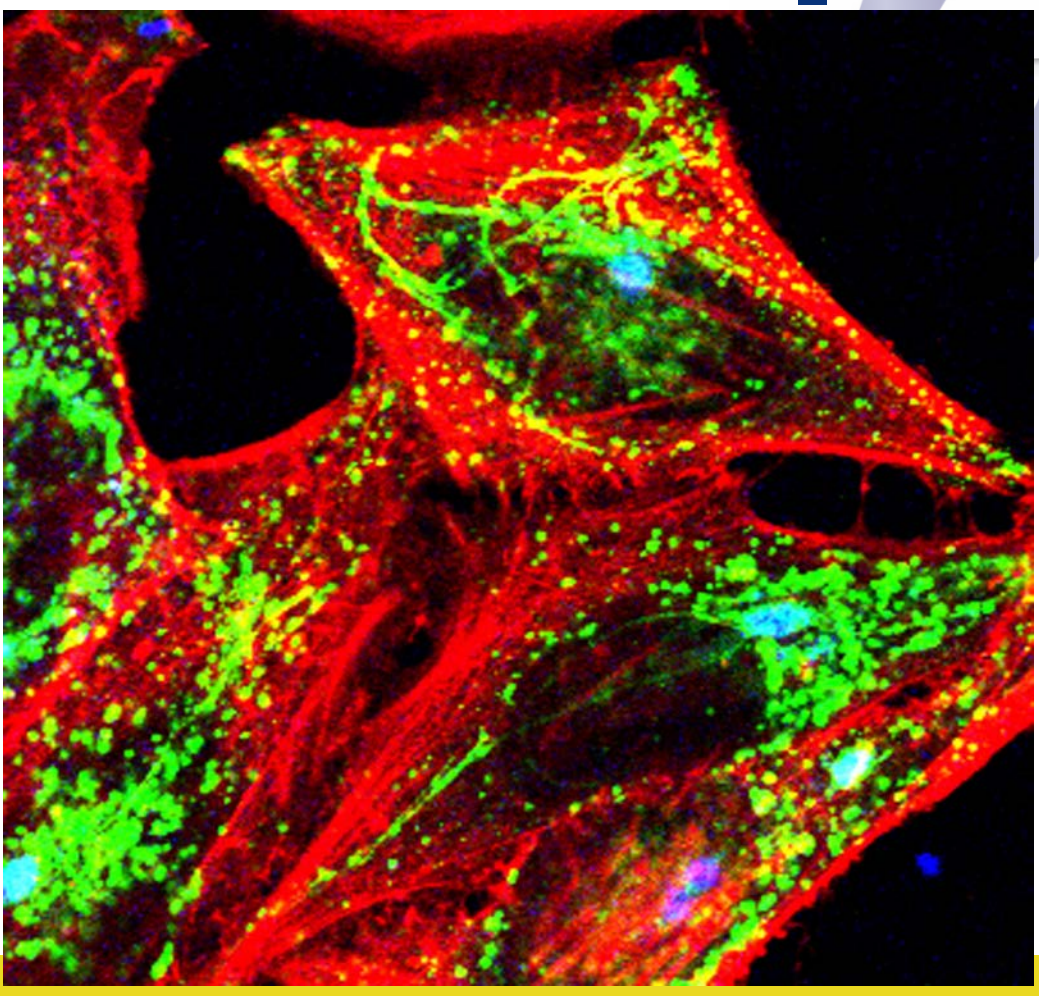
Bulletin



The Canadian Society for Molecular Biosciences
La Société Canadienne pour les Biosciences Moléculaires

2012

www.csmb-scbm.ca

Bulletin

The Canadian Society for
Molecular Biosciences

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les Biosciences Moléculaires

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Cover Image: John Brumell

HeLa cells were infected with *Salmonella typhimurium* for 8 hours and then fixed and stained for F-actin (red), LAMP1 (green) and *Salmonella* (blue).

Intracellular bacteria can be visualized within LAMP1-containing vacuoles. *Salmonella* can also replicate rapidly in the cytosol of these cells, a situation that occurs when the bacteria damage the vacuoles they occupy. However, autophagy serves as a defense against vacuole damage and protects the cytosol from bacterial colonization. In this way, autophagy limits the replication of *Salmonella* during infection of host cells.

CSMB Board for 2012

The CSMB Board at its annual Fall meeting in Ottawa, November 2012.

Front row from left: Reinhart Reithmeier (Toronto), Past-President Jim Davie (Manitoba), Frances Sharom (Guelph), Kristin Baetz (Ottawa).

Back row from left: Christian Baron (Montréal), President Art Hilliker (York), Vice-President Andrew Simmonds (Alberta), Jan Rainey (Dalhousie), David Williams (Toronto), Secretary Randy Johnston (Calgary), John Orlowski (Montréal), CSMB Secretariat Wafaa Antonious.

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President's Report – 2012

Dr. Arthur J. Hilliker

It has been an eventful year for the CSMB. Here I will report on our past and future activities.

I shall step down as President in June and will be succeeded by Andrew Simmonds of the University of Alberta, the current Vice-President. At that time I will become Treasurer replacing Vincent Duronio.

Vince Duronio (UBC) has done an outstanding job both as Treasurer and as a member of the CSMB Board providing great leadership to us for many years. His commitment to the CSMB and his wise counsel have been invaluable. I thank him for his service to the CSMB.

One challenge that now faces the Board is ensuring that annual meetings do not run at a loss. The 2012 meeting in Whistler although a scientific and social success resulted in a deficit. The upcoming meeting at Niagara-on-the-Lake will also likely result in a significant deficit and this is primarily due to lower than projected attendance. Although these loses do not threaten the financial viability of the CSMB we must not continue this way. This issue will be fully addressed at the Board Meeting in June.

The planning of the upcoming annual meeting for 2014 is well advanced. A detailed draft program has been provided and the Conference will be held at the Banff Centre from April 9 to April 15, 2014. The Conference is entitled "Membrane Proteins in Health and Disease" and will cover a wide range of topics relevant to the Conference theme. It will undoubtedly be of great interest to many of our members, so please enter it into your calendars and plan to attend if possible.

In the past year we have been approved to cosponsor two future (2016 and 2018) major international meetings. The first of these is with the International Union of Biochemistry and Molecular Biology (IUBMB). The conference theme is "Signaling Pathways in Development, Disease and Aging" and it will take place in Vancouver July 16-23, 2016. This is a great example of our service to our members, very many of whom will be interested in attending this important meeting. The Panamerican

Association for Biochemistry and Molecular Biology (PABMB) supports us in this endeavor. Our CSMB Annual Conference and that of the PABMB will be held in conjunction with the IUBMB Conference. The active participation of CSMB members is essential to the success of this meeting and in promoting Canada's international scientific reputation.

Second, we have successfully submitted a bid to host the International Congress of Genetics in 2018. The Congress is held once every five years and generally draws thousands of attendees. This meeting will be held in Vancouver in July 2018. With the Genetics Society of Canada joining the CSMB two years ago we are now the Canadian representative and a member of the International Genetics Federation (IGF), the sponsor of the Congress. We have received letters of support from many sources including all levels of government as well as from NSERC and CIHR. We have received financial commitments towards the Congress from the Genetics Society of America, Genome BC, Genome Canada and the Vancouver Convention Bureau. Again, the active participation of Canadian scientists is essential to the success of this meeting.

The theme of the 2018 IGF Congress will be "Genetics Horizons: Evolution, Development, Sustainability, Health". The Local Organizing Committee has been struck with Dr. Phil Heiter as Chair. A North American Advisory Committee has also been created with Dr. Brenda Andrews as Chair. I shall be Conference Chair.

Dr. Randal Johnston, our General Secretary, has been instrumental in the construction and success of our two bids and he has agreed to remain on the CSMB Board as General Secretary through 2018. His leadership like that of Treasurer Vince Duronio has been invaluable and will undoubtedly continue to be so.

The successful bid documents with many details regarding the committees, the venues and the draft budgets will be posted on the CSMB website. We welcome any suggestions/comments from the CSMB membership on topics and speakers for the two meetings. Randy Johnston, Phil Heiter and I as well as Suzanne Gill from Genome BC will be meeting in June to begin the more detailed planning for both meetings.

CSMB is concerned about declining levels of financial support for biological and for biomedical research. A major concern is that of support for basic research, which is addressed in our response to the recent NSERC consultation request. The response drafted by me and approved by the Board is posted on our website. We continue to support lobbying for research support for biomedical research through our membership in Research Canada. The Board has also recommending a letter writing campaign to our members. The Board suggests that all recently successful applicants for research support from NSERC and/or CIHR write to the government expressing their appreciation and outlining the importance of this support for the advancement of important scientific research in Canada.

Finally, I would like to thank all of the current Board members for their service to the CSMB and for the leadership they provided.

Incoming Members of the CSMB Executive Board

Christian Baron, Councillor

Dr. Christian Baron was born in Toronto, but he moved to Germany early in his life and had all his school and University education in this country. He received his diploma in Microbiology from the University of Munich in 1990 and his Ph.D. (RNA structures and RNA-protein interactions in selenocysteine metabolism) in Microbiology from the same institution in 1993. He then switched gears working as a postdoc on bacterial type IV secretion systems using the *Agrobacterium tumefaciens* model with Pat Zambryski in the UC Berkeley Plant and Microbial Biology Department (until 1997). After that, he returned to the University of Munich Microbiology Department where he built his independent research group as a University Assistant, the German equivalent of an Assistant Professor. His research was funded by the Deutsche Forschungsgemeinschaft (DFG), the Ministry of Research and Education and the European Union. In 2002, he moved to the McMaster University Biology Department as Associate Professor, and since 2008, he is Professor and Chair at the Université de Montréal Biochemistry Department.

His research continues to focus on macromolecular interactions, particularly on the assembly mechanism of protein complexes and on the application of knowledge on protein-protein interaction sites as drug targets. He is funded for work on the mechanism of bacterial type IV secretion systems by the CIHR and by NSERC for research on selenocysteine metabolism. His group is an active member of the FRQ-S funded membrane protein research group GÉPROM and he is principal investigator of the NSERC-CREATE training program CDMC (cellular dynamics of macromolecular complexes). He served as member of an NSERC Discovery grant evaluation panel and he continues to serve as member of CIHR grant evaluation panels.

His activities as Department Chair and as CIHR University representative have made him aware of the importance of advocacy and outreach activities and he has developed an appreciation of the use of social media for this purpose. As CSMB councilor he hopes to help increase the public profile of the society as an important voice for Canadian science and research.

Kristin Baetz, Councillor

Dr. Kristin Baetz grew up in North York and her love of science was fostered by family trips to the Ontario Science Centre, the Royal Ontario Museum, the Kortright Centre for Conservation, and kitchen / backyard experiments. While in high school she had her first opportunity to do bench work in the lab of Dr. Gill Wu, in the Department of Immunology at the University of Toronto. It was there that she decided to become a scientist. She received her BSc in Biochemistry at Queen's University in 1995 and during undergrad she worked on killer T-cells with Dr. Gillian Griffiths at the Basel Institute of Immunology and zebra fish development with Dr. Martin Petkovich at Queen's University. But once she was exposed to the power (and lovely doughnut smell) of the budding yeast *Saccharomyces cerevisiae*, she knew she had found her model organism of choice. She received her PhD in Molecular and Medical Genetics from the University of Toronto in 2000 where she worked in the laboratory of Dr. Brenda Andrews on the regulation of G1 transcription factor SBF. This was followed by postdoctoral work with Dr. Phil Hieter at UBC where she used yeast functional and chemical genomics to identify novel regulators of chromosome segregation.

Dr. Baetz is presently a Canada Research Chair Tier II in Functional and Chemical Genomics, and an Associate Professor at the Ottawa Institute of Systems Biology, Department of Biochemistry, Microbiology and Immunology at uOttawa and is a recipient of Early Researcher Award from the Ontario Government. Since starting her laboratory at uOttawa in 2005, she has developed and applied yeast functional and chemical genomics and proteomics to a variety of research programs including (i) identifying non-histone targets of the lysine acetyltransferase NuA4 that impact chromosome stability and cell cycle progression; (ii) deciphering the role of lipid signaling in Alzheimer's disease and (iii) improving industrial yeast for cellulosic fermentation. Her ability to apply systems biology approaches to hypothesis driven discovery research has created a unique training environment that is supported by funds from the Canadian Cancer Society Research Institute (CCSRI), CIHR, NSERC and BioFuelNet (a Network Centres of Excellence team grant).

Outside the university Dr Baetz has served on many grant panels at CCSRI, CIHR as either reviewer or scientific officer and has been a member of both the CIHR postdoctoral fellowships and Ontario Graduate Scholarship Selection Panel. In addition she is presently an Associate Editor at *BMC Genetics.* Further as she directly benefited in her youth by being exposed to science, she strongly believes it important to return the favour. She does outreach with elementary school age children performing "experiments" at their schools or in local Scout Troops and organizes yearly visits of middle school groups to visit her laboratory.

Importantly Dr. Baetz believes it is essential that scientists communicate their research to the public in order to not only increase scientific literacy but to advocate for continued support of research. As a CSMB Councillor Dr. Baetz aims to increase the membership base, engage graduate students and postdoctoral fellows in the Society and increase our advocacy efforts.

Minutes of the 2012 Annual General Meeting

Whistler, British Columbia – March 16, 2012

Attendees: D. Tsuyuki, J.P. Perreault, K. McManus, M. Hendzel, P. Hieter, V. Han, J. Dostie, E. Keirgha-Awemu, M. Bouvier, L. Esford, M. Lupien, S. Varmuza, J. Phillips, V. Duronio, J. Davie, A. Hilliker

1. Greetings from the President

Jim Davie called the meeting to order and welcomed the attendees.

2. Approval of quorum and agenda

Davie declared quorum was met. Duronio made a motion to approve the agenda, motion seconded by Hilliker, all in favour, agenda approved.

3. Approval of the minutes of 54th Annual General Meeting in Sherbrooke, QC, September 2011

Johnston made a motion to approve the minutes of the 54th Annual General Meeting, motion seconded by Hilliker, all in favour, minutes approved.

4. Business arising from the minutes

No business arising.

5. Update on Merger of Genetics Society of Canada with CSBMCB

The Genetics Society of Canada merged with CSBMCB and it was then decided to change the name of the society to reflect the merger. The membership voted in the 2011 AGM to approve the new name to be Canadian Society for Molecular Biosciences (CSMB).

6. Secretary's Report - Johnston

a) Membership - Attached

b) Update on the revised bylaws and new name

The revised constitution and bylaws were previously approved at the 2011 AGM and we are in the process of registering them with Corporation Canada. The website has been updated with the new name, and we are in the process of registering it also with Corporation Canada.

7. Treasurer's Report – Duronio - Attached

We contacted CSMB Departmental representatives in different institutions to approach their colleagues to become members of the CSMB, with some success. We lost a couple of sponsors like Merck-Frosst that previously provided up to $14,000 which we used to cover travel awards. Fortunately, we were able to recruit some new sponsors for the travel awards. On the other hand, we also have expenses arising from deposits for the 2013 and 2014 annual conferences, plus our society provides partial support for other meetings. In the past year we contributed to a Systems Biology and a China-Canada symposium. Luckily the value of the investment account has gone up in the last few months and we therefore remain in a favourable financial situation.

a) Presentation of the Accountant's Reviewed Financial Statement

Duronio stated that the society had moved from having a complete audit of the financial books to a review of engagement. This is less expensive than an audit, and the financial books of the organization are still reviewed by an accountant who provides us with a financial statement. Duronio went through the financial statement prepared by Mrs. Andrea Poole.

b) Acceptance of the Reviewed Financial Statement

Johnston made a motion to accept the financial statement prepared by Mrs. Andrea Poole, motion seconded by Perreault, all in favour, financial statement accepted.

c) Presentation of 2011 – 2012 Finances - Attached

8. Board membership for 2012 – 2013

Davie said that Guarne was leaving the board and she had been responsible for the membership drive. Two nominations were received for the councillor positions (no nominations from the floor were received). The two new councillors are Kristin Baetz, University of Ottawa and Christian Baron, Université de Montréal. Perreault made a motion to approve the two new councillor positions, Hilliker seconded the motion, all in favour, motion approved.

Davie made a motion to have Andrew Simmonds from the University of Alberta to be the incoming Vice-President (no nominations from the floor were received), Duronio seconded the motion, all in favour, motion carried. Davie noted for information that at the previous AGM Dr. Hilliker was appointed as incoming Vice-President and therefore he would become President effective July 1, and Davie would become Past-President. In addition, Duronio and Johnston would continue for another year as Treasurer and General Secretary, respectively.

9. Current & Future Meetings

Davie reported that he had submitted an application for conference support to CIHR and it was not approved (many others were also declined). This would affect the financial outcome of the Whistler Conference. The 2013 Meeting will be in White Oaks, Niagara on the Lake, June 2 – 7, 2013 theme: Cellular Dynamics During Development, Regeneration and Cancer.

Davie encouraged the members to contact the Executive to advise them if they thought a theme should be planned for a CSMB future conference.

10. CIHR Century Change - Davie

We invited CIHR to this conference to update us with the latest information related to the CIHR Century Change. It is clear from what was presented from CIHR at this conference and from Research Canada that for the next budget CIHR will not receive any increases and we hope there will be no decreases. We have heard from Dr. Jane Aubin, Chief Scientific Officer/Vice President and Dr. Eric Marcotte, Associate Director, Regenerative Medicine and Nanomedicine. They explained there will be a significant investment in the Signature Initiatives. On the other hand, there are many excellent scientists who are not getting grants. It is common to spend almost two months in the review of grants and then find only few grants are supported. Davie stated that the CSMB would like to send a letter to CIHR as feed back on the C Changes and he would like to present the main points for discussion and approval.

1. CIHR needs to restructure its envelope of funding to put more funds into the open operating grant program. Hilliker added that we as a country have a huge investment in our scientists. The training of highly qualified personnel is very important. We are not asking for funding of low productivity scientists; instead, studies indicate that Canadian Scientists are among the most productive worldwide, even above the USA when compared per capita. Hilliker made a motion to approve this point to be included in the letter, Perreault seconded the motion, all in favour, motion approved.

2. The proposed peer review mechanism for Foundation and Project grants that would be comprised of a blend of virtual and face to face staged meetings is likely inadequate to

appropriately review grant applications. The first virtual review would be of around 80 applications, then the number would be narrowed down to around 50, but guidelines for the reviewers are absent or poorly developed. In addition, the quality of review must be enhanced by reengaging our top scientists as reviewers. Hilliker further raised the issue of having one vs. two competitions a year, and whether rules would be consistent across all four CIHR pillars. Hilliker made a motion to include these points in the letter to CIHR, Johnston seconded the motion, all in favour, motion approved.

Duronio suggested we should identify and encourage the positive aspects and not simply focus on negative concerns. Hieter expressed his concern that approval ratios should approach 45%, and that we should encourage five year research plans and continuity. Davie added that we would post a letter on the CSMB website that members can refer to when sending letters to CIHR and their MPs. He encouraged them to send these letters and to convey their views and concerns.

11. Other business/Adjournment

No other business. Johnston made a motion to adjourn, seconded by Hilliker, all in favour, meeting adjourned.

CANADIAN SOCIETY FOR MOLECULAR BIOSCIENCES
Financial Statement

STATEMENT OF FINANCIAL POSITION

AS AT DECEMBER 31, 2012 (with unaudited comparative figures as at December 31, 2011)
UNAUDITED

	2012	2011
ASSETS		
CURRENT		
Cash	$ 6,406	$ 7,369
Accounts receivable - CSMB	10,718	2,541
Accounts receivable - GSC (note 4)	741	741
Conference deposit	22,000	66,714
	39,865	77,365
INVESTMENTS (note 5)	398,309	419,048
	$ 438,174	$ 496,413
LIABILITIES		
CURRENT		
Accounts payable and accrued liabilities	$ 18,582	$ 12,265
Deferred membership fees and subscription fees	2,859	4,405
Deferred conference income	-	5,036
	21,441	21,706
LONG TERM		
Deferred membership fees	4,172	5,594
UNRESTRICTED NET ASSETS	412,561	469,113
	$ 438,174	$ 496,413

Approved on behalf of the Board:

Director Director

STATEMENT OF OPERATIONS AND CHANGES IN NET ASSETS

FOR THE YEAR ENDED DECEMBER 31, 2012
(with unaudited comparative figures for the year ended December 31, 2011)
UNAUDITED

	2012	2011
REVENUE		
Memberships dues	$ 29,571	$ 28,931
Corporate contributions	34,146	8,750
Annual meeting	26,600	-
Other	1,145	1,075
	91,462	38,756
Investment income	8,770	8,539
	100,232	47,295
EXPENSES		
Secretariat	12,440	15,390
Annual meeting (note 6)	136,890	15,030
Board meetings	10,096	9,275
Meeting sponsorship	6,500	7,542
Website	5,150	3,900
Membership drive	-	3,159
Professional fees	2,200	2,191
Bank and credit card fees	2,007	2,178
Science advocacy	6,000	1,757
Bulletin	11,462	1,246
Office	530	272
Miscellaneous	-	-
Dues and subscriptions	-	-
	193,275	61,940
NET REVENUE (EXPENSES) FOR THE YEAR	$ (93,043)	$ (14,645)
Unrestricted net assets at beginning of year	$ 469,113	$ 503,345
Balance before items affecting net assets	376,070	488,700
Gains (losses) from sale of investments (realized and unrealized) (note 5)	36,491	(16,566)
Unrestricted net (deficit) transferred from GSC	-	(3,021)
UNRESTRICTED NET ASSETS AT END OF YEAR	$ 412,561	$ 469,113

STATEMENT OF CASH FLOWS

FOR THE YEAR ENDED DECEMBER 31, 2012
(with unaudited comparative figures for the year ended December 31, 2011)
UNAUDITED

	2012	2011
CASH PROVIDED BY (USED FOR)		
OPERATING ACTIVITIES		
Cash from operations		
Net (expenses) revenue for the year	$ (93,043)	$ (14,645)
Non-cash portion of investment income	(8,770)	(8,539)
	(101,813)	(23,184)
Net change in non-cash working capital balances		
Accounts receivable	(8,177)	(204)
Conference deposit	44,714	(34,654)
Accounts payable and accrued liabilities – CSMB	6,317	2,961
Accounts payable and accrued liabilities – GSC	-	(3,020)
Deferred membership and subscription fees	(2,968)	2,173
Deferred conference income	(5,036)	5,036
	(66,963)	(50,892)
INVESTING ACTIVITY		
Transfer of funds from investment account	66,000	38,000
(DECREASE) INCREASE IN CASH	(963)	(12,892)
Cash, beginning of year	7,369	20,261
CASH, END OF YEAR	$ 6,406	$ 7,369
CASH POSITION		
Cash	$ 6,406	$ 7,369

NOTES TO THE FINANCIAL STATEMENTS

December 31, 2012
UNAUDITED

1. PURPOSE OF THE ORGANIZATION

The Canadian Society for Molecular Biosciences (CSMB) was incorporated without share capital in 1979 under Part II of the Canada Corporations Act and is recognized as a not-for-profit organization for income tax purposes. The main objective of the Society is to foster research and education in Biochemistry, Molecular Biology and Cellular Biology in Canada.

During the year, the organization changed its name from the Canadian Society of Biochemistry, Molecular and Cellular Biology to the Canadian Society for Molecular Biosciences. Also, during the year the organization adopted the new Canadian accounting standards for not-for-profit organizations. These financial statements are the first prepared in accordance with these standards. There were no retrospective adjustments necessary as a result of the change in accounting standards. Accordingly, a statement of financial position as at January 1, 2012 has not been presented with these financial statements.

2. SIGNIFICANT ACCOUNTING POLICIES

These financial statements have been prepared in accordance with Canadian accounting standards for not-for-profit organizations.

(a) Capital assets
Capital assets purchased at a cost of less than $2,000 are expensed in the year of purchase. The Society does not own capital assets at this time.

(b) Basis of Accounting
Revenue and expenses are recorded on the accrual basis, whereby they are reflected in the period in which they have been earned and incurred respectively, whether or not such transactions have been finally settled by receipt or payment of money.

(c) Revenue Recognition
CSMB follows the deferral method of accounting for contributions. Restricted contributions are recognized as revenue in the year in which the related expenditures are incurred. Unrestricted contributions are recognized as revenue when received or receivable if the amount to be received can be reasonably estimated and collection is reasonably assured.

(d) Use of estimates
The preparation of the financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reported period. Actual results may differ from those estimates.

e) Financial Instruments
CSMB's financial instruments are recorded at fair value at the balance sheet date. Any changes in fair value, both realized and unrealized, are recorded as adjustments to revenue and expenses.

3. FINANCIAL INSTRUMENTS

CSMB's financial instruments consist of cash, accounts receivable and accounts payable and accrued liabilities. The fair value of these financial instruments approximates their carrying values, unless otherwise stated. It is management's opinion that the organization is not exposed to significant interest, currency or credit risks arising from its financial instruments.

4. TRANSFER OF ASSETS AND LIABILITIES FROM GSC

After December 31, 2010, the Canadian Society of Biochemistry and Molecular and Cellular Biology merged with the Genetics Society of Canada (GSC). At December 31, 2012 a prior year GSC HST receivable is still outstanding.

5. INVESTMENTS (at Market Value)

CSMB investments are recorded at market value. Any actual gains or losses on the disposal of investments during the year are included with the unrealized gains or losses on the portfolio as a whole at December 31 and recorded as "Gains (losses) from sale of investments, realized and unrealized".

BMO Nesbitt Burns Canadian Account	**2012**	**2011**
Cash and short term investments	$ 960	$ 24,546
Fixed Income	63,127	64,608
Common equity	247,701	245,828
	311,788	334,982
BMO Nesbitt Burns US Account (in $ Canadian)		
Cash and short term investments	6,056	80
Common equity	80,465	83,986
	86,521	84,066
	$ 398,309	$ 419,048

6. ANNUAL MEETING EXPENSES

	2012	**2011**
Exhibits and facility	$ 60,824	$ -
Organizing and planning	13,874	-
Travel and Expenses	46,253	4,878
Awards	8,702	10,104
Reception and Banquets	4,070	-
Supplies and other	3,167	48
	$ 136,890	$ 15,030

Meeting Report: The 55th Annual Meeting of the CSMB Whistler, British Columbia, 2012

Epigenetics and Genomic Stability

Correspondents: Drs. Christopher J. Nelson and Juan Ausió, Department of Biochemistry and Microbiology, University of Victoria

Adapted from Epigenomics, June 2012, Vol. 4, No. 3, Pages 255-259 with permission of Future Medicine Ltd.

The 55th Annual CSMB Meeting and Conference on Epigenetics and Genomic Stability in Whistler, Canada, 14-18 March 2012, brought together 31 speakers from different nationalities. The organizing committee, led by Jim Davie (Chair) at the University of Manitoba, consisted of several established researchers in chromatin and epigenetics from across Canada. The meeting was centered on the contribution of epigenetics to gene expression, DNA damage and repair and the role of environmental factors. A few talks on replication added some insightful information on the controversial issue of histone posttranslational modifications as genuine epigenetic marks that are inherited through cell division.

The opening plenary lecture was given by **Penny Jeggo** (Genome Damage and Stability Centre, University of Sussex, UK) an internationally recognised leader in the study of DNA damage responses, and the repair of DNA double stranded breaks (DSBs). She talked about epigenetic marks during DNA replication, and presented her group's latest results on how the process of DNA DSB repair is affected by chromatin folding, with special emphasis on the mechanisms that take place in heterochromatic (HC) regions[1]. She showed that the repair process, takes place at a much slower kinetics in these highly condensed regions of chromatin when compared to the transcriptionally active euchromatin (EU) domains. Furthermore, in HC regions, the molecular mechanisms involved require ATM and the DNA damage response mediator proteins (the MRN complex, H2A.X, MDC1, RNF8, RNF168 and 53BP1) which are dispensable for repair of DSBs in EU regions. Interestingly, she described how in G2 phase HC impacts upon the choice between the homologous recombination (HR) and non-homologous end joining (NHEJ) repair pathways. The former being the one preferentially used in HC-DSB repair. She also provided novel evidence for the involvement of BRCA1 in HR.

Patrick McGowan (University of Toronto, Ontario, Canada) talked about the fascinating topic of the epigenetic alterations resulting from early life events that lead to changes in neuroplasticity [2]. He described microarray analysis performed in rat offspring with low and high maternal care over extensive chromosomal regions showing that epigenetic changes (DNA methylation, H3K9 acetylation) occur in clusters. They affect genes relevant for development of the stress response [glucocorticoid receptor (GR)] and neuroplasticuity [protocadherin (PCDH)] in a way that is conserved across different species. Notably, these epigenetic signatures are conserved in humans: the pattern of differences across the syntenic region in abused / non-abused suicide victims mirrors that seen in rat studies.

Alexander Mazo (Thomas Jefferson University, Philadelphia) presented revealing recent experimental data that monitor epigenetic marks during DNA replication. This work reveals that most epigenetic histone marks are completely removed before passage of the parental histones through the replication fork. By contrast, PCNA and the trithorax (trx) and polycomb (Pc) proteins are associated with the replicating strands (single stranded DNA) and may represent and intermediate in transmission of epigenetic markings during replication. Histone epigenetic marks are only re-established 60 minutes after DNA replication into

the G2 phase of the cell cycle in *Drosophila* embryos. These results importantly challenge the involvement of replication as compared to transcription [3] in the cell inheritance of histone PTMs and question the correct use of the term epigenetics to describe the biological downstream effects of such PTMs [4]. Also addressing the fate of epigentically modified histones during DNA replication, Toshio Tsukiyama (Fred Hutchinson Cancer Research Center, Seattle) described some new techniques recently developed in his lab to measure nucleosome density and occupancy in yeast. During replication DNA polymerase must transit a nucleosomes every 2-3 seconds. These new methods, which involve comparisons of chromatin structure (micrococcal nuclease access) and histone occupancy (histone ChIPs), allow analysis of chromatin organization changes resulting from replication stress at the replication forks in yeast. Interestingly, an increase in nucleosome accessibility was observed under these conditions at the replication fork which was partially dependent on Mec1, an ATR-like kinase in the S-phase checkpoint.

Michael Kobor (University of British Columbia, Vancouver, Canada) described some of their recently published work on the high throughput analysis of different histone PTMs involved in chromatin regulation of genome function (transcription and DNA repair) [5, 6]. In particular the distribution of mono ubiquitinated K2BK123 (uH2BK123) was described in relation to its role in establishing the tri-methylated pattern of H3K4 and H3K79 during transcription and DNA repair. Of notice, the genomic distribution of H3K79Me3, which is dependent on the cross-talk with uH2BK123, is non-overlapping with that of H3K79Me2 even though both methylations are catalyzed by the same enzyme (Dot1).

Robin Allshire (Wellcome Trust Centre for Cell Biology, University of Edinburgh, UK) provided a detailed description of the specificity of CENP-A deposition at centromeres and how this is prevented from happening fortuitously elsewhere in the genome. He indicated how despite the unique DNA sequences associated with centromeric regions in some organisms, there is no "magic" underpinning sequence-related feature that is directly responsible for the discrimination between H3 and CENP-A- containing nucleosomes. By the end of his talk he described how yeast mutants defective in the FACT, a histone chaperone involved in the histone dynamics during transcription, exhibit an indiscriminate assembly of CENP-A nucleosomes to different regions of the genome including actively transcribed genes. This served to highlight how factors acting immediately before, and in the wake of transcribing RNA polymerase II (ie. Set2, HATs) are not only important in preventing spurious re-initiation events but also in abrogating the incorrect deposition of CENP-A. This strongly supports the existence of a cross talk between chromatin specific assembly and transcription.

Matthew Lorincz (University of British Columbia, Vancouver, Canada) talked about recently published data from his lab on 'writers' and 'readers' of H3K9 methylation in mouse embryonic stem cells (mESCs). His attention focused around mammalian endogenous retroviruses (ERVs) which comprise 10% of the mouse genome and can be classified in three major types: Class I, II and III. While DNA methylation plays an important role in the silencing of somatic ERVs, some of the class I and II silencing in mESCs is mediated by Setdb1/Eset methyltransferases that methylate H3K9 (H3K9Me2/H3K9Me3)[7]. Quite interestingly, the silencing histone methylation pathway appears to be independent of all known H3K9Me readers such as heterochromatin protein 1 (HP1)[8], suggesting there is still much to be learned regarding roles for this mark in chromatin regulation.

Benjamin Martin (PhD student, Leanne Howe's lab, University of British Columbia, Vancouver, Canada) nicely presented some very interesting unpublished results that conclusively show that high levels of histone acetylation at transcriptional active genes are not the cause but a consequence of ongoing transcription. Utilizing RNA polymerase II inhibitors (phenanthroline and thiolutin) in yeast they observed that within 15 minutes most of the acetylation is lost from the cell. Furthermore, in mutants lacking histone deacetylase (HDAC) complexes, such as

Rpd3, no loss of acetylation was observed, implying that this enzyme is primarily responsible for the removal of transcription-dependent histone acetylation. Thus, global histone acetylation is a mark of ongoing transcription.

Tiffany Quam (UC San Francisco, California) described the role of CHD1 in histone H3 turn-over. In *Drosophila*, the protein associates with HIRA to produce the incorporation of histone H3.3 in the paternal pronucleus during the replacement of protamines after fertilization. In salivary glands, the CHD1/HIRA complex, in conjunction with Asf1, participates in the replication independent incorporation of H3.3 at transcriptionally active regions. Replication-dependent deposition of H3.1 requires Asf1/Caf1. She presented data indicating that proper deposition of H3.3 by the HIRA/Asf1 complex requires S87 and G90 of H3.3 whereas H3.1 deposition by Asf1/Caf1complex requires the presence of the N-terminus of H3.1. Furthermore, she presented additional unpublished data describing the recruitment of Rpd3 by CHD1 to participate in the histone H3 turnover around RNA pol-II during transcription.

Continuing with histone H3.3 turnover, **Sheila Teves** (Fred Hutchinson Cancer Research Center, Seattle) presented some already published work from Steve Henikoff's lab on high resolution mapping of epigenome dynamics centered about this histoneH3 variant. She also described a couple of recently-developed powerful techniques that permit measurement of nucleosome turnover kinetics and determination of chromatin profiling at a single base pair resolution. Her presentation highlighted the relevance of nucleosome turnover for epigenetic inheritance of gene activity[9].

Gratien Prefontaine (Simon Fraser University, Burnaby, Canada) provided novel evidence for the involvement of the structural-maintenance-of-chromosomes hinge domain (Smc-HD1) protein in the DNA-methylation-mediated transcriptional repression of the growth hormone receptor gene.

Different talks by **Jennifer Mitchell** (University of Toronto, Toronto, Canada) and **Josée Dostie** (McGill University, Toronto, Canada) discussed most of their recently published observations about the 3D nuclear organization of chromosome domains[10]. This constitutes a fascinating topic that adds an extra layer of epigenetic complexity to gene expression. Mitchell focussed on the nuclear organization of RNA pol II transcription and interaction clusters. Dostie used the Hox gene clusters to exemplify how loss and gain of contacts among the multiple chromatin loops encompassing this cluster are related to the processes of gene activation.

David Bazett-Jones (Hospital for Sick Children, University of Toronto, Toronto, Canada) presented the results of his recently published work on the global chromatin structure transitions accompanying the reprogramming of fibrobasts into induced pluripotent stem cells (PSCs)[11] using electron spectroscopic imaging (ESI). This data provides additional support to the questioning by the same lab of the dogmatic existence of a canonical 30 nm folded chromatin fiber in heterochromatic regions of somatic cells nuclei[12]. It would appear that for its most part, both euchromatic and heterochromatic regions generally consist of polynucleosomal strings with different extent of coalescence. In this way, the 30 nm chromatin fiber would only be observed *in vitro* with chromatin fibers that have been purified away from their nuclear environment or in the highly compacted organization of chromatin observed within the nucleus of sea urchin sperm.

Michael Hendzel (University of Alberta, Edmonton, Canada) talked about unpublished data from his lab on the role of the polycomb repressor complex 1 (PRC1) in DNA double strand break signalling cascade through its interaction with DNA repair proteins. He provided evidence that the complex is required for H2A/H2A.X ubiquitination and early recruitment of phosphorylated ATM to DSBs. RNF8, another ubiquitin ligase that has long been involved in the repair process, appears to function downstream of PRC1 di- and polyubiquitinating phosphorylated H2A.X.

Michael Skinner (Washington State University, Pullman, Washington) dealt with the interesting data recently

published by his lab[13] on the impact of environmental contaminants (such as DEET, bisphenol A, TCDDD amongstothers) on epigenetic transgenerational effects. Both spermatogenic apoptosis and decreases in ovarian primordial follicle pool size in exposed mice affected by exposure to contaminants. Interestingly, differential DNA methylation regions (DMR) could be detected in the sperm of the F3 generation demonstrating that environment-induced epigenetic marks on chromatin can behave like classical imprinted regions. More over,

Skinner introduced the field to a new and important concept: that each tissue likely has acquires a different collection of DMRs with respect to other tissues. Of course, this adds yet another layer of complexity in the interaction of the maternal environment and the epigenome(s) of the developing fetal somatic tissues and germ cells.

Several talks focussed on chromosome and genome instability from yeast to plants. **Phillip Hieter** (University of British Columbia, Vancouver, Canada) talked about recently published data on the synthetic lethality of cohesions with PARPs and replication fork mediators and the use of yeast as a model for genes that are mutated and could cause chromosome instability in cancer[14]. **Krassimir Yankulov** (University of Guelph, Guelph, Canada) talk was on regulation of telomere effect position effect and the passing/pausing of replication forks[15] and the role of CAC1 (a subunit of histone chaperone CAF-1 in yeast) in building nucleosomes from "new" histones. The recruitment of CAF-1 is mediated by its interaction with PCNA. The presentation provided further insight in the transfer of histone epigenetic marks at stalled replication forks and nicely complemented the early talk on this topic by A. Mazo. **Olga Kovalchuk** (University of Lethbridge, Lethbridge, Canada) focused on the genomic instability (cancer) resulting from diagnostic and therapeutic exposure to radiation with special emphasis on the role played by small RNAs as a result of such exposure[16]. She described some of the transgenerational effects that result in alterations in the levels of DNA methylation and non coding RNAs in the paternal germ line. Repeat elements appear to be the major targets of irradiation (LTR being hypermethylated and SINEs and LINEs hypomethylated) in response to paternal irradiation. **Igor Kovalchuk** (University of Lethbridge, Lethbridge, Canada) also focused on transgenerational changes in genome instability in response to stress in plants[17]. Epigenetic information was gathered from the progenies obtained from seeds of plants exposed to different abiotic and biotic stresses. Changes were observed in the homologous recombination frequency (HRF), DNA methylation and histone PTMs. For instance, seeds of UV stressed plants were systematically larger and the progeny exhibited a hypermethylated genome at several analyzed genomic regions.

The last session closed on the topic that had been highlighted by the plenary talk on DNA repair and damage at the opening of the meeting. **Michael Kruhlak** (NIH, Bethesda) provided a detailed microscopic cytological view of the chromatin environment surrounding DNA regions affected by DNA breaks *in vivo*. An energy-dependent local expansion of chromatin was described that takes place immediately after DNA damage and does neither depend on phosphorylation of H2A.X nor on ATM. **Aaron Goodarzi** (University of Calgary, Alberta, Canada) referred again to the slow (heterochromatic) and fast euchromatic components of DSB DNA repair and focussed his attention on the currently ongoing experiments in his lab on the involvement of SNF2H-ACF1 involvement on the Artemis-dependent DSB repair in hetrochormatin. **Susan Lees-Miller** (University of Calgary, Alberta, Canada) described further insights into the NHEJ pathway. She presented several crystallographic images of different protein complexes involved in this process[18]. She also described the involvement in NHEJ of the IR-induced phosphorylation of human polynucleotide kinase/phosphatase (PNKP) PNKP at S114 and S126 by ATM and DNA-PK[19].

Two talks were included in this section that although they departed from its main subject brought the meeting to an interesting closure. The first by **Alain Verreault** (University of Montreal, Montreal, Canada) expanded on their recently published work on histone acetylation and DNA damage during replication. He described how mis-regulation of

H3K56Ac increases sensitivity to genotoxic agents and impairs DNA DSB by homologous recombination.[20]. Interestingly, he explained how H3K56Ac is regulated by Hst3 and RTT109 proteins of the sirtuin family in *Candida albicans* and how these studies resulted in the design of inhibitors with potential therapeutic use for the treatment of fungi virulence. In closing, **Daniel Gottsschling** (University of Colorado, Colorado) provided a comprehensive description about age-associated genome instability and how cellular subsystems break down in budding yeast using their mother enrichment program genetic system[21]. Evidence was provided that aging occurs concurrently with mitochondrial dysfunction and the associated reduced production of iron-sulfur clusters which ultimately results in a decreased activity of proteins involved in genomc maintenance.

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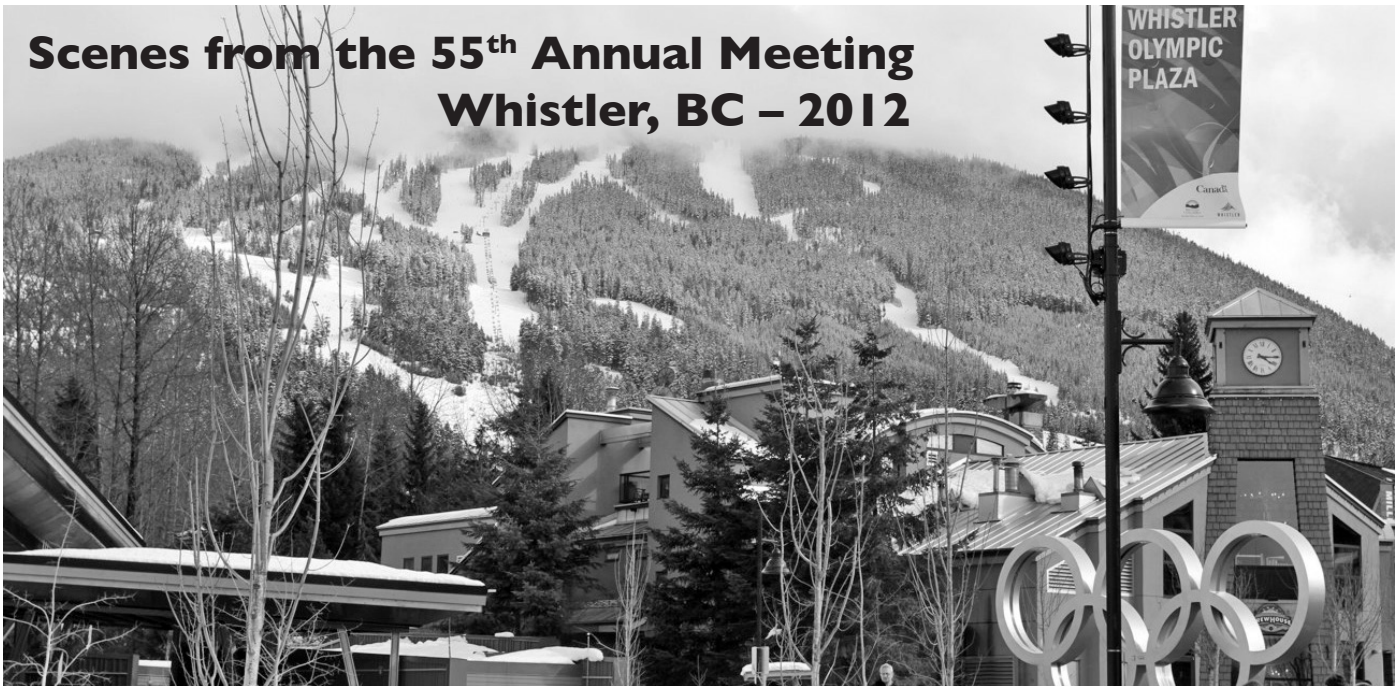
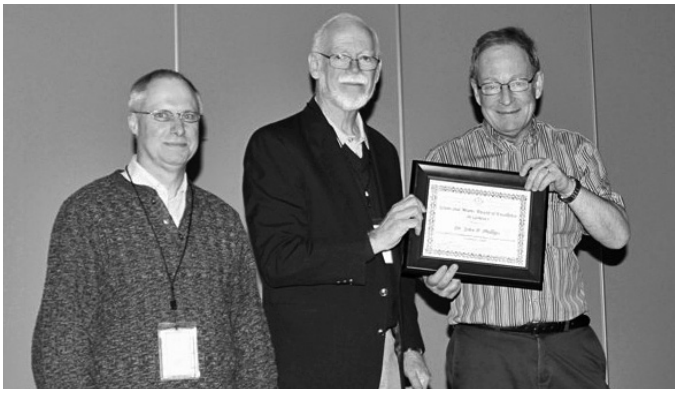
Scenes from the 55th Annual Meeting Whistler, BC – 2012



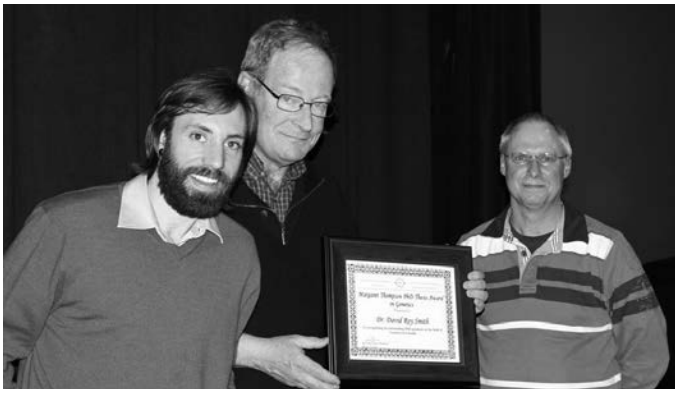
▲ Whistler was a wonderfully scenic venue for the 55th Annual Meeting

▲ Enjoying the poster sessions

▲ Taking a break between sessions.



▲ John P. Phillips, Professor Emeritus University of Guelph receives the Grant and Moens Award of Excellence in Genetics



▲ David Smith is awarded the Margaret Thompson PhD Thesis Award in genetics

▲ CSMB President Art Hilliker (right) expresses the Society's thanks to Past-President and Meeting Organizer Jim Davie

▲ Fiona Fitzgerald presents the GE Healthcare New Investigator Award to John Brumell (SickKids, Toronto)

▲ Michel Bouvier (IRIC, U. de Montréal) receives the NRC Research Press Senior Investigator Award from Jim Davie

▲ Jim Davie presents the 2012 CSMB Arthur Wynne Gold Medal to Henry Friesen

Jim Davie presents poster awards to Alice Wang, UBC, and to Peter Thompson UBC. In addition, the Jake Duerkson Poster Prize was awarded to Maxime Tremblay, Université de Sherbrooke

Travel Award Winners 55th Annual Meeting

Kathleen Attwood Dalhousie University
Supervisor: Graham Dellaire

Yannick Auclair McGill University
Supervisor: Stephane Richard

Jean-Philippe Lambert Mt. Sinai Hosp., Toronto
Supervisor: Anne-Claude Gingras

Ismail Abdou University of Alberta
Supervisor: Michael Weinfeld

Hilmar Strickfaden University of Alberta
Supervisor: Michael Hendzel

Chen Wang University of Calgary
Supervisor: Susan Lees-Miller

Uma Rajarajacholan University of Calgary
Supervisor: Karl Riabowoli

Dilshad Khan University of Manitoba
Supervisor: Jim Davie

Brent Guppy University of Manitoba
Supervisor: Kirk McManus

Rebecca Hood University of Ottawa
Supervisor: Kym Boycott

Andrea Giberson University of Ottawa
Supervisor: Robin Parks

Scott Davidson University of Toronto
Supervisor: Jennifer Mitchell

Our sincere thanks to New England BioLabs and Fisher Scientific for sponsoring several of these awards

2012 Jeanne Manery Fisher Memorial Lectureship

Dynamic complexes of intrinsically disordered proteins in biological regulation

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Introduction

Functional proteins exist in a large number of different states, from monomers to large assemblies and from relatively rigid folded structures to very flexible disordered ensembles. Much of structural biology has focused on folded low energy states, including monomers, specific homo- and hetero-oligomers and stable higher order assemblies including fibers and amyloids. More recently, specialized NMR and other approaches have enabled descriptions of monomeric excited states and folding intermediates (Baldwin and Kay, 2009; Neudecker et al., 2012), as well as unfolded and intrinsically disordered protein states (Choy et al., 2002; Mittag and Forman-Kay, 2007). However, much less studied are dynamic protein associations. These include higher order assemblies such as gels and elastic protein aggregates as well as liquid phase separated states that may function in the formation of non-membrane bound organelles (Wilson and Gitai, 2013; Wu, 2013). Dynamic protein associations also include complexes of defined oligomeric states (primarily heterodimers), which are a major focus of my research. Characterization of the biophysical properties of these dynamic complexes should provide significant insights into how and why biology exploits this piece of the continuum of protein states.

Dynamic complexes can be formed by the interaction of an intrinsically disordered protein (IDP) or intrinsically disordered region (IDR) with a folded protein partner (Mittag et al., 2010). In order to understand such complexes, it is critical to grapple with the general properties of disordered proteins (Dyson and Wright, 2005; Dunker et al., 2008; Wright and Dyson, 2009; Babu et al., 2012; Uversky, 2013). Their amino acid sequence compositions are enriched in polar and charged residues relative to hydrophobic residues and can be of low complexity. They often contain sequence motifs for recognition by modular binding domains or substrate binding regions of enzymes involved in

post-translational modification. Because of these sequence properties, electrostatic interactions can by highly significant for both intramolecular and intermolecular interactions. Configurational entropy considerations are also important. While IDPs lack a stable globular structure with a hydrophobic core, they often contain fluctuating secondary structural elements and transiently populated tertiary contacts that enable different degrees of compactness. Their dynamic sampling of multiple conformations enables exposure of binding motifs and averaging of electrostatic interactions. Post-translational modifications can lead to changes in structural properties due to effects on secondary structure propensities, specific tertiary contacts or charge effects. IDPs can function in a variety of ways, including mediating protein interactions, acting as entropic springs and linkers, and enhancing solubility. IDPs can also be considered the "polymer" form of proteins, enabling a wide phase space of large-scale assemblies to be accessed, including various fibers, gels and liquid-liquid phase separated droplets. From an evolutionary perspective, IDPs offer an ease of splicing and duplication and a robustness to sequence variability without the risk of complete loss of function due to destabilization of a folded state.

There are many benefits of disorder for protein interactions, such as the potential to impart high specificity due to large interfaces with weak or moderate binding due to configurational entropy loss upon binding, both valuable for regulatory control (Wright and Dyson, 2009). Because of their important roles in protein recognition, IDPs can function as hubs (proteins having >10 interactions partners) in interactions networks, enabling signal integration. Different binding partners can stabilize distinct structures within an IDP upon interaction, with binding leading to various degrees of disorder-to-order transitions, including only very limited and transient ordering. The latter case can be described as dynamic complexes or fuzzy complexes (Fuxreiter and Tompa, 2012). In what follows, I will provide examples of complexes of IDPs/IDRs with folded proteins along with thoughts on general principles.

Bipartitite and multi-valent interactions of IDP/IDR fragments

Modular binding domains or protein interaction domains are responsible for a significant fraction of specific protein interactions involving extended primary sequence motifs present in IDPs/IDRs. The alphabet-soup collection of these domains is responsible for a large degree of modularity in the architecture of regulatory and signaling proteins (Pawson, 2007). Consistent with the high degree of correlation of post-translational modification sites with IDRs, a subset of these domains recognize sequence motifs that have been post-translationally modified, including SH2, PTB, and 14-3-3 domains that bind phosphorylated targets and Tudor domains that bind methylated motifs (Seet et al., 2006; Deribe et al., 2010). Similarly, the over-representation of prolines in IDRs creates proline-rich or specific proline-containing target sites bound by SH3, WW and other such domains. Short segments of the target IDRs (usually <15 residues) directly contact the domain and many biophysical and structural studies have been performed with isolated peptides representing these core motifs. However, in the context of the full-length protein, the flanking sequences can play important roles, particularly contributing to electrostatic interactions, both attractive and repulsive. The flanking sequences of the IDR target motifs are not rigidly interacting with the modular binding domain, yet can have fluctuating contacts that may or may not stabilize particular backbone conformations. This dynamic picture can be thought of as fraying of the contacts at the peptide termini.

An extension of this dynamic concept is for bipartite (or multi-partite) target motifs in which a core binding element is more stably bound with immediately N- and/or C-terminal elements providing additional specificity but with greater dynamic fluctuations (Figure 1).

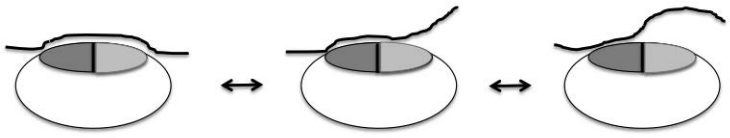

Figure 1. Schematic of a dynamic peptide complex involving a bipartite interface. (Left) fully engaged at both the core (dark grey) and secondary (light grey) sites, (center) partially engaged at the secondary site, (right) engaged only at the core site.

The core element may also have dynamic fluctuations such that no part of the target sequence is bound 100% of the time yet the fractional population of the bound state for each element can contribute to the favorable energetics of binding. An example of this is found for the binding of the Abp1 SH3 domain to a set of 24 different peptides, representing three known biological targets, three additional potential biological partners and a variety of mutant variants (Stollar et al., 2009; Stollar et al., 2012). NMR results are consistent with a picture of a primarily bipartite interface in which the canonical proline-rich core sequence is fairly stably interacting with the SH3 domain while residues C-terminal to this core dynamically exchange between contacting and non-contacting the SH3 domain within the bound state. Analyzing chemical shifts for the SH3 domain residues in the interface, "co-linear chemical shift perturbation" (CCSP) behavior is observed that is diagnostic of this inter-conversion between multiple peptide-bound conformational states having different degrees of engagement. CCSP is defined as the observation of a linear pattern of chemical shifts for resonances of the same residue in different related proteins (or protein complexes, in this case) when their 2D correlation spectra are superimposed, indicating fast exchange on the NMR timescale between two conformational states. Here these represent a "free-like" locally unengaged and a fully engaged SH3 domain-peptide complex, as observed for an Ark1 peptide. NMR relaxation data as well as gross binding affinities correlate with the CCSP values measured for the set of SH3 domain-peptide complexes. The engagement of the full bipartite binding surface appears to be important for full biological function via long-range coupling effects, suggesting that dynamic properties within the bound state of a protein complex may be a means of tuning biological responses.

Ark1, an important biological target of the Abp1 SH3 domain, actually contains two independent binding motifs that may contribute to enhanced binding by avidity effects. The presence of two or more binding motifs in protein targets of modular binding domains is very common, as is the presence of multiple related binding domains within proteins. One example is the three or four WW domains found in members of the HECT ubiquitin ligase family including Nedd4 that bind PY target motifs, which are present on each subunit in the multi-subunit complex of the epithelial sodium channel (ENaC), a target of Nedd4 (Lu et al., 2007). Another example is the six FF domains of the CA150 transcription factor that can recognize the 52 phospho-serine repeat motifs in the C-terminal portion of RNA Pol II (Murphy et al., 2009). While studies of isolated single domain-peptide complexes have revealed significant insights into binding specificity and signaling, the presence of wide-scale multi-valency within full-length binding partners argues for the need to study much longer segments of the IDR- and domain-containing regions or even full-length proteins in order to better understand biological protein recognition.

The importance of studying larger fragments of IDPs than peptides to characterize binding was recently highlighted by comparison of the Bin1 C-terminal SH3 domain binding to a peptide from c-Myc (55-68) (Pineda-Lucena et al., 2005) and the c-Myc (1-88) fragment (Andresen et al., 2012). In the first study, a stable complex of the peptide was observed involving a canonical proline-rich SH3-binding motif (residues 59-63) with a K_d value of ~4 micromolar. The second study of c-Myc (1-88) revealed a dynamic complex with SPR analysis demonstrating two separable K_d values of 33 and 200 micromolar. NMR data suggest an additional interaction with a proline-rich segment spanning residues 42-45 or other non-canonical sites and the lack of significant ordering for any residues of c-Myc(1-88), including residues 59-63, underscoring the presence of a dynamic multi-valent complex. While the binding constants in these two experiments may not be directly comparable due to different experimental approaches and protein concentration determinations, the apparent lower affinity for the longer Myc fragment may be due to repulsive electrostatic interactions from the flanking segments (see below).

The disorder-to-order continuum

Dynamic complexes involving IDPs/IDRs can involve a range of complete to partial disorder-to-order transitions as well as a range of stabilization or destabilization of secondary and tertiary structural contacts present in the free disordered protein (Mittag et al., 2010). Different degrees of each of these can be found within the same protein complex and in complexes of different disordered proteins with the same folded partner. There are a number of beautifully characterized cases of nearly complete folding upon binding, particularly involving transcription

factor complexes (Wright and Dyson, 2009). The previous description of various bipartite complexes of the Abp1 SH3 domain illustrates this principle, with full engagement of the Ark1 peptide representing a high degree of order for the core 12 interacting residues of the IDR in the complex while many other peptides can be characterized as more ordered in the canonical proline-rich segment but having transient interactions for the five residues C-terminal to that segment; increasingly significant dynamics are seen for the few extreme N-terminal and C-terminal residues of the peptides (Stollar et al., 2012).

An example that lies along the more dynamic end of the continuum is the interaction of the cystic fibrosis transmembrane conductance regulator (CFTR) regulatory (R) region with its first nucleotide-binding domain (NBD1) (Baker et al., 2007; Mittag et al., 2010; Chong et al., 2013). The free R region has elements of preferential helical structure; up to about 35% in some parts. Binding to NBD1 appears to stabilize helical structure within a dynamic complex involving multiple segments of the R region that are fractionally helical in the free R region. Phosphorylation of the R region reduces helical propensity and even induces segments with extended structure propensity, along with reducing the binding affinity and limiting the number of segments having direct interaction. This supports a model in which helical structure in the free R region enhances binding by minimizing entropy loss. However, significant helical propensity in the free state is not required for binding to NBD1 as segments without do bind, inducing (transient) helical structure in the bound state. This scenario is also consistent with crystal structures of NBD1 containing the first 30 residues of the R region (termed the regulatory extension or RE), which are immediately C-terminal to NBD1, showing different packing and specific structure but overall helical conformations for RE residues (Lewis et al., 2004; Thibodeau et al., 2005). Yet, comparison of R region resonance intensities in the presence and absence of NBD1 suggests that there is overall minimal ordering of the R region in the complex, with some residues outside the directly interacting elements in fact becoming more dynamic as intra-chain tertiary contacts within the R region are broken by competition with the R region-NBD1 contacts.

The interaction of the CFTR R region with 14-3-3 proteins is a further example of structural stabilization and destabilization upon binding in the context of dynamic complexes(Liang et al., 2012). 14-3-3 proteins interact preferentially with short extended phosphorylated segments in the context of homo- and hetero-dimers of 14-3-3 isoforms. Comparison of R region resonance intensities and chemical shifts in the presence and absence of 14-3-3beta suggests that nearly all of the 9 protein kinase A (PKA) phosphorylation sites within the CFTR R region are recognized by 14-3-3beta, with various local affinities, yielding a dynamic complex involving exchange of each of these sites in and out of the two binding pockets of the 14-3-3 dimer. (Note that this complex shares a number of features with the Sic1:Cdc4 complex described below and illustrated in Figure 2.) While some extended structural propensity is induced upon phosphorylation, beneficial for binding of the extended phosphorylated motifs to 14-3-3 proteins, there is still significant helical propensity in the R region and 14-3-3 binding must destabilize residual helical content at these sites. Importantly, there is no stable interface in the resulting dynamic complex and none of the phosphorylated sites is a good match for the canonical 14-3-3 recognition elements, yet the binding is of moderate affinity with a K_d of ~5 micromolar.

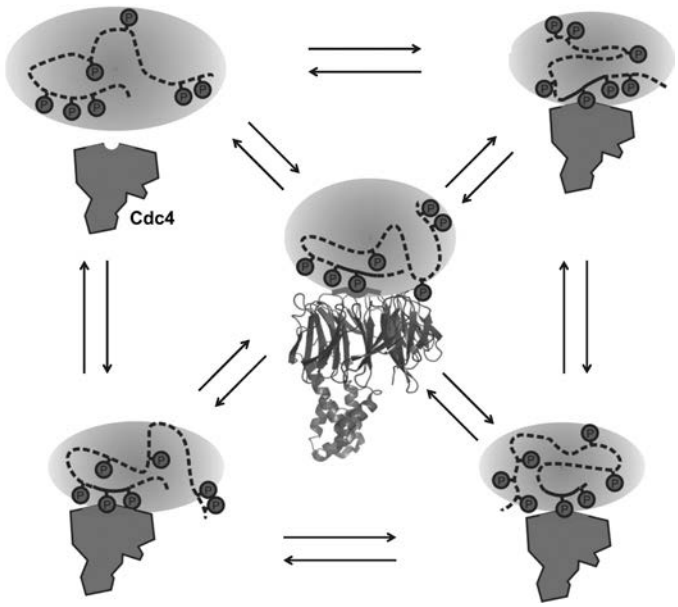

Figure 2. Schematic of the dynamic complex between Sic1 and Cdc4 showing 7 phosphorylated CPD sites exchanging on and off of the single arginine-rich binding site on Cdc4 with long-range electrostatic interactions due to the averaged electrostatic field (gray oval). Modified from (Mittag et al, 2008).

Another example that highlights the continuum of order and stabilization possible in complexes of IDPs is found in the binding of the disordered regulators of protein phosphatase 1 (PP1) to PP1 (Marsh et al., 2010; Pinheiro et al., 2011). PP1 is regulated by binding to a very large number of different targeting subunits and inhibitors, many of which are disordered. A crystal structure of the PP1 complex with the 159-residue disordered inhibitor-2 (I-2) demonstrates that only ~25% of the protein adopts stable structure, including a helix which is populated to ~70% in free I-2. Other structural elements stabilized in the complex are not observed in free-I2. Interestingly, the disorder in the PP1-bound state of I-2 increases in the context of a ternary complex with spinophilin, a disordered targeting regulator of PP1. The binary PP1-spinophilin complex, on the other hand, reveals a classic folding-upon-binding transition with a highly ordered complex observed in the crystal structure. Free spinophilin has an ~25% populated helix that corresponds to the helix seen in the complex as well as significant extended structure corresponding to one of the two beta-strands in the complex. Thus, examples exist of both conformational selection and induced fit within folding-upon-binding as well as the possibility to remain highly disordered within the bound state or even to increase disorder upon binding.

Multi-valent and poly-electrostatic interactions

The importance of electrostatic interactions in complexes involving disordered proteins is due to the significant enrichment of charged over hydrophobic residues as well as sites of post-translational modification that change charge in IDRs. The latter include serine, threonine and tyrosine phosphorylation (changing charge from 0 to -2), tyrosine sulfation (0 to -1), arginine deimination (+1 to 0), and lysine acetylation (+1 to 0) (Arif et al., 2010; Sasaki, 2012; Bicker and Thompson, 2013). These changes can have highly specific and local effects at stable binding interfaces or within folded proteins, however in the context of dynamic complexes with transient interactions, the long-range of electrostatic interactions combined with dynamic averaging of conformations suggests that overall charge distribution may play a dominant role (Borg et al., 2007). In multi-valent complexes involving exchange of multiple binding elements within an IDR on and off of the folded protein surface, this conformational exchange itself may play a role in creating a mean electrostatic field.

A clear example of this effect can be found in the binding of the 280-residue disordered Sic1 cyclin-dependent kinase inhibitor to the Cdc4 substrate recognition domain of a ubiquitin ligase in the control of yeast cell cycle (Nash et al., 2001; Mittag et al., 2008; Tang et al., 2012). In order for the G1-S transition to occur, Sic1 must be degraded by the proteasome. Recognition of Sic1 by the SCF^{Cdc4} ubiquitin ligase to facilitate proteasomal degradation is dependent on multi-site phosphorylation of Ser/Thr residues in CPD (Cdc4 phospho-degron) motifs. While cyclin E and some other cell cycle proteins targeted by SCF^{Cdc4} have a single high-affinity binding CPD site, Sic1 has nine suboptimal CPD motifs and generally requires six of them to be phosphorylated. Cdc4 has a CPD-binding WD40 domain with a single highly arginine-rich binding site for CPDs. Cdc4-Sic1 binding generates a dynamic complex in which the CPDs exchange on and off of the WD40 binding surface (Figure 2).

The K_d value for Cdc4 binding to highly phosphorylated Sic1 is ~ 1 micromolar but affinities to short peptides representing individual CPDs are much weaker (Borg et al., 2007; Mittag et al., 2008; Tang et al., 2012). The N-terminal 90 residues of Sic1 (termed the N-terminal targeting region as it is both necessary and sufficient for Cdc4 binding) contains 7 CPD sites, 11 basic residues and no negatively charged residues, yielding a net charge of +11 that is highly repulsive of the WD40 binding interface. Phosphorylation of one or a small number of CPD sites does not lead to reasonable levels of Sic1-Cdc4 binding as the electrostatics remain highly unfavorable. Multi-site phosphorylation is required, with the transition between 5 and 6 sites leading to a change in nominal net charge for the Sic1 N-terminal targeting region of +1 to -1, a transition between repulsive and attractive. This explains the observation that full-length Sic1 with only the 3 closest spaced CPDs phosphorylated binds Cdc4 with a K_d of greater than 50 micromolar while a short phospho-peptide containing these 3 closest spaced CPDs (but lacking many positively charged flanking residues) binds with a K_d of ~ 2.5 micromolar. Thus, while only one CPD is bound on the WD40 interface at a time, the overall affinity is not defined by the best affinity for any of the individual CPDs, as would be the case if local interactions dominate the binding. Rather, the longer-range electrostatic components of the binding energy (reported by net charge in a conformationally averaged system) appear to

dominate when individual CPDs have weak affinity (Figure 2).

The biological effect of a requirement for multi-site phosphorylation to enable Cdc4-Sic1 binding is that the G1 to S cell cycle transition becomes dependent on the 5th or 6th power of the concentration of the kinase that phosphorylates Sic1, leading to an ultrasensitive degradation response and very sharp cell cycle transitions (Nash et al., 2001). When a CPD peptide from cyclin E having a K_d of 1 micromolar is inserted into Sic1 lacking all the natural suboptimal CPD sequences, yeast undergo premature cell cycle transitions leading to chromosome instability and inviability, likely due to perturbation of the ultrasensitive binding. Thus, biology exploits this dynamic complex in order to create a sharp switch.

These findings further support the importance of studies of full-length or large fragments of IDPs rather than short peptides to thoroughly understand the mechanisms of regulation via binding. Interestingly, the exchange within the Sic1-Cdc4 complex also allows multi-site ubiquitination within the context of the full SCFCdc4 complex in which the catalytic cysteine is more than 60Å from the substrate binding site on the WD40 domain (Mittag et al., 2010). While the disordered Sic1 chain can easily span this distance, only sites far from a bound CPD can be ubiquitinated. Sic1 containing only a single high-affinity cyclin E CPD site at the N-terminus is preferentially ubiquitinated at the C-terminus. Thus, multi-valent binding has an additional benefit for the more uniform accessibility of the chain to other post-translational modifications.

Unlike the switch generated by Sic1-Cdc4 multi-valent binding, the multi-valent CFTR R region interactions in regulation of CFTR's chloride channel function instead appear to generate a rheostat (Baker et al., 2007; Chong et al., 2013). PKA phosphorylation reduces R region:NBD1 interactions which block NBD dimerization required for ATP hydrolysis and channel gating. Mutagenesis and electrophysiology data have shown that no single PKA site is required but increased phosphorylation leads to increased channel activity, suggesting that phosphorylation is not a switch but that it shifts the equilibrium between open and closed channel conformations. This rheostat effect is potentially important in the CFTR R region interaction with 14-3-3, as increased levels of phosphorylation enhance the biological stimulation of CFTR trafficking to the plasma membrane due to 14-3-3 (Liang et al., 2012). Rheostats are likely common regulatory components that can be generated by multi-valent dynamic complexes of IDPs.

Concluding thoughts

Disordered proteins can mediate interactions via disorder-to-order transitions that are nearly complete or partial, with significant dynamic fluctuations present in the bound state. Multi-valent interactions involving more than one segment of the disordered protein or more than one of a given type of folded binding domain can give rise to exchange between various similar transiently bound states. This exchange can create a mean electrostatic potential contributing to long-range favorable binding interactions and may generate switch-like or rheostat function. Interactions of multiple distinct folded partners with a single disordered protein can enable the IDP to act as a hub with a role in integrating various binding "signals". Conformational plasticity enables binding to target proteins in different structural modes. Post-translational modifications of IDPs/IDRs often modulate transient structural propensities and affinities for different targets. The local off-rates can be significant within dynamic complexes, even for overall moderate or high affinity binding, providing access to competing binding partners or to modifying enzymes even within or very near to the binding surfaces. Affinities for individual peptides and segments do not always reflect affinities within the context of the full IDP or IDR with net charge effects and overall compactness due to transient tertiary contacts playing a modulating role.

Our studies of dynamic complexes of IDPs have provided examples of a variety of ways in which biological function can be mediated by interactions with disordered proteins. Studies of full IDPs or large IDR regions have been required in order to observe a number of interesting features. Some of our findings contradict simple views of the structural biology of proteins and structure-function relationships. However, it is increasingly apparent that nature exploits the entire continuum of structure, dynamics and disorder. Future studies are certain to provide more evidence for the diversity of mechanisms exploiting dynamics and disorder of proteins for regulation of biological function.

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2012 GE Healthcare New Investigator Award

Autophagy: journal club misfit rises to rock star status

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Abstract

Macroautophagy (hereafter autophagy) is a cellular degradative pathway that is highly conserved in eukaryotic cells. Autophagy involves the delivery of cytoplasmic contents to the lysosome for degradation and occurs via cargo engulfment into a double-membrane compartment called the autophagosome. Fusion of autophagosomes with lysosomes leads to cargo degradation and recycling of macromolecules. Autophagy can target microbes to the lysosome for degradation, and has many other functions in innate and adaptive immunity. In turn, some pathogenic microbes have devised mechanisms to subvert, even exploit autophagy during infection of host cells. In this article I discuss my entry to the field of autophagy through studies of bacterial pathogens.

Introduction

I remember first hearing the word "autophagy" in the mid 1990's. I was a graduate student attending a journal club. The paper presented was about how autophagy was regulated by a signal transduction pathway. To the dismay of the poor student presenting, we were all perplexed about this process called autophagy. What was this structure called an autophagosome? How is it formed? Why would a cell decide to digest itself?

In hindsight the need for autophagy is obvious; cells require the ability to remove damaged or unwanted organelles. In times of metabolic need, autophagy allows recycling of essential macromolecules and generation of energy. And when microbes should invade the cytoplasm, autophagy can deliver them to the lysosome as a potent cellular defense.

Years later, autophagy has emerged as one of the 'hottest' research topics. There's even a new journal dedicated to the topic, *Autophagy*, with an impact factor of 7.5. A history of the major discoveries in the field of autophagy has been written by the editor of *Autophagy*, Dan Klionsky (1) and is recommended reading. The discovery of genes essential for autophagy in yeast, the discovery of autophagy marker proteins (e.g. LC3) and the discovery of links between autophagy proteins and human diseases (including cancer, inflammatory bowel disease and neurodegenerative diseases) have put autophagy on the radar of most medical researchers.

Bacteria and autophagy

My interest in autophagy came from an unexpected observation; *Salmonella* in the cytosol. These bacteria typically replicate within specialized vacuoles within host cells, but I became intrigued by a neglected population of bacteria in the cytosol. These bacteria had a different morphology and actually replicated faster than those in vacuoles (2). Why, if *Salmonella* can grow so fast in the cytosol, are they rarely localized to this compartment?

Then came a landmark paper by Paul Webster's group (3). Webster and colleagues showed that *Listeria monocytogenes* can be targeted by autophagy within the cytosol and killed within lysosomes. Their study inspired us to test the hypothesis that autophagy might also be targeting *Salmonella* in the cytosol. In fact we were wrong, *Salmonella* is targeted by autophagy within vacuoles, not the cytosol (4). But like so many other experiences I've had in science, proving the model wrong led to something much more interesting.

What we learned was that *Salmonella* can disrupt its vacuole using a type 3 secretion system, a bacterial translocation system. The type 3 secretion system generates a pore in the plasma membrane of host cells, allowing it to deliver 'effector' proteins into the host cell that promote bacterial growth. A population of bacteria can express high levels of type 3 secretion activity, which can damage and even disrupt *Salmonella* vacuoles shortly after invasion. We found that autophagy can target damaged vacuoles containing bacteria, engulfing these compartments and thereby preventing bacterial escape into the cytosol (4). A population of bacteria (usually about 25% in non-phagocytic cells) colocalized with the autophagy marker protein LC3 (Figure 1). Deletion of essential autophagy genes led to increased bacterial replication within the cytosol. Hence, autophagy serves as a 'defender of the cytosol' (see model in Figure 2).

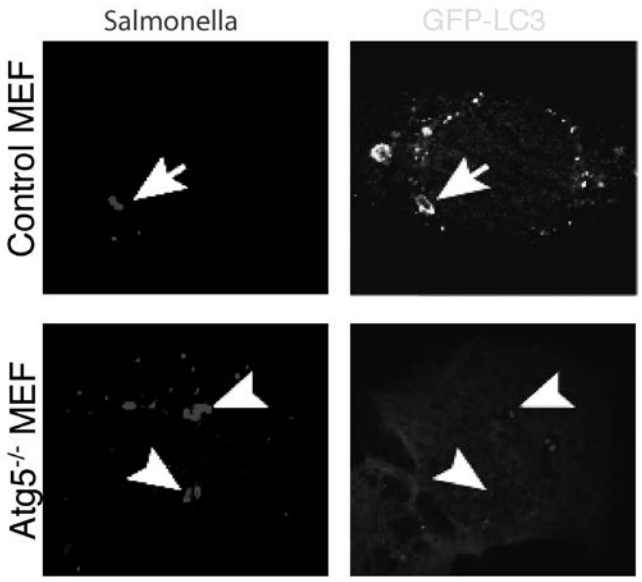

Figure 1. Autophagy targets a population of *Salmonella* during infection. Wild type (upper panels) or Atg5-/- (lower panels) mouse embryonic fibroblasts (MEFs) were transfected with GFP-LC3, a marker of autophagosomes. Cells were then infected with *Salmonella enterica* serovar Typhimurium for one hour, then fixed and stained for bacteria. Arrows indicate bacteria that colocalize with LC3 in wild type MEFs. Arrowheads indicate bacteria that do not colocalize with LC3 in Atg5-/- MEFs.

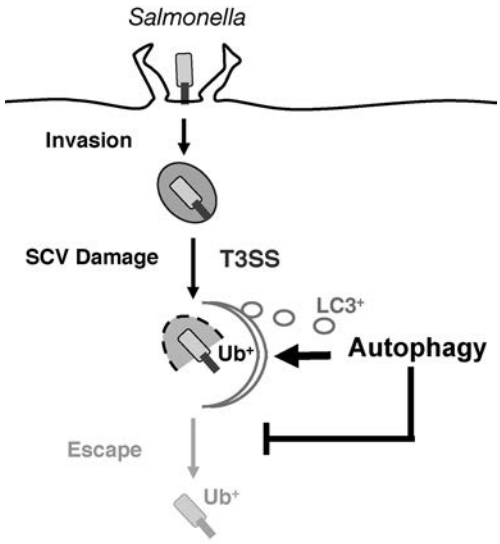

Figure 2. Model of how autophagy 'defends the cytosol' from *Salmonella* infection. *Salmonella* invades host cells using a type 3 secretion system (T3SS), a bacterial translocation system that operates by generating pores in the plasma membrane of host cells. A population of these bacteria has high T3SS activity, which can damage *Salmonella*-containing vacuoles after invasion has occurred. This damage can lead to bacterial escape into the cytosol, and rapid bacterial replication in this compartment. However, autophagy can target damaged vacuoles containing *Salmonella*, maintaining bacteria in a membrane-bound compartment and (presumably) mediating their delivery to lysosomes for degradation. Autophagy targets damaged *Salmonella*-containing vacuoles by recognizing various molecular signatures, including protein ubiquitination, complex carbohydrates and DNA (discussed in the text).

How does autophagy target *Salmonella* within damaged vacuoles? This has become a hot topic, and the answer seems manifold. First, we know that protein ubiquitination is involved, though the actual protein substrates of ubiquitination are not clear (4). Ubiquitinated proteins associated with bacteria promote recruitment of three different ubiquitin-binding autophagy adaptors: p62/SQSTM1, NDP52 and Optineurin (5-7). It is remarkable that all three adaptors seem to occupy distinct 'microdomains' around bacteria targeted by autophagy. Deletion of any one adaptor blocks autophagy of the bacteria, so presumably all adaptors provide a unique signal, or merely allow the full circumference of bacteria (typically 2 μm long) to be engulfed by autophagosomes. Second, we know that 'sugar signals' are involved. Randow and colleagues showed that the cytosolic lectin Galectin-8 can bind to complex carbohydrates presented on damaged vacuoles containing *Salmonella*, and subsequently promotes autophagy of these compartments via NDP52 (8). Third, while not specifically shown for *Salmonella*, we know that autophagy of *Mycobacterium tuberculosis* within damaged phagosomes involves 'DNA signals'. Jeffrey Cox and colleagues showed that *M. tuberculosis* can translocate DNA into the cytosol of host macrophages, leading to activation of the DNA sensor STING and initiating a cascade that leads to autophagy of the bacteria (9). In summary, it seems that eukaryotic cells have multiple detection systems to recognize damaged cellular compartments and uses these to remove them via autophagy. Pathogen removal might then be considered a 'housekeeping' function of autophagy, though there is some evidence that autophagy of bacteria is unique from canonical (e.g. starvation-induced) autophagy (10, 11).

In addition to targeting bacteria to lysosomes for degradation, autophagy has many roles in both innate and adaptive immunity (12). With so many immune functions, it should be no surprise then that bacterial pathogens have devised clever ways to subvert autophagy; blocking its initiation, evading capture by autophagosomes and blocking autophagosome maturation. Some pathogens can even exploit autophagy to replicate, or to spread from cell-to-cell. The topic of pathogen subversion of autophagy is complex and I refer the reader to this review for further insight (13). This is a fascinating area of science that is sure to illuminate bacterial virulence strategies and also to teach us a great deal about the regulation of autophagy.

Autophagy gets complicated – fast!

Notice that I started this article by qualifying that I'm discussing macroautophagy. In fact there are many forms of autophagy, which in general means 'self-eating' as translated from Greek. What originally defined macroautophagy (and differentiated it from other forms of autophagy, including microautophagy, chaperone-mediate autophagy, piecemeal microautophagy of the nucleus, etc.) was a group of Atg proteins that are essential for this process. Atg8, also known as LC3, was thought to be a specific marker of macroautophagy. Over time, it become apparent that Atg proteins have other functions (reviewed in (14)) and that LC3 could associate with structures other than autophagosomes. With relevance to bacteria, Douglas Green's group showed that LC3 could be recruited to intact phagosomes in a manner that did not involve classical autophagy (15). This process, termed 'LC3-associated phagocytosis' (or LAP as it is known in the field) is thought to promote phagosome maturation, possibly by promoting fusion with lysosomes. The Green paper made us re-evaluate LC3 as a marker of autophagy during bacterial infection. The complicating challenge in many cases is to unravel whether autophagy, or LAP (or both) is targeting bacteria during infection. Making this difficult is the fact that both pathways have the same kinetics, delivering LC3 to bacteria at precisely 60 minutes post infection! Methods to distinguish these pathways have been discussed in a recent methods review (16).

LAP seems to be an important pathway in phagocytes. In fact, we think this is the dominant pathway in these cells since the majority of bacterial pathogens don't disrupt vacuoles/phagosomes during infection, but rather face normal phagosome maturation. How is LAP activated? In my lab we showed that reactive oxygen species production by NADPH oxidases promotes LC3 recruitment to phagosomes (17). How this occurs is still an open question. We also showed that *L. monocytogenes* strain 10403S is targeted by the LAP pathway, and this leads to bacterial colonization of large vacuoles that we call Spacious *Listeria*-containing phagosomes, or SLAPs (18). SLAPs have been linked to chronic infection by *L. monocytogenes* in a mouse model of infection (19), so the LAP pathway may have an important role in maintaining the host-pathogen relationships over long periods of time.

Future directions

The autophagy 'genie' is officially out of the bottle. What started for me as an unsatisfying journal club experience has turned into a major part of my research program. Many labs now focus on autophagy and excellent reagents provided by my generous colleagues are making it easier for others to join the field. Drug companies are developing assays (including *Salmonella* autophagy!) to identify better, more specific modulators of autophagy that may help in the fight against a number of deadly diseases. How is an autophagosome formed? Ironically, this question is still hotly debated, with various compartments proposed to be involved, including the ER, mitochondria and endosomes. A recent paper by Tamotsu Yoshimori's group suggests that autophagosomes form at the ER-mitochondria interface (20). So perhaps it is the confluence of these multiple organelles, rather than their individual components, that will define autophagy. No doubt time will tell, and many journal clubs will follow the field for years to come.

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2012 NRC Research Press Senior Investigator Award

A journey through the molecular pharmacology of G protein-coupled receptors; a personal perspective of thirty-five years or so...

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My Introduction to GPCRs

I first became interested in G protein-coupled receptors when I joined the laboratory of Jacques de Champlain in 1979 to study the regulation of the sympathetic nervous system and its role in the development of hypertension. My mission as a graduate student was to test the hypothesis that presynaptic adrenergic receptors were important for the regulation of catecholamine release by the sympathetic nerves and adrenal medulla. Since detecting the presence of such receptors was part of the demonstration, the emergence of radio-ligand binding methodologies was an important methodological breakthrough for my thesis work. With the late Thomas Reader, then a professor in the department of physiology, where I was conducting my Ph.D. studies, we attended one of the practical courses on this topic offered by the Neuroscience Society. With Tom, we were among the first ones to use these techniques in Montreal. As I progressed through my pharmacological and physiological studies of the β2 and α2-adrenergic receptors (AR) in Jacques' Laboratory, I became increasingly interested in the biochemistry and molecular biology of these receptors. Therefore after demonstrating the existence of α2 and β2AR on the adrenal medulla chromaffin cells of rat and their role in controlling the secretion of catecholamines under normal conditions and in hypertensive states[1-4], I headed south to join the laboratory of Robert Lefkowitz at Duke University (Nobel prize of chemistry 2012) who was already a legend for his study of the βAR function and regulation.

A Nobel Quest

Thanks to a very productive and long lasting collaboration with a Canadian born scientist, Marc Caron, the Lefkowitz laboratory had opened the field of receptor physiology and pharmacology to the innovative approaches of biochemistry and molecular biology[5]. They had purified several receptors to homogeneity, demonstrated that reconstitution of the purified receptors with the other components of the canonical GPCR signaling pathway (ie: G protein and effectors such as adenylyl cyclase) was sufficient to confer hormone responsiveness therefore demonstrating the molecular reality of the concept of receptor. Many post-doctoral fellows working in the Lefkowitz

and Caron laboratories (including among others Jeff Benovic and later, two Canadian fellows Stephane Laporte and Steve Ferguson) then collectively unraveled the role of receptor phosphorylation and of newly discovered kinases (later named G protein-coupled receptor kinases, GRKs) and of an accessory protein (βarrestin) in the phenomenon of receptor desensitization and internalization[6,7].

When I joined the Lefkowitz laboratory, the frenzy to clone the DNAs encoding GPCRs was led by Brian Kobilka (Nobel Prize of chemistry 2012) and resulted in the cloning of almost all the adrenergic receptor family by the Duke group leading to the realization that GPCRs form a super-family of receptors sharing a common overall structure characterized by 7 trans-membrane domains. I rapidly took advantage of the then emerging tools of molecular biology to perform the first experiments involving heterologous expression of GPCRs in cultured cells[8] and used site directed mutagenesis to dissect the role of different kinases and of their phosphorylation sites in the homologous and heterologous desensitization processes[9-12]. These studies contributed to establish the now general model of receptor regulation by phosphorylation involving second messenger-dependent kinases and GRKs to control signaling efficacy[6]. In collaboration with two other Canadian post-doctoral fellows, Brian O'Dowd and Mark Hnatowich, we showed that GPCRS were also regulated by another post-translational modification, palmitoylation[13].

Back to Montréal

Back at the Université de Montréal as an assistant professor in 1989, I remained interested in the mechanisms controlling GPCR signaling efficacy and selectivity. Among our first studies was the discovery made by my first graduate student, Manon Valiquette, who showed that GPCRs were controlled not only by phosphorylation on serine and threonine residues but also on tyrosines[14-16]. These studies provided a molecular mechanism explaining some of the cross-talk regulation occurring between receptor tyrosine kinases and GPCRs. Through a collaboration that is still lasting with Stefano Marullo from the Institut Cochin in Paris and with the late Donny Strosberg, another of my Ph.D. students, François Nantel, spearheaded a series of studies characterizing the mechanism regulating the β3AR, a newly identified βadrenergic receptor that had recently been cloned by the Strosberg's lab[17-19]. This receptor turned out to be resistant to short-term desensitization as a consequence of a lack of phosphorylation and, its responsiveness largely controlled by the longer-term process of down-regulation of the receptor number through receptor degradation and regulation of mRNA stability. In addition to further our understanding of this important receptor for the control of fat cell metabolism, the studies firmly established the role of phosphorylation in the early steps of desensitization for the β2AR.

Marrying Basic and Applied Research

Since our work involved biochemical studies of the receptor, our quest for large quantities of purified receptor led us to develop the first baculovirus-insect cell expression systems for GPCRs. This work was done in collaboration with Michael Dennis, then at the Biotechnology Research Institute (BRI) in Montréal and ultimately led to the creation of BioSignal, a biotechnology company which first product was GPCR-expressing membranes sold to biopharmaceutical companies and academic laboratories. BioSignal was later acquired by Packard and then Perkin-Elmer. The studies on the baculovirus production system were pioneered, in my laboratory, by a post-doctoral fellow, Bernard Mouillac, and a graduate student, Thomas Loisel. In addition to provide tools for large production of receptors[20], the system allowed us to more easily study some biological processes. In particular, it allowed Serge Moffett and Lynda Adam then graduate students to demonstrate that palmitoylation of GPCRs was a dynamic process that is regulated by receptor activation and contributes to control its function[21-25]. While characterizing the pharmacological properties of the β2AR produced in insect cells following baculovirus infection, we discovered that receptor were spontaneously active (ie: they could activate their signaling pathway in the absence of agonist), an observation that was made possible due to the high expression level that amplified the responses. Following up on this observation, Peter Chidiac, then a post-doctoral fellow in the laboratory established the concept of inverse agonists for ligands that can inhibit the spontaneous activity of receptors[26]. Graciela Piñeyro and Mounia Azzi, also post-doctoral fellows in the laboratory, then extended the study of inverse agonists to other receptor and systems thus establishing its pharmacological and physiological importance[27,28]. Continuing our quest to better understand GPCR signaling efficacy, Mounia Azzi discovered that a ligand that acted as an agonist for a given signaling pathway

could simultaneously be an inverse agonist for a distinct pathway through the same receptor, giving rise to the concept of ligand-biased signaling also known as functional selectivity[29]. Expanding on the concept with three graduate students, Ségolène Galadrin, Geneviève Oligny-Longpré and Wayne Stallaert, we proposed that the signaling efficacy is a pluridimensional parameter such that the efficacy of GPCR ligands toward the different signaling cascades needs to be taken into consideration to obtain a comprehensive representation of drug efficacy[30,31]. This new paradigm, now widely accepted, has important consequences for drug discovery and is being integrated by many pharmaceutical companies in their drug screening strategies (Figure 1).

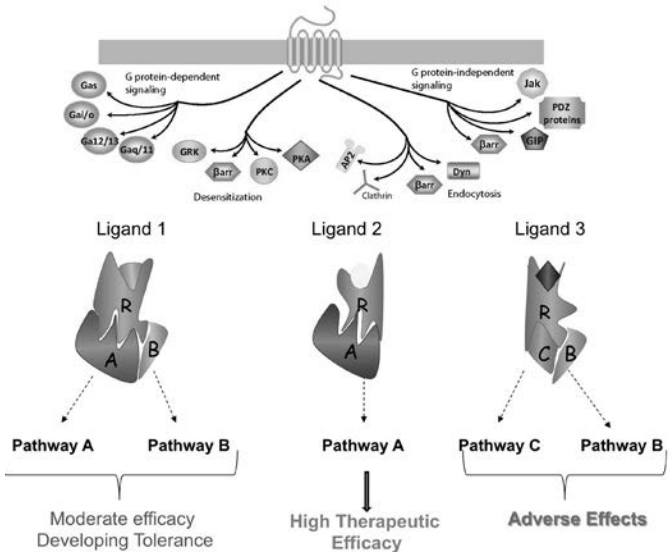

Figure 1. Functional selectivity and ligand-biased signaling. Individual G protein-coupled receptors are now known to engage multiple signaling effectors including distinct G protein-dependent and -independent pathways. Ligand have been found to have different some-times opposite efficacy on the different signaling pathways engaged leading to the concepts of pluri-dimensional signaling efficacy, functional selectivity and ligand-biased signaling.

GPCRs Come to Light

Over-expression of β2AR using the baculovirus-insect cell expression also allowed Terry Hebert to visualize GPCR dimers for the first time through co-immunoprecipitation studies[32]. Following up on these original observations, Stephane Angers and Ali Salahpour, then graduate students, established the bioluminescence resonance energy transfer (BRET) approaches that would allow us to demonstrate that dimers and most-likely higher oligomeric forms of GPCR exist in living mammalian cells[33]. Many students and post-doctoral fellows then followed in Stéphane and Ali footsteps and used this approach to uncover new aspects of GPCR oligomerization[34-39]. This discovery that led to considerable debates on its physiological relevance has now been confirmed by many laboratories and has recently received structural support[40]. The concept was also expanded to the existence of hetero-oligomers, providing a structural basis for the exquisite pharmacological selectivity and allosteric regulation observed in many systems[41-43]. Realizing the power of the proximity-based BRET assays to monitor protein-protein interactions and conformational rearrangements, Stéphane Angers, Pascale Charest, Céline Galés, Billy Breton, Julie Perroy, Stéphanie Pontier, Yann Perchérancier among other trainees of the laboratory designed and developed multiple biosensors that allow to follow the recruitment and activation of βarrestin and of G proteins, the production of second messengers as well as the ubiquitination of proteins [33,44-49] (Figure 2).

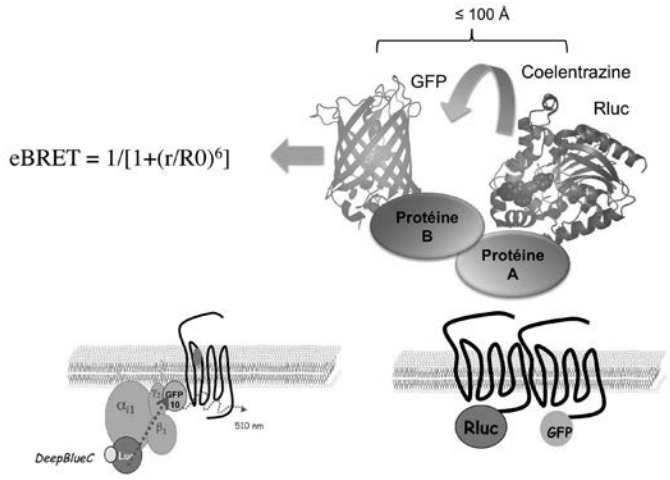

Figure 2. Bioluminescence resonance energy transfer (BRET): a proximity-based assay. BRET is a natural phenomenon occurring in marine animals such as ***Aquaria Victoria***. It consists in the non-radiative transfer of energy from a bioluminescent energy donor (typically ***Renilla*** luciferase; Rluc***)*** to a fluorescent energy acceptor (typically a green fluorescent protein; GFP). The efficiency of transfer is inversely proportional to the 6th power of the distance between energy donor and acceptor. No measurable transfer occurs when more than 10nm separates the donor and the acceptor making it a convenient tool to develop proximity-based assays to monitor protein-protein interactions and conformational reorganization. We used it to study GPCR dimerization and various cell signaling events including G protein activation.

This work laid the foundation for the creation of a GPCR biosensor consortium composed of Terry Hebert, Stéphane Laporte, Richard Leduc, Graciela Piñeyro, Eric Thorin, Christian Le Gouill and myself, which objective is to design and validate BRET-based biosensor arrays that will monitor multiple signaling activities to provide a comprehensive view of drugs' pluri-dimensional efficacy and its impact on therapeutic activity. The creation of this consortium was made possible through the support of the Quebec Consortium on Drug Discovery and continues beyond this original funding to further develop the use of BRET-based biosensors for basic science and drug discovery programs.

Rescuing GPCR Mutants with Pharmacological Chaperones

On an even more clinical note, we had the privilege several years ago to be contacted by our colleague Daniel Bichet, a nephrologist at Sacré-Coeur hospital in Montréal, who had identified mutations in the gene encoding the type-2 vasopressin receptor (V2R) as the cause for a rare disease known as nephrogenic diabetes insipidus (NDI). Daniel wanted to know if we could help him find out what was wrong with these mutated forms of the receptor that led to the incapacity of patients to concentrate their urine, resulting in urinary volumes of up to 25 liters per day. Jean-Pierre Morello, then a graduate student in the laboratory, found that most of the mutations leading to the disease (more than 200 identified today) resulted in the misfolding of the receptor and its retention in the endoplasmic reticulum (ER) by the quality control system. He then went on to demonstrate that compounds able to bind to the receptor in the ER can rescue the folding of many of these receptor mutants, allowing their escape from the quality control system and their trafficking to the plasma membrane where they can be active[50] (Figure 3).

In a continued collaboration with Dr. Bichet, and a graduate student in the laboratory, Virginie Bernier, we were then able to test these compounds that we christened pharmacological chaperones for their therapeutic efficacy in NDI patients[51]. The successful pilot clinical trial established for the first time the therapeutic potential of pharmacological chaperones. The concept of pharmacological chaperones was then extended to other GPCRs and other classes of proteins[52,53]. Two post-doctoral fellows in the laboratory, Ulla Petäjä-Repo and Patricia René have further characterized the molecular mechanisms underlying the action of pharmacological chaperones[54,55] and have identified new pharmacological chaperones that could represent therapeutic avenue for the treatment of diseases resulting from GPCR misfolding, including early onset morbid obesity resulting from mutations in the type-4 melanocortin receptor (MC4R).

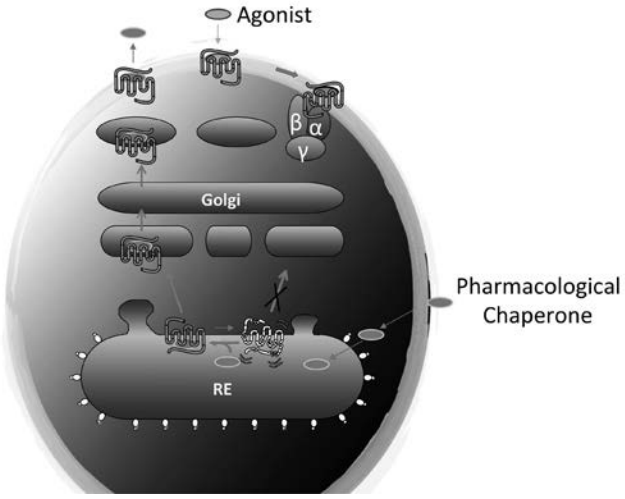

Figure 3. Mode of action of pharmacological chaperones. Human pathologies, known as conformational diseases, are caused by genetic mutations leading to improper folding of GPCR that result in their retention in the endoplasmic reticulum by the quality control system. Pharmacological chaperones, are lipophilic small molecule ligands that can selectively bind to the receptors in the ER, promote their proper folding and favor their trafficking to the plasma membrane where they can be active. Pharmacological chaperones represent a new class of therapeutic agents for the treatment of conformational diseases such as nephrogenic diabetes insipidus and familial early onset severe obesity.

Looking to the Future

These last 35 years spent to study GPCRs turned out to be fascinating. I witnessed many revolutions in our understanding of this important family of proteins and was fortunate enough to even contribute to some of them. Although they already represent the largest protein family targeted by prescribed drugs, there is no doubt that recent breakthroughs, in particular concerning the molecular and structural determinants of their function and regulation will continue to generate excitement and lead to the development of innovative therapies.

Apologies and acknowledgements: *Many students and PDFs who worked in my laboratory over the years and made important contributions were not explicitly mentioned in this brief recollection because of the limited space. I apologize to them and take this opportunity to thank them. Also, special thanks go to Monique Lagacé without whom most of what is described herein would not have been possible.*

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Department of Cell Biology

Correspondent: Paul LaPointe

The Cell Biology Department at U of A is comprised of 18 primary and cross-appointed investigators whose research interests span a variety of areas in cell biology, with a strong molecular focus in each case. In 2012 we welcomed our newest faculty member, **Ben Montpetit**, who carried out his postdoctoral work with Karsten Weis at UC Berkeley. Ben brings with him extensive expertise in mRNA export from the nucleus and complements existing strengths that include neuroscience, *Drosophila* development, organelle biogenesis and inheritance, protein folding, mitochondrial biology and metabolism, protein and lipid transport, nuclear pore function, the RNAi system, and virology.

Ben Montpetit

All told in 2012-13, members of our department were successful in attracting nearly $4.4 million in operating grants, training awards and visiting speaker awards from provincial and national sources. Our department has 32 graduate students that have been successful in obtaining prestigious fellowships including the Vanier and Dr. Fred Banting and Dr. Charles Best CIHR Graduate Fellowships. Members of our department have also been successful in adapting to the new research funding paradigm both nationally and provincially, with success in acquiring funding for basic science-clinical partnerships.

Our faculty members look forward to working through the CSMB to promote basic research across the country at the provincial and national levels; and ensure that the CIHR continues to equitable and adequately fund the important work being done in the Canadian research community.

University of Calgary

Department of Biochemistry & Molecular Biology

Correspondent: Dr. Jonathan Lytton

Jason de Koning - our newest faculty member

The Department of Biochemistry & Molecular Biology has had a very successful 2012. We were fortunate this year in recruiting **Dr. Jason de Koning** to the Department, who will expand our academic bioinformatics program. Jason uses novel statistical and computational approaches to address molecular evolution and comparative genomics that will also be relevant in interpreting personal genomic variation in humans. Last year's previous recruit to the Department, **Dr. Aaron Goodarzi**, was successful in garnering a Canada Research Chair Tier 2 in Genome Damage and Instability Diseases, as well as Canada Foundation for Innovation funds and a CIHR operating grant. This is a terrific start to Aaron's career in Calgary!

We are also proud that many of our Department members were successful in renewing or gaining new CIHR funding in these tough times. As well as Aaron, **Drs. George Chaconas**, **Jennifer Cobb**, **Susan Lees-Miller**, **Jim McGhee** and **Xi-Long Zheng**, as well as joint members, **Wayne Chen** and **Debbie Kurrasch** all received CIHR grants. In addition, **Dr. Robin Yates**, a joint member of the Department, was awarded a CIHR New Investigator Award, while joint members **Drs. Derrick Rancourt** and **Hans Vogel** were each successful as leaders of different projects funded by the recently established Alberta Innovates-Health Solutions Collaborative Research Innovation Opportunities.

The Department celebrated the research successes of both

our faculty members and trainees recently at our annual scientific and social "advance" at The Banff Centre. Awards were presented to **Drs. Savraj Grewal**, **Carol Schuurmans** and **Susan Lees-Miller** for their research achievements in 2012. We also honored MSc graduate, **Uyen Tran**, and PhD graduate, **Charlene Downey**, as well as postdoctoral researcher, **Dr. Mireille Tittel-Elmer** for their accomplishments in 2012. Another of our PhD students, **Curtis Hughey**, was honored with an Isaak Walton Killam Pre-Doctoral Scholarship, one of the University's top awards for graduate students.

Advancing BMB by putting the fun into fundamental research

This year the Department honored **Dr. Mayi Arcellana-Panlilio** with our inaugural "educational award". Mayi plays a leadership role in delivering the inquiry-based cell biology core course to our Bachelor in Health Sciences undergraduate program. Mayi also co-leads the University's international Genetically Engineered Machines team, which this year claimed the human practices award and a top 16 global ranking at the world championships in Boston, for their oil sands detection and remediation project. Check out their website: http://2012.igem.org/Team:Calgary

Several of our jointly affiliated Department members were also honored outside the University for their contributions this year. **Dr. Hans Vogel** was elected to membership in the Royal Society of Canada. **Dr. Marv Fritzler** received the Alberta Science & Technology award for "Outstanding Contribution to the Alberta Science and Technology Community ". And last, but not least, **Drs. Minh Dang Nguyen** and **Debbie Kurrasch** were honored by Avenue Magazine as two of Calgary's "Top 40 under 40". Look out for more to come from these two!

Our members also continue to be active participants in educational service roles within the Faculty of Medicine. This year, **Dr. Randal Johnston** took the reins as Director of the Master of Biomedical Technology course-based MSc program, while **Dr. Carol Schuurmans** was appointed as co-Director of the Neurosciences graduate program.

The Department continues to build on our strengths in 2013 with ongoing new recruitment in developmental biology, bioinformatics and cancer biology. Please visit our website at www.ucalgary.ca/bmb/ for more information about the Department.

University of Calgary

Department of Biological Sciences

Correspondent: Vanina Zaremberg

The Biological Sciences Department at the University of Calgary is currently organized in four clusters based on general research and teaching interests. They include Biochemistry, Microbiology, Cell Development & Physiology and Ecology & Evolutionary Biology. During this year **Elmar Prenner** and **Ken Ng** have been chairs of the Biochemistry cluster and Biochemistry program respectively.

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 elected into the Royal Society of Canada as a Fellow in 2012 and graduated five graduate students over the last half year.

Raymond J. Turner spent a 6-month sabbatical in Italy, primarily working out of the University of Bologna. His work centered on one of his interests that of microbe-metal interactions. His work in Italy focused on water bioremediation strategies but he also spent time exploring

the use of various metal resistant bacteria for metal nanoparticle production. Raymond also presented a number of seminars at a variety of universities in Italy during his visit. Through these interactions he was able to develop close relationships with groups in Bologna, Verona and Tuscia where he is now co-supervising graduate students on several related projects.

Greg Moorhead has renewed his NSERC Discovery Grant and also received funding from NSERC Discovery Accelerator Supplements Program. During this year three graduate students obtained their degrees (Glen Uhrig, Dylan Silver and David Lloyd). Glen was selected as the winner of CSPB's 2012 Ibrahim award (best student paper [national award]) and was awarded the Dean's prize for best PhD student in the Biological Sciences Department in 2012. Dylan won best poster at CSPB's 2012.

Elmar Prenner continued his teaching in Nanoscience minor and in the Biochemistry program. His basic science research focuses on lipid metal interactions, antimicrobial peptides, lipid based anticancer drugs and nanoparticle based drug delivery. His applied research deals with biosurfactants for enhanced oil release and the design of fluorescence instruments.

Teaching undergraduates continues to be one of our priorities and we take great pride in our program. The following undergraduate students were recognized for their excellent research work as honour or independent project students during our annual student conference:

Biochemistry

Andrew Cottle (**Ken Ng**), Thomas Clements (**Prenner**) - best presentation

Jae Kang (**Vogel**), Heather Smart (**Zaremberg**) - honourable mention

Cellular, Molecular and Microbial Biology

Erin Bell (**Shemanko**), Jonathan Chin (**Wong**) - best presentation

Kathleen Degner, Barry Congdon Jr. (**Cobb**) - honourable mention

Dalhousie University

Department of Biochemistry & Molecular Biology

Correspondent: Stephen L. Bearne

Dr. Petra Kienesberger

The Department of Biochemistry & Molecular Biology at Dalhousie University welcomed the arrival of new faculty member **Petra Kienesberger**, who joined us in April 2013 as part of the cardiovascular research team at Dalhousie Medicine New Brunswick in Saint John N.B. Petra will strengthen and expand our research in metabolic biochemistry, lysophospholipid-related cell signaling, and lipotoxicity.

Over the past year, a number of faculty members were successful in securing grant support despite the rather dismal success rates for national competitions. In addition, the achievements of a few members of the department were recognized through various awards. In 2013, former department head **Michael Gray** (Professor Emeritus) was elected to Fellowship in the American Academy of Microbiology. The Academy, the honorific leadership group within the American Society for Microbiology, recognizes excellence, originality, and creativity in the microbiological sciences. Several years ago, Mike established the Schnare-Spencer Prize in honor of two long-time research associates in his lab. This annual award recognizes a staff member or trainee for technical excellence, innovation, and willingness to assist others in the Department. The 2012 recipient of the award was **Robert Zwicker**. **Harold Cook**, who retired from Dalhousie as Dean of Medicine in 2010 and subsequently became Acting Dean and Principal of Dalhousie's new Faculty of Agriculture, retires from that appointment in 2013. **Christopher McMaster** was awarded the 2012 Innovation Award at the 10th Annual Discovery Awards for Science and Technology in recognition of DeNovaMed Inc., an antibiotic drug discovery company founded he co-founded with **David Byers** and Don Weaver. **Andrew**

Roger, who holds a Canada Research Chair (Tier I) in Comparative Genomics and Evolutionary Bioinformatics, was elected to Fellowship in the Royal Society of Canada in recognition of his significant contributions to our thinking about early evolution and eukaryotic diversity. **Paul Briggs**, the Senior Instructor in the Department, was the recipient of the 2012 Dalhousie University Faculty Advisor Award. This award recognizes the important role that Paul plays in counseling our students. **Richard Singer** was inducted into the Nova Scotia Health Research Foundation Decade Club for his longstanding role as Chair of the Biomedical Peer Review Committee and a member of the Board of Directors of the NSHRF. Finally, on July 1, 2012, **Stephen Bearne** was appointed to a five-year term as Head of the Department of Biochemistry & Molecular Biology, replacing **David Byers** who stepped down after providing five years of strong leadership.

We continue to celebrate the success of our students and postdoctoral fellows, many of whom are supported by national and local salary awards. Most notable are the recent recipients of the departmental Patrick Prize for outstanding research by a recent Ph.D. graduate (**Ryan Gawryluk** in 2011 and **David Langelaan** in 2012), and of the Doug Hogue Award for persistence and dedication to research: **Courtney Stairs** in 2012 and **Barry Kennedy** in 2013.

Hogue Award 2012 – Left to right Jasper Hogue, Zoe Hogue, Calla Hogue, Courtney Stairs (award recipient), Dr. Andrew Roger, and Dr. Stephen Bearne

Our alumni (and anyone else interested) are invited to find out about the latest news and events of the Department of Biochemistry & Molecular Biology at: www.biochem.dal.ca/

University of Guelph

Department of Molecular and Cellular Biology

Correspondent: Frances Sharom

Faculty news

Dr. John Dawson (left) accepts his UGFA Distinguished Professorial Teaching Award from UGFA President Ed Carter.

Dr. John Dawson was the proud recipient of a Distinguished Professorial Teaching Award, presented by the University of Guelph Faculty Association (UGFA) at a reception on October 25 2012. The annual awards were created in 1984, and recognize excellence in teaching and learning, including classroom instruction, course design, curriculum development and innovative teaching methods. John was cited for his outstanding work in teaching and curriculum development for the course "Introduction to Biochemistry", which is offered to over 1700 second year students each year.

Dr. Lucy Mutharia was honoured with a College of Biological Science (CBS) Teaching Award of Excellence in a ceremony held on November 7 2012. Lucy was cited for her passion for microbiology, in both class and lab settings, and for her important leadership in, and contributions to, the development of the microbiology program curriculum through two new introductory courses. Her advocacy for experiential and

Dr. Lucy Mutharia receives her CBS Teaching Award of Excellence

hands-on learning, and commitment to student success through involvement in biosafety and outreach, as well as her contributions to education workshops and conferences were also recognized.


Dr. Jaideep Mathur launches the Cellscapes exhibition

On 19 November 2012, **Dr. Jaideep Mathur** and his lab team opened the "Cellscapes" exhibition, which was designed to captivate the mind and fuel the imagination, while educating viewers about the living plant cell. Art and science came together in this symphony of light, colour and form, which was exhibited in the Atrium of the Science Complex, before moving to the campus McLaughlin Library for the week of November 20-25. Inaugurated by Dr. Mike Emes, Dean of the College of Biological Science, and Dr. Donald Bruce, Dean of the College of Arts, the nearly 100 stunningly beautiful images and time lapse movies provide a colourful view of plant cells and their interior. The images were obtained through state-of-the-art microscopy techniques using scintillating "living colours" at the Laboratory of Plant Development and Interactions at the University of Guelph, and a number have been featured as cover pages on prestigious international scientific journals. Colour prints of the images are available in various sizes suitable for framing; to download the image catalogue, see www.uoguelph.ca/~jmathur/pdf/Cellscapes.pdf


Some of the images on display in Cellscapes

Dr. Emma Allen-Vercoe was featured in an interview with Time magazine on 27 August 2012 (available at http://science.time.com/2012/08/27/how-gut-bugs-make-you-sick-or-well/), on the involvement of the microbiome in diseases such as autism. Allen-Vercoe has become an expert in culturing hard-to-grow species of bacteria, and she co-authored a 2012 paper about a global project to identify and catalogue the genetic material of all microbes on and in the human body. *C. bolteae*, a relative of *C. difficile*, often shows up in higher numbers in the GI tracts of autistic children than in those of healthy kids, and Emma is looking more closely at these microbes and the links between autism, diet and gut health. The Allen-Vercoe lab is also receiving a lot of attention for their development of a new treatment for *C. difficile* infection (CDI). **CDI** is an infection of growing concern in hospitals, causing pain and serious diarrhea in affected patients. *C. difficile* usually infects patients who have recently had a course of antibiotics, stripping them of their normal gut microflora and allowing space for the pathogen to flourish. Ironically, the current treatment for CDI is a further course of antibiotics to target the *C. difficile*. Unfortunately, it can be very difficult to eradicate in this way, and some patients end up with a recurrent infection that they are unable to clear, leaving them with no option but to take long-term doses of expensive antibiotics. Fecal transplants offer a potential solution to this infection, by restoring normal flora and displacing the pathogen; however these carry a fairly high degree of risk themselves, due to the potential presence of unknown pathogens in donor stool, and as well the procedure is messy and unpleasant. Together with their clinical collaborators at Queen's University/Kingston General Hospital, the Allen-Vercoe lab has developed a defined multi-species probiotic, a synthetic stool treatment called "RePOOPulate", from 33 strains of bacteria found in healthy intestines. This probiotic aims to overcome the problems of fecal transplants, while still offering a potential cure for CDI. A recent Medical Post article described their work (http://www.uoguelph.ca/mcb/pdfdocs2012/MedicalPost-rePOOPulate.pdf), and a piece on CTV's The National reported the successful use of RePOOPulate to treat a severely ill CDI patient (http://www.ctvnews.ca/health/fake-feces-shows-promise-as-treatment-for-c-difficile-1.1122319).

Department reproduction

The year 2012 saw a bumper crop of potential future scientists produced by department faculty and staff. On 18 March 2012, **Dr. Cezar Khursigara** and his wife Deborah welcomed their second child into the world, a daughter Matilda Marie Khursigara, at a very healthy weight of 9 lb. Dr. Nina Jones and her husband Todd announced the birth of their first child, Callum Rhys Jones Porter, on July 6 2012. Staff member **Dr. Amanda van der Vinne** and her husband David are the proud parents of their second child, a daughter Mya Nicole van der Vinne, born April 27 2012 weighing 6 lbs 10 oz.

Retirements

Dr. John Greenwood, **Dr. Reggie Lo** and **Dr. Frances Sharom** formally retired from the University of Guelph at the end of 2012, with 90 years of university service among them. A group retirement party was held at the University Club in early January 2013, attended by many colleagues, friends, and both current and former students, post-docs and lab staff of the three retirees.

From left to right, CBS Dean Mike Emes, Reggie Lo, Frances Sharom, John Greenwood, and department Chair Chris Whitfield.

The three retirees cut the cake!

John Greenwood received B.Sc and M.Sc. degrees from McMaster University, and then completed a Ph.D. at the University of Calgary with Dr. Derek Bewley as advisor. Research for this degree combined microscopy and physiology to study aspects of seed biology. Following this, John received an NSERC Post-doctoral Fellowship that he held at U.C. San Diego with Dr. Maarten Chrispeels, an eminent plant physiologist. In 1985, John received an NSERC University Research Fellowship (URF) which he held in the Botany Department, where he was subsequently appointed as an Assistant Professor. John's research program continued his interest in seed biology and aspects of storage compounds in plants and, more recently, involved programmed cell death in plants, utilizing his expertise in microscopy and molecular biology, Over the years, John collaborated with scientists in Canada, Germany, and the U.S.A., and is recognized internationally for his skills in microscopy. On the teaching front, John taught Life Strategies of Plants, Plant Anatomy, introductory courses in Botany and Biology, as well as various graduate courses, and he supervised many fourth year research project students.

Reggie Lo arrived in the Microbiology Department at the University of Guelph in the summer of 1982 from the University of Alberta, where he obtained B.Sc. and Ph.D. degrees in genetics. During his time at Guelph, Reggie published extensively on the molecular biology of *Pasteurella haemolytica* (later named *Mannheimia hemolytica*) even having a vanity licence plate named after it. He focussed on its toxins and potential application as vaccines, and authored a book chapter on this species in "Prokaryotes". Reggie also helped to found the International Pasteurellaceae Society, and was involved in organizing some of their meetings. He engaged in a long, productive and complementary collaboration with **Dr. Pat Shewen** in Veterinary Microbiology and Immunology (now Pathobiology) leading to a vaccine marketed as Presponse™. Reggie did the molecular work and Pat worked with the cows. Bacterial genetics courses were Reggie's teaching domain, and this was followed by a long stretch as Graduate officer for the Microbiology department, then the new Molecular and Cellular Biology department. Reggie leads a well balanced life style, playing piano after being self taught, and even giving performances at the local Kiwanis Music festival. He also participates in

weekly basketball games, raises fish, and bikes, even when it is snowing. Hawaii is one of Reggie's favourite locations, and he plans to spend more time there with his family in retirement.

Frances Sharom began her life in Canada at the University of Guelph, where she obtained a B.Sc. in Chemistry, followed by a Ph.D. in Biochemistry at the University of Western Ontario, supervised by Chris Grant. She was a post-doctoral fellow in Alan Mellor's lab at Guelph when she won an NSERC URF, and was subsequently appointed an Assistant Professor in Chemistry and Biochemistry. Frances is one of the world's experts on the structure and function of P-glycoprotein, the multidrug transporter important in pharmacology and cancer research. Her research interests also include many aspects of membrane lipid and membrane protein biochemistry, such as ganglioside biochemistry, lipid rafts, membrane protein purification, and GPI-anchored proteins. Her research group applies a wide variety of biophysical techniques, including fluorescence and NMR spectroscopy, differential scanning calorimetry, and circular dichroism to these systems, which has led to world-wide collaborations. In 2003, Frances became a Tier 1 Canada Research Chair in Membrane Protein Biology. She has graduated more than 30 M.Sc. and Ph.D. students as well as training numerous post-docs, and her lab group has published over 120 research articles. Frances has won several teaching awards, including an OCUFA award in 1992, a Lieutenant-Governor's Award in 1993, and UGFA awards in 1992 and 2002. She has also been associated for many years with the Canadian Society for Molecular Biosciences (CSMB, formerly the CSBMCB), as Vice-President, President, Councillor, Bulletin Editor, and conference co-organizer.

In 2004, the biological science departments at Guelph were reorganized, and John (Botany), Reggie (Microbiology) and Frances (Chemistry and Biochemistry) were brought together in the new Department of Molecular and Cellular Biology.

Sabbatical leave visitors and visiting scientists

Dr. Jose Casaretto, an Associate Professor from Universidad de Talca in Chile and researcher at the Institute for Plant Biology and Biotechnology, has been collaborating with **Dr. Steven Rothstein's** group since June 2011 on a project related to regulation of plant metabolism in crops grown under different conditions. The Rothstein lab also hosted Chao Yu, who was a visiting graduate student from the Chinese Academy of Sciences Institute of Plant Protection.

Michael Norris, a Ph.D. student at the University of Toronto with Dr. Theo Moraes (Hospital for Sick Children), visited the lab of **Dr. Peter Krell**. Drs. Krell and Moraes are co-applicants on a collaborative grant from the Ontario Thoracic Society (Ontario Lung Association), which investigates the respiratory syncytial virus (RSV) and its possible link to childhood asthma. Michael is interested in enhancing the immune response to RSV by including not only one of the major viral proteins M2, but also an immune enhancer, T cell co-stimulatory molecule, 4-1BBL to enhance the number of RSV-specific CD8 cells thus increasing the capacity to fight off the infection. This novel vaccine is being developed using the Krell lab's baculovirus expression system. The hope is that it will reduce the childhood incidence of RSV infection, leading to lower levels of asthma.

Dr. Anthony Clarke's lab hosted **Ana Maranha Tiago**, a visiting doctoral student from Coimbra University in Portugal, where her advisor is Dr. Nuno Empadinhas, Department of Biochemistry. Coimbra University was founded in 1290, and is now home to 10,000 undergraduates, 11,500 master's, and 2,300 doctoral students. Ana visited the Clarke lab twice, both for 3 month stints to develop an assay for the transfer of octanoate from octanyl-CoA to a sugar acceptor that comprises the methylglucose lipopolysaccharides of mycobacteria.

Marc Zuckermann, an M.Sc. graduate from the University of Osnabrück in Germany, visited the research lab of **Dr. Ray Lu** for 10 months, before returning to Germany to start his Ph.D. at the University of Heidelberg. He worked on TAP (tandem affinity purification) and embarked on isolation of the LRF protein complex; the project is now being continued by an exchange student from Austria, **Karin Olek**.

Carla Coelho, a Ph.D. student from Lavras University in Minas Gerais, Brazil, visited the lab of **Dr. Joseph Colasanti**. Carla obtained a prestigious scholarship (CAPES), which allowed her to spend one year in a lab outside of Brazil. While in Guelph, Carla analysed and isolated several genes from sugar cane that control the transition to flowering in this important crop plant. These findings will form the core of her doctoral studies in Lavras, which she will complete by the end of 2013.

Laurie Colson, a Masters student in the Faculty of Pharmacy at L'Université Paris Descartes (Paris, France), visited the lab of **Dr. Joseph Lam** from January to August 2012. This was part of the mandatory requirement that graduate students at this institution complete an internship of up to 8 months in a foreign laboratory. Her project involved the construction of chromosomal knockout mutants in five genes, and characterization of their role in the biosynthesis of a particular form of the common polysaccharide antigen (CPA) in *Pseudomonas aeruginosa*. Laurie was successful in making 4 of the 5 gene knockouts, and she then conducted complementation assays to determine the significance of these genes in the synthesis of CPA. Laurie presented her results as a poster in Summer Student Symposium in August 2012 before returning to her home institution to complete her graduate studies.

Dr. Jean Gerrath, Professor Emeritus at the University of Northern Iowa in Cedar Falls, Iowa, is a Visiting Professor for 3 years with **Dr. Usher Posluszny**, Professor Emeritus at the University of Guelph. They are currently working together on a book which is the culmination of thirty years of collaboration; "Taming the North American Grape: A Survey of the Wild and Cultivated Members of the Vitaceae and their Vegetative and Floral Biology". Jean is also beginning some collaborative transcriptome work in the Vitaceae with **Dr. Annette Nassuth**, based on sequences that she obtained via an NSF grant with colleagues at the Smithsonian Institution.

University of Lethbridge

Molecular Biosciences

Correspondent: Ute Koth

Canada Wide Science Fair 2013

The University of Lethbridge is excited to welcome the country's top young scientists to campus, May 11-18, as the 52nd annual Canada-Wide Science Fair (CWSF) 2013 comes to the city. Approximately 1,100 students, chaperones, judges, sponsors and dignitaries are attending CWSF 2013, an event that will award close to $1 million in cash, prizes and scholarships to the best students. Featuring the top 400 science projects by students from Grades 7 to 12 in the country, CWSF 2013 is a showcase of Canada's top young scientific minds. University of Lethbridge biological sciences researcher, **Dr. Roy Golsteyn**, has volunteered to be the Chief Judge "As Canada's Research University of the Year 2012 (undergraduate category), we are uniquely suited to host this event and could not be more excited to open our doors to these bright young scientists," says University of Lethbridge President, Dr. Mike Mahon. The Discovery Day is an opportunity for the finalists and delegates attending the CWSF to learn about the exciting multidisciplinary research activities at the U of L. Participants were able to choose two activities from a total of 25 being offered that showcase everything from physics, chemistry and biochemistry to new media, fine arts and neuroscience.

Students of the Canada Wide Science Fair participate in a hands-on activity during the Discovery Day

New High school iGEM group wins international award

A group of Lethbridge and area high school students who want to take NASA technology and use it to help reduce the affects of Type 1 Diabetes recently came away from an international competition with an award for their research presentation. Six students, members of the University of Lethbridge 36-person High School iGEM (International Genetically-engineered Machines) team made their first trip to the Indianapolis, IN contest as the only Canadian contingent, and presented their take on how to use an innovative, implantable capsule (developed by NASA to release medication in space) to manage the release of insulin for people with Type 1 Diabetes. The team is supervised by **Dr. Hans-Joachim Wieden** from the Department of Chemistry and Biochemistry. The group plans to engineer a bacteria that will secrete insulin in response to a person's glucose levels, then house it in the NASA biocapsule (so it is contained and not flowing freely in the bloodstream) where it will safely dispense insulin and could reduce the need for the continuous monitoring, injections and other challenges currently experienced by the hundreds of millions of people worldwide with diabetes. "When the iGEM competition expanded to include high school students, the U of L saw an opportunity to follow suit and this year 36 students participated in the program," said Dr. Andy Hakin, the U of L's Provost and Vice President, Academic. "Not only does this provide valuable hands-on learning opportunities, but it also augments the existing Alberta science curriculum. We are happy to be able to extend this world-class program into local high schools, exposing younger students to the unique opportunities available by pursuing a science education."

The University of Lethbridge high school iGEM team – the first of its kind in Canada

New book "A Life Scientist's Guide to Physical Chemistry"

Cambridge University Press has just published **Dr. Marc Roussel**'s book entitled "A Life Scientist's Guide to Physical Chemistry", which is based on his experience teaching physical chemistry to a mixed audience of chemists and biochemists at the University of Lethbridge over the last decade and a half. There are a lot of examples, many of which are of direct biological relevance. Dr. Marc Roussel says, "I've tried to discuss a few surprising applications for the life science students, such as the physical chemistry behind the wood frog's overwintering in the frozen state, and the physico-chemical evidence for the remarkable longevity of the bowhead whale." The book contains a large number of exercises (350+), many based on biological applications. The exercises aren't confined to the ends of chapters. Rather, Dr. Marc Roussel says, "I've put many of them within the chapters to encourage the students to study continuously." There's also a selection of end-of-term problems at the very end of the book that is intended to help prepare students for a final exam.

Alberta RNA Research and Training Institute – chair search

Only one year after its inception, the Alberta RNA Research and Training Institute is looking for future members as the search for two new prestigious research chairs is ongoing. For the **Alberta Innovates Health Solutions (AIHS) Translational Health Chair in the area of RNA in Health and Disease**, the candidate should have demonstrated expertise in the study of **structure and function of RNA-based systems** in vivo and/or in vitro using rational-design approaches to the biological systems under study **(synthetic biology), biochemical, biophysical or molecular biology approaches**, and bring a special focus on applications in chronic health conditions such as cancer, inherited diseases or acquired chronic conditions including but not limited to viral infections like HIV and hepatitis.

Furthermore, there is a position for a **Campus Alberta Innovates Program Chair in Synthetic Biology and RNA-based Systems**. Along with a special focus on the energy sector, candidates must bring demonstrated expertise in the engineering of biological systems **(synthetic biology) and the study of structure and/or function of RNA-based**

systems, using in vivo and/or in vitro approaches, having made major impacts in their fields of research. Candidates will be expected to play a lead role in contributing to the University's capacity in synthetic biology and RNA Research.

For more details, visit the following webpage: **http://www.uleth.ca/artsci/node/28016**

RiboWest Conference 2012

From June 10-13th 2012, the University of Lethbridge and the Alberta RNA Research and Training Institute hosted the 8th Annual RiboWest Conference 2012, taking place in southern Alberta every second year. This RiboWest Conference again attracted more than 100 RNA researchers from Canada and the northwest of the USA, who attend the Meeting to "share (their) work with the RNA community, to receive feedback and connect with like-minded individuals".

The keynote speaker at the meeting this year was Dr. Marina Rodnina from the Max-Planck Institute in Göttingen, Germany, talking in a well-attended public presentation about her work on ribosome-dependent protein synthesis. In addition, Dr. Raymund Wellinger (Université de Sherbrooke, Quebec) and Dr. Wolfgang Wintermeyer (Max-Planck Institute Göttingen, Germany) participated as invited speakers. Dr. Raymund Wellinger represented the RiboClub in Sherbrooke, Quebec continuing the tradition of strengthening the inter-Canadian network of RNA investigators. The participants of the RiboWest Conference 2012 shared their RNA research through more oral and poster presentations than ever before - 28 oral presentations held mostly by graduate and even some undergraduate students as well as more than 40 posters. But not only was the number of presentations impressive this year, but with the words of one participant: "The oral presentations were of extremely high quality this year; all talks were very interesting."

New collaborative cancer research

Two University of Lethbridge researchers are teaming up to better understand unintended side effects associated with radiation treatment of cancer cells and the difference between female and male patients. **Dr. Bryan Kolb**, a neuroscience researcher at the U of L's Canadian Centre for Behavioual Neuroscience (CCBN) and **Dr. Olga Kovalchuk**, a Biological Sciences researcher who specializes in researching the affects of radiation on cancer cells and nearby cells, are collectively putting their lab teams on the project, which is being funded by the Canadian Institutes of Health Research (CIHR). The studies, which may lead to the development of male or female-specific treatments that improve the quality of life for all cancer patients, is attempting to solve problems yet to be fully explored -- why does radiation delivered in one part of your body to help eliminate cancer cells affect your memory, balance and other behaviours normally managed by your brain -- and are those effects different in men and women? Dr. Olga Kovalchuk is also the recent recipient of a new CIHR Chair award in Gender, Work and Health. Her research project is dedicated to examining whether men and women

Participants of the 8th annual RiboWest Conference 2012 at the University of Lethbridge

are affected differently in nuclear work environments, which includes the nuclear power industry, healthcare and research departments.

CIHR Synapse Mentoring Award

Dr. Ute Kothe, an Assistant Professor in Biochemistry at the University of Lethbridge, has received the 2012 CIHR Synapse Mentorship Award – Individual Researcher. The award, which is worth $5,000, is one of three handed out nationally -- and the U of L's first -- and recognizes the efforts of a health researcher who has made exceptional efforts to promote health research among Canada's students. Dr. Kothe established a Let's Talk Science Program at the University of Lethbridge in collaboration with the national Let's Talk Science organization. This program promotes science literacy among Canadian high school students, provides hands-on science workshops and complements established school curriculum. The University Let's Talk Science Team focuses in particular on science outreach for high school students and has reached over 550 students in 2010-11 alone. "Dr. Kothe deserves this Synapse Mentorship Award for her dedication to helping Canadian students both understand and appreciate the value of science. This may ultimately help them choose career paths that will make them scientific leaders of tomorrow." says Dr. Jane Aubin, CIHR's Chief Scientific Officer and Vice President of Research and Knowledge Translation Portfolio.

University of Manitoba

Department of Biochemistry and Medical Genetics

Correspondent: Klaus Wrogemann

Trevor Pemberton

A somewhat random collection of news items from the Department of Biochemistry & Medical Genetics:

Trevor Pemberton joined the Department as Assistant Professor, coming from Noah Rosenberg's Lab at Stanford University. He studies the genetic etiology of Mendelian and complex traits, how human population history and cultural practices influence patterns of genetic variation, and the ways in which these patterns can be harnessed to advance the discovery of genes that underlie human disease. Trevor started out by setting up an impressive website for his lab (http://pembertonlab.med.umanitoba.ca).

Michelle XiaoQing Liu, M.D. (Medical College of Jiamusi University), M.S. (Johns Hopkins Bloomberg School of Public Health) is another Assistant Professor in the Department. She is interested in applying efficient statistical methods to the gene mapping of monogenic and complex traits/disorders, especially, epigenetic studies using twins and the identity-by-descent mapping method.

Cheryl Rockman-Greenberg

Cheryl Rockman-Greenberg continues as a highly prolific clinical geneticist in our Department but is also Head of the Department of Pediatrics & Child Health. She has been named as one of Canada's 100 Most Powerful Women: Top 100 award 2012 by WXN (The Women's Executive Network). Cheryl also received the "Rarities" award in the Category of Health Professional Leadership from the Canadian Organization of Rare Disorders (CORD), a selection made by lay persons and professionals dealing with such patients.

Michael Mowat

Michael R. A. Mowat, a Professor in the Department and in the Manitoba Institute of Cell Biology received an alumni award from his alma mater, the University of Alberta, and was cited for many achievements, not the least of them his discovery that p53 is a tumor suppressor gene, published in Nature in 1985. It has made p53 the most studied gene in human diseases.

Albert E. Chudley, Professor and Medical Director of the Program in Genetics and Metabolism, was part of a FORGE (Finding Of Rare disease GEnes Canada) team

effort to identify the cause for the disease that carries his name, the Chudley-McCullough Syndrome, a hereditary disease of deafness and brain malformation. Mutations were found in *GPSM2*, the G protein-signaling modulator 2 gene. **Teresa Zelinski** is the senior author of the study published in AJHG. It also included **Barbara Triggs-Raine**, and **Aziz Mhanni.**

Clinical Chemists have their academic appointments in our Department as well. **Andrew R. MacRae**, is an Associate Professor. Last summer he received the Canadian Society for Clinical Chemistry Award for Outstanding Contribution to Clinical Chemistry. It is the most prestigious award in the profession of Clinical Biochemistry in Canada.

McGill University

Department of Biochemistry

Correspondent: Kalle Gehring

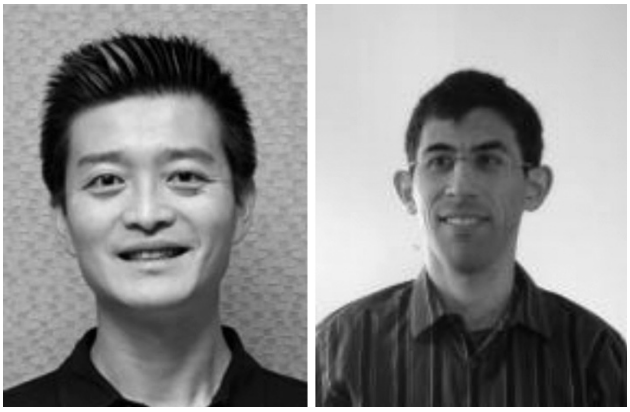
There have been substantial changes at McGill's Department of Biochemistry; one of the most recent is the appointment of **Albert Berghuis** as Interim Department Chair. Albert took the reigns in May 2013, replacing **David Y. Thomas** who served for 13 years as the Department Head. David's term was truly transformative in terms of both resources and people. David led a seventy million dollar CFI application that doubled the Department's research space with the opening of the multi-themed Life Science Complex in 2008. Along the way, David forged a collaborative spirit that continues to stimulate life science research at McGill.

David's term also saw thirteen new hires as the Biochemistry Department renewed itself and grew in size. From his first hire – incidentally, Albert Berghuis – to the most recent, David applied the same style of dialog, pragmatism and, promotion of excellence that served so well in the establishment of the Life Science Complex. He had an open door policy and acted as a mentor to many students, staff and faculty members. Whether it was in pursuit of academic excellence for the Department or individual justice for a student, David was willing to take a stand for the right thing.

While David remains at McGill, the Biochemistry Department celebrates the career of another of its members as **Maria Zannis-Hadjopoulos** retires this spring. Maria led a productive and rewarding career of over 30 years as McGill faculty. Her research on mammalian DNA origins of replication and replication factors produced over 100 peer-reviewed publications. A retirement party was held in May, bringing together past members of her lab and the department to celebrate Maria's accomplishments and wish her the best for the future.

Maria Zannis-Hadjopoulos retirement dinner, May 2013. Left-to-right, sitting: Michel Tremblay, Peter Siegel, David Thomas, Maria Zannis-Hadjopoulos, Albert Berghuis, Nahum Sonenberg. Standing: Jose Teodoro, Maxime Bouchard, Vincent Giguère, Rhoda Blostein, Nicole Beauchemin, Thomas Duchaine, Martin Schmeing, Sid Huang, Dionysis Hadjopoulos (Maria's husband), John Silvius, Bob MacKenzie, Bhushan Nagar, Josée Dostie, Alain Nepveu, Jason Young, Walter Mushynski, Kalle Gehring, Xiang Jiao Yang, Jerry Pelletier

Two new faculty members, **Sidong Huang** and **Uri David Akavia** are joining the Department this year. Sid arrived in January 2013 and uses functional genomic tools to study cancer-relevant pathways and to guide targeted cancer therapy. Uri David is arriving in August to develop computational biology algorithms to understand cancer and cancer progression.



Sidong Huan and Uri David Akavia

The past year has also marked significant milestones for several faculty members. **Thomas Duchaine**, **Jose Teodoro** and **Josée Dostie** have all been promoted to Associate Professor, and **Imed Gallouzi** has been promoted to Full Professor. **Edward Fon** of the Montreal Neurological Institute and **Gergely Lukacs** from the McGill Physiology Department joined the Department as Associate members and **Philip Awadalla** from Ste-Justine Hospital joined as an Adjunct member.

Among honours and awards, **Jason Young** and **Albert Berghuis** renewed their Canada Research Chairs while **Jerry Pelletier** was appointed a James McGill Professor. **Nahum Sonenberg** received the Lewis S. Rosenstiel Award for Distinguished Work in Basic Medical Science, the Howard Hughes Medical Institute International Scholar Award, and was made a Fellow of the American Association for the Advancement of Science. **Michel Tremblay** was awarded the Prix Michel Sarrazin du Club de Recherche Clinique du Quebec and the Canadian Cancer Society's 2012 Robert L. Noble Award. Past Chairs **David Thomas, Phil Branton,** and adjunct **Youla Tsantrizos** received Queen Elizabeth II Diamond Jubilee Medals.

Several notable research highlights are a paper by the **Sonenberg** group that dysregulation of eIF4E translational control can trigger autism-related phenotypes (Nature 2013), and a paper by **Jerry Pelletier** and collaborators on a new tumour suppressor network that regulates apoptosis (Nature 2012). The **Gehring** and **Fon** laboratories reported the structure Parkin, a protein involved in familial forms of Parkinson's disease (Science 2013) and **Bhushan Nagar**'s lab discovered how the innate immune response recognizes viral RNA (Nature 2013). **Kalle Gehring** led a funded $12M CFI project "*Structural Biology at the Crossroads of Biology and Medicine*" for new equipment and renovations at McGill and the University of Montreal.

McMaster University

Department of Biochemistry and Biomedical Sciences

Correspondent: Alba Guarné

For us, 2012 was a year of faculty renewal and exciting new projects. We continued our efforts to strengthen the stem cell research and metabolism groups. **Karun Singh** and **Eva Szabo** joined the Stem Cell Cancer Research Institute, and **Deborah Sloboda** (joint with Obstetrics and Gynecology) and **Jonathan Schertzer** came to strengthen our core metabolism group.


Eva Szabo


Karun Singh


Deborah Sloboda


Jonathan Schertzer

On the flip side of the coin, three of our senior members left to advance their career at other Universities. **John Capone** "retired" from his position as Dean of Science and it is now the Vice-President (Research) at Western University. **David Andrews** moved to Sunnybrook Research Institute, where he is now the Director of Biological Sciences and Professor in the Biochemistry Department. **Justin Nodwell**, after 15 years commuting between Toronto and Hamilton, returned to his roots as the new Chair of the Biochemistry Department, effective March 2013. John, David and Justin have made tremendous contributions to the Department and, while we are sad to see them leave, we know that they will "rock" at their new posts.


John Capone


David Andrews


Justin Nodwell

Our faculty continued to rake in accolades for their work. **Gerhard Gerber**, now Professor Emeritus and former Chair of the Department, was inducted into the Faculty of Health Sciences Community of distinction for his innovative scholarship and promotion of research at McMaster University. **Gerry Wright,** Professor and Director of the Michael G. DeGroote Institute for Infectious Diseases research, was elected a fellow of the Royal Society of Canada. **Eric Brown**, Professor and Chair, was the recipient of the Canadian Society of Microbiologists (CSM) Murray Award for career achievement and **Brian Coombes** won the CSM Fisher Scientific Award for early career achievement. **Jonathan Schertzer** received the Canadian Diabetes Association Scholar Award. **Deborah Sloboda** and **Nathan Magarvey** were awarded Canada Research Chairs in Perinatal Programming and Chemical Biology and Natural Products, respectively. **Felicia Vulcu** was one of the first recipients of the MSU Pedagogical Innovation Award that recognizes professors who are innovative with their teaching and assessment methods. **Deborah Sloboda** and **Hendrik Poinar** (associate member of the Department) received CFI awards from the Leaders Opportunity Fund. The structural biology group was out in full-force at tri-council funding competitions last year. **Joaquin Ortega**, **Alba Guarné** and **Giuseppe Melacini** renewed their NSERC and CIHR operating grants, and **Alba Guarné** received an NSERC Accelerator Award, the second ever awarded to a member of our Department.

There was also a flurry of activity at the undergraduate and graduate levels. We piloted a new first year course entitled "Current Research in Biochemistry and Biomedical Sciences" to introduce first year students to concepts in biomedical sciences, while exploring cutting edge discovery research. The course attracted a total of more than 150 students from across campus, including Business, Engineering, Health Sciences, Science and Social Sciences. Each week a different faculty member from our Department leads the class through an exploration of their research area. At the conclusion of the course this year, one of the students offered the following comment: *"I wanted to say that I honestly have really enjoyed this course. I told some of my friends at other universities (also in the sciences) about this course and they were very jealous. For me, it is definitely very different learning about research that took place decades ago (in most regular classes) and learning about research that is happening now, answering questions that do not have answers yet."*

Michelle MacDonald, Undergraduate Coordinator and Associate Chair, and **Eric Brown**, Professor and Chair, together with a team composed of faculty members from Faculties of Health Sciences and Business, developed a new undergraduate biochemistry program at the interface of discovery and business that will train the next generation of business entrepreneurs. Under the leadership of our Graduate Coordinator and Associate Chair, **Brian Coombes**, our graduate program underwent its 7-year Academic Programs Review under the new Quality Assurance Process (IQAP). After a comprehensive site visit, the review team concluded: "the graduate program in Biochemistry is a flagship program for McMaster and one that should be emulated across the country". We view this comment as a testament to the high caliber of the program, the dedication of our staff and the commitment of our students, as well as the tremendous energy that our graduate students bring to discovery research. Indeed, our trainees continued to make us proud last year by securing competitive research awards and publishing seminal papers in top scientific journals. Just as an example, trainees in the laboratories of **David Andrews** and **Mick Bhatia** published seminal papers in Cell on apoptosis at subcellular membranes and drugs that selectively target cancer stem cells. Over 40% of our graduate students were funded by competitive scholarships in 2011/2012 and biochemistry Student Chad Johnston (**Magarvey** lab) won the inaugural Michael Kamin Hart Memorial scholarship. Monica Pillon (**Guarné** lab) and Kyle Salci (**Bhatia** lab) won the top Karl Freeman awards in the PhD and MSc categories for their presentations to our graduate seminar series. Tomas Gverzdys (**Nodwell** lab) earned a distinguished service award from the Graduate Student Association.

The Guarné (centre), Brown (left) and Burrows (right) laboratories take the podium at the Biochemistry Olympics.

Of course, it was not all work. The **Guarné**, **Brown** and **Burrows** laboratories took the podium at the Biochemistry Olympics celebrated during our annual BBS picnic, the hidden musical talents in Biochemistry surfaced once again at the IIDR Holiday Reception and the Centre for Microbial Chemical Biology (CMCB) took home the first prize for our first Christmas Ornament Competition.

Andrew King (Wright lab) and Hendrik Poinar rocking the stage at the IIDR Holiday Party

Christmas ornament from the Centre for Microbial Chemical Biology (CMCB)

Université de Montréal

Département de biochimie

Correspondent : Christian Baron

Appointments and promotions

Benjamin Haibe-Kains

In 2012 a new Assistant Professor joined the Biochemistry Department. **Benjamin Haibe-Kains** established his Bioinformatics and computational genomics laboratory at the Université de Montréal-affiliated research institute IRCM (Institut de recherches cliniques de Montréal). **Gerardro Ferbeyre** was promoted to Full Professor in 2012 and **Alain Moreau**, Professor in the Departments of Stomatology and Biochemistry, was selected as scientific director of the Ste.-Justine Children's hospital research institute.

Operating and infrastructure funds

Despite the limited amount of funding available at last years **CFI** competition, the joint Leading Edge Fund application with McGill University "Structural Biology at the Crossroads of Biology and Medicine" piloted by Kalle Gehring (McGill Biochemistry) and Pascale Legault (UdeM Biochemistry) was successful. As a consequence, new equipment and crucial upgrades worth 12 million dollars will be installed at both institutions.

Our Faculty members were again very successful at **CIHR** operating grant competitions in 2012, (J. Archambault/IRCM, C. Baron, P. Chartrand, J. Drouin/IRCM, N. Heveker/Ste. Justine and S. Mader/IRIC). Our colleagues also obtained funding from other sources, such as P. Legault (CIHR POP-1), G. Ferbeyre **(NSERC)**, N. Grandvaux/CR-CHUM (NSERC), and J. Omichinski (NSERC). The IRIC commercialization arm **IRICoR** directed by Michel Bouvier received funding of 4 million dollars from Merck Canada in order to strengthen research collaborations and valorization with other Networks of Centers of Excellence in Ontario and British Columbia.

Research highlights

Researchers of the Department published several interesting articles in high-impact journals that attracted significant media attention. Gerardo Ferbeyre published articles on the effects of Metformin on aging and cancer in the journals *Ageing Cell* and *Cancer Prevention Research*. They also published their work on the tumor suppressor activity of the ERK/MAPK pathway in *Genes & Development*. **Stephen Michnick** published groundbreaking work on protein folding mechanisms in *Nature Structural & Molecular Biology and* **Christian Baron** *published research on a novel mechanism to disarm bacterial pathogens in Chemistry and Biology.*

Awards

Congratulations to **Michel Bouvier** who has received the NRC Research Press Senior Investigator Award of the Canadian Society for Molecular Biosciences. **Gerardo Ferbeyre** was named Chercheur National of the FRQ-S, which is a distinction reserved only for the most successful biomedical researchers in Québec. **Alain Moreau** received the Premio Venezia price 2012 from the Italian Chamber of Commerce and the Cotrel foundation medal for his exceptional contribution to research on the etiology of Idiopathic Scoliosis.

uOttawa

Département de biochimie, microbiologie et immunologie

Department of Biochemistry, Microbiology and Immunology (BMI)

Correspondent : Kristin Baetz

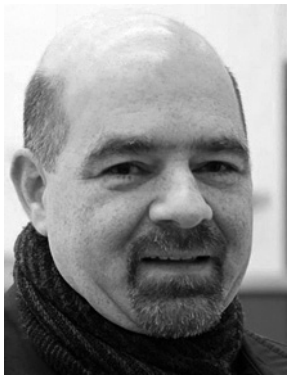
Departmental Overview

BMI is a large a diverse department with more than one hundred members conducting research over a broad area of modern biomedical sciences and life sciences. Thirty professors (or core members) are located in the Faculty of Medicine at the Health Sciences Building. Others are cross appointees from clinical departments of the Faculty of Medicine and affiliated teaching hospitals or adjunct members from research institutes and government agencies in the Ottawa area. BMI runs a Biochemistry undergraduate program for over 700 students and more than 150 graduate students are enrolled in BMI's two graduate programs: Microbiology and Immunology (MIC) and Biochemistry (BCH).

BMI has seen remarkable growth in the last eight years with more than 18 new core faculty members. BMI is also home to the Ottawa Institute of Systems Biology (OISB) and is presently developing a new research centre focusing on Inflammation and Disease.

Appointments and promotions

In 2012 two new faculty members joined the BMI core team. **Subash Sad** was recruited to BMI as full professor and moved his innovative research program on inflammation from the National Research Council to uOttawa. Subash will be leading our new initiative on Inflammation. We would also like to welcome Associate Professor **Marc-André Langlois** whose program focuses on virology and innate immunity. In 2012 **Steffany Bennett** and **Alain Stintzi** were promoted to Full Professor, while **Kristin Baetz** and **Jean-François Couture** were promoted to Associate Professor.



Subash Sad

Marc-André Langlois

Research Highlights

Researchers of the Department published over 200 papers in 2012, several of which were in high impact journals. Of particular interest, both **Alex Blais** and **Ilona Skerjanc** each published papers on the contribution of transcriptional remodeling to development in *Nucleic Acids Research*. **Alain Stintzi**, in collaboration with **Jean-Francois Couture**, solved the structure and functions of the ferric uptake regulator transcription factor of the food

borne pathogen *Campylobacter jejuni*, a major cause of gastroenteritis and Guillain-Barré syndrome worldwide, and published this work in ***PNAS***. **Andrew Makrigiannis'** work on the self-education of Natural Killer cells was appropriately published in *Blood*.

A Fond Farewell....

After more than thirty years in BMI, we wish a fond farewell to our colleague **Ken Dimock** who retired in 2012. Ken's research focused on virus interactions with host cells, in particular, mechanisms by which viruses bind to and enter cells. Over his career he published over fifty papers in the field of virology and he held numerous senior administrative position at uOttawa including Director of the BCH undergraduate program. He will be missed by many, both in BMI and across Canada, but we can't wait to hear about his travels.

Queen's University

Biochemistry Teaching Program + Graduate Program

Correspondent: Peter Davies

Sadly, we can no longer send in a Departmental report from Biochemistry at Queen's University. After a distinguished 73-year history, Biochemistry has been amalgamated with the four Life Science departments into a single basic science department. Outside consultants: Reinhart Reithmeier (U of T) and George Stewart (U of Western Australia) recommended the merger. And it was passed by a ballot in a classic example of "gerrymandering" - with the biochemists voting 11 to 1 against the merger.

Back in the 80's and 90's student enrolment in our Biochemistry program increased 5-fold during a period when the Queen's undergraduate enrolment increased 1.4-fold. Rather than shift resources to a growth area, the university capped our program numbers. After decades of departmental budget cuts or zero increases, we are now in a period of attrition where faculty who leave (like **Marlys Koschinsky** – to be Dean of Science at the University Windsor – accompanied by her spouse, **Mike Boffa**) or pass away (like **Mike Nesheim** – still sadly missed at every level) are not replaced. Any biochemist retirements will mean the load of the Biochemistry Teaching Program within the Department of Biomedical and Molecular Sciences (DBMS) will fall on even fewer shoulders.

But they are good, broad shoulders! **Steve Smith**, recently promoted to Full Professor, is the Associate Head of DBMS. Steve will be heading off for sabbatical leave this fall to U. Vic. to work with his collaborator, Al Boraston. **John Allingham** (CRCII), recently promoted to Associate Professor (with tenure) has established a dynamic research program on kinesin motor proteins and X-ray crystallography. **Zongchao Jia** (CRCI) was a recent winner of the Queen's University Prize for Excellence in Research, and before that he was both a Killam Research Fellowship holder and Steacie Award winner. **Peter Davies** (resume available on request) (CRCI) was Visiting Professor at the National University of Singapore last spring, and will be Visiting Professor at the Hebrew University of Jerusalem, Rehovot, this fall. In 2012, **Andrew Craig** won the Canadian Cancer Society Young Investigator Award. Andrew will also be on sabbatical leave (in Toronto) for the second half of 2013.

We regret to inform you that one of our former Heads, **John H. Spencer**, passed away last year. John was instrumental in strengthening the Department in the late 70's and early 80's with the help of MRC development awards.

Ryerson University

Department of Chemistry and Biology

Correspondent: Roberto Botelho

The Dept. of Chemistry and Biology encompasses multi-disciplinary interests in research and education. Our Chemistry research programs are generally focused on macromolecular, synthetic and medicinal chemistry. The research interests in Biology enjoy strengths ranging from biochemistry, molecular and cell biology to genetics, microbiology and environmental biology. The breadth and variety of research interests creates an exceptional environment that permits cross-pollination of ideas and an open-concept milieu for learning and teaching.


Dean Imogen Coe

In 2012, there were a number of exciting changes within our Department and Ryerson University. Foremost, was the creation of the Faculty of Science, hosting our Department, Physics, Computer Science and Mathematics. The Faculty of Science will promote scientific research and education within Ryerson including the disciplines represented by the CSMB. Our inaugural Dean is **Dr. Imogen Coe**, a respected cell biologist who studies membrane protein biochemistry and function, particularly nucleoside transporters. Dr. Coe comes from York University.


Warren Wakarchuk

In addition, our Department recruited **Dr. Warren Wakarchuk**, a senior scientist formerly from the National Research Council. Dr. Wakarchuk is a leading investigator in glycobiology-related processes and enzymes from microbes to eukaryotes.

The recruitment of Drs. Coe and Wakarchuk are strategically important to help our Department maintain the research momentum built over the last five years. Indeed, 2012 was a good year in terms of publication output including several publications in host-pathogen interactions (**Debora Barnett Foster**), biofilms (**Gideon Wolfaardt** and **Martina Hausner**), organelle dynamics (**Roberto Botelho**), chromatin regulation (**Jeff Fillingham**) and protein proteomics (**John Marshall**). Importantly, our research output is complemented by continued success in securing external funding, including from NSERC and CIHR. For example, **Drs. Costin Antonescu** and **Roberto Botelho** were respectively awarded CIHR Operating Grants to investigate the relationship between clathrin-mediated endocytosis and signaling and to study the function and regulation of lysosome tubules in the immune response. In addition, **Dr. Botelho** was the recipient of the 2012 Maud Menten New Investigator Award, which is given by the Institutes of Genetics at CIHR to the new investigator with the highest ranked CIHR Operating Grant application.


Roberto Botelho

Finally, an important mission for our Department, and Ryerson as a whole, is to continue advancing excellence in undergraduate and graduate education. We now have established M.Sc. and Ph.D. programs in Molecular Science that are greatly facilitating our ability to increase our research output particularly in areas relevant to CSMB. This is complemented by a new B.Sc. Program in Biomedical Sciences that will start in Fall 2013. This B.Sc. program will promote undergraduate education in molecular and cell biology, genetics and biochemistry to prepare future generation of researchers.

Overall, 2012 was a very exciting time for the Department of Chemistry and Biology at Ryerson University. We expect our Department to continue growing its research footprint and visibility within Canada and the international stage and to advance research and education on the disciplines represented by the CSMB.

University of Saskatchewan

Department of Biochemistry

Correspondent: Scot Leary

The past year has finally ushered in the opening of the much anticipated, new "D" wing of our Health Sciences Building. From an architectural perspective, it is impressive. It also adds much needed natural light, along with plenty of physical space for people to interact with one another, both professionally and personally. The new "D" wing is also home to our new, open concept lab spaces,

and the personnel and operations of roughly half of our Departmental faculty members already call it home. We anticipate that the remainder of our faculty and their trainees will complete a similar transition in the coming few months and, in general, we are excited about the multidisciplinary, inter-Departmental nature of the space.

Dovetailed with this physical move has come the news that the University is not in a strong financial position, and that it intends to make up its budgetary shortfall in two ways; by reducing its total staff and Faculty complement, and by cutting several of its undergraduate program offerings. This process, coined TransformUS, is on-going and the first two of three waves of employee layoffs have occurred. At present, it remains unclear to what extent the five Basic Sciences Departments in the College of Medicine will be affected, including our own. However, what is clear is that change is both necessary and inevitable, and a consequence of that change may be the loss of the current Departmental structure. Needless to say, we are concerned about how these developments may affect our ability to continue to deliver a strong undergraduate program, and recruit graduate and post-graduate trainees to support our research programs.

In spite of the uncertainty that lies ahead, our Faculty has had another very good year when it comes to garnering grant money from Tri-Council agencies. **Stan Moore**, **Scot Stone** and **Mirek Cygler** all received 5-year CIHR Operating Grants. **Oleg Dmitriev** and **Scot Leary** received CIHR Operating and New Investigator Salary Award grants, respectively, through the provincial partnership program. **Bill Roesler**, Oleg Dmitriev, Mirek Cygler and **Jeremy Lee** all were recipients of NSERC Discovery Grants. **Scott Napper**, whose lab is located within the Vaccine and Infectious Disease Organization (VIDO), continued to garner considerable funding from a large number of industry and government sources to develop therapeutics for the effective treatment of diseases caused by protein misfolding. Ron Geyer and **Andrew Freywald**, a new associate member of our Department, received a grant from the CCSRI to develop antibodies for cancer treatment in conjunction with the Saskatchewan Therapeutic Antibody Resource. All told, our Faculty hold a total of 43 grants from these agencies and a variety of other charities and industry sources that total more than 10 million dollars in funding a year.


Andrew Freywald

Our Department also benefitted in the past year from the sponsorship of our seminar series by Fisher Scientific. These funds, in conjunction with other Departmental and College pots of money, allowed us to host Drs. Sean McKenna (University of Manitoba), Jared Rutter (University of Utah), Heidi McBride (McGill University/Montreal Neurological Institute) and Christopher Loewen (UBC). We thank these colleagues for being so generous with their time, and for telling us about exciting developments within their own, cutting edge research programs.

We would be remiss not to acknowledge our graduate students who were also very successful this year in fellowship competitions. In particular, **Omid Tavassoli** (PI: **Jeremy Lee**) and **Jeremy Marshall** (PI: **Deborah Anderson**) were awarded traineeships from the Parkinson Society and Terry Fox Foundation, respectively. We would also like to warmly welcome **Andrew Freywald**, the newest Associate member of our Department. Lastly, we would like to send out heartfelt congratulations to **Ron Geyer** and **Scott Napper**, both of whom were promoted to Full Professor this year.

Simon Fraser University

Department of Molecular Biology and Biochemistry

Correspondent: Christopher Beh

Our previous Bulletin Reports have highlighted the many transformative developments shaping the SFU MBB Department, and this article is no exception. In addition to the many honours and awards received by the Department's faculty, the past year brought new additions to our ranks and a change of Department leadership. Among our new initiatives is an outreach program designed to engage and touch base with our graduates and postdoc alumni. If you

are an MBB Department alumnus, please contact us at the Department (mbbalumni@sfu.ca) because we welcome the chance to reestablish contact and hear about your post-graduation experiences.

Department highlights

Dr. Lynne Quarmby takes the reigns from former Department Chair **Dr. Bruce Brandhorst**, guiding the MBB Department through its second decade as an independent research and teaching unit. We are particularly pleased to announce that **Dr. Ryan Morin** has joined our Department from the Genome Sciences Centre at the BC Cancer Agency. Dr. Morin uses next generation sequencing and bioinformatics to analyze the genetic architecture of cancer and other genetic diseases, and he will also continue his affiliation with the Genome Sciences Centre.

The SFU MBB Department welcomes Dr. Ryan Morin to our ranks

Dr. David Vocadlo has formally become a member of the MBB Department with a shared position with the Department of Chemistry. Dr. Vocadlo holds a Canada Research Chair Tier II for his research in chemical glycobiology and the therapeutic targeting of O-linked glycosylation. Congratulations to **Drs. Jack Chen**, **Robert Holt**, and **Mark Paetzel** who were all promoted to Full Professor. Dr. Chen develops bioinformatic programs for genomic analysis, with primary emphasis on studying genomic organization and gene expression in *Caenorhabditis elegans*. Dr. Holt is also affiliated with the Genome Sciences Centre of the BC Cancer Agency, where he exploits next generation sequencing to analyze a variety of complex genetic diseases. Dr. Paetzel utilizes X-ray crystallography to study the mechanism of bacterial protein translocation and membrane-bound proteases.

Among the many notable distinctions, grants, and awards obtained by MBB faculty, all of which bring excellence to SFU research, a few notable examples are highlighted here. **Dr. Peter Unrau** participated in one of the international teams awarded grants in the "Origin of Life Challenge," which funds research studying prebiotic life. Dr. Unrau's entry involved the RNA World hypothesis, which proposes that molecular evolution began with RNA because it combines the catalytic and replicative functions needed for life. MBB CRC Tier 1 Professor **Dr. Jamie Scott** shared a $2.7 M National Institutes of Health (NIH) grant with collaborators at the University of Basque Country, Massachusetts School of Medicine, and UCSF. The grant proposes a novel DNA-based approach towards developing an effective HIV/AIDS vaccine. **Dr. Lisa Craig** published a key paper explaining how the unique transport mechanism for pilus retraction in *Vibro cholerae* could be exploited to deliver antibiotics specifically into these disease-causing bacteria. The findings also have ramifications for targeting antibiotics into other pathogens via their pili.

Teaching and student achievements

We are proud of the accomplishments of our graduate and undergraduate students, and now we are pleased to share news on successes of gifted high school students mentored in the MBB Department. Working with **Dr. Willie Davidson**, **Ms. Kayla Lee**, a grade 12 student at York House School in Vancouver, won prizes at the "Greater Vancouver Regional Science Fair" and "Sanofi BioGENEius Challenge Canada." Ms. Lee applied FINS (Forensically Informative Nucleotide Sequencing) to determine whether flying fish eggs in sushi were switched with cheaper smelt eggs. Together with re-establishing contact with our alumni, we hope to unite our MBB community – both graduates with established careers and those just starting right out of high school.

University of Toronto

Department of Biochemistry

Correspondent: David Williams

The Biochemistry Department is experiencing a substantial change with the completion of Reinhart Reithmeier's second and final 5-year term as Chair. Reinhart accomplished a great deal in his decade at the helm, including many new Faculty appointments, the successful bid for a CERC Chair, revamping our undergraduate curriculum, and the introduction of a new online Biochemistry course, to name just a few. The

Department gathered on Feb. 25th, 2013 to celebrate Reinhart's accomplishments and to express its appreciation for his efforts in a position he described as "the best job he's ever had". The festivities featured a slide show from various decades of Reinhart's life, videos poking fun at his passionate interest in golf, a musical tribute, and touching testimonials from colleagues from within and outside the Department. Photos of the celebration can be seen at: http://biochemistry.utoronto.ca/news/Reithmeier_Term_End_Celebration.html

Reinhart is joined by many past and present members of the Department's administrative staff

Reinhart is happily looking forward to a sabbatical year focused on research, first at UBC working on papers (and his golf game) and spending weekends with his two granddaughters. He plans to spend summer back in the lab at the U. of T. and then the Fall term at Oxford learning computer modeling of membrane transporters with time to travel to meet with collaborators and colleagues.

Passing the torch! - Incoming Chair Justin Nodwell (left) receives the Departmental master keys from outgoing Chair Reinhart Reithmeier

Of course, one can't celebrate an outgoing Chair without throwing a party to welcome our incoming Chair! The Department is very pleased to announce that Justin Nodwell, formerly of McMaster University, is our new Chair as of March, 2013. Justin heads up a very successful group that focuses on antibiotic resistance mechanisms in *Streptomyces* as well as the search for novel antibiotics. We are all looking forward to working with Justin as the Department faces new challenges and opportunities while continuing its traditions of research and teaching excellence.

Faculty News

John and Voula with Zoe

We were pleased to learn that **John Rubinstein** was awarded the 2013 Burton Medal from the Microscopy Society of America. The medal is for significant contribution to the field of microscopy and microanalysis by a scientist under the age of 40. John is the first Canadian to win the award in its 38-year history, which is particularly significant because E. F. Burton was a Canadian at U. of Toronto who played a key role in building the first practical electron microscope. John and **Voula Kanelis**, Associate Professor in the Department of Chemistry, also achieved a major milestone with the birth of their first child, Zoe Kanelis Rubinstein, on April 22nd, 2013.

University Professor Emeritus **Marian Packham** continues her long and distinguished list of accomplishments by being named a Member of the Order of Canada. She was cited for "her pioneering research in biological medical science, notably her contributions to critical breakthroughs in arterial health". **Reinhart Reithmeier** was elected a Fellow of the Canadian Academy of Health Sciences (CAHS) "having demonstrated both distinctive accomplishments and the commitment to advance health sciences". Reinhart, well-known internationally for his work on membrane proteins and human disease, has also been relentless in promoting the importance of basic research and the need for increases in funding to support excellence and to remain competitive. We were also delighted to hear that **Julie Forman-Kay** was awarded the Jeanne Manery Fisher Memorial Lectureship of the CSMB. This lectureship honours a Canadian woman scientist who has a distinguished career in the fields of either biochemistry, molecular or cellular biology resulting

from her outstanding contributions to research, teaching or society. Julie will deliver her lecture at the 56th Annual Meeting of the CSMB at White Oaks, Niagara, Ontario in June, 2013.

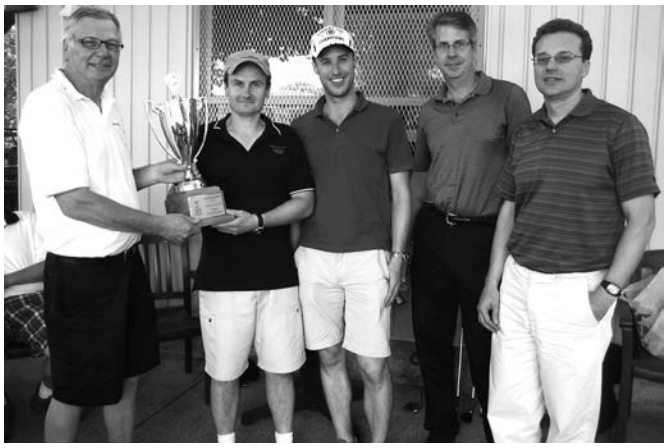
Amira Klip's research contributions were acknowledged through the prestigious Hugh Davson Award of the American Physiological Society (Cell Physiology section). Amira presented her lecture at the Experimental Biology Meeting in Boston, April, 2013. **Khosrow Adeli** was awarded the 2012 Canadian Society of Clinical Chemists Award for Education Excellence (presented at the Annual Conference in Quebec City in June 2012). He was also appointed for three years as the Chair of Publications and Communications Division of the International Federation of Clinical Chemistry (IFCC) and for a 3-year term to the Council of Scientific Advisors to the International Center for Genetic Engineering and Biotechnology (ICGEB). Finally, our Faculty members were very successful in obtaining or renewing their Canada Research Chairs. Congratulations to crystallographer **Trevor Moraes** who received a new Tier 2 CRC in the Structural Biology of Membrane Proteins to continue his work on protein and ion translocation across bacterial membranes. Congratulations also to **Stephane Angers, William Trimble, Lynne Howell, Liliana Attisano, Daniela Rotin, Amira Klip** and **Simon Sharpe** for successfully renewing their CRCs.

Events

Our **Annual Research Day** was held on May 1st, 2012 at the Old Mill Inn in Toronto. As always, the very full day featured work by our students and postdocs in the form of posters and oral presentations. Selected talks from faculty members also rounded out the day. In addition, this is the venue for our annual **Theo Hofmann lecture**, which was presented by **Michel Bouvier**, Université de Montréal, who described his lab's beautiful studies on the folding and trafficking of G protein-coupled receptors. For some photos of the event, please go to: http://biochemistry.utoronto.ca/news/Research%20Day%202012/Research_Day_2012/Photos.html

Theo Hofmann Lecturer Michel Bouvier meets....Theo Hofmann

Other events were our ever-popular **Golf Day and Year-End Party**.



Reinhart Reithmeier presents the coveted Biochemistry Cup to winning golf team, the Vesicular Traffickers (aka Allen Volchuk, Kevin Foley, Bill Trimble and Phil Bilan)

John Glover, David Williams and Debbie Hong entertain at the Year-End Party with original science parody songs. Watch the video at: http://www.youtube.com/watch?v=ihsl9ZfcCHc&feature=youtu.be

Appointments

2012 saw several new appointments to the Department. **David Andrews**, formerly of McMaster University and now located at the Sunnybrook Research Institute, was appointed as a Professor to the Department. David's research interests include apoptosis and membrane biogenesis and he currently heads up the new Sunnybrook Centre for Research in Image-Guided Therapeutics.

David Andrews


Jason Maynes

The Department was also delighted to welcome **Jason Maynes** who was cross-appointed as an Assistant Professor. Jason is a crystallographer and anaesthesiologist at the Hospital for Sick Children and also an Investigator in the Program in Molecular Structure and Function. He obtained his PhD with Michael James at the University of Alberta where he worked on the structure of protein phosphatases and their interaction with natural toxins followed by post-doctoral studies with Thomas Terwilliger (Wash. U). His current research interests centre around the role of anaesthetics on mitochondrial dysfunction, fragmentation and mtDNA damage

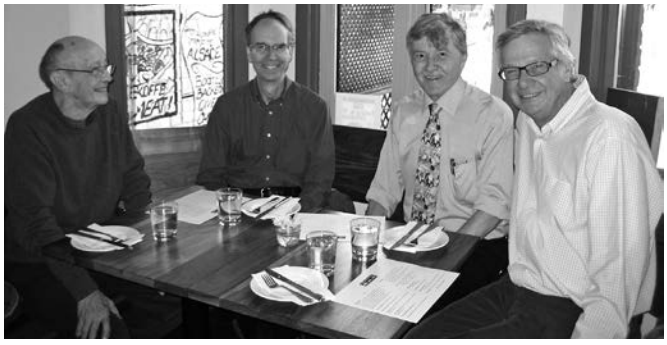

Ben Neel

Ben Neel, Director of the Ontario Cancer Institute (OCI) and a Senior Scientist in Stem Cell and Development Biology was cross-appointed at the level of Professor. Ben works in the area of cell signaling with a particular focus on protein tyrosine phosphatases.

Congratulations also to **John Rubinstein, Simon Sharpe and Allen Volchuk,** all of whom were promoted to the rank of Associate Professor.

Retirements

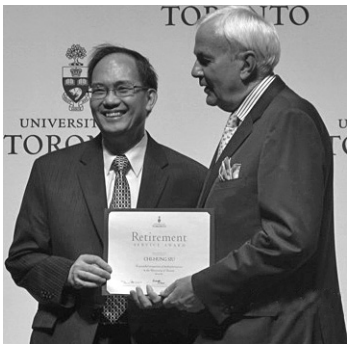
Three of our Faculty members retired in 2012. **Brian Robinson** retired from SickKids and the University of Toronto, effective March 31, 2012. Brian was first appointed to the Department of Biochemistry in 1973. His association with the Department goes back even further to 1968-70 when he was an MRC Post-doctoral Fellow with Ron Williams. Brian's research on lactic acidosis has been funding by MRC/CIHR since 1979. He has published over 250 articles and reviews and has spoken on lactic acidemia and related topics around the world. Brian is well-known for the identification of mutations in metabolic enzymes like pyruvate carboxylase and dehydrogenase and of new drugs for the treatment of mitochondrial diseases. He was awarded a Canada Research Chair in Metabolism & Nutrition in 2001. Fifteen graduate students and a similar number of post-doctoral fellows were supervised by Brian over his many years at the Research Institute at the Hospital for Sick Children and the University of Toronto. Like many of our colleagues at SickKids, Brian Robinson has been a model citizen in the Department, doing great research and contributing to the education of our graduate students, undergraduate Arts and Sciences students and Medical students.


Brian Robinson (sporting one of his signature ties) enjoys lunch with Ron Williams (left), Roy Baker and Reinhart Reithmeier

Jacqueline Segall retired from the University of Toronto on June 30, 2012. Jacqueline joined the Department in 1980 after completing fellowship training at Washington University and a Ph.D. at Harvard. She won an MRC Scholarship in 1982. In 1986 she was appointed jointly to Medical, now Molecular Genetics. Jacqueline is known for her work on gene expression in yeast, particularly during the sporulation process. She has been funded by MRC/CIHR since 1981, attesting to the recognition of the high quality of her work. Fourteen graduate students and four post-doctoral fellows trained with Jacqueline and their names feature prominently as authors on a steady stream of high-quality papers. A number of these graduates have gone onto faculty positions or other leadership positions.


Jacqueline Segall is congratulated by Chancellor (and former Ontario Premier) David Peterson

Jacqueline taught at the graduate and undergraduate level, most notably teaching and coordinating MGY420, "Regulation of Gene Expression" starting in 1984. To celebrate Jacqueline's many achievements and contributions to the Departments of Biochemistry and Molecular Genetics a luncheon reception was held on June 27th.



Chi-Hung Siu with Chancellor David Peterson

Chi-Hung Siu also retired effective 2012. For many years, Chi-Hung was a member of the Banting and Best Dept. of Medical Research and was a member of the Department of Biochemistry for many years. His research focused on structure-function analyses of cell adhesion molecules, mechanisms of signal transduction triggered by cell adhesion, and the relationship of cell-cell binding during development of the social amoeba *Dictyostelium discoideum*. In this area, Chi-Hung published over 100 influential papers that have been cited more than 2000 times. Chi-Hung has been actively involved in teaching biochemistry to our undergraduates and also in the training of Biochemistry graduate students.

Graduate Studies

Each year, our graduate students organize the **Benjamin Schachter Memorial Lecture** and they select a prominent graduate from our Department to address current students as a means to gain insights and advice on diverse career choices. The lectureship is named in honour of former graduate student Benjamin Schachter, who conducted research in the Department from 1934-1939. This year, the Biochemistry Grad Students Union invited back alumna **Jennifer Marles** who is an intellectual property lawyer in British Colombia with Oyen Wiggs Green & Mutala LLP. In her talk entitled *"An overview of patent law and its relevance to those working in academia"*, Jennifer described the process she underwent to make the transition from graduate school to law, and specifically to patent law. She also gave fascinating insights into the working life of a patent lawyer, including the strong scientific component of the work as well as the careful drafting of patent applications and the years-long process of "prosecution" wherein the claims are argued with patent offices.


Members of Benjamin Schachter's family with Jennifer Marles (right front) and Reinhart Reithmeier

One of the highlights of the Department's Annual Research Day is its **graduate student poster competition**. Our Theo Hofmann Lecturer, **Michel Bouvier**, served as guest judge to help make the hard decisions as to which posters deserved special recognition. In the end, the following students (who receive cash awards) were chosen as poster winners:

Winners in the Ph.D. category were:
Amy Cui (Palazzo lab) *"p180 Promotes the Ribosome-Independent Localization of a Subset of mRNA to the Endoplasmic Reticulum"*, **John Whitney** (Howell lab) *"A receptor for biofilm formation is a degenerate diguanylate cyclase"*, **Ryan Murchie** (Rotin lab) *"Protein tyrosine phosphatase sigma (PTPσ) targets apical junction complex proteins in the colon and modulates epithelial permeability"* and **Vikram Mulligan** (Chakrabartty lab) *"Early steps in oxidation-induced SOD1 misfolding: Implications for non-amyloid protein aggregation in familial ALS".*

Winners in the M.Sc. category were:
Feiyang Liu (Pai lab) *"Structural study of Disease-Specific-Epitope monoclonal antibodies that recognize misfolded superoxide dismutase, one of the causes of familial amyotrophic lateral sclerosis"*, **Yuqing Wang** (McQuibban lab *"ROS induces selective degradation of mitochondria by autophagy"* and **Graeme Sargent** (Kim lab) *"Identification of the E3 Ubiquitin Ligase in Pexophagy".*

The winner in the postdoc category was:
Charles Calmettes (Moraes lab) *"The structural basis of transferrin sequestration by transferrin-binding protein B"*

Additional graduate awards:
The winner of the ***Beckman Coulter Paper of the Year Award*** was **Avinash Persaud** (Rotin lab) for his paper entitled: *Nedd4-1 binds and ubiquitylates activated FGFR1 to control its endocytosis and function.* Persaud A, Alberts P, Hayes M, Guettler S, Clarke I, Sicheri F, Dirks P, Ciruna B, Rotin D. EMBO J. 2011 30(16):3259-73.

Natalia Fedianina of Beckman-Coulter presents Avinash Persaud with the "Best Paper of 2011" Award

The **outstanding PhD thesis award** went to **Sarah Rauscher** (Pomès lab) for her molecular dynamics work on elastin-like peptides.

Sarah receives the outstanding thesis award from Grad Coordinator Lil Attisano

The annual ***David Scott Prize*** for outstanding all-round graduate student was awarded jointly to **Lori Rutkevich** (Williams lab) and **Phil Ip** (Chakrabartty lab). Award winners are selected on the basis of research and teaching excellence and outstanding contributions to the Department and to fellow students.

(left) Grad Coordinator Lil Attisano presents the Scott Award to Lori and Phil

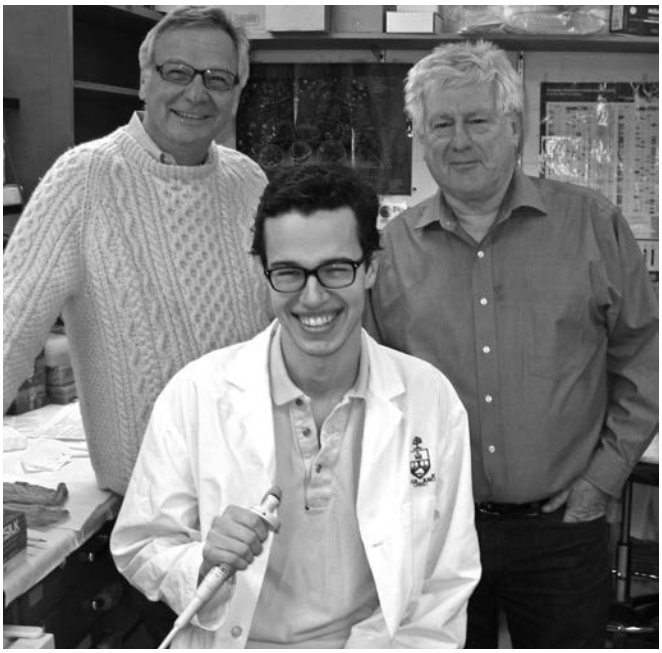
Outstanding Teaching Assistant awards went to **Mustafa Kamani** and **Kristina Han** for their excellent work as tutorial leaders in our gigantic (1200 students) intro biochemistry course BCH242Y.

Undergraduate Coordinator, Roula Andreopoulos, presents TA awards to Mustafa (left) and Kristina.

Congratulations to all winners on their achievements!

Undergraduate Studies

We were delighted to learn that one of our 4th year Biochemistry Specialist students, **Connor Emdin** was selected as one of the 11 Rhodes Scholars from Canada. A straight A+ student, Connor has always excelled in his course work. Connor was a research student in the Reithmeier lab in 2010/11 and he stayed on to continue his work on sulfate transporters and bacterial pathogenesis over the summer of 2011 and then again as a 3rd year project. Driven by his interest in global health, Connor went to South Africa the summer of 2012 to work on an AIDS clinical trial project. He will marry his interest in research and health policy for his D.Phil. studies at Oxford before going on to medical school. Connor's ultimate goal is to be a physician-researcher and global health policy adviser. Given his talent and drive, Connor will no doubt succeed in reaching his ambitious goal.



Connor Emdin poses with his favourite pipet and with his favourite Biochemistry mentors Reinhart Reithmeier (left) and Jim Ingles

University of Toronto

Department of Cell and Systems Biology

Correspondent: Tony Harris

The Department of Cell and Systems Biology is a major contributor to research and teaching at the University of Toronto. Groups in the Department combine 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.

Our labs have made numerous exciting discoveries over the last year. A few examples are highlighted here. Work from the **Tepass lab** published in *Nature Cell Biology* and the *Journal of Cell Science* revealed how the adherens junction component alpha-catenin functions in vivo. In the *Journal of Cell Science* and *Molecular Biology of the Cell*, the **Harris lab** showed how a core component of the Par polarity complex is localized to the plasma membrane. In a *Journal of Cell Science* paper the **Winklbauer lab** challenged a long-standing model of cell sorting in the developing embryo. In the *Journal of Neuroscience*, the **Peever lab** identified transmitter and receptor mechanisms responsible for REM sleep paralysis. Also in the *Journal of Neuroscience*, the **Woodin lab** found a specific sequence in KCC2 channel linked to hyperpolarizing GABAergic transmission. In *Neuroscience*, the **Lovejoy lab** described how Teneurin-1 regulates the neuronal cytoskeleton. In a paper published in *Plant Cell*, the **Goring lab** identified a ubiquitin ligase controlling the decision to accept or reject pollen. In *PNAS*, the **Guttman lab** identified innate immunity elicitors using molecular signatures of natural selection. And, in the *Plant Journal*, the **Provart lab** published a bioinformatics approach to identify orthologous genes multiple species.

These examples provide a sampling of the exciting research conducted in the Department.

Our graduate program has also excelled. In addition to the downtown group described above, our graduate program also encompasses the Scarborough and Mississauga U of T campuses. We welcomed 48 new students, and congratulate 42 students on their graduation. Currently we have 169 graduate students in the Department. We are very proud of our students' success in earning scholarships and travel awards. For example, our students won 11 NSERC Graduate Scholarships and 14 Ontario Graduate Scholarships.

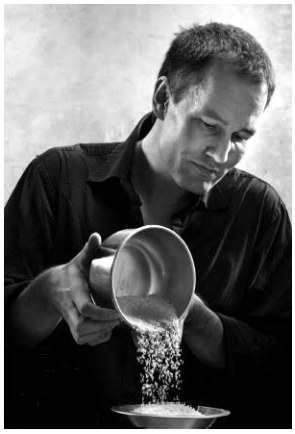
University of Toronto - Scarborough Campus

Department of Biological Sciences

Correspondent: Rongmin Zhao

The Department of Biological Sciences at the University of Toronto Scarborough campus currently has 31 full time faculty members. Most of our faculty members are also cross-appointed with the Department of Cell & Systems Biology (CSB) and/or the Department of Ecology & Evolutionary Biology (EEB) at the St. George campus. Our labs focus on research at molecular, organismal, and ecological levels, and house most of the graduate students (75 in the year 2012) in the campus. In the past year, the Department has seen several changes including a new department Chair. **Dr. Greg Vanlerberghe**, who led the Department through the recent external review process, finished his five-year term as Departmental Chair and returned to his research lab. Dr. Vanlerberghe studies the protective role of a unique component of the plant mitochondrial electron transport chain, called alternative oxidase (AOX) using biochemical and molecular approaches. **Dr. Andrew Mason**, the new Chair of the Department, leads his research group to understand the mechanisms by which the nervous system controls ongoing activity and how these mechanisms relate to behavioural adaptation by using invertebrate model systems. In the past year, **Dr. Sonia Gazzarrini**, who studies transcription factors that control plant seed development and maturation, and **Dr. Joanne Nash**, who investigates the cellular and molecular mechanisms underlying Parkinson's disease, were both promoted to the rank of Associate Professor.

The Department of Biological Sciences maintains a very successful record of attracting external research funding. Almost every faculty member holds an NSERC Discovery Grant. Additionally, in the past year, **Dr. Bebhinn Treanor** received an NSERC RTI grant, **Dr. Rene Harrison** renewed her CIHR operating grant to study the cell biology of Chlamydia infections and **Dr. Joanne Nash** received a 5-year fund from The Michael J. Fox Foundation to study the role of Sirtuin-3 in protecting brain cells from dying in Parkinson's disease. **Dr. Herbert Kronzucker**, a plant biologist with a special interest in how food crops respond to stress, and how they can be improved, received the Principal's Research Award in 2012 and gave an inaugural lecture. Dr. Kronzucker is also a Canada Research Chair in Systems Biology of Plant Nutrition and Ion Transport and he is working to establish the Canadian Centre for World Hunger Research at UTSC. Herbert was also honoured with a *Science for Better Life Award* for his work on rice from Bayer Canada.



Herbert Kronzucker examines the role of nutrient ion fluxes at cellular, whole-organism, and ecosystem levels

In the past year, graduate students in the Department also made significant achievements. **Dean Koucoulas** won the Cathy Orlando Award for Environmental Stewardship. **Caroline Tucker** won the EEB Ramsay Wright award for her excellence in research and leadership in EEB. **Marina Cvetkovska**, a recent Ph.D. from the Vanlerberghe lab, won an NSERC Postdoctoral Fellowship.

Ontario Cancer Institute

Princess Margaret Hospital

Correspondent: Linda Penn

Dr. Fei-Fei Liu

Dr. Fei-Fei Liu, OCI Senior Scientist, was recently selected as the Scientific Honouree for the Israel Cancer Research Fund's (ICRF) Women of Action, 2012. Dr. Liu was recognized for her focus in translational molecular oncology for the development of novel therapeutics for human breast and head/neck cancers. Since it's inception in 1975, the ICRF has raised more than $39 million that has been used to support over 1,600 research grants, making it one of the largest single sources of private funds for cancer research in Israel.

OCI Director Elected to AACR Board of Directors

Dr. Benjamin Neel

Dr. Benjamin Neel has been elected to serve on the American Association for Cancer Research (AACR) Board of Directors. As a member of this board, Dr. Neel will set general policy for the Association and oversee its activities, representatives and employees. He will also serve as the Chairperson of the 2012 AACR Annual Meeting. AACR is the world's first and largest professional organization dedicated to advancing cancer research and to prevent and cure cancer. Its membership includes 34,000 laboratory, translational and clinical researchers, population scientists, health care professionals and cancer advocates in more than 90 countries.

OCI Researcher Awarded a Canada Research Chair

UHN congratulates **Dr. Thomas Kislinger** on the renewal of his Tier II Canada Research Chair (CRC) in Proteomics in Cancer Research. Dr. Kislinger's CRC will provide funding over the next five years to support his research program which uses proteomics to identify biomarkers and molecular mechanisms of epithelial ovarian cancer. His research will help develop tools to improve the diagnosis of this cancer.

Dr. Thomas Kislinger

UHN Researcher Honoured by Prostate Cancer Canada

Dr. Rob Bristow

OCI Senior Scientist **Dr. Rob Bristow** has been named as a "national hero" by Prostate Cancer Canada (PCC). "In the field of prostate cancer, and especially as it applies to collaboration and leadership, Rob Bristow has no peer," said Steve Jones, President and CEO of PCC. "He is internationally respected for his achievements, and universally respected for his compassion, vision and strength of character." In recognition of his standing in the prostate cancer research community, PCC—the only national foundation dedicated to prostate cancer awareness and research—awarded him the John Ferguson Memorial Award for Prostate Cancer.

Aaron Schimmer named UHN 2011 Inventor of the Year

UHN's 2011 Inventor of the Year Award was presented to OCI Scientist **Dr. Aaron Schimmer**. This award, sponsored through UHN's Technology Development and Commercialization Office and presented by VP Research Dr. Christopher Paige, is in recognition of a UHN researcher who has made an outstanding and inventive contribution to patient-oriented biomedical research.

Dr. Schimmer was acknowledged for his efforts in advancing therapeutics from the lab to the bedside clinic. Known drugs are screened by Dr. Schimmer's research team to identify compounds that impact molecular targets responsible for cancer malignancies and thus have previously unrecognized anti-cancer activity. Through this approach, current drugs can be 'repurposed' and moved into clinical trials at a fraction of the time and resources typically needed for developing


Dr. Aaron Schimmer

cancer medicine. Fourteen patents have been applied for as a result of the successes of this research initiative. Dr. Schimmer's work has led to new insights into molecular pathways and novel treatments. Congratulations Dr. Schimmer!

The OCI has recently grown its research program in genomics and epigenetics. This included the purchase of new instrumentation and expanding the bioinformatics capabilities. In addition, three new experts in epigenetics were recruited to the Institute in 2012:
Mathieu Lupien, Daniel De Carvalho and **Hansen He**.


Dr. Mathieu Lupien

Dr. Mathieu Lupien has been a Scientist at the Princess Margaret Cancer Centre since 2012 and is an Assistant Professor in the Department of Medical Biophysics at the University of Toronto. He also has a cross-appointment with the Ontario Institute for Cancer Research (OICR). He earned his Ph.D. at McGill University in 2005, followed by post-doctoral training in medical oncology at the Dana-Farber Cancer Institute, Harvard Medical School as an Era of Hope Fellow. Dr. Lupien completed his post-doctoral training in 2008 and was recruited as a faculty member at the Dartmouth Medical School in 2009, where he became Director of the Quantitative Epigenomics Laboratory. Dr. Lupien has co-authored numerous peer-reviewed publications, including seminal work reported in high-impact journals including *Science, Cell, Nature Genetics* and *The Journal of the National Cancer Institute*. Among other honours, Dr. Lupien is a recipient of the Young Investigator Award from the OICR.

Dr. Housheng He is an accomplished young investigator with fourteen publications in peer-reviewed journals over the last five years. He has led seminal work in the field of epigenetics published in high-impact journals including *Nature Genetics* and *Genome Research*. His excellence was recognized through a series of awards including the


Dr. Housheng He

Women's Cancers Program Executive Council Award, the AACR-Aflac Incorporated Scholar-in-Training award and a postdoctoral fellowship from the Department of Defense Breast Cancer Program, US army. This clearly demonstrates his excellence in training and appreciation from his peers. He stands out amongst his peers as a bright young investigator destined for success.


Daniel DeCarvelho

Daniel DeCarvelho focuses on understanding the epigenetic mechanisms underlying tumourigenesis and translating this knowledge into more efficient approaches for epigenetic therapy. Today, a few drugs acting on DNA methyltransferase and histone deacetylase enzymes have already received FDA approval, providing validation that pharmacological alteration of epigenetic modifications has tangible clinical benefit. However, the current generation of epigenetic drugs acts by inhibiting chromatin-modifying enzymes and, consequently, has nonspecific, pan-genomic effects. This is associated with a significant dose-limiting toxicity. The DeCarvelho lab is trying to identify the molecules and pathways driving cancer-specific epigenetic modifications. They expect that future generations of cancer epigenetic therapies will target these driver molecules and pathways, instead of the core epigenetic machinery itself. The identification of these drug targets will allow more rational cancer epigenetic therapies, with increased efficiency and with fewer risks associated with the reactivation of developmental genes.

Hospital for Sick Children

Division of Cell Biology

Correspondent: John Brumell

New SickKids building almost ready!

The Hospital for Sick Children will soon complete construction of its new research building, the Peter Gilgan

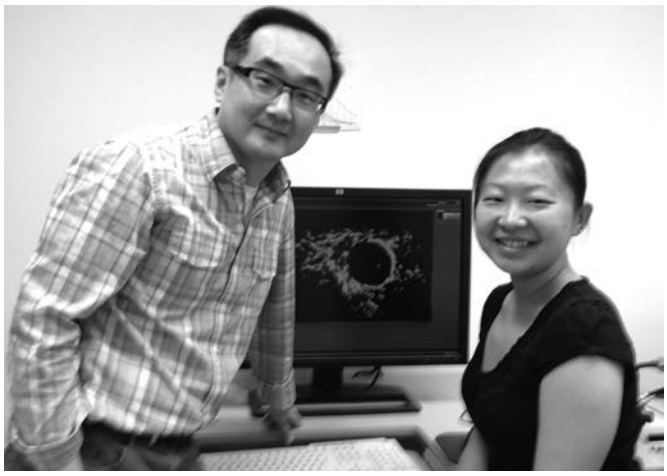
Centre for Research and Learning (PGCRL). The building is located at the corner of Elm and Bay Streets and reaches 21 stories, making it one of the biggest research facilities in Canada. The building is state-of-the art and will provide SickKids researchers with much needed facilities to pursue basic and clinical pediatric research, with both 'wet' and 'dry' labs onsite. The PGCRL will be connected via walking links to the main hospital building on Elizabeth Street.

The Peter Gilgan Centre for Research and Learning

One of the striking features of the PGCRL building is its organization into 'neighborhoods'. Each neighborhood is made up of three research floors that are linked by a shared atrium, creating a sense of community amongst researchers. The atria themselves are dramatic examples of architecture, marked by wavy glass that one can see jutting out from the building over Bay Street. Importantly, these common neighborhood spaces will provide informal meeting space for researchers to share ideas and start new collaborations. Details of the new building can be seen at: http://www.sickkidsfoundation.com/bepartofit/ Researchers will begin moving their laboratories into the PGCRL in July, 2013.

One of the young SickKids investigators moving to the PGCRL is **Dr. Peter Kim**, a member of the Cell Biology Program. Peter is excited about his new lab, which will be located on the 19th floor alongside many other members of the program. Previously members of the Cell Biology Program were located in several buildings and had limited interactions. "The new building will bring us all together" says Dr. Kim, "and allow us to bounce ideas off each other in a much more effective way".

Dr. Kim's research focuses on autophagy, a cellular degradative pathway, and how it controls organelle fate in our cells. In a recent study Dr. Kim's laboratory demonstrated that high levels of reactive oxygen species production by the mitochondria can lead to its degradation by autophagy (Wang *et al*, Autophagy, 2012). Using a novel technique of spatially and temporally induce reactive oxygen species within mitochondria, the study also showed that reactive oxygen species leads to depolarization of the mitochondrial membrane, and this change is what leads to turnover of these organelles. This is an exciting study that provides important insight into the regulation of mitochondria, which have been become a hot topic of research since their functions are linked to cancer, metabolism and neurodegenerative diseases. Dr. Kim hopes that moving to the PGCRL will open up new studies of autophagy and mitochondrial function with other members of the Cell Biology Program.



Dr. Peter Kim, Hospital for Sick Children (left) shown with his Ph.D. student Yuqing Wang (right)

Dr. Kim will not be the only young investigator to benefit from the new facilities in the PGCRL building. The Hospital for Sick Children is in the middle of a major recruitment effort, with plans to hire up to 12 new researchers. While the results of this recruitment drive are not known at this time, we are excited by the prospect of recruiting a number of top notch young investigators to SickKids. In attracting these young stars the building will begin to pay for itself in terms of its recruiting power. The PGRCL will awe and inspire!

University of Victoria

Department of Biochemistry and Microbiology

Correspondent: Robert Burke

The Department of Biochemistry and Microbiology leads in teaching and research of biomedical science and molecular biology at the University of Victoria. With 17 faculty, 40 graduate students and 14 post-doctoral fellows, our programs emphasize our expertise in structural biology and proteomics, microbial pathogenesis, and gene regulation. Our undergraduate and graduate teaching integrate biochemical and microbial approaches to problems in health and the environment.

The past few years have seen continuous growth in our undergraduate programs. We continue to emphasize hands on learning, which means our undergraduates spend a lot of time at the bench where they acquire individual skills and experience. In spite of Canada's economic woes, the Coop program thrives, in part because our courses are designed to give students skill-sets that are attractive to employers. The Co-op coordinator, **Rozanne Poulson** placed about 180 students in Co-op jobs last year and has introduced a new Internship program. One of our Co-op students, **Jenna Ries** was awarded the 2012 Association for Co-operative Education in BC Co-op Student of the Year award. The Honours program, which consists of two terms in a research lab, seminars, and a thesis examination, is an essential program for students who want to become involved in research. **Marty Boulanger** and **Doug Briant** coordinated 23 Honours students this year, and again one or our students (**Jennifer Envicio**) took the top award among over 50 Honours students on Science poster day. We are developing new curricula in proteomics, an area that is soon to be supplemented by a new Faculty appointment. The University of Victoria Genome BC Proteomics Centre has thrived under the capable leadership of **Christoph Borchers.** This year we welcomed to our department 2 faculty members who have their principal appointments at the **BCCA – Deeley Cancer Research Centre. Julian Lum** and **Brad Nelson** have become regular faculty in the department in recognition of their continued involvement in our teaching and research programs.

Steve Evans, the Graduate Advisor, has transformed our graduate program, into a structured training program that provides students with the background, opportunities, and challenges necessary for them to thrive as independent scientists. The growth in our graduate programs is steady and fulfills important roles for our research and teaching programs.

A number of faculty members have been recognized with awards over the past couple of years. **Caren Helbing** was recognized with a Craigdarroch Award for Innovation and Entrepreneurship. **Al Boraston** was recognized with an NSERC Steacie Fellowship. **Nathan West** completed his

Our Graduating class for 2013 from the Department of Biochemistry and Microbiology is a proud group of students who are looking forward to a wide range of careers and professions. We are very proud of them and their accomplishments.

PhD in the Department and is the recipient of the Governor General's Gold Medal for 2013. Nathan is currently a Cancer Research Institute Post-doctoral Fellow at Oxford. We are very proud of these important forms of recognition!

The Department continues to move forward with innovative and distinctive programs that are based on a history of excellence in research and teaching. The fundamentals of learning by doing and the captivation of imaginative research serve us well in ensuring the success of our students and our programs.

University of Waterloo

Department of Biology

Correspondent: Bernie Dunker

Andrew Doxey

2012 was a year full of exciting developments for Molecular Biosciences researchers in the Biology Department at the University of Waterloo. New faculty member **Andrew Doxey** joined us after completing his postdoctoral work at Stanford. Andrew's research uses computational methods to explore biomolecular structure, function, evolution and design, and his group (which is attracting students fast) is a great addition to our growing strength in Computational Genomics.

Members of our Department were the recipients of numerous honours this past year. Among our faculty colleagues, **Christine Dupont** won the University of Waterloo Excellence in Science Teaching Award, **Kirsten Mueller** received the Luigi Provasoli Award in recognition of her co-authorship of the year's outstanding paper in the Journal of Phycology, while **Josh Neufeld** was selected as one of Waterloo Region's Top 40 under 40.

Graduate student **Terry Lung** (Supervisor Simon Chuong) was the recipient of the 2012 Canadian Council of University Biology Chairs Graduate Student Research Prize for his paper *"A transit peptide-like sorting signal at the C terminus directs the Bienertia sinuspersici preprotein receptor Toc159 to the chloroplast outer membrane"* (Plant Cell 24: 1560-1578), **Kyra Jones** (Supervisor David Rose) won the Amit and Meena Chakma Award for Exceptional Teaching by a Graduate Student, **Laura Sauder** (Supervisor Josh Neufeld) was awarded a prestigious NSERC Vanier scholarship, while **Adriano Senatore** (Supervisor David Spafford) was recently announced as the Governor General's Gold Medal winner for his 2012 Ph.D. thesis *"Alternative Splicing of Lymnaea Cav3 and NALCN Ion Channel Genes Serves to Alter Biophysical Properties, Membrane Expression, and Ion Selectivity"*.

Terry Lung

September saw the grand opening of the **Mike and Ophelia Lazaridis Quantum-Nano Centre** (with no less than Stephen Hawking in attendance!) and, shortly thereafter, the groundbreaking for the new Science Teaching Complex. Finally, after 39 and 40 years of outstanding service, respectively, technicians **Ron Socha** and **Dale Weber** retired, and will be greatly missed.

York University

Department of Biology

Correspondent: Logan Donaldson

Room to Grow — The new Life Sciences Building at York University

Since its inception in October 2011, the Life Sciences Building is now home to thirteen laboratories from the two Faculties (Health and Science) and three Departments (Biology, Chemistry, Kinesiology). The $80 M multipurpose building was built with an emphasis on community and collaboration throughout the four floors. The first and second floors are public areas with well-equipped lecture halls, study spaces and teaching laboratories. The third and fourth floors are restricted-access areas dedicated to biochemistry and molecular biology research.

The new Life Sciences Building at York University,
Photo Credit: Chessguy01, http://commons.wikimedia.org

The decision in the early planning stages of the YorkU LSB to not include an animal facility greatly simplified the organization and maintenance of the research floors and helped amalgamate research interests. For example, nearly half of the laboratories on the third floor of the LSB focus on structural biology.

The predominantly glass building is organized into three sections along its length. Purpose-built common rooms for analytical instrumentation are found in the central sections. The outer sections comprise write-up and research areas that offer and unimpeded view across the building. The design makes it very easy to interact with colleagues (and determine what trainees are doing!). In the administrative sense, the building functions very simply owing to the innate resourcefulness of the researchers and general good will. A building PI mailing list serves most needs. A few technical staff service over $5 M in new instrumentation that includes multiphoton imaging, mass spectrometry and NMR spectroscopy.

The YorkU LSB can easily accommodate another six research laboratories. We certainly have the room to grow. But as we grow, where do we draw most of our identity? To our respective home departments and faculties? To our colleagues who share the same interests? My own experiences in the open concept building have led me to feel like more of a "global campus citizen" rather than a member of a particular organizational unit. As a result, I believe that my ability (as well as the abilities of my trainees) to collaborate and innovate has increased. Next year, I look forward to describing some of the new research synergies and joint funding successes that have occurred among my colleagues old (and hopefully new, too) in the YorkU LSB.

Inaugural researchers in the YorkU LSB:
Logan Donaldson (Professor, Dep't Biology) ; George Zoidl (Professor and CRC Tier 1 in Molecular and Cellular Neuroscience, Dept's of Biology and Psychology); John McDermott (Professor and McLaughlin Research Chair); Chun Peng (Professor, Dep't Biology); Vivian Saridakis (Assoc Professor, Dep't Biology); Yi Sheng (Assoc Professor, Dep't Biology), Mark Bayfield (Asst Professor, Dept' Biology), Terry Kubiseski (Assoc Professor, Dep't Biology), Gerald Audette (Assoc Professor, Dep't Chemistry); Dasantila Golemi-Kotra (Assoc Professor, Dep't Chemistry); Peter Cheung (Assoc Professor, Dep't Biology); Derek Wilson (Assoc Professor, Dep't Chemistry); Mike Connor (Assoc Professor, Dep't Kinesiology).

CSMB-Sponsored Events

Graduate Events

The CSMB provides financial support to graduate student societies for a variety of activities related to biochemistry, molecular biology, cell biology or genetics. Examples of supported activities include (but are not restricted to) the following:

Scientific Symposium Days, with invited scientists speaking on subjects in the areas of biochemistry, molecular biology or cell biology.
Student Research Conferences, where students display their research work as posters, or give oral presentations.
Career Fairs or Career Workshops in areas related to biochemistry, molecular biology or cell biology.

The society will support several events each year, to a maximum of $500 per event, on a first-come, first-served basis. Student organizations seeking financial support under this program should contact the Society Secretary, Dr. Randal Johnston, with a short description of the planned event and the amount of funding requested. A short report is required following the event for inclusion in the Bulletin.

Research Meetings

The CSMB also provides support for research meetings that the executive views to be of particular interest to the CSMB membership and that are within the financial means of the Society. When sponsorship is awarded, CSMB members will receive an agreed upon reduction (*e.g.*, $75) in the registration fee for the meeting.

Furthermore, the funds provided by CSMB are considered a repayable loan. The understanding is that CSMB will provide seed money to establish the meeting. The amount of the loan that is repayable to CSMB can be reduced by the aggregate fee reduction offered to CSMB members who register for and attend the meeting.

Requests for research meeting support should be directed to the Society Secretary, Dr. Randal Johnston.

6th Canadian Developmental Biology Conference

Banff, Alberta
March 8-11, 2012
Correspondent: Dr. Paul Mains, University of Calgary

More than 170 people attended the Sixth Biannual Canadian Developmental Biology Conference in Banff, Alberta. The Conference was preceded by an educational session for Zebrafish researchers. Highlights of the Conference included a keynote lecture by **Dr. Utpal Banerjee**, Professor and Chair, Department of Molecular, Cellular and Developmental Biology, UCLA entitled *"Hematopoietic lineage development in Drosophila".* In addition, there was a special lecture by **Dr. Pierre Chambon**, Director of the Institut de Genetique et de Biologie Moleculaire et Cellulaire (IGBMC) entitled *"Positive and negative control of transcription by Nuclear Receptors".* The top poster presentation by a graduate student and a postdoctoral fellow won travel awards for the Society of Developmental Biology conference in Montreal this July. There were cash awards for 18 other posters plus one for best oral presentation.

Pierre Chambon (right) with former postdoc Jeff Dilworth, Ottawa Hospital Research Institute

Louis-Philippe Bouthillier Meeting

Department of Biochemistry, Université de Montréal
May 11-12, 2012
Correspondent: Alexandre Desjardins, Graduate Student

In the name of all the members of the Graduate Student Association in Biochemistry at the Université de Montréal

(AECSBUM), I would like to thank the CSMB for its contribution to the bi-annual *Louis-Philippe Bouthillier* Meeting of the Department of Biochemistry. During this Meeting, more than 125 members of the Department including professors, graduate students and few undergraduates shared their latest results and worked on potential collaborations.

During the course of this Meeting, the AECSBUM organized a poster competition where 50 graduate students presented their work. For some, it was their first occasion to give a presentation at a scientific meeting. This first edition of the poster competition at our bi-annual Meeting was made possible by the generous contribution of the CSMB. We are really grateful of your contribution. We plan to repeat the experience for the next edition in 2014 and hope your society will be a partner of this success.

Dr. Pascale Legault of the organizing committee and Dr. Christian Baron, Director of the Biochemistry Department (both at left) and Dr. Pierre Belhumeur, Vice-Dean, Faculty of Medicine (right) flank the winners of the poster competition: Sandrine Moreira, Vincent Boudreau and Houssam Ismail

Distinguished Speaker Lecture Series

University of Alberta's Department of Cell Biology
June 14, 2012
Correspondent: N. Katie Horvat, Cell Biology Students Association Treasurer

The Cell Biology Students Association (CBSA) from the University of Alberta's Department of Cell Biology hosts an annual Distinguished Speaker Lecture Series. Every year a prestigious guest speaker is invited to the Department of Cell Biology to present a seminar on their specific field of research. This year, **Dr. Michael P. Rout from the Rockefeller University**, New York was the invited speaker.

Dr. Rout's seminar entitled, *"Before the Pore: Evolution of the Nuclear Pore Complex"* was attended by most professors, post doctorates, and graduate students in the Department of Cell Biology, as well as by members of other Departments throughout the University. Refreshments for this seminar were sponsored by CSMB and New England BioLabs. Later that day, Dr. Rout also attended a reception for approximately 50 people including professors, postdocs, graduate students, and staff from the Department of Cell Biology where a variety of refreshments were enjoyed. It was a perfect opportunity to relax and enjoy each other's company while getting to know Dr. Rout.

In addition to the seminar, CBSA hosts several other smaller events with the Guest Speaker. Firstly, Dr. Rout participated in a get-together with the graduate students of our department, entitled "Grad Student Pizza Lunch." Graduate students joined Dr. Rout for lunch and were encouraged to ask questions regarding science, research, academics, and careers within science. Dr. Rout was very knowledgeable and open to all questions from our students. It was very entertaining to have him share much of his expertise in science and experiences from his grad student and postdoc days. Secondly, CBSA hosted a "Meet the Speaker" night at O'Byrnes Pub on Whyte Avenue. Executives from the CBSA and other cell biology graduate students had an intimate evening with Dr. Rout. They were able to get to know Dr. Rout more personally and enjoy the night out. Many stories were shared and everyone had a fabulous time!

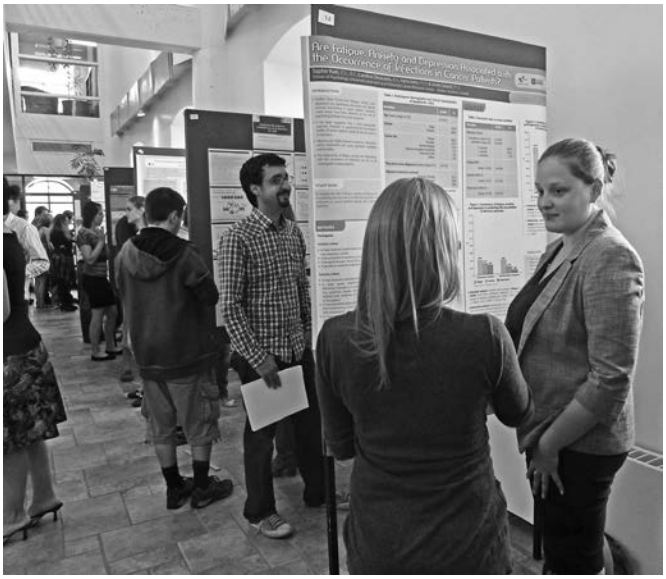
These events would not have been possible without the generous support of the Canadian Society for Molecular Biosciences (CSMB). Each year CSMB provides funding to support our Distinguished Speaker Lecture Series. Without their help, the CBSA would not be able to make these successful events possible. The CBSA as well as the graduate students of Cell Biology would like to extend a generous 'thank you' to all at CSMB. We hope to continue to host this distinguished event in future years with the proud support of CSMB.

Journée Scientifique des Étudiants 2012 (JSE 2012)

Cancer Research Centre, Université Laval
August 23, 2012
Correspondent: Gabriel Bossé, Graduate Student

The Journée scientifique des étudiants 2012 (JSE 2012) was held on August 23rd at the Université Laval Cancer Research Center in Québec city. At this meeting 75 students presented their work either by poster or oral presentation and more than 120 people attended the different presentations. **Dr. Alain Nepveu** from McGill University gave a talk as the invited speaker for JSE 2012. At the end of the day, more than 6500$ had been given as travel fellowships to more than 15 students from the Institute. These fellowships will be use to help the students go to the meeting of their choice.

Your contribution was highlighted in many ways. Your logo was convering half a page in the official program which was distributed to all the participants. All day long a Powerpoint presentation of our sponsors was presented and finally the chairman of the day mentioned the contribution of your organisation many times.



Enjoying the posters at the Journée scientifique des étudiants 2012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