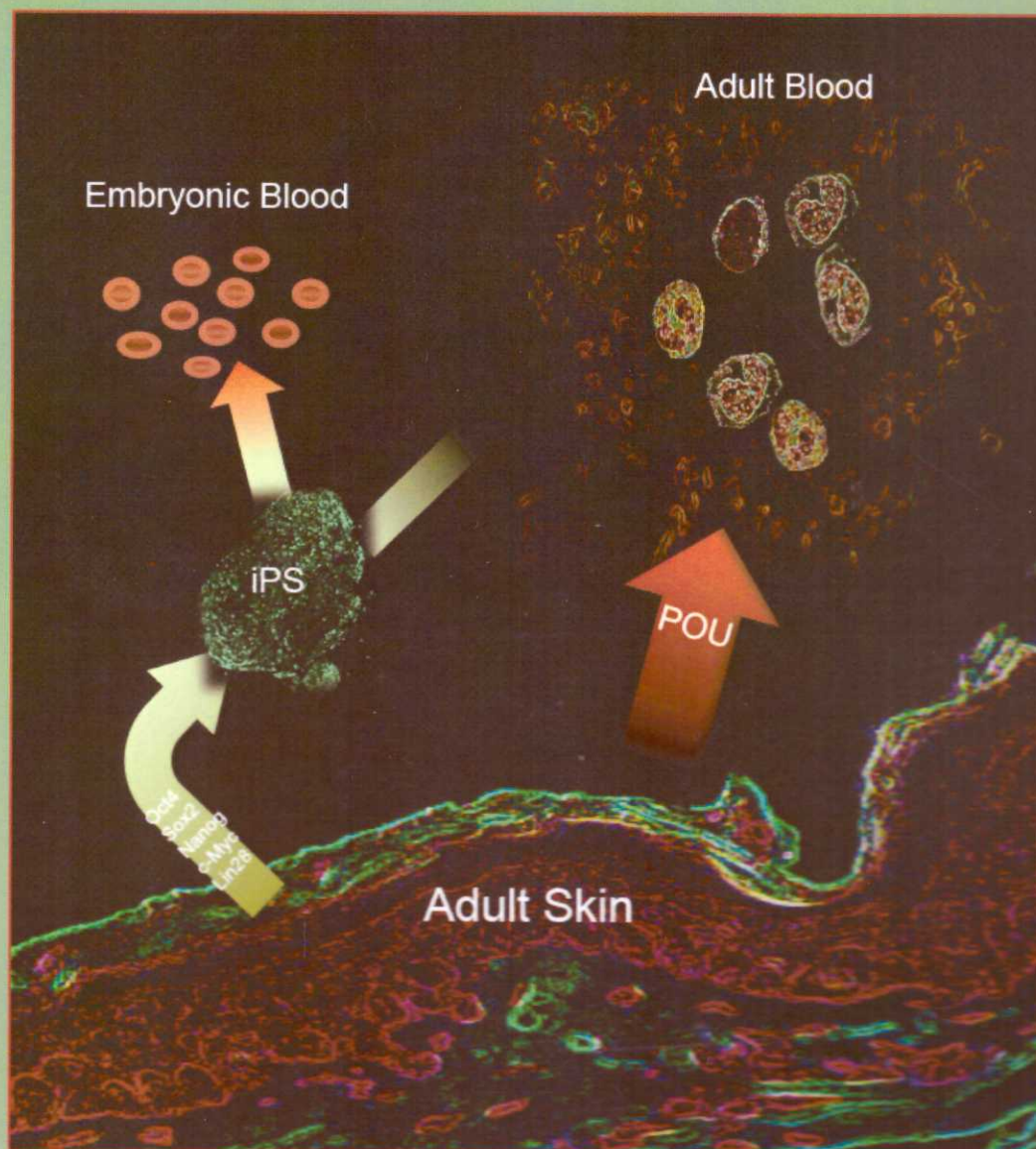


# Bulletin

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



# 2009

[www.csbmcb.ca](http://www.csbmcb.ca)

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# Bulletin



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The executive hard at work at the University of Toronto In November 2009: (left to right): Vincent Duronio (UBC, Treasurer; Alba Guarné (McMaster), Councillor; Reinhart Reithmeier (Toronto), ex officio member; David Williams (Toronto), President; Jean-Pierre Perreault (Sherbrooke), Vice President; Albert Clark (Queen's), Secretary; John Orlowski (McGill), Frances Sharom (Guelph), Councillor; Rob Reedijk (Toronto), Office Administrator; Linda Penn (OCI), Councillor; Josée Lavoie (Laval), Councillor.



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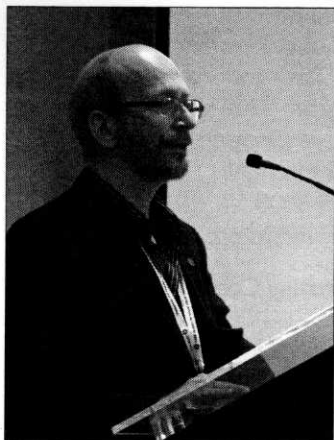
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# President's Report

David Williams



Looking back at Presidents' Reports over the years, I'm struck by recurring themes: low success rates at CIHR, lack of coherent Canadian science policy and the pressing need to advocate for basic research in Ottawa. 2009 was no exception - a low 18% success rate in the September CIHR

competition and the sorry state of Canadian science policy even attracted a scathing editorial in *Nature* [*Nature* 463, 135 (14 January 2010)]. The absence of consistency in planning is evident in the March 2010 Federal Budget. There is welcome additional funding for CIHR and Genome Canada but there is still a remarkable disparity in the level of funding for operating grants versus personnel and infrastructure. Imagine how well we'd fare with a plan that actually provides sufficient operating grants for those individuals who are hired and whose labs are outfitted by the excellent Canada Research Chairs and CFI programs! Likewise the most welcome news of \$45 million to fund a new postdoctoral fellowship program is tempered by the higher \$70,000 stipend level. Although this is intended to attract the very best, the funding would be of greater benefit if pegged at the more typical \$35-45K level, allowing many more opportunities to support this difficult-to-fund category of trainee.

Yet there are some encouraging signs on the policy front. Budget 2010 promises a comprehensive review of R & D funding and our advocacy arm, Research Canada, will be engaged in intensive lobbying to ensure that the health research sector is well represented when decisions are made concerning support for innovation. Research Canada is also "working from within" to groom health

research champions within the House and Senate, their Health Research Caucus, co-chaired by members of the Conservatives, Liberals and Bloc Québécois. Canadian scientists are invited to present cutting-edge research to our politicians as a means to raise awareness of the vital role that health research plays in the lives of Canadians. The CSBMCB is also a sponsor of a new science policy initiative, The Canadian Science Policy Centre, spearheaded largely by research trainees ([sciencepolicy.ca](http://sciencepolicy.ca)). They launched a highly successful Canadian Science Policy Conference in Toronto in 2009 and are already planning the 2010 Conference in Montreal. The Conference brings together scientists, industry, politicians and policy specialists in an effort to develop a coherent vision for science in Canada. I invite you to go to their website and watch some of the videos of their keynote addresses and panel discussions. Even better, perhaps lend your voice to the discussion at the Montreal Conference, Oct. 20-22, 2010.

Despite chronic underfunding and *ad hoc* science policy, Canadian science still manages to perform remarkably well on the world stage. In its annual Performance Ranking of Scientific Papers for World Universities, the Higher Education Evaluation and Accreditation Council of Taiwan has ranked the University of Toronto, the University of British Columbia and McGill University within the top 4 globally for the past three years in a row. The University of Toronto even cracked the top 15, surpassing Yale, Oxford and Cambridge. It seems that Canadian scientists are able to accomplish a great deal with relatively little!

## Annual Meetings

Rather than offering general annual meetings of limited interest to most members, the current CSBMCB philosophy is to host the very highest caliber meetings in focused areas in the style of Gordon Conferences. Such meetings appeal to different groups of our members each

They showcase Canadian science to the world and provide superb opportunities for our trainees to interact with top international scientists. The 2009 Annual Meeting, held from June 1-5 at the White Oaks Resort in Niagara-on-the-Lake, continued this tradition by focusing on Protein Folding: Principles and Diseases. By all accounts it was a great success, running the gamut from basic studies to human protein misfolding diseases, and attracting 155 participants.

For 2010, Joe Casey and co-organizers have put together another superb meeting in the area of Membrane Proteins in Health and Diseases to be held in Banff, April 15-18. A terrific group of speakers has been assembled, led by keynote address from Gunnar von Heijne, Stockholm University. Close to 200 participants have registered and over 100 posters have been submitted, demonstrating keen interest in the topic. Plans are underway for the 2011 Meeting in Mount Orford, Quebec: "Studying RNA, one molecule at a time" and the 2012 Meeting in Whistler, BC on "DNA repair and epigenetic regulation of genome integrity".

Do you find that these Meetings are not sufficiently close to your research interests? Then by all means do something about it! This is your Society - fire off a proposal to the CSBMCB Executive for a Meeting in your area that you know will have broad appeal. There's nothing more exciting than organizing a top notch Meeting where you can assemble your dream team of speakers. Just remember that Meetings are planned about 3 years in advance and that it will be up to you to make it happen (with lots of support from your Society!).

### Communications

Our new website is already proving to be a great asset to our Annual Meetings. Online registration allows us to save money previously charged by the Meeting venue and the online submission system has worked very well in collecting abstracts, allowing participants to view and edit abstracts in advance of the Meeting and automating output of abstracts, poster list and poster schedule to the Program Book.

The website also allows for online membership renewal, permits members to search for one another and to connect via e-mail and for the distribution of our periodic newsletters. Please take a moment to update your personal profile and upload a stunning photo of yourself. Keeping our database of members current is an ongoing challenge. As you'll see in the automated membership renewal e-mails that you are receiving, we are asking ALL members, whether dues-paying or free emeritus, postdoc and student members, to login to renew your memberships annually and update your profiles. For those who do not pay dues, this is the best vehicle we have to confirm that you remain active members of the CSBMCB.

Thanks to Councillor John Orlowski for reinstating eLink. John gathers up diverse items of interest whether it be political or financial news or intriguing scientific gossip, and delivers it in his unique and engaging style. This is a time-consuming task for John who manages it while chairing the Physiology Department at McGill. To assist him in this undertaking, feel free to send items or bring things to his attention. We really appreciate these eLinks John - please keep them coming!

### CSBMCB Awards

The financial downturn has resulted in the withdrawal of support by Merck-Frosst and Roche for our flagship awards that recognize outstanding accomplishments by young and established investigators, respectively. However, I am pleased to say that given the financial health of our Society we are able to fund these awards ourselves and have re-named them the CSBMCB Young Investigator and Senior Investigator Awards. We anticipate that this is a temporary situation as we have received encouraging signs from alternative sponsors who are interested in long term support of these prestigious awards. We will keep you posted on this front.

For 2009, the CSBMCB Young Investigator Award went to Dr. Mick Bhatia of McMaster University for his exceptional work on stem cells. I had the pleasure of presenting the award to Mick at the CSBMCB Annual

---

Meeting on Protein Folding in Niagara-on-the-Lake last June which was followed by a superb talk entitled "Cellular and molecular characterization of human pluripotent stem cells."

Dr. Hans Vogel, University of Calgary, was the recipient of the CSBMCB Senior Investigator Award. Hans received the award for his excellent work, using NMR-based methods, on structure-function relationships in calcium-binding proteins. He will receive the award at the 2010 Meeting in Banff where he will give the award lecture entitled "Iron uptake in Gram-negative bacteria: TonB or not TonB that is the question." Clearly, Hans' interests extend beyond calcium-binding proteins!

The 2010 Awards have been announced and will be presented at the Annual Meeting in Banff. The Young Investigator award goes to Dr. Senthil K Muthuswamy, Ontario Cancer Institute and the Jeanne Manery Fisher Award for outstanding Canadian woman scientist is awarded to Dr. Cheryl Arrowsmith, Ontario Cancer Institute. The Arthur Wynne Gold Medal has its second recipient, following the inaugural award to Alan Bernstein in 2008. The Arthur Wynne Gold Medal recognizes lifetime achievement by an individual who has attained an international profile in research, has played a major role in the development and promotion of the discipline in Canada, and has a long-standing record of service to the academic community. The 2010 recipient is Dr. Michel Chrétien. Dr. Chrétien will address the Society at its evening banquet in Banff. Congratulations to all of the winners on their exceptional accomplishments!

### **Membership and Merger**

The membership of the CSBMCB currently stands at 471 regular members, 82 emeritus, and 924 student/PDF members. In order to be in a financial position to mount exceptional conferences and to be a legitimate advocacy voice in Ottawa it is important to have an even stronger base of members. To this end, we are engaged in two initiatives. Councillor Linda Penn is spearheading a membership drive that is beginning with the identification

of CSBMCB representatives within all academic life science departments in Canada. These "Reps" will engage colleagues locally as a means to spread the word about the activities of the CSBMCB and the importance of membership in the Society.

The second initiative is a possible merger with the Genetics Society of Canada. Dr. Paul Lasko, president of the GSC, approached the CSBMCB with the idea of a merger following the closing of the Canadian Federation of Biological Societies. The GSC is a smaller organization than the CSBMCB and they would like to be part of a larger body in order to participate in national advocacy and to host meetings of interest to geneticists and developmental biologists. The CSBMCB Executive sees considerable advantages in such a merger as it will not only increase membership, but will enhance diversity through new members with research interests in genetics and developmental biology. We envision greater participation of the CSBMCB in national meetings in these areas which can only increase our relevance to more of our colleagues nationally. The merger proposal will be discussed and voted on at the Annual General Meeting of the CSBMCB in Banff, April 17, 2010. Stay tuned!

### **Parting words**

I've greatly enjoyed my year as President of the CSBMCB and this is largely due to the energy, good will and enthusiasm of the CSBMCB Executive. Their ideas, insights and dedication are essential to making the CSBMCB a thriving and relevant Society.

I am particularly grateful to our Treasurer Vince Duronio for keeping our finances in excellent shape despite the economic downturn and for keeping track of the myriad financial details of the Society. He will be working closely this year with our new Administrator, Mrs. Wafaa Antonious, who has taken over the position from Mr. Rob Reedijk. Rob provided much needed administrative support to the Society following the closure of the CFBS office. Wafaa assumed her role as Administrator Jan. 1, 2010 and, having previously worked for CFBS, brings



highly relevant experience as well as excellent bookkeeping and secretarial skills to the position. She will also be maintaining the Society website. We are very pleased to have her aboard.

Thanks also to Albert Clark who is ending his term as Secretary after 7 years of dedicated service. I hope Albert will continue to come to Annual Meetings armed with cameras to keep recording events for posterity! I am pleased to welcome Randy Johnston, University of Calgary, as our new Secretary and look forward to his input in the Executive. Linda Penn has been a tireless advocate for membership expansion and I am very grateful that she allowed herself to be persuaded (repeatedly!) to stay on the Executive and organize our membership drives. Thanks also to John Glover for taking on the job of Bulletin Editor. Assembling this record of our Society is an important and very time-consuming task. My job was also made much easier through the sage advice provided by past Presidents of the Society who remained as members of the Executive this year - Laura Frost, Frances Sharom, John Mikowski and Reinhart Reithmeier. It has also been a pleasure working with Councillors Alba Guarne and John Lawrie and I look forward to working with incoming Councillor Jan Rainey as well. Finally, I am pleased to transfer the President's mantle into the capable hands of Jean-Pierre Tremblay (Sherbrooke). Jean-Pierre has been a very active member of the Executive and I'm certain that his experience and energy will serve the Society well in the year ahead.

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## Incoming Board Member

Josée Lavoie, Councillor



I was born and raised in Québec and as far as I can remember, I was not expecting to become a scientist. My mother was a former teacher and my father was a banker by accident as he used to say. He was more an intellectual who put higher education at the forefront. My older sister showed an early interest

for science and physics. But I was attracted by literature, music and arts, singing for hours on the garden swing. I prepared a musical show and choreography for my parents who indulged their eccentric baby girl with enthusiastic applause.

So of course, it came as a surprise when I decided to pursue a degree in biological science. It all started when I first sat in front of a microscope to admire the beauty of cells undergoing cell division. Mitotic figures appeared to me as the most intriguing portraits I have ever seen and I became fascinated by the biology of cells. Throughout my undergrad training in Medical Biology at the Université de Trois-Rivières several classes in histology and cell biology kept intensifying my interest. I decided I wanted to learn even more about how cells modify their architecture in response to external signals to achieve complex biological processes with such precise choreography.

After graduating in 1989, I decided to pursue grad studies at the cancer research centre of Université Laval at the Hôtel-Dieu de Québec, under the supervision of Jacques Landry, a great mentor that showed me critical thinking and scientific rigor. I have been introduced to signal transduction and the cellular response to stress through investigating the protective function of the small heat shock protein Hsp27 and its regulation by phosphorylation. After some years of hard work studying the biochemistry of the protein and its influence on cell survival to stress, I found myself coming back to the microscope to “look” at the impact of heat shock-induced Hsp27 phosphorylation on its localization. I was fascinated by how deep we could look into cell structural organization using a newly acquired confocal microscope, the first one in Québec city. I made the surprising observation that the phosphorylation status of the protein had an influence on the organization of the actin cytoskeleton and on the process of fluid phase pinocytosis in the absence of stress, an effect that could be stimulated by growth factors.

At that time, the protective function of HSPs on denatured proteins was emerging and people in this field could hardly figure that chaperones would have some growth-related function. I remember Jacques telling me that since I had significant results for my thesis, I could afford having less time at the microscope anyway. And that’s what I did for the rest of my PhD. Jacques was intrigued by my findings, spending hours with me at the microscope. These years of exciting and “naïve” research led to the discovery of the phosphorylation-dependent function of Hsp27 at the level of actin dynamics during both stress and growth-regulated processes. More recently Hsp27 has been implicated in actin-based motility, in the virulence of anthrax lethal toxin and innate immunity. However,

one of the most important things that I learned during this training period is that as long as I pursue my passions and interests, and exploit my artistic nature, I could make original discoveries with unanticipated applications.

With this background in mind, I started a first postdoc in Jacques Pouyssegur's lab at the Université de Nice in France in 1984 with the aim of learning how mitogenic signals are transmitted to the cell division machinery. Again, I had the chance to be guided by a dedicated and passionate mentor at an exciting time; the functions of key molecules such as MAP kinases and cyclin-dependent kinases were beginning to emerge. I was among the first scientists to couple receptor-coupled intracellular signaling to the cell division machinery by showing that MAP kinases drive specific mitogenic responses, in part, through the modulation of cyclin D1 expression and cdk activity. These findings turned out to have major impact in cancer research. In 1996, I moved to Canada to start a second postdoc in Gordon Cohen's lab at McGill University. Intrigued by the emerging field of cell death, I wished to learn more on how cell death decisions were integrated at the cellular level. Gordon is my third fantastic mentor who provided constant support, while I was pursuing a very controversial research topic at the time, caspase-independent cell death. I started a project in collaboration with Philip Branton's group using the adenovirus E4orf4 protein as tool to probe the mechanistic underpinnings of alternative modes of cell death in cancer cells. Consequently this work formed the basis of my independent research program.

In 1998, I established my lab at the Cancer Research Centre at Université Laval as an MRC scholar. Faithful to my research interests, our work since then has been focused at the mechanisms underlying the biology of cell survival and death with the hope of getting a better understanding of the complex and precise choreography of cellular organelles and their components in response to various signals. I discovered novel functional links between Src tyrosine kinase, actin dynamics, endosomal traffic and organellar dynamics that might be relevant to the transduction of

several death pathways in the context of cancer cells, but also to normal cell division. More, recently, I have returned to the field of molecular chaperones, pursuing their role in mitotic progression and cancer cell resistance to mitotic stress in collaboration with my former mentor Jacques Landry.

Over the years, I discovered that being a mentor is one of the most gratifying activities in research. I have been blessed with family that exerted a strong intellectual influence on my life. I have also been blessed to encounter great mentors and colleagues on my cruise in basic research. I seek to pass their legacy of passion, enthusiasm and the drive to pursue even the most unexpected findings. Indeed, my history illustrates that we very often find what we were not looking for. After all, even as I was looking at the "arts" as my life's passion I serendipitously stumbled upon the fabulous world of cell biology. I recently joined the CSBMCB to serve as a Councillor with the intention of reaching young scientists and contributing to the important mission of the Society as a national advocate to promote fundamental science in Canada.

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# Minutes of the Annual General Meeting

Niagara-on-the-Lake, Ontario — June 2009

## 864. Greetings from Society President

Dr Laura Frost was unable to attend the meeting and her greetings and thanks to members for their attendance at the meeting were given by Dr Williams, Vice-President of CSBMCB.

## 865. Approval of the Minutes of the 51<sup>st</sup> Annual General Meeting

The minutes of the 51<sup>st</sup> Annual general meeting were approved as circulated (motion by Dr Orłowski, seconded by Dr Hofmann)

## 866. Business Arising From the Minutes

Items of business arising from the minutes are discussed under later agenda items.

## 867. Treasurer's Report

Dr Duronio presented the financial report and commented on the current state of the Society's finances. Starting from reports at earlier meetings the bank balance had decreased from 450K to 300K and then had risen to 396K in recent reports (amounts are approximations). The accounts are managed by BMO Nesbit Burns. Currently there is approximately \$140K in cash and bonds with \$55K in the checking account, the latter primarily from meeting registrations. Nothing has been removed from the Special Fund in over a year. There are currently approximately 100 paid up memberships. The Society website had become dysfunctional. It has cost \$32K to develop a new system which has many potential advantages over the previous one. There is a separate item of approximately \$70K listed in our books for funds transferred to the Society from PENCE two years ago when that Centre of Excellence ended. This money is being used to primarily support activities of the PENCE group many of whom are or became members of our Society.

CSBMCB pays annual dues to two international societies – PABMB (\$350) and IFCB (\$300US). We also annually contribute \$1000 to Research Canada and \$1500 to the Friends of CIHR as a donation to the Henry Friesen Award. This year the Society had to support the Young Scientist Award because of the withdrawal of support by Merck Frosst. The Executive had agreed to support Joel Weiner's attendance at the IUBMB meeting – Dr Weiner had been nominated for a position on the IUBMB Council. The Board had also agreed to contribute \$5000 toward the Canadian Science Policy Forum which is to be held in Toronto Oct 28-30. A total of \$1250 has been spent on student events. The Executive meeting in Toronto in November costs the Society approximately \$6000.

It was noted that the CFBS office had previously performed the Society's administrative tasks but their office had closed at the end of 2008. The Society now pays Rob Reedijk in the Department of Biochemistry at the University of Toronto 20 per cent of his salary and he looks after the administrative needs of CSBMCB. He will oversee that the audit for 2008 is carried out (CFBS would have previously ensured that audits were done).

A motion (moved by Dr Reithmeier and seconded by Dr Orłowski) to receive the Treasurer's report was passed unanimously.

There were questions for clarification regarding the recommendation to support Dr Weiner's attendance at the IUBMB meeting and the continued support of PABMB. It was noted that there is a Society bylaw that the Special Fund should not be allowed to go below \$300K.



### **868. Website.**

It had become necessary to find a new host for the Society website – the previous site manager had “disappeared” and was no longer available to the Society. The new site is hosted by NewGen. It is now very functional. With the new site, registrations, abstract submissions, etc. can now be done online.

### **869. Advocacy.**

CSBMCB supports the efforts of Research Canada with regard to informing politicians and the public about the results of research. The Society has written the membership regarding to letter writing campaigns to local politicians. The Society executive reviewed the CIHR strategic plan and Dr. Beaudet wrote a letter on behalf of the Society emphasising the importance of the funding to basic science research as opposed to favour support for applied research.

Dr. Orland from the University of Toronto spoke to the Senate Government S and T Commercialization Report which emphasized the commercialization of research. The University of Toronto had concurred with the report and had constituted a committee which led to creation of an Innovation Office which had lost \$11 million during its tenure. The suggestion was that its mission was to change the direction of the University. It was stated that the Liberal government had supported these documents in 2007.

Industry research had been put under Industry Canada government linkages with the private sector. There is a move to have international peer review and to obtain advice from the private sector on research programs. The University of Toronto strategic plan drives research to commercialization: the University of Medicine office have a commercialization program and there is an opinion that the university government should be criticized for their stand on the issue which they are promoting commercialization.

It was noted that the government doesn't listen to advocacy research. It is difficult to achieve such advocacy at the individual institutional level. All members were encouraged to provide input to Dr. Beaudet when input on government is requested.

### **870. Annual Conferences/Meetings.**

The current (2009) meeting is going well and will hopefully break even financially. The 2010 meeting will be held in Banff with membranes being the focus, the 2011 meeting will be held in Sherbrooke, Quebec with RNA being the theme and the 2012 meeting will be held in Whistler, BC with the topic being epigenetics/DNA damage. A question was raised about exploring the possibility of future joint meetings with the Chemistry Institute of Canada. Noted was a complaint that Society meetings are too topic oriented. It was noted that our meetings are being successful in attracting a good attendance and the meetings in general are breaking even financially.

### **871. Change to Society Constitution.**

There was a motion to amend the constitution (moved by Dr. Hofmann and seconded by Dr. Tustanoff) to remove the requirement for an application for membership in the Society be signed by two regular members. Carried unanimously.

### **872. Membership.**

As noted in the financial report there are approximately 100 paid up regular members. It was noted that it is anticipated that the new website will improve the Society's ability to remind members to renew their memberships, etc.

### **873. Society Communications.**

Dr. Glover (Editor) informed the members that the Bulletin was being assembled and would be ready for distribution within several months. Dr. Orłowski (Editor) reported that the template for eLINK had been created, the first issue had been distributed to Society members and a second issue was being prepared. Dr. Davie raised the issue of Biochemistry and Cell Biology being the official journal of CSBMCB. This latter issue will be pursued.

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#### **874. Executive Nominations.**

The nomination committee brought forward the following nominations for executive positions: Past-President; Laura Frost, President; David Williams, Vice-President; Jean-Pierre Pelletier; Councillor; Marie Josée Lavoie (Laval University). There were no nominations from the floor. A motion (moved by Dr Reithmeier and seconded by Dr Orlowski) to accept the nomination committee report was passed unanimously.

#### **875. Other Business.**

In response to a question from a member assurance was given that nominations for the Society awards are carried over from one year to the next.

#### **876. Meeting Adjournment**

As there was no further business the meeting adjourned (moved by Dr Orlowski and seconded by Dr Hofmann). Carried.

# CSBMCB/SCBBMC

## Financial Statement

### STATEMENT OF FINANCIAL POSITION

PERIOD ENDED ON DECEMBER 31, 2009  
(unaudited comparative figures as at December 31, 2008)  
UNAUDITED

	2009	2008
<b>ASSETS</b>		
<b>CURRENT</b>		
Cash	\$ 14,133	\$ 36,920
Accounts receivable	38,938	815
	<u>53,071</u>	<u>37,735</u>
<b>INVESTMENTS</b>	425,509	374,920
	<u>\$ 478,580</u>	<u>\$ 412,655</u>
<b>LIABILITIES</b>		
<b>CURRENT</b>		
Accounts payable and accrued liabilities	\$ 16,028	\$ 3,707
Deferred membership fees	3,344	2,486
	<u>19,372</u>	<u>6,139</u>
<b>DEFERRED MEMBERSHIP FEES</b>	930	4,179
<b>UNRESTRICTED NET ASSETS</b>		
Balance—beginning of year	402,283	507,005
Revenue (expenses) for the year	55,995	(104,722)
	<u>458,278</u>	<u>402,283</u>
	<u>\$ 478,580</u>	<u>\$ 412,655</u>

## STATEMENT OF OPERATIONS

FOR THE YEAR ENDED DECEMBER 31, 2009

(with unaudited comparative figures for the year ended December 31, 2008)

UNAUDITED

	2009	2008
<b>REVENUE</b>		
Memberships	\$ 30,618	\$ 20,409
Corporate contributions	22,459	16,000
Annual meeting and other	40,789	5,321
PENCE transferred funds	18,415	-
	<u>112,281</u>	<u>41,730</u>
 <b>INVESTMENT REVENUE (LOSS)</b>	 <u>50,589</u>	 <u>(61,598)</u>
	162,870	(19,868)
 <b>EXPENSES</b>		
Annual meeting	54,650	32,153
Bank and credit card fees	2,106	766
Board meetings	8,005	3,566
Bulletin	102	5,699
Dues and subscriptions	1,550	1,665
Funding and other sponsorships	6,250	3,000
Miscellaneous	609	2,228
Professional fees	2,200	506
Secretariat	13,873	19,971
Website	17,530	15,300
	<u>106,875</u>	<u>84,854</u>
 <b>NET REVENUE (EXPENSES) FOR THE YEAR</b>	 <u>\$ 55,995</u>	 <u>\$ (104,722)</u>



## STATEMENT OF CASH FLOWS

FOR THE YEAR ENDED DECEMBER 31, 2009

(Unaudited comparative figures for the year ended December 31, 2008)

(UNAUDITED)

	2009	2008
<b>CASH PROVIDED BY (USED IN) OPERATING ACTIVITIES</b>		
Revenue (expenses) for the year	\$ 55,995	\$ (104,722)
Change in non-cash working capital		
Accounts receivable	(38,123)	53,380
Accounts payable and accrued liabilities	12,321	(9,451)
Prepaid deposits	-	19,000
Deferred revenue	2,391	2,028
	<u>32,584</u>	<u>(39,765)</u>
<b>INVESTMENT ACTIVITIES</b>		
Change in investments	<u>(41,321)</u>	<u>86,201</u>
<b>NET INCREASE (DECREASE) IN CASH</b>	<u>(8,737)</u>	<u>46,436</u>
Cash and equivalents, beginning of year	<u>91,790</u>	<u>45,354</u>
Cash and equivalents, end of year	\$ 83,053	\$ 91,790
<b>Cash and equivalents include:</b>		
Bank account	\$ 14,133	\$ 36,920
Cash held with investment broker	68,920	54,870
	<u>\$ 83,053</u>	<u>\$ 91,790</u>

# The 52<sup>nd</sup> Annual Meeting of the CSBMCB, Niagara-on-the-Lake, Ontario

## Protein Folding: Principles & Diseases

Correspondents: Reinhart Reithmeier and David Williams, Department of Biochemistry, University of Toronto

The 52<sup>nd</sup> Annual Meeting of the Canadian Society of Biochemistry, Molecular & Cellular Biology (CSBMCB) on "Protein Folding: Principles & Diseases" was held at the White Oaks Resort at Niagara-on-the-Lake from June 1-5, 2009. Co-Chairs David Williams and Hue-Sun Chan (Toronto) promised an exciting meeting and they delivered. Many inherited diseases are due to a failure of mutated proteins to properly fold and attain their functional state. This effect is no more evident than during the biosynthesis and trafficking of membrane proteins that originate in the endoplasmic reticulum (ER) and traffic via the secretory pathway to their final destination. Proteins in cells do not fold on their own, but engage different families of chaperones that transiently interact to ensure that only properly folded proteins are produced. Misfolded proteins are typically targeted for rapid degradation by the proteasome. The fine balance of the life and death of proteins within cells, or proteostasis, is a very hot area of research not only because scientists are interested in how proteins fold but also how misfolded proteins cause devastating diseases like cystic fibrosis and Alzheimers.

The main meeting began with a session on protein folding in the cell. Susan Lindquist (MIT) began with a provocative presentation entitled "Happy Birthday Darwin! Protein Folding Propels Evolution". Darwin was born on February 12, 1809, 200 years before the meeting almost to the day. Dr. Lindquist described how the common Hsp90 plays a role in evolution by interacting with client proteins involved in signaling, acting as a buffer for polymorphisms. Secreted and membrane proteins contain specific disulfide bonds that stabilize or link extracellular domains. Chris Kaiser (MIT) reported on findings that these bonds are formed by the stepwise action of oxidases and thiol oxidoreductases that are part of a tightly controlled electron transport chain within the ER. While biochemists schooled in the 60's learned that structure informs function, Alan Davidson (Toronto) presented work showing that "unstructured" regions of proteins are critical

for phage assembly and other biological processes. Bill Balch (Scripps) found that pharmacological chaperones that affect protein folding may be useful drugs in the treatment of diseases like cystic fibrosis and can restore balance, or tilt the balance of the proteostasis network of proteins in the exocytic pathway. This point was emphasized by David Thomas (McGill) who showed that it is possible to identify chemical correctors that can rescue misfolded mutant CFTR and move it to the plasma membrane.

The second session revealed the power of computational approaches in developing our understanding of protein folding. Ken Dill (UCSF) explored the folding of helix bundle proteins using a 2-state model and found that folding stabilities are highly dependent on chain length, a polymer property. Vijay Pande (Stanford) simulated protein folding in the context of ribosomes, chaperonins and the crowded nature of cells, rather than in dilute solutions biochemists often employ *in vitro*. Hue Sun Chan (Toronto) emphasized the cooperative nature of protein folding, which prevents aggregation but he also provided examples of protein domains that can fold non-cooperatively.

The third session dealt with the mechanisms of protein folding and misfolding. Chris Dobson (Cambridge) showed that a wide variety of proteins can assume an amyloid fibril structure under physiological conditions, suggesting that the beta-hairpin is a primordial structure. He also showed that it is possible to study protein folding on the ribosome by NMR, mimicking what happens in a cell. Sue Marqusee (Berkeley) developed a new method using DNA handles and optical tweezers to study force-induced protein unfolding and showed that protein topology is critical in the folding cooperativity between protein domains. Art



Shawich (Yale) in a dynamic presentation introduced molecular chaperones and the role the chaperonin GroEL plays in the folding of proteins. He also reported on recent imaging and proteomics studies using transgenic *C. elegans* and mouse models of ALS. Charles Deber (Toronto/SickKids) spoke on the nature of transmembrane helix interactions and the impact of amino acid composition, sequence and packing. Lewis Kay (Toronto), like the Little Prince, demonstrated that "What is essential is invisible to the eye." He showed that sparsely populated excited states, like folding intermediates, could be detected using sophisticated NMR techniques that his lab has developed.

Session four was on cellular responses to protein misfolding. Based on solid structural studies, Walid Houry (Toronto) described his work on bacterial stress responses and a lysine acetylase pathway induced under acid conditions and regulation by ppGpp. Ron Kopito (Stanford) provided evidence that prion-like polyglutamine-based fibrils can be internalized by cells where they can then recruit similar cytoplasmic proteins. Randy Kaufman (Michigan) spoke on the ER and oxidative stress pathways involved in the unfolded protein response (UPR), suggesting that anti-oxidants can improve protein folding in the ER and prevent disease. David Ron (NYU) continued on the topic of UPR and suggested that it might be a way for cells to increase their secretory capacity while protecting the ER from protein misfolding.

As mentioned earlier, disordered regions of proteins are now recognized as having important biological functions, such as serving docking sites for interacting proteins and being important in signaling pathways. Peter Wright (Toronto) showed that NMR is particularly well suited for study of disordered regions of proteins and that linkers between domains in transcription factors allows flexibility in protein interactions. Using several protein systems, Julie Lesch (Toronto/SickKids) showed that disordered regions exist in dynamic complexes with partner proteins. Zoltan Lipp (Hungary Academy of Sciences) suggested that disordered protein regions may "moon-light" by binding differently to accommodate different partners. Michael (Toronto/UHN) showed that the folded state of a protein sensing protein is crucial for its signaling function.

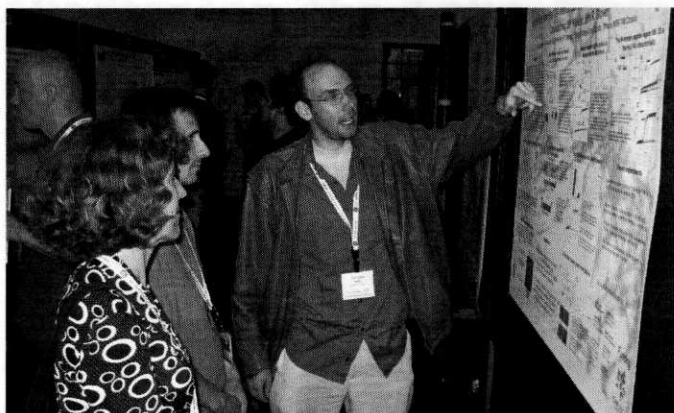
Protein misfolding plays a key role in aging and disease,

the topic of the final session. Peter St. George Hyslop (Toronto) described his lab's cutting-edge work on the genetic and molecular basis of Alzheimer's disease, now revealing new genes using genome-wide association studies (GWAS). Cynthia Lemere (Harvard) provided evidence that immunotherapy for Alzheimer's and other neurodegenerative diseases is a possibility. Jeff Kelly (Scripps) focused on cellular proteostasis and showed that modulation of the proteostasis network may be used to ameliorate disease. David Westaway (Alberta) highlighted the role of Shadoo, a neuronal glycoprotein, in modulating prion disease. In a similar vein, David Vocadlo, discussed the role of O-glycosylation in modulating Alzheimer's disease, suggesting that glycosylation inhibitors may be useful probes. PrioNet Canada and the Alberta Prion Research Institute held a workshop on prion protein misfolding and highlighted the importance of this area of research.

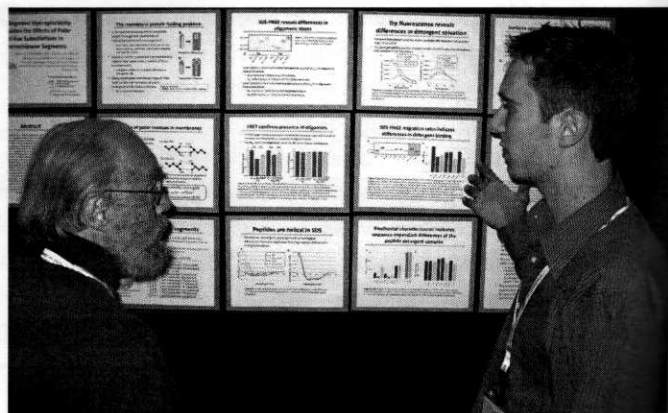
The CIHR Training Program in Protein Folding held a mini-symposium in advance of the meeting and the poster sessions during the meeting provided ample opportunity for trainees to present their work to an informed audience of over 150 participants. Mick Bhatia (McMaster) the recipient of the CSBMCB Young Scientist award presented a lecture entitled "Cellular and molecular characterization of human pluripotent stem cells". The meeting was reinforced by short talks from speakers selected from the submitted abstracts. These included presentations from Jason Young (McGill) on Hsc70 co-chaperones, Linda Foit (Michigan) on protein stability and evolution, and Lawrence McIntosh (UBC) on control of gene expression by protein phosphorylation.

A highlight of the meeting was the banquet and awards presentations. There was also a lively discussion of the CIHR Strategic Plan held immediately after the CSBMCB Annual General Meeting. Michel Chrétien was recognized for his election to the Royal Society (London) in a special tribute by Jeremy Carver. The Niagara area provided plenty of opportunity for wine tasting, cycling, hiking, golf, and a trip to the famous Falls. The many academic and corporate sponsors are thanked for their support of this important meeting, including outstanding support from the CIHR Training Programs and the Institute of Genetics. Thanks also to the organizing committee for their work, the speakers and the participants for creating a very successful meeting.

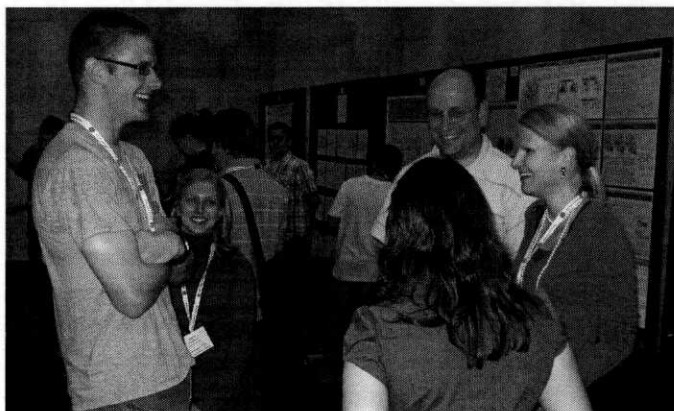
## Scenes from the AGM



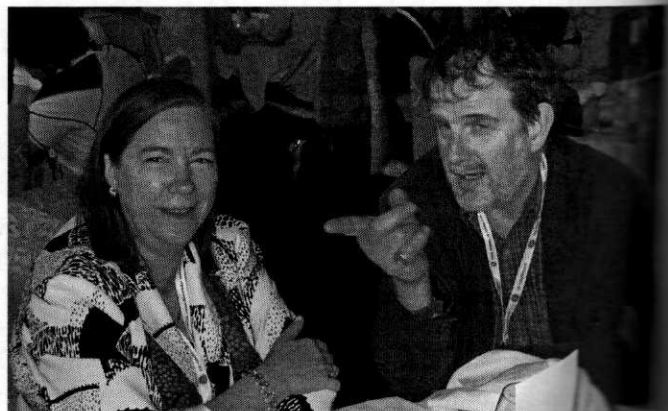
▲ Ph.D. student and poster award winner Christopher Helsen (Toronto) gives a tour of his research.



▲ Professor Emeritus Theo Hofmann (Toronto) listens attentively as Ph.D. student David Tulumello (Toronto) explains his data.



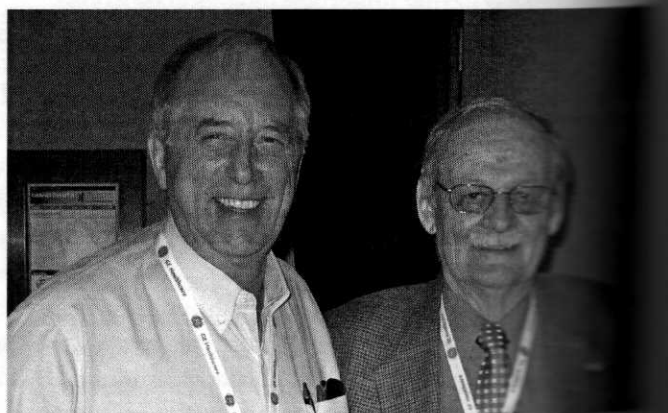
▲ Sharing a laugh during a busy poster session.



▲ Susan Lindquist (left; Whitehead/MIT) with Cliff Lingwood (right; Toronto) making a point.



▲ Scripps Research Institute's Jeff Kelley (right) enjoys a glass of wine with students.



▲ Both Fellows of the Royal Society, Michael James (left; Ottawa) and Wynne Medal Awardee designate Michel (right; Ottawa), pose for the camera.





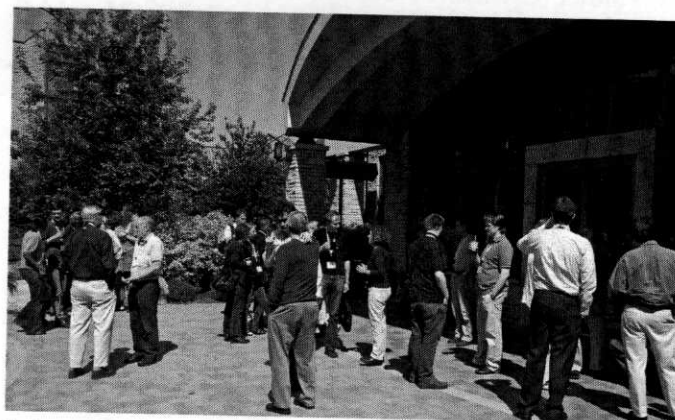
David Cant (left; Queen's), Jan Rainey (Centre; Dalhousie) and Gergely Lukacs (right; Saskatchewan)



▲ Zemin Yao (Ottawa) relaxes with his protégés.



Researchers David Thomas (left) and Gergely Lukacs relaxing with good spirits.



▲ Attendees enjoying fantastic weather outside the White Oaks Conference Centre.



◀ Vincent Duronio (left; British Columbia), Jan Braun (second from right; Calgary) are among those enjoying a tour of the vineyards of the Niagara Peninsula.

## Poster Award Winners

**Julianne Kitevski-Leblanc.** *Unfolding of a two-domain calcium binding protein by fluorine NMR spectroscopy.* Department of Chemistry, University of Toronto. Supervisor: Scott Prosser (Cedarlane Poster Award)

**Lori Rutkevich.** *Investigating functional relationships between members of the PDI family of thiol-oxidoreductases.* Department of Biochemistry, University of Toronto. Supervisor: David Williams (Jake Duerksen Poster Award)

**Valerie Walker.** *hERG trafficking is dependent on a cytosolic chaperone network*  
Department of Physiology, McGill University. Supervisor: Alvin Shrier (Cedarlane Poster Award)

**Vikram K. Mulligan.** *A novel discrete inverse Laplace transform algorithm facilitates elucidation of protein folding mechanisms from time-resolved folding experiments.* Biochemistry, University of Toronto. Supervisor: Avi Chakrabartty (Qiagen Poster Award)

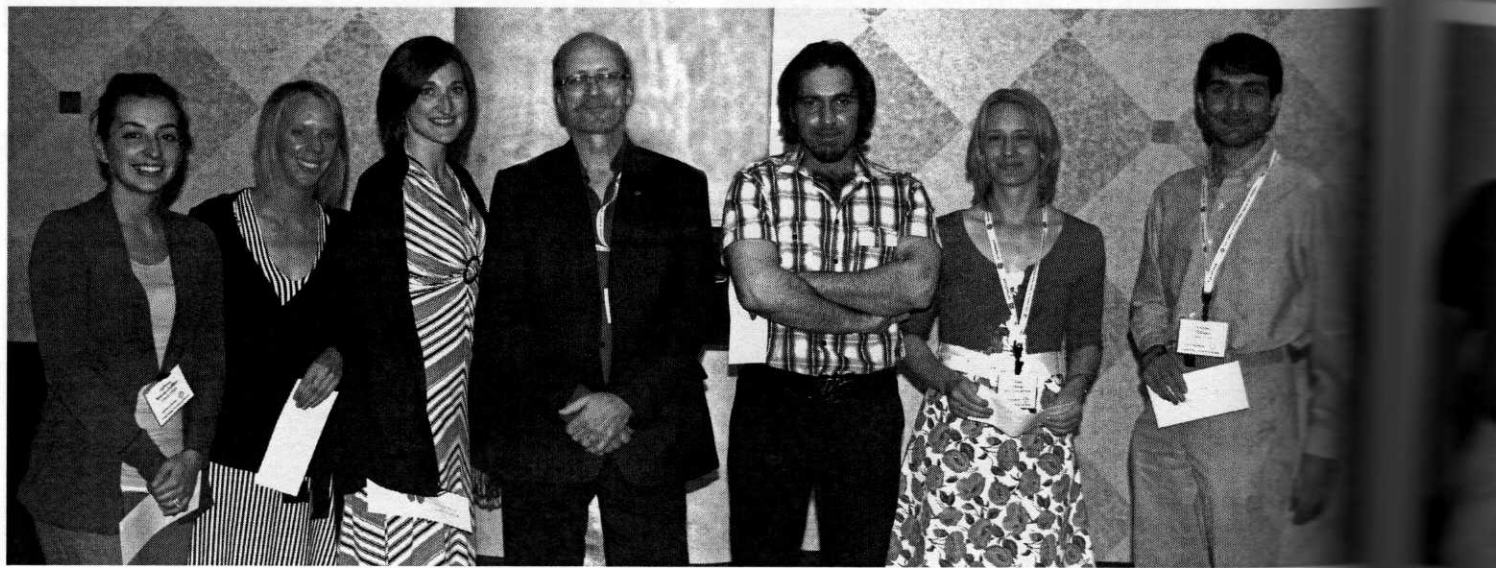
**Feng Wang** *Characterization of co-activator recruitment by FOXO3a.* Department of Medical Biophysics, University of Toronto. Supervisor: Mitsu Ikura (Diamed Poster Award)

**Alireza Roostaei.** *Aggregation and amyloid fibril formation induced by controlled dimerization of recombinant prion protein under physiological-like conditions.* Department of Biochemistry, Université de Sherbrooke. Supervisor: Xavier Roucou (Beckman Poster Award)

**Tanja Mittag** *'Fuzzy' complexes: How much disorder can a biologically relevant complex tolerate and can it even be beneficial?* Sick Kids, Toronto. Supervisor: Julie Forman-Kay (Roche Poster Award)

**Christopher Helsen.** *Identification of an Hsp104 interaction site in the yeast prion protein Sup35,* Department of Biochemistry, University of Toronto. Supervisor: John Glover (Roche Poster Award)

Thanks to all the poster judges for their hard work: Jan Braun, John Glover, Steffen Graethe, George Harauz, Jeremy Lee, Regis Pommier, Scott Prosser, Jan Rainey, Matthew Smith, Allen Volchuk, Andrew Woolley, Jason Young, and Rongmin Zhao. The CSBMC/SCBBMC is grateful to the corporations that sponsored these awards.



Poster Awardees (left to right) Julianne Kitevski-Leblanc, Toronto; Val Walker, McGill; Lori Rutkevitch, Toronto; David Williams (President); Alireza Roostaei, Sherbrooke; Tanja Mittag, Toronto; Vikram K. Mulligan, Toronto. Absent: Feng Wang, Toronto; Christopher Helsen, Toronto.

## Travel Awards Winners

**Pravas Kuma Baral**, Carleton University, Department of Biology.  
Supervisor: Michael James (New England Travel Award)

**David Langelaan**, Dalhousie University, Department of  
Supervisor: Jan Rainey (CSBMCB Travel Award)

**Mikyung Seo**, Dalhousie University, Department of  
Supervisor: Jan Rainey (CSBMCB Travel Award)

**Marie-Laurence Tremblay**, Dalhousie University,  
Department of Biochemistry. Supervisor: Jan Rainey (New  
England Travel Award)

**Gurpreet Singh**, University of Calgary, Department of  
Supervisor: Peter Tieleman (CSBMCB Travel Award)

**Alireza Roostaei**, University of Calgary, Department  
Supervisor: Peter Tieleman (New England Travel Award)

**Val Walker**, University of Alberta, Department  
Supervisor: Michael James (New England Travel Award)

Biolabs Travel Award)

**Olivier Julien**, University of Alberta, Department of  
Biochemistry. Supervisor: Brian Sykes (CSBMCB Travel Award)

**Subhrangsu Chatterjee**, University of Alberta, Department  
of Biochemistry. Supervisor: Brian Sykes (CSBMCB Travel Award)

**Andrée-Anne Lacombe**, Institut de Recherches Cliniques  
de Montréal. Supervisor: Benoit Coulombe (Beckman  
Travel Award)

**Pekka Maattanen**, McGill University, Department of  
Biochemistry. Supervisor: David Thomas (CSBMCB Travel Award)

**Alireza Roostaei**, L'Université de Sherbrooke, Département  
de biochimie. Supervisor: Xavier Roucou (CSBMCB Travel Award)

**Valerie Walker**, McGill University, Department of  
Physiology. Supervisor: Alvin Shrier (CSBMCB Travel Award)



(left to right): Pravas Kuma Baral, Alberta; Marie-Laurence Tremblay, Dalhousie; Alireza Roostaei, Sherbrooke,  
(President), Subhrangsu Chatterjee, Alberta; Val Walker, McGill; Pekka Maattanen, McGill; Gurpreet Singh, Calgary;  
Michael James, Carleton; David Langelaan, Dalhousie; Mikyung Seo, Calgary; Olivier Julien, Alberta; Tyler Reddy, Dalhousie.

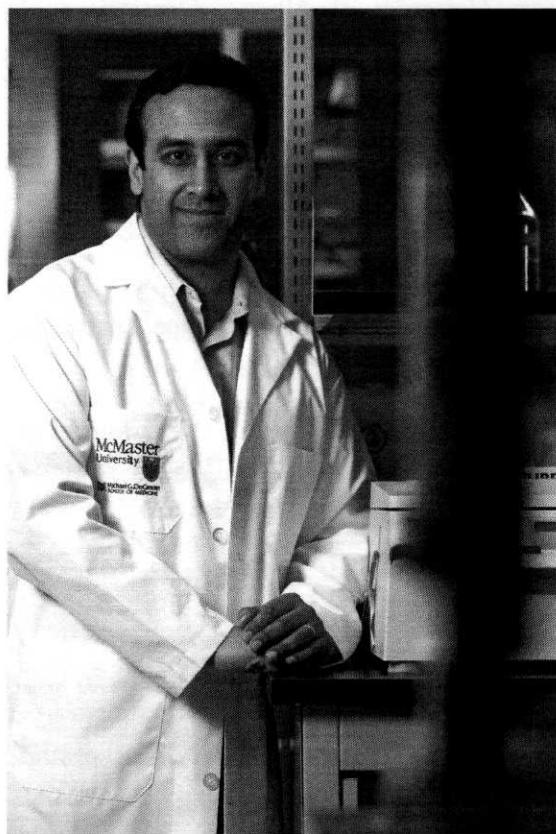


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## CSBMCB New Investigator Award Article

### Applications of human pluripotent stem cells.

Mickie Bhatia



McMaster Stem Cell and Cancer Research Institute, Michael G. DeGroote School of Medicine, McMaster University, Hamilton, ON L8N 3Z5, Canada

**Stem Cells: Here, there, and everywhere**

From cloning to political controversy, human stem cells have captured headlines over the past decade. Many may question what all the fuss is really about. Much of this was initiated during a period of time when the difficulties in organ transplantation were becoming evident. From lack of potential organ donors, to combating the immunological effects of allo-transplantation, it became more provocative to simply repair an organ or tissue vs. completely replacing it<sup>1</sup>. When arriving at this point the use of stem cells entered the already established field of regenerative medicine, of which stem cell-based cell replacement therapy represented only one aspect.

Based on a target disease or specific injury, and therefore a patient population, it became clear that the exact type of stem cell to be used for reparative therapy was important and had to be wisely chosen. Stem cells can be divided into two major sub-types; somatic (adult) vs. pluripotent. A well-known example of a somatic stem cell in biomedical research is the hematopoietic stem cell<sup>2</sup>. Hematopoietic stem cells allow bone marrow transplants to be so successful in the clinic. These rare stem cells carry two properties that operationally define putative stem cells; the first, the ability to differentiate into functional blood cells including immune cells of the hematopoietic system, and; second, being able to appropriately make copies of themselves (process termed "self-renewal") so as not to lose the original HSC pool and thereby exhaust the system. Not only are these clinically important features, but, experimentally, HSCs have established a paradigm by which to evaluate other candidate stem cells of various tissues/organs that come to the pre-clinical podium. The evaluation is based on their ability to; 1) self-renew and, 2) differentiate into the appropriate cell types expected and required to confer function in the body. An application of this paradigm is evidenced and well established in the neurological system where neural stem cells (NSCs) capable of self-renewal are equally able to give rise to all neural cell types in a hierarchical fashion similar to the structural organization of the hematopoietic system at a cellular level<sup>3</sup>. In rapid succession, researchers have identified cells with similar properties in many other tissues including liver, lung, intestine, etc. reaching a point where many predict a stem cell population exists in all tissues and organs.

though embryonic stem cells have provided incredible insights into biological processes by paving an approach to create knockout and transgenic mice<sup>5</sup>, the use of embryonic stem cells to differentiate into usable tissues that could be transplanted for tissue and organ regeneration has become of international interest. Human embryonic stem cells have been isolated<sup>6</sup>. This seminal demonstration was first shown by James Thomson's laboratory in 1998 where his paper published in the prestigious journal *Science* demonstrated the ability to isolate and expand *in vitro* embryonic cells that retained the hallmark properties of mouse embryonic stem cells<sup>7</sup>. Differing from adult/somatic stem cells, embryonic stem cells are pluripotent, meaning they're capable of forming several, if not all, of the cell types that comprise a mammal. Experimentally, this still remains a theory in that, unlike mouse embryonic stem cells where one can generate an entire adult animal from a single cell maintained in a dish, a similar demonstration is not possible using human embryonic stem cells, for ethical reasons. As such, there has been continued debate as to how human embryonic stem cells are related to mouse counterparts originally identified by Thomson's group<sup>7</sup>.

#### What is the best controlled stem cell, and how do we grow it up?

There are many arguments as to what the best stem cell is, or isn't, as there are many cells identified<sup>8</sup>. Careful

evaluation of this statement should lead to utter confusion – such is the field when it comes to the application of stem cells. There are several reports indicating that somatic stem cells are the best cells for transplantation, if the purpose is to regenerate tissue and organs that have been damaged due to injury, disease, or infection. Although many may agree with this precept, the difficulties in using somatic stem cells have become equally obvious. Unlike pluripotent cells that are derived from embryos (embryonic stem cells), somatic cells are difficult to culture *in vitro* whilst maintaining their stem cell properties. This is a two-fold problem; the survival of somatic stem cells in a dish is problematical to maintain, but equally difficult is the ability to regulate proliferation of somatic stem cells vs. their self-renewal divisions. Here, it's important not to confuse cellular mitosis (proliferation) with self-renewal, as the latter is a very unique property of stem cells which allows them to give rise to functional cell types while maintaining a critical reservoir of stem cells when called upon for endogenous regenerative processes. Although many investigators around the world have developed and are refining *in vitro* culture conditions for somatic stem cells through changes in both media and growth factors, and are even using overexpression of key transcription factors to drive increases in the survival and self-renewal properties of cultured somatic stem cells<sup>9</sup>, even the best conditions to maintain somatic stem cells fall short in comparison to the self-renewal

rates and sustainability of culturing embryonic stem cells<sup>6</sup>.

Despite the superior ability to sustain survival and self-renewal *in vitro* that allows for an expandable pool of stem cells, human embryonic stem cells come with their own limitations as compared to somatic stem cells. Perhaps due to the numerous cell fate options available for lineage-specific differentiation (over 226 different cell types), controlling differentiation of human embryonic stem cells is difficult. As these cells have yet to be identified *in vivo*, only *in vitro*, we're constantly creating and redesigning "better" conditions defined by favoring their self-renewal vs. their intrinsic and more natural aptitude for differentiation, eg. Insulin Growth Factor-1 identified recently by our laboratory that is required for human embryonic stem cell self-renewal<sup>10</sup>. Spontaneous differentiation from these cells is a constant problem, but controlling the differentiation into one cell type, neural or blood vs. other lineages, remains key to future applications of stem cell-based cell replacement therapies. Controlling differentiation would allow increased efficiencies where the majority of stem cells in the dish are participating in a specific lineage differentiation, as opposed to choosing other cellular differentiation pathways or undergoing apoptosis as a result of inadequate conditions<sup>11, 12</sup>.

Equally important to controlling lineage decisions is the ability to govern the specific ontogenic program



selected. Embryonic stem cells undergo differentiation by accessing an "embryonic-like" differentiation program that is not similar to later stages of in utero organ and tissue development. The most evident example of this problem is during the hematopoietic differentiation that our lab studies extensively starting studying several years ago<sup>13, 14</sup>. Embryonic hematopoiesis requires production of red blood cells of a different type than that seen in the adult. This is due to the simple fact that the developing fetus requires red blood cells that contain hemoglobin (for oxygen transport) that has a higher affinity for oxygen than the supportive maternal environment. This evolutionary advantage allows the fetus to access oxygen to sustain life at a greater than 20x affinity than the maternal blood that flows counter-current to fetal blood within the placental interface. Accordingly, the majority of hematopoietic cells of the erythroid lineage (red blood cells) created from human embryonic stem cells *in vitro* are of a embryonic/fetal cell type vs. an adult red cell type that would be required for clinical transplantation<sup>15</sup>. As such, overcoming this developmental program in a dish to control pathways for cellular differentiation is key to the use of human ESCs for cell replacement therapies, and is likely to affect more than the hematopoietic lineage example described here.

#### **Surrogate measures of stem cell efficacy**

There have been well over 300 independent reports/publications on differentiation methodology of human ESCs since the original isolation by Thomson in 1998. Several of these protocols vary and many have been an evolving improvement on increasing the efficiency of differentiation to one cellular pathway vs. another. Unfortunately, some of these differentiation protocols are specific to one cell line and are not broadly applicable to other cell lines. The reasons for this discrepancy remain unclear, but many feel this is due to the genetic background from which these cells were obtained, eg. unique embryo coming from diverse parental gamete providers. This is in potential contrast to inbred strains of mice used to select an ideal mouse embryonic stem cell based on its ability to give rise to chimeric animals upon blastocyst injection<sup>16</sup>. In other cases, the differentiation methodology is applicable between one cell line and another, but requires initial expansion of the stem cell population under the same initial conditions so the cells are similarly prepared to receive differentiation cues. These differences between cell lines and generalizable effects of differentiation protocols have defined the 'art' of stem cell biology at the experimental level. From an application aspect this raises the concern that embryonic stem cells defined by a specific cell line used to develop and design differentiation protocols may not be universally applicable to genetically diverse lines and therefore cannot be applied.

Given these caveats in the differentiation of embryonic stem cells, increasingly it became clear to take a pragmatic approach to determining whether one cell line vs. another was superior when using a specific differentiation protocol, or whether one differentiation protocol was only superior to a specific cell line. Our laboratory continues to be most interested in the hematopoietic system where bone marrow transplantation has been shown to be a viable and successful procedure to regenerate the hematopoietic system for several target patients; ranging from those suffering from leukemias, to infection, to having an injured hematopoietic system as an indirect effect from chemotherapy targeting an unrelated solid tumor. In the hematopoietic field, cells derived from somatic sources such as neonatal umbilical cord blood, or bone marrow, have been evaluated in their functional ability to regenerate all blood cell types in an *in vivo* model for a sustained period of time. This test uses a human-to-mouse xenograft system where immune-deficient animals such as the Non Obese Diabetic-Severe Combined Immune Deficient (NOD-SCID) mouse are used as a recipient to avoid rejection of the human cells transplanted. This has provided a powerful and consistent assay for defining hematopoietic cell populations from the somatic sources<sup>17</sup> and therefore we have used these as a functional surrogate to determine the capacity and hematopoietic cell properties of cells derived from human embryonic stem cells.

transdifferentiation *in vitro*. However, the ability to generate efficient lines of hematopoietic cells of the embryonic hematopoietic program may be the most significant hurdle making it difficult to generate cells from human embryonic stem cells lines with HSC potential to bone marrow or cord blood derived HSCs<sup>15, 18</sup>.

#### Induced pluripotent stem cells: game changer?

Use of embryonic stem cells for cell replacement therapy would suggest that specific stem cell lines would have to be matched to potential patient recipients to avoid rejection or graft-versus-host disease. Immunologically, there would have been the foundation for the use of embryonic stem cells since compatibility between recipients from which they were derived and the prospective recipient would be extremely rare. A discovery from Yamanaka's group demonstrated that dermal fibroblasts could be converted to pluripotent state by forced expression of transcription factors identified in mouse factors known to play a role in maintaining mouse and human embryonic stem cells. By applying the same conditions for culturing

embryonic stem cells, together with forced expression of these transcription factors that include Oct-4, Nanog, and Sox2, a stable cell line could be derived from patient skin-derived fibroblasts<sup>19, 20</sup>. These fibroblast-derived pluripotent cells are termed induced pluripotent stem cells, or iPSCs<sup>20</sup>. Further evaluation indicates that these cells are extremely similar to embryonic stem cells in several ways, the most significant being their developmental pluripotent differentiation potential<sup>21</sup>. Not only did this remove ethical concerns by avoiding the use of human embryos to derive lines, but also indicated that patient-specific cells could be generated while avoiding the need for therapeutic cloning (nuclear transfer) to obtain cells that could be used for either autologous transplantation after differentiation, or characterization of disease-specific cells for pathways, mutations, or identification of new small molecules that target disease associated proteins.

Ideas and directions for the use of stem cells have rapidly evolved over the past decade; moving from mouse embryonic stem cells, to additional thrust and interest of human embryonic stem cells, and comparisons to mouse counterparts. The discovery

of mouse and then human iPSCs was based on collective work and the knowledge of embryonic stem cells - a point that should not be forgotten - but it's currently unclear how useful or reasonable a substitute human iPSCs will be for human embryonic stem cells moving forward. Most recently, there have been demonstrations of direct differentiation from fibroblasts to a single neural lineage (neurons)<sup>22</sup> and hematopoietic lineage (macrophage)<sup>23</sup> without generation of an intermediate pluripotent cell type like iPSCs. This may signify the future of cell replacement therapies where skin biopsies could be used to culture fibroblasts and subsequently generate a specific cell type needed for transplantation and characterization - and "stem cells" may not even be required. Alternatively, these directed differentiation reports may be a distracting and hopeless quest, but the risk to pursue this as well as human embryonic and pluripotent stem cells is worth it - as our population suffers from continued disease that modern medicines nor surgery is able to alleviate.

Better to leave no stone unturned in cases where life and quality of life are at stake.

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## Diagnosics Award Article

### Iron uptake in Gram-negative bacteria and the battle for iron.

Research Group, Department of Biological Sciences, University of Calgary, Calgary, Alberta, T2N 1N4



#### The interplay between iron chemistry and its role in metabolism.

Iron is one of the most abundant elements in the crust of the earth. It can exist in two oxidation states but in the presence of high concentrations of oxygen it is exclusively present in the ferric ( $\text{Fe}^{3+}$ ) form, which is not highly soluble.

The ferrous ( $\text{Fe}^{2+}$ ) ion has better solubility, but it only exists under anoxic conditions or at very low pH. In aqueous solution iron can become involved in Fenton chemistry, where hydroxyl radicals are generated that would harm a living organism. In spite of these two limitations all living organisms on earth, with the exception of a few specific bacterial strains, have an absolute requirement for iron to survive and to thrive. Essential and highly conserved enzymes, such as the pyruvate reductases that produce deoxyribonucleic acid (DNA), require the  $\text{Fe}^{3+}/\text{Fe}^{2+}$  redox pair to carry out their function. Other well-known proteins such as hemoglobin and myoglobin utilize the same element to transport oxygen in blood and muscle cells, respectively. As part of the cytochrome and cytochrome oxidase systems, iron also plays a major role in the production of energy by mitochondria and bacterial cells (Crichton, 2009). When it is bound to a protein the iron is often incorporated in prosthetic groups such as iron-sulfur clusters or the characteristic heme group, while other proteins such as transferrin can bind the metal ion directly. To meet their needs for iron all living organisms have their own highly specialized systems to solubilize, transport and store ferric or ferrous iron. Moreover, within the organism as well as within a living cell, this metal is often sequestered by proteins or other ligands in

order to maintain solubility and to prevent the accidental formation of toxic radicals.

#### How do we acquire and control iron?

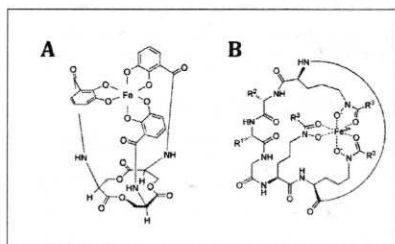
Humans and animals acquire iron directly from their diet. The metal ion is taken up in the ferrous form by the divalent metal ion transporter (DMT) proteins in the gut. However, after it enters the bloodstream, where oxygen is prevalent, it is converted to the ferric form. In serum the  $\text{Fe}^{3+}$  is bound tightly by the circulating transferrin protein, which can deliver the metal ion into cells that have a high demand for iron by binding to specific cell-surface transferrin receptors. Internalization of the transferrin receptor protein-protein complexes into endosomes allows for the intracellular release of iron and at the same time this process is extremely efficient as it also gives rise to the recycling of the receptor protein on the cell surface as well as the re-release of transferrin into the bloodstream (Crichton, 2009). By far the largest amount of iron in our bodies is found in the hemoglobin in the circulating red blood cells. At the end of their lifespan the erythrocytes are consumed by the macrophages and these carefully recycle the iron. As such our daily requirements for iron are quite low and we only need to take up a few mg per day. The major storage for iron in our body is found in the liver, where the metal ion is stored in an insoluble form inside the multi-subunit ferritin protein. The process of iron uptake and release from the hepatic or macrophage storage sites has to be carefully regulated. In some individuals, the iron uptake process is poorly controlled leading to iron overload diseases such as hemochromatosis. Conversely when there is not enough iron taken up from the diet some people can suffer from anemia. The recently discovered peptide hormone hepcidin plays an intricate role in orchestrating the regulation of iron uptake and release in our bodies. Hepcidin was originally purified as an antimicrobial peptide that is synthesized and secreted by the liver; later studies with knock-out mice revealed its essential role as the major control mediator for iron



metabolism (Ganz, 2003). This iron-regulatory peptide hormone has an unusual highly disulfide cross-linked hairpin structure (Hunter et al, 2002).

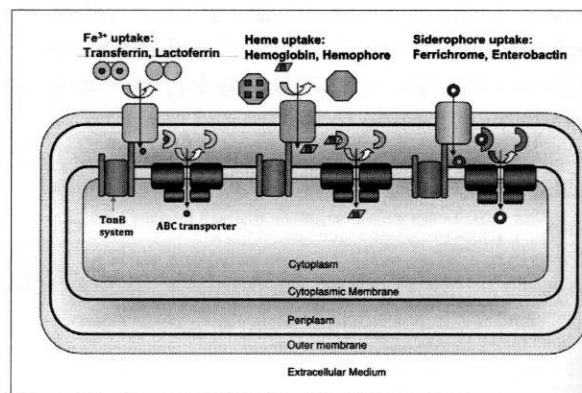
### Bacterial iron uptake and storage.

The vast majority of the bacteria also need to acquire a substantial amount of iron to survive. In the environment bacteria are faced with the problem that the iron concentration in water is extremely low and that the iron in the soil is present in an insoluble form. To overcome these barriers many bacteria can synthesize 'siderophores' which are chelators that are specific for binding  $\text{Fe}^{3+}$  (van der Helm et al, 1987; Neilands, 1995; Raymond et al, 2003). The siderophores, which are named after the Greek word for iron carriers, bind this relatively "hard metal ion" with great avidity; conversely they have a much lower affinity for  $\text{Fe}^{2+}$ , which is from a chemical perspective a much "softer metal ion". Dissociation constants of better than  $10^{-20}$  M have been reported for many of these iron-chelating agents. Siderophores are also produced and secreted by yeast, fungi and some algae; in fact numerous bacteria, including *Escherichia coli*, are quite opportunistic as they can utilize fungal siderophores, such as ferrichrome. Most siderophores are biosynthetically produced by large mutienzyme synthases that resemble the eukaryotic fatty acid synthases (Crosa and Walsh, 2002; Chan and Vogel, 2010). They often have a peptidic backbone, with modified amino acid side chains creating the iron-coordinating ligands, such as catecholate and hydroxamate groups (see Fig. 1). Also pathogenic bacteria that need to proliferate within a host enter an environment where the free iron concentration is extremely low.



**Figure 1.** Representative structures of two typical siderophores: enterobactin and ferrichrome. A) Enterobactin, a catecholate-type siderophore, is produced by numerous Gram-negative bacteria including *E. coli*. B) Ferrichrome, a hydroxamate type siderophore, is produced by the fungus *Ustilago sphaerogena*.

Nevertheless, the high affinity of the secreted siderophores allows them to compete for the iron against host proteins such as transferrin and hemoglobin. Once a siderophore is transported inside the bacterial cell, the iron is released from the siderophores by the action of dedicated enzymes that carry out the reduction of siderophore-bound  $\text{Fe}^{3+}$  to  $\text{Fe}^{2+}$  (Matzanke et al, 2004); alternatively proteolysis of the backbone of some siderophores has also been reported. Once released, the intracellular  $\text{Fe}^{2+}$  can be incorporated directly into metallo-enzymes, or if there is any excess, it is stored in the bacterioferritins or in the related Dps proteins (Chiancone et al, 2004). After the bacteria have accumulated a sufficient amount of iron from their environment, further uptake is shut down through the action of the Fur repressor protein, which shuts down the biosynthesis of the bacterial iron transport systems (for a recent review see Carpenter et al, 2009). Some pathogenic bacteria have adapted themselves even further towards the environment in the host and instead of siderophores they can actually use heme as an iron source, or they have receptors for transferrin that can extract the  $\text{Fe}^{3+}$  directly from this protein (see Fig. 2; Braun and Kilmann, 1999; Krewulak and Vogel, 2008).

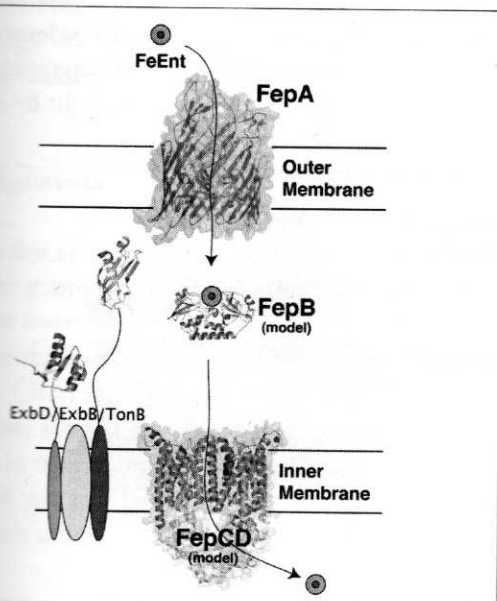


**Figure 2.** Schematic diagram of iron, heme and siderophore uptake in Gram-negative bacteria. Transferrin and lactoferrin deliver iron, while hemoglobin, hemopexin and 'hemophore' proteins deliver heme, to their specific OMT in the outer membrane. Interaction of the TonB protein with the OMT unplugs the barrel of the OMT, allowing free iron, heme or siderophores to enter the periplasmic space. A periplasmic binding protein carries each to their cognate ABC transporter complex that uses ATP hydrolysis to internalize the iron source.



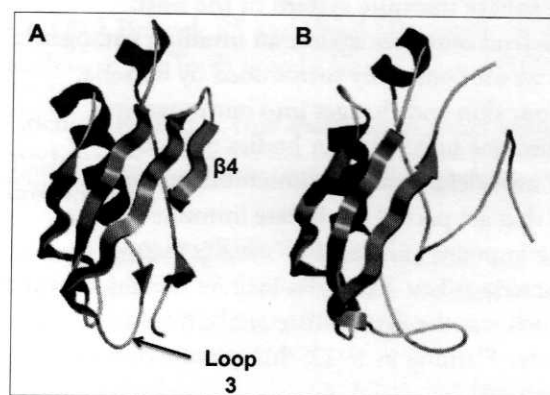
### Iron uptake in Gram-negative bacteria: TonB or not?

Gram-negative bacteria are surrounded by two separate membranes; the space between the outer and the inner membranes is called the periplasm and this compartment can make up to 30% of the volume of the bacterial cell. The outer membrane protects Gram-negative bacteria from degradative enzymes released by the host. However, the arrangement of the bacterial cell envelope creates problems for the transport of nutrients into the cytoplasm of the cell. While nutrients such as glucose, amino acids or phosphate are small enough that they can pass directly through the small pores in the bacterial outer membranes that are created by the porin proteins, the iron-siderophores and heme groups are too large to pass through the porins and hence they require their own outer membrane transporters. All outer membrane transporters (OMTs) that are involved in the uptake of iron are made up of a 22-stranded beta barrel structure (see Fig.3). The barrels are occluded by the presence of a ~150 residue independently folded 'cork' or 'plug' domain (for a recent review see Noinaj et al, 2010). In order to move the ferric-siderophore complex into the periplasmic space, the cork must be at least partially dislodged from the interior of the



**Figure 3.** A representation of the siderophore uptake pathway in *E. coli* using ferric-enterobactin (FeEnt) transport as an example (see text for details). Note that the TonB complex is made up of three proteins that associate in the inner membrane.

beta-barrel OMT structure. The energy for this process is provided by the TonB protein, which can span the entire periplasm. Together with the ExbB and ExbD proteins that are anchored in the cytoplasmic membrane, it harvests the energy from the gradients across the inner membrane (Krewulak and Vogel, 2008; Postle and Larsen, 2007). Despite years of research, the molecular details of the action of TonB on the TonB-dependent OMT's are still unclear. Several solution and crystal structures have been reported for TonB, as well as for the periplasmic domain of ExbD, but these have not yet revealed the molecular details of the action of the TonB system (Peacock et al, 2005; Pawelek et al, 2006; Lopez et al, 2009; Garcia-Herrero et al, 2007). A bioinformatic analysis, surveying all sequenced bacterial genomes, revealed that all Gram-negative bacteria have one or more TonB proteins, that are characterized by a carboxy-terminal region with a conserved fold (Chu et al, 2007; see Fig 4). Gram-positive bacteria do not have an outer membrane and, as expected, they don't appear to have the genes for the three proteins of the TonB system. Iron withholding has long been known to be a clinically useful approach to combat bacterial infections (Weinberg, 1984). Since the uptake of all ferric siderophores, heme or transferrin-derived iron are all mediated by specific TonB-dependent OMT's (see Fig 4), the TonB system presents itself as a potential target for the development of new antibiotics aimed at Gram-negative bacteria.



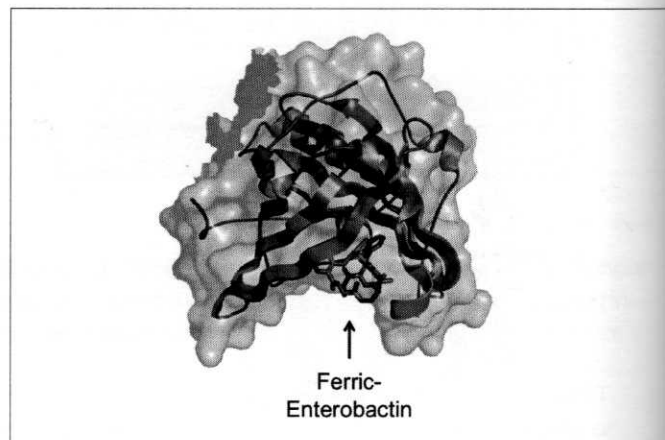
**Figure 4.** The NMR solution structures of (A) *E. coli* TonB C-terminal domain (CTD) and (B) *Vibrio anguillarum* TonB2 CTD. The primary differences between the two proteins are the lengthened loop 3 between the  $\alpha$ 2-helix and the  $\beta$ 3-strand and the absence of the  $\beta$ 4-strand in the *V. anguillarum* TonB2 CTD.

Once the ferric-siderophores have been transported into the periplasmic space by the OMT's and TonB, they are ready to be transported into the cytoplasm. This process is initiated by periplasmic siderophore-binding proteins (Clarke et al, 2000; 2002). These proteins have a characteristic structure, where the ferric-siderophore is bound between two independently folded domains. The siderophore-binding proteins form a unique class of periplasmic-binding protein that have a rather distinct arrangement of the two lobes of the protein, when compared to the periplasmic proteins that are involved in the transport of amino acids or phosphate for example (Krewulak et al, 2004). In their siderophore-bound state these proteins dock onto the periplasmic face of cognate ABC-transporters in the inner membrane. Subsequently these helical proteins mediate the transport of the siderophores into the cytoplasm in an ATP-dependent process (see Fig 3). Several crystal structures have been reported for the bacterial cytoplasmic membrane vitamin B12 uptake system, which is homologous in sequence, design and function to the siderophore transporters (Lewinson et al, 2010). It should also be noted that the uptake system for siderophores in Gram-positive bacteria closely resembles the ABC transport systems found in the inner membrane of Gram-negative bacteria; the only difference is that the siderophore-binding protein is anchored to the cell membrane, but its overall structure is conserved (Grigg et al, 2010).

#### Iron and the innate immune system of the host.

How do we defend ourselves against an invading pathogen? Even though we are constantly surrounded by bacteria, that land on our skin and that get into our lungs, it is rare that we become infected. Our bodies produce a large array of host-defense and antimicrobial proteins and peptides that are part of the innate immune system. Together these proteins and peptides usually manage to keep these bacteria at bay. Examples include the ubiquitous lysozyme, which was the first antibacterial discovered by Sir Alexander Fleming in 1922; this enzyme directly attacks the bacterial cell wall of Gram-positive bacteria (Fleming, 1922). Also the defensins are a group of small amphipathic cationic proteins that can selectively disrupt bacterial membranes and stimulate the immune system (Yang et al, 2007). Intriguingly, however, several of the

host-defense proteins interfere in the ability of the bacteria to acquire iron. In particular, the protein lactoferrin can be released by circulating neutrophils in our bodies at sites of infection (Legrand et al, 2008; Valenti and Antonini, 2005). Lactoferrin, which was originally discovered as an iron-binding protein in milk, is quite similar to the serum transport protein transferrin (Baker et al, 2002), but it binds  $\text{Fe}^{3+}$  even more tightly, thereby making the metal ion locally unavailable for bacteria. It has also been shown that the extremely low iron concentrations created by the presence of lactoferrin, prevent bacteria from aggregating with each other and forming biofilms (Singh et al, 2002); by keeping the bacteria in a planktonic state they are more susceptible to endogenous and exogenous antimicrobial compounds. Likewise lipocalin proteins are also secreted by neutrophils in the host at sites of infection; these proteins were recently shown to avidly bind various ferric-siderophore complexes, thereby again directly preventing the bacteria from obtaining iron, by competing for the bacterial iron-chelating entities (Goetz et al, 2002; Flo et al, 2004). Also the distinct class of the tear lipocalins can bind various ferric-siderophores (Fluckinger et al, 2004). Because of this newly discovered function, where these proteins are now known to strongly bind 'sidero'-phores rather than hydrophobic ('lipo') compounds, many researchers are now calling these proteins 'siderocalins' (see Fig 5). In fact, several researchers have suggested that some bacteria may have recently escalated the fight by covalently



**Figure 5.** The structure of human siderocalin (neutrophil gelatinase associated lipocalin; PDB ID: 3CMP) crystallized together with ferric-enterobactin (FeEnt), which is bound in a deep pocket.

...adding glucose to some of the bacterially-secreted siderophores; this modification does not alter their high affinity for  $\text{Fe}^{3+}$  or their uptake in bacteria, but it prevents their binding to the host siderocalins (Hantke et al, 2005; Fischbach et al, 2006). Thus the bacteria that covalently modify their siderophores in this manner, not only make them more soluble, but they cleverly evade the host defense response. Finally, it is important to note that bacterial infections also give rise to increased hepcidin biosynthesis in the liver. The increase in the serum concentration of the hepcidin peptide hormone directly decreases iron uptake by the gut and prevents the release from macrophage stores in the liver and the macrophages into the circulation; consequently the amount of iron that is available during a bacterial infection in the bloodstream decreases significantly, an effect that is clinically known as "anemia of infection" (Ganz, 2003; 2006). Obviously, to protect our invading bacteria our bodies try to create a hostile environment with a low iron concentration to prevent the bacteria from growing and multiplying. This 'battle for iron' is now considered as an integral part of the innate immune response. The corollary to this is that if we can design new compounds that block bacterial iron uptake directly, for example by interfering in the TonB system in Gram-negative bacteria, we emulate this natural situation. This strategy would clearly be advantageous, as our immune systems are already well prepared to deal with this condition.

#### Acknowledgements

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## 2010 Jeanne Manery Fisher Memorial Lectureship Awardee Designate

### Dr. Cheryl Arrowsmith

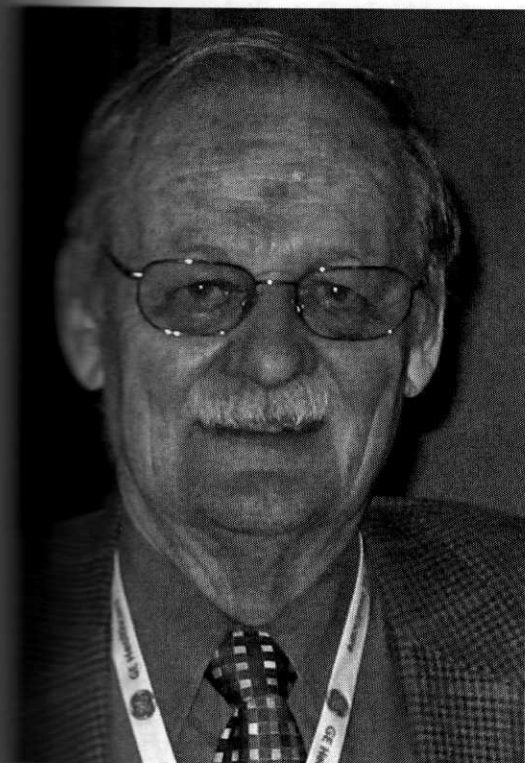


Arrowsmith holds the position of Senior Scientist at the Ontario Cancer Institute, Professor in the Banting and Best Department of Medical Research, Chief Scientist of the Toronto Site of the Structural Genomics Consortium (SGC) and holds a Canada Research Chair in Structural Genomics. Dr. Arrowsmith started her career as a chemist. She did her undergrad at Allegheny College, Pennsylvania, and earned her Ph.D. (1987) from the University of Toronto. Dr. Arrowsmith began to work on protein structure and function using NMR spectroscopy in the lab of Professor Oleg Jardetzky at Stanford University. Dr. Arrowsmith's current research focuses on the use of structural biology methods, particularly NMR and biochemical methods, for understanding the structure-function relationships of proteins and their role in cancer. Among the vast array of contributions structural biology encapsulated in the 150 or so papers Dr. Arrowsmith has authored or co-authored during her career, p53 has been a central theme. In particular her research group is interested in the structure and function of proteins such as ubiquitin ligases and deubiquinating enzymes that control the level of p53 and proteins that modulate p53 phosphorylation, methylation and acetylation. Through the Structural Genomics Consortium Dr. Arrowsmith takes advantage of economies of scale to produce large number of publically available structures of human and malaria parasite proteins intended to fuel the creation of novel treatments for cancer and infectious disease through structure-based drug design and other methodologies.

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## 2010 Arthur Wynne Gold Medal Awardee Designate

### Dr. Michel Chrétien



The CSBMCB Arthur Wynne Gold Medal is awarded to members of the research community that "have attained an international profile in research, have played a major role in the development and promotion of the discipline in Canada, and have a long-standing record of service to the academic community." This description could not more aptly describe the career of the designated recipient of our 2010 medal presentation, Dr. Michel Chrétien.

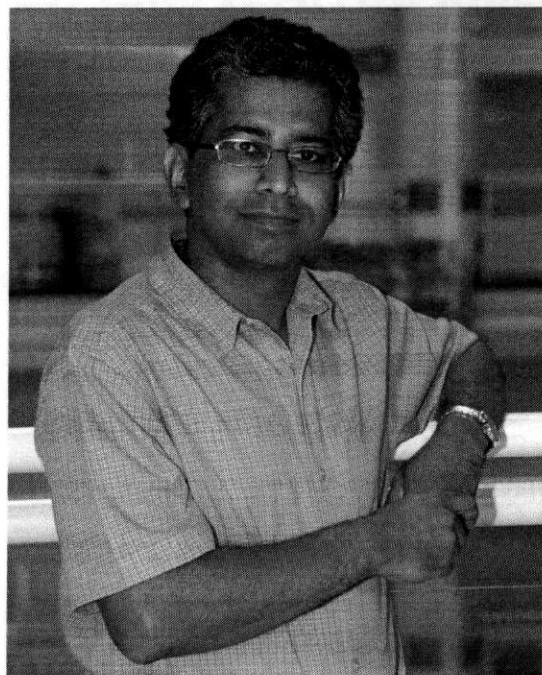
Dr. Chrétien is perhaps best known for his ground-breaking work on hormone peptide processing and the role of convertases in this as well as other biochemical processes. An Officer of the Order of Canada, Dr. Chrétien was recently elected as a Fellow of the Royal Society (London), and is a Fellow of the American Association for the Advancement of Science and the Royal Society of Canada. He holds five honorary degrees. Dr. Chrétien won the Boehringer-Mannheim Award from CSBMCB, the McLaughlin Medal of the Royal Society of Canada, the Izaak Walton Killam Memorial Prize, the Henry Friesen Award from the Royal College of Physicians and Surgeons, and the Award of Distinction from the Manning Foundation.

Dr. Chrétien founded the Laboratory of Molecular Neuroendocrinology (CRIM) in Montréal and was its Director from 1967 until 1999, when he moved to Ottawa to be the Scientific Director of the Loeb Health Research Institute. In 2005 he founded the University of Ottawa Institute of Systems Biology and helped procure the funding for a new building to house the institute. Even more recently, Dr. Chrétien co-founded and served as Scientific Director of the Foundation on Anti-Virals (FAV). Dr. Chrétien has been active in many societies including CSBMCB where he served as President from 1983-84 and a member of Council from 1981-1986.

During his research career Dr. Chrétien trained over 100 graduate student and post-doctoral fellows, many of whom are national and international leaders in their fields.

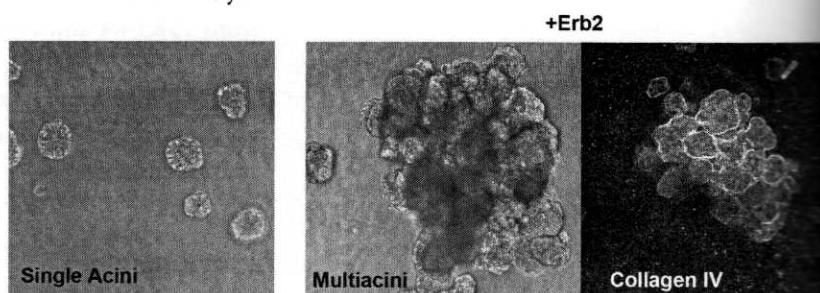
## GE Healthcare New Investigator Awardee Designate

### Dr. Senthil Muthuswamy



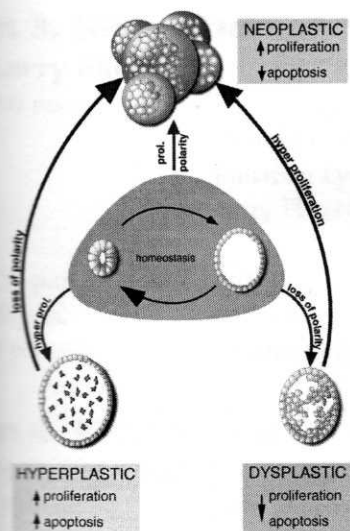
Dr. Senthil Muthuswamy received his Ph.D. in Biology from McMaster University in 1995 working under the supervision of William J. Muller. During his doctoral research, he demonstrated a role for the Src family tyrosine kinases during transformation of mammary epithelial cells using cell culture and mouse models of human breast cancer. He then moved to Boston for postdoctoral training, first at ARIAD Institute for Biomedical Research under the mentorship of Michael Gilman and subsequently at Harvard Medical School under the mentorship of Joan S. Brugge. His postdoctoral research was focused on understanding the mechanisms by which ErbB family of receptor tyrosine kinases transform breast epithelial cells. During this time Muthuswamy developed a small molecule-based strategy for inducing formation of homo- or hetero-dimers that lead to important insights into the functional differences among distinct ErbB receptor dimers.

Dr. Muthuswamy then focused his attention on development of a cell culture system that would enable activation of ErbB2 in breast epithelial cells organized into a three-dimensional acini-like (a cluster of cells resembling a soccer ball) structure, similar to that present in human breast *in vivo*. In collaboration with Dr. Mina Bissell, a pioneer in three-dimensional cell culture systems, Dr. Muthuswamy investigated the effect of activating ErbB1/EGFR or ErbB2 in epithelial cells present within the context of 3D acini. Dr. Muthuswamy discovered that ErbB2, disrupts cell polarity when activated within a 3D acinus, induces cell proliferation, inhibits apoptosis and results in the formation of multiacinar structures resembling *in situ* carcinoma seen in patients (Figure 1). These pioneering 3D culture methods have had a major impact among researchers studying breast and other types of carcinomas today.



**Figure 1.** ErbB2 induced development of multiacinar structures that resemble carcinoma *in situ*. (Nat Cell Biol. 3:785)

In 2001, Dr. Muthuswamy joined Cold Spring Harbor Laboratory as an Assistant Professor where his lab demonstrated that ErbB2-induced transformation of 3D mammary glands requires disruption of the Par cell polarity protein complex. Subsequently, they demonstrated that the loss of cell polarity protein, Scribble, or its mislocalization at cell junctions, creates a permissive environment for oncogenes like Myc to transform epithelial cells, that is in contrast to normal epithelial cells with intact Scribble function that resist Myc-induced transformation by activating a cell death pathway in a Scribble-dependent manner. Interestingly, spontaneous mammary tumors in transgenic mice expressing Myc and human breast cancer cells have dysregulated Scribble suggesting the presence of a selection-pressure for Scribble inactivation during development of cancer. These results have led the Muthuswamy laboratory to propose a model for how polarity proteins and oncogenes cooperate to transform epithelial cells (Figure 2). The model suggests that epithelial cells within 3D structures can maintain a balance of proliferation and death as part of normal homeostasis, changes in cell polarity, cell proliferation or cell death pathways will force a deviation from the normal homeostasis and lead to initiation of tumorigenesis.



**Figure 2.** Relationship between cell polarity, proliferation, and apoptosis in 3D organization of epithelial cells and initiation of tumorigenesis. While activation of hyperproliferation or loss of polarity induce hyperplastic or dysplastic growth respectively, neoplastic growth is likely to require changes in both proliferation and cell death pathways.

In 2008 Dr. Muthuswamy moved to Canada and is now a Senior Scientist at the Ontario Cancer Institute and a Professor at Department of Medical Biophysics, University of Toronto. Research at his laboratory is broadly focused on investigating the role played by polarity proteins both during normal development and during initiation and progression of cancer. Their research interests include: 1) polarity pathways that are altered in breast and other cancers and determining their clinical relevance; 2) how polarity proteins control differentiation of progenitor cells; 3) development of mouse models to study the role of polarity genes in both normal development and cancer progression; and 4) proteomic methods and genetic screens to find novel drug targets that can modify the dysregulated polarity pathways in cancer cells.

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# **53<sup>rd</sup> Annual Meeting and Conference of the Canadian Society of Biochemistry, Molecular and Cellular Biology**

## **Membrane Proteins in Health and Disease**

**Thursday, April 15, 2010 to Sunday, April 18, 2010**

Banff Centre

Banff, Alberta, Canada

### **Organizing Committee**

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Nicolas Touret, University of Alberta | [touret@ualberta.ca](mailto:touret@ualberta.ca)

Howard Young, University of Alberta | [hyoung@ualberta.ca](mailto:hyoung@ualberta.ca)

### **Wednesday April 14, 2010**

7:30 – 10:30 p.m.

Satellite Meeting on Bicarbonate Transporters



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## Thursday April 15, 2010

8:30 a.m. – 12:00 noon      Satellite Meeting on Bicarbonate Transporters  
12:00 – 5:00 p.m.          Meeting Registration in Lobby of Max Bell Auditorium

### Session 1. Main Meeting Opening Session

(Chair: Reinhart Reithmeier)

6:00 – 6:00 p.m.          Plenary lecture: Gunnar von Heijne (Stockholm University)  
6:00 – 7:30 p.m.          Dinner

### Session 2. Membrane Protein Trafficking & Folding

(Chair: Joe Casey)

9:00 – 10:30 p.m.      Ron Kopito (Stanford University)  
                                  Emmanuelle Cordat (University of Alberta)  
                                  Franck Duong (University of British Columbia)  
                                  David Andrews (McMaster University)

## Friday April 16, 2010

8:00 – 8:30 a.m.          Breakfast

### Session 3. Regulation of Membrane Proteins

(Chair: Larry Fliegel)

9:00 – 12:00 noon      Joachim Deitmer (Technical University of Kaiserslautern)  
                                  Daniela Rotin (University of Toronto)  
                                  Jonathan Lytton (University of Calgary)  
                                  Larry Fliegel (University of Alberta)

12:00 – 1:30 p.m.      Lunch  
1:30 – 4:00 p.m.      Poster Session I  
4:00 – 7:30 p.m.      Dinner

### Session 4. Membrane Protein Structure

(Chair: Howard Young)

9:00 – 10:30 p.m.      Joanne Lemieux (University of Alberta)  
                                  Kaspar Locher (Swiss Federal Institute of Technology Zurich)  
                                  Jeff Abramson (University of California Los Angeles)  
                                  Francisco Bezanilla (University of Chicago)

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## Saturday April 17, 2010

7:00 – 8:30 a.m. Breakfast

### Session 5. Membrane Proteins in Diverse Species

(Chair: Elaine Leslie)

8:30 – 12:00 Noon Ekkehard Neuhaus (Technical University of Kaiserslautern)  
Dean Price (Australian National University)  
Etana Padan (Hebrew University of Jerusalem)  
Janet Wood (University of Guelph)

12:00 – 1:30 p.m. Lunch  
1:00-5:00 pm. Satellite Meeting on Na<sup>+</sup>/H<sup>+</sup> Exchangers  
4:00 – 6:00 p.m. Poster Session II  
  
4:00 – 5:00 p.m. CSBMCB Annual General Meeting  
6:00 – 7:30 p.m. Plenary Session- CSBMCB Award Talks  
  
7:30 – 9:00 p.m. Banquet Dinner

## Sunday April 18, 2010

7:00 – 8:30 a.m. Breakfast

### Session 6. Membrane Proteins and Diseases

(Chair: Xing-Zhen Chen)

8:30 a.m. – 12:00 Noon Elaine Leslie (University of Alberta)  
Gergely Lukacs (McGill University)  
Steve Somlo (Yale University)  
Sven-Eric Jordt (Yale University)

12:00 – 1:30 p.m. Lunch

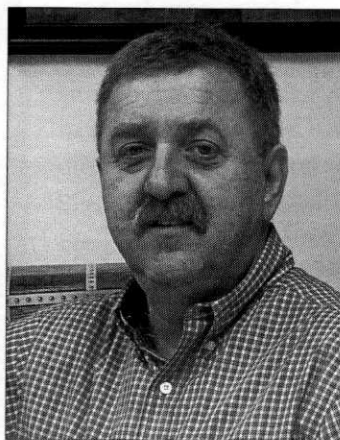
## News from Member Departments

### University of Alberta Department of Biochemistry

Department Chair: **Bernard Lemire**

It was a year of change for the Biochemistry Department. Following the appointment of Dr. Philip **Baron** as the new Dean of the Faculty of Medicine & Dentistry, **Marek Michalak** was recruited as the new Associate Dean Research. This followed shortly after his re-appointment as Department Chair for a second term on January 1<sup>st</sup>. Stepping into Marek's large shoes, **Bernard Lemire** was appointed Acting Chair. Bernard appointed **David Brindley** as Associate Chair and Graduate Coordinator. The department has embarked on a Chair recruitment search with the intent of appointing a new Chair for July, 2010. As part of the new Dean's restructuring of the Faculty, the departments of Biochemistry, Cell Biology, Pharmacology and Physiology, as well as the Center for Neurosciences now merge into the School of Molecular and Systems Medicine, creating four new schools. **Joel Weiner** was appointed the technical lead.

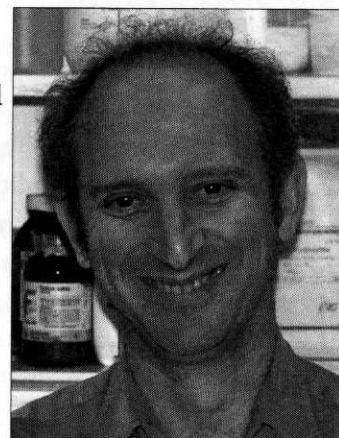
In addition to the change in leadership and Department restructuring, 2009 was a year when the Alberta Heritage Foundation for Medical Research (AHFMR), the Alberta University Fund, the Alberta Health Research Council, the Alberta Life Sciences Institute and others ceased to exist. On January 1<sup>st</sup>, the AHFMR became the Health Research Council. The Alberta Health Innovates - Health Research Council (AIHS), part of the Province's reorganization



Marek Michalak

of research funding through the Alberta Research and Innovation Act (royal assent in June, 2009). The Board of AIHS reports to the Minister of Advanced Education and Technology. The AHFMR endowment fund will continue to be used to support a balanced long-term program of research and innovation related to health, but details of the programs it will support have yet to be announced.

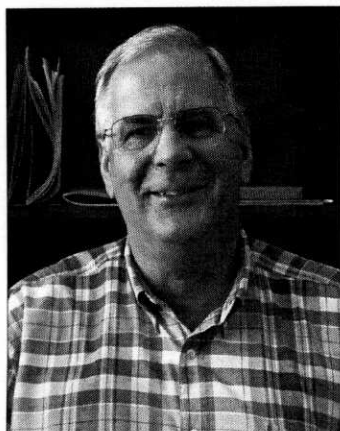
Department members garnered several awards in 2009. **Dennis Vance** received the **J Gordin Kaplan** Award for Excellence in Research, the most prestigious U of A research award. Dennis was Professor and Chair of the Department of Biochemistry at UBC (1982-86) and Associate Dean of Medicine (1978-81). He moved to here in 1986 to establish



Larry Fliegel

a Lipid Research Group. **Larry Fliegel** was awarded a Killam Annual Professorship. **Chris Bleackley** was appointed as a Distinguished University Professor, one of the highest honors the University can bestow on a member of its academic staff. **Michael James** was awarded the M. Buerger Award from the American Crystallographic Association. **Brian Sykes** was elected as a Fellow of the International Society of Magnetic Resonance (ISMAR) for outstanding contributions in the field of NMR. **Marek Michalak** was awarded the Tier I Basic Science Award for Excellence in Mentoring. **David Brindley** was awarded an AHFMR Senior Investigator Award. Both **Richard Fahlman** and **Joanne Lemieux** were recipients of awards from the CFI Leaders Opportunity Fund and the Small Equipment Grants Program. Congratulations to all. One of our graduate students, **Olivier Julien** (Brian Sykes' lab)

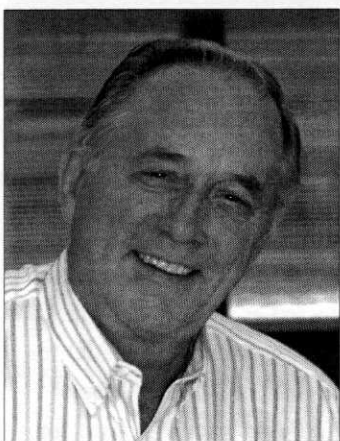
was awarded a Lionel E. McLeod (McLeod was founding president of the AHFMR) Health Research Scholarship.



Brian Sykes

The University of Alberta International Genetically Engineered Machine (iGEM), team again distinguished itself at the synthetic biology competition hosted by MIT. This year's team, with team leaders **Mike Ellison**, **Doug Ridgway** and James MacLagan developed an automated method for the rapid assembly of

complex genetic assemblies. The team competed against 111 other teams from around the world and were awarded the prize for **Best Foundational Advance**. They succeeded against teams from MIT, Berkeley, Heidelberg, Kyoto, Paris and others. This was a transformative experience for the students and we are extremely proud of them. Congratulations to all involved.



Michael James

Short notes: **Roger Bradley** (Departmental technician), **Ruthven Lewis** (Research Associate with Ron McElhaney) and **Shirley Woywitka** (office staff) retired this year after 42, 30+ and 17 years of service, respectively. **Joanne Lemieux** and **Howard Young** are the proud parents of twin boys named Quinn and Oliver, who were born on January

15<sup>th</sup>, 2009. We were saddened by the death, in September of Nancy Sykes, Brian's wife of 41 years, and of Sharon Demytruk, who worked in our wash-up facilities for 18 years.

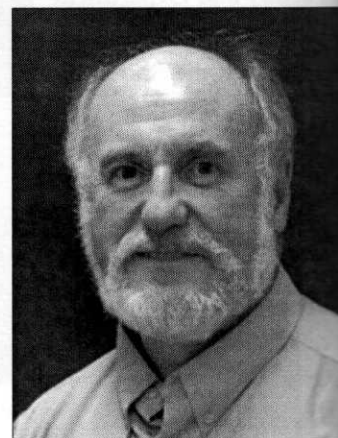
Two of our most notable visitors last year were Dr. Joseph Metzger, Director for the Center of Integrative Genomics at the University of Michigan. Dr. Metzger delivered the 22<sup>nd</sup> John S. Colter Lecture entitled "Bio-sensing Molecular Rheostat for the Failing Heart". We were also honored by the visit of Dr. Natalie Strynadka from UBC. She delivered the 5<sup>th</sup> W.A. Bridger Lecture in Biochemistry on "Antibiotic Discovery Targeting Enzymes in the Bacterial Membrane".

## University of Alberta Department of Cell Biology

Correspondent: Paul LaPointe

The Cell Biology department at University of Alberta has been largely built by our chair, **Rick Rachubinski**, over his 17 year tenure to span a variety of areas in cell biology and with a strong molecular focus in each case. In 2008 we welcomed two new faculty members, **Joel Dacks** and **Paul LaPointe**, and one more in 2009, **Moira Glerum**. Our respective research in evolution of the secretory pathway, the cell biology of the Hsp90 system and mitochondrial function broadens the spectrum of research taking place in our department which already includes neuroscience, *Drosophila* development, and organelle biogenesis and inheritance.

Several of our investigators have been recognized in the last year for excellence in their research; **Rick Wozniak** received a Scientist Award from the Alberta Heritage Foundation for Medical Research (AHFMR), a recent Cell Science publication from the laboratory of **Robert Campenot** was recognized as a Sanofi-Aventis



Rick Rachubinski





Tara Glerum

Outstanding Research Article (Mok et al., 2009, NGF-deprived distal axons of rat sympathetic neurons in compartmented cultures. *Cell Res.* 19:546-60). Members of our Department have been successful in bringing approximately \$5.5 million in research funding from provincial and national sources.



Fred Dacks

Our students have also been successful in obtaining prestigious fellowships including the Vanier, Dr. Fred Banting and Dr. Charles Best CIHR Graduate Fellowships, and the Izaak Walton Killam Memorial Scholarship. We also graduated 14 MSc and PhD grads in 2009 while welcoming nine new graduate students to our Department.



Andrew Simmonds

In June 2009, faculty members **Andrew Simmonds** and **Sarah Hughes** were on the organizing committee of the University of Alberta-hosted 10th biennial Canadian *Drosophila* Research Conference

(*Confly*) at the Sawridge Inn in Jasper, Alberta. This conference was a huge success attracting 121 researchers from across Canada, the United States and Europe.

The conference featured sessions on cell biology, cell signalling, cell adhesion/cytoskeleton, gene regulation and neurobiology.

The Department of Cell Biology hosted a number of high calibre speakers in 2009. Vivek Malhotra (Chair, Cell and Developmental Biology, Centre for Genomic Regulation, Barcelona, Spain), Yosef Yarden (Professor, Dept of Biological Regulation, The Weizmann Institute of Science, Rehovot, Israel), Lars Ellgaard (Associate Professor, University of Copenhagen, Denmark) and Mark Field (Professor, University of Cambridge) gave wonderful talks and participated in important discussions with our faculty and trainees. We also hosted Juan Bonifacio (Head, Cell Biology & Metabolism Program, National Institutes of Health), **David Kaplan** (Professor, The Hospital for Sick Children MaRs Centre Toronto Medical Discovery Tower) and **John Bergeron** (Professor and Chair, Dept of Anatomy and Cell Biology McGill University). Visits by these and other scientists contributed to the already vibrant environment of the Cell Biology Department.

The last year has seen many changes to the research landscape in Alberta. The AHFMR agency, which has funded world-class research across the Province for several decades, is being transformed into a new agency, Alberta Innovates Health Solutions (AIHS), which promises to continue in that tradition. Our members look forward to working through the CSBMCB to promote basic research across the country at the provincial and national levels.

## University of Calgary

### Department of Biological Sciences

### Faculty of Science

Correspondent: Vanina Zaremborg

In 2009, our Department has gone through a second restructuring process initiated five years ago. This has resulted in the formation of four new clusters based on

general research and teaching interests. The Biological Sciences clusters include Biochemistry, Microbiology, Cell Development & Physiology and Ecology & Evolutionary Biology. **Ray Turner** has passed the torch to **Marie Fraser** who is the new chair of the Biochemistry cluster for a two-year term, while **Greg Moorhead** is chair of the Biochemistry program for the same period. **Doug Storey** and **Wic Wildering** are the chairs of the Microbiology and Cell Development and Physiology clusters respectively. Although the role and mandate of the clusters are being better defined as we move forward, the new structure seems to be more operational than the three-cluster format previously imposed. In fact this year, clusters and undergraduate programs were challenged by the economic down turn on the financial situation of our University right before the fall term started.

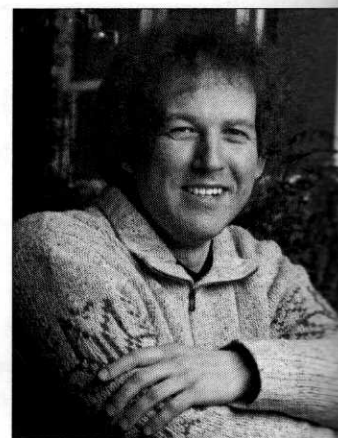
Fortunately, the Biochemistry program has been ahead in its strategic planning and the impact of the budget cuts on our courses was minimal. We were able to deliver good quality lab experiences to our students and a special recognition goes to our excellent instructors **Robert Edwards**, **Elke Lohmeier-Vogel** and **Isabelle Barrette-Ng** who all played key roles in this achievement. **Isabelle Barrette-Ng** received a Student's Union Teaching Excellence Award and **Robert Edwards** received a 'U Make A Difference' Award in 2009. Both **Elke Lohmeier-Vogel** and **Isabelle Barrette-Ng** were heavily involved in the Departmental BioCore Committee, which has a mandate for developing first-year Biological Sciences courses as well as for evaluating their alignment with second year courses.

Research in our Department is exciting at all levels and several colleagues have been recognized with distinctions/awards for their contributions or have received important funding to support future or ongoing projects. **Hans Vogel** was the recipient of the 2009 Roche Diagnostics / Senior Scientist Award in recognition to his outstanding career as a world leader in the study of metalloproteins, calmodulin and related calcium-regulatory proteins in animals and plants. Hans was also very pleased to be invited to present the annual Theo Hofmann lecture in the Department of

Biochemistry, University of Toronto, as he has collaborated and published several papers with Theo in the past. **Peter Tieleman** has received a prestigious NSERC Steacie Fellowship, which will help in further developing computer models to expand the range of membrane problems he can investigate by simulation and improve the link between the simulations and experiments. Peter continues his work on lipid flip-flop and defects and has also made progress studying human ABC transporters. He wrote an excellent review on computer simulations of membrane pores, domains, stalks and curves (BBA, 2009).

**Peter Facchini** discovered the two biosynthetic genes that give opium poppy the unique ability among plants to produce codeine and morphine. The two genes are the only known examples of *O*-demethylases in the 2-oxoglutarate/Fe(II)-dependent dioxygenase family. The work was published in

*Nature Chemical Biology* and generated worldwide media interest. Peter also launched, as Project Leader, the \$13.6 M PhytoMetaSyn Project sponsored by Genome Canada, and four regional Genome Centres. The project is aimed at the discovery of a repository of novel enzymes, the reconstitution of plant natural product pathways in yeast, and the establishment of plug-and-play functional genomics with research and commercial applications. Peter was awarded, with **Dae-Kyun Ro**, a \$1.58 M Leaders Opportunity Fund grant from the Canada Foundation for Innovation (CFI) for the purchase of a Thermo LTQ-Orbitrap mass spectrometer. They also received funds through an NSERC RTI award for the purchase of an Agilent LC-QQQ mass spectrometer. The CFI funds will also be used to build a facility in the Department of Biological Sciences housing both instruments.



Peter Tieleman

**Renar Prenner** continues teaching and research in the area of biophysics and biomembranes. He is increasingly engaged in the minor in Nanoscience that was launched in the Faculty of Sciences at the University of Calgary in 2009 by contributing to two courses. In addition, Renar continues to serve as associate editor of the *Journal of Biomedical Nanotechnology*. His collaborative work with industry was supported by a grant from Alberta Health Services under the Nanoworks program and by the Canadian Institute of Photonics Innovation. Moreover, the group participates in a new Genome Canada initiative "Hydrocarbon metagenomics" initiated by **Gerrit Klaerner** from our Department.

**Greg Moorhead** received funding from the Canadian Cancer Foundation and started his first year service on the NSERC grant panel. **Ray Turner** successfully renewed his CIHR grant to examine functions of the Twin arginine translocase system.

Graduate student Matt Workentine (**Turner**) received a presentation award at the 2009 American Society of Microbiology Biofilm conference for novel work using fluorescent proteins as markers in biofilm colonization experiments under metal stress. Teshager Bitew (**Turnberg**) won a **Graduate Poster Presentation** at the third Biological Sciences Conference and a travel award from the ASBMB to present his work on the study of the mode of action of antitumor lipid drugs at the annual meeting held in New Orleans.

**Dr. Fraser** spent six months of her sabbatical working in the pharmaceutical industry. She joined Cell, Protein and Structural Sciences, a department of approximately 100 people at the Alderley Park research facility of AstraZeneca near Manchester in the United Kingdom. Available for Marie was the insight gained into the process of drug design: target selection, biological assays, high-throughput screening, lower-throughput screening via nuclear magnetic resonance spectroscopy, surface plasmon resonance, and the interplay between microscopy and computational and medicinal

chemistry. Back in Calgary she became chair of the Biochemistry cluster.

For more information about our activities in the Department of Biological Sciences please visit <http://www.bio.ucalgary.ca/research/index.html>.

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## Dalhousie University

### Department of Biochemistry & Molecular Biology

*Correspondent: David Byers*

Two new Faculty members joined the Dalhousie Department of Biochemistry & Molecular Biology over the past year. In July, we welcomed **Claudio Slamovits** and his family to Halifax following their cross-Canada drive from British Columbia (a ritual we should all experience at least once!). Claudio is an Assistant Professor and a member of the Centre for Comparative Genomics and Evolutionary Bioinformatics (CGEB), and will complement that stellar group with his expertise in the structure, function and evolution of protist nuclear genomes. He has hit the ground running, having already been awarded a new researcher CFI grant and recruiting a number of trainees to his lab.

**Aarnoud van der Spoel** arrived a few months later in October, joining the Atlantic Research Centre (ARC) as an Assistant Professor of Pediatrics and Biochemistry & Molecular Biology. Following his graduate training in The Netherlands, Aarnoud was a postdoctoral fellow and then senior research associate at the University of Oxford, where he honed his research interests in the pharmacology and disorders of glycosphingolipids.

Several members of our Department received significant recognition in 2009. We stood by with great pride as two long time members of our administrative staff were honoured: **Barb Bigelow** received a 2009 Rosemary

Gill Award, one of Dalhousie's most prestigious non-academic awards that recognizes outstanding service to students, while **Roisin McDevitt** received a Staff Award for Professional Excellence at the annual Faculty of Medicine Community of Scholars Dinner in April. Barb and Roisin provide the bedrock support for our undergraduate and graduate students, respectively.

At the same event, **Kirill Rosen** received the Dalhousie Medical Research Foundation Award of Excellence for Basic Medical Research, an annual recognition provided to a faculty member within the first eight years of their independent career. **Rick Singer** was the 2009 faculty recipient of the Faculty of Graduate Studies Distinguished Service Award. There could be no better candidate for this honour than Rick, who has been our Graduate Coordinator for well over a decade and has presided over tremendous growth in what is currently the largest graduate program in the Faculty of Medicine. We also congratulated **Paul Briggs**, an Instructor in the Department, on receiving his Masters of Education from Mount Saint Vincent University, and **Roger McLeod** and **Andrew Roger**, who were promoted to Full Professor.

We continue to celebrate the success of our students and postdoctoral fellows, many of whom are supported by national and local salary awards. **David Walsh** (a former student of **Ford Doolittle**) received the departmental Patrick Prize for outstanding research by a recent Ph.D. graduate, while **Gerrit Volkmann** (a graduate student with **Paul Liu**) won the Doug Hogue Award for persistence and dedication to research.

Challenges in the new year will include contribution to a renewed undergraduate medical curriculum and its delivery to a new site (Saint John, New Brunswick), planning major renovations for the Comparative Genomics and Evolutionary Biology group, and maintaining and expanding our research in an ever more competitive funding environment.

## University of Guelph Department of Molecular and Cellular Biology

*Correspondent: Frances Sharom*

### New faculty and staff members

**Cezar Khursigara** joined the Department of Molecular and Cellular Biology in June 2009, bringing with him expertise in high-resolution cellular imaging. Cezar completed his undergraduate studies at Ryerson University in 1999, where he worked with Dr. Debora Barnett-Foster investigating the fundamentals of bacterial pathogenesis using enteropathogenic and enterohemorrhagic *E. coli* as model systems. During his doctoral studies in the Department of Microbiology and Immunology at McGill University, Cezar worked with Dr. James Coulton. Here he used a combination of molecular, biophysical and structural approaches to elucidate mechanisms of iron acquisition in Gram-negative bacteria. In 2005 Cezar graduated from McGill and joined the laboratory of Dr. Sriram Subramaniam at the National Cancer Institute, NIH, in Bethesda, Maryland. As a post-doctoral fellow, he helped pioneer new methods in cryo-electron microscopy and tomography. His research focused on understanding the molecular architecture of sensory proteins involved in bacterial chemotaxis. Now at the University of Guelph as an Assistant Professor, Cezar is developing and applying novel cellular imaging techniques to probe macromolecular and cellular structures involved in essential bacterial processes. Two of the current focuses of his laboratory include investigating protein complexes involved in cell division, and the cellular interactions regulating bacterial biofilm formation.



Cezar Khursigara



The high-end instrument used by Cezar's group is currently a JEOL Tecnai F20 cryo-transmission electron microscope that is capable of high-resolution single particle and three-dimensional tomographic imaging. The Department hopes to expand the EM facility to include new TEMs and a state-of-the-art DualBeam SEM for biological applications. Cezar is currently funded by an NSERC Discovery Grant to investigate macromolecular protein complexes involved in bacterial cell division, and by The Advanced Foods and Materials Network of Canada to investigate cellular architecture of bacterial biofilms. He was also awarded an NSERC equipment grant for cryo-EM tools in 2009.



Enoka Wijekoon

The Department recently recruited **Dr. Enoka Wijekoon** as an undergraduate instructor/coordinator. Enoka received a Bachelor of Veterinary Science degree from the University of Peradeniya, Sri Lanka, following which she was appointed as a Lecturer in the Department of Veterinary Clinical Studies at the same university.

Enoka then obtained a Ph.D. in biochemistry from Memorial University of Newfoundland, where she studied homocysteine metabolism in type 2 diabetes and the effect of homocysteine on vascular function. After receiving a postdoctoral fellowship from the Canadian Institutes of Health Research/Regional Partnership Program (CIHR/RRP), she carried out research on the mechanisms of hypertension in the Division of Biomedical Sciences, Faculty of Medicine, at Memorial, during which time she was also involved in teaching biochemistry courses as a seasonal lecturer. In addition to being a lecturer in the biochemistry courses offered by the Molecular and Cellular Biology Department at Guelph, Enoka is also the faculty advisor for both the regular and the Co-op biochemistry programs. This involves guiding students through course

selections, planning of academic and work term schedules for Co-op students, and evaluation of student's work-term reports. She is also an active member of the curriculum committee of the biochemistry program.

#### Faculty news

One of our relatively new faculty members, Dr. **Emma Allen-Vercoe**, was awarded a CIHR Microbiome Catalyst Grant to initiate studies on the role of human stress hormones in modulating gut bacterial community behaviour, as well as a Crohn's and Colitis Foundation of Canada grant to continue her studies of the role of *Fusobacterium nucleatum* in exacerbating inflammatory bowel disease.

#### New research initiative

A team of researchers from University of Guelph (including several members of our department) and Toronto has recently received funding from the Ontario Ministry of Research and Innovation for a commercial dynamic nuclear polarization (DNP)-enhanced solid-state nuclear magnetic resonance (SSNMR) spectrometer, which was built recently (2009) by Bruker Ltd. The funding for the instrument was only partial (\$1.8 million), and the interdisciplinary team, led by **Vlad Ladizhansky** (Physics), is currently trying to secure additional funds. The DNP SSNMR spectrometer at Guelph would be the first instrument of its kind in Canada, one of the very few in the world, and would operate at the highest magnetic field currently available for DNP (14.4 Tesla, or a proton frequency of 600 MHz). Great progress has been achieved in recent years in applying NMR techniques to the characterization of molecules in the solid state, but the poor sensitivity of the technique puts stringent requirements on the molecular weight of the systems, and demands a high amount of sample material. Improving the sensitivity of SSNMR has always been at the forefront



Emma Allen-Vercoe

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of methodological developments in the field. One of the most dramatic recent achievements has been the development of a new generation of spectrometers that combine traditional SSNMR approaches with the effect of DNP. The basic idea of the DNP technique is to transfer large electron spin polarization to nuclear spins, thus enhancing the NMR signal. Many groups have contributed to the realization and application of DNP. In particular, Bob Griffin and co-workers at MIT have developed new approaches and technologies required for the application of DNP at high magnetic fields. They have demonstrated the feasibility of DNP in a number of biological systems ranging from small molecules, to membrane proteins, to large supramolecular aggregates and amyloid fibrils. Signal enhancements routinely available with DNP are on the order of 30 or higher. The availability of such a high-field DNP-SSNMR instrument at Guelph will permit high-resolution structural studies of many challenging molecular systems. The highest priority for us is structural biology of membrane proteins, with particular emphasis on systems that have been traditionally hard to study such as G-protein coupled receptors and ABC transporters.

#### **Sabbatical leave visitors and visiting scientists**

**Dr. Charles Deutch** spent his sabbatical leave from Arizona State University in **Janet Wood's** lab from July 2008 through June 2009. While he was in Guelph, Dr. Deutch initiated a functional proteomics project that is now funded by CIHR, and continued by Research Assistant Doreen Culham and graduate student Geordie Wright: characterization of osmolytes and osmolyte transporters that confer osmotic, thermal, oxidative and urea stress tolerance on *E. coli* cells.

**Dr. Hugues Massicotte**, Ecosystem Science and Management, University of Northern British Columbia, was a visiting Professor with **Larry Peterson** from Aug-Dec 2009, to collaborate on two projects concerning the structural aspects of fungus-plant interactions in a number of myco-heterotrophic (non-photosynthetic) plant species. Two manuscripts were completed based on these projects,

and a book chapter dealing with myco-heterotrophic plants was contributed to a forthcoming book, "Plant Fungal Interactions", edited by D. Southworth, to be published by Wiley-Blackwell.

**Dr. Yaping Jin** (Professor and Associate Dean, College of Veterinary Medicine, Northwest A & F University, China) worked in the lab of **Ray Lu** for two months (Oct-Nov 2009) on an ongoing collaboration project. Dr. Jin had previously visited the Lu lab for a year (2007-2008), funded by an exchange/training program of Chinese Ministry of Education. The collaborative research focuses on LRF gene knockout mice, which have an infertility phenotype in the null mice. As an expert in the field of reproductive biology and endocrinology, Dr. Jin has been helping to figure out the underlying mechanism of the observed infertility problem.

**Dr. Rashpal Bhogal** (Mount Sinai School of Medicine, New York) worked in **Azad Kaushik's** laboratory as a Visiting Associate for a year starting in June 2009. Dr. Bhogal has contributed to a comprehensive review on bovine immunogenetics, and has learned immunoinformatic techniques in the Kaushik lab which she is applying to analyze the bovine genome.

**Dr. Bahadur Meah**, Bangladesh Agricultural University at Mymensingh, Bangladesh, paid a short-term visit to the lab of **Annette Nassuth** in April 2009 to discuss a collaborative research project on the development of molecular photomorphogenesis resistance marker(s) in eggplant. A Ph.D. student of his, Ibrahim Khalil, worked in Guelph on this project for a 6 month period with the financial assistance of a GSEP (graduate student exchange program) award from the government of Canada.

#### **Congratulations!**

**Dr. Rod Merrill's** graduate students, **Rob Fieldhouse** and **Danielle Visschedyk**, were both awarded NSERC CGS (Ph.D.) scholarships in 2009, and Danielle also received a travel award to present her work at the American Biophysical Society Meeting in 2009. The Multiple

Sclerosis Society of Canada awarded a Postdoctoral Fellowship to **Dr. Vladimir Bamm**, and Ph.D. Studentships to **Graham Smith** and **Miguel De Avila**, all in **George Harauz's** lab.

## McMaster University

### Department of Biochemistry and Biomedical Sciences

Correspondent: *Alba Guarné*

In 2009, we were thrilled to "go live" with our new web site that showcases the Department with a fresh look and improved navigation. We also saw some extraordinary new infrastructure completed. The Michael G. DeGroote Institute for Infectious Disease Research spearheaded by **Gerry Wright** officially opened its doors in newly constructed space in the M. G. DeGroote Centre for Learning and Discovery. The Grand Opening Symposium was an excellent mix of talks and posters describing outstanding science.



Professor Michael G. DeGroote, his grandson Devon DeGroote (left) and Dr. John Kelton, Dean and VP, Faculty of Health Sciences, listening to Professor Gerry Wright during the inauguration of the Michael G. DeGroote Institute for Infectious Disease Research. Picture by Ron Schessler.

Congratulations to **Mick Bhatia** who received the CSBMCB Young Scientist Award at the 52<sup>nd</sup> Annual Meeting held in Niagara-on-the-Lake, and **Felicia Vulcu** who received the MSU Teaching Award during her first year of teaching. The late Dr. **Barbara Ferrier** was inducted to the Community of Distinction in recognition of her outstanding contributions to McMaster University Faculty of Health Sciences. Dr. **Richard Haslam**, Professor Emeritus and joint member of the Department passed away this year. Richard had a long and productive scientific career and leaves outstanding contributions to cardiovascular research.

The Department welcomed 24 new students to our program and our total graduate student population now rests at 124 students, exceeding the goal that we set five years ago of doubling our graduate enrolment. Importantly, we have expanded without compromising the quality of the students who continue to do extremely well in securing scholarships including **Suzanne Osborne** (Coombes lab) who got one of the five prestigious Vanier Scholarships that were awarded to McMaster University students. Additionally, 29% of our graduate students were funded by competitive scholarships from NSERC, CIHR, Cystic Fibrosis Foundation, Heart and Stroke Foundation, Canadian Breast Cancer Foundation and OGS, a testament to the exceptional quality of our students. The outstanding work of two of our international students, **Yu Seon Chung** (Guarné lab) and **Soumaya Zlitni** (Brown lab), was also recognized with the newly minted Dean's Award for top international students. **Yu Seon Chung** (PhD), **Clinton Campbell** (PhD, Bhatia lab), **Ted Sewell** (MSc, Brown lab) and **Peter Spanogiannopoulos** (MSc, Wright lab) were the recipients of the 2008-09 Karl B. Freeman Awards that recognize students deemed to have presented the most outstanding graduate seminars of the year. Eleven M.Sc. students graduated in 2009, and thirteen Ph.D. candidates successfully defended their theses. The majority of our PhD graduates have taken postdoctoral positions at prestigious Canadian and International Universities. Good luck to all of them!



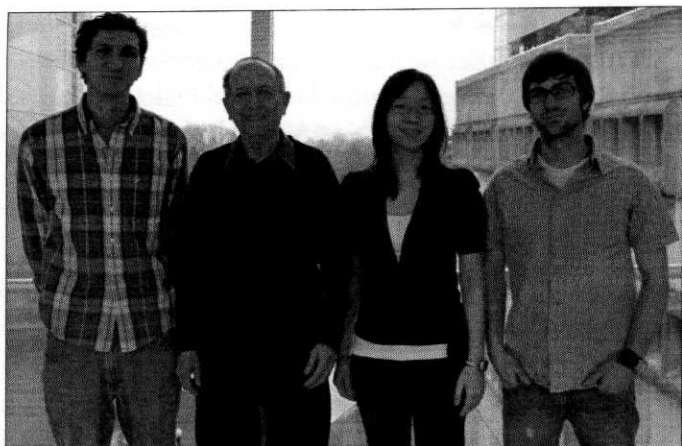


Photo Caption: Karl Freeman awardees: Peter Spanogiannopoulos (M.Sc., 2nd place), Professor Karl Freeman, Yu Seon Chung (Ph.D., 1st place) and Ted Sewell (M.Sc., 1st place). Picture by Donna Marfisi.

Through the year, students, staff and faculty also found good excuses to have fun. The 3<sup>rd</sup> Annual Photo Scavenger Hunt where the **Ray Truant** Lab took top honors for second year on a row was hilariously successful. The 1<sup>st</sup> Biochemistry Science Olympics was the highlight of this year Annual Departmental Picnic at Webster's Falls. Congratulations to the **Nathan Magarvey** lab for taking first place and to our Chair for proving that his crazy schedule has not weakened his laboratory skills. To wrap a great year up, we had a phenomenal Snow Ball Christmas Party!



Photo caption: Dr. **Eric Brown**, Professor and Chair of the Department of Biochemistry and Biomedical Sciences competing at the Biochemistry Science Olympics under the close scrutiny of graduate students Courtney Barker and Geordie Stewart. Picture by Donna Marfisi.

## Ryerson University

### Department of Chemistry and Biology

Correspondent: Roberto Botelho

The Department of Chemistry and Biology encompasses multi-disciplinary interests in research and teaching. Through 2009, 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, protein biochemistry, development and membrane signalling. 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.



Roberto Botelho

In 2009, members of our Department were quite successful in obtaining external funding, including two CFI grant awards to Drs. **Gideon Wolfaardt** and **Dérick Rousseau** to respectively study biofilm interfaces and physico-chemical properties of food materials. We also saw the publication of several articles related to the fields of biochemistry and/or molecular cell biology from the laboratories of Drs. Barnett Foster (EHEC pathogenesis), Roberto Botelho (lipid signaling), Marie Killeen (neuronal development), and John Marshall (protein complexes).

Perhaps, the most significant change to our department in 2009 was the hiring of another faculty member at the Assistant Professor level, Dr. **Jeff Fillingham**, who did his Ph.D. at York University with Dr. Ron Pearlman and his post-doctoral studies with Dr. Jack Greenblatt at the University of Toronto. His expertise in chromatin assembly and regulation is a great addition to our Department's collective expertise in biochemistry and molecular and cell biology. We are now seeking candidates with expertise in molecular evolution and ecology to hire in 2010.



For our Department, 2009 is in many ways a preparative year for expansion of the undergraduate and graduate curricula. First, we are currently planning to create specialized B.Sc. programs in Cell and Molecular Biology. Second, we have expanded the steady state number of M.Sc. students in the Molecular Sciences graduate program and thirdly, we are steps closer to establish a Ph.D. program in Molecular Sciences.

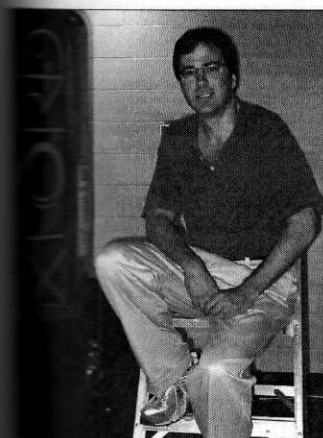
Overall, 2009 was a productive year for the Dept. of Chemistry and Biology and we expect continued growth in 2010.

## University of Toronto

### Department of Biochemistry

Correspondent: David Williams

#### Faculty News



Lewis Kay

We were delighted to learn that **Lewis Kay** has been elected to the Royal Society (UK) for his work on NMR spectroscopy. He and his group have developed many of the recent technical advances that have pushed the size limit of protein complexes that can be examined by NMR spectroscopy beyond 500 kDa. For

example, methyl-TROSY was used to elucidate the structure and aspects of the dynamics of the 670 kDa 20S proteasome core particle. He has also developed methods for studying invisible excited states of proteins by NMR and is applying them to furthering our understanding of protein folding and conformational dynamics. Lewis is the 5th member in the over 100 year history of the Department to receive this very prestigious honour. Other UK are our first Chair, Archibald Byron Macallum, James Hanes, Gordon Dixon and David MacLennan. Congratulations to Lewis!

Congratulations also to **Bibudhendra (Amu) Sarkar** who has been appointed Fellow of the Royal Society of Chemistry, U.K. The Royal Society of Chemistry is the oldest Society of Chemical Sciences in the world and dates back to 1841. He was recognized for his significant contributions in the Chemical Sciences field. Amu is well known for his discovery of the treatment of Menkes disease, a genetic disease causing neurodegeneration in children who would otherwise die by the age of three. Due to the application of his innovative research, a Menkes patient reached the age of 22. This treatment is now used throughout the world. His research not only successfully treated a fatal genetic disease, but also resulted in the discovery of a motif in proteins (the ATCUN motif), which is now being used for specific DNA cutting, the killing of certain tumour cells, and the elucidation of protein structure. More recently, the development of an accurate and inexpensive method of measuring arsenic by his team of researchers is giving hope to millions of people suffering from cancer and other diseases in remote villages in South Asia due to arsenic exposure from contaminated drinking water.

University Professor Emeritus **Marian Packham** has published a biography of Dr. Fraser Mustard entitled *Connections and Careers*. As collaborators for over three decades, Dr. Packham was able to bring a great deal of personal insight and experience to the project. One of Canada's most influential scientists, Dr. Mustard was a founding member of McMaster University's Faculty of Medicine, was founding president of the Canadian Institute for Advanced Research and was named as one of the University of Toronto's 10 Giants of Biomedical Science. His scientific accomplishments are lengthy and notable and include studies on the inhibition of platelet aggregation by aspirin and that platelet aggregation could lead to heart attacks and strokes.

**Julie Forman-Kay** is co-chair of the CFTR 3D Structure Consortium (with Christie Brouillette from the University of Alabama Birmingham or UAB), an initiative of the Cystic Fibrosis Foundation Therapeutics. By facilitating collaborative interactions, this consortium is intended to

stimulate progress towards 3D structural information on CFTR, its interactions with potential drugs and the effects of CF-causing mutations. There are about a dozen scientists involved from all over the world (UK, Netherlands, Israel, US and Canada) using a variety of experimental methods (X-ray, EM, NMR, DSC, computations, etc.). They have had two in-person meetings (March 2009 at UAB and October 2009 in Minneapolis before the North American CF Conference, the next scheduled for June 2010 in Bethesda at the CF Foundation headquarters) and have regular teleconference calls together and in subgroups. It has been quite successful in stimulating collaborations, including one involving Jack Riordan at U. North Carolina and Dev Sidhu at U. of T. who uses a phage approach for making antibodies against CFTR.

**Julie Forman-Kay** along with Co-Director **Walid Houry**, successfully renewed the CIHR Strategic Training Program in Protein Folding and Interaction Dynamics: Principles and Diseases for another 6 years. With a budget of \$320,000/yr, this highly successful program provides stipends for graduate students and postdoctoral fellows to work under the supervision of co-mentors who utilize transdisciplinary approaches to study protein folding and protein interaction dynamics. The Training Program also offers specialized courses in this discipline, travel grants for attendance at scientific meetings and focused conferences and workshops that expose trainees to top researchers in the field. To date, trainees supported by the Program have produced over 130 scientific papers. Most recently, the Training Program held a minisymposium at the 52nd Annual Meeting of the CSBMCB Meeting on Protein Folding: Principles and Diseases held June 1 - 5, 2009 in Niagara-on-the-Lake, Ontario. Mentors of the Training Program, **David Williams** and **Hue Sun Chan**, were co-chairs of the CSBMCB Annual Meeting and the Program was also the principal financial sponsor of the Meeting. For more on the Training Program, visit: [http://biochemistry.utoronto.ca/CIHR\\_folding](http://biochemistry.utoronto.ca/CIHR_folding).

**Walid Houry** co-organized the 8<sup>th</sup> International Conference on AAA+ proteins that was held just north

of Toronto, July 12 – 16, 2009. The Conference was a great success and attracted about 100 international delegates. Walid, in collaboration with Andrew Emili's and Zhaolei Zhang's groups, recently published the full physical interactome of all the yeast chaperones: Gong, Y., Kakihara, Y., Krogan, N., Greenblatt, J., Emili, A., Zhang, Z., & Houry, W. A. "An atlas of Chaperone-Protein Interactions in *Saccharomyces cerevisiae*: Implications to Protein Folding Pathways in the Cell" *Molecular Systems Biology* 5:275, 1-14 (2009).

Congratulations to **Grant Brown** who received the "Excellence in Undergraduate Teaching in Life Sciences Award." It was awarded for his excellent contributions to undergraduate laboratory teaching in the Faculty of Medicine, specifically for coordinating our 4<sup>th</sup> year project course for the past 8 years and for implementing a new research project course for 3<sup>rd</sup> year students. The latter provides undergraduates with earlier opportunities for research experience in "real-world" settings and increases one-on-one contact between students and faculty. Congratulations also to **Emil Pai** and **David Bazett-Jones** who were successful in renewing their Tier I Canada Research Chairs and to **Allen Volchuk** who renewed his Canada Research Chair in Diabetes Research (Tier II).

## Events

Our **Annual Research Day** was held on May 26<sup>th</sup>, 2009 at the Old Mill Inn in Toronto. The day highlighted work by our students and postdocs in the form of posters and oral presentations. Selected talks from some junior faculty also added to the mix. This has become the traditional venue for our annual **Theo Hofmann lecture** which was presented this year



Theo Hofmann lecturer Hans Vogel with Theo Hofmann

by **Hans Vogel**, University of Calgary, who presented an extremely engaging seminar entitled: "Calcium regulation in the EF-handome: from Theo Hofmann's calbindin D9k to brain caldendrin". Terrific science and good spirits combined to create a memorable research day experience. For some photos of the event, go to: [http://biochemistry.utoronto.ca/news/Research\\_Day\\_09.html](http://biochemistry.utoronto.ca/news/Research_Day_09.html)

Other events were our ever-popular **Golf Day, Ski Day and Year-End Party**. For some photos, visit: <http://biochemistry.utoronto.ca/news>

### New Appointments

Leading scientists, **Oliver Ernst** and **Cordula Enenkel** join U of T.

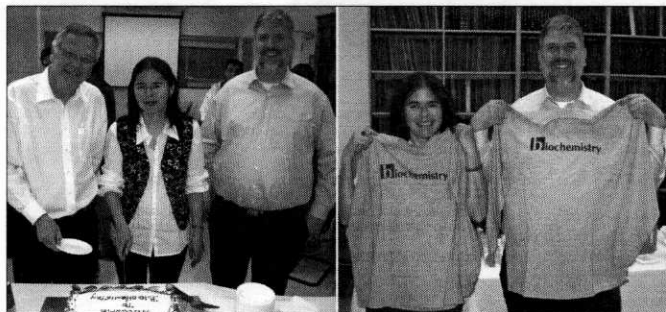
On May 17, 2010 Tony Clement, Federal Minister of Industry announced the 19 inaugural Canada Excellence Research Chairs (CERC) at a ceremony at the University of Toronto. The Faculty of Medicine was successful in recruiting two "rising stars"; Fritz Roth from Harvard University (CERC in Integrative Biology) and **Oliver Ernst** from Charité-Universitätsmedizin in Berlin (CERC in Structural Neurobiology). For each CERC, universities will receive \$10 million over seven years to support chair holders and their research teams. The CERC program is designed to attract leading researchers to Canada in areas of priority aligned with the Federal Government's Science and Technology Strategy. The complete list of CERCs is available at: <http://www.cerc.gc.ca/cpch-pctc-eng.shtml> Oliver will continue his groundbreaking work on rhodopsin, one of the most studied G-protein-coupled receptors (GPCRs) and will establish a membrane protein expression and crystallization facility in the Medical Sciences Building. He will also lead a CERC Unit, a local network of collaborators working in the area of structural neurobiology. Oliver will hold a joint full Professor position in the Departments of Biochemistry and Molecular Genetics.

The CERC program has also enabled U of T to recruit **Cordula Enenkel**, who is married to Oliver. Cordula is an outstanding scientist studying proteasome assembly and protein degradation, an area of critical importance to

diseases such as Alzheimer's. Cordula will be an Associate Professor in Biochemistry and will join a large group of scientists in the Department working on protein folding and interactions in health and disease.

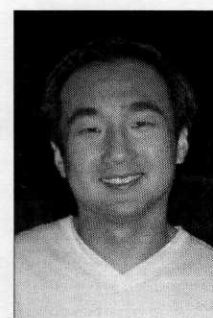
Oliver and Cordula plan to join the University of Toronto on January 1, 2011 and are keen to become part of the growing research enterprise at the U of T. As Oliver declared in an interview: "I am thankful to the federal government for creating the Canada Excellence Research Chairs program and I am eager to become part of the Canadian research success story."

A very warm welcome to Oliver, Cordula, and their family to Biochemistry and to Canada!



Cordula and Oliver are warmly welcomed to the Biochemistry Dept. by Chair Reinhart Reithmeier

We are also very pleased to welcome **Peter Kim** to the Department. Peter is a Scientist in the Division of Cell Biology at the Research Institute of the Hospital for Sick Children and was appointed to the Department of Biochemistry this year. Peter obtained his Ph.D. with David Andrews at McMaster University and completed postdoctoral training with Jennifer Lippincott-Schwartz at NIH. Peter uses sophisticated imaging methods to study peroxisomal assembly and dynamics.



Peter Kim

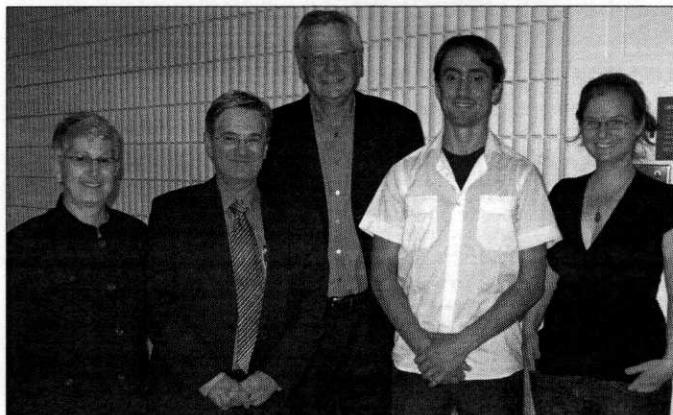
Congratulations to **Igor Stagljär** and **Walid Houry**, both of whom were promoted to the rank of Full Professor, and to **Angus McQuibban** who was promoted to Associate Professor with tenure.



## Graduate Studies

Our fifth annual **Benjamin Schachter Memorial Lecture** took place on June 17th. 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 Biochemistry Grad Students Union invited back alumnus **Michel Dumontier**. Michel's talk was entitled "*What funding? Overcoming challenges in building a multi- and inter-disciplinary research program in Canada*".

Michel's return to the Department of Biochemistry came with great interest as he has had an exciting and rapid career since his Ph.D. defense. Following only a single year as a post doctoral fellow, he is currently an assistant professor at Carleton University. His advice to current graduate students is to pursue interesting research, develop practical skills, improve communication skills, to track your own progress and the most obvious, to publish! Michel stressed the importance of a multidisciplinary approach to research and life in general, getting involved and collaborating on innovative projects and searching for novel ideas to stand out from the rest. Michel is currently developing technologies to facilitate the search and integration of biochemical data accessible via the internet.



From left, Benjamin Schachter's daughter Bonnie Druexerman and son Dan Schachter; Chair Reinhart Reithmeier; Michel Dumontier and BGSU President Eden Fussner

An integral part of the Department's Annual Research Day is its **graduate student poster competition**. Our guest poster judge was this year's Theo Hofmann Lecturer, **Hans Vogel**, University of Calgary. It's always difficult to choose poster winners and our judges had the usual challenge of deciding between many worthy posters. In the end, the following students (who receive cash awards) were chosen as poster winners:

Winners in the Ph.D. category were: **Patrick Walsh** (Sharpe lab) "*Structural characterization of a peptide from the human prion protein*"; **Stephanie Tammam** (Howell lab) "*Characterization of PilP: a protein required for the assembly of *Pseudomonas aeruginosa* Type 4 pili*"; **Patrick Kim Chiaw** (Bear lab) "*Functional rescue of deltaF508 CFTR by peptides designed to mimic sorting motifs*"; **Eden Fussner** (Bazzett-Jones lab) "*Chromatin reorganization is associated with induced pluripotency*"; **Wes Errington** (Privé lab) "*Examining the structural basis of ubiquitin ligase self-assembly and its implication as a regulatory switch*"; and **Sarah Rauscher** (Pomès lab) "*Uncovering order in disorder: exploring the structural heterogeneity of elastin-like and amyloid-like peptides*".

Winners in the M.Sc. category were: **Peter Poliszczuk** (Attisano lab) "*The search for novel Wnt pathway modulators*"; **Eliana Chan** (McQuibban lab) "*A potential mechanism to regulate rhomboid proteolytic activity*"; and **Mustafa Kamani** (Lingwood lab) "*Selective modulation of glycosphingolipid metabolism by soluble glycosphingolipid analogues*".

The winner in the postdoc category was: **Majida El Bakkouri** (Houry lab): "*The acid stress response in bacteria: the role of the novel AAA<sup>+</sup> ATPase RavA*".



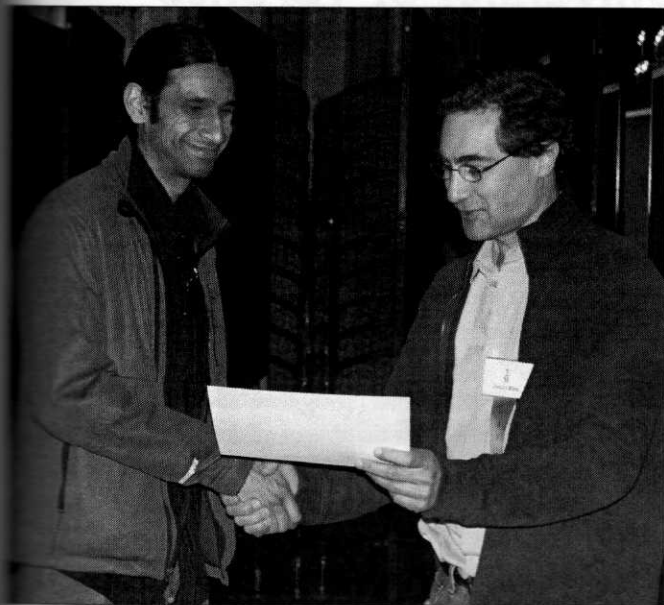
### Additional graduate awards:

The winners of the *Beckman Coulter Paper of the Year* award for 2008 were: **Kelly Stewart** and **Kristin Horton** (Kelley lab) for their paper "Mitochondria-penetrating peptides" Horton KL, Stewart KM, Fonseca SB, Guo Q, Kelley SO. Chem Biol. (2008) 15(4):375-82.



Kelly Stewart (left) and Kristin Horton present their Beckman Paper of the Year in a terrific tag-team format at the 2009 Research Day

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



Roy Baker presents the David A. Scott Award to Usheer

Outstanding Teaching Assistant awards went to **Lori Rutkevich**, **Derek Ng**, **Jean-Philippe Julien** and **Sian Patterson** for their exceptional performance as teaching assistants in our BCH371, BCH 370, BCH471 and BCH210 courses, respectively.



Undergraduate Coordinator, Roy Baker, presents TA awards to Lori, Derek (Top left to right), Jean-Philippe and Sian (Bottom left to right).

Congratulations to all winners on their achievements.

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## University of Toronto

### Department of Cell and Systems Biology

Correspondent: Tony Harris

Since its inception in 2006, the Department of Cell and Systems Biology has become a major contributor to research and teaching at the University of Toronto. Groups in the Department combine many different high-throughput, cell imaging, physiological and bioinformatics methods to characterize and understand cellular and physiological processes in both model (*Arabidopsis*, *Drosophila*, Mouse, Zebrafish, *Xenopus*) and non-model organisms. The Department's major strengths are its groups studying plant molecular biology, its labs focused on animal cell biology and tissue morphogenesis, and its groups studying neurophysiology. The Department is also home to the Centre for the Analysis of Genome Evolution and Function, a CFI-funded centre for genomics and proteomics research, in addition to a state-of-the-art imaging centre.



Jennifer Mitchell

Our faculty continues to grow, most recently with the hiring of **Jennifer Mitchell** in the last year. Dr. Mitchell studies long range interactions between genes and regulatory elements which build transcription factories and integrate transcriptional regulation in the nucleus. This adds to the many recent hires who are invigorating research and

teaching in the Department. As examples, **Alan Moses** and **Eiji Nambara** have also joined the Department in the last few years. **Dr. Moses** uses computational methods and mathematical models to study regulatory elements in DNA and proteins. **Dr. Nambara** uses metabolomics to study the regulation and activity of plant hormones.

Two especially prominent papers were published from the Department in the last year. In a paper in *Nature*, **Ulrich**

**Tepass'** group defined a new protein complex important for regulating the structure of epithelial cells. In a paper in *Science*, the groups of **Peter McCourt**, **Darrell Desveaux** and **Nick Provart** identified an elusive receptor for the key plant hormone abscisic acid.

Our graduate program also continues to grow. We welcomed 42 new students in 2009, and congratulate 30 students on their graduation. Currently we have ~140 graduate students in the Department. We are very proud of our students' success in earning scholarships and travel awards. For example, our students won eighteen NSERC Graduate Scholarships and nine Ontario Graduate Scholarships last year.

In 2009, **Ulrich Tepass** became Chair of the Department. Dr. Tepass takes over from **Daphne Goring** who was instrumental in launching our new Department. In the last year, **Vince Tropepe**, **John Peever**, **Melanie Woodin** and **Belinda Chang** were promoted to Associate Professor and **David Guttman** and **Leslie Buck** were promoted to Full Professor. **Michael Barrett** and **Stephen Tobe** are now Emeritus Professors in the Department.

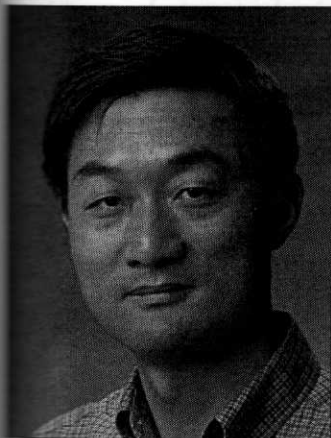
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## University of Toronto - Scarborough Campus

### Department of Biological Sciences

Correspondent: Rongmin Zhao

As a Department that produces most of the Masters and Ph.D. graduates at the University of Toronto Scarborough campus, the Department of Biological Sciences is the home of an interdisciplinary, research-intensive group with state-of-the-art facilities and extensive funding. The Department's major research programs can be clustered as Cells and Infection, Plant Cellular and Molecular Processes, Integrative Behavior and Neuroscience, Neurobiology of Stress, and Biological Dynamics of Environmental Change. One of the strengths of the Department is a cadre of scientists working in cell and molecular biology, who contribute to a very competitive and vibrant Co-op Specialist programme.



Rongmin Zhao

The faculty in the Department is rapidly growing, with 25 full time staff. In 2009, four new hires (**Drs. Ashok, Brunt, Welch and Cadotte**) joined the Department to expand and complement its research profile and instructional offerings. **Dr. Kenneth Welch's** interest is in comparative vertebrate physiology using hummingbirds and

bats as models. **Dr. Marc Cadotte** investigates species coexistence and how multi-species interactions shape ecological communities. Recent hires also include **Dr. Mark Fitzpatrick** who is using *Drosophila* as a model to study foraging behavior genetics. **Dr. Rongmin Zhao** joined the Department as a biochemist and set up his lab in late 2008. His research interest lies in cellular protein quality control systems with a focus on the role and mechanism of molecular chaperone Hsp90 in Arabidopsis growth and plant organelle biogenesis. Another research goal in his lab is to understand the mechanism of ubiquitin-independent protein degradation by the proteasome.

The Department has been very successful in attracting external research funding in 2009. All four NSERC Discovery Grants were successful. Two CFI/LOF grants were secured. The Centre for the Neurobiology of Stress, housed in the Department and led by **Professor Ian Brown**, received a \$2.7 million Leading Edge Fund from CFI, a significant boost to the Centre founded in 2001 with \$3.8 million in support from CFI/ORF at that time.

The Department supervised more than 60 graduate students. **Jeffrey Stoltz**, a Ph.D. student from the Andrade lab, studied the sexual behaviour of redback spiders and had his research recently highlighted in *Nature*. Another Ph.D. student **Michael Sheriff**, from the Boonstra lab, was awarded the Elton Prize by the British Ecological Society.

In December 2009, the Department Chair Professor **Greg Vanlerberghe** organized a one-day faculty retreat. In the retreat, the faculty discussed extensively the

undergraduate and graduate programs and how to extend the strength of the Department such as research in the field of Neuroscience. Last summer, **Dr. Stephen Reid** in the Department organized and hosted a very successful National Zoology Conference at UTSC.

## Ontario Cancer Institute Princess Margaret Hospital

*Correspondent: Linda Penn*

Princess Margaret Hospital (PMH) and its research arm, the Ontario Cancer Institute (OCI), have achieved an international reputation as global leaders in the fight against cancer. Clinical and research staff at OCI/PMH represent many of the world's leaders in oncology.

The OCI is home to over 200 researchers, 425 trainees, and 622 technical/support staff in over 373,000 square feet of research space. Last year, faculty had over 750 publications and brought in over \$100M in external research funding.

In 2009, OCI researchers were recognized nationally and internationally for their contributions to the field of cancer research. **Dr. John Dick** was recognized with two international awards for his pioneering research in the area of stem cells: the E. Donnan Thomas Lecture and Prize from the American Society of Hematology and the 2009 Clifford Prize. The Canadian Cancer Society Research Institute awarded **Dr. Brian Wilson** of OCI the Robert L. Noble Award for his pioneering research into various optical tools that can be used for minimally invasive cancer treatment and early diagnosis.

Provincially, **Dr. Benjamin Neel**, OCI Director and Senior Scientist, was awarded the prestigious Premier's Summit Award in Medical Research for his significant and distinguished ongoing contribution to the field of cell signaling in several human diseases, including cancer. Cancer Care Ontario also awarded three OCI faculty



chairs: **Dr. Lillian Siu** received a chair in Experimental Therapeutics, **Dr. Geoffrey Liu** in the area of Experimental Therapeutics and Population Studies, and **Dr. Ralph DaCosta** in the area of Cancer Imaging.

OCI has created some very important partnerships and collaborations in the past year. The Cancer Stem Cell Consortium awarded two multidisciplinary cancer stem cell projects to be co-led by OCI's **Drs. John Dick** and **Tak Mak**. Partnering investigators in California will be funded by the California Institute for Regenerative Medicine (CIRM).

Pfizer and the Ministry of Research and Innovation have partnered with the OCI to find abnormalities in the genetic make-up of colon cancer cells and to develop drugs to target the aberrations. This project is being led by **Dr. Brad Wouters**.



From top left: Drs. Geoffrey Liu, Ralph DaCosta, Benjamin Neel, Lillian Siu, Brian Wilson, Bradly Wouters. Missing photos: Drs. John Dick, Tak Mak, Senthil Muthuswamy, Nadeem Moghal, Laurie Ailles

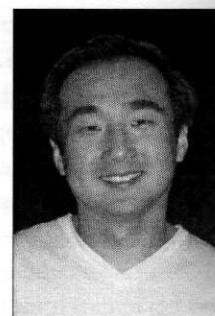
In the last couple of years, OCI has been actively recruiting great talent to the Institute. Since 2007, OCI has recruited **Dr. Nadeem Moghal** from Utah, **Dr. Laurie Ailles** from Stanford University, **Dr. Bradly Wouters** from the University of Maastricht, and **Dr. Senthil Muthuswamy** from Cold Spring Harbor.

## Hospital for Sick Children Division of Cell Biology

*Correspondent: John Brumell*

The Hospital for Sick Children has just announced that on May 4 they will break ground for their new Research and Learning building. The new 21 story building will house all SickKids researchers. The new building will centralize all SickKids research into a state-of-the-art facility and 'repatriate' those researchers who are currently located at the Medical and Related Sciences (MaRS) building, just off campus. Researchers at SickKids were recently shown a 'fly-through' video depicting how the new building will look and function. All were impressed. "I'm having new lab fantasies" said one scientist. The new building will address a long-standing need for laboratory space and will provide better synergy between different research programs.

The Division of Cell Biology's latest recruit is **Peter Kim**, a peroxisome expert who just completed his postdoctoral work with Jennifer Lippincott-Schwartz at NIH. He's studying mechanisms of peroxisome biogenesis as well as turnover by autophagy. Peter uses biochemical approaches in combination with state-of-the-art live-cell microscopic imaging to visualize peroxisomal protein targeting and organelle turnover.



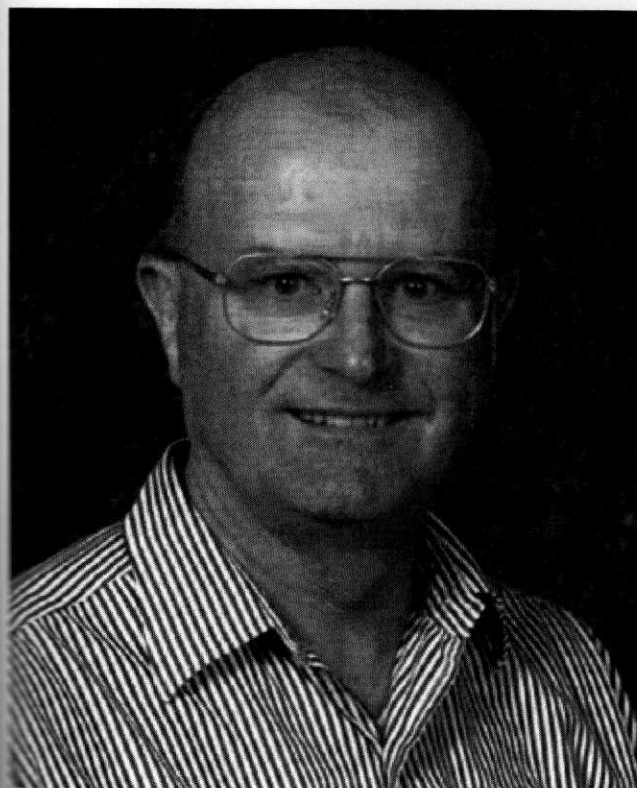
Peter Kim



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## In memorium: Louis Delbaere (1943-2009)

Bruce Waygood



Louis Delbaere died on October 5, 2009 shortly after collapsing in Toronto. At the time of his death, Louis was a Tier 1 Canada Research Chair at the University of Saskatchewan, the leader for Canadian Macromolecular Crystallography Facility at the Canadian Light Source, the leader of the Molecular Design Research Group at the University of Saskatchewan that was funded by the Saskatchewan Health Research Foundation (SHRF), and served on the Board of SHRF. He was Chair of the Canadian National Committee for Crystallography and a member of the Executive Committee of the International Union of Crystallography (IUCr), in which he had been active for many years. A year earlier, his work on these two organizations led to the award of the 2014 triennial meeting of the IUCr to Montreal, an event that will bring well over a thousand crystallographers to Canada from around the world.

Louis grew up in St. Boniface, Manitoba in a family of twelve, all of whom survive him as do his mother Mary, his wife Carol, and their two children, Christian (Joy) and Michelle (Donald Sin), and four grandchildren. Louis attended the University of Manitoba gaining his Ph.D. in Chemistry in 1970, followed by a post-doctoral fellowship at Oxford (1969-71). In 1971 he joined Michael James at the University of Alberta and worked on proteases, and then joined the Department of Biochemistry at the University of Saskatchewan in 1979, supported by a MRC Development Grant. During his years at Saskatchewan, he was funded variously by MRC, CIHR, NSERC, CFI, SHRF, Canadian Space Agency, and Connaught Laboratories, producing over 130 refereed papers on many different topics. Many of his publications were collaborations with colleagues both near and far. Louis maintained a number of collaborations through sabbatical years in Basel, Oxford, and Auckland. Louis was involved in the development of, and the funding application for the Canadian Light Source and the first macromolecule beamline. He helped develop and obtain the funding (CFI) for the Saskatchewan Structural Sciences Centre.

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Louis was a contributor to his community. He served as Department Head (1998-2003). He was active in the CSBMCB, serving as a Councillor in 1982-85, and Treasurer 1988-91. He was a Director for the CFBS (1994-96). He was President of the American Crystallography Association (2005). He served on numerous committees for MRC, CIHR, NSERC, NCI, and SHRF. Louis was active in the organization of meetings for the Societies to which he belonged. He was a member of the Faculty Club Board, and served as the President (2005-6).

As a colleague, Louis was always enthusiastic about the projects on which many of us worked with him. He was passionate about crystallography, and enjoyed the variety of projects that collaborators presented. He was a good supervisor of his students, and his research staff became long-time friends. Louis could also relax and enjoy things away from science, and especially keeping in touch with his large family, as he was doing in Toronto with a cousin, when he collapsed.



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