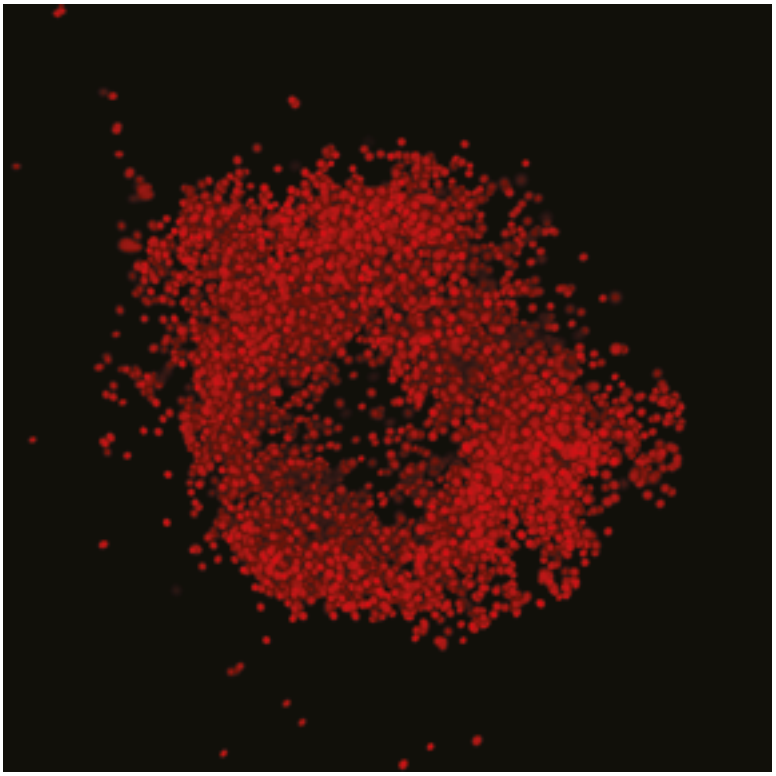
Bulletin



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

2014

www.csmb-scbm.ca

Bulletin

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Molecular Biosciences
La Société Canadienne pour les
Biosciences Moléculaires

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The CSMB Board at its annual Fall meeting, held in Montreal November 2014.

CSMB Board for 2014

From left to right: Phil Hieter, Mustapha Lhor, Martin Bisaillon, Jan Rainey, Arthur Hilliker, Kristin Baetz, Christian Baron, Frances Sharom, Andrew Simmonds, Jim Davie, Randal Johnston, Anastassia Voronova, John Orlowski

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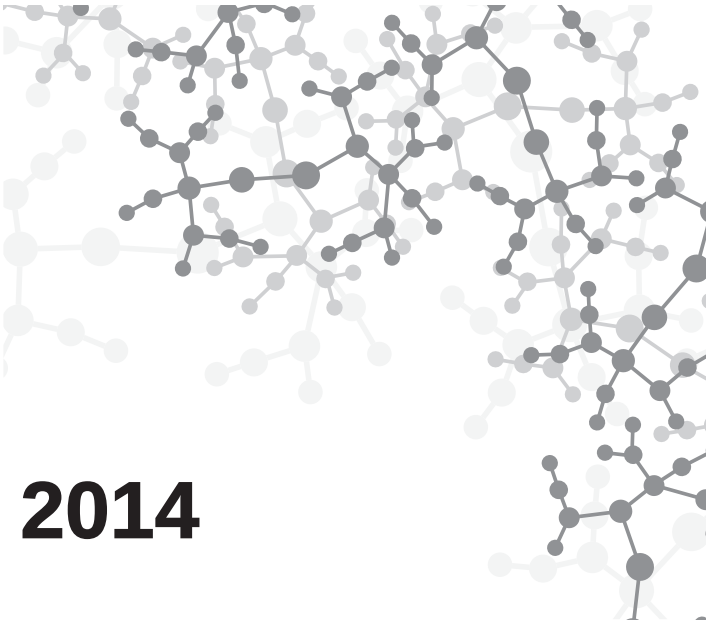

President's Report 2014

Dr. Christian Baron

My first year as President of the society is now half complete. I continue to enjoy working with the board and with our members to fulfill the society's mandate to advance and promote the molecular understanding of biology. We have advanced on several topics and advocacy work continues to be our highest priority. We have also revised our website, and the trainees now play key roles for the operation of our society. This is most important, since training and encouraging the next generation of scientists remains one of our key mandates, especially in times when budgetary challenges are preoccupying many of our members.

1. Website and social media. Our website has just been updated, giving it a much more appealing and contemporary look, check it out at http://csmb-scbm.ca/. We are now also well represented in social media (Facebook, Twitter) where we hope to provide value, rapid communication of information and of opportunities for feedback to our members.

2. Trainee involvement. The newest additions to the board of the CSMB are representatives of postdoctoral fellows and of graduate students. Their initiatives aimed at increasing trainee involvement take an increasing place in our work, as they should. The board has also decided to increase its support for scientific and social events organized by graduate students and postdoctoral fellows. These are very worthy investments into the advancement of the next generation of scientists, who will hopefully get involved in the society and help us shape what we do for them.

3. Advocacy work. The next federal election is due in October 2015. All political parties are in the progress of preparing their election platforms, and the next federal budget will be presented soon. It is therefore most important that the society, as well as individual scientists, make their voices heard now in order to educate decision makers about the challenges faced by the scientific community. In December 2014, we wrote to the Prime Minister of Canada as well as to the Ministers of Industry and Health, to the leaders of the opposition parties, and to the spokespersons for Science and Technology of the NDP and the Liberal Party of Canada. The key propositions of the CSMB remain steady; 3% annual increases of CIHR and NSERC budgets targeted to open competitions, continuation of support for the CFI, reinstatement of the NSERC RTI grant program, and a marked increase of the indirect cost program supporting research at institutions. We have received encouraging feedback, and had a very interesting conversation in person with Ted Hsu, the Liberal critic for Science and Technology. We have also

received meaningful responses from the Office of the Prime Minister and from the Minister of Industry James Moore and the Minister of State (Science and Technology) Ed Holder.

It transpires from these interactions that politicians are simply not (sufficiently) aware of the fact that there are problems concerning research funding in Canada. It is urgent that we work to change this! We strongly encourage all our members, especially trainees who are the most impacted by this situation, to contact their Members of Parliament to make them aware of the constraints of research funding, which is leading to losses of jobs, research productivity and innovation. Full documentation of the exchanges with politicians, as well as suggestions to our members, are available on our website in the Advocacy section.

We have also initiated a dialogue with other scientific societies in Canada aimed at speaking with a coordinated voice in increasing numbers with similar messages. Our exchanges with the Canadian Society of Microbiologists, the Canadian Society of Immunology, and the Canadian Society of Pharmacology and Therapeutics are very encouraging. We should soon be able to speak up for scientists and trainees in Canada in a coordinated fashion.

4. National and international conferences. The upcoming CSMB conference at Dalhousie University in Halifax in June 2015 will have the topic “Lipids: The membrane and beyond”. Preparations and networking are intensifying for the following international conference in Vancouver in 2016. We are organizing this conference jointly with the International Union of Biochemistry and Molecular Biology (IUBMB) and the Pan-American Association for Biochemistry and Molecular Biology (PABMB). We expect more than 1000 participants at this conference! We hope that many of you will participate at this landmark event that will greatly increase the visibility of Canadian molecular biosciences at the international level.

I hope that our various activities continue to meet your interests and that they will convince you to renew your membership and to motivate your colleagues to join. It is even more important to make your voice heard by politicians; as citizens of this country we have all the liberty to do so. Strength is in our numbers; please use this opportunity to help put funding for research in Canada on the political map!

Incoming Members of the CSMB Executive Board

Philip Hieter

Philip Hieter, *Councillor*

Philip Hieter is a Professor in the Michael Smith Laboratories and Department of Medical Genetics at the University of British Columbia. He received his Ph.D. in biochemistry from Johns Hopkins University in 1981 (with Phil Leder), trained as a postdoctoral fellow at Stanford (with Ron Davis), and was a faculty member at the Johns Hopkins University School of Medicine from 1985 -1997, where he was promoted to full professor in 1994. He moved to the University of British Columbia in 1997, and served as Director of the Michael Smith Laboratories until 2008. Dr. Hieter served as President of the Genetics Society of America in 2012. He is currently Chair of the CIHR Planning and Priorities Committee "Models and Mechanisms to Therapies", and a Member of the Medical Advisory Board of the Gairdner Foundation. He is a Fellow of the Royal Society of Canada, Fellow of the Canadian Academy of Health Sciences, and Member of the American Academy of Arts and Sciences.

Dr Hieter is recognized for his work on structural and regulatory proteins that ensure faithful segregation of chromosomes during cell division, including seminal studies on yeast centromeres, sister chromatid cohesion, and regulation of cell cycle progression during mitosis. His laboratory has recently established an extensive genome instability gene catalog in yeast that provides a resource to identify cross species, candidate human genes that are somatically mutated and cause chromosome instability in cancer. He has also developed a strategy to identify genes in yeast synthetic lethal interaction networks as a means for identifying novel cancer drug targets. Throughout his career, his work has demonstrated and advocated the value of model experimental organisms for understanding mechanisms of human disease.

Mustapha Lhor

Anastassia Voronova

Mustapha Lhor, *Councillor*
(trainee representative)

Mustapha Llor obtained a B.Sc. (2006) and a M.Sc. (2010) in Biochemistry from the University of Bordeaux in France where he worked on mitochondrial polymerase peptide purification and wine yeast toxin characterization. He is currently a Ph.D. student (since 2012) at Université Laval, in the Cellular and Molecular Biology program under the supervision of Prof. Christian Salesse. He is working on the characterization of an enzyme of the retina, within monolayers as a model membrane system, at the CUO-recherche unit of the CHU de Québec. Mustapha participates in different activities related to science as a member of colloqium juries, organizing committees, student helper networks, etc. Thus, he was recognized by University Laval as *"Graduate Student Associations Personality"* in 2015.

Mustapha is also involved in the entrepreneurship sphere, as a student of the MBA pharmaceutical management program, and as councillor of the *Entrepreneuriat Laval* Board. Finally, he periodically presents a chronicle in a weekly scientific radio show *Futur simple* at the CKRL FM station.

By joining the CSMB board as a student representative, Mustapha aims to express at best the voice of students and trainees involved in research across Canada and to make this voice heeded.

Anastassia Voronova, *Councillor*
(trainee representative)

Anastassia Voronova obtained her Ph.D. degree from the University of Ottawa under the tutelage of Dr. Ilona Skerjanc, where she studied the transcriptional regulation of stem cell differentiation programs by Hedgehog signalling. Anastassia has since then transferred her expertise to the laboratory of Dr. Freda Miller at the Hospital for Sick Children in Toronto, where her research focuses on environmental and epigenetic regulation of brain stem cells, more specifically in the developing cortex. Anastassia is a recipient of CIHR, Multiple Sclerosis Society of Canada, and Hospital for Sick Children Research Training Centre postdoctoral fellowships.

As a CSMB post-doctoral fellow representative, Anastassia aims to increase the visibility of CSMB for Canadian graduate students and postdoctoral fellows, and to enhance their training experience through increased support of trainee-oriented events.

Minutes of the 57th Annual General Meeting 2014

Banff, Alberta – April 12, 2014

Attendees: Janice Braun, Jim Davie, Kristin Baetz, Christian Baron, David Williams, John Orlowski, Joseph Casey, Reinhart Reithmeier, Russell Bishop, Jan Rainey, Anastassia Voronova, Joe Weiner, Mustapha Lhor, Sarah Hughes, Peter Tieleman, Andrew Simmonds, Randall Johnston, Art Hilliker, Wafaa Antonious.

1. Greetings from the President (Simmonds)

Simmonds welcomed the attendees and called the meeting to order.

2. Approval of Quorum and Agenda

Johnston stated that quorum as requested in the bylaws was met.

Motion: Johnston made a motion to approve the agenda, seconded by Hilliker, all in favour, agenda approved.

3. Approval of the Minutes of 56th Annual General Meeting in Niagara-on-the-Lake, June 2013

Motion: Johnston made a motion to approve the 56th Annual General Meeting minutes, seconded by Simmonds, all in favour, minutes approved.

4. Business Arising from the Minutes (Johnston)

a) Approval of Society Constitution and Bylaws

Johnston explained that a special resolution is needed to approve the bylaws which has been revised and forwarded for approval to adhere to the new not-for-profit act regulations for bylaws. The special resolution requires a 2/3 approval of the attendees of the annual general meeting. Johnston explained that minor amendments will be done to the presented bylaws to adhere to the antispam legislation as well. The bylaws were circulated to the membership 48 hours before the meeting.

Special Resolution: Johnston made a motion for approval of the bylaws with minor amendments, a show of hands was requested for approval, all in favour, bylaws with minor amendments has been approved.

5. Secretary's Report (Johnston)

a) Membership

Johnston reported that the CSMB is one of the largest societies. The membership has been dwindling. We are in good shape, but we need to double our efforts to increase the membership.

6. Treasurer's Report (Hilliker)

a) Presentation of the Accountant's Reviewed Financial Statement

Hilliker presented the financial statement as prepared by Ms. Andrea Poole after conducting a review of engagement.

b) Acceptance of the Reviewed Financial Statement (2013)

Motion: Reithmeier made a motion to accept the financial statement, motion seconded by Rainey, all in favour, motion approved.

c) Approval of Signing Officers

Hilliker stated that Johnston and Hilliker are the signing officers, but the CSMB account is setup with only one to sign.

Motion: Orlowski made a motion to approve the signing officers, seconded by Williams, all in favour, motion approved.

7. Board Membership for 2014 - 2015 (Simmonds)

a) Councillors

Simmonds stated that Reithmeier is stepping down from the board as a councillor after many years of service. He thanked him for his efforts. Christian Baron will be the president and Kristen Baetz will be the 1st Vice President.

b) Graduate Student and Post-Doctoral Representatives

Simmonds reported that several applications were received for these positions, he asked if there were any nominations from the floor, none was received. He stated that Phil Hieter has accepted to join the board.

Motion: Casey made a motion to approve the nomination of the new board members, Baetz seconded the motion, all in favour, motion approved.

8. Future Meetings (Johnston)

Johnston stated that the board has been very active in the planning for future meetings.

a) 2015: Halifax; Membrane Lipids in Signaling and Regulation

Johnston commented that the meeting looks like it is well in hand.

b) July 16-23, 2016: Vancouver – Signaling Pathways in Development, Disease and Aging; in partnership with IUBMB & PABMB

Johnston reported that a professional conference organizer has been hired, and the conference has a science advisory committee.

c) 2017: Ottawa

Johnston reported that it will be in partnership with Systems Biology and will be held in Ottawa. Kristin Baetz, University of Ottawa will be involved in that meeting.

d) July 14-19, 2018: Vancouver – Genetic Horizons: Evolution, Development, Sustainability and Health; in partnership with IGF and GSA

Johnston stated that the same conference organizer who was hired to manage the 2016 international conference was also hired for the 2018 Conference. He reported that both meetings will break even if there are 1,000 registrants.

Simmonds thanked Johnston and Hilliker for bringing in two international conferences. Simmonds thanked Joe Casey and his local organizing committee for organizing the 2014 CSMB meeting.

9. Other Business/Adjournment

No other business.

Motion: Bishop made a motion to adjourn, meeting adjourned.

Financial Statement
STATEMENT OF FINANCIAL POSITION

As at DECEMBER 31, 2014 (with unaudited comparative figures as at December 31 3013)
UNAUDITED

	2014	2013
ASSETS		
CURRENT		
Cash	$ 6,142	$ 10,955
Accounts receivable - CSMB	8,194	11,977
Accounts receivable - GSC	-	741
Prepaid expenses	8,080	14,316
	22,416	37,989
INVESTMENTS (note 4)	403,956	409,275
	$ 426,372	$ 447,264
LIABILITIES		
CURRENT		
Accounts payable and accrued liabilities	$ 5,053	$ 15,807
Deferred membership and subscription fees	3,091	3,207
Deferred conference income	-	5,357
	8,144	24,371
LONG TERM		
Deferred membership fees	4,049	4,643
UNRESTRICTED NET ASSETS	414,179	418,250
	$ 426,372	$ 447,264

STATEMENT OF OPERATIONS AND CHANGES IN ASSETS

As at DECEMBER 31, 2014 (with unaudited comparative figures as at December 31 2013)
UNAUDITED

	2014	2013
REVENUE		
Membership dues	$ 24,653	$ 26,099
Corporate contributions	25,811	55,459
Annual meeting	47,030	25,896
Other	415	670
	97,909	108,124
Investment income	10,073	11,855
	107,982	119,979
EXPENSES		
Annual meeting (note 5)	85,125	117,544
Secretariat	16,930	16,160
Meeting sponsorship	6,000	11,892
Board meetings	14,500	11,455
Bulletin	4,549	6,381
Professional fees	2,300	3,293
Website	2,280	2,600
Bank and credit card fees	2,533	2,282
Science advocacy	19	2,019
Office	1,067	902
Dues and subscriptions	-	658
Membership drive	-	170
Insurance	1,794	73
	137,097	175,429
NET (EXPENSES) FOR THE YEAR	$ (29,115)	$ (55,450)
Unrestricted net assets at beginning of year	$ 418,250	$ 412,561
Balance before items affecting net assets	389,135	357,111
Gains from sale of investments - realized (note 3)	13,518	8,479
Gains on investments - unrealized (note 3)	11,526	52,660
UNRESTRICTED NET ASSETS AT END OF YEAR	$ 414,179	$ 418,250

STATEMENT OF CASH FLOWS

As at DECEMBER 31, 2014 (with unaudited comparative figures as at December 31 2013)
UNAUDITED

	2014	2013
CASH PROVIDED BY (USED FOR)		
OPERATING ACTIVITIES		
Cash from operations		
Net (expenses) revenue for the year	$ (29,115)	$ (55,450)
Non-cash portion of investment income	(10,073)	(11,855)
	(39,188)	(67,305)
Net change in non-cash working capital balances		
Accounts receivable	4,524	(1,258)
Conference deposit	6,236	7,684
Accounts payable and accrued liabilities	(10,754)	(2,775)
Deferred membership and subscription fees	(710)	819
Deferred conference income	(5,357)	5,357
	(45,249)	(57,478)
INVESTING ACTIVITY		
Transfer of funds from investment account	40,436	62,027
INCREASE (DECREASE) IN CASH	(4,813)	4,549
Cash, beginning of year	10,955	6,406
CASH, END OF YEAR	$ 6,142	$ 10,955
CASH POSITION		
Cash	$ 6,142	$ 10,955

NOTES TO THE FINANCIAL STATEMENTS

DECEMBER 31, 2014
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 the molecular biosciences in Canada.

2. SIGNIFICANT ACCOUNTING POLICIES

These financial statements are the responsibility of management and have been prepared in accordance with Canadian accounting standards for not-for-profit organizations (ASNFPO) using the accounting policies summarized below.

(a) 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.

(b) 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.

(c) Use of estimates

The preparation of the financial statements in conformity with Canadian accounting standards for not-for-profit organizations requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue and expenses and disclosure of contingent assets and liabilities. These estimates are reviewed periodically and adjustments are made to net revenue as appropriate in the year they become known.

(d) Financial Instruments

The Society initially measures its financial assets and financial liabilities at fair value. The Society subsequently measures all its financial assets and financial liabilities at amortized cost, except for investments in equity instruments that are quoted in an active market, which are measured at fair value. Changes in fair value are recognized in the statement of operations.

Financial assets measured at amortized cost include cash and accounts receivable. Financial liabilities measured at amortized cost include accounts payable.
The organization's financial assets measured at fair value include quoted shares.

3. FINANCIAL RISKS AND CONCENTRATION OF RISKS

The carrying values of cash, accounts receivable and accounts payable approximate their fair values due to the short-term nature of these assets and liabilities.

Marketable securities are comprised of bonds, money market investments and segregated mutual funds. These are initially recorded at fair value based on quoted market prices and are subsequently measured at fair value at each year end. Net gains and losses arising from changes in fair value are recognized in the Statement of Operations. For the year ended March 31, 2014, the net unrealized gain was $11,526 (March 31, 2013 unrealized gain was $52,660).

Fair value approximates amounts at which financial instruments could be exchanged between willing parties, based on current markets for instruments of the same risk, principal and remaining maturities. Fair values are based on quoted market values.

Unless otherwise noted, it is management's opinion that the Society is not exposed to significant interest, currency or credit risks arising from these financial statements.

4. INVESTMENTS (at Market Value)

CSMB investments are recorded at market value. As required by CICA Section 3856 unrealized gains or losses on the portfolio as a whole at December 31 are recorded as "Gains (losses) on investments - unrealized" and included on the Statement of Operations and Changes in Net Assets.

BMO Nesbitt Burns Canadian Account	**2014**	**2013**
Cash and short term investments	$ 30,670	$ 3,238
Fixed Income	52,360	53,194
Common equity	249,247	281,347
	332,277	337,779
BMO Nesbitt Burns US Account (in $ Canadian)		
Cash and short term investments	1,012	685
Common equity	70,667	70,811
	$ 403,956	$ 409,275

5. ANNUAL MEETING EXPENSES

	2014	**2013**
Exhibits and facility	$ 7,635	$ 64,722
Travel and Expenses	54,345	35,624
Awards	15,130	8,924
Organizing and planning	6,100	6,250
Supplies and other	1,914	2,024
	$ 85,124	$ 117,544

Meeting Report: The 57th Annual Meeting of the CSMB, Membrane Proteins in Health and Disease

Joseph R. Casey, Department of Biochemistry, and Membrane Protein Disease Research Group, University of Alberta, Edmonton, Canada, T6G 2H7
www2.biochem.ualberta.ca/CaseyLab/

The 57th Annual CSMB meeting and Conference on Membrane Proteins in Health and Disease was held April 9-13 2014 at the Banff Centre, Banff Alberta. The meeting attracted 175 attendees from across Canada, the United States, Germany, Ireland, the U.K., Denmark, and Australia, who heard talks from 29 leaders in the area of membrane protein biochemistry and cell biology. The meeting's organizing committee, comprising members of the University of Alberta's *Membrane Protein Disease Research Group*, plus Reinhart Reithmeier of the University of Toronto and the CSMB Board, put together a program with seven plenary sessions (more below). In addition, the meeting featured nine short talks from speakers drawn from abstract submissions, as well as 86 posters, presented in two sessions.

This packed meeting also included CSMB award lectures (more below), a presentation by **Sylvie Roy** of NSERC about funding opportunities and an Honorary Lecture from **Reinhart Reithmeier**. Did we mention that the weather cooperated and spring skiing was great, too?

This meeting focused on the special group of "greasy" proteins that are embedded in membranes. These integral membrane proteins have distinct properties from soluble proteins, from their biosynthesis, to folding, degradation, structure, cellular roles and the diseases caused upon their failure. This meeting captured all of these topics. The inspiring setting overlooking Banff and its mountains left meeting attendees in a receptive frame of mind and terrific discussions were heard in and out of meeting sessions.

Satellite Meetings- The main meeting was orbited by two satellite meetings, before the start of the main meeting. The first, organized by **Joanne Lemieux** (Dept. of Biochemistry, University of Alberta) featured six talks on the topic "Overcoming Barriers to Membrane Protein Structure" and was attended by about 60 people. The second, organized by **Larry Fliegel, Joe Casey** and **Todd Alexander** of University of Alberta, was on "pH Regulation at the Cell Surface".

Keynote lecture- The opening keynote lecture was given by **Tom Rapoport** of Harvard Medical School. Tom's artfully-presented talk "Mechanisms of protein transport across membranes" wonderfully set the stage for the whole meeting, with his detailed description of the

events surrounding the birth of membrane proteins at the endoplasmic reticulum.

Honorary lecture- Reinhart Reithmeier presented a very entertaining lecture, targeting trainees in the audience. The talk described Reinhart's very successful career and lessons he learned that have guided him along the way. Reinhart's lecture has now been published [see (1), and this Bulletin] for anyone wanting an interesting view of a thoughtful scientist's career.

CSMB Award Lectures- Janet Rossant (Hospital for Sick Children, University of Toronto) presented her Arthur Wynne Gold Medal lecture, "A Developmental Journey", which highlighted her path to becoming one of the country's most celebrated scientists. Jeanne Manery Fisher Memorial Lectureship Award winner, **Susan Lees-Miller** (University of Calgary), presented the lecture "Structural and functional insights into the repair of radiation induced DNA damage". **James McGhee** (University of Calgary) was awarded the NRC Press Senior Investigator Award, lecturing on the topic "Development and Aging in the *C. elegans* intestine". The Robert Haynes Young Scientist in Genetics award winner was **François Bachand** (Université de Sherbrooke), who presented a lively talk on "Nuclear surveillance of coding and non-coding transcriptomes". **John Rubenstein**, GE Healthcare New Investigator Award winner, presented beautiful work on "Electron microscopy of rotary ATPases".

Plenary Sessions-

Novel Insights from Membrane Protein Structural Biology- This opening session made it clear what a huge growth area the structural biology of membrane proteins is. **Natalie Goto** (University of Ottawa) illustrated the benefits of NMR in studying membrane proteins. The next four talks strongly made the case that era of X-ray crystallography of membrane proteins is finally upon us. **Natalie Strynadka** (University of British Columbia) beautifully laid out the bacterial cell wall biosynthetic pathway in a series of structures. **Susan Buchanan** (N.I.H.) provided structural insights in the biosynthesis of bacterial β-barrel proteins. **Martin Caffrey** (Trinity College, Dublin) gave a truly encouraging talk on crystallizing membrane proteins using lipidic mesophases. **Alexander Cameron** (University of Warwick) illustrated the power of structural biology in explaining protein mechanism. His talk used the structures of four different membrane transport proteins to illustrate commonality of transporter structure and how this links to transporter mechanism.

Membrane Protein Biogenesis and Folding- Biosynthesis of membrane proteins is complex and distinct from soluble membrane proteins. Three talks provided the audience with a powerful update on the details of membrane protein biosynthesis and trafficking. **Elizabeth Conibear** (University of British Columbia) described the role of escort proteins and palmitoylation in membrane protein trafficking, using elegant experiments in yeast. Together **Johannes Herrmann** (Technical University Kaiserslautern, Germany) and **Richard Zimmerman** (Saarland University) provided great detail on events at the endoplasmic reticulum during biosynthesis, focusing on luminal disulfide bond formation and detailed roles of SEC61 complex proteins, respectively.

Molecular Events in the Immune Response- **Nicolas Touret** (University of Alberta) began the session with state-of-the-art studies illustrating how fluorescent microscopy approaches can be used to track single molecule events in immune cell signaling. **Sergio Grinstein** (Hospital for Sick Children, University of Toronto) described in crystal clear fashion complex experiments following the pH of organelles during phagosome activation. **Robert Tampé** (Biocenter of Goethe University, Germany) described multi-faceted experiments on the TAP transporter, which is responsible for loading the major histocompatibility antigen with peptide substrates. **Bebhinn Treanor** (University of Toronto) also described experiments using single particle tracking to study signaling in B-cell activation.

The Many Faces of Calcium Transport- This session explained the transport mechanisms controlling cytosolic and organellar calcium level, which provided a case study in the role of integral membrane proteins in controlling gradients across membranes. **Howard Young** (University of Alberta) explained the role of phospholamban (PLB) in regulating the sarco-endoplasmic reticulum Ca2+-ATPase and how defects in PLB cause disease. **Veit Flockerzi** (Saarland University, Germany) described recent studies of TRP Ca2+ channels. **Todd Alexander** (University of Alberta) described his recent studies linking defects in Ca2+ movement to development of kidney stones. **Jutta Engel** (Saarland University, Germany) highlighted the importance of calcium channels in signal transduction linked to hearing.

There is Nothing Basic about pH Regulation- A case study in the roles of transport proteins in homeostatic regulation focused on pH regulatory transporters. **Andrew Halestrap** (University of Bristol, U.K.) provided a clear and complete review of monocarboxylate transporters. **Christian Stock** (University of Münster, Germany) described how distinct cell surface localization of pH regulatory transporters can lead to development of pH gradients in cells, with important roles in cell signaling. **Danielle Johnson** (Hospital for Sick Children, Toronto) provided further description of pH gradients established in cells by the plasma membrane Cl-/HCO3- exchanger, AE1.

Membrane Proteins in Need of Therapy- Mutations of membrane proteins are a common cause of human genetic disease. The difficult biosynthesis of membrane proteins leaves them especially vulnerable to misfolding from minor mutations. In this session **Paul Linsdell** (Dalhousie University) and **John Hanrahan** (McGill University) described their studies of CFTR, an ion channel protein whose mutations cause cystic fibrosis. Paul discussed conformational changes during the channel's gating and John described how physiological bicarbonate secretion is impacted in cystic fibrosis. **Wayne Chen** (University of Calgary) described studies of the massive ER calcium release channel, the ryanodine receptor, and how its mutations can lead to cardiac arrhythmia. **William Balch** (The Scripps Research Institute) picked up the theme of membrane protein misfolding, describing the disease consequences of accumulation of misfolded proteins.

Cool Approaches in Membrane Biology- Ending the meeting was a session on the latest approaches being applied to membrane proteins. **Nevin Lambert** (Georgia Regents University) described a clever and exciting approach to study organellar location of membrane proteins, using bioluminescence resonance energy transfer (BRET). **John Rubinstein** (University of Toronto) showed the progress he is making on understanding rotary ATPases, using cryo-electron microscopy. **Philip Van Petegem** (University of British Columbia) presented remarkable images of the structure of the 2.2 MDa ryanodine receptor. **Michael Overduin** (University of Birmingham) showed new approaches to study membrane protein structure by NMR, with new detergents and new computational methods.

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This report was published previously: Biochem. Cell Biol. 2014 92: 425-426.
(http://www.nrcresearchpress.com/journal/bcb; doi: 10.1139/bcb-2014-0131)

Scenes from the 57th Annual Meeting Banff, 2014

James McGhee (University of Calgary) receives the NRC Research Press Senior Investigator Award from Christian Baron, President of the CSMB (2014-2015)

Susan Lees-Miller (University of Calgary) is presented with the Jeanne Manery Fisher Memorial Lecture Award by Randy Johnston, Secretary of the CSMB

A representative of GE Healthcare presents the GE Healthcare New Investigator Award to John Rubinstein (Hospital for Sick Children)

Janet Rossant (Hospital for Sick Children) receives the Arthur Wynne gold medal from Andrew Simmonds, Past President of the CSMB (2013-2014)

The Robert H. Haynes Young Scientist Award in Genetics is presented to François Bachand (Université de Sherbrooke) by Art Hilliker, Treasurer of the CSMB

CSMB Executive Board members attending the meeting

Oxford Cryosystems exhibitor booth

The vendor displays attracted much attention

John Orlowski (McGill) and Nicolas Touret (Alberta)

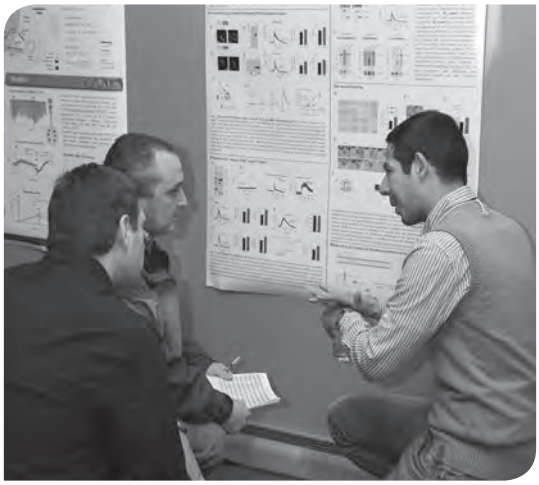
Meeting organizer Joe Casey (Alberta) introduces keynote speaker Reinhart Reithmeier (Toronto)

Wayne Chen (Calgary) and Alexander Cameron (Warwick) engaged in animated discussion

AE1 researchers discuss the latest results on their favourite protein

Lively debate at the poster sessions

Lively debate at the poster sessions



Lively debate at the poster sessions

Lively debate at the poster sessions

Lively debate at the poster sessions

Lively debate at the poster sessions

Lively debate at the poster sessions

Time for a glass of wine or beer at the posters

Membrane Proteins in Health and Disease
CSMB 57th Annual Meeting
The Banff Centre, April 9-13, 2014

Group photo of the meeting participants

Poster and Travel Award Recipients
2014 CSMB Annual Scientific Meeting, Banff, AB

POSTER PRIZES

AWARDEE	UNIVERSITY	SUPERVISOR
Jake Duerckson Poster Award in Cell Biology		
Amira Fitieh	University of Alberta, Edmonton	Dr. Nicolas Touret
Margaret Thompson Poster Award		
Anouar Belkacemi	Saarland University, Saarbrücken, Germany	Dr. Veit Flockerzi
Anatrace Poster Awards		
Huan Bao	University of British Columbia, Vancouver	Dr. Franck Duong
Matthew Patterson	University of Calgary, Calgary	Dr. Elmar Prenner
CSMB Poster Awards		
Radu Avramescu	McGill University, Montréal	Dr. Guido Veit
Linda Forero Quintero	University of Kaiserslautern, Kaiserslautern, Germany	Dr. Holger Becker

TRAVEL AWARDS

AWARDEE	UNIVERSITY	SUPERVISOR
CSMB Travel Awards		
Michael Carson	University of British Columbia, Vancouver	Dr. Franck Duong
Nigel Chapman	Dalhousie University, Halifax	Dr. Jan Rainey
Charneal Dixon	McMaster University, Hamilton	Dr. Russell Bishop
Fraser Ferens	University of Manitoba, Winnipeg	Dr. Deborah Court
Vanessa Marensi	University of Alberta, Edmonton	Dr. Elaine Leslie

Poster award winners (from left to right); Linda Forero Quintero, Amira Fitieh, Radu Avramescu, Huan Bao, and Anouar Belkacemi (missing from photo, Matthew Patterson)

Travel Award winners (from left to right); Vanessa Marensi, Nigel Chapman, Fraser Ferens, and Michael Carson (missing from photo, Charneal Dixon), Andrew Simmonds (Past-President), and CSMB Trainee Representatives Anastassia Voronova and Mustapha Llor

2015 CSMB Award Designates

GE Health Care New Investigator Award

Vincent Archambault, IRIC/Université de Montréal

Vincent Archambault is a principal investigator at the Institute for Research in Immunology and Cancer (IRIC) and an Assistant Professor in the Department of Biochemistry and Molecular Medicine at the Université de Montréal. After completing his B.Sc. in this department in 1999, Dr. Archambault obtained his Ph.D. in 2004 at the Rockefeller University in New York City, under the supervision of Mike Rout and Fred Cross. He then conducted post-doctoral research as an EMBO and HFSP fellow in the lab of David Glover in the Department of Genetics at the University of Cambridge, UK. Dr Archambault launched his group in 2009, with the aim of dissecting the molecular mechanisms controlling the cell cycle using *Drosophila* as a model.

NRC Research Press Senior Investigator Award

Michael James, Department of Biochemistry, University of Alberta

Michael James is an Emeritus Distinguished University Professor in the Biochemistry Department at the University of Alberta. He earned his doctorate in 1966 from Oxford University where he studied under the guidance of the late Nobel Laureate Professor Dorothy Hodgkin, O.M., F.R.S. His research career extends over 47 years at the University of Alberta. He is one of the founding members of the longstanding, celebrated MRC (now CIHR) Group in Protein Structure and Function at the University of Alberta. Dr. James is a structural biologist who uses macromolecular X-ray crystallography as his primary research tool. His major areas of research interest currently are: proteolytic enzymes and their protein inhibitors; glycolytic hydrolases and the enzymic mechanisms of carbohydrate hydrolysis; and the development of antiviral agents. In addition, Dr. James' group is involved in the Structural Genomics Consortium on Myobacterium tuberculosis. With the worldwide upsurge of antibiotic resistance to the isolates of this organism (MDR TB and XDR TB), the identification of new targets for antibiotic design against this diabolical organism is of paramount importance.

In the field of the glycosyl hydrolases, the James' laboratory has turned their interest to lysosomal storage diseases. In particular the group has determined the structures of β- hexosaminidases A and B, the two enzymes in which mutations are behind the genetic diseases, Tay-Sachs disease and Sandhoff Disease, respectively. More recently the group has determined the structure of α-L-iduronidase, the mutants of which are the cause of Mucopolysaccharidosis type I. Not only did this research determine the native structure, but also the structure of α-L-iduronidase in the presence of several different iduronyl derivatives has allowed for the determination of the enzymatic mechanism of α-L-iduronidase. Dr. James was elected a Fellow of the Royal Society of London in 1989 and a Fellow of the Royal Society of Canada in 1985.

Robert H. Haynes Young Scientist Award in Genetics

Luigi Bouchard, Department of Biochemistry, Université de Sherbrooke

Dr. Bouchard holds the position of Associate Professor of genetics and epigenetics at the Department of Biochemistry, Faculty of Medicine and Health Sciences, Université de Sherbrooke and is head of the Department of Molecular Biology and Genetics at the university-affiliated Chicoutimi Hospital. After his Ph.D. studies in genetic epidemiology at Université Laval under the mentorship of Dr. Louis Pérusse, he completed post-doctoral fellowships in transcriptomics (Dr. Marie-Claude Volh, CHU de Québec) and epigenomics (Dr. Arturas Petronis, University of Toronto). From 2008 to 2010, he was Assistant Professor, Department of Medicine, Université de Montréal. Since 2009, he has been leading a research group dedicated to understanding how epigenetic mechanisms are involved in the development of obesity, diabetes and cardiovascular disease, and identifying causal epigenetically-modified genes. His group is at the forefront of this growing field of research. With its analyses of specific obesity, diabetes and lipid candidate genes and the use of state-of-the-art analytical methods to survey a large fraction of the epigenome, this group was the first to report that maternal hyperglycemia and familial hypercholesterolemia are associated with DNA methylation changes (a central epigenetic mechanism) in several genes with many of them being involved in metabolic and cardiovascular disease pathways. He now has the goal to demonstrate that these epigenetic changes could explain why some children have an increased risk of developing obesity and diabetes, according to the Developmental Origin of Health and Disease (DOHaD) hypothesis, and to identify new markers for cardiovascular disease.

Grant and Moens Award of Excellence in Genetics

Graham Scoles, Department of Plant Sciences, University of Saskatchewan

Dr. Graham Scoles is currently a Professor in the Department of Plant Sciences and Associate Dean (Research and Graduate Studies) at the University of Saskatchewan. Dr. Scoles grew up on a small farm in England. He received his undergraduate education in Plant Science at the University of Reading, U.K., where he developed an interest in crop evolution and plant breeding. He worked for a year at the Plant Breeding Institute, Cambridge, and while there was offered a graduate student position by a visiting scientist from the University of Manitoba. Dr. Scoles obtained his M.Sc. and Ph.D. in plant breeding from the University of Manitoba in 1979, and immediately joined the University of Saskatchewan as a cytogeneticist. His teaching and research have been in the area of biotechnology as it applies to plant breeding, particularly the development and application of molecular markers. Dr. Scoles coordinated one of the early crop-based Genome Canada programs, and served in a number of roles on the Executive of the Genetics Society of Canada, including President. He has also served as Chair of the North American Agricultural Biotechnology Council. In 1993 he was appointed an Associate Editor for Genome, the Canadian cytogenetics/genomics journal, and now serves as Co-Editor.

2014 GE Healthcare New Investigator Award

Structure determination for membrane protein complexes by cryo-EM

John L. Rubinstein
The Hospital for Sick Children Research Institute

Abstract

Determining the structure of a protein or protein complex is an important first step in understanding how the protein works. However, structure determination is often a bottleneck in studies of a macromolecular assembly. Single particle electron cryomicroscopy (cryo-EM) offers an alternative to X-ray crystallography and NMR spectroscopy for structure determination. In principle cryo-EM should be able to determine the structure of any specimen with a well-defined structure that can be purified. Until recently, the compromise was that cryo-EM structures tended to be at significantly lower resolution than structures from other techniques. This limitation was particularly true for membrane protein complexes, which present extra complications for specimen preparation. New technology promises to increase the resolution of single particle cryo-EM, firmly establishing the technique as a mainstay of modern structural biology.

The electron microscope as tool to study biomolecular structure

Electron microscopy is not new. The first transmission electron microscope was constructed in 1931 in Berlin by Ernst Ruska and Max Knoll. This invention came just seven years after Louis de Broglie proposed (in his PhD thesis) that electrons could act as waves. The story of electron microscopy has a distinct Canadian angle, with the first electron microscope in North America, sometimes referred to as the world's first practical instrument, built in 1938 in the physics department at the University of Toronto.

Since the 1990s, electron microscopes equipped with field-emission sources have been limited by aberrations in magnetic lenses to ~2 Å resolution. Recent developments in aberration correction have allowed modern instruments to approach ~0.5 Å resolution, sufficient to resolve the details of inter-atomic bonding in inorganic materials. In biology, atomic structures of proteins can be deduced at significantly lower resolutions if the amino acid sequence of the protein is known. By producing maps of proteins or protein complexes at ~3.5 Å the known sequence of amino acids can be docked into the map to produce an atomic resolution model. Currently,

maps of proteins at these resolutions are typically obtained by X-ray crystallography of 3D protein crystals. However, growing 3D crystals of proteins can be difficult for large, unstable, scarce, or membrane-intrinsic protein complexes. Structure determination by NMR spectroscopy is limited to proteins of relative low molecular weight.

The electron microscope should be an ideal tool to determine the high-resolution structures of macromolecules without the need for 3D crystals, an approach known as single particle EM. In single particle cryo-EM [1], purified protein complexes are embedded in a thin film of ice and imaged in the electron microscope. The specimen is produced by rapidly freezing protein solution spread on an EM grid so that the water in the solution forms vitreous or amorphous ice that mimics the liquid water environment of the protein. However, using transmission electron microscopy to study the structure of biological macromolecules faces a fundamental limitation. The highly energetic electrons needed to form a transmission image destroy the structures of the molecules that they are used to image. This damage places strict maxima on the electron exposure that can be used to form an image, limiting the signal-to-noise ratio so that high-resolution features cannot be observed in images of isolated single particles of macromolecules.

This limitation can be surpassed by averaging different images. When identical views of identical particles are averaged, the signal in the images is correlated while the noise is uncorrelated and should average to zero. This approach still requires that all possible measures be taken to increase the signal-to-noise ratio available from the low-exposure images. Embedding the specimen in a thin layer of vitreous ice not only preserves the specimen in a near-native state but has the added advantage that it also limits certain mechanisms of radiation damage and increases the allowable electron exposure [2]. Use of a field-emission electron microscope allows high-resolution signal to be recovered from images obtained under the far-from-focus conditions needed to produce phase contrast. Detectors with a high detective-quantum-efficiency allow for maximum possible signal to noise ratio in low-exposure images.

Cryo-EM for membrane protein structures: rotary ATPases

Some of the first biomolecular structures studied by cryo-EM were membrane proteins. Richard Henderson and Nigel Unwin revolutionized our understanding of biological membranes by showing that bacteriorhodopsin forms an α-helical structures in lipid bilayers [3]. This pioneering structural work at 7 Å resolution in 1975 was continued by Henderson for more than fifteen more years in order to produce an atomic model of bacteriorhodopsin in 1990 [4]. These successes were made possible by the fact that bacteriorhodopsin forms a well-ordered two-dimensional crystal in lipid bilayers so that electron diffraction methods could be employed to increase the signal-to-noise ratio of images.

My own group has emphasized the structural study of rotary ATPases by single particle cryo-EM. Rotary ATPases are large membrane-bound protein complexes that convert energy stored in the form of ATP into a transmembrane proton motive force and vice versa. The most famous of these enzymes in the F-type ATP synthase found in the inner membranes of mitochondria. These enzymes makes the cell's supply of ATP [5]. However, there are other related enzymes, such as the vacuolar-type ATPases (V-ATPase) that use free energy from ATP hydrolysis to acidify intracellular compartments in all eukaryotic cells and the extracellular environment in some specialized cells. There are also distinct rotary ATPases in archaea and a few eubacteria, which some call V/A-ATPases, that appear to be similar to V-ATPases in subunit composition and structure but tend to function as ATP synthases in those organisms.

For single particle cryo-EM, membrane proteins present extra complications compared to soluble protein, as they do in many experiments [6]. In most cases, membrane protein complexes have been studied by cryo-EM in the presence of detergents. The use of detergents necessitates that extra care be taken in preparing specimens in order to suitably spread complexes on the EM grid. In my own laboratory, we have found that we obtain our best images when we nano-fabricate our own specimen grids instead of purchasing pre-fabricated grids, in order to maintain the highest possible level of control over the grid surface properties [7]. Using this approach and others we have developed in the laboratory, we have been able to obtain cryo-EM maps of a variety of rotary ATPases (Figure 1). These maps include a model at ~18 Å for the bovine ATP synthase [8], a map of the yeast V-ATPase at ~11 Å resolution [9], and a map of the *Thermus thermophilus* V/A-ATPase at ~9.7 Å resolution [10].

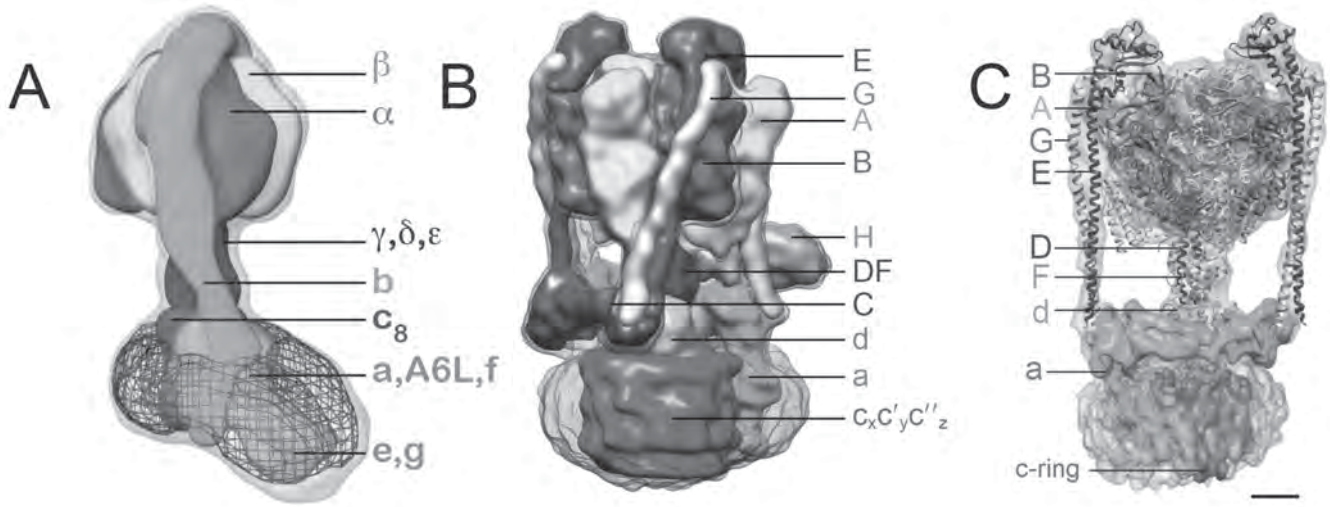


Figure 1. The structures of three rotary ATPases by electron cryomicroscopy.
Different subunits are shown in different colours and labelled with the subunit name. (A) The F-type ATP synthase from bovine heart mitochondria is responsible for the synthesis of ATP from ADP and inorganic phosphate. (B) The vacuolar-type ATPase from *Saccharomyces cerevisiae* maintains the pH of acidic intracellular compartments. (C) The V/A-type ATPase from *Thermus thermophilus* makes the supply of ATP in that organism. The scale bar corresponds to 25 Å.

Each of these maps has led to different insight. The bovine ATP synthase structure gave insight into how this mitochondrial protein complex is involved in the sharp bending of the inner mitochondrial membranes of cristae. The yeast V-ATPase structure suggested how ATP hydrolysis is regulated through a previously established dissociation mechanism. The *T. thermophilus* V/A-ATPase structure lent support to a proposal for how transmembrane proton translocation is coupled to rotation in rotary ATPases.

New technology drives higher-resolution structures

Until recently, the best detector that could be used for cryo-EM of radiation sensitive specimens was photographic film. Film allowed atomic models of icosahedral virus particles to be calculated from cryo-EM maps at better than 3.5 Å resolution [11]. It also allowed us to calculate our map of the *T. thermophilus* V/A-ATPase at ~10 Å resolution, sufficient to resolve some of the α-helices in the structure [10]. However, most structures were not at these resolutions, leading single particle cryo-EM to be dismissed as "blobology" by many structural biologists. A new generation of monolithic active pixel sensors, known as direct electron detectors, promises to change this. These detectors have significantly improved detective quantum efficiency compared to photographic film. What is more, the detectors can be read out as quickly as one desires, allowing for the creation of a movie instead of a single exposure. This movie mode of image acquisition has revealed that cryo-EM specimens undergo a beam-induced movement [12]. Fortunately, by recording a movie, one can also correct for this beam-induced movement.

Already, direct detectors, although only in use by a few groups so far, have revolutionized cryo-EM. Maps of membrane protein complexes like the TRPV1 channel have been calculated at 3.4 Å resolution [13] while a map of the 20S proteasome reached 3.3 Å resolution [14]. Cryo-EM of the mitochondrial ribosome has lead to a structure at 3.2 Å resolution [15] with reports of even higher resolutions progress. It has long been a dream of cryo-EM to obtain atomic resolution structures of protein complexes without the need for first growing 3D crystals. It seems that the next few years, biology will see this dream become reality.

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2014 Jeanne Manery Fisher Memorial Lecture

DNA-dependent protein kinase catalytic subunit (DNA-PKcs): uncovering roles in DNA double strand break repair and mitosis

Susan P. Lees-Miller
Department of Biochemistry and Molecular Biology, Southern Alberta Cancer Research Institute, University of Calgary

Abstract

The human genome encodes approximately 500 protein kinases that are involved in almost every aspect of cellular function (Manning et al. 2002). Among these is a family of large serine/threonine protein kinases, the catalytic domain of which bears amino acid similarity to the catalytic subunit of phosphatidylinositol 3 kinase (PI3K) (Hartley et al. 1995; Hunter 1995). These "atypical" protein kinases, termed the phosphatidylinositol-like protein kinases or PIKKs, include the DNA-dependent protein kinase catalytic subunit (DNA-PKcs), ataxia-telangiectasia mutated (ATM) and ATM- and Rad3 -related (ATR) that are involved in the detection and repair of DNA strand breaks (DSBs) (Abraham 2004; Lempiainen and Halazonetis 2009). Here, I will recount our work on the discovery and characterization of DNA-PKcs and elucidation of its role in the repair of DNA damage, as well as our recent studies revealing new roles for DNA-PKcs in mitosis.

Abbreviations: ATM, ataxia telangiectasia mutated; ds, double stranded; DSB, DNA double strand break; DNA-PKcs, DNA-dependent protein kinase catalytic subunit; IR, ionizing radiation; NHEJ, non-homologous end joining; PIKK, phosphatidylinositol 3 kinase like protein kinase; PP6, protein phosphatase 6

The first hint that human cells contained a DNA-activated protein kinase came from studies by Anderson and Carter who reported that extracts from human cells contained a protein kinase activity that was stimulated by the presence of double stranded (ds) DNA (Carter et al. 1990; Carter et al. 1988; Walker et al. 1985). One of the first substrates of this putative protein kinase to be identified was the 90-kDa heat shock protein, hsp90 (Lees-Miller and Anderson 1989; Walker et al. 1985). Using hsp90 as an in vitro substrate, we partially purified a DNA-activated protein kinase activity, that we termed DNA-PK, and identified a large polypeptide that we initially called p350 (now known as DNA-PKcs) and the Ku70/80 heterodimer (Ku), a protein previously shown to bind with high affinity to ends of dsDNA (Lees-Miller et al. 1990). This protein kinase activity also phosphorylated transcription factor Sp1 (Jackson et al. 1990) and the tumour suppressor protein, p53 (Lees-Miller et al. 1992). In each case, the phosphorylated amino acid (serine or threonine) was followed by a glutamine, thus the protein kinase consensus sequence became known as an SQ/TQ motif (O'Neill et al. 2000). Subsequently, Ku was shown to recruit p350/DNA-PKcs to ends of dsDNA and the interaction of DNA-PKcs with Ku and dsDNA was shown to stimulate its protein kinase activity (Gottlieb and Jackson 1993). So by the mid 1990's,

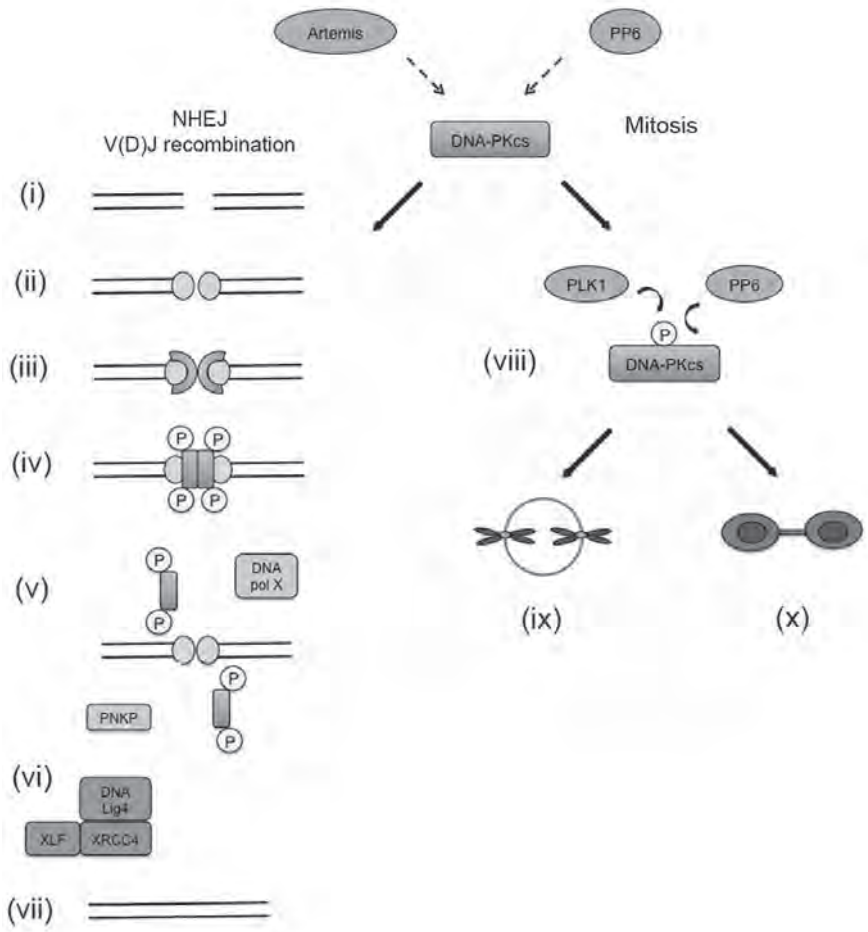

Figure 1: The roles of DNA-PKcs in DNA double strand break repair and mitosis

DNA-PKcs is a member of the PIKK family of serine threonine protein kinases with a well established role in the non-homologous end joining (NHEJ) pathway for the repair of DNA double strand breaks (DSBs). (i) DSBs can be formed either by DNA damaging agents such as ionizing radiation (IR) or during the process of V(D)J recombination in the vertebrate immune system. In both cases, DSBs are detected by the Ku70/80 heterodimer, which binds to the ends of the DSB (ii). Ku plays a key role in NHEJ, being responsible for multiple downstream proteins, including DNA-PKcs (reviewed in detail in Wang and Lees-Miller 2013)). (iii) DNA-PKcs is recruited to the DSB end, displacing Ku70/80 inwards. (iv) DNA-PKcs undergoes extensive autophosphorylation, which in vitro has been shown to induce large conformational changes and promote release of phosphorylated DNA-PKcs from the Ku-DNA complex (Dobbs et al. 2010; Hammel et al. 2010b). (v) DNA end processing enzymes such as polynucleotide kinase/phosphatase (PNKP) and DNA polymerases mu and/or lambda of the pol X family are also recruited to the DSB as is (v) the XRCC4-DNA ligase 4-XLF complex, which seals the DSB ends (vii). XRCC4 and XLF form long helical filaments (not shown) that may facilitate bridging of ends prior to ligation (Hammel et al. 2011; Hammel et al. 2010a). DNA-PKcs also interacts with Artemis (top, dashed lines) a nuclease that, with DNA-PKcs, facilitates DNA hairpin cleavage in V(D)J recombination (Goodarzi et al. 2006). The role of Artemis in repair of IR induced DSBs is not yet known. DNA-PKcs also interacts with protein phosphatase 6 (PP6, top, dashed lines) (Douglas et al. 2010). Recent studies have shown that DNA-PKcs also undergoes autophosphorylation on multiple sites in mitosis (Douglas et al. 2014; Lee et al. 2011). DNA-PKcs is phosphorylated on serine 3205 in mitosis by polo-like kinase (PLK1), which is dephosphorylated by PP6 in mitosis and after IR (Douglas et al. 2014) (viii). Via mechanisms that remain to be elucidated, DNA-PKcs is required for correct alignment of mitotic chromosomes on the metaphase plate (ix) and for cytokinesis/abscission (x) (Douglas et al. 2014; Lee et al. 2011). Our recent results suggest that the mechanism of activation of DNA-PKcs in mitosis may be distinct from that in NHEJ (Douglas et al. 2014).

the biochemical activity of DNA-PK had been defined, but its function was less clear, and roles in regulation of transcription, detection of pathogenic DNA as well as repair all seemed possible.

The breakthrough in understanding the function of DNA-PK came when Stamato and colleagues showed that Ku80 was absent in a radiation-sensitive, DNA double strand break repair-defective rodent cell line, xrs6 (Getts and Stamato 1994), a cell line that had been identified several years earlier by Kemp and Jeggo (Kemp and Jeggo 1986). Subsequently, we showed that DNA-PKcs was absent from a radiation-sensitive, DSB repair-deficient human cell line, M059J (Lees-Miller et al. 1995), and the role of both Ku (Taccioli et al. 1994) and DNA-PKcs in the repair of radiation induced DNA double strand breaks was established. At the same time, Brown and colleagues identified p350/DNA-PKcs as the gene mutated in mice with severe combined immunodeficiency (SCID) (Kirchgessner et al. 1995). Indeed, these mice had previously been shown to be not only immune deficient but also radiation-sensitive and DSB repair-deficient (Biedermann et al. 1991; Fulop and Phillips 1990). These, and other studies by our group as well as others in the field, established that DNA-PKcs and Ku are required for the repair of ionizing radiation (IR)-induced DSBs by the process of non-homologous end joining (NHEJ) (Mahaney et al. 2009; Wang and Lees-Miller 2013), as well as repair of programmed DSBs that occur in the immune system via the process of V(D)J recombination (Helmink and Sleckman 2012) (Figure 1).

The protein kinase activity of DNA-PKcs is required for NHEJ (Kurimasa et al. 1999) and small molecule inhibitors of DNA-PKcs' kinase activity sensitize cells to radiation and inhibit NHEJ (Zhao et al. 2006), thus a question that has intrigued us for many years has been "What are the physiological substrates of DNA-PK?" We showed that most of the proteins involved in NHEJ, including DNA-PKcs (Douglas et al. 2002), Ku70, Ku80 (Douglas et al. 2005), XRCC4 (Yu et al. 2003), XLF (Yu et al. 2008), PNKP (Zolner et al. 2011) and Artemis (Goodarzi et al. 2006) were phosphorylated in vitro by DNA-PK. However, although many of these proteins were phosphorylated in vivo in response to DNA damage, in most cases, the protein kinase responsible for phosphorylation in vivo was the related kinase ATM, rather than DNA-PKcs. The exception was DNA-PKcs itself. We identified multiple in vitro autophosphorylation sites in DNA-PKcs and showed that many are phosphorylated in vivo in response to DNA damage (Douglas et al. 2007; Meek et al. 2007). Phosphorylation of many of these sites was DNA-PK dependent in vivo suggesting that these sites are autophosphorylated in vivo. However, some sites can also be phosphorylated by other members of the PIKK family, ATM and ATR (Yajima et al. 2009). The most well-characterized autophosphorylation sites in DNA-PKcs are termed the ABCDE cluster, located between threonine 2609 and threonine 2647. Ablation of the ABCDE phosphorylation sites induces radiation sensitivity and inhibits DSB repair and V(D)J recombination indicating that they are important for DNA-PK function in vivo (Ding et al. 2003; Neal and Meek 2011). In vitro, autophosphorylation results in loss of DNA-PK kinase activity and dissociation of DNA-PKcs from the Ku-DNA complex (Chan and Lees-Miller 1996). Using small angle X-ray scattering, we showed that autophosphorylation of DNA-PKcs results in a large conformational change that likely facilitates dissociation of autophosphorylated DNA-PKcs from Ku (Dobbs et al. 2010; Hammel et al. 2010b). We have proposed that this autophosphorylation induced disruption of the DNA-PKcs complex is critical to DNA-PKcs' function in both NHEJ and V(D)J recombination (Dobbs et al. 2010).
As a further attempt to identify the function of DNA-PKcs, we used mass spectrometry to identify proteins that immunoprecipitated with DNA-PKcs in human cells. This study revealed that DNA-PKcs interacts with the catalytic and regulatory subunits of the protein phosphatase PP6 (Douglas et al. 2010). However, depletion of PP6 by siRNA did not affect the phosphorylation of DNA-PKcs on the sites examined at that time and the significance of this interaction was not clear. Also in 2010, the Gruneberg and Barr group at the University of Oxford showed that PP6 dephosphorylates threonine 288 in the activation loop of mitotic protein kinase Aurora A, and that depletion of PP6 leads to severe mitotic defects (Zeng et al. 2010). This observation prompted us to ask whether DNA-PKcs also had a role in mitosis. Indeed, we showed that siRNA depletion of DNA-PKcs or inhibition of its protein kinase activity using a small molecule inhibitor (NU7441) lead to multiple mitotic defects, including mis-aligned chromosomes, multinucleated cells and anaphase bridges (Douglas et al. 2014; Lee et al. 2011). Interestingly, autophosphorylated forms of DNA-PKcs were located at centrosomes and at the midbody during cytokinesis (Douglas et al. 2014; Lee et al. 2011). Moreover, serine 3205 of DNA-PKcs is phosphorylated by polo-like kinase-1 (PLK1) in mitosis and PP6 dephosphorylates DNA-PKcs serine

3205 in mitosis and after IR (Douglas et al. 2014).

In summary, our studies led to the identification of DNA-PKcs and elucidation of its role in NHEJ and the cellular response to IR. In addition, we have shown that DNA-PKcs autophosphorylation is important for NHEJ and suggested a biochemical mechanism by which autophosphorylation regulates DNA-PK activity and DSB repair. Small molecule inhibitors of DNA-PK radio-sensitize cells, making DNA-PK a potential therapeutic target for radiosensitizing tumour cells (Finlay and Griffin 2012). Our more recent studies have uncovered a new role for DNA-PKcs in mitosis. Going forward, our goal is to elucidate the role of DNA-PK in mitosis and to uncover the mechanisms that lead to genomic instability in DNA-PKcs deficient cells.

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2014 NRC Research Press Senior Investigator Award

My life with worms

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Life before worms

I obtained my undergraduate degree at the University of Toronto in Physiology and Biochemistry. I received my Ph.D. at the University of Oregon, Institute of Molecular Biology, in Eugene, Oregon, under the supervision of Peter von Hippel. The principal subject of my thesis was the study of the reaction between formaldehyde and DNA [1-4]. The aim was to establish a simple chemical model for the interaction between proteins and DNA, which could then be extended to the analysis of real DNA-protein interactions. I also dabbled in "theoretical" analysis of DNA-protein binding [5]. Pete was a pioneer in understanding, at a physical level, how genomes and genomic information could be controlled by regulatory proteins of all types and specificities. The general emphasis of Pete's lab provided an appreciation for the power of physical biochemistry, the satisfaction of a (correct) thermodynamic analysis and yet its simultaneous vulnerability. One must first understand what is actually happening in a reaction before calculating free energies, etc. and in biology, this is not always what a physical biochemist might think.

From Eugene, I went to the National Institutes of Health in Bethesda, Maryland, for post-doctoral training under the supervision of Gary Felsenfeld. Like Pete, Gary is a classically-trained physical biochemist approaching central problems in molecular biology, in particular the structure and function of chromatin. These were the mildly-heady days following the discovery of the nucleosome, the basic subunit of DNA packaging in chromatin. Over the years I spent in Gary's lab, I studied aspects of nucleosome structure, such as the surprising accessibility of the DNA on the surface of the core particle [6-8] as well as the arrangement of chains of nucleosomes into higher order structures [9,10]. Gary had developed chicken erythrocytes (and erythrocyte precursors) as a powerful experimental system in which to study the influence of chromatin structure on the transcription of the globin genes. Using this system, I also studied the association of DNA methylation patterns with globin gene activity [11] as well as local perturbations in globin gene chromatin structure that appear to signal sites of gene regulation [12]. An enduring limitation of chromatin research is to distinguish cause from effect and it was common to have authors reassure themselves by incantations such as "it is becoming increasingly clear that chromatin structure is critically important for …….". Such phrases appeared in an alarming proportion of papers that attempted to study how gene control is convoluted with chromatin structure. I thus began to feel the need to study an organism that provided classical genetics or at least some whole organism biology, with which we could test functional importance.

The answer to my "genetics vs. physical biochemistry" dilemma arrived in the person of David Hirsh, then at the University of Colorado, Boulder. David had been invited to NIH by a group of prominent scientists at NIH (Gary, Igor Dawid, Phil Leder) who were exploring biological systems to which the revolutionary new tools of recombinant DNA could be applied. David had been one of the early adopters of *C. elegans* and had done fundamental characterization of the worm's life history, germline development and genetics. To a chemist/physical biochemist (which was how I then saw myself), worms appeared delightfully simple, showing ultra-reproducible, almost clocklike development. Every experiment I have done since then has showed just how complex and sophisticated worms really are, but at the time the lure of mosaic development was irresistible. A second lure was the fact that the literature extended back only a decade or so, unlike the multi-decade literature of that other famous model organism *Drosophila*. The power of worms as an experimental animal was also apparent, applying classical genetics combined with differential interference optics to the development of a transparent living organism, where every cell division could be watched, from the first to the last. There was no hint of the technical revolutions to come, such as RNA-mediated interference (RNAi), genomic sequencing and the ever increasing ability to modify the genome.

Worms in Calgary

After so many enjoyable years at NIH with Gary, it was time to leave and perhaps to return to Canada. The Alberta Heritage Foundation for Medical Research (AHFMR) presented a once-in-a lifetime opportunity to do just this. On looking back, this opportunity really was remarkable because, among other things, it allowed me to change fields and work on worms full-time, and yet with no credible prior experience. One of these days, I'll hunt up the long-range proposal I wrote for the AHFMR and reassure myself that most of it did indeed get accomplished. The plan was to study the molecular basis of lineage specific transcription: how do only certain genes get turned on in certain lineages and only at the correct times in development. More concretely, we proposed to study the **control of digestive hydrolases in the *C. elegans* intestine.**

Why hydrolases? Because they have simple, sensitive, and potentially specific histochemical assays that could be used to follow gene expression during development (e.g. to verify that expression was indeed intestine-specific), which would provide a biochemical assay for purification of the enzyme as a route to gene cloning, and (I was dreaming here) could potentially be adapted for use in a genetic selection scheme for hydrolase mutants. The enzymatic activity would also provide a convenient assay for the expression of genes introduced back into a (null-mutant) worm.

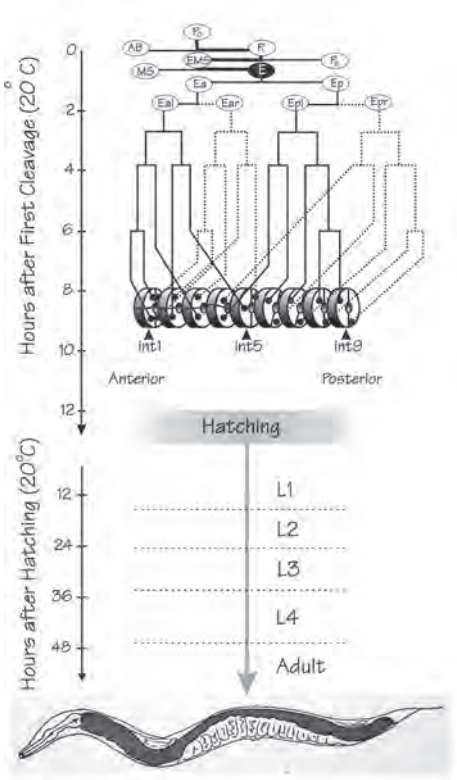

Figure 1. *Cell lineage of the C. elegans intestine (based on [44] and adapted from [13]). The entire intestine is a clone of cells derived from the single E blastomere (shown in reversed contrast near the top of the Figure). Divisions are ~anterior-posterior, except for the division of the Ea and Ep cells, which are ~transverse. Lineages on the embryo's left side are depicted by solid lines; lineages on the right side are depicted by the dashed lines. The 20 cells of the mature intestine are arranged as a longitudinal series of two-cell discs, called "ints", which surround the intestine lumen. The exception is int1, the most anterior disc, which contains four cells. Intestinal growth is ~continuous through the four larval stages (L1 to L4) to the adult, leading to an ~100 fold increase in mass. The adult worm (depicted with a dark intestine at the bottom of the Figure) is ~1.4 mm in length.*

Why the intestine? Because, of all embryonic organ-producing cell lineages in the worm, the intestine is probably the simplest. As shown in Figure 1, the intestine is produced as a simple clone of cells derived from a single blastomere (the E cell) present in the 7-8 cell embryo. The mature adult intestine still only contains 20 cells (30-34 nuclei) but each nucleus is now 32-fold polyploid. Overall, the intestine provides roughly one-third of the somatic mass of the adult worm, making purification of intestinal enzymes/transcription factors easier and making intestinal transcripts a major fraction of all somatic transcripts. At the time, the intestine (also known as the E-lineage or endoderm) was thought to develop in a completely "mosaic" manner, i.e. independent of other cell lineages. This is now known not to be true and indeed, one of the best understood examples of cell-cell interactions in all of development occurs at the cell division immediately prior to the production of the intestine progenitor cell. Overall, the simplicity of the E lineage allowed us to imagine that we could work our way backwards, up the transcription factor hierarchy, and to determine how the E cell became specified. That is, if we could only clone a gene for an intestinal-specific digestive hydrolase, then we could establish a transgenic assay for introducing modified genes back into the worm, analyze the promoter by a series of deletions and mutations to identify key regulatory sites, use these sites to clone the cognate transcription factor, and then repeat the whole process, bashing away at the promoter of the gene encoding the transcription factor. In this way, we should in principle be able to work our way from the downstream target gene to the controlling transcription factor, then to the transcription factor controlling the first transcription factor and so on, until we entered the realm of endoderm specification where the serious riddles lay. In the event, this process worked but it worked slowly and we only got part of the way back to the question of endoderm specification. Genetics (and other laboratories) got there first (for a review, see [13]). However, we ended up understanding more about endoderm differentiation than we might have otherwise and this is a fascinating topic in its own right. In this article, I will briefly describe the experimental path that we followed. For me, the path is interesting and provides occasions for nostalgia. For others, it might seem a testimony to obsolete experimental methods that have (fortunately) been superseded by the genomics revolution.

The *ges-1* esterase

During the last year that I was at NIH, I continued to work on chromatin structure and function but I was blessed by the arrival of Lois Edgar as a post-doctoral fellow. Lois had obtained her Ph.D. with David Hirsh, working on the classical genetics and developmental biology of sex determination genes in *C. elegans*. Lois was to accompany me to Calgary and it is safe to say that without her expertise and dedication, it would have been many times more difficult for me to make the transition to studying *C. elegans*. Lois was (and still is) an expert in manipulation of *C. elegans* embryos and while still at NIH, she had already defined what looked like an ideal intestine-specific enzyme for us to start the journey planned in the last paragraph: a simple carboxyl esterase named GES-1 (standing for gut esterase # 1; in worms, *ges-1* is the gene; GES-1 is the encoded protein). The esterase assay is simple, sensitive and, under the conditions that Lois established, more or less specific for GES-1 activity, even though the worm genome encodes a number of other esterases. An example of Lois's handiwork is shown in Figure 2 [14]. Embryos were permeabilized at various stages during early development and further cell division was inhibited by cytochalasin D; the arrested but still living embryos were cultured overnight and then stained for GES-1 activity. The staining pattern provides a striking demonstration of the robust lineage-restriction of "intestinal potential"; at each stage, cells in the E lineage can express *ges-1* but cells in the non-E-lineages cannot. In the normal course of embryogenesis, when cell division is not prevented by cytochalasin D, GES-1 activity appears roughly when the E lineage has only 4-8 cells and, as far as we can tell, remains expressed in the intestine for the rest of the worm's (2-3 week) lifespan.

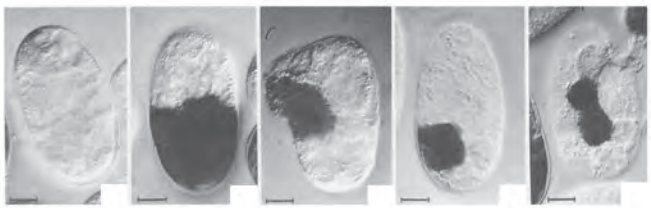

Figure 2. *Esterase expression in embryos blocked in cytokinesis by cytochalasin D (adapted from [14]). From left to right: embryo blocked before first cleavage; embryo blocked at two cells (the P1 blastomere is GES-1 positive); embryo blocked at four cells (EMS blastomere is GES-1 positive); embryo blocked at eight cells (the one E cell is GES-1 positive); embryo blocked at 16 cells (the two E cells are both GES-1 positive).*

The next part of the plan was to purify the GES-1 enzyme by standard biochemistry, using variations on the histochemical assay to follow the purification. We learned how to grow hundreds of grams of *C. elegans*, using large trays filled with mixtures of bacteria and chicken eggs (just writing this brings back memories of their ferocious smell) and learned how to disrupt worms from their protective cuticle using a Stansted Cell Disruptor, a thankfully obsolete machine based on a high pressure oil pump from the Royal Navy. The end result, after several standard chromatography steps, was pure GES-1, in an amount that eventually allowed us to determine an N-terminal sequence, reverse translate the sequence into a degenerate oligonucleotide probe that could be made highly radioactive and then to (finally) isolate the *ges-1* gene by hybridizing this probe to a *C. elegans* genomic library constructed in λ bacteriophage. I had purified the GES-1 protein [15] but all the subsequent cloning steps were performed by a post-doctoral fellow Brian Kennedy [16]. Nowadays, most of these latter steps would be completed with a computer search of the genomic sequence and might take an hour or two. Perhaps it is best not to reflect on how much time we had to spend to make even one small step of progress. The *ges-1* sequence gave few surprises, beyond the fact (still surprising to many of us) that genes in *C. elegans* are so similar to genes in humans. *ges-1* encodes a serine carboxylesterase (i.e. has serine as the key catalytic residue), highly similar to human liver esterases and normally involved (presumably) in detoxification and/or lipid metabolism.

The next step in the plan was to produce a null mutant in *ges-1* and then to introduce the *ges-1* gene back into this mutant, assaying for expression using the histochemical reactions that got us this far. We hatched a scheme to identify the *ges-1* genetic locus and it might have become popular (at least in hermaphroditic worms) if the genomic sequence had not come along and made things much easier. We first showed that the histochemical assay for esterase enzymatic activity could be used to detect GES-1 activity as a single band on an isoelectric focusing (IEF) gel in extracts of wildtype worms. This single major band (+ a few weaker bands) was comforting because it was consistent with the detection of only one gene product, one major esterase, at least under the conditions of our assay. We mutagenized worms, let them self-fertilize (one of the enormous advantages of working with hermaphrodites), picked individual F1 worms (potentially heterozygous for a *ges-1* mutation) to separate plates and let them establish a population. Each population was washed off the plate, extracts prepared and run on an IEF gel, looking for populations that produced two bands on the IEF gel, indicating that there had been a charge-change mutation introduced into one of the copies of the *ges-1* gene in the founder worm. We actually found several of these without a great deal of difficulty, isolated the homozygous charge-change mutant from the remaining worms that had failed to be washed from the plate and then used the IEF pattern as a Mendelian marker to map the *ges-1* gene to the left end of linkage group V [17]. An obvious limitation with the scheme was that this charge-change mutant still showed esterase activity and hence could not be used as a host for our planned transgenic experiments. However, knowing the map position, we were able to construct a stably balanced strain in which the *ges-1* charge-change allele was paired with a rearranged chromosome V that carried the *ges-1* wildtype allele. The main phenotype of this strain was that it now gave two IEF bands instead of one. This strain was mutagenized once again and F1-derived populations assayed for the disappearance of one of the bands, in particular the band that derived from the non-rearranged copy of LG V. After the usual rounds of outcrossing to remove extraneous mutations, we were the proud possessors of a strain of worms that lacked all activity of the GES-1 enzyme and that appeared quite healthy [18]. That is, under the normal pampered conditions of laboratory life, the *ges-1* gene is not required for worm survival, even though it might be necessary under conditions of environmental toxicity in the wild.

The stage was now set for our first attempt at transgenesis in worms, injecting the cloned wildtype version of the *ges-1* gene into the *ges-1*(null) mutant and staining the transgenic progeny by our tried and true histochemical stain for esterase activity. Remarkably, the transgene was able to reconstitute *ges-1* activity, and enzymatic activity largely was confined to the intestine. The next few years were spent gleefully bashing away at the *ges-1* promoter, deleting and mutating and re-injecting the modified constructs back into the *ges-1* null worms. This project was led by two post-doctoral fellows, Eric Aamodt and Cay Egan [19,20], aided by a summer student Cheryl van Buskirk. Typical results are shown in Figure 3. One thing we found immediately was that certain deletions abolished expression in the early endoderm (E lineage) but activated expression in cells that belonged to embryonic lineages related to the E lineage. The most prominent of these ectopically expressing lineages gave rise

to cells of the pharynx and the tail. Although the nature of the esterase stain made it difficult to determine the precise cell identities, the main source of ectopic expression appeared to derive from cells of the sister lineage MS. These observations were intriguing because they suggested that the *ges-1* activity was kept silenced in non-endodermal lineages by virtue of *ges-1* binding repressors. Other deletions were expressed only in the anterior of the intestine and we were further intrigued that this series of deletions was somehow uncovering a general anterior-posterior coordinate system in the embryo. Sean Marshall, a graduate student, showed that both of these regulatory features could also be seen with the *C. briggsae* homolog of *ges-1* [21]. Perhaps the supposition of a *ges-1* repressor is true, but we found it impossible to prove, and gradually realized that these ectopic signals might partially derive from the high activity of the *ges-1* gene used as a reporter and, even worse, could also have been influenced by the fact that the standard *C. elegans* transgene is part of a multicopy array, in which the transgenic activity significantly exceeds the activity of the endogenous gene [22]. We had narrowed down regions of the *ges-1* gene that were good candidates for repressor binding sites, together with the candidate activator sites, but were never convinced it was worthwhile to follow up diligently. In contrast, graduate student Dana Schroeder was able to exploit the anterior intestinal expression of one of the *ges-1* deletions to uncover a coordinate system within the developing intestine, based on the Wnt-wingless pathway and the critical downstream regulator POP-1 [23].

The most important result of the above analysis was homing in on a short (<30 bp) region of the *ges-1* promoter that seems to control the full intestinal expression of *ges-1* (see Figure 3). Deleting the region abolishes intestinal expression (at the same time flipping expression into the pharynx and tail); producing multiple copies of the region in such a way as to drive expression of a *lacZ* reporter from a naïve promoter showed that this short region is sufficient to drive intestinal expression. In other words, within the experimental limitations, this short region was both necessary and sufficient to drive intestinal expression of *ges-1*. The most obvious feature of this "enhancer" was that it contained a tandem pair of "TGATAA" sites, a sequence that has followed us ever since.

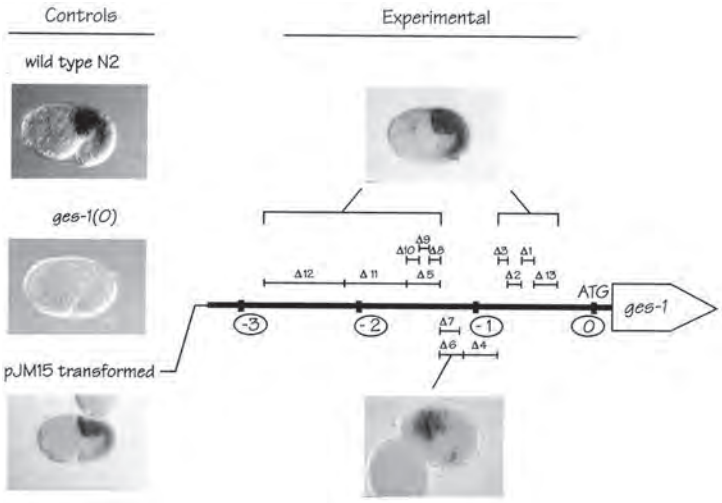

Figure 3. *Summary of the deletion analysis of the 5'-flanking region from the C. elegans ges-1 gene (adapted from [20]). Control embryos stained for GES-1 activity are shown at left: wildtype N2 embryo; ges-1 null embryo; ges-1 null embryo transformed with the plasmid pJM15 containing the intact ges-1 gene, with 3.3 kb of flanking sequence. In the area marked Experimental, promoter deletions above the line result in unchanged GES-1 staining; deletions shown below the line extinguish GES-1 expression in the embryonic intestine and activate expression in cells of the pharynx and rectum.*

Identifying ELT-2

The assumption behind our promoter analyses was that there was an intestinal transcription factor that bound directly to these TGATAA sites or to other sites in the vicinity and then activated *ges-1* transcription. Indeed, Virginia Stroeher and Brian Kennedy, both PDFs, had been able to demonstrate candidate factors in *C. elegans* embryos that were able to bind specifically to these motifs [24]. However, the most obvious approach to identifying such a factor would mean returning to old-fashioned protein purifications but now with much less material and with a much more tedious assay. Mark Hawkins, a post-doctoral fellow, set out to find this factor by a different route. There were "expression libraries" available for *C. elegans*, based on the classical bacteriophage vector λgt11, in which cDNA fragments were fused to lacZ in such a way that protein products would be produced within bacteriophage plaques upon induction. The expectation (hope) was that the binding domain of this phantom factor would also be produced and would be available for binding. Mark made a highly radioactive probe based on the TGATAA sites from the *ges-1* promoter, provided it to filters covered in plaques under conditions that a transcription factor might be expected to bind DNA, washed extensively and then put the filter up against X-ray film.

Amazingly, he found a small number of radioactive spots that corresponded to distinct plaques. After the usual rounds of purification and finally sequencing, Mark had indeed found a GATA factor [25], a member of a distinct class of zinc finger proteins that bind to variants of a GATA sequence in DNA, that were known for their involvement in vertebrate erythropoiesis, and that have since turned out to be crucial in development of the vertebrate heart as well as endoderm. At that time, there were only a few such factors that had been described and this was the second one that had been described in *C. elegans*. The first such factor had been cloned by others on the basis of sequence similarities with vertebrate factors and had been called ELT-1, standing for erythrocyte-like-transcription factor (*sic*) or erythroid-like-transcription factor (*sic*). Even though neither nomenclature was grammatically pleasing, we named our factor ELT-2. ELT-1 turned out to be crucial for development of the hypodermis (the worm's skin) and, as will be described in the next few paragraphs, ELT-2 turns out to be crucial for development of the worm's intestine.

So how do we find out if ELT-2 is indeed the transcription factor that "really" controls the *ges-1* gene in the developing endoderm? This is when Tetsunari Fukushige arrived and took on the project (and many others over the next few years). Tetsu fused the *elt-2* promoter region to a lacZ reporter, made transgenic worms and showed that *elt-2* was indeed expressed in the developing intestine and was present at the time that the *ges-1* gene became active. *elt-2* expression could be detected in some embryos as early as the 2E cell stage of the endoderm but most embryos in the population express *elt-2* when the developing endoderm has 4 cells. Tetsu could show that ELT-2 was sufficient for *ges-1* expression by constructing a plasmid in which the *elt-2* cDNA was under control of the *C. elegans* heat shock promoter, producing transgenic embryos and then heat shocking them before staining for GES-1 activity. Ectopic ELT-2 was expressed throughout the heat-shocked embryo (as detected by antibody staining) and *ges-1* activity was also driven throughout the embryo (Figure 4). Even though this process was crude, it appeared remarkably specific, in so far as a control heatshock ELT-1 cDNA construct, in similar experiments, was unable to drive ectopic *ges-1* expression. Tetsu also showed that other markers of the early intestine were also expressed ectopically under ELT-2 control, suggesting that ELT-2 might control multiple genes in the developing embryo [26].

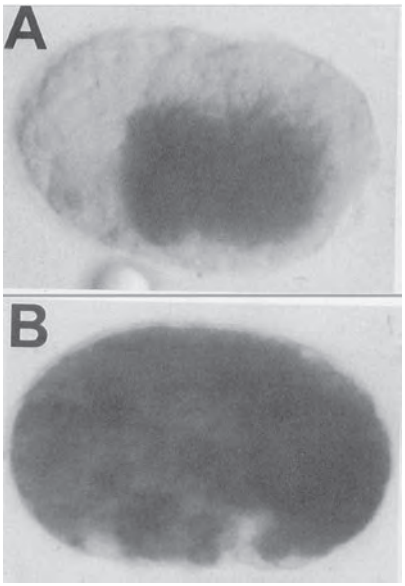

Figure 4. *Ectopic expression of elt-2 cDNA drives ectopic expression of ges-1. A) Heat shocked and arrested N2 control embryos, where GES-1 activity remains restricted to the presumptive intestine cells; B) embryos transformed with heat-shock promoter::elt-2 cDNA construct express ges-1 in essentially all cells of the embryo following heat shock.*

But how important overall was *elt-2* to the worm and was it actually necessary for *ges-1* and other intestinal gene expression? Present day technology would allow one to check *ges-1* expression in the absence of ELT-2 by using RNAi and the whole experiment might be over (including repetitions) within a few days. Although the discovery of RNAi was still a few years away, a number of investigators were working on methods to produce mutations in specific genes. I was spending a short, highly enjoyable sabbatical in Jonathan Hodgkin's lab at the LMB in Cambridge, England (the source of *C. elegans*) so it was relatively easy for me to travel to Amsterdam and spend a few weeks as a guest of Ronald Plasterk, who had developed the most successful method yet to knockout particular genes. The method was based on the ability (rather reluctant, to be sure) of a *C. elegans* transposon called Tc1 to move around the genome. Exploiting the fact that worms could be cloned and the cloned populations then frozen, the Plasterk lab had worked out an efficient PCR protocol to screen many populations of worms to identify a rare event in which a Tc1 transposon had hopped

into your favourite gene. Pools of multiple candidate populations were first screened and then positive pools were sub-divided and sub-divided until, if you were both diligent and lucky, you ended up with a single worm in which there was a homozygous insertion of the transposon into your gene. However, you were only half way there because Tc1 tended preferentially to hop into introns and the result was that the gene usually remained active. The second step was more arduous but was based on the same principles, namely PCR-screening of multiple pools of multiple candidate populations, looking for a rare worm in which the Tc1 had decided to exit from the intron but did so inaccurately, thereby removing some or all of the surrounding coding sequence. I was able to find the original Tc1 insertion during my all-too-brief stay in Plasterk's lab. Tetsu then took over to find the Tc1-pop-out, which would finally tell us whether ELT-2 was really necessary for anything, let alone necessary for driving *ges-1* activity. This Tc1 pop-out had the added complication that, if ELT-2 was as important as we hoped it would be, loss of *elt-2* activity would undoubtedly be lethal and we would have to balance the knock-out immediately. All of this, Tetsu did with his characteristic energy and determination and we finally had a perfect *elt-2* mutation with almost all of the *elt-2* coding region removed by the exiting Tc1 transposon. It turned out that the *elt-2* knock-out is indeed lethal and has to be balanced to maintain the strain but balancing was made much easier because of the emerging physical map of the *C. elegans* genome. Even with a partially completed map, the *elt-2* gene could be assigned to the middle of the X-chromosome. The entire process of identifying a mutation in *elt-2* (and in other genes in other labs) was lengthy and arduous but was soon scaled up by the *C. elegans* community to perform such screens in a more efficient high-throughput manner, replacing the reluctantly hopping Tc1 with more controllable chemical mutagens such as the combination of psoralen and UV light. In this way, mutations have been produced in roughly a third of the *C. elegans* genes, an enormously powerful community resource. All of these methods look precarious and primitive compared to the most recent CRISPR-based techniques that allow us to alter the genome almost at will.

Figure 5. *Newly hatched L1 larva homozygous for the elt-2 null mutation. Larvae arrest shortly after hatching and eventually die of starvation. The blocked intestinal lumen is apparent as is the accumulation of ingested and undigested bacteria at the intestine anterior (the gut-obstructed = "Gob" phenotype).*

The *elt-2* knockout mutants die shortly after hatching, although they clearly have an intestine and a remarkably normal one at that (Figure 5). However, closer inspection showed that the *elt-2* null intestine has a blocked lumen. Food piles up at the front of the gut and does not seem to be able to penetrate much beyond the first or occasionally the second set of intestine cells; presumably the afflicted animals die of starvation. Electron microscopy showed that the normal microvilli are irregular and stunted, but again the overall morphology of the intestine is not too abnormal, i.e. it is still clearly specified. To our unjustified chagrin, the *elt-2* mutant embryos still stain for *ges-1* activity. All of the above results showed that, although we had apparently cloned an important factor, things are more complicated; other transcription factors providing the same function as ELT-2 must also be involved in both specifying and forming the intestine.

GATA factors everywhere; how important is ELT-2?

Largely from the work of other labs, relying less on biochemistry and more on classical genetics and gene identification by RNAi, the mechanism of E cell specification has been established in admirable detail (see review in [13]). In brief, the E cell becomes specified by expression of the two GATA factors END-1 and END-3, which then proceed to activate the gene encoding a third GATA fac-

tor ELT-7 and probably all three of them then combine to activate the *elt-2* gene. A fourth endoderm-specific GATA factor, ELT-4, has little if any function that we could determine [27]C elegans and indeed, ELT-7 can also be removed without obvious consequences.

Our own work had been building the case that ELT-2 is indeed the predominant transcription factor controlling the differentiation and the function of the intestine, following endoderm specification at the 1E cell stage, and continuing through the life of the worm [28,29]. To investigate the role of ELT-2 in the mature intestine, we turned to genomics. We were able to dissect adult intestines, even from these small worms (~1 mm long), and ~1,800 such intestines (prepared by Barbara Goszczynski through her usual talents, diligence and perseverance) was sufficient to prepare a SAGE library, at that time the most sophisticated technique for investigating lists of transcripts. This project was only possible because of an extensive collaboration with Don Moerman at UBC, and by Gordon Robertson, Misha Bilenky, Monica Sleumer, Marco Marra and Steve Jones at the BC Genome Sciences Centre, together with the local bioinformatic talents of a post-doctoral fellow Stephanie Minnema. The SAGE library from the isolated intestines revealed several thousand genes that were expressed in adult intestines and we could at least argue that half or so of these genes were expressed either solely or mainly in the intestine. The second part of the study was to analyze SAGE libraries produced solely from E cells isolated by FACS sorting, as well as libraries produced from L1 larvae, comparing wildtype transcript lists to the lists produced from larvae that lacked *elt-2* (both sortings, cells and worms, were performed in Don Moerman's laboratory at UBC).

To make sense of all these genes, we focused on three subsets of ~80 genes, identified in FACS sorted embryonic E cells, in L1 larvae and in isolated adult intestines respectively, and selected because they are expressed solely or at least preferentially in the intestine. As a group, these genes were strongly responsive to ectopic ELT-2 (performed by means of a heat shock construct in the embryos) as well as to a loss of *elt-2* (in *elt-2* null L1 larvae), although there were certainly individual genes that did not respond as did the majority. There are a number of computational methods available that search for over-represented motifs in the promoters of these genes. Such sites would be candidates for binding to a transcription factor controlling this set of genes. The computational results were clearer than we had expected. The only such over-represented site that we could detect in these three sets of promoters centered on a core TGATAA site. The two bps upstream and two bps downstream of the TGATAA also contained information and we were able to assemble a position frequency matrix for these over-represented sites. Reassuringly, this matrix corresponded well to a frequency matrix assembled from the handful of studies that have analyzed intestinal promoters by experiment, the majority of which have found critical TGATAA sites. We would like to believe that this frequency matrix is a quantitative description of the binding preferences of ELT-2 but this is not yet known. There is certainly the possibility that it represents some weighted mean of, for example, the binding preferences of both ELT-2 and ELT-7. Nonetheless, the presence of such a TGATAA site and its apparent functional importance in all the intestinal gene promoters that have been analyzed is certainly consistent with a model in which ELT-2 controls most (perhaps all) of the genes expressed in the differentiated intestine. This is the most important result that we have produced in the past few years but it can only be a first approximation model. Even the worm intestine is complicated, and it is fantasy to think that its development could be completely regulated by a single transcription factor. Indeed, our SAGE library revealed several hundred recognizable transcription factors, besides ELT-2, present in the adult intestine. John Kalb, a former postdoctoral fellow and subsequently a regular and highly valued summer-and-sabbatical visitor (from Canisius College, NY), was able to investigate the importance of some of these factors by feeding worms RNAi effective only in the intestine. We were able to conclude that most of these intestinal transcription factors, at least the ones that we could test, had no necessary post-hatching function in the endoderm [28]. The single exception that we could find is the intestinal factor SBP-1 (sterol element binding protein): removal of SBP-1 by intestinal-only RNAi does indeed cause larval arrest. John had performed additional experiments to suggest that the sbp-1 gene is actually under elt-2 control but these projects were sadly interrupted by his untimely death.

Why can we not detect the binding sites for all of these other intestinal transcription factors in the promoters of intestinally expressed genes? Probably because each of these factors by itself only controls a limited number of genes, in some more specific regulatory sub-network, for example, in which the genes respond to stress or toxins

or particular nutritional demands. Indeed, there are now a handful of experimentally investigated intestinal genes where controlling elements have been identified in which ELT-2 cooperates with a second factor to confer intestinal twist or to control the assimilation of iron, heme or zinc.

Some other organs and some other genes

Up to this point, I have described our studies that have largely focused on the developing intestine and I am grateful to have been able to acknowledge the leading roles of the various talented trainees. However, other trainees in the lab have worked on other organs and other genes and I will briefly summarize these projects in order that they too can be acknowledged. Kenichi Ito performed a very pretty experiment to show that the individual DNA strands that the worm embryo receives from its parents segregate randomly during embryonic development [30]. Priti Krishna, together with Brian Kennedy, discovered that the *C. elegans* yolk proteins appear to be highly specific binding proteins for left-handed Z DNA, thereby imparting a healthy degree of skepticism into the field [31,32]. Nancy Hawkins described a set of homeobox genes in *C. elegans* at a time when everyone thought that non-segmented worms should not have any [33]. One of these genes, ceh-10, was later studied by graduate student Pia Svendsen, who showed that it was the homolog of similar genes expressed in human eyes [34], suggesting how eyes might have evolved. Marie Azzaria intrepidly led our studies into the pig parasite *Ascaris*, first studying DNA synthesis in the early *Ascaris* embryo, then describing the *Ascaris* homolog of GES-1 and finally describing the expression profile and sequence properties of the *C. elegans* homolog of the *Drosophila* forkhead factor [35-37]. Post-doctoral fellow John Kalb, mentioned earlier for his role in testing the necessity of intestinal transcription factors, followed up this last project from Marie, and was able to demonstrate that our forkhead factor, cloned on the basis of sequence similarity, was actually the product of the *pha-4* gene, previously described for its crucial role in pharyngeal development [38]. John Gilleard, a post-doctoral fellow and a veterinary in a previous life, came to Calgary to study another transcription factor that he had identified in *C. elegans*: ELT-3 is also a GATA factor and John described how it functions in the differentiation of the worm hypodermis [39,40]. Chris Beh was a graduate student who identified and then purified an acid phosphatase enzyme that is expressed along the edge of the intestinal lumen [41]. Tetsunari Fukushige led the project in which we cloned the pho-1 gene (thanks to the genomic sequence), produced a mutant by the scheme described above for *ges-1*, showed that the mutation was unexpectedly lethal, and also defined at least part of the mechanism that regulates the spatial expression pattern of pho-1 [42]. Jay Kormish, a graduate student, screened for genes that produced the same Gut-obstructed (Gob) phenotype as seen in an *elt-2* null, among which she identified and characterized the enzyme trehalose phosphate phosphatase. A clever high school student Shervin Ghafouri was able to use fluorescent beads as a proxy for bacteria, tricked worms into eating the beads and then excreting them, and by analyzing how much fluorescence exited the worm in each such excretion "event", was able to deduce that the bacteria must only reside a minute or two inside the worm. Finally, two talented undergraduate students, Tabitha Tonsaker and Ryan Pratt, were able to disprove a high-profile claim in the literature that the ELT-3 GATA factor played a crucial role in worm lifespan [43].

Current projects

We have a number of projects ongoing in the lab that continue the ELT-2 centred themes discussed above, and will occupy our time over the upcoming years.

(1) ELT-2 Chip. This is a collaboration with Erin Osborne Nishimura and Jason Lieb at the University of North Carolina. The aim is to test the model that ELT-2 directly controls every gene (or at least a majority of genes) expressed in the maturing and mature intestine. At the same time, the project is producing a more complete and much higher quality list of intestinally expressed genes.

(2) What controls *elt-2* and why do regulatory pathways evolve the way they do? This is a project almost completed by a postdoctoral fellow Tobias Wiesenfahrt, extending the work of a former graduate student Janette Berg. Analysis of the *elt-2* promoter in transgenic worms reveals conserved regions of varying strengths and contributions to *elt-2* regulation. So far, we have found no evidence for any factor other than GATA factors controlling *elt-2*, i.e. the endoderm regulatory hierarchy remains as simple as described earlier. The current model is that some redundant combination of END-1/END-3/ELT-7 is able to initiate *elt-2* expression and some combination of ELT-7/ELT-2 maintains *elt-2* expression levels thereafter, each factor acting at the same array of TGATAA sites in the extended *elt-2* promoter. Tobi's most interesting finding is that *elt-2*, when expressed under the ap-

propriate circumstances, is able to replace all four of the other GATA factors expressed in the endoderm, thereby raising questions why the *C. elegans* endoderm regulatory network evolved the way it did and not by the much simpler "ELT-2-can-do-everything" route.

(3) We mentioned earlier that *elt-2* and *elt-7* were at least partially redundant, as if *elt-7* could regulate a subset of all the genes regulated by *elt-2*. But how exactly do these two transcription factors apportion their transcriptional responsibilities? This is a general problem that comes up universally and one of the best studied examples is in vertebrate cells switching between two different GATA factors during hematopoiesis. Using the COPAS Biosorter and worm strains appropriately tagged with GFP on rescuing transgenic arrays, graduate student Aidan Dineen was able to isolate pure populations of larvae that would ordinarily be dead, e.g. *elt-2* nulls, *elt-2 elt-7* nulls, etc., as well as larvae that would ordinarily live (*elt-7* nulls along with control wildtype worms). RNA-Seq has provided a list of all transcripts produced in the various samples and it is clear that *elt-2* and *elt-7* have partially overlapping and yet distinct responsibilities. Nonetheless, our prevailing model is supported. There are many intestinal genes that are apparently controlled only by ELT-2, some other intestinal genes that are controlled by either ELT-7 or ELT-2, and few (if any) that appear to be controlled only by ELT-7. The fun now begins as we try to figure out the rules that are obeyed by the different transcription factors.

(4) The *C. elegans* vitellogenin genes encode the animal's yolk proteins and are expressed only in the intestine of the adult hermaphrodite, not males. We set out to show that ELT-2 was the major activator of one of the vitellogenin genes (*vit-2*) as suggested by previous promoter analyses performed by others. We further wanted to determine how the activity of ELT-2 was inhibited in the male intestine. We focused on the activity of a short 44 bp enhancer that contained presumptive binding sites for ELT-2 as well as a known binding site for the male vit-2 repressor. This short promoter fragment (when present in four copies) is able to drive reporter expression in the correct tissues, sex and stage, with considerable fidelity. However, the enhancer is significantly more complicated than we had expected, turning out to be the site of action of two different forkhead type transcription factors (one involved in vit-2 activation, the other in vit-2 repression) as well as an additional direct transcriptional activator currently unknown. Moreover, the enhancer responds to signaling pathways involved in regulating body size, reproductive lifespan, nutrition, aging and longevity. These experiments were started by two undergraduate students, Alicia Danielson and Vasile Captan, and then brought to completion by Barbara Goszczynski.

(5) How does the affinity of a transcription factor for its cognate binding motif influence the levels of transcription of the target gene? This is a fundamental aspect of all development and it is surprising that no definitive answer has yet emerged (to our knowledge). A graduate student, Brett Lancaster, has established an experimental system based on a gene that appears to be solely under ELT-2 control. This is the asp-1 gene, which codes for the worm's major intestinal aspartic protease. The basis for the system is that worm transgenes, at least those produced by simple injection of DNA into the gonad, consist of multiple copies of the injected DNA concatenated into an array that acts like a little chromosome. Brett has constructed two reporter genes that differ by only a single base pair from the native asp-1 gene but that now have introduced restriction sites to allow the two reporter transcripts to be distinguished and their levels to be accurately quantitated (following reverse transcription and restriction digestion). One of the reporters is driven by the wildtype promoter, the second by a reporter that has been manipulated (e.g. by mutating one of the controlling TGATAA sites to a site of lower affinity). Because of the multi-copy nature of the resulting transgenes, we can make the argument that both reporters are exposed to "identical" cellular environments, thus making the system nicely controlled internally. Brett's present results show that even apparently minor changes in ELT-2 affinity for the controlling TGATAA sites (by only altering flanking sequences) can give rise to significantly altered levels of reporter transcription.

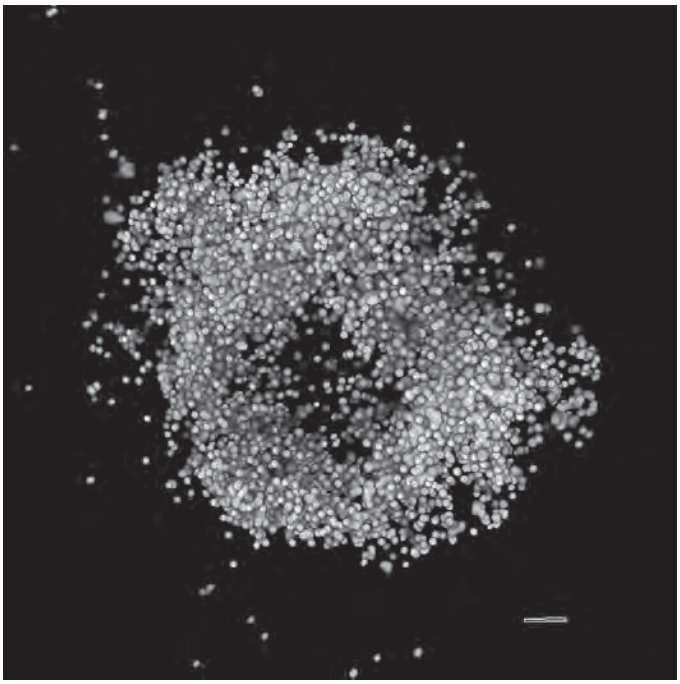

Figure 6. *A 3 micron thick section through the middle of an adult intestinal nucleus stained with a monoclonal antibody against ELT-2 followed by an Alexa647-tagged secondary antibody. Fluorescent dyes are visualized by 3D STORM (stochastic optical reconstruction microscopy). The bright dots represent individual ELT-2 molecules. The central nuclear space corresponds to the nucleolus. Scale bar = 1 micron. Image provided by Dr. Pascal DeTampel.*

(6) And finally, where do I want to go in the future? At some point, it would be nice to be able to see what is actually happening inside the living embryo. We hope to do this by exploiting powerful new microscopy techniques, generally collected under the label "super-resolution" microscopy but also encompassing all the wonderful experiments that can be done with computer controlled lasers and sensitive highly resolving cameras. Now that we know the main players in the transcriptional hierarchy, the stage is set for understanding their kinetic behavior at the molecular level, as well as the thermodynamic driving forces governing endoderm specification and differentiation. The first step in this direction is simply to see where ELT-2 protein is distributed inside a mature intestinal nucleus. An example is shown in Figure 6, provided by post-doctoral fellow Pascal DeTampel. In this case, an adult intestinal nucleus has been stained with a monoclonal antibody against ELT-2, which is then visualized by a secondary antibody tagged with a photo-switchable dye. The individual spots are detected using 3-dimensional STORM (stochastic optical reconstruction microscopy) and presumably correspond to individual molecules of ELT-2. Even at this early stage in the project, the resolution is impressive…..on the order of 30 nm in the x-y plane and 50 nm in the axial direction. As yet we clearly do not have a comprehensive understanding either of the ELT-2 distribution or the implications of this distribution. What fraction of ELT-2 do we detect? How many of these ELT-2 molecules are free in the nucleoplasm, how many are bound "non-specifically" to chromatin DNA and how many are actually bound specifically to TGATAA sites in the promoters of genes whose transcription is being controlled? What is the relation between ELT-2 and molecules of the more general transcriptional machinery, e.g. RNA Polymerase II or certain subunits of the Mediator Complex? These are all questions for the future.

Acknowledgements

Throughout this article, I have tried to acknowledge the contributions of all trainees that I have been fortunate to have in my lab over the years. If I have forgotten anyone, I apologize. I have also been blessed by a collection of the best technicians that anyone could hope for, starting with Denise Cottrell when I first came to Calgary, then Denise Ferrari, May Chung, Fran Allen (recently back in the lab as Fran Snyder), Lana Wong, Helen Tian, Indra Raharjo, Jamie Feng and finally, Barbara Goszczynski, who has been such a wonderful contributor to essentially all of the lab projects over the past many years: talented, rigorous, hard-working, level-headed and just a pleasure to have in the lab. I have also been fortunate to have had wonderful colleagues at Calgary. I'll restrain myself from listing all the members of our department but I do want to thank my long-term worm-picking colleagues who have taught me so many different aspects of worm biology over the years: Dave Hansen, John Gilleard, Jeb Gaudet and especially Paul Mains.

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2014 Robert H. Haynes Young Scientist Award in Genetics

"Trash-AAAAAid": how 3' end polyadenylation promotes RNA decay in the cell nucleus

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Abstract

Large fractions of genomes are expressed in most eukaryotic cells, generating a diverse repertoire of protein-coding and non-coding transcripts. With such complexity, and as the number of gene-specific mRNA molecules per cell are often low, it is clear that errors anywhere in the gene expression process could have profound consequences on cellular functions. My laboratory is interested in understanding how cells monitor the quality of gene expression at the transcription and post-transcriptional level. In this article, I will discuss our progress in the characterization of a previously unrecognized mechanism of RNA decay that depends on nuclear polyadenylation, which challenges the view that poly(A) tails only function to promote gene expression.

Introduction

Polyadenylation of mRNA 3' ends is a fundamental feature of eukaryotic gene expression. The addition of a poly(A) tail to the 3' end of an mRNA is a co-transcriptional process that generally involves endonucleolytic cleavage of the nascent transcript by the cleavage and polyadenylation machinery, a protein complex that functions in polyadenylation site (PAS) recognition (1). Endonucleolytic cleavage generates a free 3' hydroxyl group on the nascent transcript that serves as a template for polyadenylation by the canonical poly(A) polymerase (PAP). The mechanisms that dictates poly(A) tail length control are still poorly understood and likely involve competition between deadenylase and PAP activities, recognition by poly(A)-binding proteins (PABPs), and nuclear export (2, 3). In the cytoplasm, the poly(A) tail of the exported mRNA will be decorated by cytosolic PABPs, which are generally thought to stimulate gene expression by facilitating translation via interactions with translation initiation factors bound to the 5' cap structure.

Polyadenylation-mediated RNA degradation: The TRAMP complex

Polyadenylation has long been known to signal for RNA

destruction in prokaryotes (4) Conversely, in eukaryotes, the poly(A) tail is generally considered to positively contribute to gene expression by promoting nuclear export, RNA stability, and translational activity. Yet, in the past few years, unsuspected mechanisms of polyadenylation-mediated RNA decay have come to light in eukaryotic cells. Using the budding yeast *Saccharomyces cerevisiae*, three independent groups reported on the discovery of a novel nuclear polyadenylation complex that consist of a noncanonical poly(A) polymerase (Trf4 or Trf5), an RNA-binding protein (Air1 or Air2), and the RNA helicase Mtr4 (5-7). This complex, which has been termed TRAMP, promotes the rapid degradation of "cryptic unstable transcripts" (CUTs), which generally arise from the intrinsic nature of RNA polymerase II promoters to initiate divergent transcription (i.e. two independent pre-initiation complexes that initiate transcription in opposite directions). In yeast cells deficient for subunits of the TRAMP complex, the divergent CUT RNAs, which are not readily detectable in wild-type cells, now accumulate (7). TRAMP mutant cells also accumulate aberrant versions of structural noncoding RNAs, such as ribosomal RNAs (rRNAs) and small nucleolar RNAs (snoRNAs), which indicated that the TRAMP complex functions in RNA quality control in the nucleus (5, 6). The cellular machinery responsible for the degradation of TRAMP-sensitive transcripts is the RNA exosome, an evolutionarily conserved complex that forms a barrel-like structure (8). In yeast, the core exosome is assembled from nine catalytically inactive subunits along with the Dis3/Rrp44 enzyme, which exhibits both 3'→5' exonucleolytic and endonucleolytic activities (9). In the nucleus, the 10-subunit core exosome is associated with an additional 3'→5' exonuclease, Rrp6, which is located above the exosome core (8, 9). Although the mechanistic details of how the TRAMP polyadenylation complex stimulates the degradation capacity of the RNA exosome are not fully understood, the poly(A) polymerase and helicase activities are thought to facilitate substrate recognition by the exosome (10).

An unsuspected role for a yeast nuclear poly(A)-binding protein in RNA decay

My laboratory's interest in polyadenylation-dependent RNA decay originated as a result of a proteomic screen for the identification of substrates of arginine methylation in the fission yeast, *Schizosaccharomyces pombe* (11). Amino acid sequence analysis of a candidate protein (Pab2) showed significant homology to a human protein called poly(A)-binding protein nuclear 1 (PABPN1). PABPN1 had been studied extensively at the biochemical level, where it was found to stimulates processive poly(A) synthesis by direct and simultaneous interactions with the growing poly(A) tail and the poly(A) polymerase (12). Yet, although in vitro assays defined a biochemical activity for PABPN1 in general mRNA polyadenylation, little was known about the cellular functions of this poly(A)-binding protein. Notably, PABPN1 is the product of the oculopharyngeal muscular dystrophy (OPMD) disease gene (13). OPMD is a disorder of skeletal muscle cells that is primarily associated with eyelids drooping, swallowing difficulties, and proximal limb weakness. OPMD has now been reported in more than 35 countries (14) with one of the strongest prevalence being found in the Canadian population (15). OPMD is also more common in Bukharian Jews (16) and New Mexican Hispanics (17) than in the general population. OPMD symptoms usually appear between the fourth and sixth decade with progressive weakness in the muscles of the upper eyelids (ptosis) and pharyngeal muscles (dysphagia). As there is presently no cure to OPMD, patients compensate the progression of ptosis by reclining the head, while dysphagia is initially helped by a liquid diet; however, fluids may also become difficult to swallow as the disease progresses (18). As illustrated in Fig. 1, a stretch of six GCG-repeats is found in the normal PABPN1 allele, whereas between eight and thirteen GCG-repeats are found in OPMD alleles (13). Due to the presence of four alanine-encoding GCN codons adjacent to the (GCG)6 repeats, the amino-terminal region of the normal PABPN1 protein contains a stretch of 10 alanines, whereas the mutated PABPN1 alleles code for proteins with a stretch of 12-17 alanines. Importantly, GCG expansions in the PABPN1 gene have been found in OPMD patients from different regions of the world (19-21), confirming PABPN1 as the OPMD disease gene. Nevertheless, even 16 years after the identification of OPMD mutations, the underlying mechanism by which short GCG insertions in the PABPN1 gene causes OPMD remains unknown.

In addition to showing strong homology to PABPN1, *S. pombe* Pab2 protein showed biochemical and cellular properties consistent with being a functional homolog of human PABPN1: Pab2 binds specifically to poly(A) sequences, localizes to the nucleus, and is arginine methylated (11). Surprisingly, however, deletion of the pab2 gene in *S. pombe* did not impair growth (11). This was unsuspected, given the predicted role of human PABPN1 in mRNA polyadenylation, a critical step of gene expres-

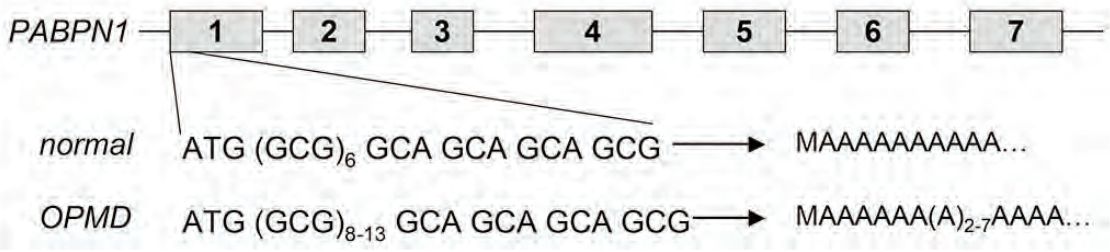

Figure 1. Mutations in the *PABPN1* gene that result in oculopharyngeal muscular dystrophy (OPMD). *The human PABPN1 gene contains seven exons, which are illustrated as blue rectangles and are not drawn to scale. In the normal PABPN1 allele, six tandem GCG repeats followed by four GCN codons are adjacent to the ATG start codon. Translation of the resulting mRNA produces a PABPN1 protein with a stretch of 10 consecutive alanines that follow the initiating methionine (M). In OPMD, the six tandem GCG repeats are expanded to 8-13 repeats, which yield a PABPN1 protein with a stretch of 12-17 alanines.*

sion. Accordingly, most proteins required for cleavage and polyadenylation are encoded by essential genes in yeast. RNAs from pab2-null cells display hyperadenylated 3' ends, indicating a key role for Pab2 in polyadenylation control in vivo. At this point, however, it was unclear whether the hyperadenylated phenotype of the pab2 mutant was due to the hyperadenylation of all RNAs or a subset of transcripts. We therefore used a genome-wide approach to get insights into the molecular mechanism responsible for detection of hyperadenylated RNAs in cells deficient for Pab2. Notably, the expression and polyadenylation status of most mRNAs were unaffected by the deletion of pab2, arguing that Pab2 is not required for global mRNA polyadenylation. Indeed, only a subset of genes demonstrated a significant change in RNA levels in the absence of Pab2 (22). Surprisingly, one class of genes that was misregulated in the pab2 mutant was encoding snoRNAs, a specific type of noncoding (nc) transcripts that functions in the post-transcriptional maturation of ribosomes. This was unexpected because snoRNAs were known to lack a 3' poly(A) tail. We were able to show that cells deficient for Pab2 accumulate 3'-extended snoRNAs with long poly(A) tails, and that this accumulation is associated with reduced levels of mature, non-polyadenylated snoRNAs (22). This observation was consistent with a model in which S. pombe snoRNAs can be matured from polyadenylated precursors via a pathway that requires Pab2. The enzymatic activity that functioned with Pab2 to promote the 3' end maturation of polyadenylated snoRNA precursors remained undetermined, however. By using functional genomics and comparing the expression profile of the pab2 mutant with the RNA profiles of several fission yeast mutants, we found a functional relationship between Pab2 and the RNA exosome (22). Importantly, we were able to show physical association between Pab2 and the RNA exosome complex, supporting a model in which Pab2 promotes poly(A) tail trimming from pre-snoRNAs by recruiting the exosome. These findings presented the first example of a PABP involved in the maturation of noncoding RNAs, contrary to the notion that PABPs function exclusively on protein-coding mRNAs.

A novel pathway of polyadenylation-dependent RNA degradation

Further analysis of Pab2-regulated transcripts indicated that a significant number of genes up-regulated in the pab2 mutant were associated with meiotic differentiation, including both mRNAs and ncRNAs. As for snoRNA precursors, the nuclear exosome complex cooperates with Pab2 in the negative regulation of meiotic transcripts (23). Our study as well as work from others (24, 25) established Pab2 as a trans-acting factor that prevents untimely expression of meiotic differentiation genes in mitosis. Our finding unveiled a previously uncharacterized mode of gene regulation in which Pab2 targets specific transcripts for rapid degradation in the nucleus. We also used next-generation sequencing (RNA-seq) to examine the global effect of pab2 and exosome mutants on the level of all pre-mRNAs. Analysis of exon-intron reads and exon-exon transreads revealed the Pab2 contributes to a nuclear pre-mRNA decay pathway that competes with pre-mRNA splicing to regulate gene expression (26) A Pre-mRNA degradation pathway that selectively targets

intron-containing genes requires the nuclear poly(A. Accordingly, in the absence of Pab2, specific genes accumulate both mRNA and pre-mRNA. To further characterize the mechanism underlying the specificity of this pre-mRNA decay pathway, we studied the rpl30-2 candidate gene that encodes for a ribosomal protein. Notably, we found that the Rpl30-2 paralog, Rpl30-1, binds to the rpl30-2 intron to inhibit splicing, and thereby sensitize the rpl30-2 pre-mRNA to Pab2- and exosome-dependent nuclear decay. This study described a new mechanism of gene regulation in which nuclear RNA decay competes with pre-mRNA splicing to control the expression of specific genes.

Pab2-dependent RNA decay is evolutionarily conserved

The characterization of an unexpected role for *S. pombe* Pab2 in a novel pathway of polyadenylation-dependent RNA decay raised the question as to whether this function was conserved in humans. As mentioned previously, the consequences of PABPN1 deficiency on global gene expression had not been examined in human cells, and therefore, the requirement of PABPN1 for general mRNA synthesis was largely based on in vitro assays. To investigate the global effect of a PABPN1 deficiency on human gene expression, a transcriptome-wide analysis of PABPN1-depleted cells using RNA sequencing was performed. Consistent with analyses of *S. pombe* pab2 mutants, it was found that the expression of only ~5% of protein-coding genes was affected by the loss of PABPN1 in human cells (27). Although the mechanism by which PABPN1 affects the expression of these specific mRNAs remains to be elucidated, it appears to be independent of the role of PABPN1 in the regulation of polyadenylation site decision (28, 29). Importantly, the transcriptome analysis of PABPN1-deficient cells by RNA sequencing revealed a greater impact on the expression of long noncoding RNAs (lncRNAs) relative to mRNA expression (27). Specifically, a majority of PABPN1-sensitive lncRNAs showed increased expression in PABPN1-deficient cells, a result that supports a prominent role for PABPN1 in the negative regulation of lncRNA expression. Mechanistically, PABPN1 promotes lncRNA turnover via a polyadenylation-dependent pathway that likely involves the RNA exosome (27, 30). Such a model for PABPN1-dependent RNA decay is remarkably similar to how its fission yeast homolog, Pab2, activates the degradation of specific transcripts in *S. pombe*. Accordingly, Pab2 promotes TRAMP-independent, exosome-mediated decay of select transcripts via the polyadenylation activity of the canonical poly(A) polymerase (23-26), suggesting that this polyadenylation-dependent RNA decay pathway has been conserved. lncRNAs have been a major point of interests in the past few years, as they have been implicated in several important biological processes (31). Yet, despite significant progress into the characterization of lncRNAs, little remains known about mechanisms that control lncRNA expression.

Future directions

The addition of a poly(A) tail at the 3' end of an RNA is a fundamental step in the course of the gene expression process in eukaryotic cells. Because the product of polyadenylation corresponds to a widespread and repetitive sequence of adenosines, the poly(A) tail is not generally considered to be involved in gene-specific regulation via trans-acting factors. However, work from several labs now indicate that the 3' poly(A) tail can function in gene regulation through the action of poly(A)-binding proteins in the nucleus. What molecular cues dictate a polyadenylation event associated with gene expression versus nuclear turnover? What distinguishes PABPN1-sensitive lncRNAs from other polyadenylated noncoding transcripts? Are PABPN1-sensitive lncRNAs involved in the development of OPMD? The answer to these challenging questions will certainly provide fascinating insights into the emerging role of noncoding RNAs to cell biology.

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2014 Young Canadian Cell Biologist of the Year

Alexandre Orthwein,
Lunenfeld-Tanenbaum Research Institute, Toronto

An award for the "Young Canadian Cell Biologist of the Year" has been established by the CSMB and the American Society for Cell Biology (ASCB) for a Ph.D. student or post-doctoral fellow at a Canadian institution to attend the ASCB Annual Meeting. The CSMB will provide $500 towards travel costs, and the ASCB will provide free meeting registration. The award winner will be a Ph.D. student or post-doctoral fellow at a Canadian institution who has published a high impact, first or co-first author, cell biology paper in the past year. They will also be judged on their ability to place their research into context. The award winner must be a CSMB member (free for students and post-docs) and their supervisor must also be CSMB member in good standing for at least the past two years.

The 2014 winner of this award, Alexandre Orthwein, provided the following report on the 2014 ASCB meeting, held in Philadelphia:

Thanks to the financial support of both the CSMB and the ASCB, I had the great opportunity to attend the 2014 ASCB/IFCB Annual Meeting in Philadelphia for the first time. The program of this year, assembled by Wallace Marshall and Michael Marks, exemplified the importance of cross-disciplinarity in science. Given the wide offering of research topics, I was exposed to certain domains of cell biology that I was not aware of, and got an overview of the current hot topics/techniques in the field.

In that matter, the Keynote speakers Steven W. Squyres and Robert M. Hazen inspired me as to how physical and earth sciences can influence our view of cell biology. Steven W. Squyres showed us breath-taking images of Mars taken by Exploration Rover's Spirit and Opportunity. He also exposed the detailed analysis of the composition of the rocks on Mars and how they may have been altered by water. For his part, Robert M. Hazen exposed his concept of mineral evolution where both the geosphere and the biosphere have co-evolved. His work put in perspective the role of minerals in the origin of life and their interdependence.

Out of all the fantastic talks and posters, I was particularly interested in the technological advancements in optogenetics, as well as the use of the CRISPR/Cas9 genome editing technology. Dr. Chandra Tucker gave a captivating talk on the use of light-inducible oligomerization for disrupting or stimulating protein activity, as well as visualizing protein-protein interaction.

Due to my background in DNA damage, I was amazed by the talk of Dr. Titia de Lange, the recipient of the Canada Gairdner International Award 2014, on 53BP1s functions at dysfunctional telomeres. She showed that 53BP1, besides its role in preventing DNA end-resection, also has a role in stimulating the mobility of dysfunctional telomeres through the LINC complex.

Altogether, this meeting was a fantastic opportunity for constructive scientific exchange and stimulation. I had the chance to appreciate the recent advances in cell biology as well as the technology developments that will help us tackle new questions in the field. I am grateful to the ASCB and the CSMB for their financial support and I hope I will attend the next edition of the ASCB/IFCB.

Keynote Lecture

Lessons from a Red Squirrel, Mentors, and the Pathway to Success

Reinhart A. F. Reithmeier
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Abstract

In this article I will review my personal career path starting with how a red squirrel got me interested in research, and the vital role that mentors played in my pathway to success – a pathway that taught me many lessons that I would like to share with the reader, particularly graduate students and post-doctoral fellows who are just starting down their own unique pathways.

I dedicate this article to my parents, Friedrich and Reinhilde Reithmeier, who taught me the value of hard work and encouraged me to find my own pathway to success.

Lesson #1: Follow your passion

It all started with a red squirrel.

I grew up in Ottawa and went to Bell High School where I was a solid B+ student. Mr. Gibson was my Grade 13 Biology teacher and he was inspiring. Near the end of the course, students had to carry out an independent research project of our own design. My parents were nature lovers and growing up in the countryside outside of Ottawa I had lots of time to explore my environment. So, I decided to do a comparative population study of red and black squirrels.

Every weekend in the Spring I trotted around the forests that surrounded our house and catalogued every squirrel sighting on a map. I found plenty of black squirrels but I couldn't find any red squirrels. As my project was to compare the two populations I was sure my project would fail. In the last week before the project was due I roamed further afield into a grove of old pine trees -a climax forest. When I entered I was greeted by incessant chattering. There, high up in a tree was a red squirrel holding a pinecone.

I searched and searched the pine forest for another but could not find any other squirrels red or black. So I wrote up the project expecting my usual B+. Boy, was I amazed when Mr. Gibson gave me an A+. He said that I had discovered a fundamental principle of biology: black squirrels are gregarious and live in communities in deciduous forests, while red squirrels are solitary, live in coniferous forests and defend their territory even from other red squirrels. It's amazing what you can learn by just looking around, even from a single red squirrel. From that moment on, I was passionate about discovering things on my own and decided research would be my life.

Lesson #2: Find something you like and are good at

I went to Carleton University in Ottawa and switched majors three times. I started out in Honours Chemistry but found the math too hard. In 2nd year I switched to Honours Biology, which I really liked and was good at. In 3rd year Carleton created an Honours Biochemistry Pro-

gram, a perfect combination of my love for biology and the rigors of chemistry. I did my 4th year project on lysozyme with Stan Tsai in Chemistry. He taught me enzyme kinetics and how come up with a well-designed experiment. I graduated in the first Biochemistry class in 1972 that celebrated its 40th anniversary in 2012. I married Kathleen Devlin the summer of '72, and she has been my greatest supporter ever since. In fact, a supportive and understanding partner is an essential key to success.

Lesson #3: Research is hard work but should be fun too

In the summers of 1971 and '72 I was fortunate to work at the NRC labs in Ottawa in an historic building on Sussex Drive. The 1st summer I worked on sequencing ribosomal proteins from diverse bacteria with Mak Yaguchi. Mak taught me that research was hard work, and it paid off a decade later with a paper on *E. coli* S14 [1]. The next summer I was back at NRC and worked on plant histones with Lou Visentin. Lou taught me that research was fun. He had a real enthusiasm for research and it was infectious. The sequence of a pea plant histone had just come out and I was amazed that it was identical to the animal histone -a lesson in protein conservation. Lou encouraged me to apply to graduate school and to write to Gordon Dixon, a leading histone expert at UBC. As my professional golf (another early passion) career was going nowhere, graduate school not Q-school it was!

Lesson #4: "When you come to a fork in the road, take it." (Yogi Berra)

I heard back from Gordon Dixon, but he was moving to England. He had passed my letter on to Phil Bragg, an expert in bioenergetics who worked on membrane proteins. I won an MRC Studentship and joined the Bragg lab to work on outer membrane proteins of *E. coli*. My first paper was published in FEBS Letters in 1974 [2]. Forty years later I am pleased that outer membrane proteins are still of broad interest. Little was I to know that membrane proteins were to become my life's work. Had Gordon Dixon stayed at UBC I might well be working on the "histone code" and epigenetics today.

Lesson #5: Aim high and do not be afraid to move afar

When I started looking for a post-doctoral fellowship, one of my committee members, Denis Vance, a new faculty member at UBC, now at the University of Alberta, recommended that I apply to Harvard to work with Guido Guidotti who led a large lab working on red cell membrane proteins. Denis had been at Harvard with Nobel Prize winner Konrad Bloch and he praised the high-powered research environment. There was a postal strike on and I remember driving down to Bellingham, Washington to send in my application to MRC for a post-doctoral fellowship and my letters to Guidotti.

Lesson #6: Come up with your own ideas, but work with smart people

Guido told me he had space, but wanted me to design my own project, just like Mr. Gibson! I knew nothing about red cell membrane proteins. I took what I had learned in the Bragg lab and decided to apply the same sort of methods (hydrodynamics, crosslinking, biophysical techniques) to the Band 3 protein of the human red cell membrane. Again, little did I know that Band 3 would be my life's work right up to today [3].

The Guidotti lab was indeed big with over 20 members, and he encouraged interactions and collaborations. So, beside my own project I developed joint projects with Anjana Rao and Lew Cantley, two of the smartest people I have ever met. Guido never put his name on papers unless he actually did experimental work, so I learned how to design my own experiments, carry them out, write up the paper and get it published. I published four papers, two with Anjana, one with Anjana and Lew, and one as a solo author [4].

Lesson #7: Be ready to go out on your own

Due to budget cuts my MRC Post-doctoral Fellowship was only for two years rather the normal three. I knew that I wanted to return to Canada and decided to apply for a Best Fellowship to work with David MacLennan at the University of Toronto, an expert in muscle proteins of the sarcoplasmic reticulum (SR). David was doing the kind of structural studies I like, but importantly he was also looking at the biosynthesis and assembly of membrane proteins using techniques like cell-free translation that I was keen to learn. These approaches led to the cloning and sequencing of the proteins of the SR. David was a leader and he was always one step ahead of the competition.

The MacLennan lab was big and well-funded, but more importantly it was like a big family. I had the good fortune of working with three star technicians: Stella DeLeon, Vijay Khanna and Kaz Kurzydlowski. The MacLennan lab was always full of smart people, many of whom (early on, Paul Holland, Amira Klip, Annelise Jorgensen, Kevin Campbell, Marek Michalak and Denis Lebel, and later on, Chris Brandl, Jonathan Lytton, Larry Fleigel, Balwant Tuana, Wayne Chen, and David Clarke, to name a few)

have gone on to successful research careers and often into leadership positions. David was an inspiration and a mentor to us all.

MacLennan reunion in 2002 of people in the lab in the late 70s. Front row from left: Varda Shoshan, Stella DeLeon, Reinhart Reithmeier, David MacLennan, Kevin Campbell. Back row from left: Annelise Jorgensen, Amira Klip, Hania Michalak, Marek Michalak, Ann Campbell and Vijay Khanna.

After a couple of years with more publications under my belt, David said I was ready to go out on my own and he encouraged me to look at the Department of Biochemistry at the University of Alberta.

Lesson #8: When opportunity knocks, open the door

In 1980 there were no faculty jobs in Canada and research funding was very tight. Alberta had just created the Alberta Heritage Foundation for Medical Research (AHFMR). John Colter, Head of Biochemistry (for life!) invited me out to the University of Alberta for a visit. To say that John was persuasive is an understatement. He pulled out all the stops to recruit me (and more importantly my wife Kathleen) to the Department that he had built up since the early 60's. With the Heritage funding about to follow and a stellar MRC Group in Protein Structure forming the core, the choice was easy. John convinced me that the opportunities were perfect for me to start my independent research career. I was lucky to win an MRC scholarship and get my MRC grant ($28,500 prorated to 1.5 years since I started in September not April) on my first try.

With the support of AHFMR, I recruited my first star technician (Debra Lieberman), graduate students (Pamela Werner and Sanjay Pimplikar), post-doctoral fellows (Valeta Gregg, Jamie Craik and Mamoru Ohnishi) and a raft of undergraduate summer and project students.

The Reithmeier lab in Alberta circa 1985. Front row from left: Joe Slupsky, Sanjay Pimplikar. Second row from left: Jamie Craik, Pamela Werner, Debra Lieberman, Kenzi Goudon, Mamoru Ohnishi. Back row from left: Perry Telzerow, Reinhart Reithmeier, Lorne Cheeseman.

The first three papers [5-7] from my own lab were published in 1983 based on quite simple and straight-forward experiments on Band 3 that I performed on my own, with Debra, and with my first post-doc, Valeta Gregg.

Joel Weiner had arrived previously from Stanford and like Phil Bragg, was an expert in bioenergetics. We share a common interest in membrane proteins that stands until this day. Along with Carol Cass and Ron McElhaney, we made up the core of membrane biochemistry at U of A in the early 80s.

Lesson #9: Face the class and speak up

I was a terrible lecturer. I was nervous and spoke very quickly. I used the blackboard and had my back to the class most of the time. Early on I watched Cyril Kay, a Professor in Biochemistry, in action and asked him to sit in on one of my introductory biochemistry lectures on metabolism. Cyril gave me some tips that have made me a better lecturer. First be very well prepared and don't lecture from notes. Make it interesting but don't dumb it down - these kids are smart and eager to learn. Face the class and speak clearly. Don't try to cram too much into a lecture, summarize as you go along. Finish on time. Design exams that allow students to apply what they

The membrane group in the Biochemistry Department at the University of Alberta at a Banff Membrane Meeting in the early 1980s. From left: Joel Weiner, Carol Cass, Reinhart Reithmeier, Ron McElhaney.

learned to real problems. Along with Charles Deber and Roy Baker, two superb lecturers, I now teach Biochemistry to over 1,000 undergraduate students in convocation Hall at U of T and enjoy every class. All three of us have won teaching awards - for me credit goes to Cyril Kay. We have even been asked to perform in fund-raising concerts in Convocation Hall as the Pro-Teens and have the courage to do so.
I even have a You-Tube video. See: How to Sleep in Biochemistry Class: http://www.youtube.com/watch?v=s0tgnJtUgdU

Lesson #10: Mentors are essential
For personal reasons we moved back to Ontario in 1986. Mel Silverman, a nephrologist in the Department of Medicine at the University of Toronto, led a research group in Membrane Biology and was looking for a membrane protein biochemist, and I fit the bill. Mel was a clinician-scientist who creating a grouping within a clinical department where basic research could flourish. Being trained in Physics he believed in the interface of theoretical and experimental approaches. Mel was a mentor to me. He helped to develop my career and was a ready source of advice and encouragement. We created an MRC Group and I developed a research stream looking into the role of membrane proteins in kidney and other diseases. I again built up a research team of excellent technicians, students and fellows. Some stayed in academia like Joe Casey, Emmanuelle Cordat, and Rongmin Zhao, some like Jeff Charuk and Yuka Okawa went into the biotech business world, and others like Hilario See, Carol Landolt, Alison Pang, Lisa Tam, Milka Popov, John Vince, Janne Quilty, Joanne Cheung, Sian Patterson, Susan Bustos and Homa Kameh became doctors, dentists, teachers, lecturers, science writers, and research administrators. I am proud of them all. My technician, Jing Li, has been with me for over 15 years and she is the backbone of my lab today.

The Reithmeier lab in Toronto circa 1990. Front row from left: Joe Casey, Jeff Charuk. Second row from left: Hilario See, Reinhart Reithmeier, Charlie Pirraglia. Back row from left: Carol Landolt, Debra Lieberman.

The Reithmeier lab in Toronto in the summer 2002. From left: Sian Patterson, Saranya Kittanankom, Susan Bustos, Emmanuelle Cordat, Jing Li, Joanne Cheung, Janne Quilty, Kevin Kuo.

Lesson #11: Follow the leaders and become one
Cathy Whiteside was a member of the Membrane Biology Group and a very successful clinician-scientist like Mel Silverman. I followed Cathy as Graduate Coordinator of

the Institute of Medical Sciences (IMS) where I continued to formalize procedures and raise standards for over 300 graduate students. Cathy went on to be Dean of the Faculty of Medicine, where she provided tremendous support to basic sciences departments like Biochemistry. One day in 2001 I received a call from then Dean David Naylor asking me to apply for the Chair of Biochemistry, as Chair Peter Lewis' term was coming to an end and he had moved to a Vice-Dean Research position. At that time, Mel was busy with administration, Cathy was already in the Dean's Office and the MRC no longer funded groups, so I applied and landed the position. My first year was very stressful, but eventually with a lot of support from colleagues like David Williams (and my wife Kathleen), and by building consensus, the Department was able to accomplish a great deal. We hired new recruits including a CERC, captured and renovated new space, developed new undergraduate programs and increased graduate enrolment and funding. I was Chair for over 10 years and I happily declare: "It's the best job I have ever had".

Lesson #12: Develop collaborations and use sabbaticals to enrich your life

Sabbaticals are a way to enrich your research and personal life, yet most people don't take them and if they do they stay in their own labs. Sabbaticals are certainly disruptive and can be expensive. I have used sabbaticals to develop new research skills: the first in molecular biology with Jacques Pouysségur in Nice, France, where I worked with graduate student Laurent Counillon; the second in membrane protein crystallography with Natalie Strynadka at UBC, where I worked with the magnificent Trevor Moraes; and the third in molecular dynamic simulations of membrane proteins with Mark Sansom at Oxford, where I worked with an outstanding (and patient) post-doc Antreas Kalli. All three labs were big and full of bright people. In all cases I developed collaborative projects with members of the lab that led to publications [8, 9] and friendships that last until today. I encourage graduate students and postdoctoral fellows to initiate collaborations.

A final lesson: Develop your skill set and build a network

The majority of graduate students today will obtain jobs outside of academia. This is not necessarily bad news, as graduate have been able to carve out their unique pathways to very diverse and successful careers. Universities but also business, government, the charitable sector, etc. need to hire PhDs, who are trained to be deep thinkers, problem solvers, innovators and most importantly, leaders.

Firstly, it is more vital than ever to use your graduate education to develop your skill set (see: http://www.conferenceboard.ca/topics/education/learning-tools/employability-skills.aspx); a diverse skill set that goes beyond technical expertise or knowledge of a system. Skills that employers are looking for include communication skills, working as an effective member of a team, time and project management, analytical and problem solving skills.

Secondly, you need to build a network beyond the confines of your research project. Do you have any contacts in business, biotech, government, hospitals etc.? A good place to start is with your own alumni. You will find many people who have developed successful career paths inside and outside of academia. These folks are usually more than willing to give back in terms of their time and experience. Contact an alumnus and arrange a meeting over lunch or a coffee. Do your research and arrive prepared with your CV or a targeted resumé. Interview the person and ask about their career path and how what they learned in graduate school helps them in their job today. Follow-up by e-mail and a Linked-In connection. You never know where this simple conversation can lead and what doors it could open. To get started, make a "cold call" to an alumnus.

Dr. Nana Lee and I created a graduate course in professional development in the Department of Biochemistry at the University of Toronto that was featured in an article in Science Careers:
(http://sciencecareers.sciencemag.org/career_magazine/previous_issues/articles/2013_10_01/caredit.a1300216)

The Conference Board of Canada has launched a Centre for Skills and Post-secondary Education in response to the changing educational landscape. The bottom line: while graduate education, especially at the PhD level must have a clear focus on research and scholarship, graduate programs should also incorporate professional development into their curricula in order to fully prepare graduates to take advantage of the diverse career and leadership opportunities available to them in today's, and more importantly, tomorrow's global job market.

Conclusion:

Throughout my career I have been very fortunate to have a supportive partner, excellent mentors, and role models.

In turn, I hope that I have been a mentor and role model to my students and fellows too. I have outlined experiences and lessons that I have learned along the way that I'm sure will resonate with others. There are many pathways to success - you have to find the right one for you. Luckily there are many people and perhaps even a red squirrel to help you along the way.

Lessons From a Red Squirrel

Lesson #1	Follow your passion
Lesson #2	Find something you like and are good at
Lesson #3	Research is hard work but should be fun too
Lesson #4	"When you come to fork in the road, take it." (Yogi Berra)
Lesson #5	Aim high and don't be afraid to move afar
Lesson #6	Come up with your own ideas, but work with smart people
Lesson #7	Be ready to go out on your own
Lesson #8	When opportunity knocks, open the door
Lesson #9	Face the class and speak up
Lesson #10	Mentors are essential
Lesson #11	Follow the leaders and become one
Lesson #12	Develop collaborations and use sabbaticals to enrich your life
Final Lesson	Develop your skill set and build a network

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News from Member Departments

Carleton University

Institute of Biochemistry

Correspondent: William Willmore

Faculty news:

The year 2014 was marked with a number of events including the development of a new Graduate Specialization in Biochemistry to be shared between the Departments of Biology and Chemistry at Carleton, approval for new hires into the Institute of Biochemistry, and new members coming into the Institute. News on the former two will be reported in the next issue of the CSMB Bulletin. New members of the Institute of Biochemistry include Drs. Bruce McKay and Alex Wong. Their bios are below.

Bruce McKay

Bruce McKay is a new member of the Department of Biology and Institute of Biochemistry at Carleton University. Despite his recent arrival at Carleton, Dr. McKay has already had a distinguished career studying genomic stability and cancer. Dr. McKay graduated with a B.Sc. in Biology from the University of Toronto (Erindale College, UTM) in 1990 where he was encouraged to continue in graduate school by Dr. Jim Anderson, a fungal geneticist. He followed one of Dr. Anderson's former post-doctoral fellows, Dr. Alan Castle, to the Department of Biological Sciences at Brock University in 1991, and he completed his M.Sc. with Dr. Castle in 1993. His project involved the cloning and characterization of the genes encoding the subunit of fungal fimbriae from *Coprinopsis cinereus* and *Microbotryum violaceum.*

In 1993, Dr. McKay joined Dr. Andrew Rainbow's radiation biology laboratory in the Biology Department at McMaster University. During his Ph.D., he used recombinant DNA viruses as a model system to study the repair of ultraviolet (UV)-induced DNA lesions in cultured human cells. Specifically, Dr. McKay and his colleagues reported that the capacity of human cells to repair UV-damaged viral reporter constructs could be increased by prior exposure to UV light or heat shock. This inducible repair response was absent in repair-deficient fibroblasts and other cells lacking functional p53. These findings provided the first evidence that nucleotide excision repair is inducible in a p53-dependent manner.

Dr. McKay started his post-doctoral studies in 1997 under the supervision of Dr. Mats Ljungman in the Department of Radiation Oncology at the University of Michigan. Together, they advanced a very important concept in DNA damage signalling. They found that the p53 tumour suppressor could be activated by DNA lesions indirectly through their effect on elongation of RNA polymerases. Conversely, the p53 response itself stimulated the recovery of transcription following transcription arrest. Therefore, they proposed the concept that p53 is not only the "guardian of the genome" by preventing the propagation of cells with irreparable DNA damage, but that p53 is tightly linked to transcriptional competence so it can be considered a "guardian of transcription".

In early 2000, Dr. McKay took a career scientist position with Cancer Care Ontario and the Ottawa Hospital Research Institute. During his 13 years at the Ottawa Hospital, Dr. McKay headed a successful research group focussed on two primary projects. In one project, his laboratory studied how DNA capacity impacted the response of human cells to platinum-based anti-cancer compounds. For example, RNA interference against the Cockayne syndrome group B protein increased the response of a variety of tumour cells to cisplatin in vitro and in vivo suggesting that this pathway may be a viable therapeutic target. In the second project, Dr. McKay found that the structural organization of p53- responsive genes (i.e. gene size, 3'UTR length and the sequence of 3'UTRs) affected their temporal pattern of expression. This work yielded several distinctions, including a Bio-

medical Research Scientist Award through the Canadian Cancer Society and an Ontario Premier's Research Excellence Award.

Dr. McKay joined the Department of Biology and the Institute of Biochemistry at Carleton University in 2013. He maintains clinical collaborations and Affiliate Investigator status at the Ottawa Hospital Research Institute. He has established a strong research group at Carleton and continues to work on these evolving projects. Dr. McKay's courses are popular with students. He is a welcome addition to the University.

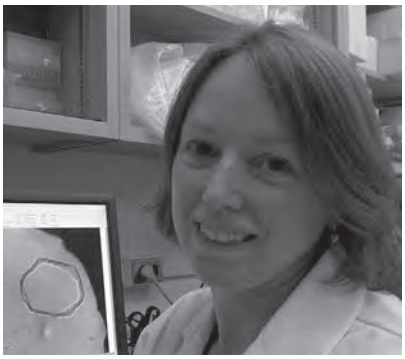

Alex Wong

Alex Wong is an Assistant Professor in the Department of Biology, and a member of the Institute of Biochemistry, at Carleton University. He has broad interests in microbiology, genomics, and evolutionary biology, with particular focus on the evolution and genetics of antibiotic resistance in pathogenic bacteria. He holds a B.A. in Biology and Philosophy and an M.A. in Philosophy from Carleton, and a Ph.D. in Genetics and Development from Cornell. He completed a post-doctoral fellowship at the University of Ottawa and a Banting Fellowship at Carleton before starting his faculty position in 2013. Dr. Wong has published 38 papers, and in 2010 was awarded the Dr. John Charles Polanyi Prize for Physiology and Medicine.

Dalhousie University

Department of Biochemistry & Molecular Biology
Correspondent: Stephen L. Bearne

The 2014-15 academic year has been a time of change within the Department of Biochemistry & Molecular Biology at Dalhousie University. In September, we were very pleased to have **Vanya Ewart** join the Department as an instructor after 17 successful years as a Research Officer at the National Research Council in Halifax. Vanya brings with her an expertise in protein structure and function, particularly applied to the study of ice-binding proteins. In addition to teaching introductory biochemistry, she will establish a new laboratory-based course for students enrolled in Dalhousie's new Medical Sciences Program.


Vanya Ewart

Carmichael Wallace will be retiring on June 30, 2015 after 28 years of service in the Department. Over the years, Carmichael and his co-workers conducted numerous studies on cytochrome c to delineate the various nuances of structure-function relationships in proteins, proposed a mechanistic model for the extended lipid anchorage of cytochrome c, characterized the ATP-binding site on cytochrome c, and demonstrated the utility of semi-synthesis for protein modification. We wish him all the best in his retirement. **John Archibald** 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 leadership in the microbiological sciences.


Carmichael Wallace


2014 Patrick Prize presentation; (left to right) Dr. Roger McLeod and Eric Fisher

During the past year, the Department has continued to celebrate the success of our students, postdoctoral fellows, and research

2014 Schnare-Spencer Prize presentation;(left to right) Dr. Michael Gray, Heidi MacKinnon, and Dr. Stephen Bearne

Beth Gourley Travel Award presentation (May 2014); (left to right) Dr. John Archibald, recipient Mary McQuaid, and Drs. Catherine and John Lazier

2013/2014 Doug Hogue Award presentation; (from left to right) Zoe Hogue, Dr. Stephen Bearne, recipient Rafaela Andrade-Vieira, Dr. Paola Marignani, and Calla Shank-Hogue

Beth Gourley Travel Award presentation (Dec 2014); (left to right) Dr. Catherine Lazier, recipient Alexandra Reda, and Dr. Stephen Bearne

associates. **Heidi MacKinnon**, the technician in our undergraduate teaching laboratory, received the 2014 *Schnare-Spencer Prize*, which was established by **Mike Gray** in honour of two long-time research associates in his lab. **Rafaela Andrade-Vieira**, a graduate student with **Paola Marignani**, received the 2013/2014 *Doug Hogue Award* for persistence and dedication to research, and Eric Fisher, a graduate student from Roger McLeod's lab, received the departmental Patrick Prize for outstanding research by a recent Ph.D. graduate. Alexandra Reda from Roger McLeod's lab and Mary McQuaid from Melanie Dobson's lab received the Beth Gourley Travel Award established by Catherine Lazier and her husband John Lazier.

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. We hope to see many colleagues at next year's CSMB 58th Annual Conference in Halifax (June 14–17, 2015).

Hospital for Sick Children Research Institute, Toronto

Correspondents: Julie Brill and Charles Deber

Cell Biology Program

Mathieu Lemaire

New faculty member: **Dr. Mathieu Lemaire** (Scientist-Track Investigator, affiliated with the Division of Nephrology) has joined the Cell Biology program at SickKids after completing his M.D. at McGill and his Ph.D. at Yale. Dr. Lemaire's main focus is on gene discovery pertaining to rare pediatric kidney diseases, as highlighted by his discovery of diacylglycerol kinase ϵ (DGKE) mutations in atypical hemolytic-uremic syndrome.

John Brumell

Sergio Grinstein

Endowed Chair: **Dr. John Brumell** became the recipient of the endowed Pitblado Chair in Cell Biology, previously held by **Dr. Sergio Grinstein**. Dr. Brumell's research dissects the cellular and genetic basis of host-pathogen interactions, focusing on the common pathogens *Salmonella* and *Listeria*. In addition, he studies how host-pathogen interactions can lead to the development of chronic inflammatory diseases.

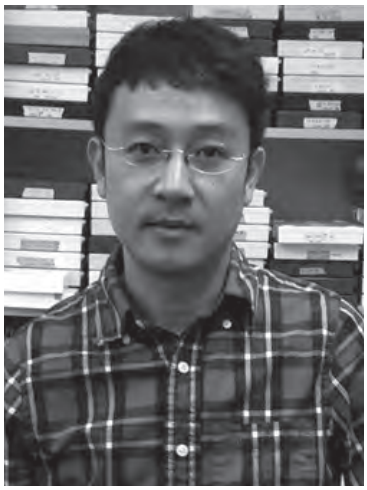
Cynthia Hawkins

Promotion: **Dr. Cynthia Hawkins** was recently promoted to Senior Scientist. Dr. Hawkins' research probes the genetic and molecular basis of pediatric brain tumors, with a particular focus on astrocytomas.

New microscopes: The **Imaging Facility** recently obtained two new super-resolution microscopes (Zeiss Elyra PS1 SIM/STORM and Leica SP8 STED) and a Zeiss Z1 light sheet microscope thanks to a CFI award led by **Dr. Sergio Grinstein**. SIM (structured illumination microscopy) allows resolution more than double that of standard confocal laser scanning microscopes. STORM (stochastic optical reconstruction microscopy) produces images that approach 20 nm resolution, a more than tenfold improvement over standard laser scanning confocal methods. STED (stimulated emission depletion microscopy) is live-cell compatible and can achieve resolution approaching 50 nm. Light sheet microscopy permits high-speed imaging without sacrificing resolution, making it possible to image live embryos over their development.

Developmental & Stem Cell Biology Program

New faculty member: **Dr. Tae-Hee Kim** (Scientist and Assistant Professor, Molecular Genetics) started as a new faculty member in the Developmental & Stem Cell Biology (DSCB) Program in Fall, 2014. He was previously an Instructor and Postdoctoral Fellow at the Dana Farber Cancer Centre with Dr. Ramesh Shivdasani. His



Tae-Hee Kim

research focuses on mechanisms of gut stem cell renewal and differentiation.

New faculty recruit: **Dr. Xi Huang** (Scientist) will be joining the DSCB Program in April 2015. He was a postdoctoral fellow at University of California San Francisco in the lab of Dr. Lily Jan. His research examines ion channels in central nervous system development and tumorigenesis.

Genetics & Genome Biology Program

Monica Justice

New program head: **Dr. Monica Justice** (Program Head and Senior Scientist) was recruited to head the Genetics & Genome Biology (GGB) Program from Baylor College of Medicine, Houston, Texas, where she was a Professor in the Department of Molecular and Human Genetics and Director of the Mouse Embryonic Stem Cell Core and the BaSH Consortium for the Production and Broad-based Phenotyping of Knockout Mice. A pioneer in mouse mutagenesis, Dr. Justice is the recipient of several awards, including an American Cancer Society Junior Faculty Award, the Burroughs Wellcome Innovation Award in Functional Genomics, and the Michael E. DeBakey Excellence in Research Award. Overall, Dr. Justice's research aims to merge mouse modeling with clinical genetics to understand the basis for many human diseases, and to use mouse models to identify new pathways for therapeutic intervention.

Stephen Scherer

In the news: **Dr. Stephen Scherer** (Senior Scientist and Director of The Centre for Applied Genomics) was selected as a 2014 "Nobel-class" Citation Laureate in the category of physiology or medicine, according to an announcement September 25, 2014 by Thomson Reuters Intellectual Property & Science (Thomson Reuters IP & Science).

Berge Minassian

Award: **Dr. Berge Minassian** (Senior Scientist and Professor of Paediatrics) received the Norman Saunders Jacob's Ladder International Research Prize for his work on Lafora and other child neurological diseases.

Rogers Heart Centre: **Dr. Seema Mital** (Scientist) and **Dr. Ronni Cohn** (Senior Scientist) are the joint scientific leads for SickKids in the new Ted Rogers Centre for Heart Research. As one of three partner institutions, SickKids will receive $32M in new funds to be used towards gaining a better understanding of the genetic underpinning and treatment of childhood heart disease.

ASHG news: GGB now sponsors a **SickKid's Trainee and Alumni reception** at the American Society for Human Genetics meetings. Please look for the location in the ASHG program, and attend!

Molecular Structure & Function Program

New program head: **Dr. Julie Forman-Kay** (Senior Scientist, The Hospital for Sick Children; Professor, Department of Biochemistry, University of Toronto) has been appointed Head of the Program in Molecular Structure and Function (MSF) at the SickKids Research Institute, for a five-year term beginning in 2015. She succeeds

Julie Forman-Kay

Dr. Lynne Howell, who held the post for 12 years. Julie brings to the Program an amazing breadth and depth of research expertise in structural and functional analysis of molecular pathways, particularly by NMR spectroscopy, with internationally-recognized contributions to our understanding of intrinsically-disordered proteins.

John Rubinstein

New Canada Research Chair: **Dr. John Rubinstein** (Senior Scientist, MSF Program, SickKids Research Institute) was awarded a Tier I Canada Research Chair in Electron Cryomicroscopy in October, 2014. Professor Rubinstein's research centres on the structural and functional analysis of macromolecular assemblies by electron cryomicroscopy. He joined the SickKids Research Institute in 2006 and holds faculty appointments in the Departments of Biochemistry and Medical Biophysics at U. of T., where he was promoted to the rank of Full Professor in 2014. Dr. Rubinstein was also awarded the 2014 G.E. Healthcare New Investigator award from the CSMB. In 2013, he was awarded the Burton Medal of the Microscopy Society of America for outstanding contributions from a scientist under the age of 40.

Jean Philippe Julien

New faculty member: **Dr. Jean Philippe Julien** has joined the MSF Program as Scientist as of September, 2014, with cross-appointment as Assistant Professor in the Departments of Biochemistry and Immunology at U. of T. Dr. Julien received his B. Sc. with Honors in Biochemistry from McGill University in 2005; and his Ph.D. in Biochemistry at U. of T. in 2010 for his detailed work on the structural characterization of an important anti-HIV 1 broadly neutralizing antibody. He then joined the laboratory of Ian A. Wilson at The Scripps Research Institute in La Jolla in 2010. A major achievement during this time was to solve the first crystal structure of a soluble HIV 1 Env trimer using integrative methods in structural biology and biophysics. This structural information now guides the design of next generation vaccine candidates. His work has led to over 35 publications in top tier journals, authorship in 43 Protein Data Bank (PDB) entries, and numerous awards. Dr. Julien is currently pursuing structure/function studies of the B cell receptor and critical co-receptors on the B cell surface.

Olivia Rissland

New faculty member: **Dr. Olivia Rissland** has also joined the MSF program as Scientist in September, 2014, with cross-appointment to the Department of Molecular Genetics at the University of Toronto as an Assistant Professor. Originally hailing from Boston, MA, Dr. Rissland received her D. Phil. from the University of Oxford, where her studies were funded by a Rhodes Scholarship. During her graduate studies, she performed seminal work in the field of mRNA decay, discovering an unexpected and conserved mRNA degradation pathway in the fission yeast *Schizosaccharomyces pombe*. Dr. Rissland then carried out her postdoctoral work in the laboratory of Professor David Bartel at the Whitehead Institute in Cambridge, MA, where she continued to study post-transcriptional regulatory pathways, focusing on those mediated by microRNAs. The over-arching goal of Dr. Rissland's laboratory is to decipher the framework underlying gene expression, especially at the post-transcriptional level. She plans to use a combination of classical molecular biology techniques and transcriptome-wide approaches to understand the fundamental mechanisms controlling gene expression and to explore how these pathways are misregulated in disease.

Neurosciences & Mental Health Program

Julie Lefebvre

Award: **Dr. Julie Lefebvre** (Scientist and Assistant Professor, Department of Molecular Genetics) was among the winners of this year's 2015 Sloan Research Fellowships, which are awarded to the most promising scientific researchers. Julie is a recent hire, who started in Neurosciences & Mental Health (NMH) in December, 2013, having done her postdoctoral training with Dr. Joshua Sanes at Harvard University. Her research addresses genetic, molecular and cellular mechanisms of neural circuit formation and function in the developing retina and brain.

Chief of Research

Award: Dr. Janet Rossant (Chief of Research, Senior Scientist, Developmental & Stem Cell Biology) is the winner of the 2015 Canada Gairdner Wightman Award. She was recognized for her contributions to developmental biology, leadership in stem cell biology, and role in promoting children's health.

Janet Rossant

McMaster University

Department of Biochemistry and Biomedical Sciences
Correspondent: Alba Guarné

2014 flew by while we were getting ready to launch our new undergraduate program in Biomedical Discovery and Commercialization. Under **Eric Brown's** leadership this multidisciplinary program will equip graduates with strong discovery research skills, business acumen and a meaningful experiential connection to the Health Sciences sector. Early adopters of the program started in January 2015 and our first full level III cohort will start next academic year.

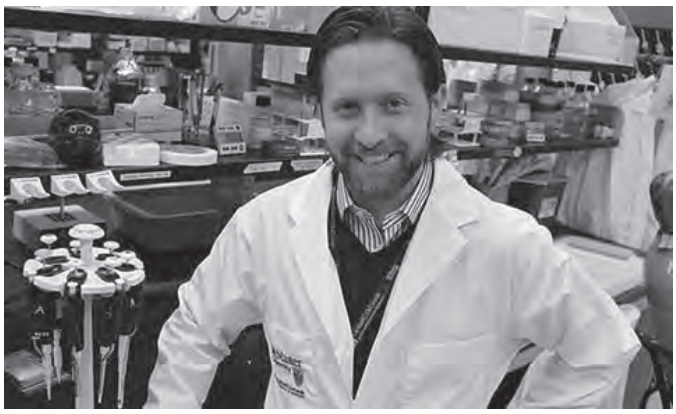
On the research front, we continued to be a hive of activity. **Joaquin Ortega** and **John Lovell** (Assistant Professor at the University of Buffalo and a McMaster alumnus) found a new mechanism to deliver cancer drugs with minimal toxicity (*Nature Communications* 5:3546). **Jonathan Schertzer** discovered one of the paths that link statins to diabetes (*Diabetes* 63:3742). **Gerry Wright** and his team discovered a fungus-derived compound that disarms one of the most dangerous antibiotic-resistance genes (*Nature* 31:922).

Despite the unstable funding climate and declining success rates, **Nathan Magarvey**, **Geoff Werstuck**, **Gerry Wright, John Hassell**, **Eva Szabo**, **Eric Brown**, **Brian Coombes** and **Marie Elliot** secured operating grants from CIHR. **Giuseppe Melacini** renewed his NSERC discovery grant, while **Eric Brown** and **Deborah Sloboda** were awarded new NSERC discovery grants. **Yingfu Li**, and his collaborator **Bruno Salena**, received an Innovation Grant from the Canadian Cancer Society to develop a novel diagnostic tool for colorectal cancer. **Mick Bhatia** received funding through the Ontario Institute for Regenerative Medicine (OIRM) to develop novel stem cell strategies for immunotherapy. **Eric Brown** and **Jonathan Bramson** (Professor in the Pathology Department and an associate member of Biochemistry and Biomedical Sciences) were awarded Tier I Canada Research Chairs in Microbial Chemical Biology, and Transitional Cancer Immunology, respectively. **Nathan Magarvey** and **Kristin Hope** were awarded Early Researcher Awards from the Ministry of Research and Innovation, and **Ray Truant** received the Michael Wright Community Leadership Award in recognition of his scientific contributions to the Huntington Disease community.

Andrew McArthur

The year also brought changes to the make-up of the department. We were sad to see **Murray Junop** move his laboratory to his alma mater, Western University, after 13 years at McMaster. He had been an excellent collaborator, outstanding educator and prolific mentor, and left big shoes to fill. On the flip side of that coin, we were excited to welcome two new recruits to the Department. **Andrew McArthur** returned to academia in September to fill the newly created Cisco Chair in Bioinformatics. **Matthew Miller**, a virologist specializing in influenza virus, returned to Canada after an extremely successful post-doctoral stint at Mount Sinai Hospital in New York City.

Our graduate program achieved a historic record with the proportion of students at the PhD level now at 70% of total students. About 40% of our students were funded through competitive scholarships, and received prestigious awards with a combined total value of over 1.7 million dollars! **Sonam Bhatia** (Draper lab) received the Thomas Nielson Scholarship, awarded to the student with the most research potential at the time of the transfer exam. **Nick Caron** (Truant lab), **Chad Johnston** (Magarvey lab) and **Soumaya Zlitni** (Brown lab) were awarded the annual publication impact awards for their papers on the flexibility of the polyglutamine domain of huntingtin (Caron et al., PNAS), gold biomineralization by a metallophore from a gold-associated microbe (Johnston et al., Nat. Chem. Biol.) and the identification of new antibacterial inhibitors (Zlitni et al., Nat. Chem. Biol.). **Nick Caron** was also a finalist in the prestigious Lap-Chee Publication Award. **Nicholas Holzapfel** (Hope lab) and **Monica Pillon** (Guarné lab) received the Karl Freeman Award for the best Ph.D. presentations in our graduate seminar series; and **Tamiza Nanji** (Guarné lab) and **Dingran Chang** (Li lab) received the Karl Freeman Award for the best M.Sc. presentations in our graduate seminar series. Ten M.Sc. and fourteen Ph.D. students graduated from our program in 2014. One of our Ph.D. graduates, **Monica Pillon** (Guarné lab), was awarded the Governor General's Academic Gold Medal for her intellectual contributions during her Ph.D. work. This was the second consecutive Governor General's Academic Gold Medal awarded to a student in our program, after **Lindsay Matthews** (also from the Guarné lab) received it last year.



Matthew Miller

As usual, the Biochemistry and Biomedical Sciences Graduate Association (BBSGA) made sure that we not only work hard, but also play hard. The Biochemistry Olympics had a record number of teams and even included a "Prof" team. Although the "profs" did very well, rumour has it that it may not have been a fair competition. At the Halloween celebrations, the **Li** gang won best group costume for their creative presentation of the Lego movie, and the **Truant** lab won first place at the pumpkin-carving contest.

The "prof team" at the 2014 Biochemistry Olympics. From left to right: Karen Mossman (Chair); Deborah Sloboda; Mike Surette; Gerry Wright; Lori Burrows; Yingfu Li; Joaquin Ortega; Eric Brown.

Princess Margaret Cancer Centre, Toronto

Correspondent: Linda Penn

John Dick

Honours and Awards (in alphabetical order):

John Dick was elected to the Fellowship of the Royal Society in recognition of his seminal contributions to the field of stem cell biology. The Society noted that his research has transformed the study of human hematopoiesis and leukemogenesis. These transformative studies have enabled the identification of long-term human hematopoietic stem cells and the development of more accurate mouse models of leukaemia.

Igor Jurisica

Igor Jurisica was included in Thomson Reuters 2014 list of Highly Cited Researchers and 'The World's Most Influential Scientific Minds: 2014 Report', prepared by Thomson Reuters. The list was created by analyzing researchers' citations - the number of times publications were referenced by peers - over an 11 year period in 21 fields of science. Researchers that ranked within the top 0.1% by citations in their field were included in the ranking. Igor's research focus is on integrative computational biology, and representation, analysis and visualization of high dimensional data to identify prognostic/predictive signatures, condition specific protein interactions, drug mechanism of action and in silico repurposing of drugs.

Tak Mak

Tak Mak was awarded the 2014 Dr. Chew Wei Memorial Prize in Cancer Research from the University of British Columbia. The prize is awarded annually to a Canadian physician or scientist who has made transformational and internationally recognized contributions to the fight against cancer.

Catherine O'Brien

Catherine O'Brien received an Early Researcher Award from the Ontario Ministry of Research and Innovation. The program helps promising, recently appointed Ontario researchers to build their research teams of trainees and technical staff. Catherine's research focuses on cancer stem cells, colorectal cancer and new anticancer therapies. The ERA will support her research into the identification of new adjuvant therapeutics to be used in combination with cetuximab - a targeted therapeutic that is used to treat colorectal cancer.

Ian Tannock

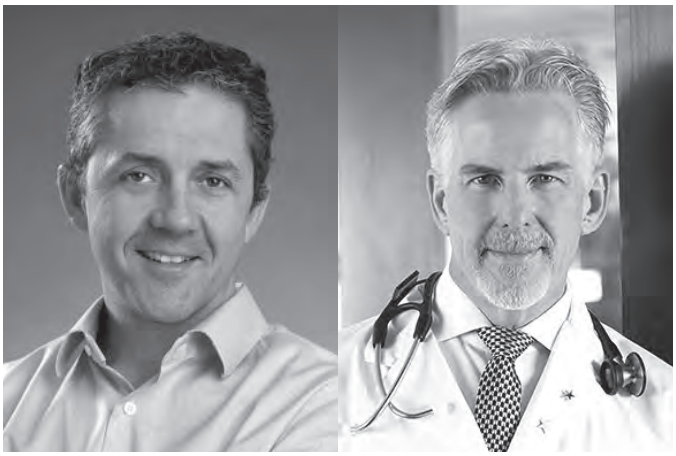
Ian Tannock was appointed to the Order of Canada, one of the country's highest civilian honours. He was recognized for his contributions to understanding the behaviour of tumour cells and im-

Brian Wilson

proving chemotherapy treatments.

Brian Wilson was elected a Fellow of the Optical Society and was awarded the 2014 Britton Chance Biomedical Optics Award by the International Society for Optics and Photonics. Dr. Wilson was recognized for his pioneering contributions to biophotonics - a field focused on the development and use of optical tools to study biological molecules, cells and tissues.

Bradly Wouters and Robert Bristow, both Senior Scientists at Princess Margaret Cancer Centre, were awarded $6.6 million from The Terry Fox Foundation. These funds will support research to develop new and more personalized treatments that target the low oxygen levels in tumours - a characteristic that may contribute to cancer's ability to resist treatment and spread.



Bradly Wouters *Robert Bristow*

Canada Research Chairs renewed:
PMCC is proud to announce the renewal of Canada Research Chairs for **Tak Mak** (Tier 1 Canada Research Chair in Inflammation Responses and Traumatic Injury), **Linda Penn** (Tier 1 Canada Research Chair in Molecular Oncology) and **Benjamin Neel** (Tier 1 Canada Research Chair in Signal Transduction and Human Disease).

Linda Penn *Benjamin Neel*

Retirements:

Brenda Gallie

Brenda Gallie, a world-renowned ophthalmologist (eye specialist), retired as a Senior Scientist at the Princess Margaret Cancer Centre at the end of August 2014. Dr. Gallie was named to the Order of Canada in 2014 for her molecular research focused on elucidating the biological mechanisms underpinning a rare form of eye cancer afflicting children, known as retinoblastoma. She remains an Associate Scientist leading the Health Informatics Research team within the Techna Institute. Dr. Gallie's new lab is global, using collaboration and Internet technologies to build a learning health system, "One Retinoblastoma World", to achieve optimal care for children with retinoblastoma everywhere. She continues to treat patients with retinoblastoma at SickKids Hospital.

Ian Tannock is retiring after 40 years at Princess Margaret Cancer Centre. Dr. Tannock has made significant contributions to cancer research and treatment. In 1990, he led an international study that laid the foundation for the first approved chemotherapy for prostate cancer. Later in 2004, he led a study, published in the prestigious New England Journal of Medicine, that revealed that the drug

docetaxel was able to improve survival and symptom control for certain types of prostate cancer. His achievements were recognized in 2012, when he received the European Society of Medical Oncology Award, and in 2013 when he was appointed to the Order of Canada.

Ryerson University

Department of Chemistry and Biology
Correspondent: Roberto Botelho

The Department of Chemistry and Biology at Ryerson University 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.

In 2014, there were several important events within our Department. Among these was the recruitment of three new faculty, including Dr. **Stephanie Melles**, a specialist in "Big Data" with relevance to ecology and environmental biology, and relevant to the CSMB membership, Drs. **Joseph McPhee** and **Sarah Sabatinos**. The last two hires will further strength our expertise complement in molecular biosciences including in microbiology and molecular cell biology.

Dr. Joseph McPhee

Joseph McPhee completed his PhD under Bob Hancock at U.B.C. before conducting post-doctoral research with James Bliska at Stony Brook University and Brian Coombes at McMaster University. He started at Ryerson University in January 2015 where he will study the microbiology of Crohn's disease (CD). In particular, he will study how adherent-invasive *Escherichia coli* (AIEC) adapts to the inflammatory conditions associated with the disease. He plans to use comparative genomic, molecular biological, microbiological, biochemical and immunological techniques to achieve this.

Dr. Sarah Sabatinos

Sarah Sabatinos completed her B.Sc. at the University of Guelph (Biochemistry) and Ph.D. at the University of Toronto (Department of Medical Biophysics). As a post-doc, she studied how the DNA replication and damage checkpoints influence genome instability, in the lab of Susan Forsburg (University of Southern California). She developed and used high-resolution and live-cell imaging methods to study the causes and effects of genome instability and their effect on replication fork structures in fission yeast (*Schizosaccharomyces pombe*). At Ryerson, she plans to pair microscopy and biochemical assays to explore how genome instability develops in yeast and human cells after drug exposure. She will focus on conditions where DNA damage checkpoints are modified or lost and ultimately how individual cells may survive chemotherapy and repopulate.

In addition to the new research faculty hires, there were several events that helped to further mature our community and graduate program. We hosted our third Annual Research Symposium - with a record of 69 poster presentations excluding talks - this showcased our exciting and emerging research activities across various disciplines and highlighted both undergraduate and graduate-based research. Dr. Molly Shoichet from the University of Toronto was the keynote speaker.

Our graduate program in Molecular Science now hosts ongoing events including the Departmental Picnic in the Toronto Islands, Alumni Meetings, Career Developmental Workshops and our new annual ski trip. It is exciting to see our student body take charge of its community and enliven our department. In addition, there

were several new initiatives towards promoting undergraduate engagement in research through programs like RyeSciMatch that matches undergraduates to faculty and graduate students, the CaB Leaders Challenge, where students team up to develop a proposal to address a scientific problem, and the Space Station Experimental Program, where a team of students design an experiment to be performed in microgravity. All these activities aim to foster an interest in research early and entice a student to consider a research career, including in the molecular biosciences.

In addition, a new National Centres of Excellence called GlycoNet was announced in 2014. Prof. **Warren Wakarchuk** is the theme leader for Therapeutic Proteins and Vaccines within this pan-Canadian glycomics network (http://www.canadianglycomics.ca/). The network incorporates the Wakarchuk lab glycobiology research and elements of the glycobiology course being taught at Ryerson.

Overall, 2014 was an exciting time for the Department of Chemistry and Biology at Ryerson University with new hires, increased publication output and new infrastructure grants, including those from NSERC RTI and CFI. We expect our Department to continue growing its research footprint and visibility within Canada and the international stage, and to advance research and education in the disciplines represented by the CSMB. Indeed, 2015 is poised to be an even better year than 2014 with a recent agreement to lease research space in MaRS Facilities in Toronto.

Keynote speakers and poster winners from our Third Annual Departmental Research Symposium. The student winners include graduate and undergraduate students across a variety of research fields.

Simon Fraser University

Department of Molecular Biology and Biochemistry

Correspondent: Christopher Beh

In addition to highlighting the awards and achievements of our faculty, this report salutes two retiring colleagues who were instrumental to our current successes. **Bruce Brandhorst**, former Chair and tireless advocate for this Department, became Professor Emeritus this year and he continues to impart his valued knowledge of science and academic administration. **Don Sinclair** also formally retired this year. As a teaching award recipient, Dr. Sinclair was a stalwart lecturer who taught many of our core courses. We gratefully thank both Drs. Brandhorst and Sinclair for their service and contribution during the past 15 years since the Department's founding.

Department highlights:

Many significant awards were presented to our faculty members this past year. As one of the Department's newest faculty members, we congratulate **Ryan Morin** again this year. In addition to his previous awards, Dr. Morin received a *CIHR New Investigator Award* for his work on applying high-throughput sequencing and bioinformatics to study cancer and other heritable and sporadic genetic diseases. We also congratulate **David Vocadlo**, who started his *Tier I Canada Research Chair* this year and received the *Teva Canada Award* from the Canadian Chemical Society for his work on chemical glycobiology. Finally, we applaud **Steven Jones** for becoming a *Fellow of the Canadian Academy of Health Sciences* in 2014. Dr. Jones, along with MBB Professor **Fiona Brinkman** and Adjunct Professor **Marco Marra**, was also listed on the Thomson Reuter's list of "The World's Most Influential Scientific Minds: 2014."

In the past year there were several news-making projects from MBB Department researchers and adjunct faculty. As reported by *CBC News*, Adjunct Professor **David Granville** captured public attention with his observation that mice lacking Granzyme B, a cytolytic protease released by cytotoxic T lymphocytes and nature killer cells, actually prevented skin damage due to aging. In the *New York Times*, an article described the work by **Dipankar Sen** (originally appearing in *Nature Chemistry*) suggesting that vitamins might be evolutionary holdbacks from when RNA catalysis dominated primordial life. Dr. Sen generated an RNA that used "vitamin B1 to pull carbon dioxide from another molecule" just like "proteins use B1 for today…" These examples of newsworthy findings

represent just a sampling of the research diversity from our faculty.

Faculty promotions:
We congratulate **Jonathan Choy** on his promotion to tenured Associate Professor as well as **Peter Unrau** on his promotion to full Professor. Dr. Choy's research program focuses on the regulation and effects of T cell responses. Dr. Unrau, like Dr. Sen, has made significant contributions towards understanding origins of prebiotic life as proposed by the "RNA World hypothesis." We also congratulate our many successful undergraduates, graduate students, and post-doctoral fellows on their many scholarships and research awards.

Sunnybrook Research Institute

Biological Sciences Platform
Correspondent: David Andrews

Our scientists in the Biological Sciences platform at Sunnybrook Research Institute (SRI) continue to conduct innovative research aimed at understanding the molecular mechanisms underlying healthy and diseased states. By working with our peers in the Physical Sciences and Evaluative Clinical Sciences platforms, we are using interdisciplinary approaches to translate basic science research findings into improved diagnostic and therapeutic tools for clinical use. Over the last year, our people have been the focus of our progress.

Dr. JoAnne McLaurin, senior scientist at SRI

In 2014, we were delighted to welcome two new recruits: Drs. JoAnne McLaurin and Saied Amini-Nik. **Dr. JoAnne McLaurin** joined the platform in May. Her research on novel small molecule therapies to target Alzheimer's disease has identified a family of compounds that inhibit the formation of toxic protein aggregates. These compounds are in Phase II clinical trials, with additional work underway to examine their utility in treating other protein-misfolding disorders such as Huntington's disease and amyotrophic lateral sclerosis. Dr. McLaurin is also a Professor in the department of Laboratory Medicine and Pathobiology at the University of Toronto.

Dr. Saied Amini-Nik, junior scientist at SRI

Dr. Saied Amini-Nik joined us in July as a junior scientist under the direction of Dr. Marc Jeschke, where he leads the stem cell and skin regeneration group. His research focuses on characterizing the cellular pathways involved in skin healing and skin regeneration. Dr. Amini-Nik is also an Assistant Professor in the Department of Surgery at the University of Toronto.

We are pleased to announce that **Dr. Laurence Klotz** was named to the Order of Canada for his pioneering work in developing a novel approach to monitoring and treating men at risk of prostate cancer. This approach, termed active surveillance with selective delayed intervention, has since been adopted as the standard option of patient care.

Dr. Laurence Klotz, affiliate scientist at SRI

We are also pleased to report that the current good manufacturing practice (cGMP) laboratory located within the Centre for Research in Image-Guided Therapeutics is now operational and slated to open within the coming weeks. **Dr. Nickett Donaldson-Kabwe** was brought on board last year as the facility manager to guide the lab through a lengthy cer-

tification process. The facilities include four clean rooms and separate quality assurance and quality control areas to ensure that all biological compounds produced meet Health Canada's safety and quality standards for clinical testing. There has been a lot of interest from researchers within and outside of SRI to use the facility, as it is only one of seven academic GMP facilities in Ontario. The cGMP lab will be an invaluable resource to our scientists in expediting the movement of innovative discoveries from the lab to the patient.

Last year was fruitful for our scientists, many of who were successful in government agency competitions. **Dr. Isabelle Aubert** received a CIHR operating grant to study the use of magnetic resonance imaging-guided focused ultrasound in targeted delivery of therapeutics to the brain in preclinical models of Alzheimer's disease. NSERC discovery research grants were awarded to **Drs. Michele Anderson**, **Isabelle Aubert**, **Bojana Stefanovic** and **Juan Carlos Zúñiga-Pflücker**. Dr. Zúñiga-Pflücker also received funding from the National Institutes of Health to study cellular signalling pathways involved in γδ T cell differentiation. **Dr. Alain Dabdoub** (a new recruit last year) was recognized with a John R. Evans Leaders Fund grant from the Canada Foundation for Innovation to study sensory and neural cell development in the mammalian cochlea.

Dr. Dan Dumont received a Genomic Application Partnership Program grant from Genome Canada to examine the angiopoietin peptide mimetic vasculotide in treating vascular inflammation and destabilization in atherosclerosis and ischemia. Dr. Dumont received additional support for this work from the Heart and Stroke Foundation.

Dr. Rena Buckstein, affiliate scientist at SRI

Dr. Rena Buckstein was awarded an innovation grant and a quality of life research grant from the Canadian Cancer Society Research Institute to study myelodysplastic syndrome mutations as early markers of disease in aging populations and to conduct a pilot and feasibility study on red blood cells transfusions thresholds and quality of life in patients with myelodysplastic syndrome.

For his work on developing mouse models of spontaneous bone metastasis, **Dr. Robert Kerbel** was awarded an innovation grant from the Canadian Cancer Society Research Institute and a research grant from the Canadian Breast Cancer Foundation.

Drs. Arun Seth and **Robert Nam** received an operating grant from the Cancer Research Society to study microRNA signatures in prostate cancer recurrence and metastasis. Also in the area of prostate cancer research, **Dr. Stanley Liu** was awarded a Movember Rising Star in Prostate Cancer Research grant from Prostate Cancer Canada to study the role of microRNAs in prostate cancer. **Dr. Urban Emmenegger** won a Relay for Life Award from the Canadian Cancer Society to continue his research on developing molecular therapies for breast cancer.

Dr. Stanley Liu, scientist at SRI

Trent University

Department of Biology

Correspondent: Carolyn Kapron

It has been some time since a report from the Biology Department at Trent was submitted to the Bulletin and so this news will span several years. Research in the department is diverse, in fields that include Aquatic Biology, Ecology and Conservation Biology, as well as in various areas of Molecular Biosciences, such as Molecular Biology and Biochemistry, Virology, Behavioural Neuroscience, Cancer Biology, Molecular Ecology, Developmental Biology and Birth Defects, Physiology and Genetics.

The Biology Department, with 21 faculty members, completed its move into the new LEED Gold-certified Life and Health Sciences building in 2011. This move brought most faculty members, along with administrative offices and teaching facilities, under one roof, after a period of being

scattered across campus. The wings of the new building house offices for Biology faculty, graduate students in the interdisciplinary Environmental and Life Sciences Graduate Program, laboratory personnel and departmental technicians. There are six undergraduate teaching labs to support the department's focus on undergraduate laboratory experience and hands-on learning, as well as 16 research labs and related infrastructure, including an animal care facility, environmental chambers and an imaging suite. The building also houses administrative offices and research space for Anthropology, Psychology and the Trent/Fleming School of Nursing. Common areas for students and staff allow ample opportunity for interaction and collaboration. These facilities are adjacent to the modules of the DNA building, which houses the Forensics Sciences program, the Natural Resources DNA Profiling and Forensic Centre, and scientists from the Ontario Ministry of Natural Resources.

Collaborations that have grown in this stimulating research environment often give students unique opportunities for study. Master's student Shawn MacFarlane has undertaken a project under the supervision of **Dr. Leslie Kerr**, who specializes in behavioural neurosciences and cancer, and **Dr. Dennis Murray**, Canada Research Chair in Integrative Wildlife Conservation. Mr. MacFarlane will be studying the role of the HPI axis in mediating morphological, physiological and behavioural responses to chronic stress and the effects on regenerative processes in salamanders.

Recent Ph.D. graduate, **Dr. Andressa Lacerda** received attention from Trent's Showcase magazine in the fall of 2014 for her research that deepened the understanding of the molecular basis of Charcot Marie Tooth disease (CMT). While Dr. Lacerda's doctoral research in Dr. Craig Brunetti's lab began with an attempt to understand the role of the protein LITAF in viral replication, the investigation broadened to an analysis of the cellular localization of LITAF in CMT. The results of the study, carried out with the assistance of undergraduate student **Emily Hartjes**, were published in PLoS One in July 2014.

The work of the Wildlife Forensics DNA Laboratory, directed by Prof. **Brad White**, in identifying a new hybrid species, the coywolf, was highlighted in a documentary on CBC and PBS, and the varied research on wildlife and agricultural genetics carried out in this lab was profiled in University Affairs in April 2014.

The coming year will be an exciting one for the Biology Department, with joint faculty recruitment under way with the Nursing program to support the new Kinesiology pathway at Trent. More information about the department can be found on our website: www.trentu.ca/biology.

Université de Montréal

Department of Biochemistry and Molecular Medicine
Correspondent: Christian Baron

In May we celebrated the **50th anniversary** of the Department jointly with the celebration of the **25th anniversary of the Simon-Pierre Noël Prize** (travel award and graduate fellowship) that is named after a former professor. The celebrations extended over two days and comprised graduate student talk and poster competitions, a symposium with talks given by graduates who now work in different professional fields, as well as a gala dinner celebrated in the Université de Montréal Hall d'honneur. The successes of our graduates are a result of our strong tradition of excellence in teaching and research. The diversity of the presentations showed the various career paths to which training in biochemistry leads. Keeping up these traditions, and the ability to adapt to a changing funding environment, will be key to our future development.

22 members of the Department, including four professors, participated in the **Movember** fundraising effort as team "Biochimistes à la moustache" and raised $2,700 for research on male health issues. This was our second participation in this initiative; fundraising has also been a focus of other departmental activities aimed at providing support for new recruits and for other priorities. In December we celebrated the 75th birthday of the late **Robert Cedergren**, who inspired many RNA and bioinformatics researchers, with a symposium with presentations by faculty members who trained in his group.

Appointments and promotions:

John Pascal, a structural biologist interested in DNA repair processes, was recruited from Thomas Jefferson University in Philadelphia. He will join the Department as Associate Professor in 2015. The Department was equally involved in the recruitment of **Elitza Tocheva** as an Assistant Professor in the Faculty of Dentistry. Dr. Tocheva

was trained as a crystallographer in Michael Murphy's group at UBC for her Ph.D. She had a stunning success as postdoctoral researcher, pioneering novel approaches for structural analyses of bacteria by cryo-tomography in Grant Jensen's laboratory at Caltech. She will greatly strengthen the field of molecular imaging at our institution after her arrival in 2015. **Michel Bouvier** was appointed as director of the Institut de recherché en immunologie et cancérologie (IRIC), a research institute on the Université de Montréal main campus. In his new role he will further advance the development of this leading cancer research institute including its innovative platform for drug development and commercialization (IRICoR). **Pascal Chartrand** and **Nikolaus Heveker** were promoted to Full Professor status.

Operating and infrastructure funds:

Despite historically low success rates, several of our faculty members obtained or renewed operating grants from the CIHR: **Vincent Archambault**, **Michel Bouvier**, **Nicole Francis**, **Natalie Grandvaux**, **Éric Lecuyer**, and **Stephen Michnick**. **Pascal Chartrand** obtained a major contract from the pharmaceutical company Roche for his research on the development of drugs for treatment of the heritable disease Myotonic Dystrophy (Steinert disease). The Québec government provided 13.9 million $ to a team led by **Michel Bouvier** for research on drug development in partnership with pharmaceutical companies.

Research highlights:

James Omichinski and **Jacques Archambault** published the results of their collaborative work combining structure and molecular biology approaches to understand the mechanism of gene regulation of Epstein-Barr virus in the journal PLoS Pathogens. This work could reveal novel targets for cancer therapies.

Awards and Distinctions:

Christian Baron was elected president of the CSMB and **Michel Bouvier** was elected as a member of the Royal Society of Canada. Michel was also one of three researchers at our institution on the list of highly cited researchers and influential scientific minds published by Thomson Scientific. **Jacques Drouin** received the distinction of doctor honoris causa from the University Aix-Marseille in France. **Stephen Michnick**, who is a world leader in interactome research, received a Tier 1 Canada Research Chair in Cellular Architecture and Dynamics.

Université Laval

Department of Molecular Biology, Medical Biochemistry and Pathology

Correspondent: Jean-Yves Masson (Director)

Since December 2013, I have been appointed as the new director of the Molecular Biology, Medical Biochemistry and Pathology department. Our department, which celebrated its 70th anniversary, comprises 41 professors working mostly on basic research and molecular and cellular biology. I organized the first meeting retreat in January 2015, which helped to foster the sense of belonging to the department. The atmosphere was excellent and **Jacques Huot** and **Jean-Claude Forest** were named "*professors emeritus 2015*" of our department. **Josée Lavoie** became director of our molecular and cellular biology program at Laval University. Josée is one of the most acclaimed teachers we have in the department. This is a perfect fit! **Jacques Côté** renewed his Tier 1 Canada Research Chair in Chromatin Biology and Molecular Epigenetics. **Martin Simard** received the André Dupont prize from the club de recherches cliniques du Québec. **Guy Poirier** was awarded an Honoris Causa doctorate from Université de Rennes 1 in France, for his outstanding work on poly(ADP)ribose polymerase enzymes.

Many professors were involved in meeting organization: The Cell Stress Society International Workshop on Small Heat Shock Proteins (**Robert Tanguay**); the 19th Annual Congress of the RNA society (**Martin Simard**); the 2nd Canadian Symposium on Telomeres and Genome Integrity (**J.-Y. Masson**); the 6th Signalisation Québec meeting (co-organized by **Nicolas Bisson**, **Marc-Étienne Huot**, **Patrick Laprise** and **Darren Richard**). Sadly, **Manjapra Govindan** passed away in January 2015. It should be noted that **Jacques Landry**, an expert in heat-shock proteins, retired in 2014. We wish all the best to Jacques, who will spend a lot of time working on the identification of mushrooms (http://www.mycoquebec.org/bienvenue.php). Our department will welcome **Amélie Fradet-Turcotte** as an Assistant Professor in September 2015.

University of Alberta

Department of Biochemistry

Correspondent: Joe Casey

Canadian and German Scientists at the IRTG in Membrane Biology Symposium, Banff April 2014

The International Research Training Group (IRTG) in Membrane Biology (composed of members of the Membrane Protein Disease Research Group (MPDRG)) has continued to be a focus of activity for several department members. In April 2014 the IRTG hosted their partner graduate students and principal investigators from Germany at a research Symposium at the Banff Centre. This was followed by the 57th Annual meeting of CSMB, whose organizing committee was composed of members of the MPDRG.

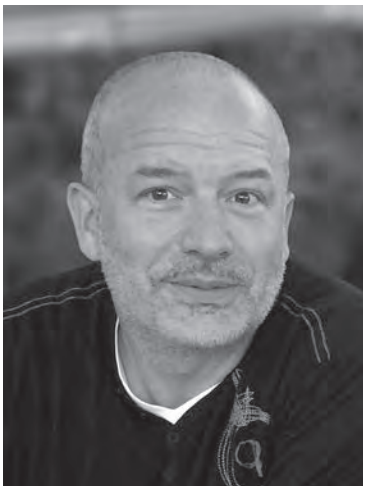
In 2014 two Biochemistry graduate students, **Sampath Loganathan** (supervisor, **Joe Casey**) and **Aruna Augustine** (supervisor **Larry Fliegel**) completed three-month research visits to German partners respectively at Technical University Kaiserslautern and Saarland University, as part of their enrollment in the IRTG in Membrane Biology. **Joanne Lemieux** and **Larry Fliegel** also hosted German graduate students in their lab as part of the training program.

Mark Glover on top of Sulfur Mountain, after hiking up during a free afternoon at the 2014 departmental retreat in Banff

In October the full Department of Biochemistry held a retreat at the Banff Centre. Linkages between department members were strengthened by research talks and posters presented by department members. Drinking beer together in a spectacular mountain setting helped, too.

Following his years as Vice-Dean, Research, **Marek Michalak** has been on administrative leave as a Visiting Professor in the Department of Biological Sciences, Hanyang University, Seoul, South Korea, working on the role of calreticulin mutants in *C. elegans*. Two of his CIHR grants were renewed this year. **Marek** was also appointed as Honorary Professor at the University of Exeter, UK.

Promotions and appointments:



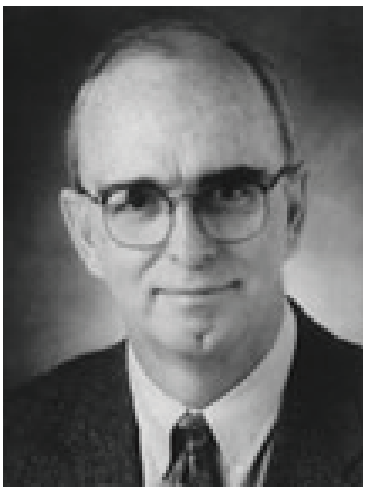
Nicolas Touret, the department's newest Associate Professor

Nicolas Touret was promoted to Associate Professor, starting July 2015. **Peter Hwang**, a new Assistant Professor of Medicine who completed his Ph.D. with **Lewis Kay** (University of Toronto) and postdoctoral fellowship with **Brian Sykes** (University of Alberta), was cross-appointed to Biochemistry. Peter's research program applies NMR approaches to clinical problems he sees in his clinical medicine practice.

Retirements:

In 2014 **Jim Stone** and **Ron McElhaney** both formally retired. Jim has moved on to raise turkeys on his Vancouver Island farm, while Ron is active as a Professor Emeritus with years of backlogged research remaining to be written up. Jim and Ron's retirements were marked by a research symposium held at the Banff Centre in October. The symposium featured talks by Ron's former students **Peter MacDonald** (University of Toronto), **John Silvius** (McGill) and **Todd McMullen** (University of Alberta), and Jim's close collaborators **Hanne Ostergaard** (Medical Microbiology and Immunology, University of Alberta) and **Mike Schultz** (Biochemistry, University of Alberta).

In Memoriam: Dr. Bill Bridger, Chair Department of Biochemistry 1987-1993



The late Bill Bridger, Chair of the Department of Biochemistry at the University of Alberta, 1987-1993

William (Bill) Bridger passed away on Thursday, December 18, 2014 at St. Michael's Palliative Care Centre in Lethbridge Alberta. Bill Bridger was a native of Winnipeg, who obtained a B.Sc. in Honours Chemistry at the University of Manitoba. Following a Ph.D. in Biochemistry at the same institution, supervised by L.H. Cohen, he moved to University California Los Angeles (UCLA) for postdoctoral studies with one of the world icons of biochemical enzymology, Nobel Prize Laureate, Paul D. Boyer. During his time in Boyer's lab, Bill was beguiled by the enzyme succinylCoA synthetase, and this complex protein became the major focus of his research, finally culminating with a full description of the enzyme's structure at the atomic level by X-ray crystallography thirty years later.

Bill Bridger joined the Department of Biochemistry at the University of Alberta in 1967. He moved through the ranks to full professor (1977), spent 1984-85 as a visiting professor at the Rockefeller Institute in New York and in 1987 became Chair of the Department of Biochemistry. Six years later, Bill took on the role of Associate Vice-President (Research) at the University of Alberta and served in that position, whilst maintaining his research group, until January 1996, when he became Vice-President (Research) at the University of Western Ontario. In 2001 Bill became Founding President and CEO of the newly established Alberta Ingenuity Fund. In this capacity he played a key role in the Province of Alberta in the development of long-term strategies for knowledge discovery, and top-quality training of scientific personnel. He has also been active in national science bodies, including serving the Canadian Biochemical Society (CBS) as Secretary, Vice-President and then President. In 1980 Bill was the recipient of the Ayerst Award of the CBS, given for outstanding biochemical research, and in 1989 he was named a Fellow of the Royal Society of Canada. Bill's career demonstrated the highest levels of achievement in research, teaching and administration. To commemorate his many achievements, the William A. Bridger Lectureship in Biochemistry was inaugurated as an annual event in 2005.

University of Alberta

Department of Cell Biology

Correspondent: Paul LaPointe

The Cell Biology department at the University of Alberta comprises 17 primary and cross-appointed investigators whose research interests span a variety of areas in cell biology, with a strong molecular focus in each case. Research in our department includes mRNA export, nuclear pore structure and function, neuroscience, *Drosophila* development, organelle biogenesis and inheritance, protein folding, protein lipidation, mitochondrial biology and metabolism, protein and lipid transport, evolutionary cell biology, the RNAi system, and virology.

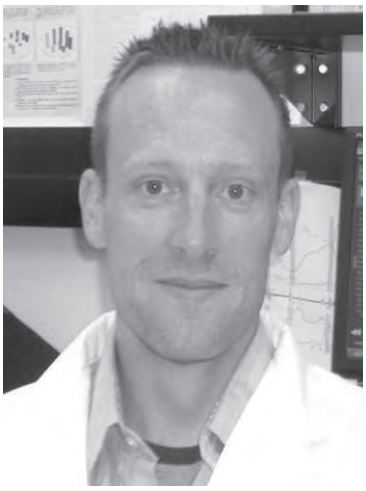
Dr. Richard Rachubinski, has recently been reappointed as our department chair. Our department has 32 graduate students, many of whom have been successful in obtaining prestigious fellowships including the Vanier, and Dr. Fred Banting and Dr. Charles Best CIHR Graduate Fellowships. Members of our department 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. We welcome **Dr. Michael Hendzel** to our department, who brings with him a robust research program focused on understanding the dynamics and function of chromatin and non-chromatin structures in the cell nucleus.

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 equitably and adequately fund the important work being done in the Canadian research community.

University of Alberta

Department of Physiology

Correspondent: Emmanuelle Cordat



Jamie Mitchell

2014 has been a busy year in the Department of Physiology at the U of A! In 2014, our Department welcomed several new faculty members. **Dr. Silvia Pagliardini** joined our Department as an Assistant Professor after completing a PhD under the supervision of Dr. John Greer followed by a postdoc with Dr. Jack Feldman at UCLA. Her research is focused on the control of breathing under physiological and pathophysiological conditions. **Dr. Jamie Mitchell** joined our Department as an Assistant Professor dedicated to teaching, with a research expertise on heart-lung physiological interactions. Finally, **Dr. Jessica Yue** is the latest recruited Assistant Professor after completing her Ph.D. degree under the supervsion of Drs. Mladen Vranic and Adria Giacca, and postdoctoral studies with Dr. Tony K. T. Lam at the University of Toronto. Her research focuses on brain mechanisms that coordinate whole-body metabolism, with an emphasis on stress-related hormone signalling pathways in the brain. **Drs. Declan Ali** and **Darren Freed** were also cross-appointed to the Department of Physiology, bringing expertise in synaptic development and cardiac transplantation, respectively.

Jessica Yue

This year, Membrane Protein Disease Research Group members from our Department participated in the organization of the 57th Annual Meeting of the Canadian Society for Molecular Biosciences that was held in Banff, AB, from April 9-13, 2014. The meeting focused on Membrane Proteins in Health and Disease, with two satellite meetings on “pH regulation at the membrane surface” and another entitled “Overcoming barriers to membrane protein structure determination”. We had a terrific turnout with more than 100 participants, including many young researchers from Canada but also the UK, Germany and Denmark.

Finally, 2014 marked the centennial of our Department, which was created in 1914 under the leadership of **Dr. Heber Moshier**, just 6 years after the official opening of the University of Alberta, and one year after the creation of the Faculty of Medicine. To celebrate this milestone, the current Chair, **Dr. James Young** and former Chair **Dr. Esmond Sanders** launched a book entitled “One Hundred Years of Physiology 1914-2014: The Department of Physiology at the University of Alberta” on November 11, 2013, since Dr. Moshier died in action during the first World War. This launch was followed by a highly attended Centennial Symposium held on May 29 and 30, 2014. This two-day celebration started with a keynote lecture delivered by Professor Denis Noble from the University of Oxford, a pioneer in mathematical modelling of the heart and systems biology, and ended by an enlightening seminar from Dr. Diane Finegood, President and CEO of the Michael Smith Foundation for Health Research in B.C. We are now looking forward to another century of exciting research and teaching in the Department of Physiology at the University of Alberta!

University of British Columbia

Department of Biochemistry and Molecular Biology

Correspondent: Roger Brownsey

External review:

2014 was a momentous year for the Department in many respects. The year began with preparations well advanced for an external review of the Department. This was to be the first such review for 10 years, so we had begun in earnest with an academic retreat in June 2013, to map out priority areas and to establish working groups with responsibilities for each of those key areas. For those who have gone through this exercise, you will appreciate the

time and effort but hopefully also the rewards that come from careful review of past events coupled with looking to the future. Preparing for the review provided a singular opportunity to discuss key activities and establish updated strategic plans, and particularly to engage the next generation of leaders, including junior faculty and trainees. The self-study report came together in March and the visiting external team came in April. Considering that the University as a whole, and the Faculty of Medicine in particular, are facing stiff fiscal challenges (what's new?) we now have a solid external endorsement and strategic plans to take us forward. At the time of writing, we also look forward to the arrival of the new Dean of the Faculty of Medicine, **Dermot Kelleher**, who will take up his role in October 2015.

Faculty news:

Please check out the Department website (www.biochem.ubc.ca) for updates on our activities and for information about the research and teaching programs that could not be incorporated in this message. I have given a brief overview of those faculty members who have joined the Department in most recent years (see below) so I'd like to draw your attention, through the website, to our more established colleagues, many of whom will be well known to you. **Ross MacGillivray** had a very popular and productive term as Vice-Dean in the Faculty of Medicine and has now returned to his "day job" in the Department and Centre for Blood Research. **Gary Brayer** and **Grant Mauk** are both currently on leave, Gary for medical reasons and we are all wishing him a speedy recovery. **Lawrence McIntosh** continues to manage the NMR core of the LSI and is supporting efforts by **Natalie Strynadka** and others to complement our strength in structural biology by adding to the EM resources developed by **Bob Molday**, and to exploit the extraordinary advances in structural resolution now possible. This will require a major and concerted effort of many, but equally will support many fundamental studies that rely on detailed understanding of protein structure. New CFI funding awarded to Natalie, **Calvin Yip** and others have provided a substantial base upon which to build. Other major areas of interest are the focus of LeAnn Howe and **Ivan Sadowski**, who are also members of the LSI "Molecular Epigenetics Group". LeAnn is fresh off a sabbatical leave in which she has been developing *in silico* and big data approaches to tackle the mechanisms and functions of histone modifications. Ivan, meanwhile, has been extending his established interests in gene transcriptional control in yeast and has been applying his efforts to understand latency in HIV infection. This exciting work promises new molecular-based avenues to understand how latent HIV infection might be eliminated.

Retirements:

George Mackie the older

The past year saw retirements of long-time colleagues **Bruce Tiberiis** and **George Mackie**. Bruce's affiliation with the Department went back to his time as a trainee in the early 1980s and for many years he was a senior instructor and leader of our contributions to teaching in the M.D. undergraduate program. Bruce was instrumental in developing new M.D. program course materials when "problem based learning" was first introduced more than 10 years ago and was very popular with the M.D. classes. George will be well known to many of you. He joined us to take over as Department Head in 1994 and served two full terms in that capacity. His broad knowledge of science and of administration is unparalleled and George is still in demand to provide advice to senior levels of administration. To mark his retirement, the Department organized a series of research talks, culminating in a reflection by George himself with an appropriate reception in the Life Sciences Centre. UBC President Stephen Toope, Provost David Farrar and VPRI John Hepburn all attended and provided heart-felt reflections of George's contributions. For one individual to have the skills to operate so effectively in these very different spheres is rare indeed and George will be sadly missed, although we all wish him a long and rewarding retirement.

George Mackie the younger

"THE MACKIE SERIES"

- Dr. Sidney Kushner (Department of Genetics, University of Georgia, Athens): "New Insights into Polyadenylation in Bacteria"
- Dr. Stanley Dunn (Department of Biochemistry, University of Western Ontario): "The Right-handed Coiled Coil of the ATP Synthase Stator Stalk"
- Dr. George Chaconas (Department of Biochemistry, University of Calgary): "From Molecules to Mice: Biochemistry and Molecular Biology of the Lyme Disease Spirochete"

On the topics of research talks, we were especially fortunate to attract Bob Sauer (Luria Professor of Biology, MIT) to give the 10th Annual Michael Smith Lecture: "Machines of Protein Destruction". The Michael Smith lecture preceded a fortuitous visit from Professor Venki Ramakrishnan, a result of Venki being a close friend of Julian Davies, one of our colleagues in Microbiology and Immunology. Venki, of course, won the 2009 Nobel Prize for his pioneering work on the structure of ribosomes and he left a packed lecture theatre buzzing with his latest revelations using single-particle EM approaches. We learned recently that Venki has been elected President of the Royal Society.

Closer to home, **Dr. Michel Roberge** was the winner of the 2014 UBC Faculty of Medicine Distinguished Medical Researcher Award Lecture: "Chemical biology and drug discovery". Those of you interested in Chemical Biology will likely know of Michel through his role in the Canadian Chemical Biology Network or his recent role as Scientific Director of the Centre for Drug Research and Development.

Pieter Cullis and the Life Sciences Institute:

In 2005 a number of Departments joined a cross-cutting initiative to establish the Life Sciences Institute. This development was sparked by the expansion of the medical school M.D. program and the building of the Life Sciences Centre. As well as providing the learning spaces for the expanded M.D. program (the annual intake is now close to 300 students) the LSC is the home to 90 research laboratories and more than 800 researchers. Pieter Cullis, a long-time member of the Department, was appointed Director of the LSI in 2013 and is leading a broad initiative in "Personalized Medicine" that aims to build critical links between basic scientists, commercial partners, clinical researchers and the health care community. A major symposium is planned for the summer of 2015 to promote the potential and emerging realities of the revolutionary changes in the applications of science to medicine.

The "new generation" of faculty:

Franck Duong joined the Department in 2004 and has since been promoted to Associate Professor with tenure. Franck has held a Tier 2 CRC from the outset and has brought new cutting-edge approaches to the study of membrane proteins through the use of "nano-discs", adding to our existing strength in membrane protein structure and function. Protein translocation machinery and specific studies of the maltose binding/transport systems are among Franck's specific interests.

Leonard Foster was recruited as part of the proteomics and bioinformatics initiatives in 2005 and is also a member and now Director of the Centre for High Throughput Biology (CHiBi). Leonard is also a Tier-2 CRC and has been a leader in grant applications that have provided resources to establish a large suite of equipment for mass spectrometry. He is now responsible for oversight of mass spectrometry core resources in the Michael Smith Laboratories, the Biomedical Research Centre and the Life Sciences Centre. These cores support a large number of research groups across the Faculties of Medicine, Science, Pharmaceutical Sciences, Dentistry, Applied Science and Land and Food Systems. Leonard's core interests are in pioneering mass spectrometry methods and applying these particularly to understanding host-pathogen interactions.

Eric Jan joined us in 2006, was promoted to Associate Professor with tenure and has held MSFHR and CIHR Investigator Awards. Dr. Jan's expertise in viral control of protein translation has impacts on diabetes, viral pathogenesis in humans and other species of economic importance, notably honey bees. His work is therefore integrated with that of the Diabetes Research Group of the LSI as well as work in the Michael Smith Laboratories (Dr. Foster) and has considerable potential for application in other important human diseases that are mediated by viruses.

Thibault Mayor was recruited as a member of CHiBi in 2007 and was recently promoted to Associate Professor with tenure; he has held MSFHR Career and CIHR New Investigator awards. Dr. Mayor has added further strength in computational biochemistry, with special application to diseases mediated by defects in protein "quality control". His novel work on the ubiquitin-proteasome system has major relevance for neurodegenerative diseases, an-

other key priority area of the Faculty of Medicine that will likely gain further momentum with the recent opening of the Centre for Brain Health.

Filip van Petegem was also recruited in 2007 and has been promoted to Associate Professor with tenure. Filip has also held MSFHR and CIHR Investigator Awards and is leader of the Cardiovascular Research Group of the Life Sciences Institute. Dr. van Petegem has made remarkable progress in defining the structure of the ryanodine receptor, one of the largest of all proteins and is pursuing further work on this and other ion channel proteins.

Joerg Gsponer was also recruited as an Assistant Professor (in 2009) as a member of CHiBi and holds an MSFHR Career Investigator Award. Joerg is particularly interested in understanding the structure and function of intrinsically disordered proteins with an emphasis on computational approaches, so his recruitment has added greatly to our emerging strength in computational biochemistry applied to protein structure and function.

The most recent recruits all joined the Department in 2011, two of these being through collaboration with the Michael Smith Laboratories (MSL).

Calvin Yip

Calvin Yip trained with Natalie Strynadka and returned to UBC following post-doctoral work with Tom Walz at Harvard Medical School. Calvin has been awarded MSFHR Career and CIHR New Investigator Awards and has added a critical new element to the expertise in structural biology through high-resolution single-particle electron microscopy.

Nobu Tokuriki (recruited as a member of MSL) holds MSFHR Career and CIHR New Investigator Awards and has added to the emerging strength in computational biochemistry applied to directed protein evolution.

Christian Kastrup (recruited as a member of MSL) holds Peter Wall Early Career and CIHR New Investigator Awards and has provided new cross-cutting initiatives with colleagues in the Centre for Blood Research and Chemical and Biological Engineering by applying fundamental chemistry to the development of new bio-materials to treat cardiovascular disease.

Nobu Tokuriki

The earlier retirement of senior instructors **Ev Trip** and **Richard Barton**, coupled with that of **Bruce Tiberiis**, opened the way to the recruitment of a new generation of tenure-stream instructors. The new instructors, **Scott Covey**, **Warren Williams** and **Jason Read** have assumed leadership roles in the renewal and continuing evolution of the Biochemistry undergraduate B.Sc. programs. They have greatly enhanced our outreach to current undergrads in Science as well as their continuing mentorship through the laboratory courses and informal advising.

Christian Kastrup

Post-doctoral Fellows and Research Associates:

It is important to recognize the many roles, often understated or easily unnoticed, that are played by post-doctoral fellows, research associate and longer term staff and lab managers. Without them, the continuity of training of younger researchers, the maintenance and oversight of core equipment and unspoken hours of quiet mentorship would all be lost. Together, these groups currently make up a population of 63 senior researchers, of whom 30 are post-doctoral fellows. We were very saddened to learn of the sudden death of former trainee **Michael Page**. Mike had trained with and earned his Ph.D. with Ross MacGillivray and went on to post-doctoral and further work. Mike died in 2013 at the young age of only 36 and Ross worked with Mike's family to establish the Michael John Page Post-doctoral Fellow Award to "recognize a

Post-doctoral Fellow who reflects Dr. Pages' academic excellence and his passion for life". Drs. Julien Bergeron (2013) and Michael Yuchi (2014) were the first two recipients. The award is funded jointly by the Page family, the Department and the Centre for Blood Research.

PDFs present their work at the regular Department poster sessions and at annual retreats. In addition, we have initiated new activities specifically for post-doctoral fellows, including a short series of research talks to enable more senior PDFs to present and finally a "mock interview day" for a post-doc to give a full research talk and then meet one-on-one with a number of faculty members to discuss their future plans. The first "applicant" took up this offer in June 2013 and promptly went for the real thing and obtained his first academic position.

As part of the preparations for external review, we attempted to track the career progress of former post-doctoral fellows. 147 individuals had spent periods as post-doctoral fellows in the Department and moved to subsequent positions in the period 2003-2013 and we have so far been able to track 135 of these former fellows. In view of current and continuing interest in the quality and outcomes of training programs we would like to share the rough "job classifications" that have come to light:

Position	Number
1. Academic tenure/tenure-track	**34**
2. Academic research (RA etc.)	**42**
3. Further PDF training	**18**
4. Research in industry	**20**
5. Research in government unit	**6**
6. Professional (e.g. Law, M.D.)	**8**
7. Commerce	**4**
8. Home	**3**
9. Current location not yet known	**12**
Total	**147**

Based on a survey of our current post-doctoral fellows, we are planning further development of resources for our fellows. The PDFs themselves have developed a number of recommendations relating to career development, teaching opportunities, training and supervision and we will be working to implement a number of their suggestions.

Graduate Program:

The names of 2014 graduates, with degree, supervisor and thesis title:

Huan Bao (Ph.D., Franck Duong): "The regulatory mechanisms of the maltose transporter"

Wendy Bernhard (Ph.D., Ivan Sadowski): "The effect of YY1 and small molecules on HIV-1 expression"

Alina Yujia Chan (Ph.D., Philip Hieter): "DNA:RNA hybrid genome-wide profiling and links to genomic instability"

Leon Chew (M.Sc., Calvin Yip): "Structural characterization of the ATG1 kinase by single-particle electron microscopy"

Genevieve Desjardins (Ph.D., Lawrence McIntosh): "Structural characterization of DNA binding and auto-inhibition in the Ets1 transcription factor"

Elizabeth Dunn (Ph.D., Stephen Rader/Eric Jan): "Investigation of Free U6 snRNA structure and function"

Nancy Neng Fang (Ph.D., Thibault Mayor): "Good riddance to bad proteins: Identification of novel protein quality control pathways targeting cytosolic misfolded proteins for degradation"

Lynn Kimlicka (Ph.D., Filip van Petegem): "Structural and biochemical characterizations of the skeletal muscle and cardiac ryanodine receptor N-terminal disease-associated mutants"

Kelvin Lau (Ph.D., Filip van Petegem lab): "Binding and structural insights of the ryanodine receptor"

Alex Leung (Ph.D., Pieter Cullis): "Biophysical characterization of lipid nanoparticles containing nucleic acid polymers as produced by microfluidic mixing"

Alym Moosa (M.Sc., Michel Roberge): "Characterization of cellular abnormalities due to loss of TSC2"

Faraz Quazi (Ph.D., Bob Molday): "The role of photoreceptor ABC transporter ABCA4 in retinal and lipid transport and Stargardt macular degeneration"

Qian Ren (Ph.D., Eric Jan): "Characterization of alternative reading frame selection by a viral internal ribosome entry site"

Leslie Williams (Ph.D., Gary Brayer): "Structural studies of alpha-amylase inhibition"

As with the prior major review of the undergraduate program, a corresponding effort to review the graduate program is now under way. Feedback from graduate students has helped with this planning. Ideas being developed relate to course content and professional development. To kick start a trial of potential new offerings, the students themselves have worked with post-doctoral fellows to provide a series of "how to" workshops on a range of

key techniques and basic computational tools. Professional development is a significant concern of graduate students in Biochemistry and Molecular Biology. While a career in academia was traditionally the major goal and outcome of graduate studies, this is no longer the major career outcome for students today. The changing landscape of career options for graduate students is a major consideration through the current program review.

Undergraduate teaching programs:
A major undergraduate curriculum review began in 2009 with a broad survey of current and former students and faculty. The recommendations that emerged from the surveys and subsequent discussions led to a number of changes that have now been implemented:

- Expansion of the programs with new introductory courses in second year
- Addition of a new research-oriented course in third year
- Development of a suite of new options in fourth year to provide a broader range of upper level topics and to reduce class sizes at that critical phase
- Enhanced capacity in the advanced fourth year laboratory, to accommodate a larger number of majors students
- Further promotion and expansion of Coop internship opportunities – almost half of our major and honors students now take an extra Coop year to gain practical experience
- Greater "outreach" to students through "Imagine Day", careers advisory and "meet the prof" evenings, research lab tours and invitation to keynote lectures
- Greater involvement of graduate students as teaching assistants to provide parallel tutorial sessions to more courses and to enable smaller tutorial groups
- Increased development of scientific literacy and presentation skills

The process of curriculum renewal is continuing with further consideration of new course options to exploit expertise in emerging areas including computational and structural biology, regulatory RNAs, nano-medicines, "omics" and others. A new collaborative joint degree program in Forensic Biochemistry, developed in collaboration with colleagues at the BC Institute of Technology has also been developed and should be implemented within the next year. The joint specialization will provide a focused and compact program which enabling students to gain core scientific competencies in the field of biochemistry while achieving the requirements of the Forensic Science Education Programs Accreditation Commission (FEPAC).

The final element of change in undergraduate B.Sc. training relates to the space in which most of the laboratory teaching takes place. The condition of the D.H. Copp building has been deteriorating for many years and although some remediation has been possible, longer range planning has led to the incorporation of our needs into broader plans for new consolidated teaching laboratories for all undergraduate science programs. Planning is now well advanced for a major overhaul and expansion of the UBC Biosciences Building to accommodate teaching laboratories, offices and many other resources for undergraduate education. This project is now a major academic building priority and it is hoped that the new space will come on stream in the summer of 2018.

In addition to our major undergraduate science programs, the Department has always been significantly involved in the M.D. undergraduate program, notably in the first two foundational years. The M.D. program will evolve from problem-based to "case-based" learning over the next four years and the new paradigm will alter the delivery of basic science elements, the exact nature of integration of basic science is still being established at the time of writing.

University of Calgary

Department of Biochemistry & Molecular Biology, Cumming School of Medicine
Correspondent: Jonathan Lytton

Despite uncertain economic times, the Department of Biochemistry & Molecular Biology at the University of Calgary continues to thrive. This year our Faculty was renamed as the **"Cumming School of Medicine"** and a new Strategic Plan was launched. We are thrilled that our senior leadership are investing in, among other things, a bigger and better **centre for genomics and bioinformatics**, academic **recruitment in bioinformatics**, a better **grant-bridging program**, and expanded **support for trainee stipends** at the PhD and postdoctoral levels. The Department also launched a **new graduate specialization in Bioinformatics** as part of our BMB graduate program, and welcomed our first three students to the stream.

Our members continue to be highly successful in their research programs. This year **Justin MacDonald**, **Karl Riabowol**, **Jennifer Cobb**, **Jay Cross**, **Peng Huang** and **Raylene Reimer** were all successful in increasingly tough CIHR operating grant competitions. In addition, **Peng Huang** was awarded a CFI grant to help establish his new zebrafish lab, and **Debbie Kurrasch** was successful with her colleagues in garnering support from Brain Canada for a large drug development platform that will use zebrafish as a model.

Susan Lees-Miller

Research success was also recognized by several distinguished awards this year. **Susan Lees-Miller** won the CSMB's Jeanne Manery Fisher Memorial Award for her accomplishments, and **Jim McGhee** won the CSMB's NRC Research Press Senior Investigator Award for his outstanding career achievements. Both gave excellent lectures at the CSMB's 2014 Banff meeting.

In addition, **Karl Riabowol** was honored with a Killam Annual Professorship from the University, **Jason de Koning** received a research mentor award from the Bachelor of Health Sciences program, while our Department recognized **Aaron Goodarzi** (Leon Browder Rising Star Award), David Schriemer (Associate Professor Award), **Carol Schuurmans** (Schultz Award for General Excellence), and **Mike Walsh** (Hans van de Sande Leadership & Service Award) for their excellent achievements and contributions.

Jim McGhee

The passage of time has also marked our Department with some changes. The Department underwent a positive external review and **Jonathan Lytton** was renewed as Department Head for a second term, while **Paul Mains** was appointed as Director of the Medical Sciences Graduate Program. Several members moved on to new phases of their lives and careers. **Christoph Sensen** moved to the Technical University of Graz, in Austria, where he will lead their Institute for Molecular Biotechnology, while both **Roy Gravel** and **Dallan Young** retired. We are, of course, saddened by the departure of our good colleagues, but we wish them well in their new adventures!

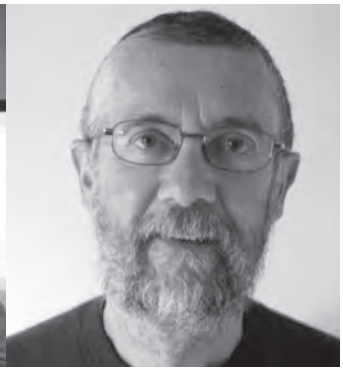
Karl Riabowol

Jason de Koning

Aaron Goodarzi

David Schriemer

Carol Schuurmans



Mike Walsh

The Department will continue to build on our strengths in 2015, with ongoing new faculty recruitment in bioinformatics and brain tumour biology. We also continue to seek top students for our strong graduate program. Please visit our website at www.ucalgary.ca/bmb/ for more information about the Department.

University of Calgary

Department of Biological Sciences, Faculty of Science
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 **Sergei Noskov** and **Marie Fraser** have been chairs of the Biochemistry cluster and Biochemistry program respectively.

Teaching undergraduates continues to be one of our priorities and we take great pride in our programs. Our B.Sc. Honours Biochemistry program was accredited by the Canadian Society of Chemistry (CSC) in 2014. The program is accredited as a Biochemistry program, not a pure Chemistry program. It meets the requirement of having students complete a minimum of 400 hours of labs in the fields of general chemistry, biochemistry, analytical chemistry and organic chemistry. The CSC maintains national standards of education and promotes the portability of the qualifications of graduates from such programs. We are very grateful to **Marie Fraser** for her dedication and commitment throughout the process.

Raymond J. Turner serves currently as Associate Department Head - Graduate Program. He visited the University of Manitoba as a participant in the Western Canada Biochemistry professor exchange. **Hans Vogel** continues to be very active as the Executive Editor of BBA-Biomembranes. He is currently enjoying a half-year sabbatical leave at UBC in the laboratory of Bob Hancock in the Department of Microbiology and Immunology, working on host-defence peptides. **Elmar Prenner** continues teaching and research in the areas of biophysics and Biomembranes, and is heavily engaged in the minor in Nanoscience by contributing to three courses, one of them a lab based-course. His group is funded by a NSERC Discovery Grant and participates in an AIHS-CRIO grants on tear film structure and function with Drs. Kubes and Vogel from the University of Calgary, and an AIHS-CRIO grant on the formulation of virus particles with Drs. Riabowol, Jirik, Dort and Morris. He is also involved in the start-up company, Alberta BioPhotonics. The **Tieleman** group develops computer models to study lipids and membrane proteins, at both atomistic detail and increasingly at a slightly coarser level of detail, in the now widely-used MARTINI force field for biomolecular simulation. Finishing a series of studies over the past ten years, they have published papers on monolayers and on lipid membrane defects, while a new plasma membrane model is likely to form the basis of a new research program for the next few years. The simulation groups in Chemistry and Biological Sciences have come together in the *Centre for Molecular Simulation*, promoting a range of activities including a very successful summer school in Calgary in 2014.

Elke Lohmeier-Vogel continued to teach and coordinate laboratory sections in two Biochemistry courses: the advanced laboratory course for biochemistry majors (20 students, 7/10 labs coordinated), and the introductory biochemistry course for non-science students (54 students, 6 labs coordinated). In these courses she team-

scenes from the 2014 Biosciences Graduate Poster competition

taught with **Elmar Prenner** and **Marie Fraser**. She also introduced two new guided-inquiry lectures in a 400 level Biochemistry course, one dealing with the phosphoketolase pathway used by the pro-biotic bacterium *L. reuterii*, and the other dealing with the deregulation of fat metabolism in alcoholics. These had been developed the previous year, after taking a C-LAB (classroom as a laboratory) course offered by the Faculty of Science. Five out of the six labs in this course were switched up from the year before in order to reduce student plagiarism (200 students). She also team-taught the first year biology course with her colleague **Kathreen Ruckstuhl** for the first time (400 students, no labs).

Several of our graduate students and post-docs have been recognized with distinctions/awards for their excellent research achievements: **Joseph Lemire** from the **Turner** lab was the recipient of a 2014 *Banting Postdoctoral Fellowship*. He was one of five University of Calgary scholars to receive this prestigious award. In the **Noskov** group, Dr. **Hristina Zhekova**, who completed her Ph.D. studies in Chemistry at the University of Calgary (2013), received the *Eyes High Post-Doctoral Award* and Dr. **Van Ngo**, who completed his Ph.D. studies in Biophysics at the University of Southern California (2014), received an *Alberta Innovates Health Solutions Post-Doctoral Award*. Among our graduate students **Yibo Wang** (Noskov) was awarded with an Eyes High International Graduate Scholarship. **Weiam Daear** (Prenner) won the biochemistry section of the 2014 *Sigma Xi* Student Research Showcase - The effect of polymeric nanoparticles on the stability of a biomimetic model of the lung surfactant. **Matthew Patterson** (Prenner) received an award for best poster at the 57th CSMB meeting: Membrane Proteins in Health and Disease held in Banff. **Ola Czyz** (Zaremberg) received the *Gene Huber* graduate thesis prize in Biological Sciences for her work on the effect of lysophosphatidylcholine analogues on pH homeostasis and membrane structure in budding yeast. **Isha Nasa** (Moorhead) was the winner (BCEM) of the annual *Biosciences Graduate Poster competition*.

University of Guelph

Department of Molecular and Cellular Biology

Correspondent: Frances Sharom

Faculty news

The four new faculty members who joined the department in 2013 were all successful in obtaining CFI funding to support their growing research programs:

Jim Uniacke's CFI JELF award of $311,648 will help grow his research program through the acquisition of specialized equipment for studying the cellular adaptation to low oxygen environments (hypoxia) through the reorganization of the protein synthesis machinery. This includes a state-of-the-art hypoxia workstation (Whitley HypOxygen H35), which is a "lab-in-a-box" where cells are cultured through glove ports. Dr. Uniacke also acquired a polysome gradient fractionation system from Brandel to isolate and study factors directly involved in protein synthesis. Hypoxic adaptation is linked to tumour progression and malignancy. This award will allow Dr. Uniacke to maintain a leadership role in the field of hypoxic adaptation where he is investigating novel therapeutic approaches targeting specialized protein synthesis machineries in cancer therapy

The funds received by **Scott Ryan** and **John Vessey** ($250,000 from CFI, matched by the Ontario MRI) will be used to establish a Neural Regeneration and Degeneration Laboratory. This will include an animal surgery facility, a stem cell culture room and a live cell imaging suite (live cell deconvolution microscope with optical sectioning) as well as a biochemistry work station. The research programs of Drs. Ryan and Vessey focus on fundamental aspects of neuroscience, with emphases on the generation and degeneration of the neurons of the brain, respectively, creating a research environment that strives to improve our understanding of the life of neurons from birth to death. This infrastructure investment will help Drs. Ryan and Vessey meet their research goals by establishing four research and technology suites to complement the existing expertise and infrastructure. The Stem Cell Culture and Analysis Suite will house all of the necessary equipment for generating and working with human induced pluripotent stem cells (hiPSCs). Here, trainees will learn to reprogram somatic cells, screen colonies for pluripotency and establish novel hiPSC models of neurological disorders. Their combined training in stem cell

biology and developmental biology will enable trainees to subsequently differentiate hiPSCs to disease-relevant cell types for mechanistic study. In parallel, the Animal Surgery and Primary Cell Culture Suite will allow *in vivo* study of both the development and degeneration of the nervous system, including *in utero* electroporation of recombinant DNA into neural stem cells at very early time points in development. Finally the Biochemistry Suite and the Live Cell Imaging Suite will allow new analysis of these systems to better understand neurodevelopment and degeneration.

Tariq Akhtar's award (a total of $310,000 from CFI and the Ontario MRI) will be used to purchase several "modules" for his plant metabolic biochemistry laboratory, including a high performance liquid chromatography system equipped with a variety of detectors. This system will be used to perform small molecule analysis, which is a vital component of any plant biochemistry research lab. A second module will be a Fast Protein Liquid Chromatography system, which will be dedicated to plant enzyme/protein purification and biochemistry. The combination of these two high-end pieces of equipment will allow Dr. Akhtar's research group to detect and quantify important plant compounds, with the added capability of identifying the enzymes that are responsible for their synthesis.

Retirements

The department wished a happy retirement to **Christine Schisler**, a dedicated instructor whose commitment to undergraduate teaching has been exemplary over a period of many years.

New additions

Jim Uniacke and his wife welcomed their first child, a boy, in July 2014, and **Cezar Khursigara** and his wife expanded their family with a little boy in June 2014.

Marc Coppolino receives his UGFA teaching award from Dean Mike Emes

Awards

The University of Guelph Faculty Association (UGFA) 2014 Distinguished Award for Excellence in Teaching was awarded to **Marc Coppolino**. Marc was recognized for his outstanding dedication and commitment to student academic and personal development at both the undergraduate and graduate levels, or as Marc put it "all, ostensibly, for being easily distracted during lectures!"

Dean Mike Emes (back left) with the award-winning CBS teaching team of (left to right) Jaspreet Kaur, Paula Russell and Enoka Wijekoon

The team of **Enoka Wijekoon**, **Paula Russell** and **Jaspreet Kaur** was one of two recipients of the College of Biological Science 2014 Award for Excellence in Teaching. The award recognized the collaborative efforts of this team towards supporting student learning in biochemistry, and enhancing the quality of the Biochemistry (and Biochemistry Coop) undergraduate programs. The other recipient of the award was **Wendy Keeleyside**, who was recognized for her numerous and diverse contributions to student learning and her longstanding dedication to undergraduate education. Wendy is a course instructor and faculty advisor for the Microbiology and Microbiology Co-op programs in the department, and has had made many outstanding contributions to this program, and to teaching and teaching scholarship.

Ph.D. candidate **Melanie Wills** (advisor Dr. Nina Jones) was honoured as one of Guelph's "Top 40 under 40" for 2014. Melanie has won many awards for academic achievement, including the WC Winegard Medal, The Governor General's Silver Award and the CIHR Vanier Scholarship. Her other passions include photography and film. She started taking photographs when she was 10 years old and at the

Wendy Keenleyside receives her CBS teaching award from Dean Mike Emes

Ph.D. student Melanie Wills was named one of Guelph's "Top 40 under 40" for 2014

age of 12 started working with film, which she says was a natural progression of photography and storytelling. Melanie's search for stories led her briefly into the field of broadcast journalism. When she was 14, she had her own teen news program on the local cable channel 10 in Lindsay called Minor Issues, and after her stint in television she started her own film company, Double Helix Creations. That is still active, and Melanie makes short films and documentaries, some of which have been screened at local festivals.

Emma Allen-Vercoe in her "robo-gut" laboratory, which simulates the microflora of the large intestine

Emma Allen-Vercoe received the 2014 YMCA-YWCA Women of Distinction Award in science and research for her research and efforts to change health-care practices by including effective caretaking of the human "inner ecosystem". Dr. Allen-Vercoe created the "robo-gut" scientific laboratory at the University of Guelph, which mimics the environment of the large intestine. In 2013, she released a groundbreaking discovery that an artificial fecal transplant created in her lab (RePOOPulate), which is essentially synthetic "poop" created to replace human fecal matter in stool transplants, can cure gastrointestinal infections caused by *Clostridium difficile*. Dr. Allen-Vercoe was interviewed by New Scientist in March 2014 for a story on using fecal transplants to cure inflammatory bowel diseases such as ulcerative colitis. She discussed the lack of regulations and said some people are conducting transplants themselves without medical supervision and increasing their health risks. She was also interviewed by the National Post in Sept 2014 for a story examining a recent Israeli study which suggested that the additives in diet soft drinks could negatively affect cell bacteria and microorganisms living in the gut.

Conferences

The University of Guelph hosted the 21st International Symposium on Plant Lipids 2014 (ISPL2014) from July 6-11, with Dr. Rob Mullen (our department chair) as conference Co-Chair. The conference, which was a huge success, offered a one-of-a-kind program highlighting recent achievements and future directions in basic and industrial-related aspects of plant lipid biology. It included the latest information and insights from a number of areas, ranging from the biosynthesis of cellular lipid components, to increasing oil yields in plant crop platforms and algal production systems, and developing new oil compositions to match human nutritional requirements and industrial material specifications.

Research news

Several senior researchers in the department made high-profile discoveries in 2014.

Rod Merrill's research team found a toxin released by the pathogen that causes American foulbrood disease in bees (*Paenibacillus larvae*), and developed a lead-based inhibitor against it. The Merrill team researchers identified a toxin, C3larvin, believed to be necessary for the bacteria to colonize a hive. The study was published in December in the *Journal of Biological Chemistry*, and was also featured in the Globe and Mail. American foulbrood is found throughout Canada, and affects the honeybee pollinator population, whose numbers are already falling globally because of disease, pesticide use, climate change and other factors. The disease spreads readily through spores transmitted within and between colonies by adult bee carriers, killing the larvae. Since American foulbrood is now antibiotic-resistant, and the spores may remain viable for 40 years, the only effective control method is to burn the hive and associated equipment. A new inhibitor-based approach could lead to natural and more effective approaches for fighting this widespread

and destructive bee disease. The Guelph team plans to begin field studies on honeybees in spring 2015 with the Institute of Bee Research in Hohen Neuendorf, Germany.

An international group including **Chris Whitfield's** team and researchers from the UK and Germany was the first to show how bacteria use a "molecular ruler" in making chains of sugar molecules for their protective coats. The study appeared in *Nature Structural and Molecular Biology* in December 2014. The molecular ruler - actually a coiled protein complex - enables bacteria to add right-sized chains to the microbe's outer membrane, and is critical for protecting some bacterial invaders from their host's immune system. The team used X-ray crystallography and small-angle X-ray scattering to determine the structure of the complex, which consists of three protein strands twisted together. Whitfield's team then showed how genetically altering the length of the ruler itself affected the ability of *E. coli* bacteria to make sugar polymers.

University of Lethbridge

Department of Chemistry and Biochemistry
Correspondent: Ute Kothe

Nehal Thakor

The University of Lethbridge has appointed **Dr. Nehal Thakor** as its fourth Campus Alberta Innovates Program (CAIP) Chair of Synthetic Biology and RNA-based Systems. Nehal Thakor, an Assistant Professor, brings his expertise in metabolic engineering and synthetic biology to the Alberta RNA Research and Training Institute (ARRTI) as its newest member. His research into the regulation of gene expression has implications for many fields, from biofuel production to cancer treatment. Before coming to the U of L, Nehal was a senior scientist at BioVectra, a supplier to the pharmaceutical and biotechnology industries, in Prince Edward Island. Originally from India, he obtained his bachelor's and master's degrees in microbiology from Sardar Patel University in Gujarat, India. Nehal did his doctoral work on microbial technology at Sardar Patel and at the University of Münster in Germany with Profs. Kamlesh C. Patel and Alexander Steinbüchel respectively. Afterwards, he studied bacterial protein translation and the mechanism of Tet(O) mediated tetracycline resistance in the labs of Diane E. Taylor and Kevin S. Wilson at the University of Alberta. Subsequently, he transitioned to the eukaryotic protein translation control field and worked with Martin Holcik at the Apoptosis Research Centre in Ottawa to investigate deregulation of protein translation during cancer and apoptosis. Specifically, using X chromosome-linked inhibitor of apoptosis protein (XIAP) IRES as a model, Nehal delineated the mechanism of internal ribosome entry site (IRES) mediated translation of cellular mRNAs during stress conditions. At the University of Lethbridge, he will continue investigating protein translation regulation during oncogenesis. Additionally, Nehal will establish a research program to develop novel RNA synthetic biology tools which will expand the available tool-kit for metabolic engineering in bacteria.

Brian Dempsey

Dr. Brian Dempsey joined the department on November 1 as a biochemistry instructor. Brian obtained a B.Sc. from McMaster University before moving to the University of Western Ontario and completing a Ph.D. in 2007. His Ph.D. work focused on using X-ray crystallography and NMR to study targeting in bacterial preprotein translocation. As a post-doctoral fellow at Agriculture and Agri–Food Canada, Brian studied methods of over-expressing therapeutic proteins in plant systems. Following that he became a Research Associate in Gary Shaw's lab at the University of Western Ontario, where he used NMR to examine the formation of protein complexes involved in membrane repair and neuronal signaling. At the University of Lethbridge, Brian will be teaching Biochemistry classes and labs, in addition to being an instructor in the successful iGEM synthetic biology program.

The University of Lethbridge is now an **affiliated academic partner with the CDRD (Centre for Drug Research and Development)** based at the University of British Columbia in Vancouver. The CDRD is Canada's fully-integrated national drug development and commercialization centre, providing expertise and infrastructure to enable researchers from leading health research institutions to advance promising early-stage drug candidates. Through this partnership the University of Lethbridge is connected to the other CDRD partners representing 10,000 Principal Investigators and enabling the CDRD to play an instrumental role in translating their breakthrough discoveries into viable commercial opportunities.

On the strength of a project that may one day lead to a new cell therapy to repair damaged neurons in the brain, the University of Lethbridge iGEM (international genetically engineered machine) team was awarded a gold medal at the iGEM Giant Jamboree 2014 in Boston from Oct. 30 to Nov. 3. Known as the Lethbridge Brainiacs, the iGEM team chose an ambitious project that involved using the brain's own immune cells to facilitate recovery following a brain injury such as stroke. The team picked a neuroscience project that involves engineering immune cells to identify astrocytes (cells that play a role in the scarring process) and reprogram them to become normal neurons. "When you have a stroke your neurons die and they don't grow back. By this system, we would be able to replace those lost neurons and hopefully enhance functional recovery after a stroke and traumatic brain injury," says Zak Stinson. "We were able to take some pretty big steps towards getting this targeting and delivery system built. We weren't able to test it fully because it was a really ambitious project for one summer, but we got quite a long ways towards showing that we could package these genes in these cells and send them over to astrocytes."

The University of Lethbridge iGEM team for 2014

The University of Lethbridge is actively planning for a new Science and Academic Building. In 2014, the university chose a design option for the new building called the Hub, a concept that creates a vibrant core in the heart of the building where paths between laboratory blocks and the general campus intersect. "The design encourages interaction and collaboration between faculty, students and the community, while the building respects the wonderful coulee landscape presented by the Oldman River valley and our campus." says Provost and VP Academic, Andrew Hakin. The Government of Alberta has invested $12.5 million towards the planning process of the Destination Project, and in December 2013, announced a $200-million commitment towards construction.

University of Manitoba

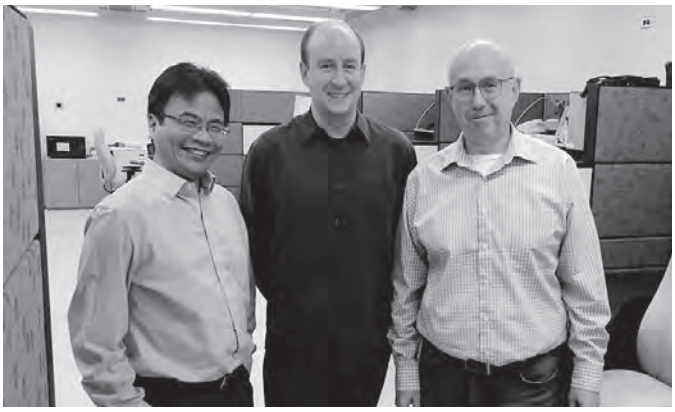
Department of Biochemistry and Medical Genetics
Correspondent: Klaus Wrogemann

Genomics and Bioinformatics are pervading everywhere, including our Department. In May 2014, work on the department's new computational biology laboratory was completed. Funded by the George & Fay Yee Centre for Healthcare Innovation, this facility is now home to the research groups headed by bioinformatician **Pingzhao Hu**, computational proteomicist **Ron Beavis**, and computational geneticist **Trevor Pemberton**. The opening of this facility follows closely on the heels of the College of Medicine's investment in a new secure data storage server to house the extremely large biological datasets being created by our faculty and those in other college departments.

James (Jim Davie) was re-appointed for another five years (2014 to 2019) as Editor of the journal Biochemistry and Cell Biology. In 2014, Jim was invited to present his research at symposia held in Edmonton, Jerusalem (Israel), Winnipeg, London (Ontario), Nassau (Bahamas), Bologna (Italy), and Barcelona (Spain). The symposium in Spain celebrated the 50 years of histone acetylation, which has been Jim's research interest since starting his graduate training at the University of British Columbia. Jim manages the Manitoba Next Generation DNA sequencing platform. In 2015, he will be launching the Manitoba Epigenetic Network website, which will serve as a resource for Manitoba epigenetics researchers.

Grant Hatch, primary appointment in Pharmacology, and our expert on cardiolipin, received new grants from the Barth Syndrome Foundation Inc., the Heart and Stroke Foundation of Canada, and NSERC. He served on the Organization Committee for the 2nd Cardiovascular Forum for Promoting Centres of Excellence and Young Investigator, held in Winnipeg, September 4-6, 2014, was a Senior/KeyPerson for a successful NIH R13 grant application for the 2014 Barth Syndrome Scientific & Medical Conference, Clearwater, Florida. Grant was also an Invited Symposium Speaker at the American Society for Neurochemistry annual meeting, Long Beach, CA and served as an Associate Editor for a Special Issue of Biochemistry and Cell Biology on Type 2 Diabetes.

Barbara Triggs-Raine, our Associate Head, has been named Researcher of the Month by Canadians for Health Research for her work on hyaluronidases in rare genetic diseases in unique populations. **Patrick Frosk**, known for his work on monogenic diseases, has joined the Clinical Genetics Section as an Assistant Professor.



In the new Computational Biology Lab (left to right): Pingzao Hu, Trevor Pemberton, and Ron Beavis.

University of Saskatchewan

Department of Biochemistry

Correspondent: Scot Leary

Our Department has experienced considerable change in the two years since our last communiqué to the CSMB. In the Spring of 2013, the new, research intensive D-wing of the Health Sciences building was opened and, almost without exception, the stand-alone lab structure of old was abandoned. Principal Investigators and their personnel from across the five basic sciences Departments within the College of Medicine now belong to Research Clusters, which are themselves contained within larger, more dynamic open concept lab spaces. Echoing this consolidation of our research potential, a mandate from the Deanery came down shortly thereafter urging that we merge the five basic science Departments into a single Departmental structure that would then deliver a unified undergraduate curriculum. This proposal met with considerable resistance from Faculty and, after striking an appropriate working committee, strong support was found for a two Department model. Although Faculty subsequently ratified this structural model, it is unclear if and when such changes will be implemented, and for now we remain as the Department of Biochemistry.

Mary Pato

Perhaps the biggest change to our Department occurred in July 2014, when **Mary Pato** retired after 32 years on Faculty. Mary was a valued colleague, who poured her heart and soul into our undergraduate program, particularly in the latter years of her academic career. Not surprisingly, our students loved her and they miss her sincere commitment, deep engagement and genuine interest in the betterment of their education. We miss her too! We also miss **Ron Geyer**, who moved laterally from our Department to a full-time position in the Department of Pathology. We certainly have nothing but the warmest of wishes for

both Mary and Ron going forward.

Bill Roesler remains Department Head, and it is fair to say that we have leaned heavily on his stewardship in a time of significant uncertainty. In fact, we are frequently reminded of how fortunate we are to have a Head who dedicates so much of his daily ATP to thinking about how to make our academic lives better, so that we can be more productive. His decision to host a working lunch every two months at the Faculty Club allows us to deal with Departmental issues but, equally importantly, gives many of us an opportunity to reconnect on a collegial level since we no longer see each other on a day to day basis.

Bill Roesler

Despite the considerable uncertainty about the organization and structure of our Department, our Faculty continue to acquit themselves well in national grant competitions. **Stan Moore** (2012) and **Scot Leary** (2013) received 5 year CIHR Operating grants, while **Oleg Dmitriev** received 2 years of operating funds from the CIHR in the final installment of the Regional Partnership Program (2012). **Jeremy Lee** and **Hong Wang** were both awarded 5 year NSERC Discovery grants in the 2012 competition. Several other Faculty also excelled at garnering extramural funding from a variety of charities or governmental agencies, and the achievements of **Scott Napper** (Agriculture Development Fund [6 total], Alberta Meat & Livestock Agency) and **Yuliang Wu** (CFI, Canadian Breast Cancer Foundation, and Leukemia and Lymphoma Society) are particularly noteworthy in this regard.

We would be remiss to end without acknowledging that this year Yuliang Wu was granted a second, three year probationary period as he continues to strengthen his case file for tenure. Equally encouraging news was received by Scot Leary and **Erique Lukong**, who learned that the Department and College had approved their case files for tenure and promotion to Associate Professor.

University of Toronto

Department of Biochemistry

Correspondent: David Williams

Faculty News

The past year has been a busy one for Chair **Justin Nodwell**. In his second year at the helm he has undertaken a two-year review of our undergraduate education program with emphasis on optimizing our Biochemistry Specialist stream. A more career-focused Master's program is also in development that is tailored to career paths other than academic research. Our Departmental website has been completely overhauled and now sports a much more contemporary look (please visit us at: biochemistry.utoronto.ca). Justin is also working hard to expand Biochemistry's influence in Toronto by creating new Departmental research nodes through appointments of scientists at St. Michael's Hospital, Sunnybrook Hospital and the Tanz Centre for Research in Neurodegenerative Diseases, as well as enriching our Faculty complement at SickKids (see below). Another key undertaking is the Department's participation in the new Centre for Collaborative Drug Research (CCDR; www.collaborativedrugresearch.ca), a multidisciplinary initiative designed to spur networking, collaboration and innovation in drug research. The CCDR is actively involved in developing new models for collaboration and innovation with the pharmaceutical industry and other partners. Justin heads the natural products/anti-infectious disease node of the CCDR.

Former Chair **Reinhart Reithmeier** has been appointed Special Advisor to the Dean of the School of Graduate Studies for Graduate Professional Development and Engagement. The goal of this position is to transform graduate education to ensure that our MSc and PhD graduates have the skill set and network to be able to take advantage of the diverse opportunities available to them in today's and tomorrow's global workplace. In keeping with this theme, Reinhart presented an Honorary Lecture on "Lessons from a Red Squirrel, Mentors, and the Pathway to Success" at the 2014 CSMB Annual Meeting

and Conference in Banff that was published in the special meeting issue of Biochemistry and Cell Biology: (http://www.nrcresearchpress.com/doi/abs/10.1139/bcb-2014-0058).

Freshly minted Associate Professors Trevor Moraes (left) and Alex Palazzo dish up some celebratory cake to the Department

We were delighted to learn that **Alex Palazzo** and **Trevor Moraes** were promoted to Associate Professor with Tenure in recognition of their "outstanding contributions to the Department and the University and of their promise for future scientific leadership." Alex and Trevor were also awarded Ontario Premier's Research Excellence Awards. The Department extends its warmest congratulations on their achievements!

John Rubinstein also celebrated several milestones in 2014. In a veritable scientific hat trick, he was promoted to Full Professor, awarded a Tier I Canada Research Chair and received the CSMB GE Healthcare New Investigator Award. We can't wait to see what John has in store for 2015!

John Rubinstein (left) receives the GE Healthcare New Investigator Award at the CSMB Meeting in Banff, April 2014

Walid Houry was appointed Associate Editor of the Frontiers in Molecular Biosciences section on "Protein Folding, Misfolding and Degradation" and was also Editor of the book "Systems Biology & Interactomics: The Molecular Chaperones Interaction Networks in Protein Folding and Degradation", Springer Science + Business Media.

Julie Forman-Kay, together with her past post-doc Tanja Mittag (now faculty at St. Jude's, Memphis), proposed a new symposium for the 2014 Biophysical Society meeting on the topic of phase separation of disordered proteins. Subsequently, they co-organized and co-chaired the "Liquid Protein Assemblies in Spatial Organization and Ultrasensitive Signaling in Cells" symposium at the Biophysical Society 58th Annual Meeting February 15–19, 2014, at the Moscone Center, San Francisco. Julie also spoke on the topic "Phase separation of disordered protein in the formation of membrane-less organelles", describing collaborative work that is now published: Nott et al., Molecular Cell 57:936, 2015. In another influential paper, Julie and co-workers describe how the folding of an intrinsically disordered protein by phosphorylation functions as a regulatory switch: Bah et al., Nature 519:106, 2014.

Alex Palazzo and collaborator **T. Ryan Gregory** (University of Guelph) published a well-received article in PLoS Genetics 10(5):e1004351, 2014 entitled "The Case for Junk DNA" which was covered on the National Geographic website and in the New York Times Magazine. In this review Palazzo and Gregory challenge a major interpretation of the ENCODE project that the majority of the human genome is functional. They present an overview of the experimental work and conceptual arguments that support the notion that a large portion of most eukaryotic genomes lacks an organism-level function. They demonstrate that the concept of "Junk DNA" is well supported by our current understanding of genomic content, and from experimental work from a number of different fields including biochemistry, genomics and molecular evolution.

Events

A major event of the year is our **Annual Research Day**. **The 2014 Research Day** was held on June 12th, a little closer to home this time, right on campus. As usual, the day began with a buffet breakfast which offered opportunities to socialize, followed by talks from our students and postdocs. One of the highlights of the morning was our annual **Theo Hofmann lecture** which was presented by **Dr. Hendrik Poinar**, McMaster University, who gave a fascinating talk on the origins of Yersinia pestis as gleaned from plague victims of old.

After a pleasant lunch, the afternoon featured a lively

Theo Hofmann lecturer Hendrik Poinar meets Theo Hofmann

Close to 200 biochemists squeeze onto the steps of the Medical Sciences Building during our Annual Research Day

poster session followed by several talks by recently appointed faculty members. All in all, it was a great day of science and collegiality capped off with our annual effort to squeeze everyone into our group photo!
For some additional photos of the event, please go to: http://biochemistry.utoronto.ca/2014/06/research-day-2014

The CIHR Training Program in Protein Folding and Interaction Dynamics winds down after 13 successful years!
Through the generous support of CIHR and several Departments at the University of Toronto and the surrounding Research Hospitals, the CIHR Training Program in Protein folding was established in 2002 and was continuously funded until 2015 (http://local.biochemistry.utoronto.ca/CIHR_folding). The program brought together scientists from various disciplines within the large Toronto protein folding community to encourage cross-disciplinary research encompassing *in vitro*, *in vivo*, computational, and disease-related aspects of protein folding. The program involved 33 member PIs and 26 non-member PIs with Professors **Walid Houry** and **Julie Forman-Kay** serving as co-Directors and Professors **Hue Sun Chan**, **David Williams** and **Khosrow Adeli** as members of the Program Advisory Committee. Prospective trainees, both graduate students and postdoctoral fellows, became part of a network of laboratories working in the broad field of protein folding. These trainees were co-supervised by at least two mentors working on different aspects of protein folding-related research. The unique and rich environment provided by the program trained graduate students and post-doctoral fellows to make substantial contributions to this important and multidisciplinary field.

The Program supported the establishment and continued offering of three new graduate courses at the University of Toronto. Under its auspices, high-profile international symposia were run on a biennial basis in addition to annual retreats. In total, the Training Program supported 39 graduate students, 45 postdoctoral fellows, and provided 130 travel awards. The trainees of the program were very successful in making important contributions to the area of protein folding resulting in more than 220 publications.

The Training Program has provided a unique and rich training environment for our students and has been instrumental in encouraging innovative and collaborative research between many PIs in Toronto. This STIHR model allowed the creation of a closely interacting community of researchers. We hope that CIHR will make the positive decision to continue these programs.

Trainees and mentors at the CIHR Training Program Symposium - CSMB Meeting on Protein Folding, Niagara, 2009

Other events were our ever-popular **Golf Day and Biochemistry-Immunology Baseball Challenge.**

A happy group of golfing biochemists!

The Biochemistry "Mutants" Baseball Team

Twenty faculty, staff and trainees (plus the odd ringer) gathered at Flemingdon Park Golf Course for our Annual Golf Day. There was a vast range of abilities, but each team had its share of novices and pros and, with a scramble format, things were pretty well matched. Great weather and excellent company combined to make for an excellent day. In the end, the coveted Biochemistry Cup changed hands in a cliff hanger 3-way tie that had one team nosing ahead on a technicality. For more photos: http://biochemistry.utoronto.ca/2014/08/annual-biochemistry-golf-day

Challenged by the Department of Immunology to a softball game, 12 intrepid biochemistry faculty and students heeded the call, ably captained by PhD student Tomas Gverzdys. Despite extensive trash-talking by the well-practiced immunologists, the inexperienced but well-tolerized biochemistry team showed heart and determination, losing a squeaker to their opponents in the final inning. Notably the biochemists turned the only two double plays of this Fall Classic!

Appointments

The Department welcomed four new faculty members as primary appointees in 2014.

Vito Mennella

Dr. Vito Mennella, a Scientist in the Cell Biology research program at The Hospital for Sick Children (SickKids) was appointed as an Assistant Professor. As a Fulbright Fellow, he completed his MSc and PhD at the Albert Einstein College of Medicine in Dr. David Sharp's lab. He then joined the lab of Dr. David Agard at UCSF as a postdoctoral fellow. Vito is using super-resolution microscopy to probe the architecture and dynamics of centrosomes and cilia. His strategy is to build nanometer-scale molecular maps of organelle structures by combining two super resolution microscopies (3DSIM and STORM) with 3D alignment and averaging techniques borrowed from cryo-electron microscopy analysis.

Joel Watts

Dr. Joel Watts, Scientist at the Tanz Centre for Research in Neurodegenerative Diseases, joined the Department as an Assistant Professor. Joel did his PhD with Dr. David Westaway at the University of Toronto, which involved the first characterization of the novel prion protein family member, Shadoo. He then pursued postdoctoral studies in the lab of Nobel Laureate Dr. Stanley Prusiner at UCSF where he developed new transgenic mouse models of prion disease and explored the prion-like properties of Aβ and α-synuclein. Joel is continuing this theme as an indepen-

Jean-Philippe Julien

dent investigator.

Dr. Jean-Philippe Julien was welcomed back to the Department as an Assistant Professor. Jean-Philippe did his PhD degree in the Department with Prof. Emil Pai and then undertook postdoctoral studies with Dr. Ian Wilson at the Scripps Research Institute. He has had a long-standing interest in immune recognition of viral antigens both in terms of solving crystal structures of immune complexes as well as the development of novel vaccine strategies. As a Scientist in the Molecular Structure and Function research program at the Hospital for Sick Children, Jean-Philippe will focus on the characterization of B cell receptors by using a combination of biochemical, biophysical, immunological and structural techniques. The study of their interactions with cognate molecules, therapeutics and pathogens is also an active area of research in the laboratory.

Nana Lee

We were also fortunate to recruit academic and industrial scientist **Dr. Nana Lee** back to the Department as a part-time Lecturer. Nana received her PhD from our Department, then did a postdoctoral fellowship at the University of Michigan and was a Visiting Scholar at the Whitehead (Broad) Institute for Biomedical Research, MIT. Subsequently, she moved to industry with positions as Senior Research Scientist for Ellipsis Biotherapeutics and Senior Research Scientist, Product Manager and Director of Application Science for DNA Software. She brings her expertise as an industry scientist into her current position as Coordinator of our Graduate Professional Development Program that focuses on developing the academic and professional skills required to succeed during and beyond graduate education in basic biomedical sciences. For more information on the program visit: http://biochemistry.utoronto.ca/professional-development

We were pleased to cross-appoint four additional faculty members to the Department. An important new node was established at the Saint Michael's Hospital Keenan Centre for Biomedical Research through the appointments of Drs. **Gregory Fairn** (Asst. Professor), **Warren Lee** (Asst. Professor) and **Andrew Kapus** (Professor). These appointments bring expertise to the Department in the areas of cell biology of lipids, membrane biology and organelle function (Fairn), mechanisms of endothelial permeability (Lee) and the cytoskeleton as a fate-determining device (Kapus). We also welcomed **Dr. Deborah Zamble** of the Department of Chemistry who was appointed at the level of Professor, bringing new strength to the Department in the area of transition metal homeostasis.

Retirements

Students, staff and Faculty members gathered Sept 18 2014 in the delightful setting of the University Faculty Club to celebrate the 37-year career of **Professor David Pulleyblank**. We were joined by several former students of David's who shared in the celebration and regaled us with stories of their times in the Pulleyblank lab.

David grew up in Cambridge, England where his father was a Professor of Chinese history. The family moved to Vancouver when his father took up a position there in 1966. David completed an undergraduate degree at the University of British Columbia then moved to Edmonton where he finished a Ph.D. in the biochemistry department with Richard Morgan. During his post-doc with Jerome Vinograd at CalTech, he worked on DNA structure and supercoils. When Vinograd died in 1976, David applied for a job in the Biochemistry Department at the University of Toronto. He started in January 1977.

Seven of David's Ph.D. students currently hold faculty positions at universities in Canada and other countries. Our Department recently hired one of David's scientific grandchildren, Trevor Moraes. Many of David's papers on DNA and chromatin structure are still being cited. During his 37 years with the department, David has interacted with, and influenced, dozens of colleagues and students – both undergraduate and graduate. Although retired,

David Pulleyblank chats with former students Duncan Jones (centre) and Simon Ives (right)

we still enjoy David's company as he frequently drops by student seminars and invariably manages to pose questions from a novel perspective.

Graduate Studies

Once again our graduate students selected a prominent alumnus to present the **Benjamin Schachter Memorial Lecture**. This lecture provides our students with insights and advice on diverse career choices and 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 **Dr. Arash Zarrine-Afsar** of the Techna Institute. This is an institute of the University Health Network, in collaboration with the University of Toronto, which focuses on the accelerated development and exploitation of technology for improved health. Arash is also co-founder and Chief Technology Officer of VertoNova Analytical, a federally registered Canadian venture dedicated to the commercialization of a new ion source for biodiagnostic applications and image guided surgery.

Arash Zarrine-Afsar (second from left) with Chair Justin Nodwell and Benjamin Schachter's daughter Bonnie Druxerman and her husband Peter Druxerman

Arash gave a fascinating account of his development of ultra fast laser tools which are dramatically more precise and less damaging to tissues in surgical applications and how this can be coupled to mass spectrometry in near real time to analyze small molecules in tissue samples.

The centrepiece of the Department's Annual Research Day is its **graduate student poster competition**. Our Theo Hofmann Lecturer, **Professor Hendrik Poinar**, McMaster University, served as guest judge to help make the hard decisions as to which posters deserved special recognition. As usual, the quality was high and the decisions tough but, in the end, the following students (who receive cash awards) were chosen as poster winners:

Winners in the Ph.D. category were:

Tomas Gverzdys (Nodwell Lab) *"Genomic-era methods for antibiotic discovery"*, **Tina Sing** (Brown Lab) *"The RSC complex functions to maintain ploidy in Saccharomyces cerevisiae"*, **Edith Cheng** (Brown Lab) *"Re-modeling of the BLM-TOP3A-RMI1-RMI2 genome stability complex during replication stress"* and **Theodore Pham** (Trimble Lab) *"The role of septins in the compartmentalization of the mammalian plasma membrane"*.

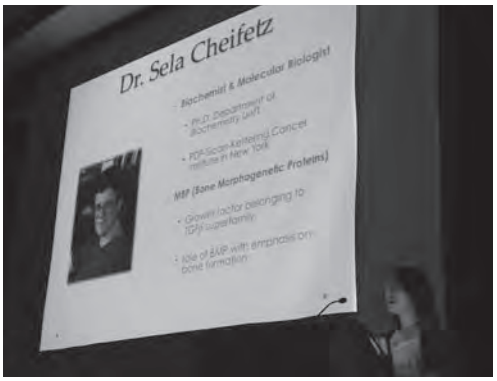
Winners in the M.Sc. category were:

Martin Daniel-Ivad (Nodwell lab) *"Identification of 'cryptic' antibiotics by a constitutively active AfsQ1"* and **Anthony Chen** (Rotin lab) *"RNA interference screen to identify kinases that suppress rescue of ΔF508-CFTR"*

The winner in the postdoc category was:

Carina Buttner (Davidson Lab) *"Phage baseplate assembly - as simple as that!"*

Kethika Kulleperuma presents her Beckman Coulter Paper of the Year (2013) Award talk



Amy Cui offers a touching memorial to Sela Cheifetz during her award talk

Undergrad coordinator Roula Andreopoulos and Chair Justin Nodwell with outstanding TAs Vince Nadeau and Tracy Stone

Additional graduate awards:
The winner of the ***Beckman Coulter Paper of the Year Award*** was **Kethika Kulleperuma** (Pomès lab) for her paper entitled:
Construction and validation of a homology model of the human voltage-gated proton channel hHV1.
Kulleperuma, K., Smith, S.M., Morgan, D., Musset, B., Holyoake, J., Chakrabarti, N., Cherny, V.V., DeCoursey, T.E. and Pomès, R. (2013) *J. Gen. Physiol*. 141(4):445-65.

A new award this year, created in memory of alumna **Sela Cheifetz**, was awarded to **Amy Cui** (Palazzo lab) who received the honour as our top Ph.D. student beyond year 3.

The **outstanding PhD thesis award** went to **Eliana Chan** (McQuibban lab) for her thesis entitled *"Mitochondrial-localized phosphatidylethanolamine in mitochondrial dynamics and autophagy."* This award is based on having a well written and scholarly thesis document that provides important contributions to new knowledge and outstanding performance at the oral defense.

Chair Justin Nodwell presents the Scott Award to Graeme Sargent

Brandon Sit (left) and Tom Bateman (right) receive their awards from Chair Justin Nodwell

The annual ***David Scott Prize*** for outstanding all-round graduate student was awarded to **Graeme Sargent** (Kim lab). Award winners are selected on the basis of research and teaching excellence and outstanding contributions to the Department and to fellow students.
Outstanding Teaching Assistant awards went to **Tracy Stone** and **Vincent Nadeau** for their exceptional performances as tutorial leaders.

Congratulations to all winners on their achievements!

Undergraduate Studies
Congratulations to Brandon Sit and Tom Bateman for exceptional achievement at the top of their classes in our 3rd and 4th year laboratory courses, respectively.
We were also pleased to learn that Biochemistry undergraduate student **Moustafa Abdalla** was one of Canada's 11 students named as Rhodes Scholars. He plans to study computational biology and computational medicine research at Oxford and hopes to one day contribute to the advancement of medicine through the ethical use of technology and artificial intelligence.

In a conversation with U of T News, Moustafa reflects: "We are currently developing artificial intelligence that is capable of teaching itself, and teaching other artificial intelligence. The stock exchange is an example of computers teaching other computers how to trade stocks. We don't realize the implications of this.... ultimately, I want to develop an ethical, compassionate framework for technology, and apply that within the context of medicine."

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 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 CFI-funded microscopy centre.

Our labs have made numerous exciting discoveries over the last year. A few examples are highlighted here. Research from the **Woodin** lab published in *Cell Reports* identified that Kainate receptors coexist in a functional complex with the neuron-specific K^+-C^{l-} cotransporter KCC2 and regulate chloride homeostasis in hippocampal neurons. A collaborative project from the **McCourt, Desveaux, Moses** and **Provart** labs published in *Developmental Cell* defined an abscisic acid (ABA) signaling network made up of 138 interconnected proteins in higher plants. In *Development*, the **Winklbauer** lab identified a fundamental relationship between the resistance of a tissue to flow (tissue viscosity) with the cohesion of a tissue (how strongly its cells adhere to each other), providing a basis for the comparison of tissues with mechanical properties that may vary by orders of magnitude. These examples provide a sampling of the stimulating research conducted in the Department.

Our graduate program has also excelled. For example, we are very proud of our students' success in earning scholarships. NSERC CGSM: Molly Allen (Bruce lab), James Colapinto (Berleth lab), Yan Li (Harris lab), Jing Lu (Godt lab), Amanda Miles (Tropepe lab), Ashley Miles (Buck lab), Amir Sabouhanian (Chang lab), Natalie Sorfazlian (Tropepe lab); CIHR CGSM: Matthew Snow (Peever lab); NSERC PGSD: Christine Cao (Yoshioka and Desveaux labs), Jessica Pressey (Woodin lab), Jordan Silver (Tepass lab); NSERC CGSD; Raphael Brisset Di Roberto (Chang and Peisajovich labs), Timothy Lo (Desveaux and Guttman labs), Jarlath Rodgers (Ryu lab); OGS: Janine Cajanding (Kim lab), Thomas DeFalco (Yoshioka lab), Peter Hawrysh (Buck lab), Charline Khademullah (Woodin lab), Nina Kirischian (Guttman and Desveaux labs), Virlana Shchuka (Mitchell lab), Zoltan Torontali (Peever lab), Taraneh Zarin (Moses lab); QEII-GSST: Donghoon Lee (Harris lab); Vision Science Scholarships: Nihar Bhattacharya, Gianni Castiglione, and Alex van Nynatten (Chang lab).

Our faculty members were recognized in a numbers of ways:

- **Ulrich Tepass** was named a Fellow of the Royal Society of Canada
- **Eiji Nambara** ranked among 19 U of T scholars recognized as one of the world's most highly cited researchers
- **Darrell Desveaux** received the 2014 C.D. Nelson Award in Plant Biology from the Canadian Society of Plant Biologists


Sergey Plotnikov

Last but not least, we welcomed a new faculty member, **Sergey Plotnikov.** Sergey comes to us from Claire Waterman's lab, and will advance our understanding of how cells integrate positional cues to guide their migration. In particular, Sergey discovered that cells use focal adhesions to pinch the extracellular matrix to judge, and respond to, its mechanical properties. His lab will explore the molecular mechanisms involved using advanced microscopy and biophysical approaches.

University of Toronto

Department of Molecular Genetics
Correspondents: Leah E. Cowen and Julie M. Claycomb

This has been an eventful year for the Department of Molecular Genetics, with 2014 marking the 45th anniversary of the founding of the Department, which is also the 25th anniversary of the establishment of its graduate program. Whereas, in 1969 the Department had 10 faculty members housed solely in the newly constructed Medical Sciences Building (MSB), it now comprises over ten times as many faculty members, half on campus in the MSB and the Donnelly Centre, and half in hospital-based research institutes including the Peter Gilgan Centre for Research and Learning, the Lunefeld-Tanenbaum Research Institute, and the Ontario Institute for Cancer Research. This growth reflects the success of the Department in establishing and maintaining key partnerships both on and off campus. We hope that you will enjoy our research highlights and coverage of exciting faculty and student achievements and initiatives.

Research highlights:

Researchers solve a longstanding mystery in cell division - cells do not repair damage to DNA during mitosis because telomeres could fuse together with catastrophic consequences. (Science 2014, 344: 189-93). MoGen team lead by **Daniel Durocher** discovered that at the moment of cell division cells lose the ability to distinguish between damaged DNA strands and telomeres. They found that reactivation of DNA double-strand break repair machinery that is normally shut down during cell division leads to fusion of telomeres, as shown.

Discovery of an "obesity gene" that encodes a master energy regulator in the brain, contributing to obesity and likely diabetes. (Nature 2014, 507: 371-5). An international team co-led by MoGen scientist **Chi Chung Hui** found that obesity-associated genetic variants control weight gain by tuning the expression levels of the gene *IRX3*. *IRX3* in turn controls a group of neurons in the brain that regulate energy expenditure. Mice lacking *IRX3* showed reduced weight gain and more efficient glucose processing compared to control mice, providing a foundation for developing new therapeutic approaches for obesity and diabetes.

Study discovers a pre-leukemic stem cell that may be the first step in initiating disease and also the culprit that evades therapy and triggers relapse in patients with acute myeloid leukemia. (Nature 2014, 506: 328-33). MoGen team led by **John Dick** lays the groundwork to detect and target pre-leukemic stem cells in the bone marrow that give rise to an aggressive blood cancer. Mutation in the gene DNMT3a cause the pre-leukemic stem cells to proliferate abnormally, creating a reservoir of cells that is resistant to chemotherapy and can lead to relapse

Researchers make great strides towards cracking the autism code. (Nature Genetics 2014, 46: 742-7). An international team lead by **Stephen Scherer** discovered a unifying set of characteristics in DNA that define a genetic formula to calculate which mutations have the highest probability of causing autism. They key to solving the enigmatic code was in recognizing exons of genes that are highly conserved in human evolution and highly expressed during early brain development.

Discovery of a new link between the cell membrane and the mitochondrial matrix that controls metabolic state. (Cell 2014, 158;1293-208). MoGen team led by **Helen McNeill** discovered that the large cell-surface cadherin Fat, known for its role in the regulation of planar cell polarity and the Hippo pathway, is also essential for normal oxidative phosphorylation. Fat is proteolytically processed to release an intracellular fragment, which is targeted to mitochondria, where it interacts with components of the electron transport chain. Loss of Fat leads to increases in reactive oxygen species and a switch to aerobic glycolysis that is reminiscent of the Warburg effect.

Study reveals the architecture of cellular homeostasis circuitry. (Cell 2014 158:434-48). An international team led by MoGen scientists Mikko Taipale and **Anne-Claude Gingras**, and Whitehead scientist Susan Lindquist, systematically investigated protein-protein interactions of key chaperones required for modulating the folding and function of target proteins. They identified a complex landscape of interactions for Hsp90 and its co-chaperones, with implications for understanding cancer and neurodegenerative disease.

Team led by Ben Blencowe has identified and characterized a large network of conserved brain-specific alternative exons that is critical for neurogenesis. (Molecular

Cell 2014, 56:90-103). A neural-specific splicing regulator previously discovered in the Blencowe laboratory, nSR100/SRRM4 (Calarco et al. Cell, 2009), activates this exon network by binding to adjacent, specialized intronic splicing enhancer motifs, and by facilitating the recruitment of multiple early splicing complex assembly factors. Discovery of this global splicing activation mechanism facilitates our understanding of the molecular mechanisms underlying neuronal differentiation, evolution for brain complexity, and neuronal developmental disorders such as autism.

Study led by Jack Greenblatt illuminates structural and functional features of regulation of human RNA polymerase II. (Nature Structural and Molecular Biology 2014, 21:686-95). Human RNA polymerase II carboxyl-terminal domain (CTD) contains 52 heptapeptide repeats that are important for transcriptional regulation and transcription-coupled RNA processing. This work demonstrates that dimeric RPRD proteins specifically recognize serine 2 and serine 7 phosphorylated (S2P, S7P) CTD repeats so as to organize the CTD into "CTDsomes" and recruit the phosphatase RPAP2 for CTD serine 5 (S5P) dephosphorylation.

MoGen researchers identify novel molecular origins of congenital and idiopathic forms of adolescent idiopathic scoliosis (AIS). (Nature Communications 2014, 5:477). The team led by **Brian Ciruna** pioneered a zygotic _ptk7_ zebrafish model of AIS, deficient in a key regulator of Wnt signalling. They identify genetic links between congenital and idiopathic forms of scoliosis and implicate dysregulated Wnt signaling in AIS, which manifests as a late onset spinal deformity that occurs in 3% of school children worldwide.

International team led by Michael Wilson demonstrates that comparing transcription factor binding between species is a powerful way to locate the DNA necessary for tissue specific gene expression. (eLife 2014, 3:e02626). They mapped the precise binding locations of a set of essential liver transcription factors in five mammalian species. As expected, only a minority of combinatorial transcription factor binding locations were shared between species. However, the shared combinatorial binding events were frequently found near genes involved in critical liver metabolic pathways and coincided with numerous regions mutated in liver-related diseases.

Discovery of tiny gene fragments linked to brain development and autism. (Cell 2014 159:1511-23). MoGen team led by **Ben Blencowe** found that very small segments of genes called "microexons" influence how proteins interact with each other in the nervous system. They identified a new landscape of splicing regulation that is highly specific to the nervous system. Many of the microexons that they detected are misregulated in people with autism. This article was highlighted in Cell, EMBO Journal, the London Free Press, and the Toronto Star.

Writing the genetic instruction manual to decode the human genome. (Cell 2014 159:1212-26). An international consortium co-led by MoGen professor **Fritz Roth** has systematically mapped how 13,000 proteins in the human proteome interact with one another. They found that proteins involved in cancer are more likely to interact with each other than with other types of proteins. An appreciation of protein interactions is key to deciphering the human genome, just as fixing a car requires more than a list of parts.

Discovery that C2H2 zinc finger proteins greatly expand the human regulatory lexicon. (Nature Biotechnology 2015 doi: 10.1038/nbt.3128). MoGen team led by **Tim Hughes** performed the first systematic study of the largest group of human transcription factors. They found that the C2H2 ZF transcription factors recognize more motifs than all other human transcription factors combined, and that they broadly bind to regulatory regions. These transcription factors may have evolved to defend our ancestral genome from damage caused by parasitic DNA.

Uncovering distinct genetic causes for sibling's autism. (Nature Medicine 2015 21:185-91). Study led by MoGen professor **Stephen Scherer** provides the largest whole genome sequencing analysis of families with autism. They discovered that siblings with autism spectrum disorder often carry different genetic mutations, and that those with distinct mutations showed more clinical variability than those with a shared mutation.

Finding needles in haystacks of genomic data. (Nature Methods 2015 12:154-9). An international team led by MoGen Professor **Fritz Roth** develops a powerful computational method to identify disease-associated genes from genome-wide association studies (GWAS). This approach leverages a "guilt-by-association" technique, and

outperformed existing algorithms in an analysis of 100 genome-wide association studies focused on 10 cancer types.

Discovery of a molecular basis for disease severity in patients with Cerebral Cavernous Malformation (CCM). (Nature Communications 2015 6:6449). MoGen team led by Brent Derry and **Anne-Claude Gingras** uncovers novel mechanisms underpinning CCM, which is caused by the progressive development of large lesions in blood capillaries, afflicting ~1 in 500 individuals. They identify novel _in vivo_ roles of CCM3-STRIPAK in regulating biological tube development and membrane integrity.

Discovery of a mechanism by which animals generate rhythmic motor activity that outlasts sensory stimuli. (Nature Communications 2015 6:6323). By combining genetics, optogenetics and electrophysiology, **Mei Zhen's** team found that a small group of premotor interneurons are required for sustained activation of motor output, and that this requires a new class of channel that mediates leak of sodium.

Research establishes that drug combinations could be a powerful approach for fungal infections. (Cell Reports 2015 10:809-19). **Leah Cowen's** team discovered that antifungal drug combinations can minimize the evolution of drug resistance, and that pathogens that ultimately evolve multi-drug resistance often suffer trade-offs such that they are vulnerable to killing by immune cells.

Faculty highlights and awards:

John Dick

John Dick was elected as a Fellow to the Royal Society (London). Prof. Dick has transformed the study of human hematopoiesis and leukemogenesis, with his development of methodologies for transplanting human bone marrow into immune-deficient mice. He has identified long-term repopulating human hematopoietic stem cells and generated mouse models of leukaemia. His studies showing that a specific subset of leukemic cells can recapitulate tumour growth are foundational for current work on cancer stem cells and applications to cancer therapy.

Charlie Boone

Charlie Boone was awarded the Edward Novitski Prize by the Genetics Society of America. This award recognizes an extraordinary level of creativity and intellectual ingenuity in solving significant problems in genetics research.

Igor Stagljar has been named a Corresponding Member of the Croatian Academy of Sciences and Arts. Prof. Stagljar uses a combination of molecular, cellular, chemical genomic and proteomic approaches to study the function of yeast and human membrane proteins, as well as bacterial proteins involved in pathogenicity.

Igor Stagljar

Janet Rossant has been awarded a 2014 honorary Doctor of Laws from the University of Windsor, and is a lead investigator for the Canadian Rare Diseases Models and Mechanisms (RDMM) Network — a first of its kind collaboration. The network was awarded $2.3 million from the Canadian Institutes of Health Research (CIHR), in partnership with Genome Canada, to advance rare disease research using model organisms. MoGen faculty members serve on the Network's advisory committees: Scientific Advisory Committee (Lipshitz, Rossant) and Clinical Advisory Committee (Cohn).

Bret Pearson was awarded the 2013 Early Career Award

Bret Pearson

in Cancer from the CIHR Institute of Cancer Research. This award was established to recognize the excellence of research being conducted in Canada by a new investigator in the field of cancer. Dr. Pearson's project entitled "Understanding the mechanism of stem cell lineage development and tumour suppression using freshwater planarians" received the highest ranking (by percent rank) in the 2013 Spring Operating Grant competition.

Professor Lap-Chee Tsui received the 2014 Henry G. Friesen International Prize in Health Research. The Prize, established by Friends of the Canadian Institutes of Health Research (FCIHR), in collaboration with the Canadian Academy of Health Sciences recognizes leaders of exceptional achievement in science and health policy of international stature. Dr. Tsui was a professor in Molecular Genetics when he cloned CFTR, and his current U of T appointment is as an emeritus professor in the Department. He was also instrumental in our establishment of the joint PhD with Hong Kong U.

Lap-Chee Tsui

Brenda Andrews

Brenda Andrews leads a team awarded a $1 million Connaught Fund Global Challenge Prize. Their project focuses on the cutting edge field of personalized medicine. The project is called Connaught Network for Modeling and Mapping Complex Disease: Addressing the Global Challenge to Understand our Personal Genomes.

Welcome to new Professors:

We are delighted to welcome eight new professors to the Department of Molecular Genetics since July 2013.

Ronald Cohn

Ronald Cohn joined The Hospital for Sick Children as the Chief of the Division of Clinical and Metabolic Genetics, Co-Director of the Centre for Genetic Medicine and Senior Scientist in September 2012. He also became the Inaugural Women's Auxiliary Chair in Clinical and Metabolic Genetics in April of 2013, as well as joining the department of Molecular Genetics as an Associate Professor in July of 2013.

James Dowling is a clinician scientist at the Hospital for Sick Children who is focused on gene discovery and therapy development for childhood muscle diseases. He was appointed to the department of Molecular Genetics as an Assistant Professor in September of 2013.

James Dowling

Ran Kafri was appointed to the department of Molecular Genetics as an Assistant Professor in November 2013. Prior to this appointment, he was a Postdoctoral Research Fellow at the Department of Systems Biology, Harvard Medical School hosted jointly by the laboratories of Marc W. Kirschner and Galit Lahav. His research focuses broadly on cell growth and proliferation, signal transduction, and genetic redundancy.

Ran Kafri

Monica Justice is the Head and a Senior Scientist in the Genetics & Genome Biology program at The Hospital for Sick Children and a pioneer in the field of mouse mutagenesis. Prof. Justice was recruited from Baylor College of Medicine, Houston, Texas, and was appointed to Molecular Genetics as a Professor in April 2014.

Julie Lefebvre is a Scientist in the Neurosciences and Mental Health Program at The Hospital for Sick Children, and was appointed to the department Molecular Genetics as of July 1, 2014. Prior to this appointment, she pursued her postdoctoral training in the laboratory of Joshua Sanes at Harvard University. She studies how nerve cells establish highly specific patterns of connections in the developing nervous system and links defects in these processes to neurodevelopmental disorders and brain diseases.

Mikko Taipale

Mikko Taipale was appointed to the Department of Molecular Genetics as an Assistant Professor in October 2014, and is located in the Donnelly Centre Research Node. Prior to this appointment, he was a Postdoctoral Fellow in Susan Lindquist's laboratory in the Whitehead Institute for Biomedical Research (Cambridge, MA). His plan is to take advantage of high-throughput proteomics and genomics approaches to understand how the mammalian proteostasis network is organized and how it is regulated in health and disease.

Tae-Hee Kim was appointed to the Department of Molecular Genetics as an Assistant Professor in November 2014, and is located in the SickKids Research Node. He completed postdoctoral training at the Dana-Farber Cancer Institute. Applying mouse genetics, epigenomics and gut organoid cultures, his lab investigates the developmental basis of gut stem cell renewal, differentiation, and cancer.

Olivia Rissland was appointed to the Department of Molecular Genetics as an Assistant Professor in November 2014, and is located in the SickKids Research Node. She was previously a Postdoctoral Fellow in David Bartel's laboratory in the Whitehead Institute for Biomedical Research (Cambridge, MA). She plans to use a combination of classical molecular biology techniques and transcriptome-wide approaches to understand the fundamental mechanisms controlling gene expression and to explore how these pathways are misregulated in disease.

Graduate Student Highlights:

The Department of Molecular Genetics has initiated a new Quantitative Biology Track within its graduate studies program.

Antonija Kreso

Former Molecular Genetics student Dr. **Antonija Kreso** was featured in the Toronto Star for her graduate work with Dr. John Dick on the characteristics of colon cancer cells. Dr. Kreso also received the CIHR Lap-Chee Tsui Publication Award.

Graduate student **Joseph Bondy-Denomy** was finalist and runner-up for the Three Minute Thesis competition, in which doctoral students have three minutes or less to present their doctoral research to a panel of non-specialist judges. Joe's talk was about Harnessing Viruses as the Next Generation Antibiotic.

Launch of new Career Development Workshops

Although academic careers are common for ~20% of our trainees, up to 80% of our students pursue careers outside of the academic sphere, including consulting, biotechnology, patent law and policy making, among others. Thus, among our >1,400 alumni, we have expertise in a

Joseph Bondy-Denomy (left) at the awards ceremony

remarkable breadth of career pathways. Notably, >1/3 of our alumni live in the Greater Toronto Area or within a few hours drive, providing a phenomenal and highly accessible resource for career mentorship. In response to requests for career development opportunities, Drs. **Julie Claycomb** and **Leah Cowen** have worked with our Graduate Student Association to hold a series of professional development workshops on subjects that include: strategies to maximize the graduate school experience, networking in science and beyond, MoGen alumni career trajectories, mental and physical health in graduate school, and career opportunity panel discussions. A larger Career Development Alumni Symposium is planned for the department in June 2015.

Career Development Workshop

Genetic Counselling student **Amanda Carnevale** was awarded the 2014 Jane Engelberg Memorial Fellowship Student Research Award. This prestigious award of the National Society of Genetic Counselors recognizes her research project on "Psychosocial Impacts Related to Receiving a Diagnosis of Klinefelter Syndrome in Adulthood."

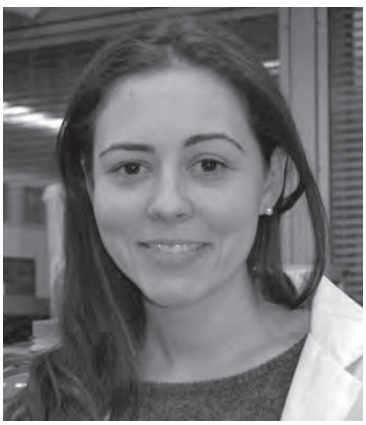
Ken Grisé has been elected as MoGen GSA president. Ken

Amanda Carnevale

is a doctoral student in the van der Kooy lab. As Graduate Student Association president, his role is to communicate the interests of the graduate student body to the MoGen faculty, other Faculty of Medicine departments and the university at large, and conversely, to keep MoGen grad students apprised of initiatives and issues arising from these different levels of the university. Ken also coordinates the GSA leadership team to ensure that grad life in the MoGen department is an engaging experience.

Ken Grisé

Joseph Bondy-Denomy received a Sandler Fellow position at the University of California, San Francisco. This fellowship enables recipients to establish their own independent research program immediately after they obtain their Ph.D. and is one of the most sought-after postdoctoral positions in the world. Bondy-Denomy completed his Ph.D. with Dr. Alan Davidson where his studies focused on a bacterial immune system called CRISPR-Cas.



Amber Couzens

Amber Couzens is the recipient of the Canadian Institutes of Health Research-Institute of Genetics (CIHR-IG) Lap-Chee Tsui Publication Award (2014). Dr. Couzens award winning paper published in Science Signaling was from her postdoctoral work with Dr. Anne-Claude Gingras

and focused on the protein interaction network of the mammalian Hippo pathway to identify mechanisms of kinase-phosphate interactions (Science Signaling, 6(302): rs15). Mohamed Solimen, also a MoGen student who trained with Dr. Anthony Pawson and Dr. James Dennis, was a finalist for his Science Signaling paper on the adaptor protein p66SHc inhibiting mTOR-dependent anabolic metabolism (Science Signaling, 7(313): ra17).

Monika Schmidt

Monika Schmidt was inducted into the American Society of Human Genetics Training and Development Committee (ASHG-TDC). Schmidt is currently pursuing her graduate studies in Dr. Christopher Pearson's laboratory, and will be one of only eight members, including graduate students, post-docs, and early career/industry scientists on the committee. The ASHG, founded in 1948, is the primary professional membership organization for human genetics experts worldwide, and includes nearly 8,000 members.

Undergraduate student highlights:

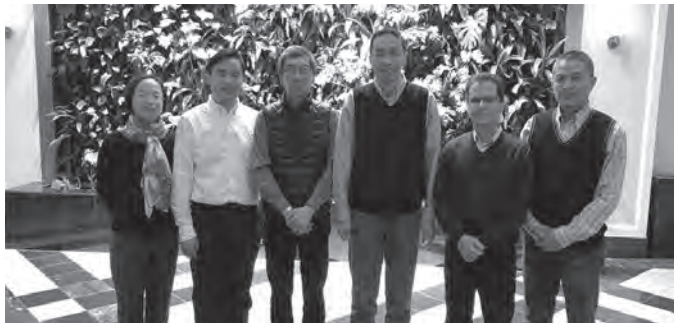
Revamped MoGen Specialist program. Our new Specialists have been paired with a faculty mentor. and over the coming year, they will participate in a variety of activities including lunchtime discussion groups with eminent faculty members, increased interactions with the graduate students and the Graduate Student Association, and lab shadowing. The intensive training our Specialists receive both in the lab and in the classroom will expand their perspectives and give them a unique and powerful advantage as they embark on the next stages of their careers, whether those careers are in biomedical science or something completely different.

Innovative online MoGen course. We launched our first entirely online course in January - "An Introduction to Medical Microbiology." This course, led by Prof. **William Navarre**, is pioneering in several respects. It is not only the first online course developed by our Department, it is also the first course at the University of Toronto to be simultaneously available to students inside the school and through the School of Continuing Studies for students outside of the university who wish to learn more about microbiology. This course also pioneers a collaborative approach that is unusual among typical offerings. Many units have been designed in collaboration with scientists and clinicians at Public Health Ontario and St. Michael's Hospital. This foundational online course introduces students to the fundamental principles of medical microbiology as they relate to health and disease. The partnership with hospitals and public health agencies provides a unique opportunity for students to learn directly from professional medical microbiologists.

International Partnerships:

Molecular Genetics partnerships with China featured in the Norman Bethune Celebration. The University of Toronto's Faculty of Medicine celebrated the legacy of one of its most famous graduates - Dr. Norman Bethune - 75 years after the death of the renowned humanitarian.

Toronto hosted the 5th Joint Symposium for researchers from the Shanghai Institute of Biochemistry and Cell Biology and the University of Toronto Faculty of Medicine. The Hospital for Sick Children hosted the event at the Peter Gilgan Centre for Research and Learning on November 11-12, 2014. Scientists presented their latest findings to hundreds of faculty members, staff and students, and talked about ways to work together. U of T's Department of Molecular Genetics, Donnelly Centre for Cellular and Biomolecular Research and SickKids Research Institute have worked with the Shanghai Institute since 2007.



5th Joint Symposium for researchers from the Shanghai Institute of Biochemistry and Cell Biology and the University of Toronto Faculty of Medicine. Left to right: Jian Zhao (SIBCB), Weiguo Zou (SIBCB), C.C. Hui (U of T), Naihe Jing (SIBCB), Howard Lipshitz (U of T), Jinsong Li (SIBCB). Photo by Yi Zhen.

University of Toronto Scarborough

Department of Biological Sciences
Correspondent: Bebhinn Treanor

Research in the Department of Biological Sciences at the University of Toronto Scarborough covers a diversity of fields, which are focused into seven research clusters: Biodiversity and Conservation, Cells and Infection, Comparative Physiology, Environmental Epigenetics and Development, Integrative Behaviour and Neuroscience, Plant Cellular and Molecular Processes, and the Neurobiology of Stress.

Tod Thiele uses optogenetics and imaging to identify sensorimotor circuits in zebrafish that guide behaviour

In the past year, we welcomed two new members to the Department. **Dr. Péter K. Molnár**, whose research focuses on the ecological impacts of climate change, blends field data collection with mathematical modelling to identify biological mechanisms by which environmental change affects ecosystems. **Dr. Tod Thiele** studies how the nervous system uses sensory information to guide behaviour. His research focuses on identifying sensorimotor circuits in zebrafish involved in the selection of visually driven behaviours using optogenetics, imaging, and behavioural approaches. This year also saw the promotion of three faculty members; **Dr. Marc Cadotte** and **Dr. Mauricio Terebiznik** were promoted to Associate Professor, and **Dr. Aarthi Ashok** was promoted to Senior Lecturer.

Several faculty members were awarded NSERC Discovery Grant funding including Professors **Herbert Kronzucker**, **Nicholas Mandrak**, **Blake Richards**, **Greg Vanlerberghe**, **and Rongmin Zhao**. The 2014 Bhagirath Singh Early Career Award, conferred by the CIHR Institute for Infection and Immunity, was awarded to **Dr. Bebhinn Treanor**. **Dr. Marc Cadotte**, whose research focuses on the role of different species in maintaining the ecosystem, received an Early Researcher Award from the Ontario Ministry of Research and Innovation. Professor **Rudy Boonstra**, whose research focuses on the role of stress in maximizing fitness in natural populations, received the UTSC Principal's Research Award. **Dr. Aarthi Ashok's** innovative teaching methods were rewarded with the Faculty Teaching Award.

Our labs have also made many exciting discoveries this year. The **McGowan** lab reported DNA methylation modifications associated with Chronic Fatigue Syndrome in *PLoS ONE*. The **Zhao** lab demonstrated an essential role for the molecular chaperone HSP90.5 in plant growth and chloroplast biogenesis (*BMC Research Notes*). The **Welch** lab reported that hummingbirds are able to use either exogenous glucose or fructose in order to fuel energy expensive hovering flight (*Functional Ecology*). The **Harrison** lab characterized various inflammatory stimuli in the modulation of osteoclastogenesis (*PLoS ONE*). The **Andrade** lab demonstrated that male black widow spiders prefer the pheromones of well-fed females – a preference which helps them avoid being eaten by a hungry female during mating! These examples demonstrate not only the diversity of research within the department, but the diversity of organisms under investigation.

University of Victoria

Department of Biochemistry and Microbiology
Correspondent: Robert Burke

John Burke joined the Department as an Assistant Professor

It has been another busy year in Victoria. In March 2014 we welcomed **John E. Burke** (no relation to your correspondent) as a new faculty member to the Department. John did his Ph.D. in San Diego and then had a very successful post-doc in Cambridge. He and his family are getting settled into life in Canada, and his lab is being transformed

from an empty space to a functioning lab filled with students and activity. John is interested in lipid signalling pathways, and will teach Proteomics and Biochemistry of Cellular Signalling.

For the past couple of years our **Biochemistry and Microbiology Student Society** has been very active and has become a vital part of the department. The BMSS organizes a wide range of events for students; movie nights, student help groups, mentoring for new students, pub-crawls, and term-end socials. The socials are popular for the quizzes and the irreverent imitations of faculty. The BMSS have also taken the lead on student recruitment and they are very effective at communicating the advantages of our programs to first year students. The department benefits enormously from the energy and enthusiasm of our students and this year they have been particularly helpful.

The department is also bracing itself for two retirements this year. The first of these is **Terry Pearson**, who has been a faculty member in the department since 1980. Terry's research on African sleeping sickness has achieved international prominence. His focus is on developing diagnostics using immunological methods; most recently coupling antibodies with mass spectrometry. His spin-off company is likely to make his retirement very busy! Terry has lived and travelled extensively in Africa and continues to do collaborative research with laboratories in Europe, North America, and Africa on sleeping sickness. Terry has delighted thousands of students with his unique lectures on immunology, replete with first person accounts of the early days of molecular biology at the MRC Labs in Cambridge.

Terry Pearson has been a faculty member for 35 years and this year will join the ranks of emeritus faculty.

Albert Labossiere, a member of the department for 39 years and head of the Biotechnology Support Centre, will retire this year.

The second retirement is that of **Albert Labossiere**, who has been a staff technician since 1976. Albert has been the department's Mr. Fixit for as long as anyone can remember. He conceived and built the Biotechnical Support Centre - his vision was a facility where faculty, staff, and students could get professional technical assistance in the maintenance and repair of equipment. "The Shop" is Albert's legacy to the department and it has been one of our secret weapons for teaching and research. Getting immediate, expert assistance with everything from a gel box to a mass spectrometer has substantially enhanced our research and lab teaching programs. Albert was a critical part of the design and construction of several buildings on campus and we have also lent him out to look after Animal Care and Aquatic Facilities. Albert is going into retirement gracefully, but, as he will be devoting more time to martial arts (he is the owner and head instructor for Sandalwood Martial Arts), retirement may be an exaggeration of his activity level.

Another key change for the department will be a new chair. **Perry Howard** will be taking over as Chair of Biochemistry and Microbiology in July 2015. We are fortunate to have someone of his calibre and experience to serve the department and we all look forward to his leadership.

University of Waterloo

Department of Biology

Correspondent: Bernie Duncker

Paul Craig

2014 was an eventful year in the Biology Department at the University of Waterloo. We were excited to welcome new faculty member **Paul Craig**, who studies the role of epigenetic regulation on phenotypic responses to environmental stressors in teleosts. **Barbara Katzenback** joined us twice, in a sense: first as a Banting Postdoctoral Fellow working with Brian Dixon, after which she successfully competed for a faculty position in our Department (she'll take up the latter after completing her fellowship). The focus of Barbara's research is the effect of climate change on fish immunity.

Barbara Katzenback

The accomplishments of our faculty members and students were recognized by a number of honours in 2014. **Brian Dixon** was the recipient of both an NSERC Synergy Award as part of a team working with Yellow Island Aquaculture Ltd. to rear quality salmon that are free of antibiotics or other contaminants, as well as the Partners in Research Virtual Researcher on Call Award, for outreach to public school and high school students. **Josh Neufeld** also picked up two awards, the Canadian Society of Microbiology Fisher Research Award and the Ontario Undergraduate Student Alliance Teaching Excellence Award. Once again our iGEM team achieved gold status at the annual Jamboree in Boston, this time for a project aimed at inhibiting antibiotic resistance in *Staphylococcus aureus* through gene silencing.

Finally, we were all shocked and saddened over the news that one of our former students, **Andrei Anghel** had died as a passenger on Malaysia Airlines Flight MH17, shot down over Ukraine on July 17th 2014 We have dedicated a beautiful new table in his honour in our Gleave Library, created from the wood of a Dawn Redwood (*Metasequoia glyptostroboides*) that was harvested to make room for our new Science Teaching Complex.

Gleave Library table named in honour of Andrei Anghel

York University

Department of Biology

Correspondent: Logan Donaldson

York University, like many others, is concerned with enhancing the first year experience (FYE) on its commuter campus. In addition to creating a better learning environment, it is hoped that retention will increase, and students will develop a deeper relationship with the University.

Towards stimulating the development of new programs, York University established an Academic Innovation Fund. **Dr. Logan Donaldson** received $80,000 in total funding from the first two rounds of the AIF program to create a first year learning community (or FLC, as its commonly known) in the life sciences. The goals for the FLC were to promote socialization beyond the confines of the large Introductory Biology course and to promote lateral thinking. Gaining membership in the FLC was straightforward - any student just had to be available on Friday afternoons to participate in the activities.

Genomics and personal medicine were two contemporary themes that really resonated among the first year life sciences students. As a result, part of the FLC funding was used to recruit **Dr. Tanya DaSylva**, an experienced genetics instructor, to develop classroom activities that raised questions about the application of these technologies. **Dr. Amro Zayed**, also in the Biology Department, gave an entertaining description of how human genomics initiatives in the areas of SNPs and sequence used by companies such as 23andMe could be extended to organisms like honey bees. **Dr. Steven Scherer** graciously gave the students a tour of The Centre for Applied Genomics facility.

The capstone event each year was a "spit day", where students supplied their own saliva sample for genetic analysis by the company, 23andMe. The personal genomics data provided to each student from 23andMe served as a foundation for discussions on ethics, technology and the role of science in culture. Students also had the opportunity to visit the Donaldson laboratory, isolate genomic DNA and analyze a SNP by PCR analysis.

The FLC was assessed through yearly written surveys and focus groups led by social research specialists on campus. To the surprise of the developer, the qualitative survey demonstrated that the FYE program gave no benefit to the students, despite a substantial commitment of both time and resources to the program and a self-selected, high achieving student cohort. One prevailing theme emerging from the focus group data was a feeling among the students that they were too burdened with demands of their on- and off-campus commitments for an enrichment program to make an impact. This unintended outcome challenges the idea that all FYE programs by nature are helpful, and it has informed future policy at York University. Logan Donaldson is currently exploring the possibility of working with Bethune College (the college that services York science students) to recast the FLC program as a degree credit course that would replace a general elective in a student's calendar. As a result, the net academic cost of the program would be zero.

Considering that most students will not elect to pursue a research path, improving scientific literacy is a worthy goal we can all work towards. Logan Donaldson is always interested in hearing the experiences of other CSMB members.

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, cell biology or genetics.
Student Research Conferences, where students display their research as posters, or give oral presentations.
Career Fairs or Career Workshops in areas related to biochemistry, molecular biology, cell biology or genetics.

Requests for graduate event support should be directed to the CSMB Secretary.

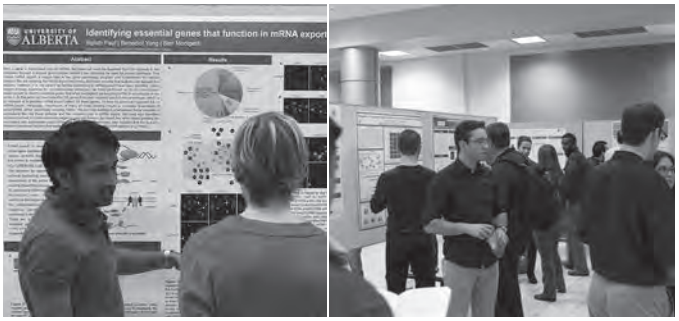
Cell Biology Invited Speaker and Research Day 2014

Department of Cell Biology, University of Alberta

Correspondents: Emily Herman (former President of the Cell Biology Student's Association) and Azra Lari (current President of the Cell Biology Student's Association)

The Cell Biology Student's Association hosted distinguished guest **Dr. David Drubin** from the University of California, Berkeley. Our event began with a "Meet the Speaker" evening for students and faculty to mingle with Dr. Drubin. Early the next day Dr. Drubin gave a very exciting and well-received keynote lecture titled *"Harnessing Actin Dynamics for Endocytosis".* We were able to highlight our own research through selected student talks and a competitive poster session. These sessions were very well attended by members within and outside our own department. We also hosted a pizza lunch for graduate students who grilled Dr. Drubin with questions about his research, academic career, and opinions about science in general.

Keynote lecture and student posters at the Research Day



Student posters at the Research Day

The second part of the day was our "Careers in Science" discussion led by a panel of guest speakers. This year our speakers included **Dr. Andrei Fagarasanu** who is currently a Hematology Fellow at the University of Alberta Hospital, **Dr. Melissa Dobson** who is a Bachelor of Technology and Technology Management Instructor at the Northern Alberta Institute of Technology (NAIT), and **Dr. Stephanie Minnema** who is a management consultant at KPMG LLP. This diverse panel gave the Cell Biology graduate students a chance to engage with successful individuals who have established careers outside of traditional academics.

This event created an environment of learning, discussion, networking, and sharing of knowledge and skills. This is imperative for students to experience to be successful in their graduate studies and future careers paths, regardless of where that will be. Research Day was also beneficial to the many guests outside our department from the Faculty of Medicine & Dentistry and promoted an environment for collaborative discussion within our own University.

Ontario Ecology, Ethology, and Evolution Colloquium 2014 (OE3C)

University of Guelph

Correspondent: Sara Kafashan

For decades, OE3C has brought together top researchers across Ontario to share findings in an intimate academic environment. Originally known as the Ontario Ecology and Ethology Colloquium, the recent addition of the third E – Evolution – significantly broadened the scope of this conference. In 2014, the Ontario Colloquium, with all of its three Es, was held at the University of Guelph, hosted by graduate students of the University of Guelph's Integrative Biology, Animal and Poultry Science, and Psychology departments (Jamie Ahloy Dallaire, Kate Eisen, Kelsy Ervin, Sara Kafashan, Tony Kess, Heather Kinkaid, Richard Matta and Zachary Ramsay). We welcomed over 120 attendees, ranging from undergraduate students to graduate students, post-doctoral students, and faculty members, to share their exciting findings. Presentation topics were highly diverse, ranging from animal welfare, climate change, and conservation biology, to evolutionary psychology and social behaviour.

We were also proud to have four plenary speakers present the most recent and intriguing findings within the fields of ecology, ethology, and evolution. Speakers included **Dr. Hafiz Maherali**, Department of Integrative Biology, University of Guelph; **Dr. Nicole Mideo**, Department of Ecology and Evolutionary Biology, University of Toronto; **Dr. Bennett Galef**, Department of Psychology, Neuroscience, & Behaviour, McMaster University; and **Dr. Amy Newman**, Department of Integrative Biology, University of Guelph.

Posters and participants at OE3C 2014

OE3C was a great way for young researchers to receive constructive feedback about their research, and for faculty to recruit, and interact with, top prospective students. Like past OE3Cs, this conference was entirely organized by a subset of dedicated graduate students. Together, we strove to make this conference a friendly, collaborative, fun and positive academic experience for all.

Plenary lecture, posters and participants at OE3C 2014

2014 Graduate Student Symposium

College of Biological Sciences, University of Guelph

Correspondent: Elyse Roach

The College of Biological Sciences Graduate Student Symposium is a student run event that aims to encourage scientific communication between students, research fellows and professors within the three departments of Molecular and Cellular Biology, Integrative Biology and Human Health and Nutritional Sciences. This year the 10th Annual Graduate Student Symposium was held on April 28 2014, and was organized by Shawn Beaudette, Alison Berezuk, Jennifer Bernard, Danve Castroverde, Thanushi Eagalle, Dita Moravek, Liliy Nasanovsky, Elyse Roach, Veronique Taylor, Jessica Ralston, Meghan Yip, Tegan Williams, Derek Zwambag, Dr. Glen Van der Kraak (Associate Dean of Research), and Karen White. It was held at the Science Complex and Alexander Hall, University of Guelph, and had 230 registrants consisting of graduate students, post-doctoral fellows, lab technicians, lab coordinators and professors. The event featured a keynote address by **Dr. Hendrik Poinar** of McMaster University, who talked about his research related to the evolution and origins of the "Black Death". The symposium also showcased graduate student research across the college in student oral presentation sessions, and the day concluded with a student poster session and social.

Graduate students during the poster session and social, which concluded the 10th Annual Graduate Student Symposium

2014 College of Biological Sciences Graduate Student Careers in Biology Day

College of Biological Science (CBS) University of Guelph

Correspondent: Scott Mazurkewich

On April 22 2014, the graduate students from CBS held the second annual Graduate Student Careers in Biology day. This was a free, all-day event focused on informing the graduate students in CBS of career opportunities that exist in industry, government and academia. There were over 200 graduate students from across the three departments of CBS, and additionally over 30 students from outside the college, who registered and attended the event which included 37 alumni and other professionals on hand describing the sectors in which they work.

The event was organized and run primarily by a committee of graduate students under the advisement of the College of Biological Sciences Associate Dean of Research, Dr. Glen van der Kraak. The graduate student members were: Scott Mazurkewich, Jonathon Samson, Christian Carlucci, Tara MacDonald, Erin Connelly, Anna Deboer, Cory Schilling, Tony Kess, Elizabeth Sears, Alena Mammone, and Jose Maloles.

The event was held in the Science Complex at the University of Guelph and the day was started by a keynote address in the atrium by **Dr. Nana Lee**, the Coordinator of the Graduate Professional Development program for the Departments of Biochemistry and Immunology at the University of Toronto. Her talk on "Success after Gradu-

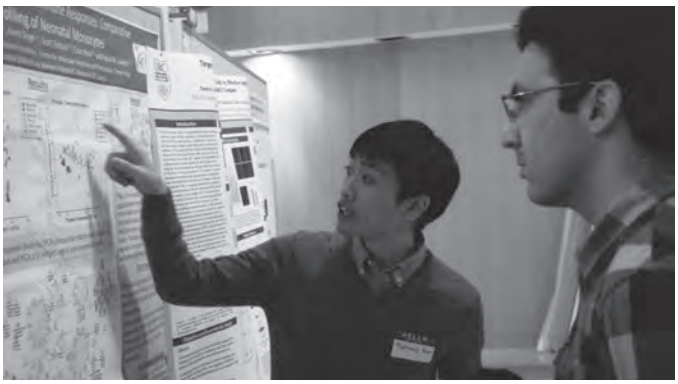
Keynote address by Dr. Nana Lee, Coordinator of the Graduate Professional Development Program for the Departments of Biochemistry and Immunology at the University of Toronto

Small discussion on entrepreneurship lead by Dr. Jamie Doran, CEO at Innovation Guelph

Outgoing student representative, Eric Pesarchuk, and Graduate Student Society representative Enav Zusman

ate School" integrated topics on developing critical skills during graduate school and how to pursue your passions after your degree. The keynote address was followed by a series of concurrent smaller round-table discussion sessions with alumni and other professionals to give students an opportunity to hear about careers in their sectors. The day concluded with a career fair/networking mixer with representatives from companies and organizations in southern Ontario on hand to interact with students and the university community as a whole.

We have since surveyed the student attendees to gauge the impact of the event. We have received an overwhelmingly response from the students remarking that this 2nd annual event was a success, useful in informing their future career choices and recommending that the event be run again next year.

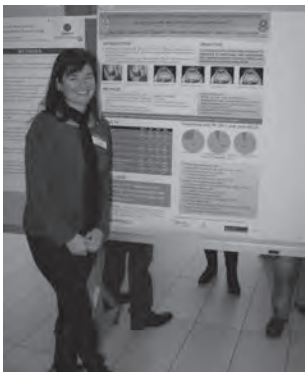


Bernard Kan discussing his poster with fellow student Mohsen Khosravi

Experimental Medicine Program Student Research Day

University of British Columbia

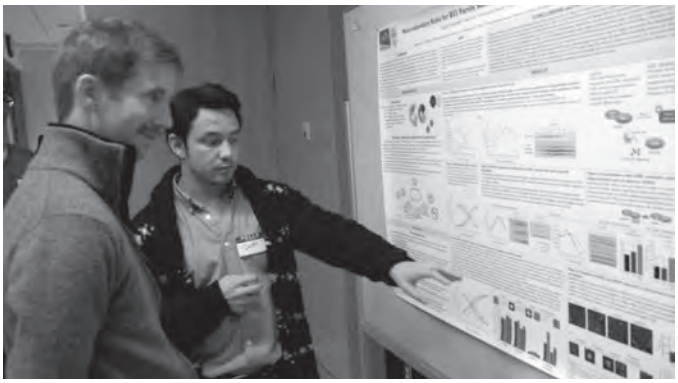
Correspondent: Eric Pesarchuk



2014 Vanier Scholar Erin Macri

With over 200 students, Experimental Medicine is the largest graduate program in the Faculty of Medicine at the University of British Columbia (UBC). Twice per year we hold a Student Research Day to allow students to present their research in oral and poster formats. We have a wide variety of research interests including molecular mechanisms of disease, drug development, biomaterial engineering, human physiology, and public policy analysis. These conferences also provide networking opportunities for students and faculty in our program, who are located at numerous research facilities throughout Vancouver. Our Student Research Days are always wholly organized and implemented by the Experimental Medicine Student Committee.

This year's events were held in June and November at the Children and Family Research Institute and Vancouver General Hospital, respectively, and were each attended by approximately 120 people. We always seek out talented and inspiring keynote speakers for these events. In June we heard from **Dr. Jeremy Hirota**, who is a new faculty member in the Department of Medicine at UBC. He not only outlined his respiratory medicine research but also gave pointed advice on how to land desirable post-doctoral fellowships, foster productive collaborations, navigate faculty interviews, and secure a tenure-track position in today's job market. For November we recruited **Karimah Es Sabar**, President and CEO of



Incoming student representative, Dominik Sommerfeld, presenting his poster to a judge

Keynote speech by Karimah Es Sabar, President and CEO of The Centre for Drug Research and Development

the Centre for Drug Research and Development, who has been voted one of Canada's Top 100 Most Powerful Women. Her inspiring talk highlighted the growing overlap between academia, industry, and government, and how scientists with diversified skills in business, project management, and entrepreneurship will be the most successful in this changing climate.

VanWoRM (Vancouver Worm Research Meeting)

Correspondent: Jennifer Grants

VanWoRM (Vancouver Worm Research Meeting) is a student-run seminar series for Caenorhabditis elegans (nematode) researchers from the University of British Columbia (UBC) and Simon Fraser University (SFU). It has been at the heart of a vibrant *C. elegans* research community in Vancouver and Burnaby since 2005. VanWoRM is run by five students from UBC and SFU, Jennifer Grants (Chair), Khang Hua, Grace Goh, Troy MacDiarmid, and Kwangjin Park. In 2014-2015, VanWoRM hosted seminars at UBC, the Centre for Molecular Medicine and Therapeutics, and at SFU on November 5th, 2014, and January 13th, March 4th, and April 1st, 2015. Speakers at VanWoRM included graduate students and postdoctoral fellows from UBC and SFU, as well as new UBC faculty member Dr. Kota Mizumoto and a visiting faculty member, Dr. Frédéric Picard, from the University of Laval, Quebec. Presentations covered diverse areas of C. elegans research, including neurobiology, metabolism, behaviour, and transcriptional regulation. VanWoRM united over 40 graduate and undergraduate, postdoctoral, and faculty member attendees from 10 labs across the UBC and SFU campuses. In April 2015, VanWoRM hosted the seminar at UBC, with excellent presentations on diverse topics from Catrina Loucks (SFU), Victor Jensen (SFU), George Chung (UBC), and Tiffany Timbers (SFU).

Department of Biochemistry and Molecular Medicine Poster Competition

Université de Montréal

Correspondent: Samuel Tremblay-Belzile

The Biochemistry Graduate Student Association of the Université de Montréal (AÉCSBUM) organized the poster competition to allow students and professors to familiarize themselves with the research activities of the Department of Biochemistry and Molecular Medicine. This year's event had the distinction of taking place as part of the celebrations of the 50th anniversary of our department, and was held on May 9 and 10 2014 in the Roger-Gaudry building of the university. Because of the context, many alumni of the department were present, bringing the total number of participants to approximately 150, including 33 poster presenters.

Students, professors, and alumni of the Department of Biochemistry and Molecular Medicine browse the posters

La Journée Scientifique des Étudiants du Centre de Recherche sur le Cancer de Québec et l'Axe Oncologie du CHU de Québec

Correspondent: Claire Dziengelewski

Discussions at the poster session

La 18ème édition de la Journée Scientifique des Étudiants (JSE) du Centre de Recherche sur le Cancer de Québec et l'Axe Oncologie du CHU de Québec s'est déroulée les 20 et 21 août dernier au Centre de Recherche sur le Cancer de l'Université Laval. Organisée par les étudiants du Centre de Recherche, cette journée a rassemblé environ 140 participants provenant des diverses équipes de recherche en cancérologie fondamentale et clinique, en radio-oncologie ainsi qu'en néphrologie. Plus de 105 stagiaires de premier cycle, étudiants diplômés, professionnels de recherche et stagiaires post-doctoraux ont profité de l'occasion pour présenter leurs travaux de recherche par un exposé oral ou sous forme d'affiche. Les meilleures présentations ont été récompensées par l'octroi de plus de $6,000 en bourses de congrès et de $1600 en prix.

Chaque année, les étudiants invitent pour l'évènement un ou plusieurs chercheurs de renommée internationale qui présentent leurs travaux. Pour la 18ème édition, nous avons eu le plaisir d'accueillir les **Dr. Martin Lepage** de l'Université de Sherbrooke et **Dr. Nicole Beauchemin** de l'Université McGill à Montréal. Ils ont présenté leurs travaux de recherche portant sur l'amélioration des techniques d'imagerie pour le cancer, et sur l'implication de la protéine CEACAM-1 dans la progression et la dissémination des cellules de cancer colorectal, respectivement. Ils ont également participé activement à la journée en évaluant les présentations orales des participants tout en assistant aux sessions de présentation par affiches. Le Dr. Beauchemin a également animé une discussion avec les étudiants à propos de leur avenir dans le monde de la recherche, ce qui était la première initiative du genre dans le cadre de la Journée des Étudiants et qui a été très appréciée par les étudiants.

Le comité organisateur tient à remercier la Société Canadienne pour les Biosciences Moléculaires pour leur contribution financière à l'organisation de cette Journée qui est sans aucun doute la plus importante dans notre Centre de Recherche.

The First Annual Cell and Systems Biology (CSB) Graduate Research Symposium

Ramsay Wright Laboratories, University of Toronto

Correspondent: Donghoon Lee

The First Annual Cell and Systems Biology (CSB) Graduate Research Symposium was held on May 16th, 2014 at the University of Toronto St. George campus. The event was organized by the CSB Graduate Seminar Organizing Committee, consisting of four CSB graduate students (Helen Chen, Miranda Hunter, Donghoon Lee, and Yixie Zhang).

More than 50 CSB graduate students turned out and celebrated their ongoing research endeavours, showcasing 16 posters with topics ranging from plant/microbial biology to animal morphogenesis, and neurobiology. Participating students were engaged in vibrant discussion and had the opportunity to share their research with fellow colleagues. The invited CSB faculty, **Dr. Jennifer Mitchell,**

The invited CSB faculty member, Dr. Jennifer Mitchell, giving a career/research talk on her scientific journey, pursuing her research interests from graduate school to her current position as a faculty member.

CSB students enjoying lunch and refreshments, generously provided by the CSB department and CSMB.

Graduate student Yan Li presenting her research poster to other fellow graduate students.

Graduate student Junior West presenting his research poster to a peer.

CSB graduate students presenting their research posters to peers.

The student organizers of the CSB Graduate Research Symposium 2014 (from left): Miranda Hunter, Donghoon Lee, Helen Chen, and Yixie Zhang)

delivered an intriguing lecture on "How do transcription factors control cell states?" sharing her research interest development in transcriptional regulation starting as a graduate student till now as a principle investigator. Overall, the event was a great success with numerous positive remarks, establishing a tradition that will continue to grow and expand in the future.

2014 James Lepock Memorial Student Symposium

Department of Medical Biophysics, University of Toronto

Correspondent: William Tu

The 2014 James Lepock Memorial Student Symposium was organized by graduate students in the Department of Medical Biophysics (MBP) at the University of Toronto and took place on Thursday, May 29, 2014 at the Toronto General Hospital Helliwell Centre. The symposium gathers graduate students, post-doctoral fellows, and faculty members of MBP and its various affiliated institutes, including Princess Margaret Cancer Centre, Sunnybrook Health Science Centre, and SickKids Research Institute, to learn about the wide array of research being conducted and to provide feedback on improving the students' research. This year, over 150 people attended the symposium.

We hosted top-flight researchers to speak, including insight and engaging keynote sessions by **Dr. Robert Kerbel** (senior scientist at Sunnybrook Research Institute) on translational oncology and **Dr. Xiaoyuan Shawn Chen** (senior investigator at National Institute of Biomedical

Symposium participants listening to one of the talks

Imaging and Bioengineering) on nanomedicine, and a discussion panel on technological innovations and impact in biomedical research with **Dr. Joseph Cafazzo** (University Health Network), **Dr. Kullervo Hynynen** (Sunnybrook Research Institute), *Marco Raposo* (Illumina), **Dr. Ian Tannock** (Princess Margaret Cancer Centre), and **Dr. Aman Thind** (Colibri Technologies Inc.). M.Sc. and Ph.D. Students were also selected to give oral presentations and poster presentations, and the best speakers and posters were given awards.

Biology Graduate Research Forum

University of Western Ontario

Correspondents: Kayla Gradil and Aimee Lee Houde

The primary mandate of the Biology Graduate Research Forum (BGRF) is to provide a forum for graduate students to showcase their research in biological sciences through poster and invited verbal presentations. It is also the aim of this research forum to host an invited speaker who will present their current endeavours within the field of biological sciences. The aim of the BGRF is to bring together students within the multi-disciplinary umbrella of biological sciences to exchange novel and exciting ideas within their respective fields. It is also our hope that this annual event will foster inter-disciplinary collaborations, which would add and enhance the academic and scientific research experience of the participants here at Western.

BGRF is organized by the graduate students of the Department of Biology. There were 9 short verbal presentations, 6 short presentations, and 20 poster presentations by biology graduate students. There was also a photo contest and awards ceremony for the graduate students. The event was held on Friday 3 October 2014, and was attended by 70 graduate students and 15 faculty members from the Department of Biology.

Keynote speaker Dr. Marla Sokolowski

The keynote speaker was **Dr. Marla Sokolowski** from the University of Toronto. Dr. Sokolowski's lab studies how genes and the environment interact to influence behaviour in fruit flies. They discovered the foraging gene which influences naturally occurring behavioural variation including the rover/sitter polymorphism. This gene plays a role in behaviour in many other organisms including social insects.

There was a break for the weekly Departmental Seminar series: Dr. Mungo Marsden talked about integrin signalling in *Xenopus* Development. There was also a break for the Friday Philosophicals Graduate Seminar series: (1) Vicki Simkovic talked about genetic vs. environmental effects on nestmate recognition in the Eastern subterranean termite *Reticulitermes flavipes* and (2) Joanna Konopka talked about the success of native and exotic egg parasitoids (Hymenoptera: Scelionidae) as biological control agents of *H. halys* (Hemiptera: Pentatomidae).

Poster session

Graduate student participants

Research Meetings

The CSMB 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

The understanding is that the CSMB is providing seed money to establish the meeting, and the funds provided by the CSMB are considered a repayable loan. The amount of the loan that is repayable to the 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 CSMB Secretary.

First International Summer Institute on Course Design, Education, and Leadership for Bioscience Researchers

College of Medicine, University of Manitoba

The aim of this Summer Institute was to promote discipline-specific course design and teaching, and to create the next generation of bioscience educators who will lead curricular development in ways to enhance student learning. They were expected to acquire the knowledge, skills, and confidence to conduct research focusing on teaching in their subjects and to evaluate educational literature, with the view to use effective teaching practices. The International Network of Bioscience Educators, which is based at the College of Medicine, University of Manitoba, in partnership with the Oxford Learning Institute, University of Oxford, U.K., hosted the Summer Institute. The College of Medicine and Office of the Vice President (Academic) and Provost, University of Manitoba sponsored the Summer Institute. In addition, the Canadian Society for Molecular Biosciences provided financial support. The Institute was held at the College of Medicine in Winnipeg on 5-9 August 2014, daily from 9:00 am to 4: 30 pm.

Theme: A Problem-based Approach to Designing Courses:

The overall theme of the Institute was for the participant to acquire new knowledge on how to design a course and lead in doing so. The "problem" participants worked on was to develop an undergraduate course in the biosciences. The approach to this theme was to envision problem-based learning (PBL) tutorial groups of participants engaging in a design activity in a more integrative way

Group of invited speakers and participants

throughout the week. The participants were divided into tutorial groups. Through this activity, participants were to:

a) Identify the "Big Ideas," - the thinking processes, key concepts, or core values that define biosciences education (and invent ways to help students learn those)

b) Attend the Summer Institute's seminars, workshops, and plenary sessions

c) Apply the key concepts from the seminars, workshops, and plenary sessions to design innovative teaching and assessment plans

d) Receive and provide feedback on the "Course Designs"

e) Experience small group problem-based learning

Workshops provided were:

a) Using educational frameworks. For example, the Teaching Goals Inventory and backward design to develop learning objectives

b) Pathways to scientific teaching by designing transformed courses

c) Constructing group learning activities

d) Learning and assessing critical appraisal of a primary biomedical literature

e) Cognition and metacognition prompts

f) Feedback and assessment techniques

Each workshop was followed by a group activity to implement what participants had learned in designing a course. For example, after a seminar on active learning strategies, they would go back to their tutorial groups to design a learner-centered activity or two for "their" course. By the end of the week, tutorial groups were able to develop a number of different, innovative first year courses that we hope some participants will have the opportunity to teach at their current institution or in a future teaching role. These designs will be used in future Institutes to inspire other participants. Faculty colleagues and students in each tutorial group collaboratively designed the courses.

The tutorial groups were given a 30-minute slot in which to give a 15-minute presentation and have 15 minutes to answer questions or facilitate a discussion on their Course Designs. Each presentation was complemented by a written course outline with sufficient details to enable other participants to teach it, including:

a) Course title

b) Short "blurb" suitable for course catalogue. (No more than 100 words.)

c) Intended learning outcomes

d) Schedule of main topics or activities

e) Description of assessment processes and criteria

f) Possible key texts or recommended readings

Examples of Course Designs:

- Microorganisms: friend or foe
- Science, Scientist, and Society: why Science is important
- Current Health Related topics: dissecting facts and fictions
- Environment and Health: a project-based course
- Health Sciences in a Modern World

Some of the notable highlights of the Summer Institute were:

Keynote Presentation:

- "Creating the Future: Preparing the Next Generation of Bioscience Educators". Dr. Kathleen Quinlan, Head of Educational Development, Oxford Learning Institute, University of Oxford, UK.

Research Seminars:

- "Lessons Learned from Science Doctoral Students' Experiences" by Gregory Hum (Ph.D. candidate), Institute for the Study of Teaching and Learning in the

Some participants and the Co-chair from left to right: Dr. Muhammad Mazhar (Alfaisal Medical School, Saudi Arabia), Ms. Amanda Scott (Ph.D. Candidate Immunology), Department of Biological Sciences, University of Alberta, Dr. Saad Salim (Postdoctoral Fellow), Faculty of Medicine & Dentistry, University of Alberta, Ms. Nelly Ameyogbe (Ph.D. Student), Dept. of Immunology, University of British Columbia, Dr. Sadia Qazi (Alfaisal Medical School, Saudi Arabia), and Dr. Francis Amara (Co-chair), University of Manitoba

Workshop on "Constructing Group Learning Activities" led by Dr. Adam Ritchie, BSc, Ph.D., FHEA (UK), Course Director, Science and Public Policy, Blavatnik School of Government, University of Oxford, U.K.

Disciplines, Simon Fraser University, Canada

- "Pedagogical Values of Involving Science Undergraduate Students in Research" by Dr. Anna Wilson, Australian National University, Canberra, Australia.

Plenary Sessions:

- "Leadership models for Faculty Development". Joanne Hamilton, Assistant Professor & Director, Educational Development, University of Manitoba, Faculty of Medicine,
- "Using Self-Reflection to Integrate the Core Tenets of Invitational Education with Collaboration" by Dr. Alanna Baldwin, Centre for Health Innovation, College of Medicine, University of Manitoba, Canada.
- "Leading Change in Curriculum Development" by Professor Keevin Bernstein, Director of Curriculum Renewal, College of Medicine, University of Manitoba.

There were 5 major invited international, bioscience educators and speakers, including Professor Diane Ebert May (AAAS Fellow), Michigan State University, East Lansing, U.S.A., Drs. Simon Hunt and Adam Ritchie, University of Oxford, and Dr. Paul Seldon, Imperial College, University of London, UK.

40 participants registered for the Institute, of whom 3 participants were international faculty members from Alfaisal University, Saudi Arabia, 2 were from the University of Alberta (Ph.D. Candidate & Postdoctoral Fellow), 1 doctoral student from the Department of Immunology, University of British Columbia, and the rest of the participants were faculty, doctoral students, postdoctoral fellows, and research associates from the University of Manitoba.

Evaluation: Comments by participants:

"I would recommend this Summer Institute to those who enjoy teaching in higher education" (Assistant Professor, Faculty Member)

"It is very useful for me. I am thinking to use those teaching skills in my future teaching activity." (Ph.D. Candidate)