be Membranes and Disease. Dr. Joe Casey from the University of Alberta will be chair of the program committee.

2011 Meeting. This meeting will be organized by Dr Jean-Pierre Perreault on RNA and will be held in the Eastern Townships probably during the autumn.

2012 Meeting. There is nothing specific being discussed for 2012 but the current thought is to aim for a meeting on the West Coast.

847. Membership

Dr. Penn noted the new webpage design. All membership fees now come to the Society i.e. there is no sharing with CFBS. Email contacts are being used to work with representatives at the different institutions. Personal contacts are needed to sign people up.

848. Nominations

Dr David Williams from the University of Toronto was nominated for Vice-President (Motion by Reinhardt Reithmeier, seconded by Davie). Dr James Davie from the University of Manitoba was nominated for Councillor (Motion by Williams, seconded by Penn)

849. Adjourned

(Motion by Davie, seconded by Penn)

CSBMCB/SCBBMC Financial Statement

The attached financial statement is a result of the audit for fiscal year 2007, and reflects the strong financial position of our society. Due to a number of reasons, I am unable to provide the financial statements reflecting our position in 2008, but as many of you will realize, we were affected by the downturn in financial markets. However, I am pleased to report that this has not dramatically affected our society's finances. First of all, we did not have to sell any securities during the downturn, as most of our holdings represent solid investments. We also were holding more than one quarter of our funds in cash or bonds. At the time of writing this report, our investments are valued at just over $423,000, which is very close to the value as of Dec. 31, 2007. To put the recovery in perspective, the value of the fund was approx. $340,000 at its low point last winter. Thus, while we 'lost' $100,000 in value, we are close to recovering all of the losses, and fortunately it has not hurt our society's financial strength.

A significant investment was made recently in rebuilding an entirely new website that is now much more functional, and will be instrumental in maintaining membership in the society. In the past two years, our failing website had resulted in many members not renewing, with a resulting loss of revenues from dues. This trend has now been reversed. A final point is that the success of our annual meetings has also continued to be a source of revenue, and these meetings are the result of a fantastic contribution from our members that volunteer their time in putting them together.

For those that notice the large discrepancy in Revenues and Expenses surrounding the annual meetings of 2007 and 2006, the reason is that in 2007, our society handled all of the expenses related to the meeting, as opposed to having the conference centre do this for us.

STATEMENT OF FINANCIAL POSITION

December 31,	2007	2006
ASSETS		
Current assets		
Bank	$ 19,143	$ 9,729
GST receivable	4,337	1,892
Sponsorships & accounts receivable	49,858	7,081
Meeting deposit	19,000	17,000
	92,338	35,702
Meeting deposit 2008	-	14,000
Investments – at market value	436,518	441,001
	$528,856	$490,703
LIABILITIES AND SURPLUS		
Current liabilities		
Accounts payable & accrued liabilities	$13,158	$12,232
Deferred membership fees	3,552	2,710
	16,710	14,942
Deferred membership fees	5,141	4,487
	21,851	19,429
Net assets	507,005	471,274

STATEMENT OF CHANGES IN NET ASSETS

December 31,	2007	2006
Net assets, beginning of year	$ 471,274	$ 424,063
Excess of revenues over expenses for the year	35,731	47,211
Net assets, end of year	$507,005	$471,274

STATEMENT OF REVENUE AND EXPENSES

December 31,	2007	2006
Revenue from operations		
Memberships	$ 14,633	$ 19,963
Corporate contributions	31,461	28,254
Annual meeting & other	115,510	23,995
PENCE transferred funds	70,461	-
	232,065	72,212
Investment revenue (loss)	(4,432)	45,521
Total revenue	227,633	117,733
Expenses		
Annual meeting	149,780	35,118
Audit	2,812	2,506
Bank & credit card fees	2,555	830
Board meetings	8,997	6,461
Bulletin	7,163	6,039
Dues & subscriptions	1,692	795
Funding & other sponsorship	3,000	6,082
Management fees	10,983	8,091
Miscellaneous	160	-
Website	4,760	4,600
	191,902	70,522
Excess of revenues over expenses for the year	$35,731	$47,211

STATEMENT OF CASH FLOWS

December 31,	2007	2006
Cash flows from operating activities		
Cash received from members and events	$ 188,339	$ 88,676
Cash paid to suppliers	(178,976)	(84,697)
Cash flows from operating activities	9,363	3,979
Cash flows from investing activities		
Net flows from investing activities	(9,323)	(16,269)
Net change in cash and cash equivalents	40	(12,290)
Cash and cash equivalents, beginning of year	45,314	57,604
Cash and cash equivalents, end of year	$45,354	$45,314
Cash and equivalents is made up of:		
Bank account	$ 19,143	$ 9,729
Cash held with investment broker	26,211	35,585
	$45,354	$45,314

The 51st Annual Meeting of the CSBMCB, Banff, Alberta

A report on the 51st CSBMCB meeting, Epigenetics and Chromatin Dynamics

This year's Canadian Society of Biochemistry, Molecular, and Cellular Biology's annual meeting on epigenetics and chromatin dynamics opened with a plenary lecture by Shelley Berger (Wistar Institute), entitled The Complex Language of Histone and Factor Post-Translational Modifications in Genome Regulation. The lecture effectively set the scene for the sessions that followed.

The 2008 Jeanne Manery Fisher Memorial Award Lecture was delivered by Katherine Siminovitch (Mount Sinai Hospital, University of Toronto). Her lecture entitled Roles of the mDia1 Diaphanous-Related Formin in Immune Cell Migration and Transformation was very well received.

Epigenetics and the genome — The relationship betweenhistone dynamics and DNA replication was presented by AnjaGroth (Biotech Research and Innovation Centre, University ofCopenhagen). The role of histone H3 lysine and 56 acetylation was discussed by Alain Verreault (University of Montreal). Jacques Côté (Université Laval) described the roles of histone acetyltransferases complexes in genome stability and maintenance. Karolin Luger (Colorado State University) discussed nucleosomes and their chaperones with special reference to NAP-1. Human X chromosome inactivation was described by Carolyn J. Brown (University of British Columbia), with reference to the establishment of facultative heterochromatin by the XIST RNA. Hugh Brock (University of British Columbia) finished the session by addressing the question: Do long noncoding RNAs of the bithorax complex repress by transcriptional interference?

Nuclear architecture and function — The organization and assembly of transcriptional regulatory machinery in nuclear microenvironments was described by Gary Stein (University of Massachusetts), while Roel van Driel (University of Amsterdam) discussed the principles of large-scale chromatin folding of the human genome inside the interphase nucleus. David P. Bazett-Jones (The Hospital for Sick Children, Toronto) introduced the functional interactions between chromatin and PML nuclear bodies. Chromosome territories and nuclear organization — structural, functional, and evolutionary aspects — were presented by Thomas Cremer (Ludwig-Maximilians-Universität München).

Chromatin remodeling and gene regulation — Novel mechanisms of targeting chromatin-modifying complexes were discussed by LeAnn Howe (University of British Columbia) while Jerry L. Workman (Stowers Institute for Medical Research) described protein complexes that modify chromatin for transcription. The metabolic regulation of global histone acetylation in yeast was discussed by Mike Schultz (University of Alberta). Chromatin remodeling machines were presented by Craig Peterson (University of Massachusetts Medical School). Luc Gaudreau (Université de Sherbrooke) described the regulation of gene expression by histone H2A.Z, while Rod Bremner (University of Toronto) described lessons on remote control from the interferon transcriptional cascade.

Chromatin networks, epigenetics, and oncogenesis — The role of RNAi in heterochromatin assembly and function was described by Danesh Moazed (Harvard Medical School). Peter Cheung (Ontario Cancer Institute) discussed the epigenetic functions of mono-ubiquitylated H2A.Z. Ali Shilatifard Published by NRC Research Press (Stowers Institute for Medical Research), in a lively presenta-

tion, described how to translate histone crosstalk. In his talk entitled *Chromatin modifications, associated proteins, and disease,* Karl Riabowol (University of Calgary) described how ING tumour suppressor proteins target and regulate chromatin modifying complexes, while Yamini Dalal (Fred Hutch Cancer Research Center, Seattle) discussed the evolution, structure, and dynamics of centromeric nucleosomes. The certain and progressive methylation of H4 at lysine 20 was presented by Craig Mizzen (University of Illinois), while Jinrong Min (University of Toronto) described the division of labor among human MBT repeat proteins. The role of histone demethylation on stem cell properties was discussed by Christopher Wynder (McMaster University). Michael Bustin (National Cancer Institute, Maryland) discussed the epigenetic function of chromatin architectural proteins.

Summary — The four-day conference covered most aspects of chromatin biology and was enjoyed by all the attendees. The poster sessions were exceptional and provided ample opportunities for discussion and information exchange.

Acknowledgements — The organizers thank the following organizations and companies for their support of the meeting: Canadian Society of Biochemistry, Molecular, and Cellular Biology, National Cancer Institute of Canada (This event is supported by the Terry Fox Foundation), Canadian Institutes of Health Research, Alberta Heritage Foundation for Medical Research, National Research Council of Canada Research Press, Beckman Coulter, Carl Zeiss Canada Ltd., Cedarlane, ESBE Scientific, Fisher Scientific, IBM Canada, Illumina, Integrated DNA Technologies, Genome Prairie, Merck Frosst, Molecular Devices, Perkin Elmer and Roche Diagnostics.

PETER N. LEWIS
Department of Biochemistry, University of Toronto

Rapport sur la 51e réunion de la SCBBMC sur l'épigénétique et la dynamique de la chromatine

Cette année, la rencontre annuelle de la Société canadienne de biochimie et de biologie moléculaire et cellulaire sur l'épigénétique et la dynamique de la chromatine a débuté avec une conférence plénière animée par Shelley Berger (Wistar Institute) intitulée « The Complex Language of Histone and Factor Post-Translational Modifications in Genome Regulation » (Le langage complexe de l'histone et les modifications factorielles post-traductionnelles dans la régulation génomique). L'exposé a bien préparé le terrain pour les séances suivantes.

L'exposé de Katherine Siminovitch (Mount Sinai Hospital, Université de Toronto), présenté dans le cadre de la remise du prix Jeanne Manery Fisher de 2008 et intitulé « Roles of the mDia1 Diaphanous-Related Formin in Immune Cell Migration and Transformation » (Rôles de la mDia1 [diaphanous-related formin] dans la migration et la transformation des cellules immunitaires), a été très bien reçu.

L'épigénétique et le génome — La relation entre la dynamique de l'histone et la réplication de l'ADN a été présentée par Anja Groth (centre d'innovation et de recherche en biotechnologie, Université de Copenhague). Le rôle de l'acétylation de la lysine-56 de l'histone H3 a été abordé par Alain Verreault (Université de Montréal). Jacques Côté (Université Laval) a décrit les fonctions des complexes histone-acétyltransférases dans la stabilité et la maintenance du génome. Karolin Luger (Université d'État du Colorado) a décrit les nucléosomes et leurs protéines chaperonnes en mettant l'accent sur l'anticorps NAP-1. L'inactivation du chromosome X humain a été décrite par Carolyn J. Brown (Université de la Colombie-Britannique), en faisant référence à l'établissement de l'hétérochromatine facultative par l'ARN-XIST. Hugh Brock (Université de la Colombie-Britannique) a clôturé la séance avec la question suivante: les longs ARN non codants du complexe Bithorax exercent-ils une répression transcriptionnelle par interférence?

Architecture et fonction nucléaire — L'organisation et l'assemblage des complexes de régulation transcriptionnelle dans les microenvironnements nucléaires ont été décrits par Gary Stein (Université du Massachusetts), tandis que Roel van Driel (Université d'Amsterdam) a décrit les principes du repliement à grande échelle des chromatines du génome humain dans le noyau en interphase. David P. Bazett-Jones (Hospital for Sick Children, Toronto) a présenté les interactions fonctionnelles entre la chromatine et les corps nucléaires PML. Les territoires chromosomiques et l'organisation nucléaire – aspects structurel, fonctionnel et évolutionnaire – ont été présentés par Thomas Cremer (Université Ludwig- Maximilians, Munich).

Remodelage de la chromatine et régulation génétique — De nouveaux mécanismes de ciblage de complexes de modification de la chromatine ont été décrits par LeAnn Howe (Université de la Colombie-Britannique), tandis que Jerry L. Workman (Stowers Institute for Medical Research) a décrit les complexes protéiques qui modifient la chromatine pour la transcription. La régulation métabolique de l'acétylation globale des histones dans les levures a été décrite par Mike Schultz (Université de l'Alberta). Des complexes de remodev Department of Biochemistry, University of Toronto lage de la chromatine ont été présentés par Craig Peterson (École de médecine de l'Université du Massachusetts). Luc Gaudreau (Université de Sherbrooke) a décrit la régulation de l'expression génétique par l'histone H2A.Z, tandis que Rod Bremner (Université de Toronto) a décrit des cours sur un mécanisme de contrôle à distance à partir de la cascade de signalisation liée à la transcription de l'interféron.

Réseaux de chromatines, épigénétique et oncogenèse — Le rôle de l'ARNi dans l'assemblage et la fonction de l'hétérochromatine a été décrit par Danesh Moazed (Harvard Medical School). Peter Cheung (Ontario Cancer Institute) a décrit les fonctions épigénétiques de l'H2A.Z mono-ubiquitylée. Ali Shilatifard (Stowers Institute for Medical Research) a, dans un exposé très animé, décrit comment interpréter le mécanisme d'interaction croisée (crosstalk) lié à l'histone.

Modifications de la chromatine, protéines associées et maladie — Karl Riabowol (Université de Calgary) a décrit comment des protéines de la famille des suppresseurs de tumeurs ING (« inhibitor of growth ») ciblent et régulent les complexes modificateurs de chromatine, alors que Yamini Dalal (Fred Hutch Cancer Research Center, Seattle) a présenté l'évolution, la structure et la dynamique des nucléosomes centromériques. La méthylation assurée et progressive de la lysine- 20 de l'histone H4 a été présentée par Craig Mizzen (Université de l'Illinois), alors que Jinrong Min (Université de Toronto) a décrit la division du travail entre les protéines de répétition (« repeat proteins ») MBT. Le rôle de la déméthylation de l'histone sur les propriétés des cellules souches a été décrit par Christopher Wynder (Université McMaster). Michael Bustin (National Cancer Institute, Maryland) a décrit la fonction épigénétique des protéines architecturales de la chromatine.

Sommaire — Durant le colloque de quatre jours, qui a été apprécié de tous les participants, la plupart des aspects biologiques de la chromatine ont été abordés. Les séances de présentation d'affiches étaient exceptionnelles et ont fourni de nombreuses occasions pour discuter et échanger de l'information.

Remerciements — Les organisateurs aimeraient remercier les organismes et entreprises suivants de leur soutien dans le cadre de la réunion: la Société canadienne de biochimie et de biologie moléculaire et cellulaire, l'Institut national du cancer du Canada (ce colloque est commandité par la Fondation Terry Fox), les Instituts de recherche en santé du Canada, l'Alberta Heritage Foundation for Medical Research, les Presses scientifiques du Conseil national de recherches du Canada, Beckman Coulter, Carl Zeiss Canada ltée, Cedarlane, Les Produits Scientifiques ESBE, Fisher Scientific, IBM Canada, Illumina, Integrated DNA Technologies, Genome Prairie, Merck Frosst, Molecular Devices, Perkin Elmer et Roche Diagnostics.

PETER N. LEWIS
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Award Winners: 51st Annual General Meeting, Banff, Alberta

Arthur Wynne Gold Medal Award

Dr. Alan Bernstein
Executive Director of the Global HIV Vaccine Enterprise

Jeanne Manery Fisher Memorial Award

Dr. Katherine Siminovitch, MD
Samuel Lunenfeld Research Institute

Merck Frosst Award

Dr. Frank Sicheri
Samuel Lunenfeld Research Institute

TRAVEL AWARDS

Merck Frosst

AWARDEE	SUPERVISOR	UNIVERSITY
Kirk Hooper	Ronald Pearlman	York University
Dax Torti	Rod Bremner	University of Toronto
Leslie Mitchell	Kristin Baetz	University of Ottawa
Nancy Thorogood	Carolyn Brown	University of British Columbia
Rachel Elves	Louis Lefebvre	University of British Columbia
Alice Wang	Michael Kobor	University of British Columbia
Anita Thambirajah	Juan Ausio	University of Victoria
Kevin Dong	Matthew Lorincz	University of British Columbia
Amy Svotelis	Luc Gaudreau	Université de Sherbrooke
Jean Philippe Lambert	Daniel Figeys	Ottawa Inst. of Systems Biology
Andrew Rust	Linda Penn	University of Toronto, Ontario Cancer Institute

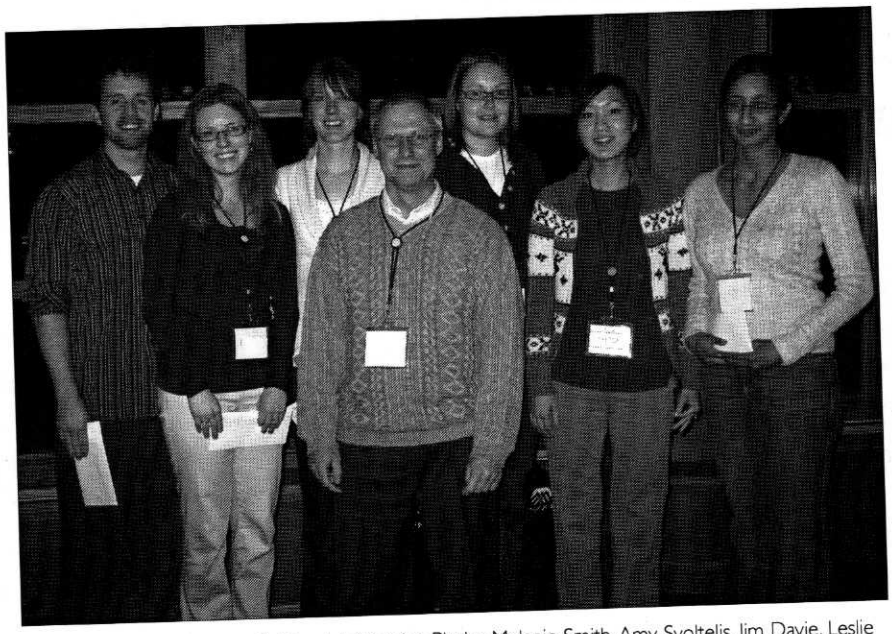
TRAVEL AWARDS

AWARDEE	SUPERVISOR	UNIVERSITY
Integrated DNA Technologies		
Jordon Pinder	Melanie Dobson	Dalhousie University

POSTER AWARDS

AWARDEE	SUPERVISOR	UNIVERSITY
Jake Duerkson Poster Award		
Anita Thambirajah	Juan Ausio	University of Victoria
Roche Diagnostics Poster Award		
Stephen Hoke	C.J. Brandl	University of Western Ontario
Rosemary Oh	Louis Lefebvre	University of British Columbia
Genome Prairie Poster Award		
Leslie Mitchell	Kristin Baetz	University of Ottawa
Genome Prairie Poster Award		
Amy Svotelis	Luc Gaudreau	Université de Sherbrooke
Carl Zeiss Poster Award		
Melanie Smith	Dallan Young	University of Calgary
Carl Zeiss Poster Award		
Jordon Pinder	Melanie Dobson	Dalhousie University

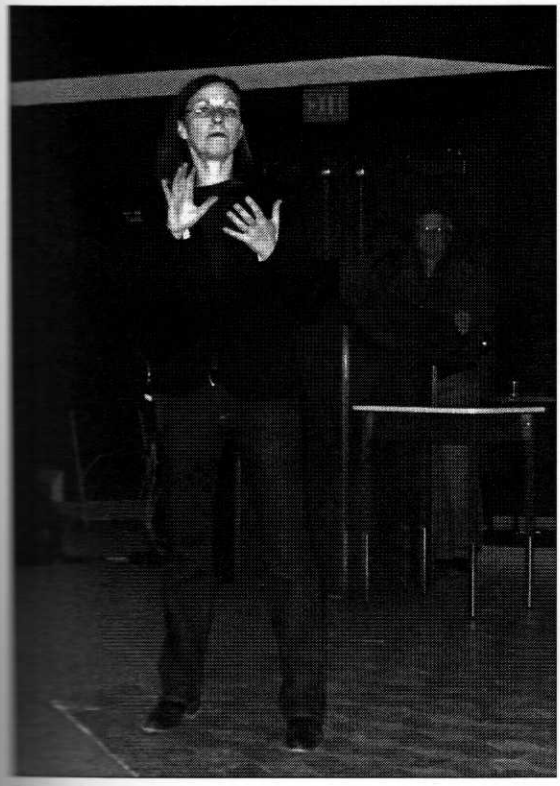
Trainee Award Winners at the 51st Annual General Meeting, Banff, Alberta



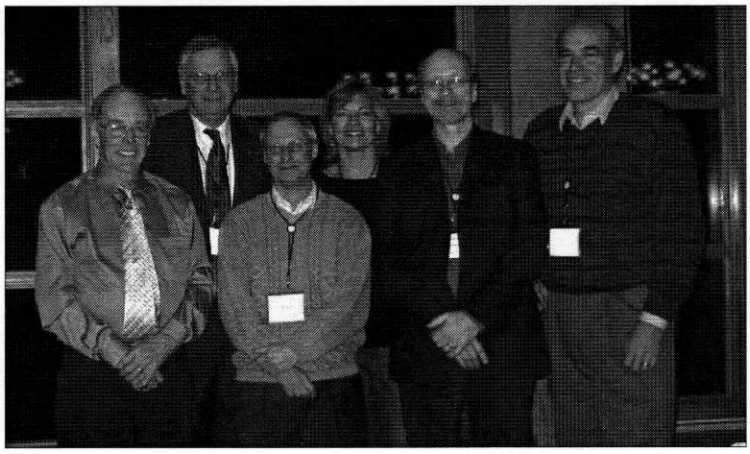
Poster Award Winners. (left to right) Jordan Pinder, Melanie Smith, Amy Svoltelis, Jim Davie, Leslie Mitchell, Rosemary Oh, Anita Thambirajah

Travel Award Winners. Back row: (left to right) Jean-Phillipe Lambert, Amy Svotelis, Kevin Dong, Rachel Elves, Leslie Mitchell, Dax Torti, Jordan Pinder, Kirk Hooper. Front row (left to right) Andrew Rust, Anita Thambirajah, Alice Wang, Jim Davie, Nancy Thorogood.

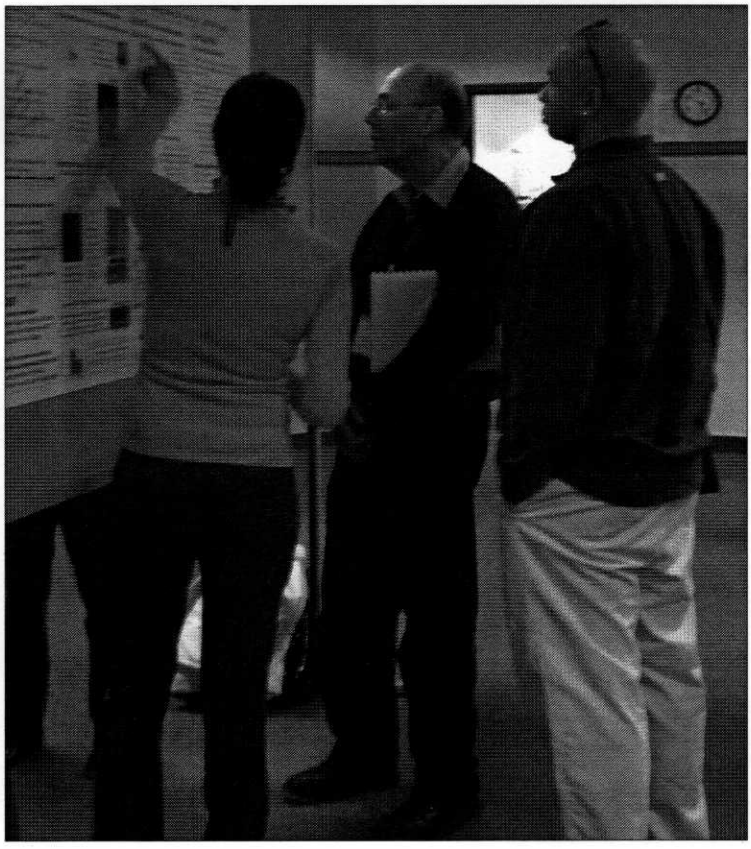
Scenes from the 2008 CSBMCB Meeting



Berger answers questions following her keynote address



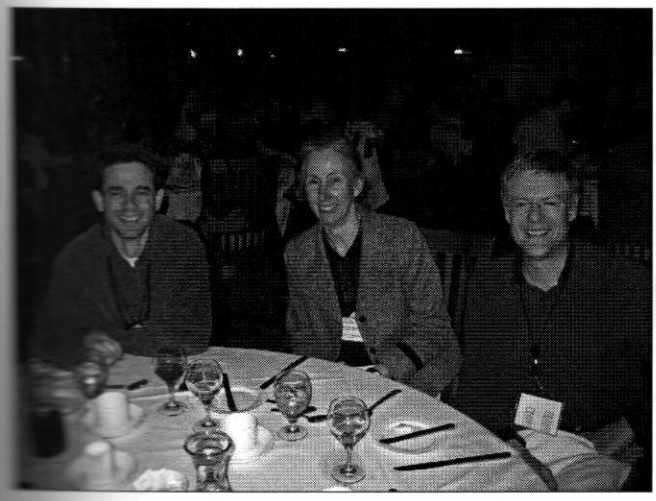
The CSBMCB executive, (left to right) Albert Clark, Reinhart Reithmeier, James Davie, Linda Penn, David Williams, Vince Duronio.

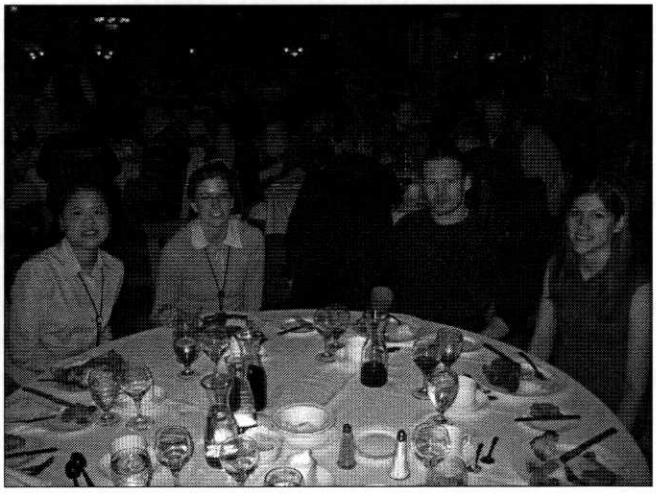


Poster judging

View from the Banff Centre

Attendees enjoying the banquet.





enjoying the banquet.

52nd Annual Meeting of the Canadian Society of Biochemistry, Molecular and Cellular Biology

Protein Folding: Principles and Diseases

June 1 - 5, 2009

WHITE OAKS CONFERENCE RESORT, NIAGARA-ON-THE-LAKE, ONTARIO

Scientific Program

MONDAY JUNE 1

CIHR Training Program in Protein Folding: Trainee Minisymposium

2:00 pm	Welcome - Walid Houry
2:05	Sarah Rauscher (Trainee) Research Institute, Sickkids. Uncovering Order in Disorder: Characterizing the Structural Heterogeneity of an Elastin-like Peptide
2:20	Derek Ng (Trainee) Research Institute, Sickkids. Peptide Approaches to the Mechanism of Myelin Proteolipid Protein (PLP) Oligomerization
2:35	Andrew Wooley (Mentor) - Department of Chemistry, University of Toronto. Photo-Control of Protein Folding.
3:00	Stephen Lin (Trainee) - Dept. of Biochemistry, University of Toronto. Effect of Peptide Secondary Structure Propensity on Binding Kinetics of Sho1 SH3 Domain
3:15	Yoshito Kakihara (Trainee) Dept. of Biochemistry, University of Toronto. The Role of the R2TP Complex and Hsp90 in rRNA and snoRNA Biogenesis
3:40	Janice Robertson (Mentor) - Centre for Research in Neurodegenerative Diseases, University of Toronto. Misfolded SOD1 in Amyotrophic Lateral Sclerosis
4:05	Angela Rutledge (Trainee) - Research Institute, Sickkids. Mechanisms Targeting Apolipoprotein B100 to Proteasomal Degradation: Evidence that Degradation is Initiated by BiP Binding at the N-Terminus and the Formation of a p97 Complex at the C-Terminus
4:20	Greg Clark (Trainee) Ontario Cancer Institute. Loss of the Chaperonin GroEL in the Mycoplasma
4:35	Cliff Lingwood (Mentor) Molecular Structure & Function, Research Institute, SickKids. Hsp70-Glycolipid Interactions Can Regulate Chaperone Function

CSBMCB Young Scientist Award Lecture

9:00 pm	Mick Bhatia (McMaster) Cellular and molecular characterization of human pluripotent stem cells

TUESDAY JUNE 2

Session 1: Protein Folding in the Cell

CHAIR: GERGELY LUKACS (MCGILL)

8:15 am	Susan Lindquist (Whitehead Institute) Happy Birthday Darwin! Protein folding propels evolution
8:50	Chris Kaiser (MIT) The Meaning and Mechanisms of Redox Homeostasis in the ER
9:25	Alan Davidson (U Toronto) The important role of unstructured protein regions in bacteriophage assembly
10:30	Jason Young (McGill) Functional diversity of Hsc70 co-chaperones
10:50	Bill Balch (Scripps) Managing folding and traffic in human misfolding disease
11:25	David Thomas (McGill) Correcting the trafficking defect of F508 CFTR
4:00 pm	Poster Session I

Session 2: Theoretical & Computational Approaches to Protein Folding

CHAIR: RÉGIS POMÈS (SICKKIDS, TORONTO)

7:30 pm	Régis Pomès (SickKids, Toronto) Molecular mechanism of beta-sheet formation at water-nonpolar interfaces
8:05	Ken A. Dill (UCSF) Modeling protein stabilities and solubilities
9:00	Vijay S. Pande (Stanford) Simulating protein folding in vitro and in vivo on experimentally relevant timescales
9:35	Hue Sun Chan (U Toronto) Cooperativity in Protein Folding: Theory and Experiment

WEDNESDAY JUNE 3

Session 3: Mechanisms of Protein Folding and Misfolding

CHAIR: CHARLES DEBER (SICKKIDS, TORONTO)

8:15 am	Chris Dobson (Cambridge) Protein Misfolding and Disease: From the Test Tube to the Organism
8:50	Charles Deber (SickKids, Toronto) Peptide approaches to membrane protein folding
9:25	Susan Marqusee (UC Berkeley) Manipulating the folding landscape using the optical tweezers
10:30	Art Horwich (Yale) Chaperone action in vitro and in an ALS model
11:05	Linda Foit (U Michigan) Optimizing protein stability in vivo offers new insights into the conflicting forces in protein evolution
11:25	Lewis Kay (U Toronto) Seeing the invisible by solution NMR spectroscopy
4:00 pm	Poster Session II

Session 4: Cellular Responses to Protein Misfolding

CHAIR: ALLEN VOLCHUK (UHN, TORONTO)

7:30	Walid Houry (U Toronto) The role of nucleotides and amino acid decarboxylases in the bacterial acid stress response
8:05	Ron Kopito (Stanford) Prion-like properties of polyglutamine amyloids
9:00	Randy Kaufman (U Michigan) Interactions between protein misfolding in the ER and oxidative stress
9:35	David Ron (Skirball Inst., NYU) Prospects for tuning the Unfolded Protein Response

THURSDAY JUNE 4

Session 5: Protein Dynamics and Disorder

CHAIR: SCOTT PROSSER (U TORONTO)

8:15 am	Peter Wright (Scripps) Promiscuous proteins: folding and interactions of intrinsically disordered proteins
8:50	Julie Forman-Kay (SickKids, Toronto) Disordered Protein Interactions within Highly Dynamic Regulatory Protein Complexes
9:25	Lawrence Macintosh (UBC) Rheostatic control of gene expression: conformational flexibility and phosphorylation-dependent regulation of Ets transcription factor
10:30	Peter Tompa (Budapest) Unusual modes of molecular recognition by disordered proteins
11:05	George Harauz (U Guelph) Induced Secondary Structure and Polymorphism in Myelin Basic Protein, an Intrinsically Disordered Organizational Linker of the CNS
11:25	Mitsu Ikura (UHN, Toronto) STIM1-mediated store-operated calcium entry uses a protein unfolding/oligomerization-coupled mechanism?

1:00- 4:00 pm	Featured Workshop: Prion Protein Misfolding - Canadian Contributions to Protein Structure and Dynamics Organized by PrioNet Canada and the Alberta Prion Research Institute Speakers include: Avi Chakrabartty, University of Toronto; Will Guest, University of British Columbia; Michael James, University of Alberta; Nahid Jetha, University of British Columbia; Olivier Julien, University of Alberta; Nat Kav, University of Alberta; Braden Sweeting, University of Toronto; David Wishart, University of Alberta
4:00 - 5:00 pm	CSBMCB Annual General Meeting
6:00 - 7:00 pm	Mixer
7:00 - 9:30 pm	Banquet and Awards Presentation

FRIDAY JUNE 5

Session 6: Protein Misfolding in Aging and Disease

CHAIR: NEIL CASHMAN (UBC)

8:15 am	Peter St. George-Hyslop (U of Toronto) Molecular insights into protein misfolding in Alzheimer's Disease and Frontotemporal Dementia
8:50	Cynthia Lemere (Brigham and Women's) Immunotherapy for Alzheimer's and Other Neurodegenerative Diseases
9:25	Jeff Kelly (Scripps) Restoring Proteostasis to Ameliorate Disease
10:30	David Westaway (U of Alberta) Attributes and Overlaps of the PrP and Shadoo proteins
11:05	Jeremy Lee (U Sask) Nanopore analysis of the interaction of metal ions and antibodies with prion proteins
11:25	David Vocadlo (SFU) Modulators of intracellular glycosylation limit microtubule-associated protein tau phosphorylation in vivo

The Toronto Biochemical and Biophysical Society 1930-1974

Marian A. Packham
University Professor Emeritus

Recently, at the back of a storeroom in the Department of Biochemistry at the University of Toronto, a large box was discovered containing all the detailed records of the Toronto Biochemical and Biophysical Society (TB&BS) from its beginning in 1930 to 1961. Unfortunately, only fragmentary reports of its activities between 1961 and 1974 were included. The story of the TB&BS is an almost forgotten chapter of the history of biochemistry in Canada. The Society began at a time when scientific societies of the sort with which we are familiar today were almost non-existent, so it fulfilled a need for a forum in which scientists in Ontario could report their research results and engage in discussions with other investigators.

Relationships with Universities and Societies outside Toronto

During the years when the Toronto Biochemical and Biophysical Society (TB&BS) was active, it frequently arranged joint meetings at which scientists at McGill University, Queens University, the University of Western Ontario, the University of Ottawa, McMaster University, and the Ontario Agricultural College in Guelph described their current research findings. A yearly meeting in the fall at Guelph, attended by at least 50 members from Toronto, became routine in the 1930s, but travel to meetings was interrupted by World War II. Afterwards, a number of joint meetings took place in Toronto, London, Guelph, Kingston, and Hamilton. Meetings with the Toronto Quality Control Society took place at the Ontario Research Foundation in the 1940s.

The Society also exchanged meeting notices with the Montreal Physiological Society, The Biological Sciences Association of Saskatchewan, and the Nova Scotia Institute of Sciences in Halifax. Many of the graduate students who made their first presentation at a meeting of the TB&BS moved on after graduation to faculty positions at universities across Canada. These include H.B. Stewart and I.G. Walker (UWO), R.O. Hurst (Queens), L.B. Smillie (Alberta), C.W. Helleiner (Dalhousie), G.H. Dixon (Calgary), C.K. Harris (UBC), J.M. Neelin (Carleton) and G.C. Butler, M.A. Packham, G.E. Connell, R. Sheinin, and R.R. Baker (Toronto).

The lists of members of the TB&BS over the years would form a large part of a "Who was Who" in Canadian biochemistry.

Organization of the TB&BS

Up until the end of 1930, some members of the Canadian Chemical Association who were interested in biological chemistry met periodically and were referred to as the Toronto Biochemical Group. In a meeting in December of that year, a change in name to The Toronto Biochemical Society was discussed and approved. (In 1937 the name was changed to the Toronto Biochemical and Biophysical Society.)

The original constitution of the Toronto Biochemical Society that was drawn up in 1931 provided for an elected president, secretary, treasurer and an executive committee of 5 ordinary members. Booklets published by the Society in 1933/34 and 1941 list the officers and the other members of the executive. The changes in these positions are detailed in the minutes of the annual meetings that were held each May. Minutes of all the scientific meetings and of the executive meetings were laboriously hand written in two hard cover, 200 page minute books, used until 1961.

In 1931/32 there were six meetings held on Thursday evenings during the academic year; 27 papers (about 20 minutes each) and three demon-

strations were presented, with attendance averaging 60 of the 72 members. These arrangements continued for the more than 400 meetings held by the Society, although few demonstrations appear to have been given after the 1930s. The membership rose to a high of 114 in 1937-38, but attendance at the meetings showed little change. In the beginning, the meetings in Toronto were held at various sites on and off campus, but eventually nearly all were in Room 13 of the old Medical Sciences Building until it was about to be demolished. Regular meetings were moved then to the Ramsay Wright Building of the Department of Zoology in 1966.

Members of the Society included not only members of all the relevant departments at the University of Toronto, but also of the Connaught Laboratories, the Ontario Research Foundation, the Ontario Department of Health, the Dominion Government, the Hospital for Sick Children, Toronto Western Hospital, Canada Packers Ltd., the Ontario Agricultural College at Guelph, and the University of Western Ontario. From the beginning, graduate students were included in the membership, and after 1947, the fourth year Physiology and Biochemistry students in Toronto were invited to join as junior members (fee of $1/yr instead of $2/yr).

Early officers and members of the executive committee whose energy and enthusiastic support were responsible for the strong beginning of the TB&BS include Professors V.E. Henderson (Pharmacology), E.J. King (Medical Research), P.J. Moloney (Connaught Laboratories), C.H. Best (Physiology), L. Irving (Physiology), D.A. Scott (Connaught Laboratories), A.M. Wynne (Biochemistry/Zymology), and H. Wasteneys (Biochemistry).

Relationship with the Canadian Chemical Association

The TB&BS began as the "Biochemical Group" of the Toronto Branch of the Canadian Chemical Association. Close ties with the Toronto Chemical Association continued until 1942. Of the annual fee of $2 set in 1931, $1 went to the Toronto Chemical Association. In 1938, the TB&BS agreed instead to pay a yearly fee of $25 to the Toronto Chemical Society, but continued to collect $2/year from its members until 1974. The journal of the Canadian Chemical Association, "Canadian Chemistry and Metallurgy" (that changed its name in 1938 to "Canadian Chemistry and Process Industries") published 200-word abstracts of papers presented at the meetings of the TB&BS up until January of 1945 (Volume 29), and supplied 100 reprints free of charge in the early days.

In addition, a joint meeting of the TB&BS and the Toronto Chemical Association was held each year in the 1930s, usually with a distinguished visiting speaker such as James F. Danielli, Vincent du Vigneaud, and James B. Sumner.

In 1944, the chairman of the TB&BS, David A. Scott, announced that the Society would no longer be a member of the Toronto Chemical Association because the latter would disappear in January, 1945, when the newly formed Chemical Institute of Canada took over three existing chemical organizations.

The Years of World War II (1939-1940)

During WWII, attendance at the meetings of the TB&BS declined and some were postponed or cancelled because (as the minutes in 1942 noted) "many members are engaged on problems relating to the war and feel hesitant about publishing results of their work at this time". Meetings were shifted from Thursday to Wednesday evenings because "many members are regularly tied up by military courses, drills etc." The executive decided in September of 1941 that "wartime conditions make it difficult and perhaps inadvisable to hold a meeting in Guelph." Fourteen members of the Society were listed as on "active service" in 1941 and although the Biochemical Society of London, U.K., invited biochemists from the Dominions to attend their meetings, it is not known whether any members of the TB&BS accepted this invitation.

Some of the papers presented in Toronto, however, do appear to have been related to wartime concerns. Professor R.E. Haist's group reported

their studies on shock in five papers during the war, and there were papers on 'Methods of penicillin assay', 'Nitrogen balance after burns', 'The problem of "immersion foot"' and 'New tests for vision'.

In October of 1945 the minutes of the executive record that "It was hoped that some war research might now be reported. It was pointed out, however, that much of the more interesting material will be secret."

By December of 1946, most of the veterans had returned to Canada and a decision was made to resume the joint, yearly meeting at the Ontario Agricultural College at Guelph.

1945-1961

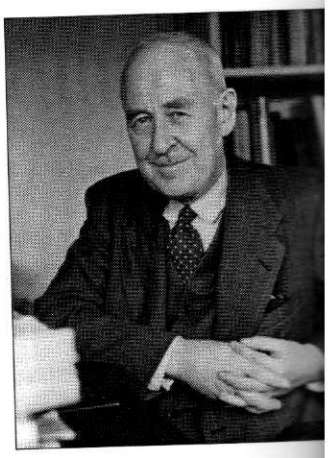
Records of the TB&BS in the 16 years after WWII are quite complete. Joint meetings at the Ontario Agricultural College in Guelph, the University of Western Ontario, and Queens University resumed, usually as the first meeting in the fall of each year. The Society had a meeting in 1952 at the Research Division of Canadian Breweries Ltd., including a tour of the research and control laboratories. In 1954 the meeting was held at the Medical Research Laboratories of the Defence Research Board.

In November of 1947, the treasurer's report stated that, "For some years past, the membership has remained fairly constant at about 45 (on the basis of fees collected)".

This report led to a reduction of the $2 annual fee to $1, and the enlistment of the members of the executive committee to contact those who might be interested in membership. As a result, the membership rose to 106. However, in 1952 the membership fee for senior members returned to $2, although junior member continued to pay $1.

By 1952 the executive committee noted that, "Papers are now submitted more or less voluntarily". (Previously, the secretary of the Society had often found it necessary to contact a number of members to find papers for the programs.) The executive concluded that, "This probably indicates an increasing tempo of fundamental research in the biological sciences". It was agreed "to continue the policy of inviting presentation of papers on investigations still not complete to obtain the benefit of criticism and discussion".

The Society celebrated some of its milestones with speeches from members of the first executive in 1930. To mark the 150th meeting in December of 1952, Arthur Wynne, presented "Comments on the Achievements and Aims of the Society". On the 25th anniversary of the Society in 1955, a dinner for members, spouses and friends was held at Hart House with Laurence Irving as guest speaker. Hardolph Wasteneys's speech on "The Origins of the Society" marked the occasion of the 200th meeting in 1960.


Arthur Wynne

In 1958, The TB&BS held a combined meeting with the Clinical Research Society of Toronto and this became an annual affair. The first joint meeting at McMaster University occurred in 1961.

1961-74

Most of the records of the TB&BS during 1961-74 are concerned with membership lists and treasurer's reports, although a few of the program notices have survived. Paid up members in1969/70 totaled 71 and the receipt books indicate that the membership included scientists from the newly formed York University. There are also copies of some of the correspondence, but no minutes of the meetings of the executive committee.

In November of 1963, a joint meeting in Toronto with scientists from other Ontario universities was devoted to phospholipids. It was held on the day that Gerald M. Edelman of the Rockefeller Center had presented a graduate lecture at the University of Toronto. The joint meeting took place in the afternoon and was followed by a dinner for 50 people at the Art Gallery of Ontario. In subsequent years, other distinguished scientists were invited as guest lecturers, supported by an anonymous donor. These included Albert L. Lehninger of Johns Hopkins University in October of 1965, who spoke on "Dynamics and Mechanism of Ion Transport in Mitochondria"; Eugene P. Kennedy of

Harvard University in 1966, who gave a lecture on "Biochemical Aspects of Membrane Function"; and Erwin Chargaff of Columbia University in 1968 who discussed "Problems in the Separation of DNA Strands".

Women in the TB&BS

Of the 99 members listed in the 1941 booklet, 21 were women, and they were often co-authors of the presentations. However, their presence was scarcely noticed as shown by an exchange of letters in 1933 between Prof. Wasteneys (the president of the Society) and Prof. A. Bruce Macallum of the University of Western Ontario. In their correspondence they agreed that "The Toronto **men** could supply part of the programme". Except for the first three years, women were not elected as members of the executive of the TB&BS until 1961. (Indeed, the meetings of the executive were held in Hart House from which women were barred.) In 1955, Amy Britton had been appointed chairman of a committee to improve arrangements for the serving of refreshments, and in 1961 she was elected as an ordinary member of the executive and then agreed to take over as the secretary of the Society to replace the officer who was ill.

Jeanne Manery Fisher

Jeanne Manery Fisher served as president of the TB&BS in 1962, but the only other woman recorded as an officer of the Society was Rose Sheinin as treasurer in 1969.

Female graduate students (including the author of this article) served refreshments after the meetings, but their names are recorded in the minutes only between 1948 and 1953. It is interesting to note that during this time, Kenneth C. Fisher (husband of Jeanne Manery Fisher) was one of the presidents of the TB&BS; Gordon Butler was another. In 1957, the minutes of the executive committee stated, "The practice of having coffee prepared exclusively by the female members of the society should be discontinued". It is not known how refreshments were managed after this time, but Amy Britton was still buying the supplies in 1964.

The secretarial assistance and guidance of support staff, particularly Miss D. Caldicott (Department of Pharmacology) from 1937-1957, is acknowledged each year in the minutes of the executive committee. These women prepared and sent out the notices and programs of the meetings, dealt with correspondence, and kept the affairs of the Society running smoothly. The honoraria they received did not begin to cover the hours that they must have spent on these tasks.

Presentations at the TB&BS

The TB&BS not only served as a venue for graduate students to make their first presentations to a scientific audience, but also provided discussions and constructive criticisms that were helpful to the principal investigators as they prepared papers for publication. A few of the over 1500 papers presented have been chosen to illustrate the breadth of the subjects and the participation of well-known scientists.

1938 Protamine and the anticoagulant action of heparin by Louis Jacques and C.H. Best
Charles H. Best was very active in the Society, serving as its president and as a member of the executive committee between 1932 and 1935. His name appears on 19 of the papers presented between 1931 and 1958, many of them dealing with his research interests in diabetes, choline and heparin.

1945 Thiamine in milk products by Mary McArthur and Clara C. Benson
In 1907, Clara Benson had been one of the first two women at the University of Toronto appointed as an Associate Professor. She later became Professor of Food Chemistry. This paper was published in the year that she retired.

1949 Studies on the nutrition of animal cells in tissue culture by J.F. Morgan, Helen J. Morton and R.C. Parker.
In **1950**, this group also published a paper with this title, including the addition of "I. Initial studies on

a synthetic medium" in Proc. Soc. Exp. Biol. Med. This landmark paper described the famous medium 199 that that was used by Jonas Salk in the development of the first polio vaccine.

1961 Hidden genetic differences in the human haptoglobins by G.E. Connell, G.H. Dixon and O. Smithies
All three of these scientists went on to outstanding careers. George Connell became president of the University of Western Ontario and then of the University of Toronto; Gordon Dixon's scientific achievements were recognized by the award of the Flavelle Medal of the Royal Society of Canada in 1980; Oliver Smithies shared the Nobel Prize in Medicine in 2007.

1961 Measurement of the proliferative capacity of mouse marrow cells by E.A. McCulloch and J.E. Till
These investigators published their groundbreaking paper on stem cells in 1961. They are credited now with establishing the concept of stem cells, and setting the framework in which stem cells are studied today.

Closure of the TB&BS

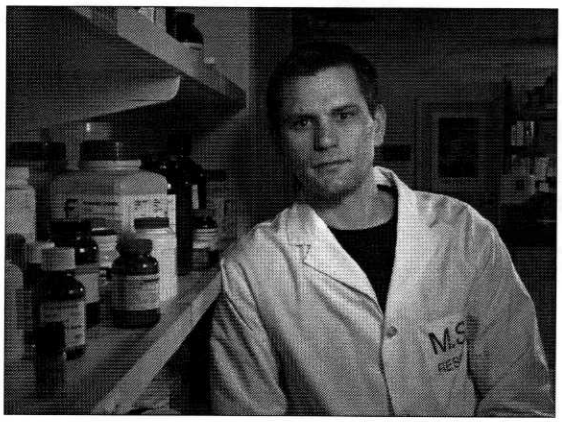
Information about the final 13 years of the TB&BS is incomplete. An annual joint meeting with the Clinical Research Society of Toronto began in 1958 and there is some speculation that the TB&BS may have merged with it. A note in Jeanne Manery Fisher's archived material fixes the last year of the operation of the TB&BS as 1974, and its president at the time, Harry Schachter, has confirmed this. It seems likely that the increase in seminar programs and visiting scientist speakers in all the biological sciences departments took the place of the TB&BS. In addition, the meetings of the Canadian Federation of Biological Societies, including the Canadian Biochemical Society, provided a venue for graduate student presentations.

2008 Merk Frosst Awardee

Frank Sicheri, Samuel Lunenfeld Research Institute and University of Toronto

The structure and regulation of eukaryotic Protein Kinases

Introduction



Frank Sicheri

The transmission of signals from the surface of the cell to the cytoplasm and nucleus is mediated by networks of interacting proteins. The temporal and spatial integrity of the network interactions are regulated by a limited repertoire of enzymatic activities and second messengers. Protein kinases regulate numerous biological processes through their ability to influence signaling networks by transferring phosphate from ATP to an acceptor hydroxyl group in a substrate. This transfer function is carried out by a conserved bilobal structure termed the kinase domain. Phosphorylation by protein kinases can exert a biological effect by (i) inducing structural changes that impact on target protein function or (ii) by promoting a change in protein localization or the formation of macromolecular assemblies. The latter occurs through the action of specialized interaction modules such as the prototypical phospho-tyrosine binding SH2 (Src Homology 2) domain (reviewed in ref. 1). Importantly, aberrant protein kinase function arising from mutation or viral subversion mechanisms gives rise to cellular dysfunctions that underlie human disease including many cancers. As demonstrated by the potency of the first clinically approved protein kinase inhibitor Gleevec in treating chronic myeloid leukemia and gastrointestinal stromal tumors, the ability to counteract aberrant kinase function has validated protein kinases as drugable targets[2,3]. This provides the impetus for further research into how protein kinases function.

The pervasiveness of protein kinases as regulators of cell biology arises from a plasticity of structure that enables diversity in switching and substrate recognition mechanisms (reviewed in refs. 4 & 5).

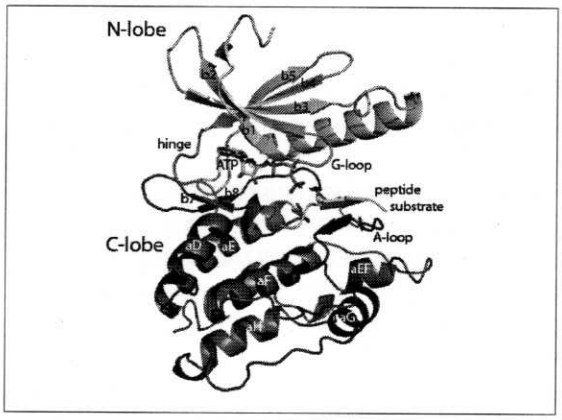


Figure 1. Structure of the kinase domain and mechanism of regulation and substrate recognition. Ribbons representation of the protein kinase domain of phosphorylase kinase in complex with ATP, magnesium and a canonical peptide substrate (PDB id: 2PHK).

While inroads have been made in understanding these mechanisms for a subset of protein kinases, our understanding of how the majority of human protein kinases function is less advanced. Here I provide a brief review of the general architecture of the protein kinase domain and provide specific examples of protein kinases studied in my lab for

which regulatory and substrate recognition mechanisms have been elucidated by high-resolution structural methods.

Structure and Function of the Kinase Domain

The eukaryotic protein kinase domain is an autonomously folding unit of ~250-300 amino acid residues (reviewed in ref. 6). Twelve sequence elements termed subdomains are highly conserved across the protein kinase superfamily with most play essential roles in ATP binding, substrate binding, and catalysis. The first protein kinase structure solved by X-ray crystallographic methods was that of protein kinase A[7,8]. The structure revealed a bilobal architecture with an ATP binding pocket and active site within the inter-lobe cleft that is maintained by all proteins kinases solved to date (see representative kinase domain structure in Figure 1). The amino terminal lobe (or N-lobe) of the kinase domain possesses a β-sheet architecture, while the carboxy-terminal lobe (or C-lobe) is rich in α-helices. The two lobes are linked through a flexible hinge.

ATP Binding Pocket: The majority of conserved subdomains localize to the cleft region of the protein kinase domain and act to bind and orient ATP. Subdomain I, termed the G-loop, serves to coordinate the ATP phosphate groups from a top position. An invariant lysine (subdomain II) and glutamate (subdomain III) residue function to coordinate ATP from a lateral position. The hinge region (subdomain V) hydrogen bonds with the adenine nitrogen atoms and contributes to the hydrophobic pocket surrounding the adenine ring. A large number of conserved residues in the C-lobe also bind and coordinate ATP. For example, an aspartic acid side chain of the highly conserved Asp-Phe-Gly triplet (subdomain VII), coordinates two magnesium ions, which in turn coordinate ATP phosphate groups from a bottom position.

Peptide binding and catalytic residues: In addition to contributing to ATP binding pocket, the C-lobe contributes residues that function in the catalytic transfer mechanism and in peptide substrate binding. In addition, C-lobe residues compose an element termed the activation segment that plays an important role in auto-regulation. A conserved sequence element termed the catalytic loop (subdomain VIB), plays an important role in the phosphotransfer mechanism. Specifically, an invariant Asp residue within this loop functions as the catalytic base by abstracting protons from the acceptor hydroxyl group of the protein substrate. Multiple regions of the C-lobe participate in peptide substrate binding through a combination of electrostatic and hydrophobic interactions. These interactions, which are directed at residues immediately flanking the phospho-acceptor site of the substrate, dictate the preferred peptide sequence phosphorylated by each protein kinase.

The activation segment resides between the conserved triplet motifs Asp-Phe-Gly (subdomain VII)

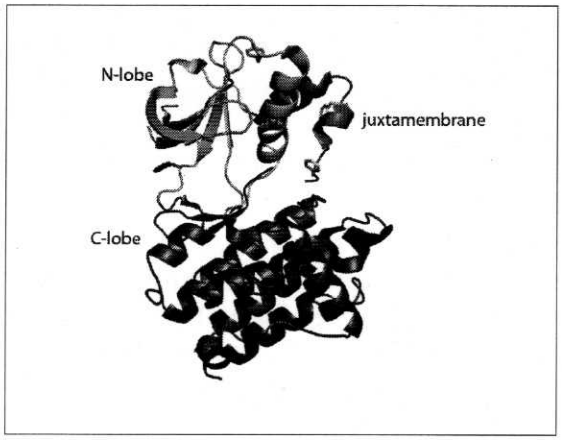
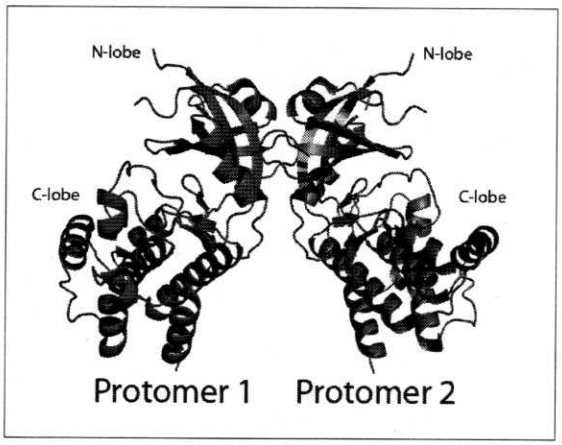


Figure 2. Juxtamembrane region regulation of the Eph receptor tyrosine kinases. In its un-phosphorylated state, the juxtamembrane region sprawls across the N- and C-lobes of the kinase domain to restrain inter-lobe flexibility and to impede the activation segment from attaining a productive conformation

and Ala-Pro-Glu (subdomain VIII). Both the sequence of the A-loop, its precise conformation, and the interactions that maintain it in productive and non-productive conformations are highly variable (reviewed in ref. 9). The productive conformation of the A-loop functions to orient the peptide substrate to accept phosphate. Many protein kinases have one or more phospho-regulatory sites within their A-loops that transition the activation segment between productive and non-productive conformations.

Regulation of catalysis by elements external to the kinase domain



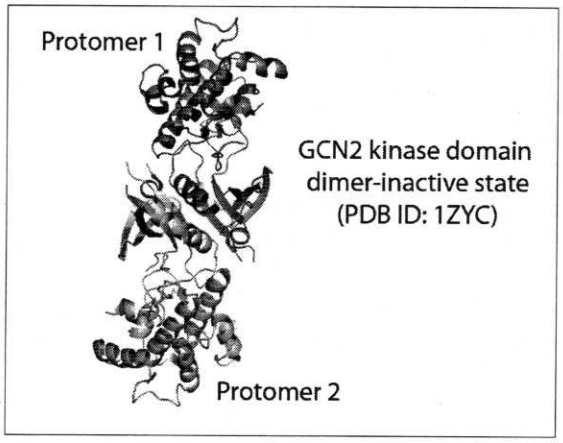


Figure 3. The active state of PKR is defined by a back-to-back mode of dimerization involving the N-lobe of the kinase domain (top panel). The inactive state of Gcn2 is defined by an alternate mode of dimerization characterized by a non-productive positioning of helix aG (bottom panel).

The precise position of active site elements is a point of regulation for many protein kinases. In many instances, regulation is achieved by the action of protein sequences external to the kinase domain. These sequences can be part of the same protein giving rise to cis modes of regulation, or they can be part of other proteins giving rise to trans modes of regulation (reviewed in refs. 4 & 5). Examples illustrating cis and trans modes of regulation follow.

Receptor tyrosine kinase regulation by the juxtamembrane region in cis: The Eph receptor tyrosine kinases (RTKs) are the largest family of RTKs in human with 14 members. Their domain structure consists from the N-terminus of an extracellular ligand-binding domain, a membrane-spanning segment, a juxtamembrane segment, a tyrosine kinase domain, followed by a sterile alpha motif (SAM) domain. Contained in the juxtamembrane region is a conserved sequence (Y_{604}IDPFTY$_{610}$EDP in EphB2) with two conserved phosphoregulatory sites. When not phosphorylated, the juxtamembrane region represses the catalytic function of the adjacent protein kinase domain and once phosphorylated, this repressive function is relieved[10]. The crystal structure of a cytoplasmic fragment of murine EphB2, encompassing the juxtamembrane segment and the protein kinase domain, revealed how autoregulation is achieved[11] (Figure 2). In its dephosphorylated state, the juxtamembrane region binds across the N- and C-terminal lobes of the kinase domain to hamper inter lobe flexibility. In addition this binding mode prevents the A-loop from attaining a productive conformation. Follow-up NMR analyses revealed that auto-phosphorylation of the juxtamembrane segment causes it to dissociate from the kinase domain to yield a catatlytically competent enzyme[12]. Subsequent studies by other groups revealed a similar mode of regulation at play for the Kit and Flt3 RTKs[13, 14]. Strikingly, mutations that disrupt the ability of the juxtamembrane region of these two RTKs to auto-regulate gives rise to constitutive activation and cancer causing abilities[13, 14].

Allosteric regulation of protein kinase function by dimerization in trans: The original paradigm for receptor kinase activation envisioned that ligand binding to the extracellular portion of the receptor would activate protein kinase activity by promoting receptor dimerization and then trans-phosphorylation on regulatory sites within the kinase activation segment. Our work on PKR and more recently on RAF revealed an altogether different means by which dimerization can regulate protein kinase function.

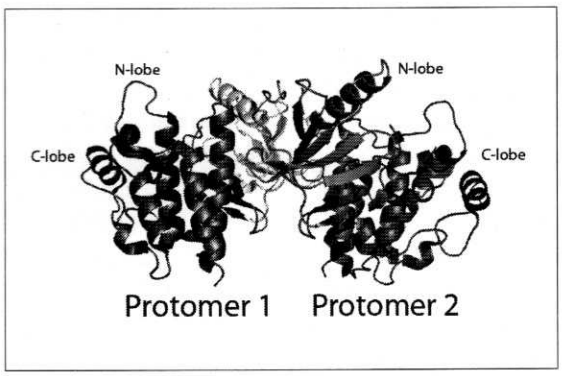


Figure 4. The active state of RAF is defined by a side to side mode of dimerization involving the N-lobe of the kinase domain. The inactive state of RAF has yet to be characterized at an atomic level.

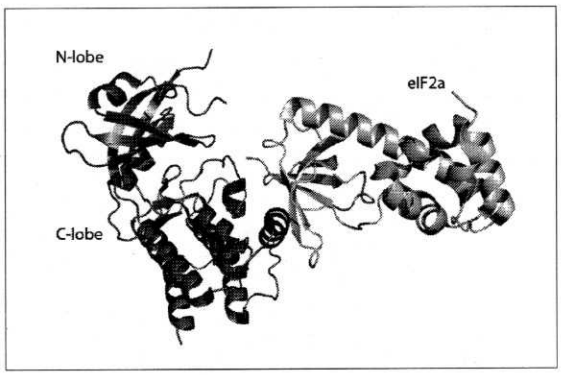


Figure 5. PKR engages eIF2α through a surface on its C-lobe centered on helix aG.

PKR: In response to binding viral double stranded RNA byproducts within the cell, the RNA dependent protein kinase PKR dimerizes, auto-phosphorylates and then phosphorylates the a subunit of the translation initiation factor eIF2, on Ser51. This triggers the general shutdown of protein synthesis to arrest the propagation of viruses (reviewed in ref. 15). To understand how PKR recognizes eIF2α and how dimerization and autophosphorylation regulate PKR function, we determined the X-ray crystal structure of the catalytic domain of PKR in complex with eIF2α[16, 17]. In its active state, the kinase domain of PKR adopts a specific mode of dimerization, which we term the back to back configuration, which allosterically regulates the ability of the kinase domain to transfer phosphate (Figure 3: top panel). The structure of a related eIF2α kinase, GCN2, provides an explanation for how in the absence of the back to back dimer configuration, the kinase domain is rendered incompetent for enzymatic activity[18] (Figure 3: bottom panel). Specifically, structural distortions to helix aC in the N-lobe resulting from the adoption of an alternate (inactive state) dimer configuration by the protein kinase domain disrupts the proper coordination of ATP phosphate groups. Transition to the back to back dimer configuration restores a productive orientation of helix aC and as a result, optimal ATP coordination and catalytic function.

RAF: The ERK (extracellular signal-regulated kinase) pathway is an evolutionarily conserved signal transduction module that controls growth[19]. Activation of RTKs by the binding of growth factors initiates the loading of RAS with GTP, which activates the ERK pathway by modulating RAF kinase activity. Once activated, RAF in turn activates MEK, which in turn activates ERK. Dysregulated signaling through the ERK pathway has been linked to many human cancers[20]. Indeed, B-RAF, is the most often mutated oncogene in the kinase superfamily[21]. In collaboration with Dr. Marc Therrien's lab (U. Montreal) we recently discovered that RAF catalytic function is allosterically regulated in response to the attainment of a specific dimer configuration by its kinase domain, which we term the side-to-side configuration[22] (Figure 4). We also discovered that the RAF-related pseudokinase KSR can also form side-to-side dimers with RAF to activate RAF catalytic function. What remains to be determined is how in the absence of dimerization, RAF is rendered incompetent for catalytic function.

Higher order Substrate Recognition by the eIF2α protein kinases

The ability to recognize and discriminate substrates represents a second means for controlling and diversifying protein kinase function. While we understand the basis by which many kinase domains bind and discriminate a target acceptor site, this represents the tip of the proverbial iceberg of how protein kinases recognize a fully intact substrate. Our work on the eIF2α protein kinase PKR, highlights how determinants far beyond the immediate site of phosphorylation in eIF2α contributes to the substrate targeting mechanism.

The eIF2α protein kinases, which include the RNA dependent protein kinase (PKR), GCN2, the heme-regulated eIF2α kinase (HRI), and the pancreatic eIF2α kinase (PEK) respond to distinct stress stimuli within the cell but share a common ability to phosphorylate eIF2α at an identical site, Ser51, to potently inhibit protein translation (reviewed in ref. 15). The recognition of eIF2α by the eIF2α protein kinases is defined by two sets of determinants both encoded by their kinase domains. PKR can phosphorylate linear peptide sequences (ILLSELS$_{51}$RRIR) corresponding to the acceptor site in eIF2α but it does so very inefficiently and non-specifically[23]. In contrast, in the context of an intact eIF2α protein, PKR phosphorylates Ser51 in a highly efficient and specific manner.

The structure of PKR in complex with eIF2α revealed the basis for this specificity[16,17]. Recognition of intact eIF2α by PKR occurs through the C-terminal lobe of the kinase domain by a conserved surface centered on helix aG (Figure 5). This convex surface engages a concave surface of the globular fold of eIF2α. In addition to imparting specificity to PKR substrate recognition, the unusual binding mode observed for eIF2α also serves to orient the Ser51 phospho-regulatory site towards the catalytic cleft of PKR.

Conclusions

Structures of protein kinases in their active and repressed states and in complex with substrates provide great insight into the diverse mechanisms by which protein kinase turn on and off and recognize their substrates with high fidelity. As so many of the protein kinases in the human genome have yet to been characterized in great detail, there are likely many more mechanism of regulation and substrate recognition that remain to be uncovered in future studies.

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2008 Jeanne Manery Fisher Memorial Awardee

Katherine Siminovitch, Samuel Lunenfeld Research Institute and University of Toronto

Src kinase Hck association with the WASp and mDia1 cytoskeletal regulators promotes chemoattractant-induced Hck membrane targeting and activation in neutrophils

Katherine Siminovitch

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ABSTRACT

The haemopoietic cell kinase (Hck) plays an important, but poorly understood role in coupling chemoattractant stimuli to the actin cytoskeletal rearrangement required for neutrophil polarization and chemotaxis. Here we show that Hck co-immunoprecipitates with the cytoskeletal regulatory Wiskott-Aldrich syndrome protein (WASp) and mammalian diaphanous-related formin 1 (mDia1) in chemoattractant-stimulated neutrophils and that the three proteins inducibly colocalize with one another at the leading edge of chemotaxing cells. Hck interaction with WASp was found to be mediated by Hck SH3 domain binding to the WASp proline-rich region, while Hck interaction with mDia1 was indirect, but required for binding to WASp. In contrast to wild-type cells, both WASp and mDia1-deficient neutrophils showed severe impairment of chemokine-induced Hck membrane translocation and induction of Hck binding to WASp, Hck activation and WASp tyrosine phosphorylation were impaired in mDia1$^{-/-}$ cells. Thus chemotactic stimulation appears to induce an mDia1/Hck/WASp complex required for Hck membrane targeting and for induction of the Hck-mediated WASp tyrosine phosphorylation thought to be required for WASp-driven actin polymerization. These findings reveal Hck functions in neutrophils to be realized at least in part via its interaction with mDia1 and WASp and identify the mDia1/Hck/WASp axis as a cytoskeletal signaling interface linking tyrosine phosphorylation to chemotactic and possibly other actin-based neutrophil responses.

Key words: Wiskott-Aldrich syndrome protein, Diaphanous-related formin, haematopoietic cell kinase, tyrosine phosphorylation, chemotaxis, actin cytoskeleton

INTRODUCTION

Ability to migrate to sites of infection is critical to neutrophil roles in immunity, enabling these cells to provide the first line of defense in the innate immune response to bacterial pathogens (Nathan 2006). Neutrophil movement to such sites is guided by N-formyl-methionyl-leucyl-phenylalanine (fMLP), macrophage inflammatory protein 2 (MIP-2) and other bacteria-derived chemoattrac-

tants which bind to cognate heterotrimeric G-protein-coupled surface receptors on neutrophils so as to evoke actin cytoskeletal rearrangements that promote cell polarization, altered adhesive behaviour and other facets of cell chemotaxis (Kobayashi 2006). Extensive studies of the downstream signaling cascades induced by neutrophil chemoattractant receptor engagement have identified activation of protein tyrosine kinases, the phospholipase C, protein kinase C and PI3 kinase/Akt pathways, and Rho family GTPases as key events in linking these receptors to the cytoskeletal changes driving neutrophil migratory responses (Thelen 2001; Niggli 2003; Fumagalli *et al.* 2007).

Among the Src family tyrosine kinases expressed in neutrophils, the haemopoietic-restricted Hck enzyme has been shown to play particularly important roles in regulating such actin-based processes as chemotaxis and adhesion (Scholz *et al.* 2000; Giagulli *et al.* 2006; Evangelista *et al.* 2007) as well as integrin and FcRγ-mediated phagocytosis (Wang *et al.* 1994; Suzuki *et al.* 2000). In addition to the plasma membrane-localized p59 and lysosome-localized p61 Hck isoforms, Fgr is another prominent Src kinase in neutrophils and the severe defects in mobility, adhesion and filopodia formation detected in Hck/Fgr-deficient neutrophils and macrophages suggest that these kinases act in concert to promote actin-dependent functions in these cells (Lowell *et al.* 1996; Lowell and Berton 1998; Suen *et al.* 1999; Fitzer-Attas *et al.* 2000; Zhang *et al.* 2006; Totani *et al.* 2006; Giagulli *et al.* 2006). However, a particularly important role for Hck in actin dynamics is implied by data identifying Hck as an activator of the Wiskott-Aldrich syndrome protein (WASp), another haemopoietic-restricted molecule implicated in many actin-mediated cell processes (Cory *et al.* 2002; Badour *et al.* 2004). This multimodular cytosolic protein regulates actin dynamics via its C-terminal verprolin/central/acidic (VCA) domain, a segment that binds and activates the actin-nucleating Arp2/3 complex so as to induce actin polymerization (Machesky *et al.* 1998; Pollard *et al.* 2003). WASp effects on Arp2/3 activity are constitutively inhibited by intramolecular conformational constraints, but are induced following cell stimulation by interaction of the WASp GTPase binding domain (GBD) with activated cdc42 (Prehoda *et al.* 2000) and binding of its proline-rich region to SH3 domain-containing adaptors (Rohatgi *et al.* 2001; McGavin *et al.* 2001; Badour *et al.* 2004). Importantly, WASp coupling to Arp2/3 induction and actin polymerization also requires that WASp undergoes tyrosine phosphorylation (Badour *et al.* 2004). In T cells, WASp is specifically tyrosine phosphorylated by the Fyn kinase (Badour *et al.* 2004), while in macrophages, this role has been shown to be subserved by Hck (Cory *et al.* 2002). This observation, together with data implicating Hck in activation of the Vav1 Rho/Rac guanine nucleotide exchange factor and Rac target p21-activated kinases required for fMLP-induced actin polymerization (Fumagulli *et al.* 2007), are consistent with a critical role for Hck in coupling chemotactic stimuli to the actin remodeling required for neutrophil migration.

While Hck can tyrosine phosphorylate and thereby activate WASp in macrophages, the relevance of Hck-WASp interaction to neutrophil function has not been defined. As WASp has been implicated in chemotaxis of neutrophils and several other haemopoietic lineage cells (Badolato *et al.* 1998; Hadded *et al.* 2001; Gallego *et al.* 2005; Zicha *et al.* 1998), modulation of WASp is likely relevant to Hck effects on actin-driven neutrophil chemotactic responses. However, another important actin cytoskeletal regulator expressed in haemopoietic cells, the mammalian diaphanous-related formin 1 (mDia1), has also very recently been shown to play essential roles in chemotaxis of mature haemopoietic cells (Vicente-Manzanares *et al.* 2003; Eisenmann *et al.* 2007; Sakata *et al.* 2007; K.A. Siminovitch and J. Zhang, unpublished data). In contrast to WASp, mDia1 directly nucleates actin via a formin homology 2 (FH2) domain, but its regulation is otherwise similar to that of WASp, the formin constitutively inactivated by structural constraints and its activity induced by interaction with activated Rho GTPase (Watanabe *et al.* 1999; Copeland *et al.* 2004; Higgs *et al.* 2005). While mDia1 tyrosine phosphorylation status has not been studied, Src has been shown to bind mDia1

and regulate its actin modulatory properties (Tominaga *et al.* 2000; Satoh and Tominaga 2001). Conversely, activation of Src family kinases, such as Src, Yes and Fyn, is dependent on actin polymerization, actin rearrangement enabling the peripheral membrane targeting required for induction of kinase activity (Sandilands and Frame 2008; Sandilands *et al.* 2007; Kaplan *et al.* 1994; Fincham *et al.* 2000). These data suggest an important functional relationship between Src family kinases and actin cytoskeletal regulators in driving actin-mediated processes such as chemotaxis. To explore this possibility, we investigated the potential for Hck to associate with and modulate mDia1 and/or WASp in neutrophils. Our data reveal the capacity of Hck to interact with both mDia1 and WASp in chemoattractant-stimulated neutrophils and to colocalize with both cytoskeletal regulators and F-actin at the leading edge of chemotaxing cells. Disruption of this complex in the context of mDia1 or WASp-deficiency abrogates Hck translocation to the leading edge following cell stimulation. While Hck does not bind mDia1 directly, fMLP-mediated induction of Hck activity, binding to WASp, and WASp tyrosine phosphorylation are severely impaired in mDia1-deficient neutrophils. Thus Hck activation downstream of chemoattractant stimulation requires its association with both mDia1 and WASp and its spatial and functional regulation via this trimolecular complex appear key to Hck capacity to modulate neutrophil actin dynamics.

MATERIALS AND METHODS

Mice, cells and reagents: mDia1$^{-/-}$ and WASp$^{-/-}$ mice generated as previously described (Zhang *et al.* 1999; Peng *et al.* 2007) were maintained on the C57BL/6 background and under pathogen-free conditions at the Samuel Lunenfeld Animal Facility. Human leukemia HL-60 cells were maintained in RPMI-1640 supplemented with 10% fetal calf serum, 2mM L-glutamine and penicillin/streptomycin (Gibco BRL). MIP-2, fMLP, enolase and mouse monoclonal anti-FLAG antibody were purchased from Sigma-Aldrich, mouse monoclonal anti-mDia1 antibody was from BD Transduction Labs, mouse monoclonal anti-DsRed antibody from Clontech, rabbit polyclonal anti-WASp and mouse monoclonal anti-phosphotyrosine antibodies from Upstate Biotechnology and mouse monoclonal anti-GFP, GST and His tag antibodies and goat polyclonal anti-Hck and rabbit polyclonal anti-Hck antibodies were from Santa Cruz Biotechnology Inc. Fluorescently-labeled secondary antibodies (including FITC, Cy3 and Cy5) were obtained from Jackson ImmunoResearch Lab Inc. HRP-conjugated goat anti-rabbit, goat anti-mouse and rabbit anti-goat secondary antibodies were from BioRad and FITC and Alexa 635-conjugated phalloidin were from Molecular Probes.

Constructs: Expression constructs were derived by subcloning cDNAs encoding full-length WASp, WASpΔEVH1 (Δaa1–170), WASpΔPRO (Δaa309–430) and WASpΔVCA (Δaa422–502) into the pEGFP-C1 vector (Clontech), and Flag-tagged (C-terminal tag) Hck p59 (provided by T. Miller), HckΔSH3 (Δaa1-113) and HckSH2 (aa121-240) into pcDNA3.1 (Invitrogen), and full-length mDia1 into pDsRed (Clontech). Fusion proteins containing the WASp Ena/Vasp homology 1 (EVH1, aa1-159), VCA (aa422-502) or C-terminal EVH1 and N-terminal proline-rich (N321; aa50-371) domains were constructed in the pGEX4T-2 vector, expressed in *Escherichia coli* and purified as previously described (Badour *et al.* 2004) with glutathione-linked Sepharose 4B beads (Amersham Biosciences). A fusion protein containing 6x His-Hck was derived by subcloning full length Hck into the pQ30 vector (Qiagen). All construct sequences were directly confirmed by DNA sequencing.

Isolation of neutrophils: Neutrophils were obtained from mouse bone marrow by flushing femurs with Hank's buffer supplemented with 10mM HEPES (pH7.2) and 0.1% BSA (HBSS). After removing red blood cells using RBC lysis buffer, cells were resuspended in HBSS containing calcium and magnesium supplemented with 0.1% BSA and the neutrophils purified by percoll density gradient (52%, 65% and 75%) centrifugation at 2600 rpm for 30min. Neutrophil purity was determined to be at least 90% by forward and side scatter and Gr-1 staining.

Immunofluorescence microscopy: Purified neutrophils were adhered to glass coverslips and stimulated with a uniform concentration of MIP-2 (25ng/ml) at 37°C for 3 min. Cells were fixed in cytoskeleton buffer containing 3.7% paraformaldehyde for 10 min, then permeabilized with 0.2% Triton-100X/PBS for 10 min, washed and blocked with 3% BSA/PBS for 20 min. Following incubation with appropriate primary and fluorescently-labeled secondary antibodies, stained samples were mounted in anti-fade mounting medium (Dako Cytomation) and the images collected and analyzed using the Leica SP2 scanning confocal microscope.

Immunoprecipitation and immunoblotting: Cos-7 cells transiently transfected with cDNAs for WASp and/or mDia1 and/or Hck using Lipofectamine 2000 (Invitrogen) and fMLP (1μM)-stimulated HL-60 cells or bone marrow neutrophils were lysed in buffer containing 20mM Tris-HCl, pH 7.5, 1% Triton-X100, 150mM NaCl, 20mM sodium fluoride, 1mM PMSF, 40mM b-glycerophosphate and 1 mM Na_3VO_4 and 10mg/ml each of pepstatin A, leupeptin, chymostatin, and aprotinin (Amersham Biosciences). After 1 hour incubation on ice, lysates were purified by centrifugation at 12,000g for 30 min at 4°C. For immunoprecipitation, lysates were precleared by incubation with Protein A or G beads for 1 hour at 4°C followed by overnight incubation with specific antibody. Immunoprecipitated proteins were collected over Protein A or G beads and eluted by boiling in Laemmli sample buffer. Total lysate or immunoprecipitated proteins were electrophoresed through SDS-polyacrylamide, transferred to nitrocellulose (Schleicher & Schnell) and the blocked membranes sequentially incubated with primary antibody and horseradish peroxidase-conjugated secondary antibody as previously described (Zhang *et al.* 1999). For Far Western analyses, membranes were incubated at 4°C overnight with 4 μg/ml 6xHis-tagged Hck or GST-WASp fusion proteins and then probed sequentially with either anti-His tag, anti-Hck or anti-GST antibodies.

In vitro protein-binding assays: For *in vitro* binding studies, 5μg GST-fusion proteins (WASp EVH1, PRO and VCA) immobilized on glutathione-coupled Sepharose 4B beads or mDia1 or WASp immunoprecipitates prepared from Cos-7 cells were incubated for 1 h at 4°C with 2 μg 6xHis-Hck. After extensive washing, the protein complexes were electrophoresed through 10% SDS-polyacrylamide gel, transferred to nitrocellulose and visualized by immunoblotting analysis with anti-His antibody.

In vitro kinase assay: Hck immunoprecipitates prepared from fMLP-stimulated neutrophils were washed in kinase buffer (20mM HEPES, pH7.6, 0.25mM Na_3VO_4, 8 mM $MgCl_2$, 1.4 mM EDTA, 1 mM EGTA and 0.1mM 2-β-mercaptoethanol). Complexes were then incubated for 30 min at 30°C in kinase buffer containing 10μCi [γ-^{32}P] ATP (Amersham Biosciences) with 5μg enolase, resolved over SDS-PAGE and transferred to nitrocellulose. Phosphorylated proteins were visualized by autoradiography and the membranes then probed with anti-Hck antibody to confirm equal loading of Hck. Protein phosphorylation was quantitated by densitometry using a Fluor-S™ multi-image scanner (Biorad),

RESULTS

Hck associates with both the WASp and mDia1 cytoskeletal regulators at the leading edge of chemotaxing neutrophils.

The pathways linking Hck to modulation of the actin dynamics underpinning neutrophil chemotactic or other actin-based responses are not well-understood. However, Hck capacity to induce WASp tyrosine phosphorylation in macrophages (Cory *et al.* 2002) and the reported link between Src kinases and mDia1 formin function (Tominaga *et al.* 2000) suggest that Hck effects on neutrophil actin remodeling may be realized at least in part via Hck interactions with these cytoskeletal modulators. To ascertain whether Hck associates with mDia1 as well as WASp, these three effectors were co-expressed in Cos-7 cells and anti-Hck immunoprecipitates then examined for the presence of

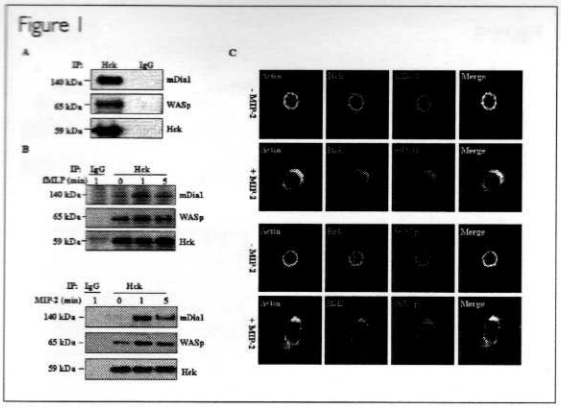

Figure 1. Hck binds and colocalizes with WASp and mDia1 in neutrophils. (A) Lysates prepared from Cos-7 cells transfected with the Hck, WASp and mDia1 cDNAs were immunoprecipitated with anti-Hck antibody or IgG control and the immunoprecipitated proteins subjected to sequential immunoblotting analysis with anti-mDia1, WASp and Hck antibodies. (**B**) Lysates prepared from HL-60 cells at the indicated times after fMLP (upper panel) or MIP-2 (lower panel) stimulation were immunoprecipitated with anti-Hck antibody or IgG and the immunoprecipitated proteins subjected to sequential immunoblotting analysis with anti-mDia1, WASp and Hck antibodies. (**C**) Primary bone marrow neutrophils from C57BL/6 mice were adhered to glass coverslips, stimulated with a uniform concentration of MIP-2 (25ng/ml) and the fixed cells stained for F-actin, Hck, mDia1 and/or WASp and visualized by immunofluorescence microscopy. A merge of all three panels is shown on the far right. All figures are representative of at least four independent analyses.

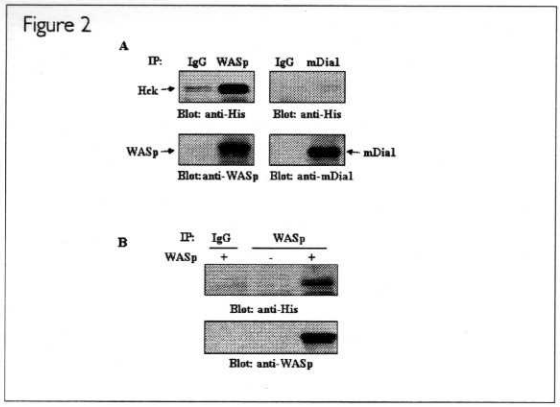

Figure 2. Hck binds directly to WASp. (**A**) Cos-7 cells were transiently transfected with pEGFP-WASp or pDsRed-mDia1 and WASp or mDia1 then immunoprecipitated with anti-GFP or anti-DsRed antibodies. After extensive washing, the immunoprecipitated proteins were incubated with purified His-Hck protein and the complexes then boiled in SDS sample buffer and subjected to immunoblotting analysis with anti-His antibody. (**B**) Far Western blot analysis of WASp-Hck interaction. GFP-WASp was immunoprecipitated from Cos-7 cells transfected with pEGFP-WASp and the complexes resolved by SDS-PAGE and transferred to nitrocellulose membranes. Membranes were then incubated with His-Hck protein and bound Hck detected by anti-His antibody. All figures are representative of at least four independent analyses.

WASp and mDia1. As shown in Fig. 1A, both cytoskeletal regulators were immunoprecipitated with Hck in these cells. To ascertain whether these effectors interactions occur in myeloid cells in the context of chemotaxis, the association of Hck with WASp and mDia1 was also explored in chemoattractant-stimulated HL-60 cells. Results of this analysis revealed mDia1 and WASp to be coimmunoprecipitated with Hck (Fig. 1B). While Hck interacted with WASp constitutively in these cells, the kinase association with WASp was markedly increased after fMLP or MIP-2 stimulation and its association with mDia1 was essentially detected only after cell stimulation. Immunofluorescence analysis of bone marrow neutrophils stimulated with the MIP-2 chemokine confirmed the inducible association of both mDia1 and WASp with Hck in primary cells, revealing that Hck translocates to the front of polarizing cells where it colocalizes with each of mDia1 and WASp as well as the intense F-actin band that accumulates at the cell anterior to constitute the leading edge (Fig. 1C). Thus Hck forms a complex with mDia1 and WASp at the leading edge of chemotaxing neutrophils, a finding that is consistent with the paradigm of Src kinase regulation by actin polymerization-dependent membrane targeting.

Characterization of the Hck/WASp/mDia1 interaction.

To ascertain the molecular basis for Hck interaction with WASp and mDia1, GFP-WASp and DsRed-mDia1 were expressed in and then immunoprecipitated from Cos-7 cells and capacity of these proteins to bind recombinant Hck *in vitro* was examined by immunoblotting analysis. As shown in Fig. 2A, Hck protein was precipitated in this assay by protein A Sepharose-bound GFP-WASp, but not DsRed-mDia1, suggesting that Hck binds WASp directly and mDia1 indirectly. Similarly, incubation of nitrocellulose-immobilized GFP-WASp (Fig. 2B) or DsRed-mDia1 (not shown) with His-tagged Hck followed by anti-His antibody in a Far Western immunblotting analysis confirmed

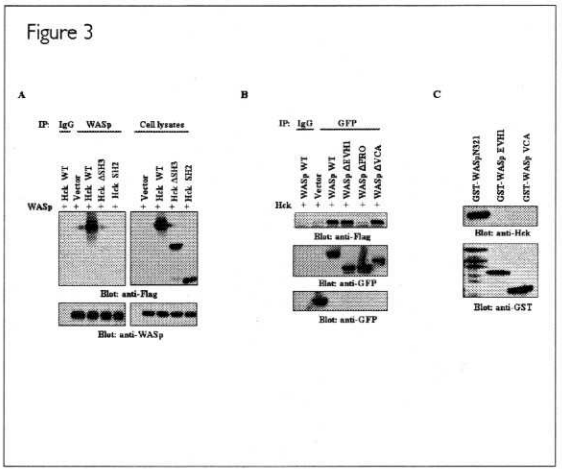

Figure 3. The SH3 domain of Hck is required for the Hck-WASp interaction. (**A**) Cell lysates were prepared from Cos-7 cells transfected with pEGFP-WASp and pcDNA3.1 Flag-tagged Hck, HckΔSH3 or HckSH2. Cell lysates (right panel) or lysates immunoprecipitated with anti-GFP antibody (left panel) were fractionated on SDS-PAGE and subjected to sequential immunoblotting with anti-Flag and anti-WASp antibodies. (**B**) Lysates prepared from Cos-7 cells co-transfected with pcDNA3.1 Flag-Hck and either pEGFP-WASp(WT), pEGFP-WASpΔEVH1, pEGFP-WASpΔPRO or pEGFP-WASpΔVCA cDNAs were immunoprecipitated with anti-GFP antibody or IgG (control), resolved over SDS-PAGE and subjected to sequential immunoblotting with anti-His and anti-GFP antibodies. (**C**) Polyhistidine-tagged Hck was incubated with GST-WASp N321, EVH1 or VCA fusion proteins immobilized on glutathione sepharose and the complexes resolved by SDS-PAGE and sequential immunoblotting with anti-Hck and anti-GST antibodies. All figures are representative of at least four independent analyses.

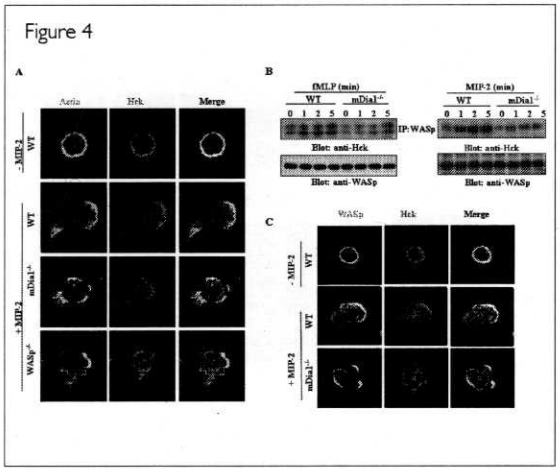

Figure 4. Effects of WASp and mDia1 deficiency on Hck subcellular distribution. (**A**) and (**C**) Wild-type (WT), mDia1$^{-/-}$ and WAS$^{-/-}$ neutrophils adhered to glass coverslips were stimulated with a uniform concentration of MIP-2 (25ng/ml), stained for F-actin and Hck (**A**) or Hck and WASp (**C**) and the images visualized by immunofluorescence microscopy. WASp immunoprecipitates obtained from fMLP-stimulated wild-type (WT) and mDia1$^{-/-}$ bone marrow neutrophils at the indicated time points after fMLP (upper panel) or MIP-2 (lower panel) stimulation were subjected to sequential immunoblotting analysis with the indicated antibodies. All figures are representative of at least four independent analyses.

the direct binding of Hck with WASp, but not mDia1. To characterize the structural basis for Hck-WASp binding, GFP-WASp expressed in Cos-7 cells was assessed for capacity to immunoprecipitate co-expressed Flag-tagged full-length Hck or Hck species lacking the SH3 (HckΔSH3) or containing only the SH2 (HckSH2) domains. Although equivalently expressed in these cells, only full-length Hck, but neither mutant Hck protein was co-immunoprecipitated with WASp (Fig. 3A). Thus the Hck SH3 domain is essential for and likely mediates binding of this kinase to WASp. Conversely, when co-expressed with WASp mutants lacking the EVH1, PRO, or VCA domains, Hck co-immunoprecipitated with all WASp species except WASpΔPRO (Fig. 3B). Similarly, an evaluation of GST fusion proteins containing the WASp EVH1 domain, VCA domain or region encompassing the C-terminal EVH1 and N-terminal half of the PRO domain (N321) for *in vitro* binding to recombinant His protein, confirmed that Hck binding to WASp is direct, not dependent on the WASp EVH1 or VCA domains, and most likely mediated by interaction of the WASp proline-rich region with the Hck SH3 domain (Fig. 3C). Importantly, when co-expressed with WASp and either Hck or the HckΔSH3 or HckSH2 proteins, mDia1 also coimmunoprecipitated with the full-length, but not mutant Hck species (data not shown), suggesting that mDia1 participation in the trimolecular mDia1/Hck/WASp complex also depends on SH3 domain-mediated binding of Hck to WASp.

Disruption of the mDia1/Hck/WASp complex abrogates chemokine-induced Hck translocation to the neutrophil leading edge.

Activation of Src family kinases requires their targeting to the cell membrane, a process in turn, requiring actin polymerization and shown to be

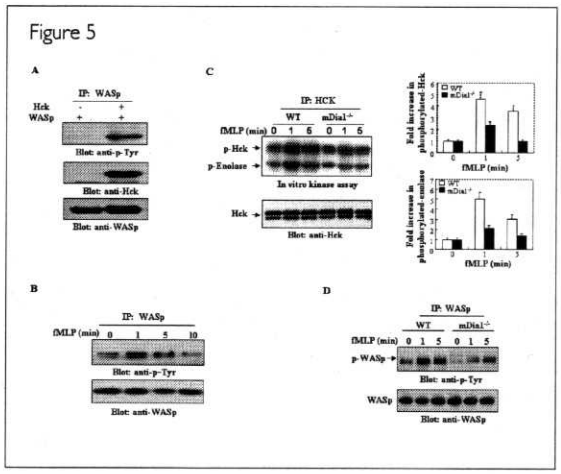

Figure 5. Hck activation and WASp tyrosine phosphorylation are impaired in mDia1$^{-/-}$ neutrophils. (**A**) Cos-7 cells were transfected with WASp alone (–) or with (+) Hck, the lysates then immunoprecipitated with anti-WASp antibody and the immunoprecipitated proteins sequentially immunoblotted with anti-phosphotyrosine, Hck and WASp antibodies. (**B**) HL-60 cells were stimulated with 1 μM fMLP for the indicated times, the lysates then immunoprecipitated with anti-WASp antibody, and the complexes resolved by SDS-PAGE and sequential immunoblotting with anti-phosphotyrosine and anti-WASp antibodies. (**C**) Lysates prepared from wild-type and mDia1$^{-/-}$ bone-marrow-derived neutrophils were stimulated with 1 μM fMLP for the indicated times and subjected to immunoprecipitation with anti-Hck antibody. Immunoprecipitates were then incubated with enolase and ^{32}P-ATP in an ***in vitro*** kinase assay. Complexes were resolved over SDS-PAGE, transferred to nitrocellulose and phospho-labeled enolase and auto-phosphorylated Hck visualized by auto-radiography (upper panel). Equal loading of all lanes was confirmed by reprobing the membranes with anti-Hck antibody (lower panel). Phosphorylation of Hck (upper panel) and enolase (lower panel) were quantitated by densitometry and plotted as the fold increase in phsosphorylation relative to baseline level. (**D**) WASp immunoprecipitates from wild-type and mDia1-/- neutrophils stimulated with 1 μM fMLP for the indicated times were subjected to sequential immunoblotting analysis with anti-phosphotyrosine and anti-WASp antibodies to detect tyrosine-phosphorylated WASp (p-WASP, upper panel) and total WASp (lower panel), respectively. All figures are representative of at least four independent analyses.

SH3 domain-dependent (Sandilands *et al.* 2007). To investigate the relevance of mDia1 and WASp to Hck membrane targeting during chemotaxis, chemoattractant effects on Hck subcellular positioning were compared between wild-type neutrophils and neutrophils obtained from WASp-deficient (Zhang *et al.* 1999) or mDia1-deficient (Peng *et al.* 2007) mice. As shown by immunofluorescence microscopy, both MIP-2 (Fig. 4A) and fMLP (data not shown)-induced Hck translocation to the leading edge was essentially abrogated in both WASp and mDia1-deficient neutrophils, Hck remaining evenly distributed around the periphery of the stimulated cells and showing minimal colocalization with F-actin. Thus, despite its indirect association with Hck, mDia1 effects on anterior polarization of the kinase in response to chemotactic stimulation appear similar to those of WASp. Similarly, the marked reduction in amount of Hck co-immunoprecipitated with WASp in mDia1-deficient relative to wild-type fMLP or MIP-2-stimulated neutrophils (Fig. 4B), and severe disruption of inducible Hck colocalization with WASp and anterior translocation in mDia1$^{-/-}$ cells (Fig. 4C) identify a requirement for mDia1 in Hck binding to WASp and in the triggering of Hck movement to the cell membrane. Interestingly, lack of mDia1 was also associated with impairment in polarized redistribution of WASp, WASp moving to a number of regions across the cell membrane rather than concentrating at the anterior of the mutant cells. Thus Hck and WASp association with mDia1 within a multimolecular complex appears to be required for Hck and WASp to translocate together to the neutrophil leading edge in response to chemotactic stimuli

mDia1 promotes Hck activation and WASp tyrosine phosphorylation in response to chemotactic stimulation.

The association of Hck with mDia1 and WASP raises the possibility that this kinase phosphorylates and thereby coordinately regulates both cytoskeletal regulators. However, antiphosphotyrosine immunoblotting analyses of WASp (Fig. 5A) or mDia1 (data not shown) immunoprecipitates from Cos-7 cells coexpressing either of these proteins with Hck revealed only WASp and not mDia1 to be tyrosine phosphorylated by Hck. Similarly, WASp (Fig. 5B), but not mDia1 (data not shown) was inducibly tyrosine-phosphorylated following fMLP stimulation of HL-60 cells. To further explore the biologic relevance of Hck-mDia1 association, the possibility that mDia1 influences Hck activation as well as localization was also explored. As shown in Fig. 5C, evaluation of Hck immunoprecipitates from

mDia1-deficient neutrophils for *in vitro* kinase activity revealed fMLP-induced Hck activation to be severely reduced in the mutant relative to wild-type cells. Consistent with this finding, fMLP-triggered WASp tyrosine phosphorylation was also markedly diminished in mDia1$^{-/-}$ compared to wild-type neutrophils (Fig. 5D). Thus disruption of Hck-WASp interaction and localization in mDia1-deficient neutrophils appears to impede Hck activation and its induction of WASp tyrosine phosphorylation, findings which suggest a critical role for Hck juxtaposition to mDia1 and WASp in promoting actin dynamics during neutrophil chemotaxis.

DISCUSSION

The Hck Src family kinase is thought to play essential roles in modulating actin-dependent processes in myeloid/monocytic lineage cells. However, the mechanisms whereby Hck subserves this cytoskeletal modulatory role remain unclear. In the current study, we demonstrate the inducible association of Hck with WASp and mDia1 in chemoattractant-stimulated neutrophils and show that Hck is recruited with both cytoskeletal regulators to the leading edge of polarizing cells. While Hck associates directly with WASp, but only indirectly with mDia1, its inducible translocation to the cell anterior is abrogated in the context of either mDia1 or WASp deficiency, suggesting that the macromolecular complex formed by Hck, mDia1 and WASp is required for Hck membrane targeting in response to chemotactic signals. The capacity of Hck to phosphorylate and, by inference, activate WASp and the disruption of fMLP-evoked Hck activation, Hck-WASp binding and WASp tyrosine phosphorylation in mDia1-deficient neutrophils also demonstrate an integral role for mDia1 in regulating Hck function and imply that this role is realized by virtue of the mDia1/Hck/WASp complex. Thus Hck association with mDia1 and WASp appears to constitute a signaling axis of critical importance to neutrophil actin dynamics and to provide a mechanistic framework for linking tyrosine phosphorylation to cytoskeletal remodeling downstream of chemotactic stimulation.

Biochemical studies of the Hck-mDia1 interaction reveal this association to be indirect and dependent on the presence of WASp. While mDia1 and WASp do not appear to interact directly (data not shown), both these effectors have been shown to bind the Dia-interacting protein (DIP, aka WISH and SPIN90), a widely-expressed cytosolic adaptor independently implicated in actin cytoskeleton remodeling (Satoh and Tominaga 2001; Fukuoka *et al.* 2001, Sano 2001; Lim *et al.* 2001; Eisenmann *et al.* 2007). As different DIP domains appear to mediate its respective binding to mDia1 and WASp (Fukuoka *et al.* 2001; Eisenmann *et al.* 2007), this adaptor may enable mDia1-WASp linkage in at least some cell lineages and thereby form the structural nidus for a DIP/mDia1/Hck/WASp complex. This possibility requires further evaluation, but is highly consistent with the current data identifying the mDia1/Hck/WASp complex as a cytoskeletal regulatory signalosome linking chemoattractants and potentially other cell stimuli to actin-based biological responses.

In addition to confirming Hck effects on WASp tyrosine phosphorylation and, by extension, WASp-driven actin polymerization, the data presented here reinforce the reciprocal importance for actin dynamics in regulation of Src kinase activation. Thus, for example, Src activation has been shown to be tightly regulated by its membrane targeting and its translocation from the perinuclear region to plasma membrane depends upon Rho GTPase-mediated generation of actin filaments enabling its intracellular redistribution (Fincham and Frame 1998; Timpson *et al.* 2001). Such subcellular redistribution is thought to modulate not only activation of Src kinases, but also their access to specific substrates and, as a consequence, capacity to influence a diversity of cellular responses. Whether WASp and mDia1 effects on Hck positioning similarly influence the repertoire of neutrophil responses modulated by Hck remains to be determined. However, the current findings implicating both WASp and mDia1 in Hck membrane targeting and activation downstream of chemotactic stimuli are in keeping with an integral role for actin polymerization in Hck function.

These findings are also consistent with previous data showing Src activation in fibroblasts to be dependent on mDia1 activity (Satoh and Tominaga 2001) and recent data revealing the Fyn Src family kinase to be associated with endocytic vesicles and to require RhoB activity for its membrane translocation and activation (Sandilands *et al.* 2007). As Hck has been shown to localize in neutrophil secretory granules (Möhn *et al.* 1995) and to trigger biogenesis of actin-rich podosomes in a lysosome-dependent manner (Cougoule *et al.* 2005), mDia1/WASp regulation of Hck positioning may be mediated at least in part by modulation of Hck vesicular trafficking. This possibility, while hypothetical at present, is supported by prior data suggesting mDia1 involvement in regulation of endosome recycling and motility (Gasman *et al.* 2003).

In addition to linking Hck function to a WASp and mDia1 interaction, the current data raise the possibility that WASp and mDia1 activities are coordinately regulated in neutrophils. Such coordinate regulation is suggested by the disruption of WASp anterior polarization, tyrosine phosphorylation/activation engendered by mDia1 deficiency and would provide a mechanism for juxtaposing mDia1 actin filament extension with WASp actin filament branching activities so as to imbue specific cytoskeletal sites with both these structural properties. Although again speculative at present, this possibility is consistent with the data reported here showing WASp/mDia1 to be required for Hck membrane/targeting activation and implicating mDia1 and Hck in WASp-mediated cytoskeletal rearrangement. While the molecular mechanisms whereby mDia1 influences Hck-WASp association and the functional sequelae of these effector interactions requires further investigation, the current data identify mDia1/Hck/WASp complexes as a cytoskeletal signaling interface potentially underpinning a diversity of actin-based cellular responses.

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2009 Award Designates

2009 Roche Diagnostics Award

Dr. Hans Vogel

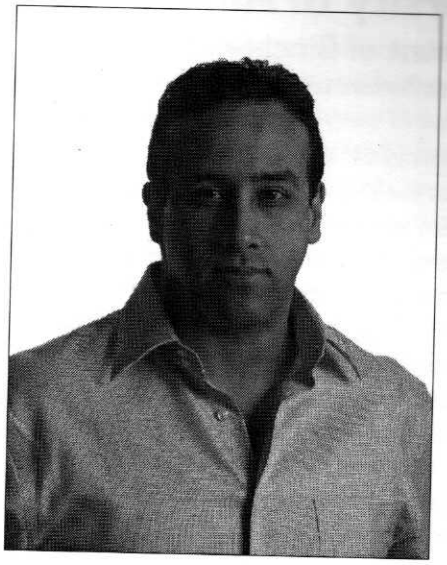
Dr. Hans Vogel is a Professor of Biochemistry and a Scientist of the Alberta Heritage Foundation for Medical Research at the University of Calgary. Hans was born in the Netherlands where he obtained his initial academic degrees at the University of Groningen. He then joined the University of Alberta, where he obtained his Ph.D. degree. As a postdoctoral fellow he worked for almost four years in the group of Dr. Sture Forsen at the University of Lund in Sweden. He returned to the University of Calgary in Canada in 1985 where he has established a large and diverse research program. He was promoted to Full Professor in 1991.

Dr. Vogel's research interests encompass a rather broad area. His studies are often focused on metalloproteins and he is considered one of the world leaders in the study of calmodulin and related calcium-regulatory proteins in animals and plants. His favorite experimental tool has been NMR spectroscopy, but to answer specific research questions his team has utilized many other biochemical and biophysical techniques. Since the early 1990's his group has actively studied mammalian and bacterial proteins involved in iron uptake and transport. The objective of the latter studies is to target the proteins involved in bacterial iron metabolism for the development of new antibiotics. In parallel his group has also determined the structures and the mechanism of action of numerous antimicrobial peptides, as these may also provide an alternative for combating resistant pathogenic bacteria. Recently his research group has been using an NMR metabolomics approach to obtain more direct biological, diagnostic and prognostic information about inflammatory and infectious diseases, such as arthritis and sepsis. At the moment his research spans all the way from basic structural protein work to translational research collaborations with clinicians.

To date the research in Dr. Vogel's group has already led to well over 300 publications, many of them in the leading biochemistry journals. He has trained almost 35 Ph.D. and M.Sc. students, as well as 30 postdoctoral fellows, several of whom have gone on to distinguished independent research careers in academia, industry or government. In addition more than 80 undergraduate students have carried out research projects in his laboratory. Dr. Vogel has served on many national and regional grant review and advisory panels. Moreover, for several years he has been chair of the Biochemistry Group in Calgary; as well, he has been a member of the Board of Directors of the Canadian Light Source in Saskatoon. Over the years Dr. Vogel has been an invited speaker at nearly 100 international and national conferences and symposia. He also regularly presents invited lectures at various universities and institutes around the world. Since coming to Canada, his research endeavors have been directly supported by the Canadian Institutes of Health Research, the Natural Sciences and Engineering Research Council, the Canada Foundation for Innovation, the Heart and Stroke Foundation, and the Alberta Cancer Board. Dr. Vogel has been the recipient of several awards including the CSBMCB Merck Frosst Prize.

2009 CSBMCB New Investigator Award*

Dr. Mickie Bhatia



Dr. Mickie Bhatia is a recognized leader in human stem cell research. Although Dr. Bhatia believes stem cells can serve as sources for cellular and organ replacement in tissue damaged by trauma or genetic influences, and for disease intervention, he will focus on human cancer and using human stem cells to understand how cancer begins, and how treatment may be revolutionized.

Dr. Bhatia joined McMaster University in 2006 as the inaugural Scientific Director of the Stem Cell and Cancer Research Institute (SCC-RI), has been appointed as the Chair in Stem Cell and Cancer Biology, and is a full Professor within the Faculty of Health Sciences. As a highly respected scientist, his work has been published in journals including *Nature, Nature Medicine, Nature Cell Biology, Nature Biotechnology, PNAS, Developmental Cell* and *Immunity.*

Dr. Bhatia serves as a scientific consultant to government and industry, and to medical companies interested in stem cell-based technologies, and sits on numerous editorial and scientific advisory boards

**Formerly Merk Frosst Award*

News from Member Departments

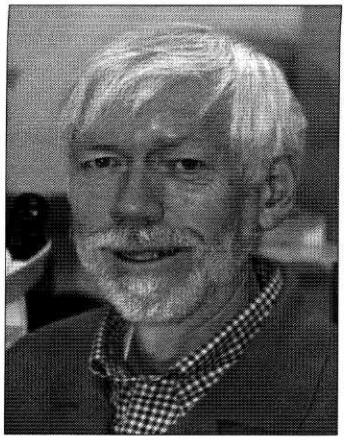
University of Alberta

Department of Biochemistry

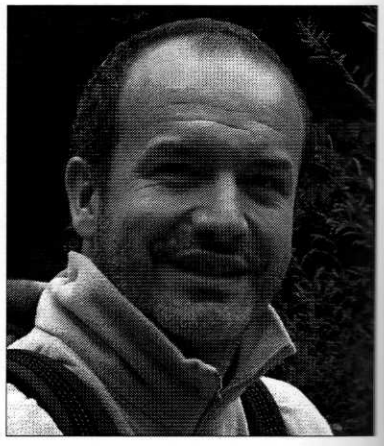
Correspondent: Bernard Lemire

The Biochemistry 21st Century Summit celebrated the history of the Department of Biochemistry during the University of Alberta's centenary year. The keynote speaker was Dr. Jay Ingram with a talk entitled: 'Watson and Crick...Lennon and McCartney'. Among the dignitaries in attendance were Dr. Indira Samarasekera, President of the UofA and the Honourable Doug Horner, Minister, Advanced Education and Technology. Congratulations to **Charles Holmes** and **Adrienne Wright** for organizing an excellent summit. To coincide with the centenary celebrations, **Vern Paetkau** and **Neil Madsen** edited a book entitled 'Spectrum. A history of the Biochemistry Department at the University of Alberta'. This book, dedicated to **John Colter** contains 2 parts: Neil Madsen wrote part one, which covers the first 45 years of the history of the Department; the second part opens with the arrival of John Colter and consists of a series of essays by current and former faculty members.

Department members garnered several awards in 2008. **Dennis Vance** was the recipient of the **J Gordin Kaplan** Award for Excellence in Research, the most prestigious University of Alberta research award. Dennis was Professor and Chair of the Department of Biochemistry at UBC (1982-86) and Associate Dean of Medicine (1978 –81). He moved to the University of Alberta in 1986 to establish a Lipid Research Group. Dennis and his colleague **Joel Weiner** also became University Professors at the UofA in 2008. The American Crystallographic Association awarded **Michael James** the Buerger Award for his contributions of exceptional distinction. He will receive the award at the annual meeting in Toronto in July, 2009. **Mark Glover** was named a Howard Hughes Medical Institute International Research Scholar. **Ing Swie Goping** received the Alberta Cancer Board Recruitment/Retention award. **Nicolas Touret** was awarded an AHFMR Scholarship. **Joanne Lemieux** is now the holder of a CRC Tier II award. Congratulations.



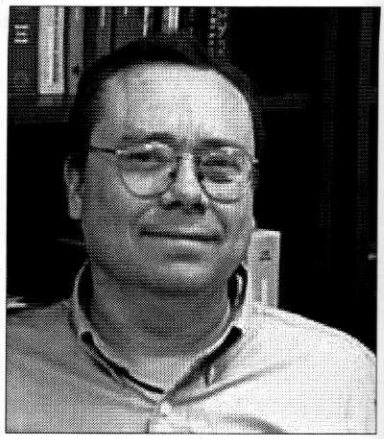
Dr. Dennis Vance



Dr. Nicholas Touret

Dr. Joanne Lemieux

The University of Alberta Butanerds took first place in the energy division of the 2007 International Genetically Engineered Machine jamboree (iGEM), a synthetic biology competition hosted by MIT. Student teams are challenged to design and build biological machines. The Butanerds engineered *E. coli* to produce butanol, a biofuel superior to ethanol. The success of the Butanerds has led to the introduction of two biochemistry



Dr. Michael Ellison

courses in synthetic biology, the first offered anywhere in Canada and taught by **Mike Ellison**. It has also led to a $1.1 M dollar grant to commercialize butanol production and the Alberta Genetically Engineered Machines competition (AGEM). One of this year's iGEM teams, the Bisphenolics is trying to program bacteria to find, metabolize and neutralize bisphenol-A, a toxic chemical found in many plastics. Congratulations to all involved.

Short notes: **Michael James** was recognized for 40 years of service at the UofA and **Colleen Iwanicka** for 25 years of service. Colleen started with the Department 25 years ago and returned to us this year as Assistant Chair Administration following the retirement of **Gail Redmond**, who served the Department for 30 years, 25 as Administrative Professional Officer. Congratulations are in order to **Joanne Lemieux** and **Howard Young** upon the birth of their twin sons, Quinn and Oliver, and to **Nicolas Touret** and his wife Emmanuelle for the birth of their daughter, Zoey.

Two of our most notable visitors last year were Dr. Randall Moon from the University of Washington. Dr. Moon delivered an exciting presentation entitled "Wnt Signaling in Regeneration and Regenerative Medicine" as the 21st John S. Colter Lecturer in Biochemistry. We were also honored by the visit of Dr. Brett Finlay from UBC. He delivered the 4th W.A. Bridger Lecture in Biochemistry on "Pathogenic *E. coli*: The role of the pathogen, the host and the microbiota".

University of Calgary

Department of Biological Sciences

Faculty of Science

Correspondent: Raymond J. Turner

Our department has a range of disciplines in it ranging from Ecology to Biochemistry. Of the ~70 faculty in this department just under half are biochemists, molecular or cell biologists. We contribute to undergraduate programs in cell and molecular biology, microbiology, plant biology and biochemistry. Our research areas are diverse with strengths in structural biology, Cell and developmental, membrane biochemistry, computational biology with emerging strengths in metabolism, environmental microbiology, and systems biology.

Several of our group have been recognized with a number of distinctions and awards. Outstanding recognitions/awards went to **Peter Tieleman** receiving the Rutherford Memorial Medal in Chemistry, Royal Society of Canada. **Stuart Kauffman**, director of the institute of biocomplexity and informatics (IBI) became a Fellow of the Canadian Royal Society. **Andre Buret** was awarded the Robert A. Wardle Medal by the Canadian Society of Zoologists, for outstanding contributions to parasitology research on the national and international scenes. He also was awarded an Endeavour Research Fellowship Award, Government of Australia, for research and innovation. **Gordon Chua**, received a Maud Menten New Principal Investigator Prize from the CIHR Institute of Genetics. **Isabella Barrette-Ng** received a Student Union Teaching Excellence Award.

Peter Facchini led a major Genome Canada grant application in the area of synthetic biology (reconstituting plant secondary metabolism in microbes; plug-and-play functional genomics); **Hans Vogel** initiated Calgary's contribution to a CFI proposal on proteomics and metabolomics. Another large-scale initiative included a Genome Alberta initiative on metagenomics of oil sands led by **Gerrit Vourdoow**.

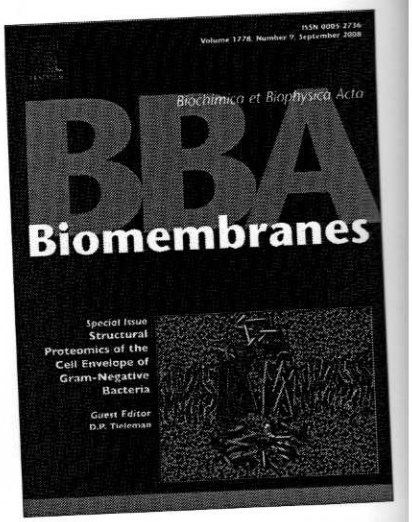
Several of our students have also been recognized and/or presented significant contributions. Justin MaCallum (PhD student with **Tieleman**) received the Huber PhD Thesis Prize for his computational work on membrane partitioning of amino acids. Joe J. Harrison (PhD with **Turner** & **Ceri**) received the CanGene Gold Medal award for microbiology graduate student of the year and presented several talks at meetings and to the department on his work on heavy metal resistance mechanisms. Jake Pushie (PhD with **Vogel**) developed a new model of how

copper binding to the prion protein can potentially initiate the original misfolding event (published recently in Biometals). Amy Laderoute (PhD with **Chua**) presented her work on microarray analysis of transcription factors in fission yeast Yeast at the Genetics & Molecular Biology Meeting in Toronto. Denice Bay (PDF with **Turner**) presented her work on combining bioinformatics and proteomics to study multidrug resistance transporters. Undergraduate biochemistry and cell biology students Adam Kulaga, Jing Cheung, and David Burrows who had received university undergraduate student research awards were involved in a poster presented at the Genetics & Molecular Biology Meeting in Toronto. Undergraduate student Bozhena Liyak was selected to present her summer project work at the student union research symposium. Many of these students were present at our annual biochemistry undergraduate dinner, which was a great success, an event that has been organized over the years by **Gene Huber** (now professor emeritus).

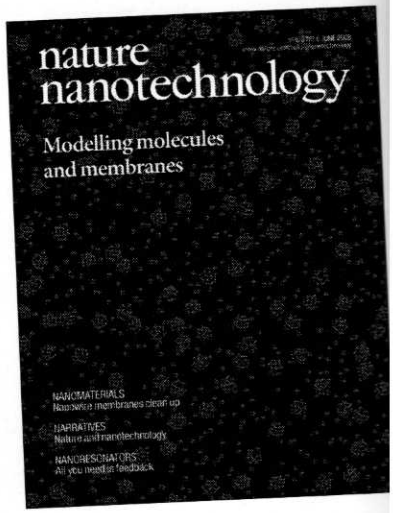
Peter Tieleman organized/chaired a workshop at the Biophysical Society in 2008 "Modeling the membrane" and was one of the speakers. **Sergei Noskov** and **Peter Tieleman** were involved in chairing a biomedical modeling section at the international conference on theoretical Chemical Physics in Vancouver. **Peter Facchini** organized the 1st Banff Conference on Plant Metabolism in July, with the success of this event, including participants from 10 countries, leading this to be a regular bi-annual event.

Raymond Turner and **Sui-Lam Wong** were co-chairs of a session on Bacterial secretion systems and membrane proteins at the Canadian society of microbiology annual meeting held in Calgary on the University Campus. This provided a structural biology twist to a microbiology meeting. **Steve Zimmerly** and **Michael Hynes** convened the symposium on mobile genetic elements. The meeting in Calgary was a great success; **Raymond Turner** and the president of the society **Michael Hynes** performed with the Swing-Jazz band (Woodhouse Big Band) at the society banquet providing a rousing party for all.

Peter Facchini gave invited talks at the Canadian Society of Plant Physiologists and the International Atomic Energy Agency - International Symposium on Induced Mutations in Plants in Vienna; Italian Federation of Life Sciences Meeting in Italy. **Elmar Prenner** and **Vanina Zaremberg** were key contributors to the ASBMB special meeting on Cellular lipid transport in Canmore, Alberta.



Some other research highlights include **Greg Moorhead** being invited to write a review on phosphatase evolution for a special issue of the Biochemical Journal to mark the Darwin Bicentenary (published in the Jan 09 issue). **Peter Tieleman, Raymond Turner** and **Hans Vogel** with Joel Weiner (UofA) worked together editing a special issue of BBA-Biomembranes on the topic of structural proteomics of the cell envelope of Gram-negative bacteria. This volume included may excellent contributions from our Canadian colleagues in the field. **Peter Tieleman** contributed a cover story in Nature Nanotechnology on the interactions of fullerenes with membranes, as well as a paper in PNAS using a new simulation model to study monolayer/lung surfactant collapse in PNAS. Peter found that he needs to be careful with his artistry, as one never knows how journals may use ones figures of membranes (see attached Christmas trees). Work in **Hans Vogel**'s lab led to a solution structure of the calponin homology domain of SMTNL1 protein with apo-calmodulin published in J. Biological Chemistry.



Several of our faculty are now key players in the Alberta Ingenuity Centre for Carbohydrate Science

including **Ken Ng**, **Greg Moorhead**, and **Elke Lohmeier-Vogel** along with the new recruit in the department of chemistry, **Chang-Chun Ling**. Chang-Chun also received a CFI grant to establish his Carbohydrate research lab.

Several groups have explored moving aspects of their research to industry and to market. For example **Robert Edwards** and **Raymond Turner** solidified agreements with NuSep Inc. (Australia) for their halocompound chemistry for fast visualization of proteins in PAGE gels without staining. The chemistry is also now used in BioRad's Criterion Stain Free system.

Andre Buret was on sabbatical in the fall with Prof. RCA Thompson, at the School of Veterinary and Biomedical Sciences, Murdoch University (Western Australia). His work has led to some very significant findings on the pathogenesis of *Giardia* infections, which will shed a new light on therapeutic targets not only for enteric infections, but also the development of chronic inflammatory disorders of the gut. **Peter Tieleman** was on sabbatical in the winter, at the Centre for Blood Research, UBC where he explored membrane fluctuation dynamics by computational approaches. **Marie Fraser** also began her leave this fall catching up on carry over projects from her graduated students. **Sui-Lam Wong** chose to remain in house for his leave focusing his work on the production of enzymes for cellulotic biofuel production.

As we have a large role in undergraduate education we are constantly reworking courses, adding and subtracting as we gain or lose faculty. A great loss this past year was the deletion of our nucleic acids course due to the absence of key individuals from the faculty of medicine. However, we are bouncing back with **Sui Huang** and **Gordon Chua** offering our first new systems biology undergraduate course at the fourth year level in the fall. They determined that this course would be best split into two courses (one in third year and one in the fourth year). The two courses will be System Biology I: Functional Genomics and Cellular Networks. Description: Introduction to high-throughput methods for global functional and network analysis of genes and proteins. Topics include microarrays, chromatin immunoprecipitation, synthetic genetic array analysis, next-generation sequencing and network topology. System Biology II: Network Dynamics and Biocomplexity. An overview of theoretical concepts and modeling paradigms in systems biology and biocomplexity including genetic circuits, gene-regulatory networks (continuous and discrete systems), Boolean functions, gene expression noise and systems dynamics as applied to the control of development.

Elmar Prenner and **Vanina Zaremberg** developed a course on the biochemistry of lipids first offered in the Fall semester. Topics include properties of lipids and bilayers, lipid-lipid and lipid-protein interactions, technological applications, biosynthesis and regulation, lipids as second messengers, intracellular trafficking, and lipids in physiology and disease. Literature review and student seminars are significant components of this course.

Another new course available to our students is Medicinal Plant Biochemistry developed by two of our CRC chairs, **Peter Facchini** and **Dae-Kyun Ro.** This course overviews the biochemical potential of the genome of plants metabolism and how the new technologies allow for their exploration.

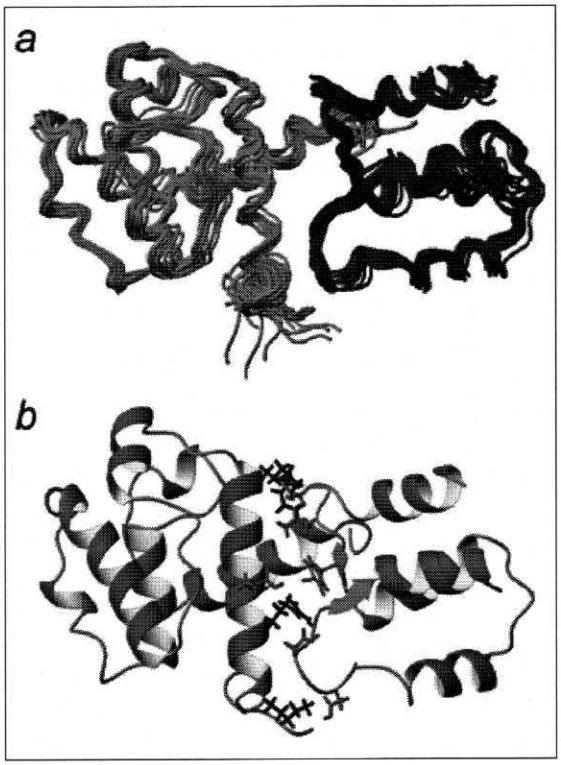
Elmar Prenner along with David Cramb (Department of Chemistry) established a Faculty wide minor in Nanotechnology. Elmar has been recognized for his bio-nano work and will be participating in contributing a biological sciences course in this area.

Our department with its breadth needs to continually evaluate its first year core courses. **Elke Lohmeier-Vogel,** one of our key Biochemistry instructors, has been our important link influencing the redesign of such courses. **Isabelle Barrett-Ng** has been involved in implementing several changes to the laboratory exercises in the Introductory Genetics and Introductory Biochemistry courses, through the help of a grant from the Alberta Teaching and Learning Fund. In

the genetics course, students are now able to get hands-on experience with PCR and agarose gel electrophoresis through a new, inquiry-based laboratory exercise that tests whether various types of food have been genetically-modified. Students are also asked to bridge classical genetics with molecular genetics through a bioinformatics project, where they select a human genetically-inheritable disease, perform bioinformatics analyses on the gene and protein, and prepare and present a poster summarizing their findings to their peers. The top three posters are then selected for presentation at the Department's annual science students' conference. In the biochemistry course BCEM 393, several new inquiry-based laboratory exercises have also been introduced. Students are now studying hydrolysis of carbohydrates and artificial sweeteners by probiotic bacteria, purifying proteins from yeast, and designing their own experiments on metabolic regulation.

Several members of our group play key roles in academic service. **Peter Tieleman** joined the CIHR BMA panel. **Michael Hynes** completed his 3rd year on the NSERC panel 32. **Sergei Noskov** is now an editorial board member for the journal Computational Life Sciences. **Greg Moorhead** continued as the Biochemistry program director and played a large role chair of our Bio core courses committee. **Doug Storey** took on the role as the program director for cellular, molecular, and microbiology program from **Sui-Lam Wong** in the fall. **Howard Ceri** was appointed president elect of Sigma Xi and becomes president of the Society in July 09. **Vanina Zaremberg** became involved with the Argentinean Minister of Science developing discussions towards collaborative research initiatives between Argentina and Canada. **Raymond Turner** finished his role as department subgroup/cluster chair and was key in helping develop a new department management structure.

A number of new people were recruited in the past couple of years and now have started to solidify their research labs and programs. However, not without some frustrations, as after a little more than a year **Gordon Chua's** lab is still to be renovated for him, but he has made efforts to establish a group using our overflow lab. He has been successful in obtaining CIHR operating funds for "Deciphering Pathways of Transcriptional Regulation in *Schizosaccharomyces pombe*". He has also begun a new project working on Pumilio proteins in fission yeast to determine their function in the post-transcriptional regulation of mRNA targets. Gordon received funding from CFI this past year to establish a functional genomics lab.



Solution structures of SMMTNL-1 with C-terminal domain of apo-calmodulin.
a) superposition of 15 models of the complex of SMTNL1-CH (***green***) with the C-terminal domain of apo-CaM (***blue***) ***b***, ribbon representation of the lowest energy model. The side chains that contribute to the formation of intermolecular hydrogen bonds are also shown. The acidic and basic side chains are colored in ***pink*** and ***blue***, respectively, whereas Tyr is shown in ***green***.

Dae-Kyun Ro has recently established his plant genomics and biochemistry laboratory as part of his CRC appointment in Plant Bioproducts, and obtained a CFI infrastructure fund for terpenoid metabolism. His research activities are further supported by a new faculty award from the Alberta Ingenuity Fund, and operating funding from the

Alberta Agriculture Research Institute. Ro was invited several times to present his hybrid research (biochemistry plus engineering) in the area of drug precursor synthesis in microbes at various academic institutions in Denmark, Slovenia, Israel, and USA and also for the biotech company, Amyris Biotechnologies (USA).

Our most recent recruit is **Marcus Samuel,** arriving late in the fall, who is interested in exploring the cellular signaling mechanisms that regulate compatible pollination events during plant reproduction, and elucidating the complex interplay between compatibility and incompatibility pathways. He comes to us from University of Toronto with a PhD from UBC.

Sergei Noskov is one of our new computational biologists, who over the past year has now a well established his lab with a couple of PDF's and graduate students. Sergei was successful in receiving an AHFMR scholar salary award and establishment funds as well as funding from CIHR for operating and CFI for his computational laboratory set up. His research focuses on computational studies of transport proteins and ion channels. Additionally he received a France-Canada Research Awarded for development of QM/MM techniques for modeling biological systems. Sergei was also active in presenting talks at various meetings including Gordon Research conference (USA) and an International school on ion channels (Italy) as well as at the Biophysical Society meetings in Long Beach USA.

Peter Dunfield, our new environmental microbiologist who is interested in the ecology, physiology and biogeochemistry of extremophiles, has now established his lab. He has been active in giving talks on the 'hot' topics of organism life in geothermal soils and hot springs (talks to Nature Calgary, Gordon Research conferences and UBC). His research will examine saline lakes in Alberta and hot springs in the Rocky Mountains. He has also focused interest on methane oxidases from acidophiles.

John Cobb received AHFMR scholar support for his work to study how transcription factors control the development of specific structures. He is seeking to identify the genes downstream of *Shox2* that are responsible for its function and the evolutionarily conserved enhancers that control *Shox2* expression. His lab is also close to completion with some good students in place.

For more information about our activities in the department of Biological Sciences visit: www.bio.ucalgary.ca/research/BCM.html.

Dalhousie University

Department of Biochemistry & Molecular Biology

Correspondent: David Byers

The Dalhousie University Biochemistry & Molecular Biology Department is delighted to announce that two of our most renowned members, **W. Ford Doolittle** and **Michael Gray**, have been appointed as Professors Emeriti. Ford and Mike officially retired in 2007 and 2008, respectively, but continue to be very active in research. Both are associated with Dalhousie's new Centre for Comparative Genomics and Evolutionary Bioinformatics (CGEB), which is directed by fellow Department member **Andrew Roger**. CGEB received official Dalhousie institute status last year, and with generous financial support from the Tula Foundation and the Canadian Institute for Advanced Research (CIFAR), will keep Dalhousie in a leadership position in molecular evolution research for years to come. **Ford Doolittle** was also named a CIFAR Institute Fellow at a gala dinner held in Toronto in November, a prestigious and rare honor recognizing his outstanding administrative and scientific contributions to that organization.

Our most recent faculty addition is **Claudio Slamovits**, slated to arrive on July 1, 2009 as an Assistant Professor and a member of the CGEB

centre. Claudio hails from the U.B.C. group of **Patrick Keeling** (himself a Dal alumnus) and his research will focus on the structure, function and evolution of protist nuclear genomes. **Catherine Currell** also joined the Department as its Administrator in May, 2008, after 20 years of outstanding service at Dalhousie Legal Aid. In addition, we welcomed **Heidi Berry** as a technician in charge of the undergraduate student laboratories, as well as all-round computer guru and webmaster. Finally, we said goodbye to **Carl Breckenridge** who retired in July, 2008. Carl was an esteemed and beloved member of our Department for almost 30 years (and its Head from 1988-98), so we forgive him for spending his last few years on the "dark side" in senior administration as VP Research.

We were all saddened to note the passing of **Syd Patrick** last May at the age of 89. Syd was a longtime member of our Department (1960-89), an expert in carbohydrate metabolism and a passionate defender of teaching basic biochemical principles to medical students. Syd retired many years ago to the beautiful Okanagan valley (Winfield, B.C. to be precise), but his memory has lived on through the endowment of the Patrick Prize, awarded annually for the best Ph.D. thesis and defence in the Department of Biochemistry & Molecular Biology. An eloquent tribute to Syd Patrick (written by **Chris Helleiner**), along with information on all current and former Department members, can be found on our website (www.biochem.dal.ca/faculty/index.php).

On a brighter note, several of our faculty and staff received awards and achieved career milestones in the past year. **John Archibald** and **Kirill Rosen** were both recipients of New Investigator Awards from CIHR, and John was further honored with the Dalhousie Medical Research Foundation's Award of Excellence In Basic Science Research, a prestigious prize given to annually to a Faculty of Medicine researcher within their first eight years of appointment. **John Archibald** and **Christian Blouin** (jointly appointed with Computer Science) were promoted to the rank of Associate Professor with tenure in July, 2008. In other news, your humble correspondent was awarded the Dalhousie Student Union prize for Graduate Teaching Excellence, while **Chris McMaster** received the Greg Ferrier Award from the Heart and Stroke Foundation of Nova Scotia. Finally, **Catherine Currell** was a winner of the 2008 Rosemary Gill Award, which celebrates a high level of commitment and service to Dalhousie students.

Despite the rather grim news on the national research funding scene, all of our research faculty continue to be supported by CIHR, NSERC and/or other national agencies. New or renewal CIHR operating grants were awarded to **Andrew Roger**, **Kirill Rosen**, **Jan Rainey** and **Roger McLeod**, while **Steve Bearne** and **David Byers** saw their NSERC grants renewed. **John Archibald** and **Mike Gray** received an NSERC Special Research Opportunity grant to study the impact of secondary endosymbiosis on eukaryotic genome evolution, while **David Byers** and **Chris McMaster** (with **Don Weaver**, PI) received a CIHR Emerging Team grant to further their antimicrobial drug discovery research. New grants were also awarded to **Paola Marignani** (Canadian Breast Cancer Foundation, Nova Scotia Lung Association), **David Waisman** and **Chris McMaster** (Heart and Stroke Foundation of Nova Scotia), **Jan Rainey** (Nova Scotia Health Research Foundation) and **Hyo-Sung Ro** (Canadian Breast Cancer Research Alliance). Department members continued to be successful in national and regional equipment grant competitions; acquisitions in the past year include a stopped-flow spectrofluorometer, new phosphoimager, and chemically-resistant lyophilizer. Personally, I can't wait to start pulling proteins apart with **Jan Rainey**'s new atomic force microscope.

Many of our trainees received scholarships and awards in 2008-09. A highlight was the Governor General's Gold Medal won by **Laura Hug**, for the most outstanding Masters thesis in the natural sciences and engineering. Graduate student awards were also received by **Ryan Gawryluk** and **Jordan Pinder** (Killam Scholarships), **Ameer Jarrar**, **Meghan Bebbington**, **Alya Arabi**, **David Langelaan** and **Tyler Reddy** (NSERC), **Suchita**

Nath-Sain, **Eric Fisher** and **Craig Steeves** (Nova Scotia Health Research Foundation), **Dale Corkery** (Canadian Breast Cancer Research Foundation), **Paul O'Connell** (Dalhousie Cancer Research Training Program) and **Michelle Leger** (Fonds National de la Recherche Luxembourg). **Anastasios Tsaousis** was awarded an EMBO postdoctoral fellowship as well as a Marie Curie International Outgoing Fellowship from the European Commission. Finally, **Tim Shutt** (a former student of Mike Gray) was the winner of our Department's Patrick Prize for excellence in graduate research, while **Patricia Mitchell** (Roger McLeod) received the Doug Hogue Award for persistence and dedication to research.

University of Guelph

Department of Molecular and Cellular Biology

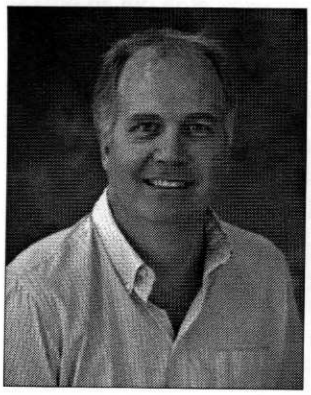
Correspondent: Frances Sharom

It has been a very busy year for the department. With the merger of four different departments/faculty groups (biochemistry, plant cellular biology, microbiology, and molecular biology and genetics) into the Molecular and Cellular Biology department, the individual graduate programs have been merged to reflect our integration. OCGS approval was granted rapidly, and the new graduate program opened for business in Fall 2008, with newly designed graduate courses coming on-stream at that time. The Molecular and Cellular Biology graduate program offers opportunities for interdisciplinary studies in molecular and cellular biology leading to the M.Sc. and Ph.D. degrees. The research groups directed by the faculty are engaged in the pursuit of fundamental and applied research questions involving diverse biological systems (plants, humans and other animals, prokaryotic and eukaryotic microbes), with areas of emphasis in Biochemistry, Cell Biology, Microbiology, Molecular Biology and Genetics, and Plant Biology.

The department currently has around 130 graduate students registered in our programs, as well as students in other interdisciplinary programs, such as Biophysics and Toxicology. **Frances Sharom** stepped down as Director of the Biophysics Interdepartmental Group graduate program after over 5 years at the helm, and was replaced by Michele Oliver, from the School of Engineering.

New faculty addition

Terry Van Raay joined the Department as an Assistant Professor in July 2008, strengthening the department's developmental cellular biology group. Terry completed his undergraduate studies at the University of Windsor in 1991 and pursued a Master's Degree under the supervision of Dr. Teresa Crease at the University of Guelph (1993). His Master's research focused on the molecular evolution of a fresh-water crustacean, *Daphnia*, in the Canadian High Arctic. Terry's training in molecular biology and sequence analysis at the Master's level provided him with the proper skill set to land a job at a biotech company (now part of Genzyme) outside Boston, MA. He spent several years in the biotech sector before returning to graduate school. He then pursued his Ph.D. in the Neuroscience Program at the University of Utah (2003) under the supervision of Dr. Monica Vetter. His project focused on how Wnt signaling controlled the transition of a neural progenitor into a more lineage restricted neural precursor in the developing *Xenopus* retina. Following his Ph.D., Terry took up a collaborative postdoctoral position with Drs. Robert Coffey and Lilianna Solnica-Krezel at Vanderbilt University in Nashville, Tennessee. Here he pursued the role of the Wnt antagonist gene, *naked*, in the early development of the zebrafish embryo. As an independent investiga-

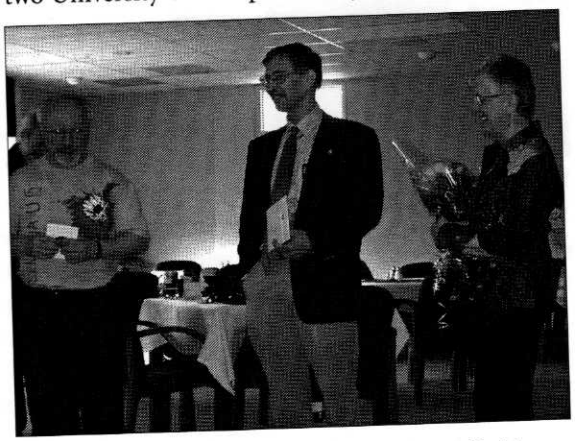


Terry Van Raay

tor, Terry is continuing to study the role of Naked during zebrafish development, but now he is focusing his attention at the biochemical, molecular and cellular level to determine exactly how Naked and other negative feedback regulators can turn off Wnt signaling.

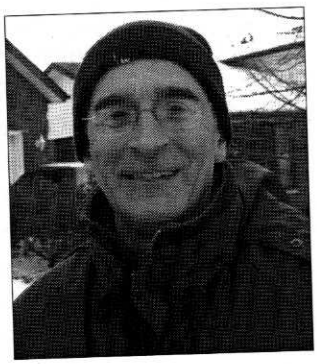
Retirement

Bob Keates officially retired on April 1 2008, after over three decades of service to the University of Guelph. Bob was a major contributor to the Biochemistry teaching program during the time that the biochemistry group was located in the Department of Chemistry and Biochemistry, and continued this after we joined Molecular and Cellular Biology. For many years, Bob did an outstanding job of teaching lecture theatres packed with students taking Introductory Biochemistry, where he soon became a legend in his own time. Over the course of an outstanding career, Bob received many accolades for his teaching, including two University of Guelph Faculty Association



Bob Keates and his wife Ingrid Boesel with colleague David Josephy at the retirement celebration held in April 2008.

(UGFA) Awards. He received a Special Merit Award for his innovative contributions to the development of web-based instruction, and was lauded for developing a truly world-class web resource based on protein structure and function, which proved to be a highly effective mode of teaching. Bob always found the time to keep up with the biochemical literature, and his colleagues have long considered him to be a veritable encyclopedia of biochemical information. Bob's research interests initially focused on the dynamics of microtubule polymerization and the role of micro-tubule-associated proteins. More recently, he had been engaged in collaborations with several researchers at Guelph, notably the groups of **Janet Wood, Joe Lam, Rickey Yada** and **Dev Mangroo**, where he provided protein structure modelling and bioinformatics expertise. A reception was held on April 30 2008 to honour Bob, and he and his wife, **Ingrid Boesel**, said their goodbyes to their colleagues and friends. Bob and Ingrid have relocated to warmer climes on Saltspring Island, British Columbia, and they moved into their newly built retirement home at the end of February 2009. There will be excellent opportunities for Bob to indulge his life-long passion for rock climbing, and Ingrid (a former plant physiologist and Master Weaver) will be joining the many artists on the island and continuing to run her weaving business, Fiberworks, from the island. The multi-talented Bob also designs and writes specialized weaving software for Fiberworks, which is distributed world-wide. An undergraduate biochemistry scholarship was set up in Bob's name, and was awarded for the first time in March 2009.



Bob Ford

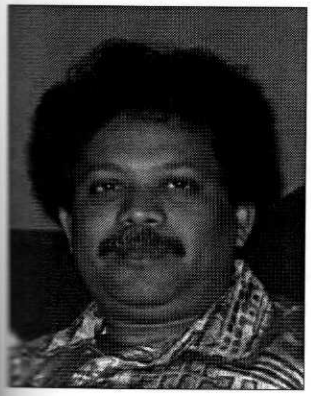
Sabbatical leave visitor

The department is pleased to be hosting **Bob Ford**, who is visiting Guelph on a 12-month sabbatical leave from the U.K., where he is Professor of Structural Biology at the University of Manchester. Bob is collaborating mainly with Chris Whitfield and Joe Lam while here in Guelph, focussing on membrane protein structural studies. So far, this has all been done by cryo-EM, using the new 200 kV FEG Tecnai G2 transmission electron microscope in the Science Complex building. Bob is hoping to take advantage of the excellent structural biology equipment in Guelph to learn new techniques and to update his knowledge in electron tomography, NMR, X-ray crystallography and fluorescence studies, as well as taking the opportunity to work on pre-existing projects that are continuing in Manchester.

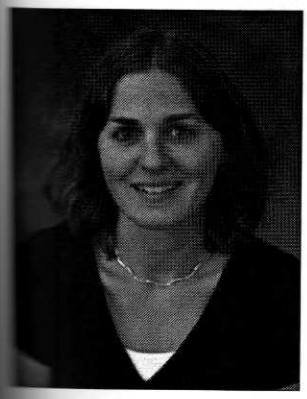
Perhaps foremost among these are studies of CFTR, the protein that when mutated gives rise to cystic fibrosis in humans. The first EM structural data on the mutated CFTR protein have been collected in Guelph in the last few months.

Congratulations!

The department now has two faculty members that hold ERAs (Early Researcher Awards), **Jaideep Mathur and Nina Jones**. Funded by the Ontario Ministry of Research and Innovation, Jaideep's award is spread over 5 years, 2008 to 2012, and will partially fund a graduate student and post-doctoral researcher to work on understanding signalling mechanisms in environment-plant cell interactions. Plants are masters at survival and manage to do so while staying rooted to one location. However, how plants respond so quickly to their environment is not well understood. Jaideep's research uses live-imaging techniques, including the use of multi-coloured fluorescent proteins and transgenic plants, to dissect rapid sub-cellular interactions that form the basis for plant growth and development. Besides adding to basic knowledge, the resulting data will serve as an effective public education tool concerning the rapid effects of environmental change on living cells.



Jaideep Mathur



Nina Jones

Nina's ERA award runs from 2007-2012, and supports her research focus on characterizing the phosphotyrosine-based signal transduction pathways that occur during the biological process of blood vessel development. Her laboratory is investigating the function of a number of signalling adaptor proteins in vascular cells, including endothelial cells and kidney podocytes. A second focus within the lab involves the study of adaptor proteins in neuronal signalling pathways. A variety of multidisciplinary techniques are used to address these research questions. The ERA in particular has been used to recruit two graduate students and a technician, who are working on projects that focus on kidney development and disease. Nina also holds operating grants from CIHR (2009-2014), NSERC (2006-2011) and the Kidney Foundation of Canada (2007-2010), and recently obtained a new Investigator Salary award (2008-2011) from the KRESCENT program, and a Hospital for Sick Children Foundation/CIHR New Investigator Award (2009-2011).

University of Lethbridge

Departments of Biological Sciences, Chemistry and Biochemistry, Kinesiology & Physical Education, and Physics

Correspondent: James E. Thomas

Biochemistry at the University of Lethbridge is a multidisciplinary major delivered by several Departments. Focus within the group is varied with expertise in agriculture, cancer research, microbial biochemistry, nucleic acid biochemistry (in particular in RNA), and nutrition, as well as areas of health and theory.

Dr. Ute Kothe is Assistant Professor in Biochemistry at the Department of Chemistry and Biochemistry since October 2006. Based on her experience in studying the prokaryotic ribosome, Ute's research now focuses on the complex process of **ribosome biogenesis**. In particularly, she is investigating the early stages of ribosome formation when the ribosomal RNA becomes modified by small ribonucleoproteins. **RNA modification** is of particular importance since it is affected in several genetic diseases. Furthermore, ribosome biogenesis

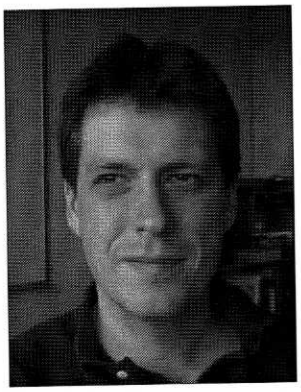
Ute Kothe

might be a limiting factor for rapidly dividing cancer cells and thus represent a new drug target. However, currently the functioning of complexes involved in ribosome formation is only poorly understood. Thus, detailed biochemical knowledge of these processes is much required.

For her investigations, Ute is using a multi-disciplinary approach of molecular biology, biochemistry and biophysics. With the help of highly purified, *in vitro* reconstituted systems, the Kothe group studies the function of different RNA modifying enzymes by biochemical, rapid kinetic and advanced fluorescence techniques. These *in vitro* experiments are complemented by yeast *in vivo* studies. In particular, Ute is interested in understanding the differences between prokaryotic and eukaryotic ribosome biogenesis since this pathway might also be a new antibiotic target. Therein, the Kothe group is focusing on a prokaryotic stand-alone model enzyme for RNA modification with the aim of identifying its kinetic and catalytic mechanism. Other projects in the Kothe lab address the function of archaeal and yeast small ribonucleoproteins. Highly stable archaeal complexes allow Ute's PhD student Raja Kamalampeta to investigate the conserved general features of RNA modification. This is complemented by the research of Jessica Durand, an MSc student, who develops a eukaryotic model system to specifically address the causes of genetic diseases. Also, many highly motivated undergraduate students are participating in these projects during summer research, honour theses and research independent studies. In combination, research in the Kothe lab will reveal the critical steps in RNA modification. Insight into the molecular mechanism and the building principles of small and large ribonucleoproteins will ultimately also lead to the development of new nanobiomachines.

Research in the Kothe group is supported by the Canada Foundation for Innovation, Alberta Science and Research Authority, the Banting Research Foundation and the University of Lethbridge (http://people.uleth.ca/~ute.kothe).

Dr. Hans-Joachim Wieden joined the Department of Chemistry and Biochemistry in January 2005 and was awarded a Canada Research Chair in Physical Biochemistry as well as an Alberta Ingenuity New Faculty award in 2007. HJ is studying Molecular Mechanisms of Antibiotics. With the steady emergence and spread of antibiotic resistant pathogens, the development of new antibiotics is increasingly important. This research program focuses on the study of antibiotic function in order to develop novel antibiotics. In particular antibiotics that target the cellular machinery of the pathogen, that is responsible for translating genetic information into functional proteins. A process called translation. The detailed mechanistic understanding of the involved processes is of fundamental importance for the development of new types of antibiotics. In his research program he approaches the problem of how antibiotics interfere with these processes, in order to inhibit translation, on the molecular level. His research group will identify the molecular requirements for the inhibition of translation and analyze how resistance mechanisms work. On the basis of these results we will develop novel tests that will allow us to search for chemical compounds that will effectively inhibit translation. The research will significantly contribute to our understanding of the structural and functional requirements of antibiotic function, providing the framework for rational inhibitor design.

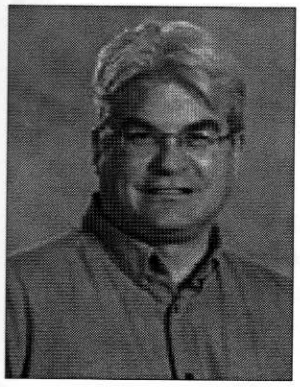


Hans-Joachim Wieden

Other research is looking at the **Molecular Dynamics of Elongation Factors**. This part of his research program is supported through the AIF New Faculty award. During translation, growth of the polypeptide chain is facilitated by consecutive binding of two Elongation factors (EF), Tu and G, to the elongating ribosome. Protein molecules are intrinsically flexible, and typically undergo a wide variety of motions at normal temperatures. Crystal structures of the free EFs as well as Cryo-electron microscopic studies of ribosome-bound EFs demonstrated a high degree of conformational flexibility to be important for the function of these factors. The flexibility and dynamics of proteins such as elongation factors has been optimized by evolution for their activities and functions. In order to analyze the role of the dynamical properties on their

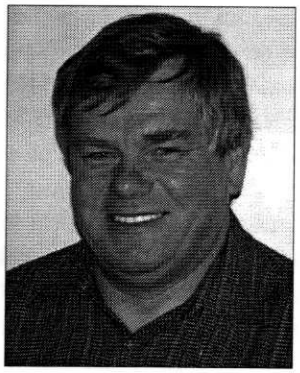
function, and to bridge the gap between the static structural data and the huge amount of biochemical and kinetic information that is available, the conformational flexibility of elongation factors such as EF-Tu and EF-G is studied using molecular dynamics simulation and structural alignments.

HJ's work focuses around a unique combination of state-of-the-art biophysical techniques involving fluorescence spectroscopy, fast kinetics (Quench Flow / Stopped Flow), biochemistry, molecular biology, and molecular dynamics. He has four graduate students; Jeff Fischer (PhD) is working on alternative elongation factors, Evelina DeLaurentiis (MSc) focuses on EF-Tu's role during ribosomal A-site binding, Evan Mercier (MSc) studies the structural dynamics of EF-Tu using molecular dynamics simulations., while Adam Smith is working on the functional mechanism of RNase II (co-supervised by Dr. Steve Mosimann). He also is strongly committed to undergrad research and maintains an active undergrad research program. During the summer of 2007 four undergraduates researchers (Funded through AHFMR, NSERC and Chinook stipends.) worked on individual research project in his lab. . He is currently looking for two PDFs to join his research team (Applications are welcome; funding is available for 3 years). (http://people.uleth.ca/~hj.wieden/index.html)



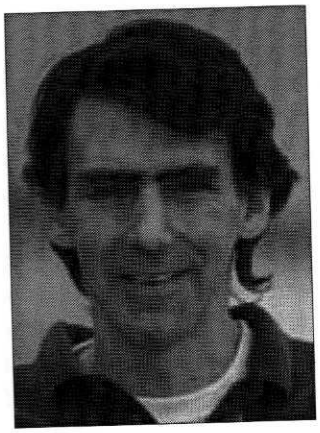
Brent Selinger

Dr. Brent Selinger is an Associate Professor in the Department of Biological Sciences and Coordinator of Agricultural Biotechnology at the University of Lethbridge. Brent is interested in the genetics and biochemistry of microbial hydrolytic enzymes, microbial ecology of animal digestive tracts and surface waters and biological control of cattle ectoparasites. His research group in currently characterizing a unique family of phytate degrading enzymes related to protein tyrosine phosphatases (PTP). A large collection of PTP-like phytase genes is currently being used to address questions about the molecular and biochemical characteristics of this family as well as mechanisms of action, structure/function relationship and biological function. A variety of techniques are used in Brent's research, including aerobic and anaerobic microbiology and molecular biology (e.g., gene cloning and overexpression, protein purification and characterization, and mutagenesis). Collaborations with Steve Mosimann and Hans-Joachim Wieden from the U of L and Ralf Greiner (Federal Research Centre for Nutrition and Food, Centre for Molecular Biology, Karlsruhe, Germany) have allowed questions on phytase structure/function relationships, molecular dynamics and dephosphorylation pathways to be addressed. Brent is supervising or co-supervising a number of graduate students working on i) the biochemistry, structure/function relationships and evolution of PTP-like phytases; ii) *Campylobacter* pathogenesis and persistence in the environment, iii) antibiotic resistance in enteric bacteria from feedlot cattle, iv) stability of *Esherichia coli* O157:H7 lineages, v) gene expression in triticale and bacteriophage of *Mannheimia haemolytica.*



Roman Przybylski

Dr. Roman Przybylski is an AVAC Chair in the Department of Chemistry and Biochemistry. Roman is working on (1) development of antioxidants for edible oils and food systems; (2) the effects of endogenous edible oil components on stability, performance and nutritional value; (3) assessment of food products and raw materials for compounds with nutritional and nutraceutical properties. Recent projects include (1) development of analytical techniques to assess antioxidant potency of different plant origin components: (2) assessment of chemical activity of minor oil components during frying; (3) formation of trans fatty acids during processing and food preparation; (4) Designing oils for specific food application by manipulating their composition: (5) formation of compounds with negative health and nutritional effects during food processing. He is

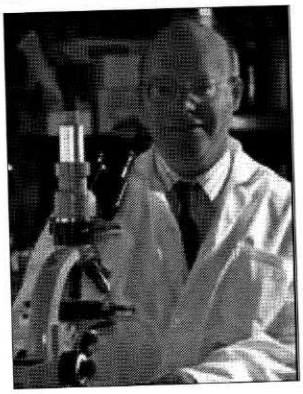


Steve Mosimann

interested in making contact with potential graduate students at the Masters and Ph.D. levels and prospective Post Doctoral Fellows. **Dr. Steve Mosimann** is an Associate Professor with the Department of Chemistry and Biochemistry at the U of L. Steve's research involves development of an understanding of the mechanism of mRNA turnover and the formation of long-lived mRNA species. One area of interest is in **messenger RNA turnover in bacteria.** The hallmark property of mRNA is its rapid turnover within the cell. Ultimately, it is the balance between the production and degradation of mRNA species that control the levels of proteins within a cell. Accurate, three-dimensional models of the enzymes, proteins and complexes responsible for 'general' mRNA turnover can reveal the recognition events that lead to degradation of a given mRNA species. The longer-term goals of this research program are an understanding of mechanism of mRNA turnover and the development of long-lived mRNA species. Other research involves **ribosome biogenesis in Archaea.** Ribosomes are assembled in a stepwise, vectorial process that involves a number of characterized RNA processing events. Archaeal ribosome biogenesis share common features with eukaryotic ribosome biogenesis and can serve as a less-complex model for study.

Structural studies of archaeal enzymes, proteins and complexes required for ribosome biogenesis will shed light on related processes in eukaryotes. Steve currently has a PhD Student, **Rob Gruninger** working with him, who is being co-supervised by **Brent Selinger** (Department of Biological Sciences, University of Lethbridge) and is working on the structure and functional relationships of phytases.

Much of Steve's research involves X-ray Crystallography. Homogeneous samples of macromolecules and macromolecular complexes can be crystallized in aqueous solutions. The diffraction of monochromatic X-rays by these crystals can yield intensity data that is used to create a three-dimensional map of the electron density associated with the macromolecule(s) of interest and ultimately a three-dimensional structural model. As the structure and function of macromolecules are intimately connected, these models provide functional insights and lay the groundwork for an understanding of biological function at the molecular level.



James Thomas

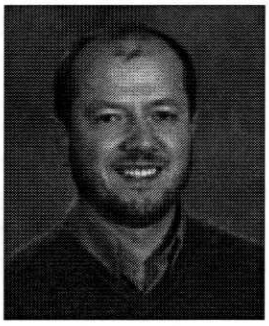
Dr. James Thomas is an Associate Professor in the Department of Biological Sciences, and Coordinator of Biochemistry at the University of Lethbridge. Part of his research focus is in the area of microbiology, looking at cause and effect associations in the occurrence of waterborne pathogens, in particular in relation to agriculture, ecology and urban/industrial activities. In collaboration with **Dr. Victor Gannon and Dr. Eduardo Taboada** from the Public Health Agency of Canada, Jim is using metabolic fingerprinting of environmental isolates of *Enterococcus* and *Salmonella* as a means of bacterial source tracking, and genomic characterization of environmental isolates of *E. coli* O157:H7 and *Campylobacter* to develop clinical assays for use in environmental testing. Part of this research has involved assessment of water quality within the Oldman River basin of southern Alberta using geographical information systems to assess spatial and temporal distribution of the fecal coliforms, *E. coli* O157:H7 and *Salmonella* within the watershed. Three graduate students, Sara-Jo Paquette, Susan Ross and Chad Laing currently are being co-supervised by Jim and **Victor Gannon,** Adjunct Professor with the University of Lethbridge and a Research Scientist with the Public Health Agency of Canada, and are working on this research. Another Master's Student, Jennyka Hallewell successfully defended her thesis in the Spring of 2009.

Jim also is working with **Dr. Surya Acharya,** Adjunct Professor with the University of Lethbridge and a Research Scientist with

Agriculture and Agri-Food Canada, **Dr. Manjula Bandara** and **Dr. Darcey Drieger**, Adjunct Professors with the University of Lethbridge and Research Scientists with Alberta Agriculture Food and Rural Development in Brooks, Alberta to develop new forages for the livestock and dairy industries and, new value added functional food and nutraceutical crops to help diversify our agricultural industry. Much of this work has been focused on fenugreek which is an annual legume which can be used in crop rotations and is adapted for growth in semi-arid environments. Ee Lynn Lee is a Master's Student (co-supervised with Manjula Bandara) who is working to develop new varieties of fenugreek with enhanced production qualities for the food and pharmaceutical industries and, as a dietary supplement for the nutraceutical industry. Rajib Prasad is a new Master's Student (co-supervised with Surya Acharya) who is selecting for high quality fenugreek seed and early maturation.

Theresa Burg

Dr. Theresa Burg is an Associate Professor in the Department of Biological Sciences at the University of Lethbridge. Her predominant research interests focus on how intrinsic and extrinsic factors influence the evolution of natural populations. Theresa uses a broad-scale, comparative phylogeographic approach to examine evolutionary patterns and processes in a wide range of organisms including fish, birds and mammals. In her research she has examined a diverse array of topics from mating systems in albatrosses to genetic structure of harbour seals. Current research projects include metapopulation dynamics of the wandering albatross complex, investigating temporal components of a range expansion in the northern fulmar and patterns of post-glacial population expansion in northern North American birds including chickadees, jays and woodpeckers.



Igor Kovalchuk

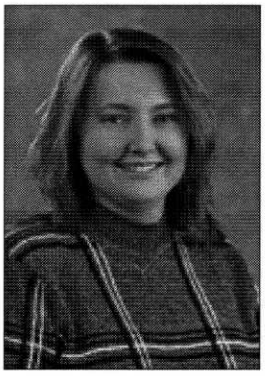
Dr. Igor Kovalchuk is an Associate Professor and Board of Governor Research Chair with the Department of Biological Sciences at the University of Lethbridge. Igor is working on plant genome stability. Specifically, he is looking at:

- the influence of various abiotic (UV, draught, heavy metals, high temperatures) and biotic (pathogens, specifically viruses) factors on plant genome integrity;
- the mechanisms of protection that are developed by plants against the pathogens;
- various types of signals that plants use to warn non-targeted tissues;
- genes involved in various steps of DNA repair, specifically, double strand breaks.

This work has potential to help with generation hardier more resistant crop and could provide an insight to the role of stress in plant evolution.

The lab is the home for the following graduate students: Scott Greer

(MSc), Franz Zemp (MSc), Lidia Luzhna (MSc), Alex Boyko (PhD), Palak Kathiria (PhD), Saikat Basu (PhD).



Olga Kovalchuk

Dr. Olga Kovalchuk is an Associate Professor, a CIHR Chair in Gender and Health, and Board of Governor Research Chair with the Department of Biological Sciences at the University of Lethbridge. She also is the Associate Member (Fundamental Stream) of the Southern Alberta Cancer Research Institute and an Honorable Professor of the Kavetsky Institute of Experimental Oncology NAS Ukraine. Dr. Kovalchuk is an active member of several professional societies and Editorial Board member of the Mutation Research.

The Kovalchuk laboratory works in the rapidly evolving, challenging area of cancer research. Despite a plethora of research in the area, there is still no clear cut answer as to exactly why and how cancer arises. Many powerful cancer treatment modalities have been developed, but they cause serious side effects. Our program is devoted to uncovering the molecular mechanisms of cancer development and new approaches to cancer prevention, diagnostics and treatment.

We have a particular interest in the effects of radiation and chemotherapy agents. Radiation is a double-edged sword – on one hand it is a powerful cancer treatment regiment, on the other hand it can cause cancer.

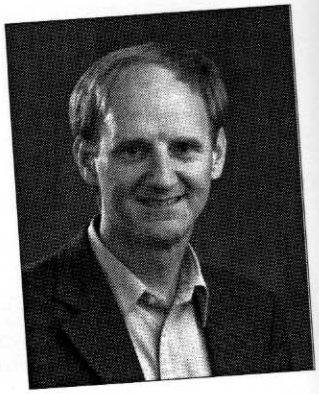
The Kovalchuk laboratory works to minimize the harmful effects of radiation, while maximizing its therapeutic potential. The research program consists of several interconnected lines of research:

- Molecular and cellular mechanisms that underlie cancer development
- Epigenetic regulation in normal and cancer cells
- Radiation and cancer: why and how does radiation cause cancer in the exposed individuals and their unexposed progeny?
- Radiation and cancer: role of radiation in cancer treatment
- Radiation and cancer: mechanisms of radiation side effects
- Sex differences in radiation responses and cancer occurrence.

Amongst various cancer types we are specifically interested in breast, skin and blood cancers. Kovalchuk lab is also analyzing molecular mechanisms of chemotherapy responses and chemoresistance.

Research in the Kovalchuk Laboratory is funded by the Canadian Institutes for Health Research, Alberta Cancer Research Institute/Alberta Cancer Foundation, NSERC, Canadian Breast Cancer Foundation Prairies/NWT Chapter, and the USA Department of Energy.

Dr. Kovalchuk's lab has I have built a rigorous collaborative network. We productively interact with Dr. Dr. Carole Yauk (Health Canada), Dr. Francesco Marchetti (LLNL, USA), Dr. Brian Hemmings (Friedrich Miescher Institut (Basel, Switzerland), Dr. Bevin Engelward (MIT Bioengineering Division, USA), Dr. Igor Pogribny (National Centre for Toxicological Research, USA), Drs. William Bonner and Olga Sedelnikova (Molecular Toxicology Laboratory at NCI/NIH, USA). We also collaborate with the researchers at the Department of Genetics, University of Leicester (UK), the Canadian Centre for Behavioral Neuroscience, Health Canada, McMaster University, University of Calgary, Savannah River National Laboratory, University of Georgia and William Beaumont Hospital Research Institute.

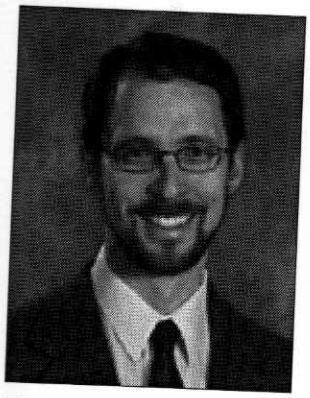

Roy Golsteyn

Dr. Roy Golsteyn is an associate professor in the Department of Biological Sciences at the University of Lethbridge. Roy is studying how cancer cells respond to clinical treatments, with the goal of identifying new biochemical pathways that might be used in future treatments. When cancer cells have damaged DNA, they engage the DNA damage checkpoint. This pathway permits cells to repair the damage, or if that is not possible, it causes them to die. Cancer cells can escape a DNA damage checkpoint by checkpoint adaptation which leads cells to enter mitotic catastrophe. Checkpoint adaptation and mitotic catastrophe are poorly understood at the molecular level although they are believed to have an important role in the cellular response to cancer therapies.

Roy's laboratory is working on the following projects:

- Characterization of the enzyme Checkpoint kinase 1 (Chk1) in checkpoint adaptation in cancer cells.
- Identification of potential biomarkers in cancer drug therapy.
- Characterization of early-stage anti-cancer compounds to understand their mechanism of action.

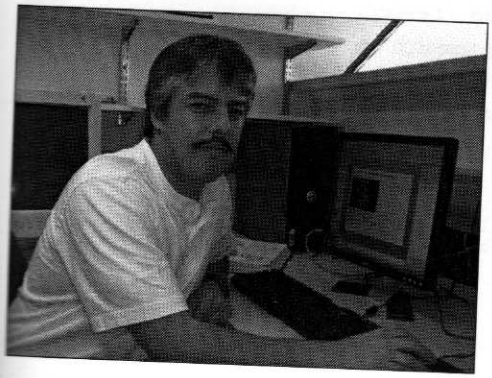
Roy is working with the Servier pharmaceutical company and with clinical research laboratories in France. His laboratory uses the techniques of cell imaging, human cell culture and protein biochemistry.



Marc Roussel

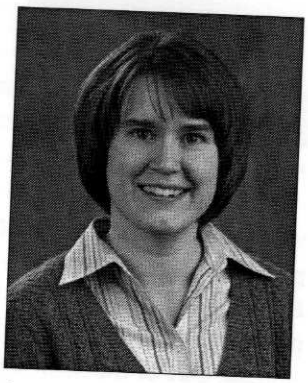
Dr. Marc Roussel is a mathematical chemist appointed to the Department of Chemistry and Biochemistry. His main research interests centre on the development of tools for the mathematical modeling of biochemical systems, from the smallest (subcellular) scales all the way up to the intermediate spatial scales represented by tissues. In addition to fundamental theoretical work, recent projects have included applied modeling research in developmental biology, and collaborative projects in which modern time-series analysis methods are applied to study physiological dynamics.

Dr. Tony Russell joined the Department of Biological Sciences at the University of Lethbridge in August 2007 as an Assistant Professor. Tony's research background has involved using both biochemical and molecular biological approaches to identify and functionally characterize classes of ribonucleic acids in both archaeal and unicellular eukaryotic organisms. His research has provided the first structural information about these RNAs and their associated proteins in several different groups of organisms and most recently he identified the first known minor spliceosomal components in unicellular eukaryotes (Russell *et al.*, Nature (2006), 443: 863-866). These findings have also provided important insights about the age and evolution of these ribonucleoprotein (RNP) complexes. Tony's future research will be to further explore the structure, function and evolution of these macromolecular complexes by using selected protist organisms as model experimental systems. His laboratory will study both small nucleolar (sno) and small nuclear (sn) RNPs. Amongst several research objectives is the development of the first eukaryotic *in vitro* systems to study the mechanism of action of these protein-RNA complexes. Since several human diseases are associated with aberrations to the functioning of these RNPs, his research may provide novel strategies to combat these physiological abnormalities. Additionally, some of the protists being studied in his lab (*i.e.*, *Giardia* and *Phytophthora*) are either animal or plant pathogens that cause serious human health or agricultural concerns.



Tony Russell

Dr. Stacey Wetmore is appointed in the Department of Chemistry and Biochemistry as an Associate Professor and Canada Research Chair in Computational Chemistry. Stacey's research uses calculations on computers to understand DNA damage and repair mechanisms, as well as the properties of modified DNA components that have a variety of biochemical and medicinal applications. Computational chemistry provides a unique approach to study these problems since information about short-lived, highly reactive, reaction intermediates can be obtained more readily than from experimental studies. Current areas of research in the Wetmore lab include understanding DNA damage due to phenoxyl radicals and the mechanism of action of enzymes involved in the base excision repair process, where particular emphasis is being placed on understanding the glycosidic bond cleavage in damaged nucleotides catalyzed by DNA glycosylases. Although calculations on biological systems require significant computer resources, these calculations are possible at the University of Lethbridge due to the recent establishment of a high-performance computer cluster that is composed of 170 quad-core processors (680 cores in total). The Wetmore group currently includes four graduate students (Andrea Millen, Lesley Rutledge, Adi Chhikara, Jennifer Pryzbylski)

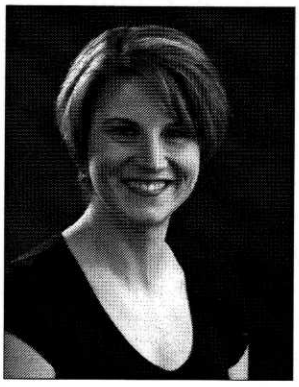


Stacey Wetmore

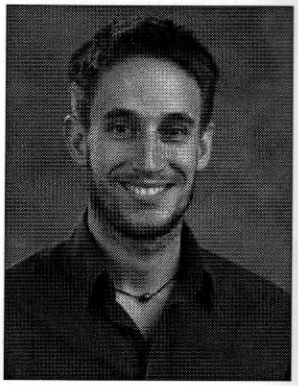
and five undergraduate researchers (Cassandra Churchill, Terri Peterson, Eunjung (Jenny) Shim, Alexis Navarro-Whyte and Siyun (Linda) Wang).


Alicja Ziemienowicz

Dr. Alicja Ziemienowicz joined the team of Dr. Igor Kovalchuk in October 2007, as a Research Associate, and later as a Research Professor in the Department of Biological Sciences at the University of Lethbridge. Alicja's research interests include: (1) genetic transformation of eukaryotic cells, (2) nucleo-cytoplasmic transport of proteins and nucleic acids, (3) DNA replication, repair and recombination in plant cells, and (4) plants as renewable energy sources. One of the main topics of her study is *Agrobacterium*-mediated plant transformation. In particular, Alicja is investigating the mechanism of integration of *Agrobacterium* T-DNA in the plant genome, by identifying plant factors involved in this process. This work not only will contribute to better understanding of the mechanisms of "genetic" colonization" of plants by *Agrobacterium* and of the inter-kingdom gene transfer, but also has the potential to improve the plant transformation technologies.

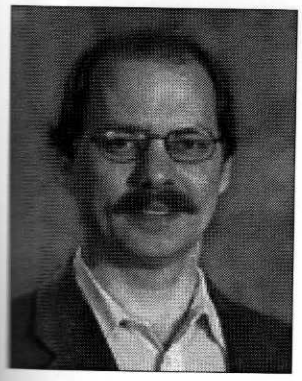

Jennifer Copeland

Dr. Jennifer Copeland is an Associate Professor in the Department of Kinesiology and Physical Education at the University of Lethbridge. Jennifer's research focus is in the areas of exercise physiology and endocrinology. Her primary objective is to understand the relationships between human aging, physical activity, and endocrine function, with emphasis on anabolic and catabolic hormones that play a role in tissue growth, repair and remodeling. She is particularly interested in the gonadal hormones, adrenal steroids, and growth hormone/insulin-like growth factor-1 as changes in these hormone axes have been implicated in the development of sarcopenia and some types of cancer. Jennifer will continue to investigate the role of body composition, physical activity, and nutritional status on age-related changes in endocrine function and this work will potentially lead to the development of evidence-based interventions to promote healthy aging. Jennifer's laboratory is one of three interconnected labs in Kinesiology that constitute the Southern Alberta Centre for Successful Aging.


François Billaut

Dr. François Billaut joined the Department of Kinesiology and Physical Education at the University of Lethbridge in July 2006 as an Assistant Professor in Exercise Physiology. In 2008, he was awarded a **Canada Foundation for Innovation – Leaders Opportunity Fund** for his research on cerebral perturbations provoked by exercise. His main research interest attempts to characterize the neurophysiological mechanism(s) by which O_2 delivery regulates sex-based differences in motor neuron cortical activation and to ultimately shed some light on the unique cerebrovascular responses of women to physical activity. Preliminary work from his lab suggests that men may be more sensitive to reduced arterial O_2 levels than women; further work on cerebral functional activation and haemodynamics is to come. Techniques used range from electrophysiological event analysis to transcranial magnetic stimulation and near-infrared spectroscopy. A comprehensive characterization of sex differences in neurophysiology has wide implications for human biology and physiology research and also in medical research (e.g. altitude medicine). Importantly, all studies using men and women will have to consider sex differences in physiology when evaluating physical activity, neurological disorders or drugs. His lab,

The Integrative Physiology Unit, currently includes 1 graduate and 2 undergraduate students. (http://people.uleth.ca/~f.billaut/)

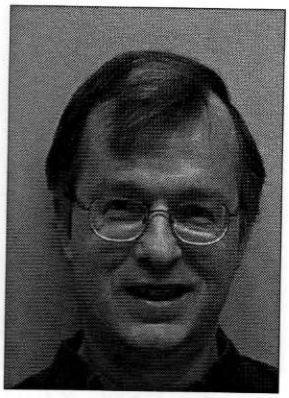


Ken Vos

Dr. Ken Vos is an Associate Professor in the Department of Physics at the University of Lethbridge. Ken is a theoretical physicist and one of his research interests is pharmacokinetics. Pharmacokinetics describes the motion of a drug in the human body and its interaction with the human body. The human body is highly heterogeneous and hence the transport and chemical reaction processes occurring within the human body are highly anomalous. The primary focus of the research is to develop physiologically accurate theoretical models of the drug transport and interaction with the human body. The research focuses on the administration of drugs; but has applications in all stages of drug discovery, development, and administration. This work is being done in collaboration with researchers at the Cross Cancer Institute in Edmonton, Alberta.

David Siminovitch

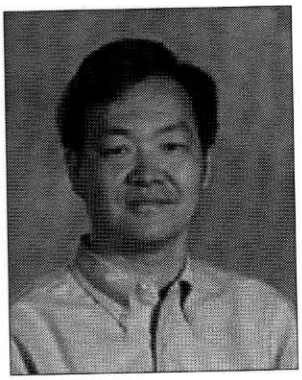
Dr. David Siminovitch is an Associate Professor in the Department of Physics at the University of Lethbridge. David now is working in collaboration with the Laboratory of Physics and Helsinki Institute of Physics (Finland). Because of the hydrogen-bonding capacity of sphingomyelin phospholipids, they have been implicated in the formation of lateral domains ("lipid rafts") in eucaryotic cell membranes. David is investigating the dynamic structure of sphingomyelins using solid-state NMR techniques (Lethbridge) and molecular dynamics simulations (Helsinki). David and his colleagues hope to unravel the unique properties of these unusual lipids, and for the first time, integrate experimental NMR results from the study with theoretical molecular dynamics simulations.



André Laroche

Dr. André Laroche is an Adjunct Professor in the Department of Chemistry and Biochemistry at the University of Lethbridge, and a Research Scientist in Plant Molecular Genetics with Agriculture and AgriFood Canada at the Lethbridge Research Centre. André currently is investigating stress biology in plants due to abiotic (e.g., low temperature) or biotic (e.g. pathogenic fungi) factors and more recently at the development of transgenic triticale as a bio-industrial crop for materials and energy production. He is using functional genomic tools such as large scale sequencing; transcriptome profiling with DNA chips for screening large arrays of genes; real-time PCR to focus on specific genes, and transient and stable expression of candidate genes to assess their role and contribution in a plant cell; and proteomic analyses using 2D-gel electrophoresis and protein sequencing. Within his multidisciplinary research group, he is looking to use this information to improve and accelerate the selection of germplasm toward the development of commercial wheat and triticale cultivars. These tools provide complementary information to enable André and his team, to decipher plant responses to specific forms of stress in order to better understand plant responses and better devise strategies for plant protection and adaptation to unfavorable climatic conditions and to develop triticale lines with value-added traits.

Dr. Oliver Lung is an Adjunct Professor with the Department of Biological Sciences. Oliver is a Research Scientist at the Canadian Food Inspection Agency in Lethbridge. His research is focused on: 1) developing methods for rapid and simultaneous identification and typing of agriculturally important animal viruses such as avian influenza virus,

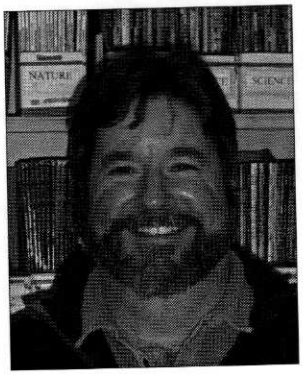

Oliver Lung

food-and-mouth disease virus and their differentials; and 2) improving and expanding baculovirus-based agri-biotechnological applications. His group uses biochemistry, molecular biology, cell biology and virology techniques as well as tools such as electronic microarrays, microsphere arrays and slide microarrays for genetic typing of animal viruses. Research in Oliver's lab is funded by The Chemical, Biological, Radiological or Nuclear Research and Technology Initiative (CRTI), Agriculture Funding Consortium, and the Canadian Food Inspection Agency.

University of Manitoba

Department of Biochemistry and Medical Genetics

Correspondent: Klaus Wrogemann


Geoff Hicks

The new Faculty-wide initiative in Regenerative Medicine is taking off with several members from our Department. **Geoff Hicks** has been appointed the director and **Mojgan Rastegar** is the first new recruit with primary appointment in Biochemistry and Medical Genetics.

Jim Davie has stepped down as director of the Institute of Cell Biology. **Leigh Murphy** has become acting director. **Barbara Triggs-Raine** is acting co-director of the Manitoba Institute of Child Health (MICH). **Jim Davie** is now the new Executive Director of the MHRC (Manitoba Health Research Council). Funding to MHRC has finally increased significantly. Two members have been awarded newly created MHRC Research Chairs, **Spencer Gibson** and **Jeff Wigle**.

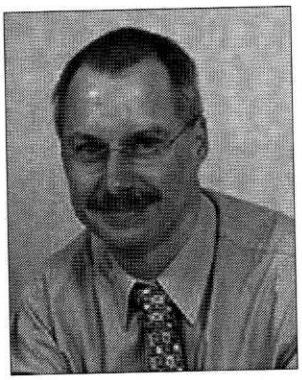
Louise Simard received the David Green Award which is presented to a scientist or researcher who has made a significant contribution to Muscular Dystrophy Canada in the areas of neuromuscular research or the advancement of care of clients with neuromuscular diseases.

Jane Evans received the Dr. John L Hamerton Distinguished Service Award, presented by the Canadian College of Medical Geneticists

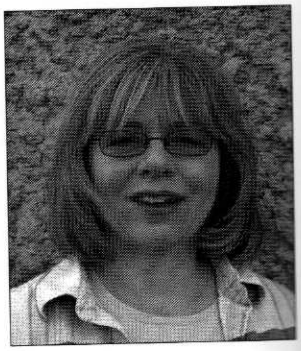
Klaus Wrogemann is spending 6 months in Berlin at the Max Planck Institute for Molecular Genetics

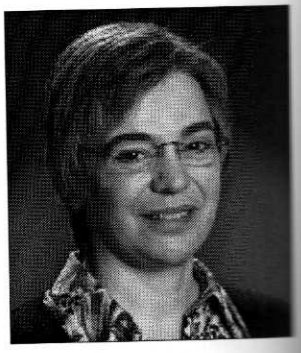
Dr. Albert Chudley received the Founders Award from the Canadian College of Medical Geneticists (CCMG) presented at the annual meeting in September 2008. This award is in recognition of members of the CCMG who have had an outstanding career in medical genetics in Canada or abroad.

Dr. Cheryl Greenberg received the Manitoba Medical Association - Scholastic Award for scholarly activity in the health professions as well as the Michael Wright Award for Community Leadership, the highest honour the Huntington Society can bestow on an individual.

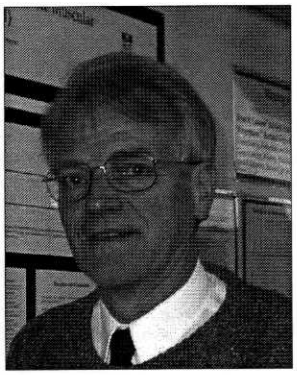

Jim Davie


Leigh Murphy

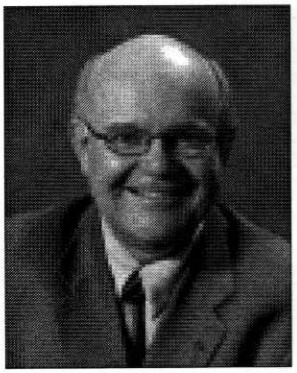

Barbara Triggs-Raine


Louise Simard

Jane Evans



Klaus Wrogemann



Albert Chudley

Cheryl Greenberg

The Biochemistry Department, McGill University

Correspondent: David Y. Thomas

The past year has seen many changes in the McGill University Biochemistry Department. The new buildings of the McGill University Life Sciences Complex (MULSC) - the Bellini Life Sciences Building and the linked Goodman McGill Cancer Centre were opened and you can watch this on You Tube http://www.youtube.com/watch?v=-EtA-BA5K3eQ . This has enabled the department to finally consolidate in a single location and we are already enjoying the benefits. Even in these days of Skype, iChat and Blackberries, there is still a lot to be said for proximity. This expansion has enabled us to repatriate the Molecular Oncology Group - Morag Park, Bill Muller, Alain Nepveu and Vincent Giguère from the Royal Victoria Hospital. Also to bring together the structural biologists Kalle Gehring from rented underground accommodation at La Cité and Albert Berghuis together with Bhushan Nagar and Jason Young. The new Bellini Life Sciences Building contains four thematic groups - Chemical and Structural Biology (Director, David Thomas), Complex Traits (Director, Philippe Gros), Development and Cell Information Systems. Mike Hallett, Director of the McGill Centre for Bioinformatics has also moved his research group to the MULSC, where they have an extensive network of projects and interactions embedding. The increased space that the Biochemistry Department now enjoys has enabled us to expand our graduate program and we now have 135 talented and happy graduate students registered at present.

New members of the Biochemistry Department are Josée Dostie who is working on chromatin conformational capture, Joe Teodoro, on tumour angiogenesis and apoptosis, Thomas Duchaine from Craig Mello's laboratory working on miRNA, and Julie St-Pierre from Bruce

Spiegelman's lab at Harvard working on cancer and metabolism. In 2009 we will also welcome as a new member of the Biochemistry Department Rod McInnes, former director of the CIHR Institute of Genetics. Rod will be the new director of the Lady Davis Institute, Jewish General Hospital, McGill University.

On a sadder note, our distinguished colleague

Annette Herscovics

Professor Annette Herscovics, FRSC, died on September 6, 2008 after a courageous battle with cancer. The Department held a celebration of Annette's many achievements in science. She was a founder of the discipline that we now term "glycobiology" and also an accomplished violinist. This poignant celebration was held in the atrium of the new Bellini Building of the MULSC, and was attended by her many friends, colleagues, fellow orchestra members, and her son Philippe, his wife Jackie and their three children, of whom Annette was the proud and adoring grandmother. (http://reporter.mcgill.ca/2008/09/professor-annette-herscovics-1938-2008/)

A unique assembly of four 4 chairs of the McGill Biochemistry Department; from left to right Angus Graham, Phil Branton, David Thomas and Rose Johnstone.

Former chair of the Biochemistry Department, Professor Angus Graham, FRSC (Chair 1970-1980) also passed away in 2008. Angus was invited to McGill from the Wistar Institute and stick-handled the hiring of our first molecular biologists. In typical Angus fashion, he had already organized a celebration for this sad occasion that was attended by friends and family and we had a wee drop of Scotch in his fond memory.

Recent notable awards to the members of the Biochemistry Department were to Nahum Sonenberg, elected as a Fellow of the Royal Society of London, as a Foreign Honorary Member of the American Academy of Arts and Science, and the 2008 Gairdner Award in Health Sciences. He also was the awardee of the CSBMCB Roche Diagnostics award in 2007. Philippe Gros was awarded the Prix Wilder-Penfield of Québec for his many contributions to our knowledge of host resistance. Morag Park has been installed as the new director of the CIHR Institute of Cancer Research, replacing the indefatigable Phil Branton who is on a well-deserved sabbatical at Cancer Research UK in London. Morag Park and Michel Tremblay were both elected as Fellows of the Royal Society of Canada. Thomas Duchaine, Nahum Sonenberg, Michel Tremblay, Morag Park and Mike Hallett were all honoured by the magazine Québec-Science for making some of the "top ten" important discoveries of the year. Maxime Bouchard, Albert Berghuis, Bill Muller, Arnim Pause and David Thomas all renewed their Canada Research Chairs. The CIHR new investigator awards and FRSQ chercheur-boursier awards to Josée Dostie, Thomas Duchaine, Joe Teodoro and Maya Saleh brings the number of faculty in our department who have external salary awards to 23 out of 33 full and jointly-approved members. Albert Berghuis was promoted to full professor and Imed Gallouzi to Associate Professor this year.

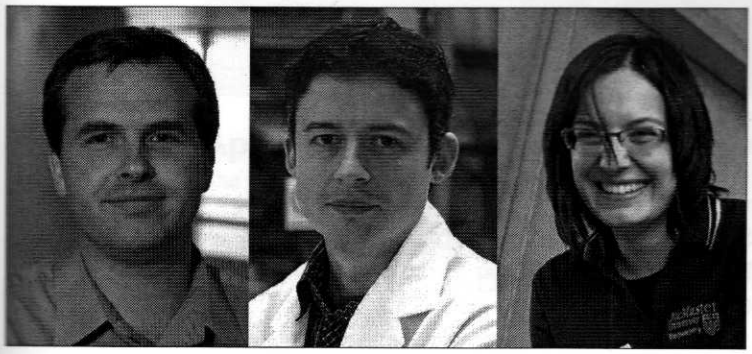
As with many, probably all, research departments, we are concerned with the continuing support and maintenance of our CFI acquired equipment. Some relief for this came from an FRSQ team award to the Chemical and Structural Biology Group. The team "Groupe Axé sur la structure des proteins" is directed by Kalle Gehring, and has participants from the Université de Sherbrooke, UQAM, Concordia and Université de Montréal.

McMaster University

Department of Biochemistry and Biomedical Sciences

Correspondent: Alba Guarné

In 2008, we have welcomed three new Assistant Professors. **Jonathan Draper**, a joint appointment with the Department of Pathology and Molecular Medicine, will develop a research program concerned with the genetic mechanisms that govern lineage determination within human embryonic stem cells. **Nathan Magarvey**, a joint appointment with Chemistry, will develop a research program in understanding the action and molecular mechanisms of bioactive small molecules produced by bacteria. **Felicia Vulcu**, a home-grown biochemist from McMaster, is covering for Michelle



From left to right Nathan Magarvey, Jonathan Draper, Felicia Vulcu

Macdonald, our Associate Chair of Undergraduate Studies, while she is on parental leave.

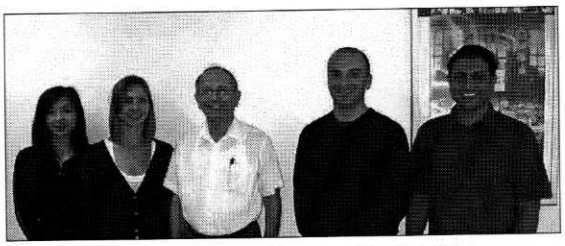
The rest of our Faculty continued to thrive. **David Andrews** published a seminal paper in Cell that lays bare the key steps in programmed cell death. **Gerry Wright** and **Murray Junop** joined efforts to understand a novel mechanism of rifamycin antibiotic resistance (PNAS, 105(12)). **Karen Mossman**, in collaboration with **Ali Ashkar** (Pathology & Molecular Medicine), published a cutting edge paper in the Journal of Immunology. **Richard Epand** published in JACS how bacterial membranes can function as predictors of animicrobial potency. **Mick Bhatia** and **Sheila Singh** (Stem Cell and Cancer Research Institute) were named Canada's Top 40 under 40 this year. **John Capone** was honoured with the Spirit of Ontario Award presented by the National Congress of Italian Canadians. **Jonathan Draper** was awarded a Canada Research Chair (Tier 2) in Human Stem Cell Biology. **Brian Coombes** was named the recipient of the 2007 Most Promising Researcher Merit Award from the Public Health Agency of Canada and was awarded an Early Researcher Award from the Ontario Ministry of Research and Innovation.

Our Faculty members also continued to succeed at securing research and infrastructure funds. **Gerry Wright** and **Eric Brown** were awarded a grant from the Canadian Cystic Fibrosis Foundation. **Gerry** also successfully headed a New Emerging Teams grant on Antibiotic Adjuvants including **Lori Burrows** and **Murray Junop**. **Brian Coombes** and **Murray Junop** secured funds from NSERC. **Dino Trigatti** was awarded a 5-year Heart and Stroke Foundation of Ontario Program Grant and **Ray Truant** was awarded grants from the CHDI and the Krembil Foundation. The Macbiophotonics Facility has now two new life cell imaging systems (http://www.macbiophotonics.ca). The Canadian Centre for Electron Microscopy has two new high-resolution transmission electron microscopes and was officially inaugurated last October by the President and CEO of the Canada Foundation for Innovation (http://ccem.mcmaster.ca). The build-out of the

From left to right Prof. Mo Elbeswati (VP Research, McMaster University), Dr. Eliot Phillipson, President and CEO of Canada Foundation for Innovation), Prof. Gianluigi Botton (Scientific Director of the CCEM), Prof. Peter George (President, McMaster University)

new Centre for Microbial Chemical Biology, spearheaded by **Gerry Wright**, is ahead of schedule and researchers are scheduled to move into the new facilities this spring.

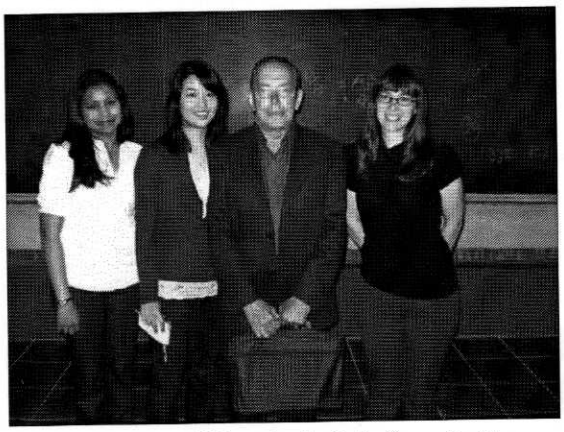
In 2008, our graduate community continued to grow. 24 new students enrolled in our program and our total graduate student population is now 114 students, more than twice what it was 6 years ago. A total of 32% of our graduate students were funded by rather competitive scholarships from NSERC, CIHR, Cystic Fibrosis Foundation, Heart and Stroke Foundation, Fred & Helen Knight Enrichment Fund, Canadian Breast Cancer Foundation and OGS, a testament to the exceptional quality of our students. **Soumaya Zlitni** received the 2008 Thomas Neilson Award, the highest award offered by our Department. **Chand Mangat** (PhD), **Chris Delvecchio** (PhD), **Carly Desmond** (MSc) and **Grace Lou** (MSc) were the recipients of the 2007-08 Karl B. Freeman Awards that recognize students deemed to have presented



From L to R: Grace Lou, Carly Desmond, Dr. Karl B Freeman, Chris Delvecchio, Chand Mangat

the most outstanding graduate seminars of the year. Nine Ph.D. candidates successfully defended their theses: **Tim Bowes** (Gupta Lab), **William Chiuman** (Li/Higgs lab), **Ryan Noyce** (Mossman lab), **Morag Stewart** (Bhatia lab), **Jaeok Park** (Gupta lab), **Mark Pereira** (Brown lab), **Victor Pau** (Yang lab), **Rahul Das** (Melacini lab) and **Felicia Vulcu** (Andrews lab). Another 17 students graduated with M.Sc. degrees.

The postdoctoral fellows in the Department, the Institute for Infectious Disease Research and the Stem Cell and Cancer Research held a one-day Career Development Workshop. The event, covering careers in academia and government and how to give a successful job talk, was a great success. Our Biochemistry and Biomedical Sciences Graduate Association maintained a very active profile this year. Dr. David Hopwood, a renowned leader on antibiotic production in soil bacteria, was the 2nd Annual Student Invitational Speaker. The BBS-GSA also kept us having fun with a Snow Sculpture Contest (conquered by the Ortega-Zhorov-Epand Team), the 3rd Annual Spring Cleaning Clothing Drive Challenge (a smashing



From L to R: Vanessa D'Costa, Stephanie Au-Young, David Hopwood, Emma Griffiths

victory of the Wright Lab), the 2nd Annual Photo Scavenger Hunt where the Truant Lab took top honours, the ever-popular Pumpkin Carving and Costume Contest dominated by the Burrows Lab and a Holiday Party that was a fantastic way to finish off the year!

Welcome BBQ

In September, we hosted the traditional "Welcome Barbecue" to welcome back all of our students including 103 new students to level II of our program. In October, the Department hosted a "Twist and Turns" event for the seventh year, as part of the Engineering and Science Olympics. About 1,000 high school students from across Ontario converged on campus to participate in a variety of events to compete for McMaster University entrance awards.

NOTE: Louis Delbaere sadly passed away in October 2009. The Canadian and world-wide crystallography community lost a colleague, a friend and a spokesman on the world stage. A.G.

Université de Montréal

Département de Biochimie

Correspondent : Christian Baron

Appointments.

The year 2008 was characterized by the appointment of a new Department Chair as of June 1st (**Christian Baron**, formerly at McMaster) and the Bioinformatician **Nicolas Lartillot** (formerly Montpellier, France) joined the Department at the same time as Assistant Professor. These hires reflect the strength and future development of the Department with emphasis on structural biology/molecular design and bioinformatics/genomics.

Operating and infrastructure funds.

In competitive times members of the Department had a lot of success at recent operating grant competitions. In the spring 2008 competition, no less that five groups received CIHR operating funds (**Jacques Archambault**, **Pascal Chartrand**, **Serguei Steinberg**, **Nathalie Grandvaux** and **Luis Rokeach**) and awards for **Jacques Drouin** and **Pascale Legault** were announced as result of the fall 2007 competition. Examples of other operating grant awards are that for **James Omichinski** from the NCIC and that for **Natalie Grandvaux** from the CBCRA. Members of the Department played key roles in the development of three institutional CFI initiatives that are currently under consideration and CFI leader's opportunity funds were awarded to **Christian Baron** and **Gerardo Ferbeyre.** A major renovation project is already underway as a result of these awards and others are planned in future linked to the initiatives that are under consideration.

Research highlights.

The group of **Stephen Michnick** described a novel method to monitor protein-protein interactions in living cells in *Science* and they also co-authored an important publication on the epigenetic control of transcription in *PLoS Biology*. **Nicolas Lartillot**, newly appointed as an Assistant Professor, had an excellent start crowned by co-authoring a publication on the early evolution of life in *Nature.*

Awards.

Gerardo Ferbeyre received the Prix André Dupont from the Club de recherches cliniques du Québec (CRCQ), acknowledging the potential for clinical applications of his research in the area of cancer biology. G. Ferbeyre is also a senior fellow supported by the FRSQ as of this year, which further underlines his achievements in research. The research of **Alain Moreau** is in the area of genetically determined musculoskeletal disorders and he received the Génome Québec price "Biotechnology of tomorrow" acknowledging his excellent track record of pursuing innovative approaches.

Teaching activities.

The Université de Montréal was the first one in Canada that established Bioinformatics undergraduate and graduate programs since 2000, and this effort was spearheaded by **Gertraud Burger.** As a consequence, the first Bioinformatics Ph.D. student (**Emmanuelle Permal**) graduated from this program in 2008 and she conducted her research on the prediction of RNA structures in the group of **François Major** (associate member if the Department). Bioinformatics research is also at the heart of the

annual international Bioinformatics Symposium in Memory of Robert Cedergren that is integrated into the CIHR-funded Bioinformatics training program. At the undergraduate level, we have started a major reform of the Biochemistry program. This project is being conducted in close collaboration with our very active undergraduate student society, a collaborative approach we will continue in future.

Ryerson University

Department of Chemistry and Biology

Correspondent: Roberto Botelho

Our first report to CSBMCB will serve to introduce our Department. The Dept. of Chemistry and Biology encompasses multi-disciplinary research and teaching interests. As of 2008, the research interests in Chemistry were enriched in macromolecular and synthetic chemistry and research on the properties of surfaces, interfaces and materials. The research interests in Biology enjoyed strengths in ecology and environmental biology, microbiology and biofilms, virology, cellular microbiology, biochemistry, development and cell biology. The breadth and variety of research interests creates a unique environment that permits cross-pollination of research ideas and an open-concept milieu for learning and teaching.

Despite our diversity, there is a core group whose research fits neatly within the realm of Biochemistry and Molecular and Cellular Biology.

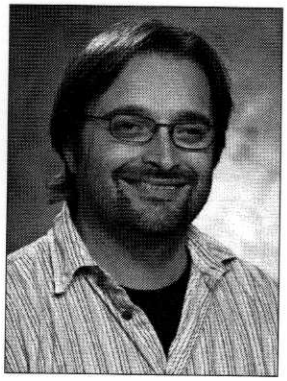
Mario Estable investigates the molecular biology and biochemistry of retroviruses, particularly HIV-1. He is interested in the effects of environmental conditions on retroviral gene mutations and their role in human disease and gene transcription. Current projects are focused on the characterization of the host protein MCEF that appears to repress HIV-1 replication and the molecular characterization of the MFNLP HIV-1 sequence that binds transcription factors.

Debora Barnett Foster is the Director of the Molecular Science Graduate Program and investigates host-pathogen interactions of diarrheagenic *E. coli* including the molecular basis of pathogenesis, the impact of environmental stress on pathogen virulence, and the development of antimicrobial treatment and prevention therapies. Her laboratory is currently investigating the effect of various ingestion stresses on the expression and function of virulence factors in enterohemorrhagic and enteropathogenic *E. coli* using DNA microarray, real time PCR and mutagenesis. A second area of interest is the role of DNA repair mechanisms in these pathogens after exposure to acid stress and the effect of antimicrobial peptides in inhibiting acid-induced DNA repair.

Kim Gilbride is our current Biology Program Director and a molecular microbiologist. She uses molecular techniques to study bacterial communities in wastewater. She is currently designing molecular assays for rapid detection of microbial pathogens in drinking water sources and to better describe the protozoan community in wastewater treatment systems. Her laboratory is also interested in examining and understanding the effect of pharmaceuticals on the nitrification process driven by bacteria in wastewater secondary treatment systems. Please see the Can. J. Microbiol. (2007) for a recent example of her work.

Marie Kileen is concerned with understanding the mechanisms and molecules that govern the guidance of cell and axon migrations during development. She uses the microscopic, non-parasitic nematode, *Caenorhabditis elegans*. She has been conducting a classic genetic screen to find new mutants that enhance the defects of UNC-5, in guidance of motor neurons. UNC-5 is one of the receptors for the axon guidance cue UNC-6/Netrin. The mutants are being detected by visually screening the animals under a dissection microscope with epifluorescence. Several candidates have been found and are being characterized. She recently published an insightful review in *Dev Biol.*, 2008.

John Marshall is an analytical biochemist interested in the identification and characterization of extracellular proteins and receptor complexes using biochemical assays and mass spectrometry. He has published and analysed data sets of blood peptides and proteins using mass spectrometry. His laboratory recently described the Live-cell Affinity Receptor Chromatography (LARC) that uses ligand coated microbeads to capture an activated receptor-complex from the surface of living cells and identify them using mass spectrometry (Anal. Biochem., 2008). Dr. Marshall is a driving force for proteomics in Canada and wishes to remind one and all about the impending HUPO meeting in Toronto Sept 26-29th, 2009.



Dr. Robert Botelho

Finally, yours truly, **Roberto Botelho**, was recruited in 2008. I am interested in the regulation and function of phosphoinositides, which modulate a myriad of processes including membrane trafficking, the cytoskeleton and organelle identity. I will use a combination of yeast and mammalian cell culture to study how these lipids are synthesized, degraded and interconverted and how they regulate downstream events. I obtained my Ph.D. from the Dept. of Biochemistry at U. of Toronto with Dr. Sergio Grinstein and undertook my Post-doctoral studies with Dr. Scott Emr, initially at UCSD and then at Cornell University. During my post-doctoral studies, I identified a protein complex that conjoins an antagonistic phosphoinositide kinase and phosphatase to regulate phosphatidylinositol-3,5-bisphosphate (Mol. Biol. Cell, 2008). In turn, this phosphoinositide regulates the organelle properties of the late endocytic pathway in yeast and mammalian cells.

While our department is relatively small, we are in a dynamic phase of growth. We are currently searching for candidates with research and teaching interests in molecular genetics and/or molecular evolution/ecology. As part of our growth, we are seeking to form research and teaching connections with other Universities and Institutions.

We have a thriving Undergraduate program with specialties in biochemistry and molecular and cellular biology. Our enrollment has increased 60% from 2005 to 2008 and is expected to keep growing. Similarly, in 2006, the M.Sc graduate program in Molecular Sciences was established and our first cohort of graduate students are graduating. The program has been successful and we are now developing a proposal for the Ph.D. program to start in 2011.

Developing and expanding our research core in biochemistry and molecular and cell biology is an important focus for the Department and the University. We most definitely look forward in connecting and collaborating with members of the Canadian Society of Biochemistry and Molecular and Cellular Biology.

University of Saskatchewan

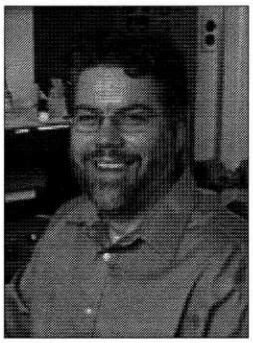
Department of Biochemistry

Correspondent: Yu Luo

Highlight:

Louis Delbaere is a protein crystallographer who joined the Department in 1979. He is a Tier 1 Canada Research Chair in Structural Biochemistry and this CRC was renewed for a seven-year term in 2008. Also in 2008, he was appointed for a six-year term to the Executive Committee of the International Union of Crystallography. Dr. Dealbaere also heads an intramural Molecular Design Research Group.

New faculty:



Dr. Scot J. Stone

Dr. Scot J. Stone joined our department in 2007. His group is focused on understanding the basic mechanisms of neutral lipid synthesis and storage. Of particular interest are the class of triglycerides and the roles played by diacylglycerol acyltransferases.

Simon Fraser University

Department of Molecular Biology and Biochemistry

Correspondent: Christopher Beh

This year was relatively quiet except for hires associated with new initiatives being developed. However, with the looming possibility of a $42 million cut in funding to British Columbia's public universities, the SFU Faculty of Science and our Department anxiously await how this might impact our programs.

Department highlights

We congratulate **Dr. David Baillie** for the renewal of his Tier 1 Canada Research Chair in genomics, and during the past year there were also several promotions. **Dr. Jenifer Thewalt** was promoted to full professor for successes in her work on membrane structure and dynamics. **Drs. Mark Paetzel** and **Christopher Beh** were both promoted to associate professor with tenure. Dr. Paetzel's research program involves the crystallographic study of protein targeting and translocation across membranes, while Dr. Beh's group examines cholesterol transport and lipid signaling during cell polarization.

New faculty and teaching programs

In 2008 we welcomed several new faculty to our ranks. **Dr. Jonathan Choy** joined us from Yale University, and he brings to our Department further expertise in immunology. Dr. Choy's research focuses on the regulation of T cell responses by the endothelium, and how T cell activation impacts blood vessel structure and function. His work has direct implications for transplant rejection and immune-involved vascular diseases. This research complements the work done by **Dr. Jamie Scott**, who holds a Tier 1 Canada Research Chair for her studies of peptide antigen recognition by antibodies, particularly as it pertains to HIV-1 vaccines. As part of a new interdepartmental BSc program in genomics being developed at SFU, four half-time faculty positions were offered to scientists from the Michael Smith Genome Sciences Centre (operated by the BC Cancer Agency). **Drs. Sharon Gorski, Steven Jones**, and **Robert Holt** have active teaching roles in the new program administered by the MBB Department, and **Dr. Angela Brooks-Wilson** is involved through her appointment with the School of Kinesiology. These positions further strengthen SFU's academic and research programs in genomic sciences.

We are also pleased to welcome several new associate faculty including: **Drs. Tim Beischlag** and **Gratien Prefontaine** from the Faculty of Health Sciences; **Drs. Tom Claydon** and **Peter Ruben** from the School of Kinesiology; and **Dr. Hogan Yu** from the Department of Chemistry. These new associates, as well as our new hires, add to our ever-increasing research diversity.

University of Toronto

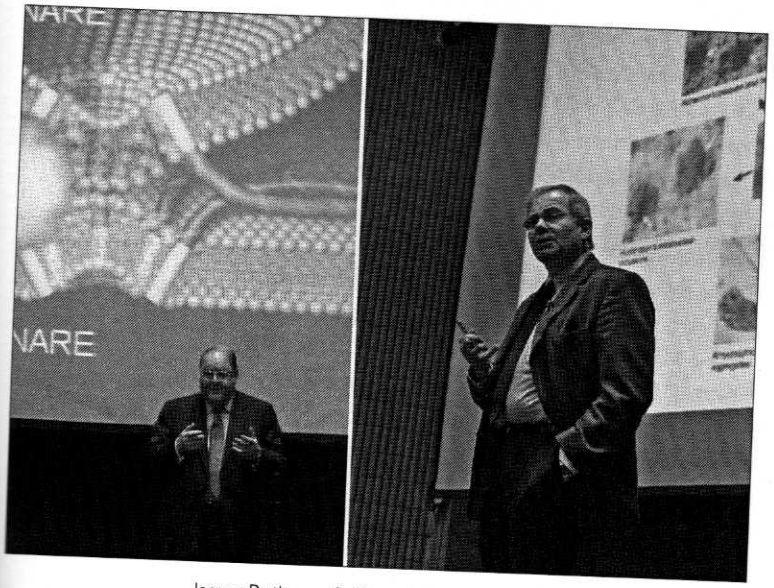
Department of Biochemistry

Correspondent: David Williams

About 200 current and past U. of T. Biochemists gather to celebrate 100 years of Biochemistry at U. of T

Events - What a Century!

The big news from the Department of Biochemistry at U. of T. this year was the celebration of our 100th Birthday. The Department was founded in 1907-08 by Professor Archibald Byron Macallum, the first department dedicated to this discipline in Canada, and amongst the very first in the world. Over the past century, we've graduated over 350 Ph.D. and 370 Masters degree students and teach thousands of undergraduate life science and medical students. Growing from just two professors in 1908, the current Department is thriving with 60 faculty members and roughly 200 graduate students and post-doctoral trainees. Noted for its highly productive research programs, the Department has published over 1000 papers in the past five years alone.



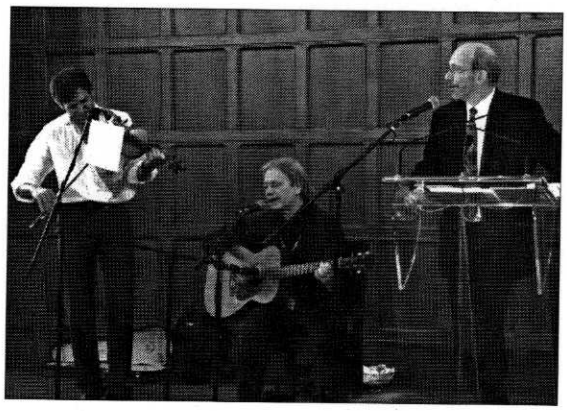
James Rothman (left) and Gregory Petsko speak at the 100th Anniversary Symposium

Between May 28th - 30th, 2008 Departmental alumni spanning the past five decades joined with current faculty, staff and trainees to celebrate our centennary with a 100th Anniversary Symposium. Kicked off by a most stimulating **Connell Centennial Lecture** by **James Rothman**, Columbia University. The program featured a **Theo Hofmann Lecture** by **Gregory Petsko**, Brandeis University, and talks from past and current Department members who spoke within the major scientific themes of the Department: Proteins, Molecular Information Transfer, and Molecular Cell Biology (for program info. see: **http://biochemistry.utoronto.ca/news/100_birthday_program.html**). Interspersed among the scientific talks were Historical Vignettes of the Department highlighting "The Early Years", the "1960's Expansion Phase" and "Modern Times", presented by Marian Packham, George Connell and Peter Lewis, respectively.

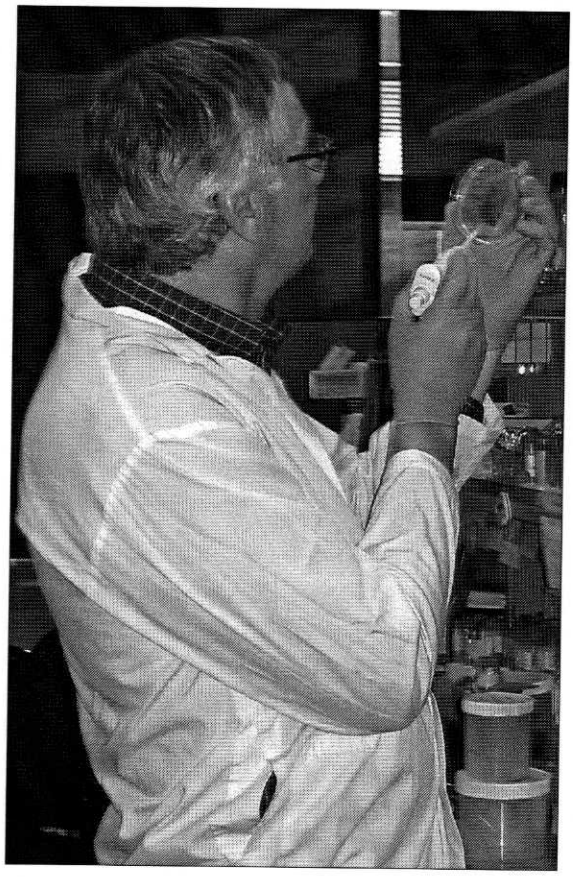
Current and past chairs of the Department dedicate a bronze plaque commemorating Archibald Macallum and our 100th Anniversary

Other highlights of the Symposium were the annual trainee poster session (see Graduate Studies below), a gala banquet at Hart House (featuring our popular Biochemistry Idol Contest and songs by John Glover and David Williams about student and faculty life **biochemistry.utoronto.ca/graduate_studies/biochem_student_videos.html**) as well as a host of very enjoyable opportunities for

Enjoying the 100th Anniversary Gala



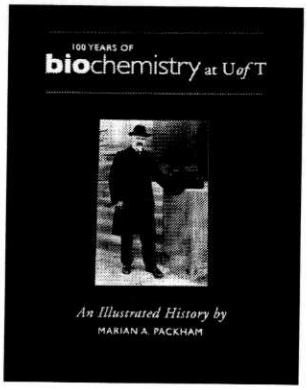
Mark Glover, John Glover and David Williams entertain at the Gala



Reinhart Reithmeier is back to picking colonies

past and current members of the Department to meet and swap stories. For a photo gallery of the Event, please visit our website at: **http://www.biochemistry.utoronto.ca/news/100_Symposium**

The Symposium was also the perfect venue for the installation of bronze plaques commemorating our centennary as well as the launch of Professor Emeritus Marian Packham's new book on the many achievements of the Department entitled, "100 Years of Biochemistry at the University of Toronto: An Illustrated History".



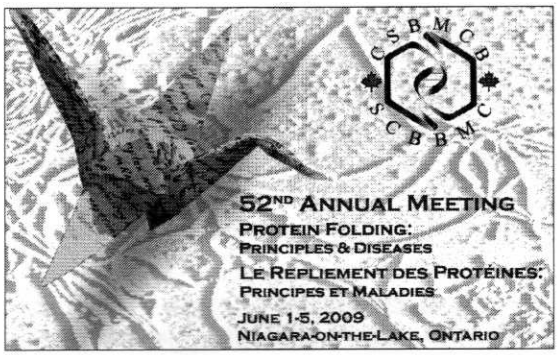
Marian Packham's Illustrated History of the Department

Other events this year included our ever-popular **Annual Ski Day** and **Annual Golf Day** as well as our first-ever **Biochemistry-Immunology Challenge Baseball Game**, all of which are organized by graduate students. We may have lost this year but the bats are already warming up for a rematch! Photos can be found at: http://biochemistry.utoronto.ca/news

Faculty News

Chair Reinhart Reithmeier is on a well-deserved mini-sabbatical as he enters the half-way point of his second term. Reinhart is working in the laboratory of Natalie Strynadka in the Blood Center at UBC learning to express and crystallize membrane proteins in bacteria with the goal of solving the structure of a bicarbonate transporter. Reinhart completed his Ph.D. in Biochemistry at UBC in 1976, so after 30+ years of career development, he finds himself back at a bench where he started.

David Williams has been very active as the new Vice President of the CSBMCB. He has been working on a brand-new Society website which features the ability to pay dues online, produces stylish e-Newsletters, and permits online meeting registration and abstract submission. David, along with **Hue Sun Chan**, is also organizing the 52nd Annual Meeting of the CSBMCB with the theme of "Protein Folding: Principles and Diseases". It will be held at the White Oaks Conference Resort in Niagara-on-the-Lake from June 1-5, 2009. The objective of this Meeting is to apply mechanistic principles of protein folding and misfolding to protein misfolding disease models as a means to develop novel approaches to preventing or



Visit **http://www.csbmcb.ca** for Meeting information.

treating such diseases. The Meeting will feature world renowned speakers describing their work in the areas of Mechanisms of Protein Folding and Misfolding, Theoretical and Computational Approaches to Protein Folding, Protein Folding in the Cell, Protein Dynamics and Disorder, Cellular Responses to Protein Misfolding and Protein Misfolding in Aging and Disease. There will also be a Featured Workshop on Prion Protein Misfolding sponsored by PrionNet and the Alberta Prion Research Institute.

Also organizing a major meeting this year is **Walid Houry** who, together with Joaquin Ortega of McMaster University is running the 8th International Meeting on AAA Proteins to be held in Toronto, July 12 – 16, 2009. The website for the conference is http://www.utoronto.ca/aaaplus/

Amu Sarkar was the honourary president of the Fourth International Conference on Metals and Genetics (ICMG) at the Université Paris Descartes, France, July 21 to 24, 2008. The ICMG was started in 1994 by Amur as a way to bring together top professionals from around the world who specialize in the research and treatment of metal-caused diseases. Jean-Marie Lehn, winner of the 1987 Nobel Prize in Chemistry and Professor at the College de France, was patron of the 2008 ICMG. The Conference focused on the broad discipline of metals and genes, related diseases and their therapeutics, the role of the metals in nutritional supplementation, as well as themes related to the environment, characterization of proteins and systems biology. Participants came from 22 countries around the world. The fifth ICMG will be held in Kobe, Japan, 19 to 23 September, 2011. Amu has also been invited to join the Editorial Board of a new journal "Metallomics" launched by The Royal Society of Chemistry, UK. The first issue started in January, 2009.

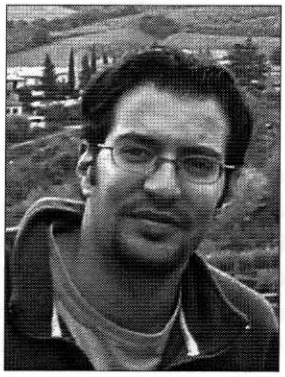
David MacLennan was appointed to the Order of Ontario in the Fall of 2008 with the investiture taking place Thursday, Jan 22, 2009. David was honoured for his contribution to the field of science and was praised as an international expert in biochemistry, genetics and physiology of muscle function. The University of Toronto selected **Marian Packham** for the prestigious Arbor Award for outstanding volunteer service. This award celebrates university volunteers who inspire others through their exceptional work. **Sergio Grinstein** was chosen as the Davson Award winner of the American Physiological Society. This is the highest award, given by the Cell Physiology section. **Khosrow Adeli** was awarded the 2008 Merck Senior Investigator Award, by the Canadian Lipoprotein Conference, at their annual meeting held October 2-5, 2008, Whistler, BC. This national award recognizes annually a senior investigator in the field of lipid and lipoprotein metabolism who has made outstanding contributions to the field of research both nationally and internationally. It recognizes major advances made by Dr. Adeli's laboratory in elucidating the molecular mechanisms linking fructose-induced insulin resistance and the development of cardiovascular complications. Finally, **Morris Manolson** received the CIHR-Institute for Gender Health/Ontario Women's Health Council Senior Investigator Award as well as the CIHR-IMHA Quality of Life award.

Appointments

We are very pleased to welcome three new Assistant Professors to the Department.

Trevor Moraes

Trevor Moraes will arrive April 1, 2009 following his postdoctoral work with Natalie Strynadka at UBC. The primary focus of his research will be on protein and ion translocation machineries within the membranes of pathogenic bacteria. In addition to the structural and biochemical characterization of these transport system components, he will examine the mechanisms that facilitate the proper localization, insertion and assembly of these membrane protein complexes.



Alex Palazzo

Alex Palazzo will be joining us July 1, 2009. Alex did his Ph.D. at Columbia and is currently a postdoc with Tom Rapoport at Harvard. The focus of his research is to determine how the nuclear export, cytoplasmic transport and subcellular distribution of mRNA contributes to the regulation of gene expression in mammalian cells. In particular, he plans to investigate how mRNAs, which code for secreted proteins, are exported from the nucleus and targeted to the surface of the endoplasmic reticulum and how these processes contribute to the proper functioning of secretory cells.

Walter Kahr

Walter Kahr, a Scientist at the Research Institute of the Hospital for Sick Children, and an Assistant Professor in the Department of Paediatrics, was cross-appointed to the Department of Biochemistry this year. Walter is one of our own, having obtained his Ph.D. with David Pulleyblank and his M.D. from the University of Toronto in 1994. He completed his Residency in Internal Medicine in 1999 and Fellowship Training in Hematology in 2002. Walter received a Clinician Scientist career award from the Heart and Stroke Foundation and his research focuses on the pathophysiology of inherited platelet disorders.

We've also had some changes in our Departmental office. **Carrie Harber** was promoted to Graduate Program Administrator and she now has help handling our ever-growing grad student population with the hiring of **Carol Gordon** as Graduate Program Assistant. We also bid a fond farewell to **Mike Folinas**, our Administrative Assistant - Finance, and welcomed **Anthoula Vlahakis** who has assumed this position.

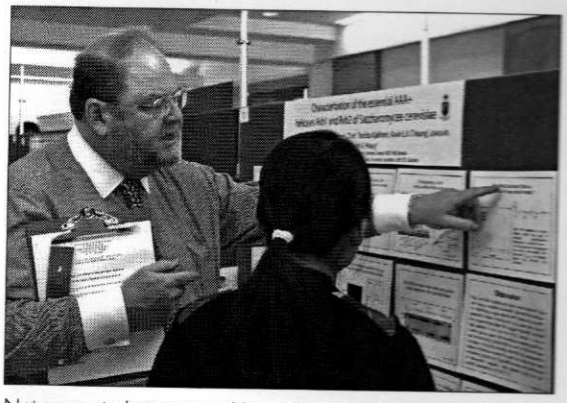
Carrie Harber, Carol Gordon and Anthoula Vlahakis

Graduate Studies

Our fourth annual **Benjamin Schachter Memorial Lecture** took place on November 27th this year. Named in honour of former graduate student Benjamin Schachter, who conducted research in the Department from 1934-1939, this lectureship is organized by our graduate students who select a prominent graduate from our Department. This year, the students welcomed back two of their alumni, **Walter Kahr** and **Carolina Landolt-Marticorena**. Both are clinician scientists, Carol in the Division of Rheumatology at Toronto Western Hospital and Walter in the Division of Haematology/Oncology at SickKids. Their tag-team styled talk, entitled "Remembrance of Experiments Past" chronicled their transition from grad school, to medical school, through residency and finally their careers as clinical researchers. This dynamic duo shared their experience as a scientific couple, the advantages of having someone who understands the challenges and small triumphs, and someone who can accompany you to the lab at all hours of the day, even spending a memorable New Years Eve together in the lab! They also shared their five stages towards financial acceptance, warning to never, ever calculate one's hourly wage. It's their passion for science and discovery that has pulled them through life, juggling the many tasks of clinic duty, research and being parents of twins.

from left, Walter's Ph.D. supervisor David Pulleyblank, Benjamin Schachter's son Dan Schachter, Walter Kahr, Carol Landolt-Marticorena, and Chair Reinhart Reithmeier

During our **100th Anniversary Symposium**, the work of our graduate students and postdocs was featured in a special **Trainee Poster Session**, featuring celebrity judges James Rothman and Greg Petsko.



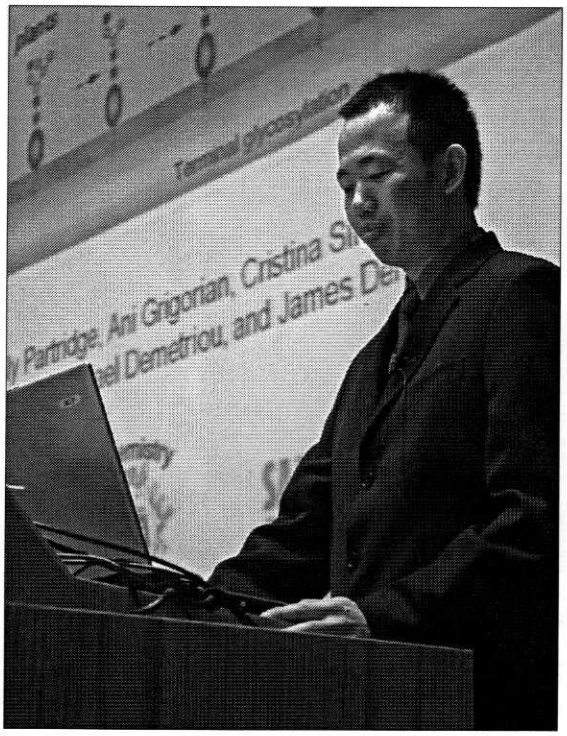
Not many students get a critique of their work from the likes of Jim Rothman, but Jennifer Huen (Houry lab) is up to the challenge

The following students (who receive cash awards) were chosen as poster winners:

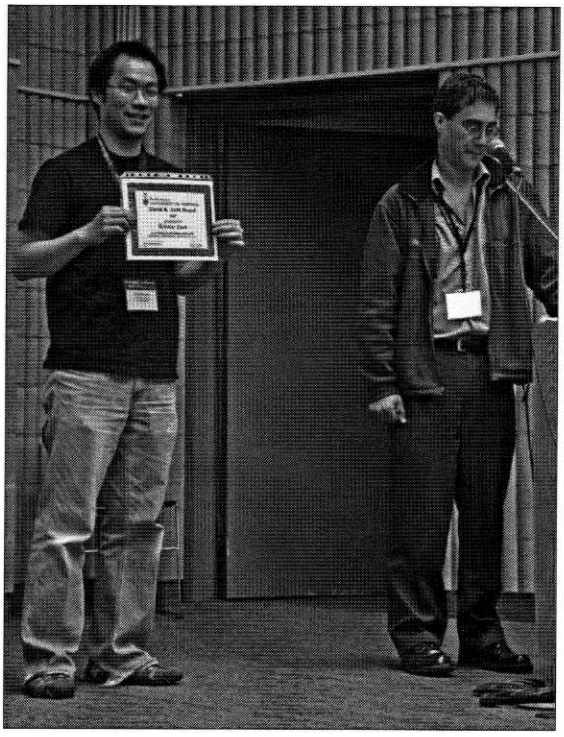
Winners in the Ph.D. category were: **Monica Podkowa** (Attisano lab) "The role of c-Jun N-Terminal Kinase, JNK, in BMP-dependent dendritogenesis"; **Lia Cardarelli** (Davidson lab) "Aberrant Oligomerization of a Head-Tail Connector Protein and Its Role in the Assembly of Bacteriophage HK97";

Lisa Pell (Howell and Davidson labs) "Solution structure of the bacteriophage lambda major tail protein, GPV, insights into viral tail assembly"; **Stephanie Tammam** (Howell lab) "Characterization of PilP, a Protein Required for the Assembly of *Pseudomonas aeruginosa* Type 4 Pili"

Winners in the M.Sc. category were: **Rowan Henry** (Pomès lab) "Molecular Mechanism of Proton Uptake in the D-channel of Cytochrome c Oxidase"; **Mathew Estey** (Trimble lab) "Mitotic Regulation of Mammalian Septins"; **Karen Stanger** (Davidson lab) "Characterizing the role of Nbp2p in the Cell Wall Integrity Pathway of *Saccharomyces cerevisiae*"



Ken Lau presents his Beckman Paper of the Year research at the 100th Anniversary Symposium



Jim Rini, presents the David A. Scott Award to Ronnie

The winner in the postdoc category was: **Tanja Mittag** (Forman-Kay lab): "Multiple phosphorylation in a disordered protein creates a dynamic and largely disordered complex"

Additional graduate awards:

The winner of the ***Beckman Coulter Paper of the Year Award*** for 2007 was**: Ken Lau** (Dennis lab) for his paper "Complex N-glycan number and degree of branching cooperate to regulate cell proliferation and differentiation" Lau KS, Partridge EA, Grigorian A, Silvescu CI, Reinhold VN, Demetriou M, Dennis JW. (2007) *Cell* 129:123-134

The annual ***David Scott Prize*** for outstanding all-round graduate student was awarded to **Ronnie Lum** (Glover lab). Ronnie was selected on the basis of research and teaching excellence and outstanding contributions to the Department and to his fellow students.

Outstanding Teaching Assistant awards went to Costin Antonescu, Lisa Pell and David Tulumello for their exceptional performance as teaching assistants in our BCH371 and BCH 370 lab courses.

The hand of undergraduate Coordinator, Roy Baker, presents TA awards to Costin (left), Lisa and David.

We were also pleased to hear that **Chris Neale** (Pomès lab) received an Exceptional Research Trainee Award from SickKids in 2008.

Congratulations to all winners on their achievements.

University of British Columbia

Department of Biochemistry and Molecular Biology

Correspondent: Roger Brownsey

2008 has proved to be an eventful year for the UBC Department of Biochemistry and Molecular Biology in a number of respects and some of the highlights are briefly outlined here. The most dramatic news is that former Department Head Dr. Christopher Proud, departed in July 2008 to return to the U.K. Chris had joined UBC in May 2005 and after a successful, albeit relatively short term, has returned to the U.K. to join the Institute for Life Sciences in Southampton. We wish Chris and his wife and daughter, Min and Sofie, all the best in their new home and endeavours. The subsequent search for a new Department Head has not yet concluded and your correspondent is still serving as Acting Head at the time of writing this report.

Another departure during the past year came about with the retirement in the summer of 2008 of one of our long-time senior instructors. Dr. Everard Trip had been with the Department as an instructor since September 1978 and had for many years run our large undergraduate teaching laboratory. The teaching lab is now in the very capable hands of a new instructor, Jason Read. Warren Williams is another new full-time instructor to join the tenure-track ranks in the Department. Warren was formerly a graduate student with Dr. Caroline Astell and had been employed as a sessional instructor for the past several years and has fully justified his new appointment with outstanding teaching performances in undergraduate science courses and in the medical student tutorial program. Warren is also a very effective and popular undergraduate advisor and somehow finds time to coordinate our web-based information offerings. The retirement of Dr. Richard Barton, another long-time instructor, at the end of 2007 led to the recruitment of Dr. Scott Covey who has assumed responsibility for the senior undergraduate laboratory and other duties. Scott was formerly a post-doctoral fellow working with Dr. Tim Kieffer (Cellular and Physiological Sciences, UBC) and still maintains some of his diabetes research interests. Scott officially joined the Department as a tenure track Instructor in May, 2008. In view of the continuing popularity and increased enrollments across in the Biochemistry programs, it is hoped that additional instructor positions can be secured in the not too distant future.

We are very sorry to report the passing of former Department member Dr. Gordon Tener. Gordon will be known to many of you and passed away on September 7, 2008 after a brief illness. Gordon was associated with the Department as long as anyone I can recall and throughout his 30-year career at UBC, was an active teacher and researcher who inspired generations of undergraduate, graduate and postdoctoral trainees, many of whom went on to distinguished careers. Gordon graduated in Chemistry from UBC and then obtained his PhD in Biochemistry from the University of Wisconsin at Madison, one of the most active Biochemistry Departments in the USA at that time. Following postdoctoral studies with Professor E. Lederer in Paris, he joined the research group of Dr. Gobind Khorana at the BC Research Council and made significant contributions to the early work on the chemistry and biochemistry of nucleotides and coenzymes, particularly in developing new analytical techniques. It was a testament to Gordon's contributions that Nobel Laureate Khorana records in his own memoirs that Gordon was one of the most creative scientists he knew. In 1960 Gordon joined the Department of Biochemistry at UBC as an Assistant Professor and Career Investigator of the Medical Research Council and remained in the department until his retirement. In his new position at UBC he developed a chromatographic material called BD-cellulose which enabled the separation of nucleic acids. This methodology became widely used, most notably in the Nobel Prize-winning work of Professor Holley, who was the first to sequence a ribonucleic acid. In his own lab, Gordon had great success in separating the

multiple tRNA species involved in protein synthesis and subsequently, in collaboration with Drs. David Suzuki and Robert Miller, he studied the location of the genes for tRNA on the chromosomes of the fruitfly, Drosophila. This was a ground-breaking study as gene location on chromosomes was then in its infancy. Experience with Drosophila further suggested that this organism would be ideal for a study of aging and in typically intuitive style, Gordon decided to focus on the role of superoxide dismutase, an enzyme involved in detoxification. This led to the discovery that increasing SOD expression resulted in increased longevity. Gordon added further to our understanding of aging by recognizing that a number of compounds become progressively limiting with aging and therefore might take on the role of vitamins. Gordon maintained an active role in the Association of Professors Emeriti at UBC for many years and was until recently the treasurer of this organization. It is sad to think that Gordon passed away only days before the dedication of the new "Nobel Parks", located in a peaceful and beautiful part of the UBC campus. This is surely a spot that Gordon would have enjoyed.

Faculty members have continued to excel in many areas of research and during the past year and several have won prestigious awards. Dr. Robert Molday won the Faculty of Medicine 2008 Bill and Marilyn Webber Lifetime Achievement Award, a tribute to his leadership in the field of vision research. Since joining UBC in 1975, Bob has made an impressive number of pioneering discoveries in the fundamental molecular mechanisms of vision and the genetic bases of human diseases that lead to blindness. Natalie Strynadka has also continued her remarkable work in protein structure determination and in recognition has been awarded a National Killam Research Prize to add to her already impressive set of awards. Another senior faculty member, Dr. Stephen Withers, has been re-appointed for a further five-year term as the Gobind Khorana Chair in Biological Chemistry in the fall of 2008, a position held jointly between Chemistry and Biochemistry. In his "spare time", Steve has also led the establishment of the Centre for High-Throughput Biology, a multidisciplinary group of investigators established to develop and apply high-throughput methods of biological analysis. This new UBC Centre is located in the Network of Centres of Excellence (NCE) and Michael Smith Laboratories and will also be the home of our newest assistant professor, Dr. Joerg Gsponer. Originally from Switzerland, Joerg will shortly be arriving from Cambridge University in England, where he has been a postdoctoral trainee for the past few years. Joerg has a background in both medicine and science and is applying computational approaches in combination structural methods to understand fundamental aspects of protein stability and dynamics. His recent publications in Science and Nature suggest a very bright future is in store. Further recognition is in order for other younger recruits to the Department including Dr. Eric Jan (CIHR new investigator award and Michael Smith Foundation of Health Research career investigator award), Dr. Thibault Major (CIHR Operating grant) and Dr. Filip Van Petegem (CIHR new investigator salary award; Michael Smith Foundation of Health Research career investigator salary award). Among students who achieved distinction in the past year, our top graduating student, Timothy Au-Yeung, was also the top-ranked student overall in the Faculty of Science; the result of remarkably consistent performance over four years among a cohort of over 2,000 science undergraduates. For this, Timothy was awarded to BC Governor General's Silver Medal in Science. Another notable award, the Violet and Blythe Eagles Prize for best graduating essay went to Wendy Tay. Finally, the top graduate student award went to Chris Jang, who is supervised by Dr. Eric Jan and who won the Zbarsky award for his seminar entitled" Lost in Translation: The Mechanics of Viral Internal Ribosome Entry Sites".

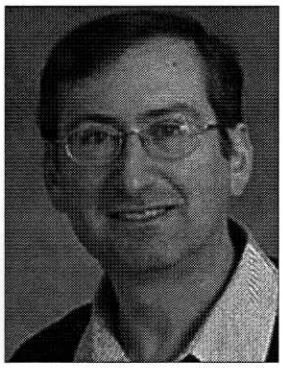
The series of invited speakers has been impressive again in the past year, the particularly notable events being the visits of Dr. David Botstein from the Princeton University who was invited to give the Michael Smith Distinguished Research Lecture. His title was entitled "Genomics, Computation and the Nature of Biological Understanding". In addition, the 2008 Gairdner Symposium involved lectures by two Gairdner International awardees, Dr. Alan

Bernstein ("Global Science for Global Challenges") and Dr. Gary Ruvkun ("The Small RNA Pathways of *C. elegans*"). Among Canadian colleagues who were welcomed to UBC in 2008 were included Moshe Szyf, (McGill), Terry Pearson and Christoph Borchers (Victoria), Warren Wakarchuk , (NRC, Ottawa), Peter Davies (Queens) Nick Shah, Amira Klip and Peter Cheung (Toronto) and Marek Michalak (Alberta). In addition to the formal seminar program, the Department has continued it's recent tradition of monthly poster sessions in which several labs present their recent work, aided by suitable refreshments. The seminar and poster events, together with the annual retreat (held at the Loon Lake Resort over three days) have been orchestrated by the active "events" committee and others, with special thanks to Eric Jan, Leonard Foster and LeAnn Howe. The retreat attracted some 70 participants including teaching faculty and research personnel, with Dr. Brett Finlay as the keynote speaker. A wide variety of excellent research seminars, interspersed with social time was concluded with valuable discussions late into the evening around the campfire. Arguably the best time and place to plan the next great experiment...

University of Waterloo

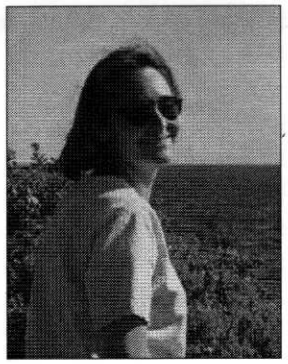
Department of Biology

Correspondent: Bernard P. Dunker

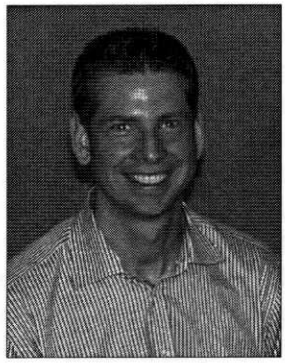


Dr. David Rose

In 2008, the Department of Biology at the University of Waterloo set the stage for a fresh chapter in its evolution, with the selection of a new Chair, and the start of a strategic planning process. After an extensive search, we chose **Dr. David Rose** as our new Chair. David is a structural biologist, who joins us from the Department of Medical Biophysics at the University of Toronto. His research focus is on enzymes involved in protein glycosylation and starch digestion. Other new faculty in the Department over the past year include **Dr. Kim Cuddington**, who was formerly at Ohio University and studies invasive species and biological control, and **Dr. Bryce Pickard**, from the University of Western Ontario, who will be a lecturer for cell and molecular biology, genetics and physiology courses. Last year we hired GBB Inc. to facilitate our strategic planning exercise. A very productive two day retreat for all faculty was held last December, and the process is continuing in 2009 with the goal of having a plan in place by this summer.



Dr. Kim Cuddington



Dr. Bryce Pickard

University of Western Ontario

Department of Biochemistry

Correspondent: Eric Ball

After an eventful few years involving renovation of the Departmental space and attracting a new Chair (Dr. **David Litchfield**), 2008 was relatively calm for the Department.

In terms of awards, Dr. **Murray Huff** won a Faculty Scholar award in recognition of his achievements in teaching and research. Murray is a long time career investigator of the Heart and Stroke Foundation of Ontario. His research deals with lipoproteins and atherosclerosis. Dr. **Hong Ling** of the Department received an Ontario Early Researcher Award - an award to help promising new researchers build their research teams.

Hong is a structural biologist specializing in DNA polymerases.

Over the last several years the Department has established six managed, multi-user core facilities housing equipment for the analysis of protein structure and function, and these have been integrated to create the London Regional Proteomics Centre (LRPC) under the leadership of Dr. **Stan Dunn**. Structural determinations by NMR or crystallography take place at the Biomolecular NMR and Macromolecular Crystallography Facilities, respectively. Mass spectrometry of proteins or peptides for identification or analysis of covalent structure is done at the Biological Mass Spectrometry Laboratory and the MALDI Mass Spectrometry Facility. A Functional Proteomics Facility provides instrumentation for running and imaging 2D gels, automated spot picking, and phosphorimaging. Finally, the Biomolecular Interactions and Conformations Facility is equipped for the biophysical analysis of proteins; instrumentation includes an analytical ultracentrifuge, calorimeters, fluorimeters, and a CD spectropolarimeter. The facilities of the LRPC (http://www.lrpc.uwo.ca) have strengthened our overall research enterprise and enriched our Honors and Graduate Studies programs by providing hands-on training opportunities. The instrumentation and services of the RPC are available to researchers both inside and outside UWO.

RETURN POSTAGE GUARANTEED

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