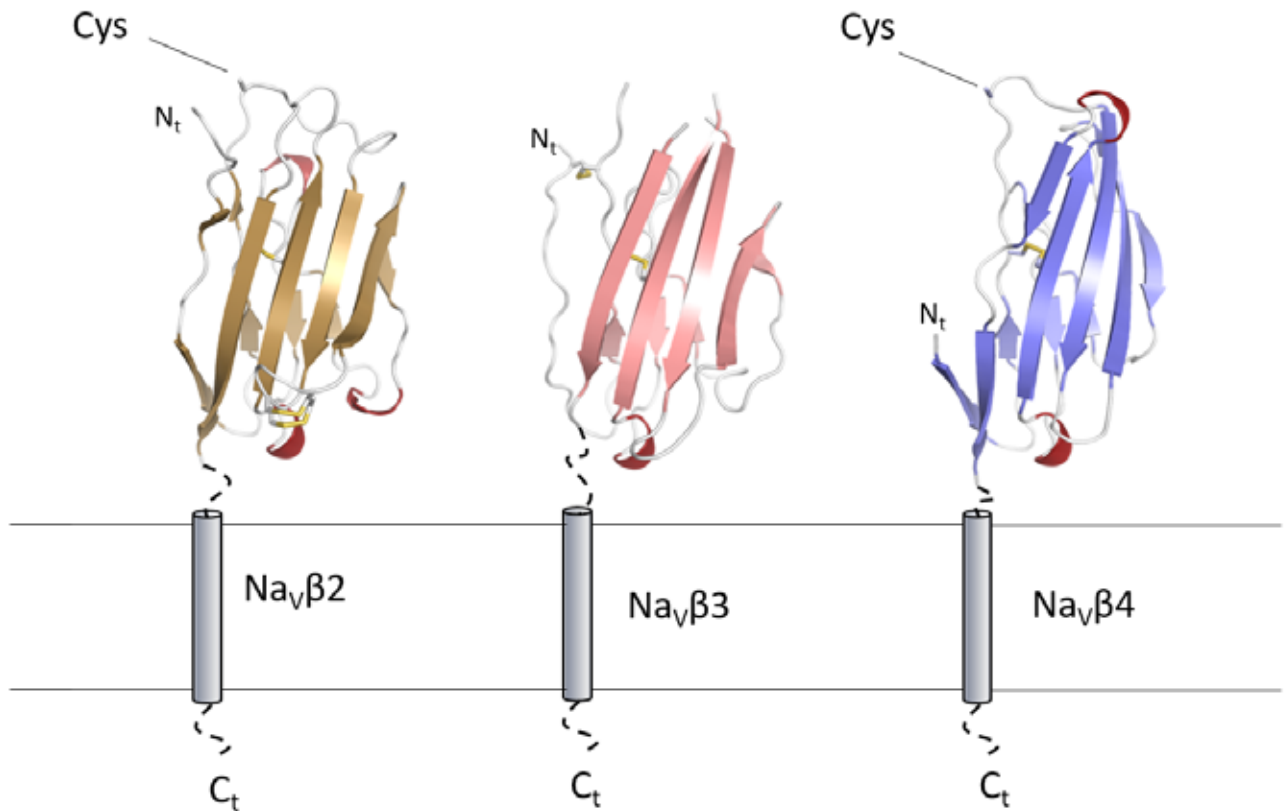


Bulletin



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

2016
www.csmb-scbm.ca



Bulletin



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

2016

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CSMB President, Kristin Baetz

President's Report 2016

Dr. Kristin Baetz

2016 was another noteworthy year for the CSMB and scientists across Canada. Through the continued efforts of societies like CSMB and individuals across Canada, science remained on the national agenda. We saw the release of the new Liberal government's budget which outlined a strong vision for Canada's Innovation Agenda. Not only did both CIHR and NSERC receive budget increases, but Budget 2016 contained the announcement of a Chief Science Advisor of Canada and the Fundamental Science Review.

Though there is renewed hope by scientists across Canada, funding for fundamental science remains a serious concern for our members. While I continue to work with the board to fulfill the society's mandate to advance and promote the molecular biosciences in Canada, my number one priority was to increase the advocacy efforts of the CSMB. Most importantly we aim to increase our presence in Ottawa to promote the concerns and solutions of our members to parliamentarians. Moving forward, with Canada's new Innovation Agenda, we have an unprecedented opportunity to work together to build a country where science and research plays a critical role.

Below I highlight some of the CSMB initiatives that have taken place in 2016.

1. Increased trainee engagement. During what has been challenging budgetary times for scientists in Canada, the CSMB believes it is extremely important to encourage our next generation of scientists. During 2016 the CSMB provided financial support to 9 trainee-organized activities from coast to coast,

including career days and scientific symposia. Given the increased demand for funding, CSMB will now run [two yearly competitions](#) for trainee activity sponsorships. We have also been working with Canadian Science Publishing to establish a travel award for a trainee who publishes in *Biochemistry and Cell Biology*.

CSMB also believes that in addition to awards, we can help support young scientists through unique workshops. After the success of the one day Young Scientist Program at the 16th IUBMB Conference in Vancouver (59th Annual CSMB conference), CSMB will offer a slate of trainee-specific workshops at all future CSMB-sponsored meetings.

2. Scientific meetings. The 59th CSMB conference was held in collaboration with the International Union of Biochemistry and Molecular Biology (IUBMB) and the Pan-American Association for Biochemistry and Molecular Biology (PABMB) in Vancouver on "Signalling Pathways in Development, Disease and Aging". Bringing this conference to Canada took years of preparation, and while this landmark event greatly increased the visibility of Canadian molecular biosciences at the international level, it was poorly attended by Canadians. While CSMB was able to mitigate the financial loss of this meeting, many valuable lessons were learned.

Moving forward CSMB will be introducing new meeting guidelines, and will strive to offer you affordable conferences that will be of interest to

larger numbers of our members. Our guidelines will ensure that our CSMB conferences are not only high quality scientific meetings in diverse areas of Genetics, Biochemistry and Cell Biology, but they offer affordable registration and accommodations, added-value events for trainees, and speakers reflecting the diversity of our members including visible minorities and approximately 50% women. We will also use our annual meetings to conduct open-forums to discuss federal science funding issues, to aid in shaping CSMB recommendations and policy positions.

For Canada's Sesquicentennial year, the CSMB 60th annual conference called "Celebrating Canadian Molecular Biosciences: from organelle to systems biology" will take place in Ottawa May 16-20 2017. This meeting aims to serve as model for the new mandate of CSMB meetings. Given the outstanding scientific program and affordability, we anticipate that CSMB2017 may be one of the most successful meetings to date. I sincerely hope you were able to attend CSMB2017 to see the revitalized CSMB conference structure.

3. **Advocacy work.** In 2016, CSMB remained focussed on advocating for the importance of fundamental research. While we continue working with both our lobbying partners [Research Canada](#) and the [Partnership Group for Science and Engineering](#), CSMB is also increasing its own efforts to ensure that your voice is heard on Parliament Hill. Here I highlight some of the activities CSMB has done this past year and I encourage you to check out our advocacy web-pages to stay informed of our efforts <https://www.csmb-scbm.ca/advocacy/Petition.aspx>.
4. **Response to Budget 2016.** After launching our first petition in 2015 to increase support for federal funding of fundamental research, CSMB continued to advocate through both letters and meetings with our elected representatives and their staff right up until the first Liberal budget. CSMB was extremely pleased by the first Liberal budget, which focused on innovation and included welcomed 30 million dollar increases to each of the budgets of CIHR and NSERC. CSMB applauded this effort and landmark shift for science through a [press release](#), full page thank you ad in the Hill Times and a solicited opinion piece for the [Canada Science Policy Centre](#). CSMB was

also asked to comment on the 2016 Budget by Ivan Semeniuk of the [Globe and Mail](#).

5. **Working to reform the CIHR reforms.** Many of us have been directly impacted by the CIHR reforms that created a funding gap during its tumultuous implementation, but the virtual review process eroded our trust in CIHR. Starting in late 2015, CSMB started to directly address this issue through our "[Time to Demand Change at CIHR](#)" e-mail campaign. Later in 2016, CSMB launched a petition for quality face-to-face peer review for federal research funding. Through the efforts of many societies and individuals, CIHR was forced to hold the July 13 2016 meeting in Ottawa to find solutions to the flawed peer-review system. Both Christian Baron, CSMB past-President and I attended the July meeting, where not only did we present the concerns of our members, but also worked to improve the CIHR system for you. We also raised the profile of the CSMB through multiple media interviews (read them all at [CSMB in the News](#)) for the Globe and Mail, Ottawa Citizen and Science Magazine. It is not an understatement to say that the consolidated efforts of the greater research community on this issue played a significant role in the change of CIHR leadership that was announced in December 2016.
6. **CSMB submission to the Fundamental Science Review.** The June 2016 announcement by Science Minister Dr. Duncan of the Fundamental Science Review gave the research community of Canada a unique opportunity to not just voice their concerns about, but to provide recommendations to build a fundamental research environment that would allow for innovation to be the bed-rock of Canada's economy. Through consultation with our members and our board we submitted [three key recommendations](#) to the Fundamental Science Review. Further, Dr Christian Baron and I were invited to present and discuss our key recommendations with the Minister of Science's policy advisor in Ottawa.

Looking towards 2017 and the release of the Fundamental Science Review, the CSMB will continue being a strong voice for fundamental research in Canada. Our primary goals will be to continue to advocate for increases in funding for non-targeted principal investigator-driven research programs

such as NSERC's Discovery Grants and CIHR's Foundation and Project Grants, to continue to work towards building a rigorous peer-review process for all federal funding, and to work with Minister Duncan and the Liberal Government to implement the recommendations of the Fundamental Science Review. We all need to work together to achieve our goal of building sustainable and robust funding mechanisms that are essential for breaking new ground in molecular biosciences research and for Canada to truly become an innovative society.

I hope this illustrates the dynamic efforts and activities of the CSMB and that they convince you to not only renew your membership, but to motivate your colleagues to join us. We have a unique window of opportunity to improve the research environment in Canada, and this requires strengthening our political voice in Ottawa by raising our membership numbers.

In conclusion, it is an honour to serve as President of the CSMB. Do not hesitate to reach out to me or any other members of the board. We are here to work for you.

Incoming Members of the CSMB Executive Board



Barbara Karten

Barbara Karten, *Councillor*

Barbara Karten is a Professor in the Department of Biochemistry and Molecular Biology at Dalhousie University. She received her undergraduate training in chemistry at the University of Hamburg, Germany and then moved to Graz in Austria for graduate research on lipid peroxidation with Dr. Wolfgang Sattler. After obtaining her PhD degree in 1999, she received fellowships from the German Research Foundation and the Alberta Heritage Foundation for Medical Research to pursue post-doctoral studies with Dr. Jean Vance in the Department of Medicine at the University of Alberta. It was there that she started working with primary neuron cultures and became deeply fascinated with these intriguing cells. In 2005, she joined the faculty at Dalhousie University.

As an independent investigator, Dr. Karten continues to work on cholesterol metabolism in the brain and neurodegeneration. Her group investigates how cholesterol influences mitochondrial function and energy metabolism in neurons, and how abnormalities in cholesterol metabolism affect neuronal and synaptic function. In addition to research, she is teaching courses at nearly all levels of post-secondary education, from introductory biochemistry to graduate level molecular and cell biology of lipids, and she is also Associate Graduate Coordinator for her department.



Michelle Scott

Michelle Scott, Councillor

Michelle Scott is an Associate Professor in the Department of Biochemistry at the Université de Sherbrooke. Following studies in Biochemistry and Computer Engineering (Université de Montréal, University of Calgary and McGill University), she obtained her PhD in Bioinformatics from McGill University in 2005 under the co-supervision of Mike Hallett and David Thomas, studying the prediction of protein subcellular localization. She then moved to Geoff Barton's group at the University of Dundee in Scotland for her post-doctoral training, focussing on protein targeting to the nucleolus and non-canonical functions of small nucleolar RNAs. She joined the Université de Sherbrooke in 2011.

Dr. Scott has maintained a long-standing interest in the characterization of protein subcellular localization, creating machine learning predictors of protein localization and of protein target signals. Her group currently characterizes the pre-translational regulation of the inclusion of protein targeting motifs as well as the visualization of differential protein motifs. The other main interest of her group is the characterization of small nucleolar RNA, a group of highly abundant cellular non-coding RNA involved in ribosome biogenesis, but with many additional emerging functions. Her group is computational and is specialized in the analysis of high-throughput sequencing datasets.



Hans-Joachim Wieden

Hans-Joachim Wieden, Councillor

Dr. Hans-Joachim (HJ) Wieden is Professor of Physical Biochemistry in the Department of Chemistry and Biochemistry at the University of Lethbridge. He is the founding Director of the Alberta RNA Research and Training Institute (ARRTI), home to one of the largest groups of primarily RNA-focussed research labs in Western Canada, as well as the SynBridge open synthetic biology maker space. Dr. Wieden holds an Alberta Innovates Strategic Research Chair with focus on RNA Bioengineering. Research in his group ranges from the rational design of biological nano-machines, to the over-designing and re-programming of genetic circuits, to the development of novel antibiotics.

Dr. Wieden received his Ph.D. in Biochemistry from the University of Witten/Herdecke in 2000, followed by a post-doctoral diploma in Bioinformatics from the Ruprecht-Karls-University in Heidelberg in 2003. Following his time as a visiting scientist in the Department of Cellular Biochemistry at the Max-Planck-Institute for Biophysical Chemistry from 2001-2004, he joined the University of Lethbridge as an Assistant Professor in 2005.

Dr. Wieden is dedicated to teaching and training the next generation of scientists. In addition to the undergraduate and graduate students in his research group, he has also been a team leader for iGEM teams since 2006, both at the collegiate and high school levels. The collegiate iGEM teams have won gold medals at 8 of the last 10 jamborees, and the high school team was the World Championship winner in 2013. He has been recognized for his dedication to teaching by receiving both the University of Lethbridge Distinguished Teaching Award and the University of Lethbridge Student's Union Teaching Excellence Award in 2011.

Minutes of the 59th Annual General Meeting 2016

Vancouver, British Columbia – 20 July 2016

Attendees: Christian Baron, Kristin Baetz, Liliana Attisano, Jim Woodgett, Logan Donaldson, Paola Marignani, Sarah Hughes, Andrew Simmonds, Philip Hieter, John Dawson, Joe Casey, Frances Sharom, Jim Davie, Jan Rainey, Kalle Gehring, Vincent Duronio, Gerry Wright, Kaitlin Kharas, Mustapha Lhor, Tarik Mörröy, Randy Johnston, Arthur Hilliker, Wafaa Antonious.

1. Greetings from the President (Baetz) – Power Point Presentation

Baetz welcomed the attendees. She talked about the relevance of CSMB as a Society and listed some of the activities that CSMB had undertaken recently. She did a short presentation about the 2017 meeting and encouraged the attendees to participate and encourage their colleagues to attend. She then stated that 2018 will be an international meeting and it will be at the University of British Columbia with the International Genetics Federation. She also introduced Kaitlin Kharas as the CSMB Video Challenge winner. Then she talked about advocacy activities. She stated that CSMB advocacy activities are of two kinds. The first is done through other organizations. For example, CSMB is a member of Research Canada and PAGSE and participates in their organized events. The second kind is the activities that the CSMB undertakes directly. Then she highlighted some of the advocacy activities that were led by the CSMB. CSMB updated its website to be able to do petitions and be more active in advocacy activities. Baetz has been very active in conveying the researchers' messages and concerns to the politicians and the media. She participated with her trainees with a Kiosk on the Hill. 70 MPs attended that event, which was organized by Research Canada. She emphasized that it was important at this stage, since we have a government willing to listen, that we do not make too much noise but rather identify and agree on main points that we need to convey to the politicians. She would like the attendees to identify three key messages and invited feedback.

Duronio asked if there was an appetite to have a virtual CFBS. Wright asked if CSMB was working with other societies to join together in advocacy activities. Baetz stated that she was in constant contact with the Neuroscience Society. There are some societies that are more active than others.

Marignani asked about having more women involved. She also asked how we can reach out to the public.

The Naylor Fundamental Science review committee is supposed to look at multiple items and it is important that we do not only focus on CIHR.

2. Approval of Quorum and Agenda

Johnston declared that quorum was met since 24 were in attendance.

Motion: Mörröy made a motion to approve the agenda, Gehring seconded the motion, all in favour, agenda approved.

3. Approval of the Minutes of 58th Annual General Meeting in Halifax, June 2015

Motion: Rainey made a motion to approve the 58th AGM Halifax Minutes, Sharom seconded the motion, all in favour, minutes approved.

4. Business arising from the minutes (Johnston)

Johnston stated there was no business arising.

5. Secretary's Report (Johnston) – Attached

a) Membership

Johnston stated that CSMB membership numbers

for 2013-2015 have been roughly stable, but have declined compared to 2012 numbers. The 2016 membership numbers are expected to be less than 2015. He emphasized the importance of increasing the CSMB membership and encouraged the attendees to approach their fellow colleagues and encourage them to support the Canadian Society that works on their behalf. He added that the Canadian participation in the IUBMB Conference was very low and disappointing in spite of all the efforts to market the conference within Canada.

6. Treasurer's Report (Hilliker) - Attached

a) Presentation of the Accountant's Reviewed Financial Statement

Hilliker presented the Reviewed Financial Statement. The Conference generates revenue, but the expenses are more than the revenue it generates. If we remove the awards and board travel, then the 2015 Halifax conference can be considered to have broken even.

b) Acceptance of the Reviewed Financial Statement (2015)

Motion: Hieter made a motion to accept the financial statement as prepared by Mrs. Andrea Poole, Davie seconded the motion, all in favour, financial statement accepted.

c) Approval of Signing officers

Motion: Hilliker made a motion to add Jan Rainey as a signing officer in addition to the current signing officers: Randy Johnston and Arthur Hilliker. Joe Casey seconded the motion, all in favour, motion approved.

Hilliker will stay on as a Treasurer during a transition time to finish paying expenses related to the 2016 conference until Jan Rainey can take over and the needed paperwork is completed at the bank to set him up as a signing officer.

7. Board Membership for 2016 - 2017 (Baron)

Baron presented a PowerPoint presentation showing the nominations received and identified the candidates. He stated that this year 6 nominations were received. Baron stated that the board looked at the nominations and looked at gender equity. Currently only 3 board members are females, the president, one of the trainees and the bulletin editor.

The board also took in account regional distribution when making its recommendations. The CSMB Board recommends Barbara Karten, Michelle Scott and Hans-Joachim Wieden for the positions of councillors. He then asked if there were nominations from the floor. None was received.

a) Call for nominations from the Floor

Motion: Hilliker moved to close the nominations from the floor for new board members, seconded by Simmonds, all in favour, nominations from the floor closed.

b) Councillors and Executive

Motion: Hilliker made a motion to approve the slate recommended by the board, Davie seconded the motion, all in favour, motion approved.

Johnston stated that CSMB bylaws allow electronic voting and next year we will enable electronic voting to elect Board members.

8. Meeting Reports

a) July 17-21, 2016: Vancouver - Johnston

Signalling Pathways in Development, Disease and Aging; in partnership with IUBMB & PABMB

Johnston reported on the 2016 IUBMB Conference. We were anticipating attendance to be from 1,000-1,500. Last year in Brazil 3,000 attended and in Taiwan they had 1,000 attending. Johnston stated that we advertised, had a good program and with two Nobel Prize winners and multiple Gairdner Awardees and other distinguished guests as speakers - both IUBMB and PABMB were extremely pleased with the scientific quality of the program. We made sure that this conference was more affordable for the attendees than previous IUBMB conferences and other comparable international meetings, by around 30%. We offered \$100 discounts for CSMB members, and a further \$100 off for those who booked their accommodation through the conference website, plus further fee reductions for attendees from developing nations. The services of a professional conference organizer were engaged and a professional website was created. We are looking at financial set back of \$290,000, the lowest financial loss would be \$220,000. As per the financial

statement CSMB membership revenue is around \$24,000. A request for support was submitted to CIHR, but it was ranked #7, with only 6 events supported for \$10,000 each. To cut down on the financial loss, PABMB was approached for support, it might provide from \$2,000 - \$3,000 in support. A request for support was submitted to the IUBMB, and they requested additional paper work. We are expecting to have the final numbers by the end of this month. Canada invited the World to come; the World came but Canadians did not come. We have obligations to the hotels that reserved large blocks of rooms for the 2016 IUBMB conference, there is a concert in town, so hopefully most of the rooms that were released will be sold and CSMB will not be liable. Joe Casey stated that the funds that CSMB has been relying on for decades were profits from the IUBMB 1979 conference.

Marignani said that the students stated that hotels were expensive. Johnston stated that the hotels' cost is the same as other conferences held in previous IUBMB meetings. Baetz said that in the future university residences should be part of the accommodation available for the conference. Wright stated that the CSMB conferences tend to be very focused. The CSM meeting tends to be broader and attract more attendance. Joe Casey stated that it was not fair to count the board travel and awards against the conference. Simmonds stated that we need to get proposals to support future meetings. There has to be a call for bids.

b) 2017: Ottawa - Baetz
Celebrating Canadian Molecular Biosciences
May 16 - 20, 2017

Baetz stated that the 2017 meeting is a merger with colleagues at Ryerson. The board will be formulating the format of future CSMB Conferences, and discussing this issue at its upcoming December board meeting.

c) July 14-19, 2018: Vancouver - Johnston

Genetic Horizons: Evolution, Development, Sustainability and Health; in partnership with IGF and GSA. Hieter stated that they are looking into holding the 2018 Congress at the University of British Columbia rather than the Vancouver Convention Centre. UBC has good residences that will allow for

affordable accommodation and the facilities' cost will be much cheaper than the convention center. Gehring commented that it was important that CSMB ensures that the upcoming 2 conferences are profitable financially.

9. Other Business/Adjournment

No other business. Meeting adjourned.

List of Motions:

Motion: Mörröy made a motion to approve the agenda, Gehring seconded the motion, all in favour, agenda approved.

Motion: Rainey made a motion to approve the 58th AGM Halifax Minutes, Sharom seconded the motion, all in favour, minutes approved.

Motion: Hieter made a motion to accept the financial statement reviewed by Mrs. Andrea Poole, Davie seconded the motion, all in favour, financial statement accepted.

Motion: Hilliker made a motion to add Jan Rainey as a signing officer in addition to the current signing officers: Randy Johnston and Arthur Hilliker. Joe Casey seconded the motion, all in favour, motion approved.

Motion: Hilliker moved to close the nominations from the floor for new board members, seconded by Simmonds, all in favour, nominations from the floor closed.

Motion: Hilliker made a motion to approve the slate recommended by the board, Davie seconded the motion, all in favour, motion approved.



Andrea Poole, C.A.
Licensed Public Accountant

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REVIEW ENGAGEMENT REPORT

To the Members of the Canadian Society for Molecular Biosciences

I have reviewed the statement of financial position of Canadian Society for Molecular Biosciences as at December 31, 2016 and the statements of operations and changes in net assets and cash flows for the year then ended. My review was made in accordance with Canadian generally accepted standards for review engagements and, accordingly, consisted primarily of enquiry, analytical procedures and discussion related to information supplied to me by the management.

A review does not constitute an audit and, consequently, I do not express an audit opinion on these financial statements.

Based on my review, nothing has come to my attention that causes me to believe that these financial statements are not, in all material respects, in accordance with Canadian accounting standards for not-for-profit organizations.

Andrea Poole, CPA, CA
Licensed Public Accountant
Ottawa, Ontario May 18, 2017

CANADIAN SOCIETY FOR MOLECULAR BIOSCIENCES

Financial Statement

STATEMENT OF FINANCIAL POSITION

As at DECEMBER 31, 2016 (with unaudited comparative figures as at December 31 2015)

UNAUDITED

	2016	2015
<hr/>		
ASSETS		
CURRENT		
Cash	\$ 9,646	\$ 15,600
Marketable securities - short term (note 3)	211,898	350,121
Accounts receivable	35,492	4,343
Prepaid expenses	38,410	15,557
	<hr/>	<hr/>
	\$ 295,446	\$ 385,621
	<hr/>	<hr/>
LIABILITIES		
CURRENT		
Accounts payable and accrued liabilities	\$ 12,150	\$ 15,617
Deferred membership fees - short term	3,343	2,476
	<hr/>	<hr/>
	15,493	18,093
DEFERRED MEMBERSHIP FEES - LONG TERM	<hr/>	<hr/>
	5,337	3,778
	<hr/>	<hr/>
	20,830	21,871
	<hr/>	<hr/>
	274,616	363,750
	<hr/>	<hr/>
BALANCE	<hr/>	<hr/>
	\$ 295,446	\$ 385,621
	<hr/>	<hr/>

STATEMENT OF OPERATIONS AND CHANGES IN NET ASSETS

As at DECEMBER 31, 2016 (with unaudited comparative figures as at December 31 2015)

UNAUDITED

	2016	2015
REVENUES		
Annual meeting revenue	\$ 570,820	\$ 78,410
Membership fees	23,075	24,707
Investment income	10,282	8,823
Miscellaneous	2,796	727
	\$ 606,973	\$ 112,667
EXPENDITURES		
Annual conference expenses	628,507	81,524
Board meetings and travel	18,763	19,132
Secretariat	18,111	19,579
Website	15,896	10,543
Funding and other sponsorship	13,000	6,500
Science advocacy	12,907	4,521
Bank, credit card, and investment management fees	5,312	2,955
Bulletin	5,250	5,300
Accounting fees	2,325	2,300
Insurance	1,763	1,726
Office expenses	510	2,569
	722,344	156,649
DEFICIENCY OF REVENUES OVER EXPENDITURES BEFORE OTHER ITEMS	(115,371)	(43,982)
OTHER INCOME		
Gain on sale of marketable securities	26,684	38,263
DEFICIENCY OF REVENUES OVER EXPENDITURES	(88,687)	(5,719)
NET UNREALIZED GAIN ON MARKETABLE SECURITIES	447	44,709
DEFICIENCY OF REVENUES OVER EXPENDITURES	(89,134)	(50,428)
BALANCE, BEGINNING OF YEAR	363,750	414,178
BALANCE, END OF YEAR	\$ 274,616	\$ 363,750

STATEMENT OF CASH FLOWS

As at DECEMBER 31, 2016 (with unaudited comparative figures as at December 31 2015)

UNAUDITED

	2016	2015
OPERATING ACTIVITIES		
Deficiency of revenues over expenditures	\$ (89,134)	\$ (50,428)
Adjustment for gain on sale of marketable securities	(26,684)	(38,263)
	(115,818)	(88,691)
Change in non-cash working capital items		
Marketable securities – short term	164,907	92,098
Accounts receivable	(31,149)	3,851
Prepaid expenses	(22,853)	(7,477)
Accounts payable and accrued liabilities	(3,467)	10,563
Deferred membership fees – short term	867	(615)
	(7,513)	9,729
FINANCING ACTIVITY		
Deferred membership fees - long term	1,559	(271)
NET (DECREASE) INCREASE IN CASH	(5,954)	9,458
CASH, BEGINNING OF YEAR	15,600	6,142
CASH, END OF YEAR	\$ 9,646	\$ 15,600

NOTES TO THE FINANCIAL STATEMENTS

DECEMBER 31, 2016, UNAUDITED

1. NATURE OF OPERATIONS

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

The organization 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 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 and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. By their nature, these estimates are subject to measurement uncertainty. The effect of changes in such estimates on the financial statements in future periods could be significant.

(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. MARKETABLE SECURITIES – SHORT TERM

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 “Net unrealized gains on marketable securities” and included on the Statement of Operations and Changes in Net Assets.

All amounts below are quoted in Canadian dollars.

	2016	2015
Cash and short term investments	978	14,068
Fixed income	73,300	96,825
Common equity	77,248	97,238
Cash and short term investments (US account)	424	832
Common equity (US account)	59,948	141,158
	<u>\$ 211,898</u>	<u>\$ 350,121</u>

4. ANNUAL CONFERENCE EXPENSES

	2016	2015
Exhibit and facility expenses	155,547	\$ 4,000
Receptions and banquets	18,656	30,490
Speakers travel and expenses	204,027	16,278
Awards	1,301	15,408
Meeting organizer fees	111,794	3,989
Supplies and other	137,182	11,359
	<u>\$ 628,507</u>	<u>\$ 81,524</u>

5. FINANCIAL INSTRUMENTS RISKS AND UNCERTAINTIES

The organization’s financial instruments consist of cash, short-term investment, accounts receivable, and accounts payable and accrued liabilities. Unless otherwise noted, it is management’s opinion that the organization is not exposed to significant interest rate, currency, credit, liquidity or cash flow risks. The fair value of these financial instruments approximate their carrying values, unless otherwise noted.

Market risk is the risk that the value of a financial instrument will fluctuate as a result of changes in market prices, whether the factors are specific to the instrument or all instruments traded in the market. The CSMB is exposed to market risk due to the volatile nature of equity investments.

Meeting Report: The 59th Annual Meeting of the CSMB

Signalling Pathways in Development, Disease and Aging

Dr. Randal N. Johnston

General Secretary, Canadian Society for Molecular Biosciences, and IUBMB 2016 Conference Chair, Department of Biochemistry and Molecular Biology, University of Calgary, Calgary AB

E-mail for correspondence: rnjohnst@ucalgary.ca

The Canadian Society for Molecular Biosciences served as the national host for the 2016 IUBMB conference, in partnership with IUBMB and the Panamerican Association for Biochemistry and Molecular Biology (PABMB). The conference was held July 17-21 at the Vancouver Convention Centre, located on the waterfront of the beautiful Vancouver Harbour, adjacent to the main Vancouver downtown area, Stanley Park, and with a great view of the nearby Coastal Mountain range.

Over 500 researchers from around the world attended this meeting, representing more than 50 countries. Canadians amounted to almost 40% of the attendees, and participation was especially strong from Pacific Rim nations, including 49 attendees from Latin America and 113 from Asia and Australia. We were very pleased by a high level of engagement with the special Young Scientists Program (YSP), and had 38 graduate or postdoctoral researchers attending both the main conference, plus a special pre-meeting series of YSP events conducted at the University of British Columbia campus. This included

very popular shared presentations on research being conducted by the trainees, plus career counselling and tours of research facilities. Travel support for many of these students was provided through a generous contribution by the Tang Prize Foundation, plus YSP funding through IUBMB.

The main conference was structured around 8 Plenary sessions, plus 28 Concurrent Sessions and 4 special purpose Workshops. Special invited speakers included two Nobel Laureates: **Drs. Harald zur Hausen**, Deutsches Krebsforschungszentrum and **Andrew Fire**, Stanford University, who spoke about their work in the areas of nutritional risk factors for cancer, and regulatory RNA, respectively. We also had 5 Gairdner award winning speakers, including **Drs. Tom Pollard** (Yale University), **Michael Young** (Rockefeller University), **Tak Mak** (University of Toronto), **Ulrich Hartl** (Max Planck Institute) and **Nahum Sonenberg** (McGill University). In addition, there were 2 winners of IUBMB Conference Award speakers (**Drs. Alexandra Newton**, University of

California, San Diego; and **Nahum Sonenberg**, McGill University) and 5 CSMB award winners (**Drs. Morag Park**, McGill University; **Laurence Pelletier**, University of Toronto; **Filip van Petegem**, University of British Columbia; **Esther Verheyen**, Simon Fraser University; and **Gerry Wright**, McMaster University). Topics that were covered by these and many other speakers were under the main conference themes of Signalling Pathways in Development, Disease and Aging, and included sessions on Membrane Proteins and Channels, Cancer Signalling Pathways, Regulation of RNA and Proteins, Signalling and Immune Function, Circadian Rhythms, Cell Death and Aging, plus many others.

Workshops were very well attended, and included sessions on Education in the Biochemical Sciences, the Art of Science Communication, an Update on Research Funding, and Writing Skills in Science. Not only was this an IUBMB Conference, it also served as the annual conference for both CSMB and PABMB, plus it provided a venue for the Annual General Meetings for the latter two Societies. Finally, the conference benefited greatly from over 50 exhibitors and sponsors, with booth spaces that operated in the same hall as the many poster presentations, and where coffee breaks and refreshments were provided.

In summary, we were extremely pleased with the very high quality of the science that was presented at this meeting and with the high level of international participation. Dr. Jorge Babul, Past-President of PABMB, indicated that when he attends these conferences he often feels like a warrior on behalf of science, fighting to keep the traditions of open communication, funding and international excellence moving forward. The next IUBMB Congress will be held in Seoul, Korea, in 2018, and we wish our colleagues there every success in maintaining those same traditions.

Scenes from the 59th Annual Meeting *Vancouver, 2016*



Conference attendees enjoyed the scenic Vancouver waterfront



Participants in the IUBMB 2016 Young Scientist program



Young Scientists enjoying networking and social interactions



Welcome Reception hosted by Pascal Spothelfer from Genome BC



Esther Verheyen (Simon Fraser University) receives the Grant and Moens Award of Excellence in Genetics from CSMB President, Kristin Baetz



Conference speaker Harald zur Hausen (Nobel Laureate 2008, German Cancer Centre, Heidelberg) with Esther Verheyen (Simon Fraser University)



Esther Verheyen (Simon Fraser University) delivers her conference talk



The E.C. Slater Lecturer, Alexandra Newton (UC San Diego), receives her award from Joan Guinovart, President of the IUBMB



Kaitlin Kharas (University of Ottawa), winner of the CSMB 2016 Video Challenge, is congratulated by Mustapha Lhor (Université Laval), Trainee Representative on the CSMB Executive Board



Gerry Wright (McMaster University) receives the Canadian Science Publishing Senior Investigator Award from Jim Davie, Editor of Biochemistry and Cell Biology



Kristin Bates, President of the CSMB, congratulates Morag Park (McGill University), winner of the 2016 Arthur Wynne Gold Medal



Gerry Wright (McMaster University) introducing his talk at the podium



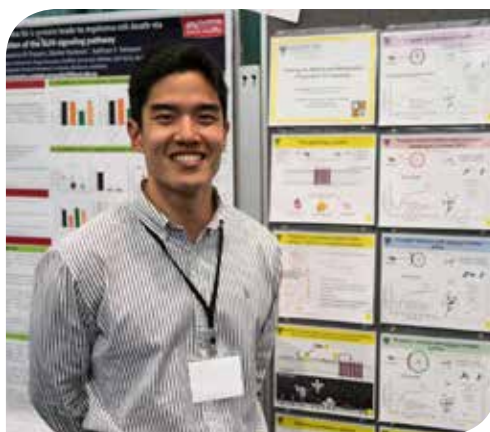
Tarik Moroy (ICRM, Montreal) delivers a Rapid-Fire Presentation in the session on Cellular Regulation



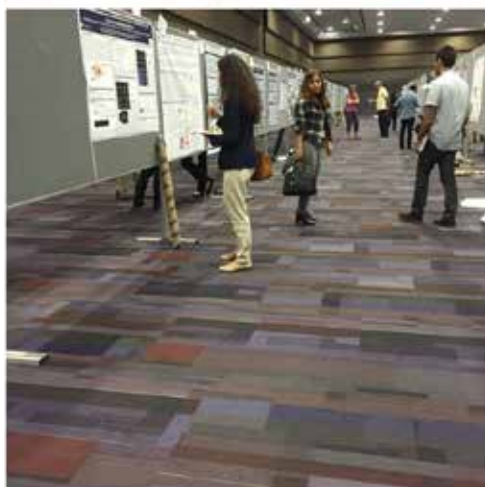
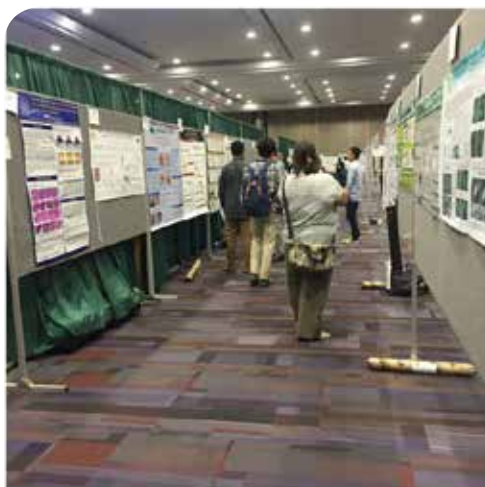
Laurence Pelletier (Lunenfeld Tanenbaum Research Institute and the University of Toronto), winner of the Robert H. Haynes Young Scientist Award in Genetics, delivers his conference talk



Martin Montecino, of the Universidad Andres Bello, Chile, presents a talk in the session on Epigenetic Signalling and Regulation



Kyungsoo Shin (Dalhousie University), winner of the Tang Prize Foundation poster award; Kyungsoo was also awarded an IUBMB Travel Award



Discussions at the poster sessions



Exhibitors at the IUBMB meeting



Kristin Bates, President of the CSMB, presents Filip Van Petegem with the CSMB New Investigator Award



Exhibitors at the IUBMB meeting



Filip Van Petegem, CSMB New Investigator Award winner, gives the closing lecture at the IUBMB 2016 conference



Tom Pollard (Yale University) gives a talk at the session on Signalling in Cell Biology and Development

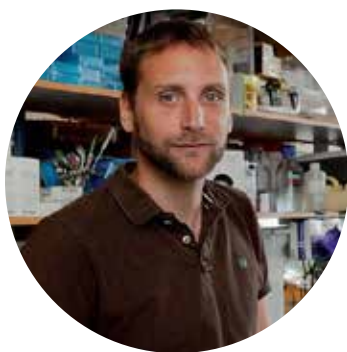


It's a wrap! Closing ceremonies at IUBMB 2016

2017 CSMB Award Designates

CSMB New Investigator Award

The CSMB New Investigator Award recognizes meritorious research in one or more of the fields of biochemistry, molecular or cellular biology in Canada. Recipients have ten years or less of independent research experience, and demonstrate outstanding research accomplishments.



Dr. T. Martin Schmeing

Associate Professor, Department of Biochemistry, McGill University

Martin Schmeing received his B.Sc. from McGill University (1998), before obtaining his M.Sc. and Ph.D. degrees with Dr. Thomas Steitz at Yale University (2002, 2004). He then carried out post-doctoral research with Dr. V. Ramakrishnan at the Laboratory of Molecular Biology, Cambridge, UK (2006-2010). He was appointed Assistant Professor in the Department of Biochemistry, McGill University in 2010, and was promoted to Associate Professor in 2016. He holds a Tier 2 Canada Research Chair in Macromolecular Machines, and serves as the Associate Director of the Centre for Structural Biology. The main focus of his research is on elucidating the structures and functions of non-

ribosomal peptide synthetases (NRPSs). NRPSs are large microbial enzymes that synthesize their products through amide bond formation between building block monomers (most commonly amino acids). The chemical and biological properties of these compounds often make them useful to society as therapeutics (antibiotics, antivirals, anti-tumours, and immunosuppressants) and as natural green chemicals (emulsifiers, siderophores, and research tools). Two aspects of particular focus in Dr. Schmeing's research are the catalytic event which links substrate building blocks, and the manner in which NRPS domains and modules work together in a complicated and productive catalytic cycle.

NRC Research Press Senior Investigator Award

This award recognizes a record of outstanding achievement in research in one or more of the fields of biochemistry, molecular or cellular biology, undertaken in Canada by a Canadian scientist.



Dr. Sergio Grinstein

**Senior Scientist and Pitblado Chair
in Cell Biology at The Hospital for
Sick Children Research Institute,
Toronto, and Professor, Department of
Biochemistry, University of Toronto**

Dr. Sergio Grinstein completed his Ph.D. in 1976 at the Centro de Investigacion y Estudios Avanzados, in Mexico City. He then spent two years as a post-doctoral fellow at the Hospital for Sick Children in Toronto, followed by a year in the Department of Biochemistry at the Federal Institute of Technology in Zurich. He is currently a Senior Scientist

at the Hospital for Sick Children in Toronto, and has been Professor in the Department of Biochemistry at the University of Toronto since 1988. Dr. Grinstein is interested in the cell physiology and biophysics of innate immunity, particularly phagocytosis and host-pathogen interactions.

Jeanne Manery Fisher Memorial Award

This award is given out in honour of the late Jeanne Manery Fisher, Professor of Biochemistry, University of Toronto. Dr. Fisher was not only an outstanding biochemist, but a remarkable teacher. She was instrumental in creating the Society's Equal Opportunity Committee and fought diligently for the position of women in science. This award recognizes an eminent Canadian woman scientist who has a distinguished career in the fields of biochemistry, molecular or cellular biology or genetics, resulting from her outstanding contributions to research, teaching or society.

Dr. Brenda Andrews

Professor, Department of Molecular Genetics, University of Toronto



Brenda Andrews is the Charles H. Best Chair of Medical Research, Director of the Donnelly Centre for Cellular and Biomolecular Research, and Professor of Molecular Genetics at the University of Toronto. Dr. Andrews completed her PhD in Medical Biophysics (with Paul Sadowski) at the University of Toronto, and post-doctoral training in genetics with the late Dr. Ira Herskowitz at the University of California San Francisco. In 1991, Dr. Andrews was recruited to the Department of Medical Genetics (now Molecular Genetics) at the University of Toronto. She became Chair of the Department in 1999, a position she held for 5 years before becoming Chair of the Banting & Best Department of Medical Research and the inaugural Director of the Donnelly Centre. Dr. Andrews' current research interests include analysis of genetic interaction networks in budding yeast and mammalian cells, using high through-put genetics platforms that include high content microscopy for systematic analysis of cell biological phenotypes. Her research is currently funded by the Canadian Institutes for Health Research, the National Institutes of Health, the Ontario Research Fund,

Genome Canada and the Canadian Institute for Advanced Research (CIFAR). Dr. Andrews sits on many editorial and advisory boards and is the founding editor-in-chief of the journal *Genes/Genomes/Genetics*, an open access journal of the Genetics Society of America. She has recently served as member or chair of grant review panels for the Canadian Institutes for Health Research, the National Institutes of Health, the European Research Council, the Wallenberg Foundation (Sweden), the March of Dimes (USA), the American Association for Cancer Research, the California Institute for Regenerative Medicine and the Gordon and Betty Moore Foundation (USA). Dr. Andrews was recently named a Companion of the Order of Canada for her "globally significant research in systems biology and for developing and nurturing prominent scientific communities in molecular genetics". Dr. Andrews is also an elected Fellow of the Royal Society of Canada, and the American Association for the Advancement of Science and the American Academy of Microbiology. She was the inaugural Director of the Genetic Networks Program of the CIFAR, and remains a Senior Fellow.

2016 Arthur Wynne Gold Medal

Met receptor tyrosine kinase; feedback inhibition, rewiring and mechanisms of resistance

Crista Thompson and Morag Park

Goodman Cancer Research Centre, McGill University



Biology of the Met receptor

The Met receptor tyrosine kinase (RTK) was first identified in the early 1980s in a human osteosarcoma cell line that was exposed to the mutagen *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine (MNNG). The chromosomal translocation generated by MNNG resulted in a novel fusion protein between the translocated promoter region (TPR) and Met kinase domain. Dimerization of the fusion protein mediated by TPR led to the oncogenic activation of Met (Cooper et al., 1984; Park et al., 1986). Subsequent isolation of the full-length proto-oncogene identified Met as a unique RTK. Met is a disulfide-linked heterodimer that is created by the cleavage of a precursor chain into a shorter extracellular α chain, and a longer membrane-spanning β chain. Met has a high affinity ligand, hepatocyte growth factor (HGF), a plasminogen-related growth factor involved in epithelial tissue remodelling and cell migration (Graveel et al., 2013). Under normal physiological conditions, HGF, which is predominantly produced by mesenchymal cells, acts in a paracrine fashion on epithelial cells expressing the Met receptor. In normal epithelial cells, ligand-dependent Met activation promotes a cell-scattering phenotype in 2D culture and an invasive morphogenic phenotype in 3D culture (Peschard and Park, 2007) which also includes resistance to anoikis. This activity is phenocopied *in vivo* where during development, paracrine Met signalling is crucial for the epithelial-to-mesenchymal transition (EMT) and long-range migration of myogenic progenitor

cells, as well as the survival and proliferation of hepatocytes and placental trophoblast cells (Organ and Tsao, 2011). Given that the signalling networks required for the developmental processes of EMT, wound healing and invasion are exploited by tumour cells to promote invasive growth, it is not surprising that Met and a Met-induced EMT signature (Ponzo and Park, 2010) play an oncogenic role in a wide variety of human cancers.

Signalling

The invasive morphogenic phenotype stimulated by HGF requires a prolonged signal downstream from the Met receptor, whereas the transient signal induced by other RTKs typically promotes a proliferative but non-invasive response (Maroun et al., 1999). HGF binding promotes Met dimerization and trans-phosphorylation of tyrosine residues within the activation loop of the Met kinase, resulting in its activation. The induction of Met catalytic activity allows for the phosphorylation of tyrosine residues in the C-terminal tail of Met (Y1349 and Y1356), which are essential for all biological functions of the Met receptor. These tyrosines create a unique multisubstrate docking site that engages the adaptor proteins Grb2 and Shc, thereby coupling Met to the Ras–mitogen-activated protein kinase (MAPK) and Akt pathways respectively (Figure 1) (Lai et al., 2009). In addition, Grb2 indirectly recruits multiple proteins including the docking protein Gab1 and the ubiquitin ligases c-Cbl and Cbl-b, which negatively regulate the Met signal.

In epithelial cells, Gab1 is the major substrate for Met, and genetic and biological studies have demonstrated that Gab1 is essential for Met-dependent phenotypes

(Maroun et al., 1999). Met activation promotes prolonged Gab1 phosphorylation, which is not observed upon activation of other RTKs such as the proliferative

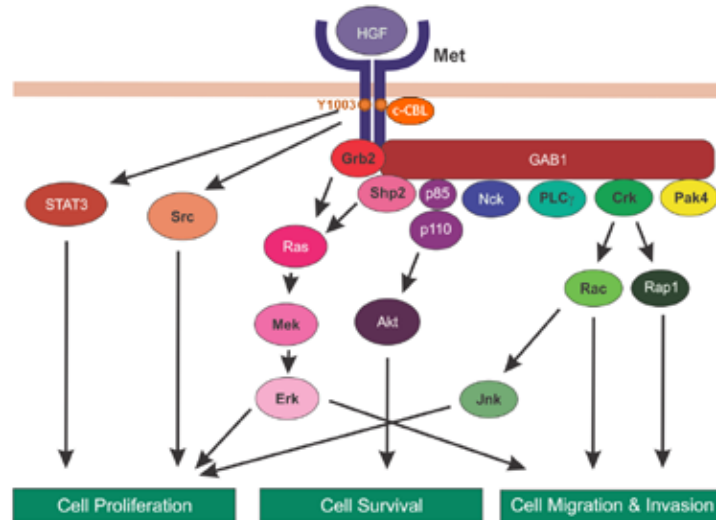


Figure 1. Met signalling adaptor and effector proteins

Activation of Met receptor tyrosine kinase by the binding of its ligand hepatocyte growth factor (HGF) promotes receptor dimerization and autophosphorylation. Met phosphorylation creates docking sites for a variety of downstream interactors. Recruitment of adaptor and effector proteins links Met activity to signalling pathways promoting cell proliferation, survival and migration. Met phosphorylation also recruits casitas B-lineage lymphoma (c-CBL) to tyrosine 1003 (Y1003) in the juxtamembrane domain. c-CBL mediates the transfer of ubiquitin to promote degradation of Met. Proteins have not been drawn to scale, and other known interactors have been omitted for clarity.

signal downstream from the epidermal growth factor receptor (EGFR). Sustained Gab1 phosphorylation is mediated through a distinct mode of recruitment of Gab1 to Met (Lock et al., 2003) which facilitates a direct and robust association between Gab1 and Met that is essential for enhanced and sustained phosphorylation of Gab1 in response to HGF (Maroun et al., 1999; Peschard and Park, 2007). Met-dependent phosphorylation of Gab1 creates phosphotyrosine docking sites that recruit multiple signalling proteins, including the p85 subunit of PI3-K, PLCγ, the tyrosine phosphatase SHP-2, the Crk adaptor protein and the serine–threonine kinase Pak4 (Figure 1) (Peschard and Park, 2003; Peschard and Park, 2007; Paliouras et al., 2009). Recruitment of PI3-K to Gab1 permits activation of Akt and its downstream pathways, and is required for cell migration and escape from apoptosis (Organ and Tsao, 2011). Recruitment of Shp2 to Gab1 and Shp2 catalytic activity is essential for the sustained activation of MAPK required for invasive growth (Lamorte et al., 2002). Gab1 also coordinates pathways that modulate the actin cytoskeleton, cell adhesion and migration, where association of Crk to Gab1 couples Met signalling to activation of Rap1 and Rac, and recruitment of Pak4, Nck and Cortactin to Gab1 are required for cell invasion (Lamorte et al., 2002;

Rodrigues et al., 2005; Paliouras et al., 2009; Abella et al., 2010b; Rajadurai et al., 2012). In response to HGF, Met, Gab1 and Gab1-associated proteins (SHP2, Crk, Pak4) relocate from the cytosol to dorsal ruffles, peripheral ruffles and lamellipodia, thereby assembling localized signalling networks (Frigault et al., 2008; Paliouras et al., 2009; Abella et al., 2010a).

Downmodulation

Met is predominantly downregulated via rapid internalization and subsequent degradation by the lysosome, although a role for the proteasome in Met degradation has also been proposed (Hammond et al., 2001). Trafficking to the lysosome is regulated through ligand-dependent ubiquitination of Met. Ubiquitination is mediated by the Cbl ubiquitin ligase which is recruited to pY1003 of the Met juxtamembrane domain (Figure 1) (Peschard and Park, 2007). Ligand-dependent ubiquitination of Met promotes recognition by endocytic adaptor proteins that contain ubiquitin-binding domains, thus targeting Met for inclusion into the multivesicular body (MVB). This acts to terminate signalling through sequestration of Met from the cytosol, and subsequently promotes lysosomal degradation (Abella et al., 2005; Abella and Park, 2009). Met RTK

mutants that are uncoupled from Cbl (Y1003F) have decreased ubiquitination and are inefficiently targeted for degradation (Abella et al., 2005). This results in increased stability and prolonged signalling, particularly to the Ras–MAPK pathway, and in the oncogenic activation of Met. The cytoplasmic Tpr-Met oncoprotein lacks the juxtamembrane region containing Y1003, and its transforming activity is caused, in part, by its resistance to Cbl-mediated downregulation (Peschard and Park, 2003; Mak et al., 2007). Met signalling can also be attenuated by tyrosine-specific phosphatases such as protein-tyrosine phosphatase 1B (PTP1B), T-cell phosphatase (TCPTP), and density enhanced protein tyrosine phosphatase-1 (DEP-1) (Palka et al., 2003; Sangwan et al., 2008). It has been observed that the absence or disruption of these negative regulators can promote receptor stability and contribute to the oncogenic capacity of Met.

Met in cancer

Multiple mechanisms have been identified that confer oncogenic potential on Met. These include autocrine/paracrine stimulation, Met overexpression, genomic amplification, translocation, point mutation and alternative splicing (Peters and Adjei, 2012; Maroun and Rowlands, 2014). Establishment of an HGF/Met autocrine loop is associated with many types of cancers, including melanomas, osteosarcomas, breast carcinomas and gliomas (www.vai.org/met), and might play a role in driving cell motility and metastasis. *MET* amplification has been detected in nonsmall cell lung cancer (NSCLC), medulloblastoma, glioblastoma, esophageal and gastric cancer, and is associated with poor outcome, particularly in lung and gastric cancer (Maroun and Rowlands, 2014). In general, when amplified, the growth of these tumours is dependent on Met catalytic activity. However, elevated expression of Met in the absence of amplification occurs in multiple human cancers (www.vai.org/met), and can be induced under hypoxic conditions (Pennacchietti et al., 2003). Met expression is negatively regulated through microRNAs, e.g. miR-34a, miR-34b, miR-34c and miR-199a* (He et al., 2007; Migliore et al., 2008). Interestingly, miR-34a itself is negatively regulated by p53, and elevated levels of Met are associated with loss-of-function p53 mutations (Rong et al., 1995). Hence, elevated Met might be causally associated with the increased invasive capacity often found in p53 null tumours (Lewis et al., 2005). Various *MET* germline and somatic mutations have been identified and found to be associated at low incidence with human cancers.

Mutations of the extracellular domain have been noted in solid tumours (breast, colon, lung, ovarian, renal), although their functional consequences are unknown (Ma et al., 2005; Ma et al., 2008). Met knock-in mice expressing kinase-activating mutations found in renal cancers develop carcinomas in multiple organs as well as lymphomas (Graveel et al., 2004), highlighting the involvement of dysregulated Met signalling in tumorigenesis. Reminiscent of the fusion protein that led to the discovery of Met (TPR-Met), genomic rearrangements of *MET* that fuse the kinase domain in-frame with multiple different N-terminal partners are oncogenic and sensitive to Met inhibitors in a rare subset of melanoma (Yeh et al., 2015). A fusion transcript involving *PTPRZ1* and *MET* occurs in 15% of secondary GBM and is associated with aggressive clinical behaviour and poor prognosis (Bao et al., 2014). Recently, the International Cancer Genome Consortium pediatric brain tumour project identified recurrent *MET* fusion genes in approximately 10% of cases, which provides a new drug target in pediatric glioblastomas, one of the most common and deadly brain tumours in childhood (Bender et al., 2016).

Mutations in the juxtamembrane domain that disrupt the negative regulation of Met have also been reported and extensively studied in lung cancer (Reungwetwattana et al., 2017). Specifically, mutation of the Cbl binding site Y1003, or deletion of exon 14 (which contains Y1003) as a consequence of alternative splicing, attenuates downregulation of Met and promotes receptor stability. Evidence suggests that mutations resulting in *METex14* skipping prolong Met activation, and case reports have indicated that patients with *METex14*-altered NSCLC respond to Met tyrosine kinase inhibitors (TKI) supporting MetΔex14 as an oncogenic driver (Togashi et al., 2015; Mendenhall and Goldman, 2015; Paik et al., 2015; Waqar et al., 2015).

Research over the last decade has also identified Met as a key player in the development of resistance to other RTK targeted therapies (Hochart et al., 2017; Ko et al., 2017). The role of Met in resistance to EGFR family inhibitors through receptor crosstalk was one of the first demonstrations of drug resistance through RTK bypass signalling. It was observed that amplification of *MET* occurs in patients with NSCLC who develop resistance to EGFR inhibitors (Bean et al., 2007; Engelman et al., 2007; Cappuzzo et al., 2009). In NSCLC cells selected

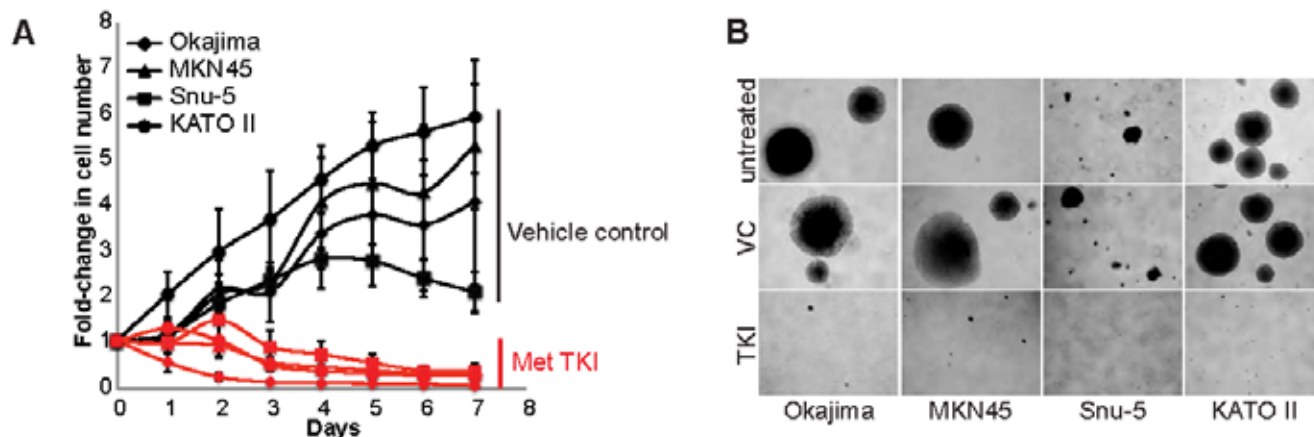


Figure 2. Gastric cancer cell lines with *MET* amplification are dependent on Met signalling for proliferation and anchorage-independent growth

A. Proliferation of cells cultured in vehicle control or Met tyrosine kinase inhibitor (TKI). **B.** Representative images of soft agar (3D) colonies untreated, treated with vehicle control (VC) or Met TKI. Images are at 40H magnification. Adapted from Lai et al., 2014.

for resistance to gefitinib *in vitro*, active Met via gene amplification stimulates HER3 phosphorylation and signalling to Akt, a key molecule promoting cell survival and proliferation (Engelman et al., 2007). Because *MET* amplification or overexpression can lead to HGF-independent activation of Met (Rodrigues et al., 1991), this provides a mechanism for constitutive Met activation and crosstalk in these tumours. The established role of Met in resistance to EGFR-targeted therapies has prompted clinical trials targeting Met and EGFR in combination in NSCLC, colorectal cancer, and head and neck cancer (Ko et al., 2017). While preliminary results have shown promise, the reports from previous phase III trials dictate that careful patient selection based on concurrent Met and EGFR activity will be essential for improved patient outcome and overall survival.

Met-dependent signalling in *MET* amplified gastric cancer

Historically, amplification of *MET* was considered a frequent event in gastric cancer based predominantly on cell lines isolated from patient metastases (Kuniyasu et al., 1992; Smolen et al., 2006). Gastric cancer is the fifth most common cancer and the third leading cause of cancer death worldwide (Ferlay et al., 2015) highlighting Met as a potential therapeutic target in this disease. The Cancer Genome Atlas (TCGA) analyses of 295 primary tumours classified gastric cancer into four molecular subtypes: Epstein-Barr virus-positive (EBV), microsatellite instable (MSI), genomically stable (GS),

and tumours with chromosomal instability (CIN) (TCGA, 2014). Amplification of *MET* was the most frequent Met alteration discovered (approximately 4%), and virtually all amplified samples fell into the CIN category characterized by marked aneuploidy, focal amplification of RTKs, and high expression of mitotic genes. This is consistent with our observation that strong Met expression resulting from *MET* amplification in gastroesophageal adenocarcinoma correlates with nuclear Ki67, an established marker for cell proliferation (Lai et al., 2014). The association with increased proliferation links Met expression with a more aggressive phenotype, in keeping with previous observations that amplification of *MET* is associated with shorter overall survival (Christensen et al., 2005; Lennerz et al., 2011; Lee et al., 2012; Kawakami et al., 2013; Catenacci et al., 2016; Metzger et al., 2016).

In order for gastric cancer patients to benefit from Met-targeted agents, their tumours must exhibit Met dependency and consequently, sensitivity to Met inhibition. To verify a requirement for Met signalling in *MET* amplified gastric cancer, we used gastric cancer cell lines with amplification of the *MET* gene and high levels of constitutively active Met protein: KATO II, Okajima, Snu-5 and MKN45 (Lai et al., 2014). Treatment of each cell line with a Met TKI, PHA-665752 (PHA) (Christensen et al., 2003), efficiently inhibited constitutive Met phosphorylation and abrogated cell proliferation and anchorage-independent growth *in vitro* (Figure 2). In addition, cells injected subcutaneously into nude mice

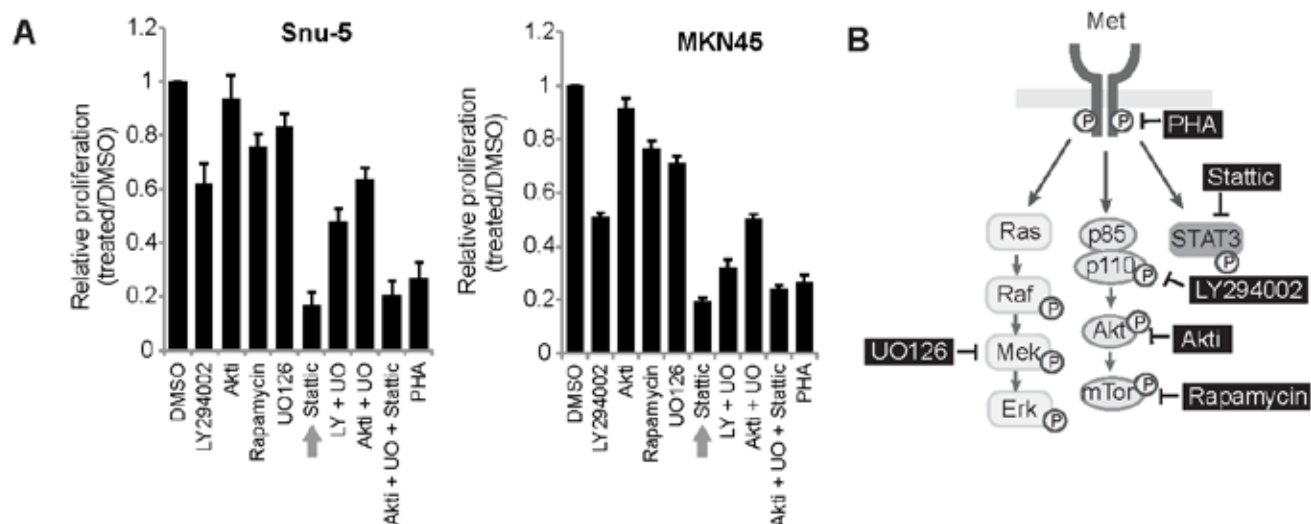


Figure 3. STAT3 is an essential mediator of Met-dependent proliferation

A. Proliferation of cells cultured in different inhibitors compared to DMSO as vehicle control. STAT3 inhibitor (arrow) had the greatest effect on proliferation. Data are means \pm SEM from three biological replicates. **B.** Model illustrating signalling pathways and specific inhibitors downstream from Met. Adapted from Lai et al., 2014.

were unable to form tumours following treatment with a Met TKI currently in clinical use, crizotinib (Lai et al., 2014). These results confirmed that *MET* amplified gastric

cancer cells are dependent on Met for their tumourigenic capacity.

To identify ligand-independent oncogenic signalling pathways activated downstream of amplified *MET* in gastric cancer, we used reverse-phase protein array (RPPA) (Lai et al., 2014). This revealed that the AKT and STAT3 pathways were predominantly inhibited by treatment with Met TKIs. Moreover, a Met-dependent, STAT3-mediated gene expression signature was the predominant gene expression signature lost following Met inhibition by TKI (Lai et al., 2014). Inhibition of STAT3 by siRNA or small molecule inhibitors, but not PI3K or ERK, significantly reduced cell proliferation in 2D and 3D, supporting that STAT3 dependent pathways are essential mediators of Met-driven proliferation and anchorage-independent growth of *MET* amplified gastric cancers (Figure 3). This corresponded with our *in vivo* data demonstrating that STAT3 inhibition attenuated growth of gastric xenografts where phosphorylation of STAT3 is highly dependent on Met activity, and confirmed STAT3 in *MET* amplified gastric cancer cells as a key mediator of tumourigenesis.

Mechanisms of resistance to Met inhibition

The development of a wide variety of Met-targeted therapeutic agents and their evaluation in clinical trials

has been accompanied by an increased interest in the mechanisms of resistance to Met inhibition. Our investigation of the downstream effectors of Met-driven tumourigenesis in *MET* amplified gastric cancer revealed a potential mechanism of Met inhibitor resistance. STAT3 proved to be an important Met-dependent target in all gastric cancers tested for tumourigenic growth, whereas ERK showed differential phosphorylation following Met inhibition. In gastric cancer cell lines where Met inhibition was cytostatic (KATO II) rather than cytotoxic (Okajima), ERK phosphorylation was elevated following Met inhibition, supporting the presence of feedback inhibition of the ERK pathway (Figure 4). Notably, after 4 h of Met inhibition, expression and protein levels decrease for dual-specificity phosphatases (DUSP4 and DUSP6) that dephosphorylate ERK in the nucleus and cytoplasm. Expression of DUSP4/6 is regulated by the MAPK pathway as part of a negative feedback loop (Patterson et al., 2009). Hence, these results support a mechanism whereby inhibition of Met promotes loss of negative feedback regulation by DUSP, allowing ERK reactivation by upstream signals other than Met in gastric cancer cells.

The loss of the negative regulators DUSP4 and DUSP6

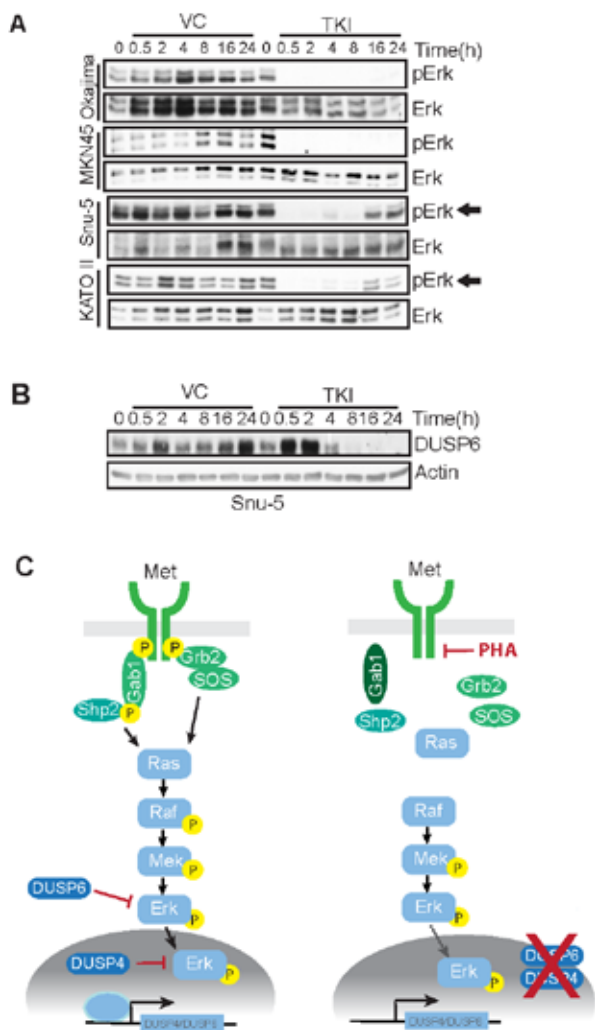


Figure 4. Met inhibition results in reactivation of ERK through loss of negative regulators of ERK signalling

A. Western blots of phosphorylated ERK (pErk) and total ERK in cells treated with vehicle control (VC) or Met tyrosine kinase inhibitor (TKI) for up to 24h. ERK is reactivated in two of the cell lines (arrows). **B.** Western blot demonstrating the loss of one of the negative regulators of ERK, dual-specificity phosphatase 6 (DUSP6), following treatment with Met TKI. **C.** Model depicting the ERK pathway in gastric cancer cell lines in conditions in which Met is activated (left panel) or inhibited (right panel). Adapted from Lai et al., 2014.

following Met inhibition and reactivation of ERK in *MET* amplified gastric cancer cell lines that display a cytostatic response (Lai et al., 2014) is consistent with evidence indicating that loss of negative feedback loops mitigating oncogenic signalling may render

tumours more susceptible to the development of resistance to targeted therapies (Chandarlapaty, 2012). To investigate mechanisms of resistance to Met inhibition, we subjected *MET* amplified gastric cancer cell lines to chronic treatment by Met TKIs and isolated drug-resistant clones and populations (*manuscript in preparation*). Interestingly, resistant (Res) cells were only isolated from cytostatic cell lines, confirming that altered signalling resulting from targeted therapy may promote a non-proliferative but stable state that facilitates the development of drug resistance. Resistance was Met-independent, and many of the downstream effectors of Met were decreased, e.g. AKT. However, in resistant cells, phosphorylation of ERK correlated with the loss of negative regulators such as DUSP4 and DUSP6, reminiscent of gastric cancer cells following short-term treatment with Met TKI. Treatment with ERK inhibitors abrogated proliferation demonstrating dependency of the resistant cells on ERK activation. This has interesting clinical implications, as the treatment of established tumours with Met-targeted agents may prevent tumour growth but not promote tumour regression. Hence therapy-induced stabilization of Met-driven tumours may facilitate additional adaptive events that promote drug resistance, tumour progression and/or metastasis. To overcome resistance and foster tumour regression, dual inhibition of Met and ERK could be clinically relevant in Met-addicted gastric cancer.

Conclusion

Since its discovery, numerous studies have established the significant role of the Met receptor in tumour growth and metastasis. But it is still unclear why Met activates growth in one cell type while promoting invasion in another. Understanding the context-specific oncogenic pathways controlled by Met activation is critical to the development of successful therapeutics. Moreover, the ability to predict the sensitivity of cancer patients to Met-targeted agents is vital for achieving significant clinical benefit. We, and others, have shown that *MET* amplification may be a suitable biomarker for response to Met-targeted therapy, and have investigated the downstream signalling cascades in *MET* amplified gastric cancer to identify the key oncogenic players and elucidate possible mechanisms of resistance to Met inhibition. We have shown that loss of the negative regulators DUSP4 and DUSP6 provide a survival advantage leading to drug resistance by promoting the reactivation of ERK signalling. An increasing body of work highlights the role

of ERK in therapeutic resistance. ERK reactivation has been observed in response to targeted therapy in BRAF V600E melanoma (Johannessen et al., 2010), thyroid carcinoma (Piscazzi et al., 2012), lung cancer (Huang et al., 2013), colorectal cancer (Misale et al., 2012), hepatocellular carcinoma (Xu et al., 2016), and head and neck cancer (Bian et al., 2015), among others. New drugs that inhibit MEK1 and MEK2 (as the 'gatekeepers' of ERK activity) have been recently approved or are undergoing late-stage clinical evaluation (Caunt et al., 2015), and the cumulative experimental evidence indicates that dual RTK-MEK inhibition would be an attractive therapeutic combination.

We have also demonstrated that STAT3 is an essential mediator of Met-driven proliferation and can be reactivated in Met TKI resistance. This indicates that STAT3 may be a critical target in *MET* amplified gastric tumours and raises an important question if STAT3 phosphorylation should be a companion diagnostic for Met dependency in these tumours. This is important, as approximately 70% of human solid and hematological tumours display overexpression or constitutively active STAT3, and its activation has been shown to play a pivotal role in tumourigenesis (Zhuang, 2013). *MET* amplification has been shown to predict sensitivity to Met-targeted agents in the clinic. In a subset of gastroesophageal cancer patients, high level *MET* amplification correlated with sensitivity to the Met TKI crizotinib, although the response was transient (Lennerz et al., 2011). The transient nature of the response could reflect the loss of negative regulators of ERK signalling, or upregulation of STAT3 activity as we have observed in our studies. Future studies on the mechanisms of resistance to Met inhibition using clinical data and samples will be informative in clarifying the dynamic signalling downstream of Met inhibition. For now, it appears that the greatest potential of Met-targeted agents resides in combination therapies where multiple molecular drivers and/or mechanisms of resistance are simultaneously inhibited.

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2016 Canadian Science Publishing Senior Investigator Award

Mechanistic diversity in antibiotic resistance

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Antibiotics are keystone medicines that enable much of modern medicine. The discovery of antibiotics in the mid 20th Century launched the Antibiotic Era and ended the millennia-old hegemony of bacterial infection on human health. For the first time, clinicians could expect to successfully manage and prevent bacterial infections. Before the discovery of antibiotics, acute infections caused by what we now consider to be routine injuries or afflictions were often fatal. Medical interventions such as lengthy and complicated surgeries, immune debilitating cancer chemotherapies, organ transplantation, and a myriad of other procedures, which before the antibiotic era would be considered highly radical or even impossible, are now routine. These advances are imperiled due to the unchecked emergence and dissemination of antibiotic resistance genes and their accumulation in bacterial pathogens across the globe. The reality is that it is now common for pathogens to harbour multiple resistance genes resulting in a multidrug resistance phenotype. These are the so-called “superbugs” that cause infections not easily treated with current drugs. We are now in the Resistance Era of antibiotics (1).

Understanding of the molecular mechanisms of antibiotic resistance is essential to address the current antibiotic crisis. Such foundational knowledge is key to 1) establish the origins and evolution of resistance, and therefore how best to predict and track its emergence, 2) guide the development of new drugs and determine any potential resistance weaknesses prior to clinical launch, and 3)

develop countermeasures such as inhibitors of resistance mechanisms that can directly overcome resistance.

The domain of such understanding is in fundamental, basic biomedical research on resistance in all its guises. There are obvious potential applications of this knowledge, but underpinning it is an unimpeachable requirement for open-ended i.e. curiosity driven, detailed, and cross-disciplinary basic research.

Origins of resistance

Resistance to the first widely used antibiotics, the sulpha drugs, was reported soon after their development in the 1930s. Resistance to penicillin was famously described in 1940, years before its widespread use during the second World War (2). To antibiotic researchers and clinicians at the time, this resistance was consistent with the knowledge that bacteria were not universally susceptible to the antibiotics that were being discovered, i.e. certain bacteria were intrinsically resistant. The early 1950s saw the first reports of acquired and mobile resistance, accounts that at first were not widely accepted by the medical and scientific communities (3). We now know that the acquisition of resistance genes on mobile genetic elements such as plasmids and transposons and their distribution vertically and horizontally in bacterial communities is a hallmark of resistance. It is these properties, enhanced by gene capture mechanisms such as integrons, which are at the heart of the current resistance crisis. It is now unremarkable for pathogenic

strains to be resistant to most, and increasingly all, available antibiotics (4-6). Furthermore, the accretion of redundant mechanisms in the same strain can increase resistance phenotype complexity. For example, genome sequencing of a strain of *Acinetobacter baumannii* revealed an 86 kb genomic resistance island consisting of 45 resistance elements conferring resistance to all the main drug classes, including genes encoding five β -lactamases and nine aminoglycoside inactivating enzymes (7).

What is now evident through retrospective analyses is that before the Antibiotic Era, pathogenic bacteria were mostly antibiotic sensitive and that they harbored mobile genetic elements including plasmids. However, these plasmids rarely included resistance genes (8). The use of antibiotics selects for the capture of antibiotic resistance elements and their mobilization.

Where did these genes come from?

In 1973, Julian Davies recognized that a biochemical mechanism of aminoglycoside resistance in pathogens, specifically *N*-acetylation of the antibiotics, was identical to the self-protection mechanisms used by the environmental bacteria that produced aminoglycosides (9). Twenty-five years later, we discovered that the biochemically complex mechanism of glycopeptide antibiotic resistance involving remodeling of the bacterial cell wall that emerged in the clinic the late 1980s was also identical in mechanism, gene content, and gene synteny with drug producing bacteria (10, 11). These studies implied a link between benign environmental bacteria and pathogens. In 2006 we reported the first systematic search for resistance in these bacteria and found that all the ~500 spore forming bacteria that we had collected from a variety of soil environments were multidrug resistant (12). The mechanisms of resistance were both similar and different to those circulating in pathogens. We termed the global pool of resistance elements in all bacteria, the antibiotic resistome (Figure 1) (13).

The environmental resistome is broad, mechanistically diverse, and the source of resistance genes that are stochastically captured and mobilized that eventually make their way into pathogens via the selective pressure of antibiotic use (14). Many other studies and laboratories have confirmed the resistome concept and the hypothesis that the environment is the source of many resistance genes currently circulating in the clinic (15-19).

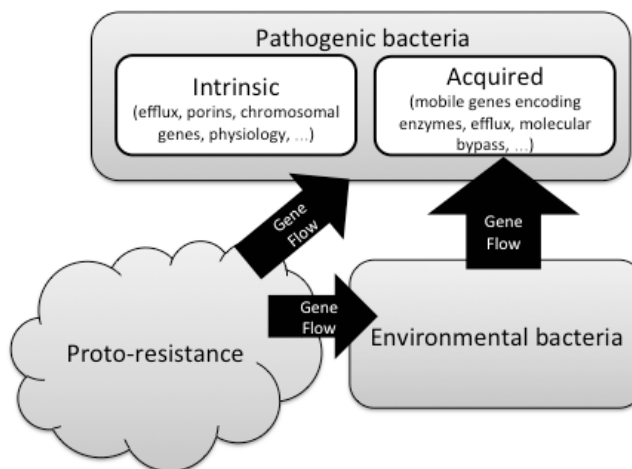


Figure 1. The antibiotic resistome.

Bacteria can be intrinsically resistant via the presence of efflux, porins, physiological structures such as the outer membrane in gram negative bacteria, etc., or they can acquire resistance genes from other bacteria. The source of these genes in pathogens is likely the vast numbers of highly antibiotic resistance environmental bacteria. The ultimate origins of resistance are the proto-resistance elements that are necessary for metabolism, but which have little or no effect on antibiotics. Natural selection molds these genes into the elements that are responsible for high-level drug resistance.

The presence of the vast number of resistance elements in environmental bacteria suggests that, unlike the situation in pathogens, human use of antibiotics over the past decades is not causally linked to the multidrug resistance phenotype of these bacteria (20). We presented evidence for this hypothesis using two approaches. First, with Hendrik Poinar from McMaster, together with colleagues from the University of Alberta and the Yukon government, we sampled ancient metagenomic DNA isolated from 30,000-year-old Yukon permafrost (21). In these samples, we identified DNA sequences from extinct Beringian megafauna including mammoth, along with resistance genes to the glycopeptide, tetracycline, and β -lactam antibiotics. We were able to 'revive' one of these genes, *vanA* encoding a D-alanyl-D-lactate ligase essential for glycopeptide resistance. We overexpressed and purified the enzyme, confirmed its enzymatic activity, and solved its 3-dimensional structure. In all ways, ancient VanA was equivalent to the modern enzyme that plagues clinics across the globe.

In a second strategy, we measured antibiotic resistance in a panel of bacteria isolated by Hazel Barton from the Lechuguilla Cave system in New Mexico. Lechuguilla is the deepest and longest cave system in North America. Entry to the cave was only achieved in 1986 and it had been sealed from the surface for ~4M years. Microorganisms living in the cave form a biofilm on the rock surface and have not been contaminated or exposed to human activity including antibiotic use. A survey of both gram positive and gram negative bacteria isolated from Lechuguilla demonstrated multidrug resistance phenotypes in all organisms (22). Consistent with our studies on surface organisms, we found that these cave bacteria, uninfluenced by human activity, were highly resistant to antibiotics using known mechanisms that are found in pathogens in addition to new strategies not yet reported (22, 23). These studies demonstrate that the resistome is ancient and an essential constituent of microbial chemical ecology in the environment. What is now evident is that the human use of antibiotics provides the selection conditions for the movement and capture of resistance genes by previously sensitive pathogenic bacteria, increasing the chances of clinical failure.

Mechanisms of resistance

A key to understanding resistance and to managing its inevitable emergence is a thorough understanding of its molecular mechanisms. Bacteria become resistant to antibiotics using one or more of the following strategies: prevention of penetration of the drug into the cell, active efflux of the agent, alteration of the cellular target, molecular bypass of the target, or production of enzymes that modify the antibiotic itself (Figure 2) (24). All of these strategies can be engaged by pathogens to overcome antibiotic activity.

Barriers to drug penetration and efflux systems are significant components of the 'intrinsic resistome' (25). These mechanisms can, independently or working in concert, significantly limit the efficacy of antibiotics, often in a genus or species-specific manner. Environmental bacteria are regularly highly antibiotic resistant as a result of such intrinsic mechanisms. Not surprisingly, opportunistic pathogens that are increasingly problematic in the clinic such as *Pseudomonas* and *Acinetobacter* have their reservoirs in the environment and are intrinsically drug resistant. These intrinsic mechanisms, evolved over millennia to overcome a myriad of toxic compounds produced by bacteria, fungi, plants, and

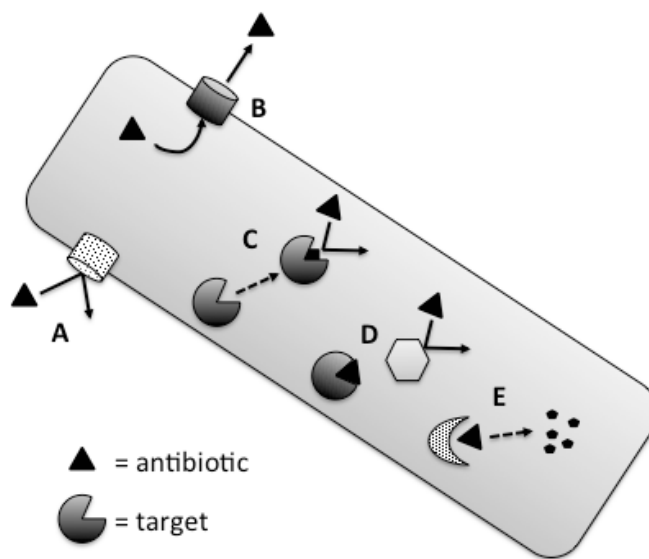


Figure 2. Mechanisms of antibiotic resistance.

Bacteria evade antibiotic through a variety of mechanisms including preclusion of drug penetration into the cell (A), active efflux (B), alteration of the cellular target (C), molecular bypass of the target by making the target redundant (portrayed by the hexagon that has no susceptibility to the antibiotic) (D), and production of drug inactivating enzymes.

animals, represent some of the most daunting challenges to modern antibiotic drug discovery.

The 'acquired resistome', unlike the more passive intrinsic mechanisms, evolve in direct response to antibiotic exposure. Mechanisms include the mutation of cellular targets to insensitive versions, the upregulation or horizontal acquisition of dedicated enzymes that can bypass or modify cellular drug targets, and the expression of enzymes that inactivate the drugs themselves. An example of exposure linked to acquired resistance is the selection of point mutations in type II topoisomerases in gram negative bacteria and type IV topoisomerase in gram positives, the targets of the fluoroquinolone antibiotics such as ciprofloxacin.

The resistance to the glycopeptide antibiotics such as vancomycin offers a compelling example of target bypass. Vancomycin binds to the D-alanyl-D-alanine terminus of cell wall precursors, physically preventing essential the cross-linking reactions necessary for wall rigidity. Resistant bacteria have acquired an alternative metabolic pathway, encoded by three enzymes and a

two-component regulatory system, which replaces the dipeptide D-alanyl-D-alanine with the ester D-alanyl-D-lactate, a structure that no longer binds vancomycin (26).

Erm and Rmt/ArmA are S-adenosylmethionine-dependent methyltransferases that modify respectively the exocyclic amine of A2058 of the 23S rRNA and N7 of G1405 of the 16S rRNA. These relatively minor chemical modifications (the molecular weight of a bacterial ribosome is $>1.3 \times 10^6$ Da compared to a 15 Da for a methyl group) result in high-level resistance to macrolide, lincosamide, type B streptogramin, and aminoglycoside antibiotics respectively.

Antibiotic resistance via inactivation of the compound itself is perhaps the apogee of resistance evolution. Enzymes that act on almost all drug classes are known and are highly efficient at overcoming antibiotic activity. They use a myriad of mechanisms including hydrolysis, group transfer (kinases, acyltransferases), lyases, and oxygenation among others (27). Analysis of the detailed molecular mechanisms of the enzymes and their 3-dimensional structures reveal similarities to enzymes of cellular metabolism. For example, the kinases that inactivate aminoglycoside antibiotics share structure, function, and inhibitor susceptibility to Ser/Thr/Tyr kinases (28-30). Similarly, acetyltransferases that modify histones and aminoglycoside antibiotics share

ADP-ribosylation is an unusual mechanism of antibiotic resistance. It requires the seemingly metabolically expensive sacrifice of a molecule of NAD⁺ as the source of the ADP-ribose, a mechanism shared by several bacterial toxins such as cholera, pertussis and diphtheria toxins. We established that ADP-ribosylation occurs on a key hydroxyl group of rifampin required for target binding providing the molecular logic of resistance (Figure 3) (36). Determination of the structure of the enzyme demonstrated similarity with bacterial toxins in the catalytic domain (36). Similarly, glucosylation of rifampin occurs at the same key hydroxyl group, thereby blocking the ability to bind to the antibiotic target (37). Characterization of the enzyme mechanism and protein sequence reveals substantial similarity to glycosyltransferases essential in the biosynthesis of glycopeptide antibiotics such as vancomycin.

Our survey of rifampin resistance in a panel of ~500 spore forming bacteria identified five strains that inactivated the

structure and mechanism (31, 32). We term the genetic elements encoding standard metabolic enzymes that can either give rise to drug resistance or that share common ancestors proto-resistance genes by analogy to proto-oncogenes (33). These are the wellspring of resistance.

The diversity of these mechanisms is exemplified through the example of the rifamycin antibiotics (Figure 3). Rifamycins are natural product antibiotics first discovered in the late 1950s by researchers at Lepetit laboratories in Milan (34). Chemical modification of the naphthalene core of rifamycin SV generated the semi-synthetic antibiotic rifampin, a drug that is on the WHO essential medicines list for its pivotal role in treating tuberculosis. In addition to mycobacteria, rifamycins are broadly useful vs. gram positive bacteria. Rifamycins bind to the mRNA exit tunnel of bacterial RNA polymerase, thereby disrupting transcription (35). Resistance to rifampin in the clinic is dominated by point mutations in the rifamycin-binding site of RNA polymerase. These mutations arise frequently, and as a result, rifampin is given in a cocktail of other antibiotics. Despite this seemingly straightforward path to resistance, there exist many enzymatic inactivation mechanisms in the environment and paradoxically in gram negative bacteria, which are intrinsically insensitive. These mechanisms include ADP-ribosylation, O-glycosylation, O-phosphorylation and destruction following monooxygenation.

antibiotic via phosphorylation (12). Identifying the kinase responsible for this activity proved challenging but was successful when we realized that in actinomycetes, genes encoding rifamycin resistance genes were downstream from a 19 base pair inverted repeat sequence (38). This finding enabled us to identify a candidate gene in a resistant strain we had sequenced. The gene was originally annotated as a phosphoenolpyruvate synthase. Overexpression of the enzyme, which we termed RPH, enables us to confirm the predicted activity both in cells and *in vitro* (38). Determination of the 3-dimensional structure of the enzyme made it possible to propose an unprecedented mechanism in antibiotic resistance for RPH. First, the β -phosphate of ATP is transferred to a catalytic His residue on a mobile domain that swivels toward a rifampin binding domain resulting in phosphate transfer to a hydroxyl group on the antibiotic. This hydroxyl is distinct from the target of rifampin ADP-ribosyltransferase and rifampin glycosyltransferase, but nevertheless equally important to target binding (39).

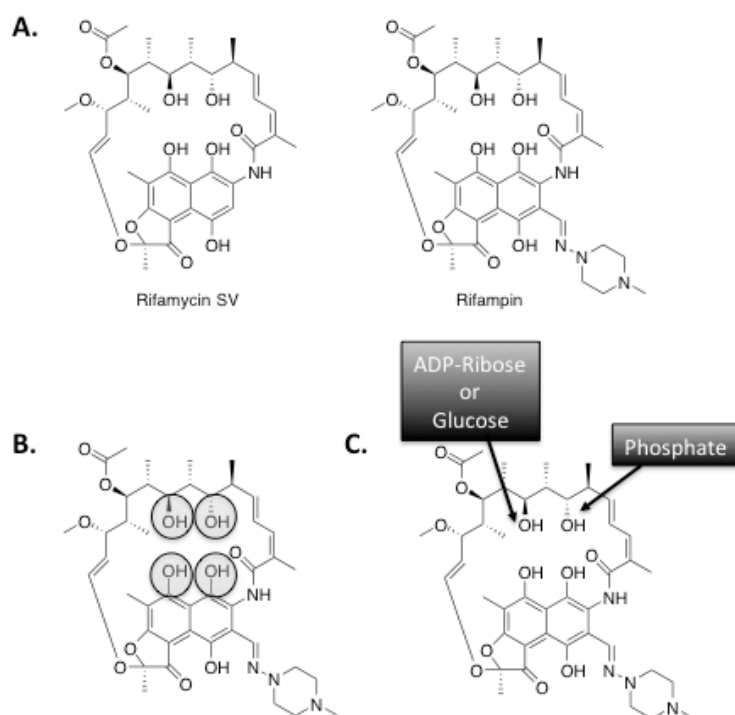


Figure 3. Enzyme-mediated resistance to rifamycin antibiotics.

A. Rifamycin SV (natural product, poor drug properties), Rifampin (Semi-synthetic derivative, excellent drug properties). **B.** Rifamycins interact with the target RNA polymerase via four conserved hydroxyl groups. **C.** Enzymes modify the key hydroxyl groups ADP-ribosylation, glucosylation, or phosphorylation, providing the chemical logic of drug resistance.

The remaining rifamycin resistance mechanism, hydroxylation followed by compound destruction is proving to be equally interesting with a novel mechanism (unpublished results). The theme of the rifampin inactivating enzyme saga parallels our work with other antibiotics and supported by many other labs. It is the recurring co-opting of metabolic enzymes with activities unrelated to antibiotic resistance (proto-resistance elements) that are reshaped through the force of natural selection to achieve new activities in drug resistance. Knowledge of the details of these enzymes, their structures, and molecular mechanisms can be leveraged in shaping next generation antimicrobial strategies.

Application of mechanistic knowledge in antibiotic discovery and detection

Research on the diversity and mechanisms of antibiotic resistance is essential to addressing the current antibiotic crisis. The lack of a central well-curated resource of resistance, essential to the surveillance of resistance and the discovery of new mechanisms, prompted the establishment with Andrew McArthur of the

Comprehensive Antibiotic Resistance Database (CARD; card.mcmaster.ca) (40). The CARD is now the most accurate resource of curated and up to date information on bacterial antibiotic resistance. It includes not only information on individual genes, proteins and their structures, molecular mechanisms, bacterial species, antibiotics, and links to the peer-reviewed literature, it also incorporates bioinformatic tools that enable the prediction of resistance gene genotype from genomic and metagenomic data. The CARD is accessed daily by researchers across the globe working on all aspects of resistance from populations to the clinic to the lab. Fundamental mechanistic information is essential to inform the algorithms that enable prediction of new resistance genes and ultimately the development of diagnostic tools.

A second application of basic research in mechanisms of antibiotic resistance is in the discovery and development of new antibiotics and alternatives to traditional drugs. In the first instance, we established a platform that arrays individual resistance genes, clustered by mechanism and

resistance phenotype, in isogenic hosts, in single and multiple gene copies under the control of constitutive low and high expression promoters (41). This platform is used to support antibiotic discovery in several ways. First is the dereplication of known antibiotic classes from crude extracts of natural product-producing organisms. Dereplication is the process of identifying known compounds and compound classes early in the discovery process to avoid their re-isolation. Second is the assessment of susceptibility of candidate drugs to known resistance mechanisms. In this mode, candidate compounds are challenged against a panel of known resistance alleles that can quickly identify any resistance liabilities early in the development process. Third is in the screening for inhibitors of antibiotic resistance. Here we have successfully used the platform to identify candidate molecules that block specific resistance mechanisms. Such compounds can in principle be co-formulated with existing antibiotics thereby overcoming resistance and rescuing drug activity.

In an example of the latter strategy, we used our platform to screen a panel of our in-house collection of extracts of compounds produced by environmental microbes against the resistance element NDM-1 (42). NDM-1 is a metallo- β -lactamase conferring resistance to almost all β -lactam antibiotics, including the 'last resort' carbapenems. NDM-1 emerged in 2010 and has rapidly spread across the globe (43). This screen identified a fungal natural product, aspergillomarasmine A (AMA) as a novel inhibitor of NDM-1 and other metallo- β -lactamases that re-sensitized resistant bacteria to β -lactam antibiotics. With Brian Coombes, we demonstrated that AMA could be co-formulated and cure infections caused by NDM-1-expressing bacterial pathogens in mouse models of infection (42). AMA is currently undergoing pre-clinical evaluation as a potential human drug candidate.

Knowledge of fundamental mechanisms of antibiotic resistance also shapes efforts to explore alternatives to traditional antibiotics. In collaboration with Eric Brown and Mike Tyers, we rationalized that combining antibiotics with bioactive non-antibiotic compounds could overcome resistance, in particular, intrinsic resistance. Our first screening efforts in this area identified compounds that enhanced the antibiotic activity of tetracycline antibiotics in intrinsically resistant gram negative bacteria such as *Pseudomonas aeruginosa* (44). This work demonstrated the unexpected synergy

between tetracyclines and loperamide, better known as Imodium. We term these non-antibiotic enhancers of antibiotic activity antibiotic adjuvants (45). Further screening efforts have identified a number of adjuvant molecules in *E. coli* (46), methicillin *Staphylococcus aureus* (MRSA) (47) and even in fungal pathogens (48). This strategy can also extend to enhancers of antibiotic action that act on the host (49). Antibiotic adjuvants offer an orthogonal approach to new antibiotic discovery that can contribute to the antibiotic crisis.

Conclusions

Antibiotics are essential to medicine, and it is inconceivable that we can maintain and advance human health without them. Yet, they are imperiled, and the almost daily news reports of organisms untreatable with current drugs are sobering (5). Numerous avenues can be used to address this crisis. Disease prevention strategies including aggressive public health measures, vaccine development, and well-coordinated surveillance are essential. Equally important is the awareness that antibiotic resistance is a One Health issue (50). That is it integrates humans, animals, and the environment. Antibiotic stewardship, therefore, is critical to the human and animal health and the agricultural sectors. Finally, we will continue to need new antibiotic drugs and to preserve our existing ones. Here fundamental research in resistance, microbial physiology, host biology, and their associated biochemical targets must be leveraged with more applied discovery strategies. Discovery cannot occur without basic research, and basic research needs the outlet of application to fulfill one of its mandates, which is to improve health.

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2016 CSMB New Investigator Award

Regulation of voltage-gated sodium channels by calcium ions and auxiliary subunits

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Abstract

Excitable cells such as neurons and myocytes use ion channels to generate and shape electrical signals. Voltage-gated sodium channels are responsible for the upstroke of the action potential. In mammals, these channels typically consist of two subunits (α and β), and can associate with multiple cytosolic proteins that modulate their properties. The α -subunit forms a large protein with four homologous repeats of six transmembrane helices each. β -Subunits contain a single transmembrane helix and an extracellular domain. They modulate the functional properties and can affect the pharmacology. Among the cytosolic binding partners is calmodulin, a universal Ca^{2+} sensor that endows sodium channels with Ca^{2+} -dependent modulation. Crystal structures are available for different β -subunit isoforms, and for calmodulin bound to two different cytosolic portions of the α -subunit. These allow mapping of disease mutations associated with cardiac arrhythmia and congenital epilepsy, and investigation of the primary disease mechanisms.

Electrically excitable cells, such as neurons and myocytes, have the ability to rapidly change the potential across their plasma membranes. This process is mediated by ion channels, membrane proteins specialized in allowing passage of either one type or a subset of ions. Sodium ions are in large excess in the extracellular environment, and voltage-gated sodium channels (Na_v s), when triggered to open, allow them to enter the cytoplasm. In doing so, they mediate a very rapid depolarization of the plasma membrane, contributing to the upstroke of the action potential in many excitable cells. An example is shown in Figure 1, which shows the action potential in ventricular myocytes. Two features are absolutely essential for the physiological role of Na_v s: they must be selective for sodium over other ions, and they need to be able to 'gate', i.e. open or close in a regulated manner.

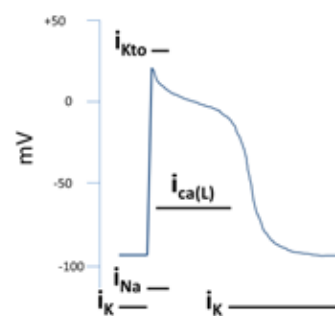


Figure 1. Action potential in a cardiac ventricular myocyte

The curve shows the membrane potential as a function of time. The black bars indicate some of the currents that contribute to the action potential (note: more currents than the ones shown here are actually present). i_k = potassium current; i_{Na} = sodium current; i_{Kto} = transient outward potassium current; $i_{Ca(L)}$ = L-type calcium current.

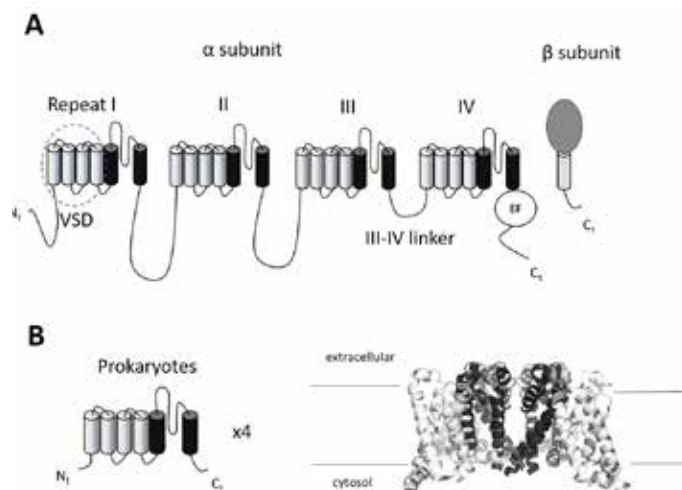


Figure 2.

A. Schematic view of a mammalian sodium channel, showing the 24-TM helix α -subunit and the smaller β -subunit. The α -subunit is arranged in 4 repeats, with the first four helices in each forming a voltage-sensing domain (VSD), and the last two (dark) contributing to the pore. **B.** topology and crystal structure of NaVAAb, a prokaryotic sodium channel. Four identical subunits form a four-fold symmetric pore.

As suggested by their name, the primary trigger for opening of Na_v s is the membrane potential. Under resting conditions, excitable cells such as neurons have a net negative charge inside the cell relative to the outside, leading to a negative or 'polarized' membrane potential. Depolarization is the event by which this potential difference dissipates, making the inside of the cell less negative. This depolarization activates the Na_v s, triggering them to open and allowing the rapid influx of sodium ions. This event depolarizes the membrane even further, so Na_v s can both sense and mediate depolarization.

The ability of Na_v s to sense the membrane potential is achieved by their voltage-sensing domains (VSDs), which contain several arginine residues that are sensitive to the membrane electrical field. Figure 2a shows the predicted topology of a mammalian Na_v . The main α -subunit consists of 24 transmembrane (TM) helices, arranged in four homologous repeats (I-IV) of 6 TM helices each (S1-S6). Helices S1-S4 together form a VSD, whereas S5 and S6 contribute to the channel pore. Additional short helices are also located in the pore-forming domain. The four repeats are connected by long cytosolic loops, termed the I-II loop, II-III loop, etc. The C-terminus of the protein is located within the cytoplasm and contains an

EF-hand domain, immediately downstream of the last transmembrane segment.

The human genome encodes nine different Na_v α -subunit isoforms ($\text{Na}_v1.1$ - $\text{Na}_v1.9$). These commonly associate with an auxiliary β -subunit, for which four isoforms have been identified ($\text{Na}_v\beta1$ -4). $\text{Na}_v\beta$ is not essential for channel function, and has a much simpler architecture, consisting of an extracellular N-terminal domain, a single TM helix, and a short unstructured cytosolic tail.

Structure of the α -subunit

Currently no high-resolution structure is available for the TM region of the α -subunit of any mammalian Na_v . However, much more is known about prokaryotic Na_v s. Figure 2b shows the topology and crystal structure of a bacterial sodium channel (Na_vAb), isolated from *Arcobacter butzleri*, at 2.7 Å resolution.¹ Much simpler than the mammalian isoforms, Na_vAb forms a homotetramer of 4 identical subunits with 6 TM helices each. The pore-forming regions of each subunit arrange around the 4-fold symmetry axis, and each VSD interacts with the pore-forming domain of a neighbouring subunit. Since then, several structures have been reported, including versions where the VSDs have been removed.²⁻⁷

The prokaryotic Na_v s provide useful blueprints to understand their mammalian counterparts, but several important differences distinguish them: 1) Prokaryotic Na_v s form fully symmetrical pores, whereas mammalian Na_v s display pseudo-symmetry. 2) Prokaryotic Na_v s lack the long cytosolic linkers. These linkers endow the mammalian Na_v s with distinct properties. 3) Prokaryotic Na_v s lack additional β -subunits. More recently, a cryo-EM structure has been reported for an insect Na_v at 3.8 Å resolution.⁸ This structure confirms the expected arrangement of the transmembrane helices, with a pseudo-fourfold symmetric arrangement. Although this provides a better template to understand mammalian Na_v s, the structure still lacks an auxiliary subunit and also misses some of the essential regulatory properties of mammalian channels, discussed below.

Inactivation

Voltage-gated channels open and close as a function of voltage. However, many ion channels have evolved additional mechanisms that can regulate the passage of ions. Na_v s can 'inactivate' over the course of just milliseconds after opening. The mechanism of

inactivation is not completely understood, but it is essential for normal Na_v function and any misregulation can lead to serious disorders. A prevailing theory for Na_v s is that the loop connecting repeats III and IV (the 'III-IV loop') acts as an inactivation gate, blocking the passage of sodium ions by associating with a portion of the α -subunit. This was shown in dramatic fashion by mutating three hydrophobic residues ('IFM') within the III-IV loop, yielding channels that no longer undergo fast inactivation.⁹ Due to the lack of 3D structures, the exact identity of the interface with the III-IV loop is unknown, and it remains to be proven whether the 'IFM' motif truly forms a blocking particle.

Sodium channel inactivation is strongly dependent on a number of factors. Foremost is the membrane potential. Upon depolarization, sodium channels open and rapidly inactivate. However, it can also be shown that they can inactivate prior to opening. This is most readily observed in the experiment in Figure 3, a so-called 'steady-state inactivation' experiment. The curve shows the availability of the sodium channels after a long pre-pulse. For example, keeping the channels for a long stretch of time (>50 ms) at very negative potentials (such as -120 mV), followed by a test pulse to e.g. -20 mV, yields a large sodium current during the test pulse. However, keeping the channels for a long time at a less negative potential (e.g. -40 mV), followed by the same test pulse to -20 mV, shows almost no currents. The interpretation is that most of the Na_v s were inactivated at -40 mV, so that none were available to mediate currents during the test pulse. In comparison, at -120 mV, virtually none of the channels were inactivated. The curve shows that progressively more inactivation occurs at less negative membrane potentials.

Mammalian Na_v s have adopted an additional layer of complexity. Intracellular Ca^{2+} has the ability to influence inactivation in an isoform-dependent manner.¹⁰ In $\text{Na}_v1.5$, the cardiac isoform, Ca^{2+} seems to impede inactivation, as now stronger depolarizations are required for full inactivation. This is shown in Figure 3, whereby μM concentrations of intracellular Ca^{2+} cause a right-shift in the steady-state inactivation curve. This can have profound effects on the availability of sodium channels. For example, on the curve shown, a resting membrane potential at -75 mV would mean that only ~20% of the channels are ready to provide currents during a depolarization, but

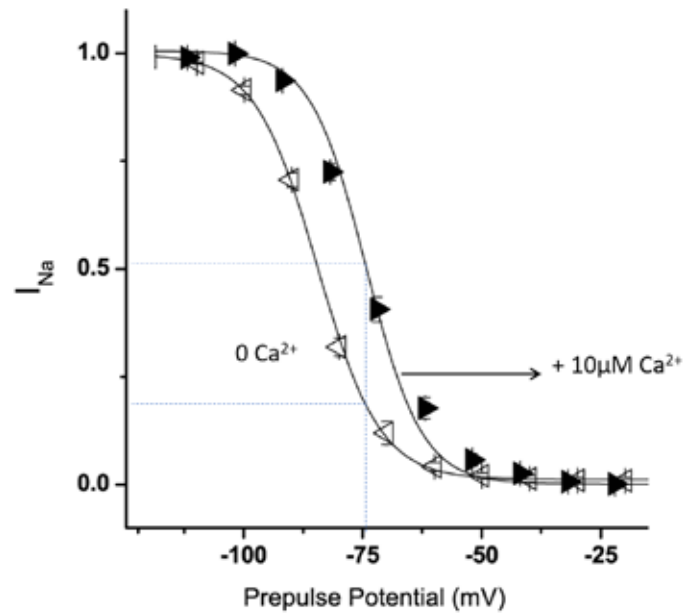


Figure 3. Steady-state inactivation curve for a cardiac sodium channel ($\text{Na}_v1.5$) in the absence and presence of intracellular Ca^{2+}

Each data point on the curve shows the Na^+ current, obtained during a test pulse to -20mV, after a long (500 ms) prepulse to the voltage shown on the x-axis. On the plot, the Na^+ currents are normalized to the maximum current. A prepulse at -120 mV yields near maximum possible currents at the test potential, whereas a prepulse to -40 mV yields almost no current during the test pulse because the Na_v channels were inactivated during the prepulse. Intracellular Ca^{2+} shifts the curve to the right, resulting in less inactivation over a range of voltages. For example, the dotted line shows that for a cell held at -75mV, only 20% of the maximum possible current is visible, but this goes up to more than 50% in the presence of 10 μM intracellular Ca^{2+} .

in the presence of μM Ca^{2+} levels this would more than double. This observation for the effect of Ca^{2+} on $\text{Na}_v1.5$ has been challenged¹⁰, but the experiments differ in the composition of the intracellular solution.

Na_v s thus have very complex gating landscapes. Depolarization and repolarization trigger channel opening and closing, respectively. On top of that, they can inactivate in a manner that is dependent on both voltage and intracellular Ca^{2+} .

Calmodulation

Na_v s are targets for a multitude of proteins that can

change their functional properties. Among these is calmodulin (CaM), a ubiquitous Ca^{2+} sensor. CaM contains four EF-hands, arranged into two domains (termed N-lobe and C-lobe). Upon binding Ca^{2+} , both lobes expose a hydrophobic surface. The C-terminal tail of the $\text{Na}_v\alpha$ -subunit contains an EF-hand motif, followed by an IQ domain. IQ domains are well-known CaM interaction motifs, and CaM can associate with the Na_v IQ motif in both the presence and absence of Ca^{2+} . Several structures are available for complexes of apo-CaM with the individual IQ domain or larger portions of the C-terminus that include the EF-hand domain.¹¹⁻¹⁵ Figure 4a shows a structure of apoCaM bound to $\text{Na}_v1.5$, the isoform expressed in cardiac tissue. Crystal structures are also available in the presence of higher Ca^{2+} concentrations, but the C-lobe is not present in a typical Ca^{2+} -bound form.¹⁴ An exact structure of full-length Ca^{2+} /CaM bound to the C-terminal region of the Na_v thus remains to be described.

In addition to the IQ domain, another binding site for CaM is present within the III-IV linker.^{16,17} A crystal structure shows the C-lobe of CaM bound to a region just downstream of the 'IFM' motif (Figure 4b). This is confirmed via isothermal titration calorimetry (ITC) experiments, whereby only the C-lobe shows appreciable binding. This interaction only occurs in the presence of

Ca^{2+} , in contrast to the IQ domain which binds CaM both in the presence and absence of Ca^{2+} . Electrophysiology experiments confirm the functional importance of the interaction with the III-IV linker, as a mutation in the III-IV linker that decreases the affinity for CaM leads to a loss of the effect of Ca^{2+} on inactivation. Conversely, a mutation that increases the affinity potentiates the effect, as now less Ca^{2+} is required to shift the inactivation curve. Based on these observations, a simple gating scheme can be proposed (Figure 5), whereby apo-CaM is bound to the IQ domain. Depending on the membrane potential, the channel can inactivate or recover from inactivation to a particular steady state. Upon binding Ca^{2+} , the C-lobe can bind the III-IV linker, thus reducing the amount of inactivation. Since Ca^{2+} -loaded CaM can also associate with the IQ domain via either its C-lobe or N-lobe, a possibility exists whereby CaM bridges the IQ domain and the III-IV linker, but this remains to be confirmed.

Interestingly, the elements involved in inactivation are targets for a multitude of disease-causing mutations. In $\text{Na}_v1.5$, the cardiac isoform, these are mostly associated with long-QT and Brugada syndromes, two types of inherited arrhythmias. Mutations are found within the III-IV linker, the EF-hand, the IQ domain, and even within CaM itself.¹⁸ These highlight the importance of channel inactivation and its modulation by cytoplasmic factors.

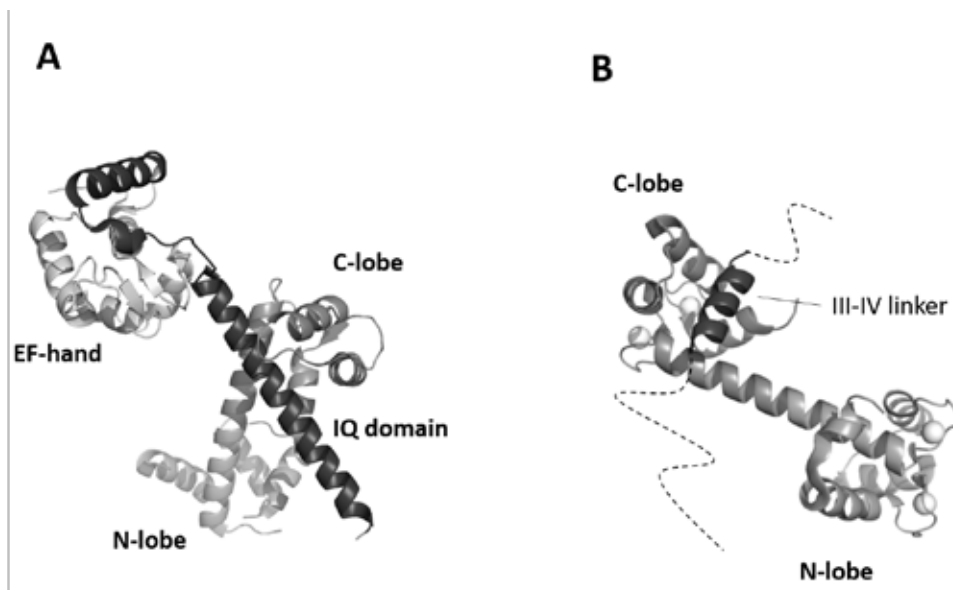


Figure 4.

A. Crystal structure of apo-CaM bound to the C-terminal region of $\text{Na}_v1.5$, including the EF-hand and IQ domains. The two CaM lobes are labeled. An FGF-like domain bound to the EF-hand is not shown for clarity. **B.** Crystal structure of Ca^{2+} /CaM bound to the $\text{Na}_v1.5$ III-IV linker. Only the portion bound to CaM is structured. The interaction is entirely mediated by the C-lobe.

The auxiliary β -subunit

Although the α -subunit can produce currents on its own, native Na_v channels typically associate with an additional β -subunit. Four different isoforms are known, each consisting of an extracellular domain, a single transmembrane helix, and a short cytosolic tail. The exact functional effects depend on the specific α - β combination, and includes increased membrane trafficking and modulation of inactivation. Crystal structures are now available for the extracellular domains of three isoforms ($\beta 2$, $\beta 3$, $\beta 4$).¹⁹⁻²¹ These show an immunoglobulin fold with a conserved buried disulfide bond (Figure 6). $\beta 2$ and $\beta 4$ both contain an exposed cysteine that is highly reactive.

Among the multiple functional effects of β -subunits is the ability to change the pharmacological properties.^{19,20} For example, protoxin II is a peptide toxin produced by the green velvet tarantula, and it can rapidly block currents through neuronal sodium channels. This likely

contributes to the ability of the tarantula to paralyze its prey. The Bosmans lab showed that in the presence of either $\beta 2$ or $\beta 4$, this block is less effective, suggesting a direct competition between the toxin and the β -subunit to associate with the α -subunit. The exposed cysteine appears crucial, since mutating it renders the $\beta 2$ or $\beta 4$ ineffective in neutralizing the toxin. Through careful analysis of various cysteine mutations in the α -subunit, we propose the likely model that $\beta 2$ and $\beta 4$ can form direct disulfide bonds with an exposed cysteine on the α -subunit.¹⁹

The different β -subunits are also targets for a multitude of disease-causing mutations, mostly linked to inherited epilepsy. One of the first described mutations affects the conserved central disulfide bond within the $\beta 1$ -subunit. Although this isoform remains to be crystallized, the equivalent mutation could be made in $\beta 4$. Surprisingly, it did not cause a complete misfolding, but rather

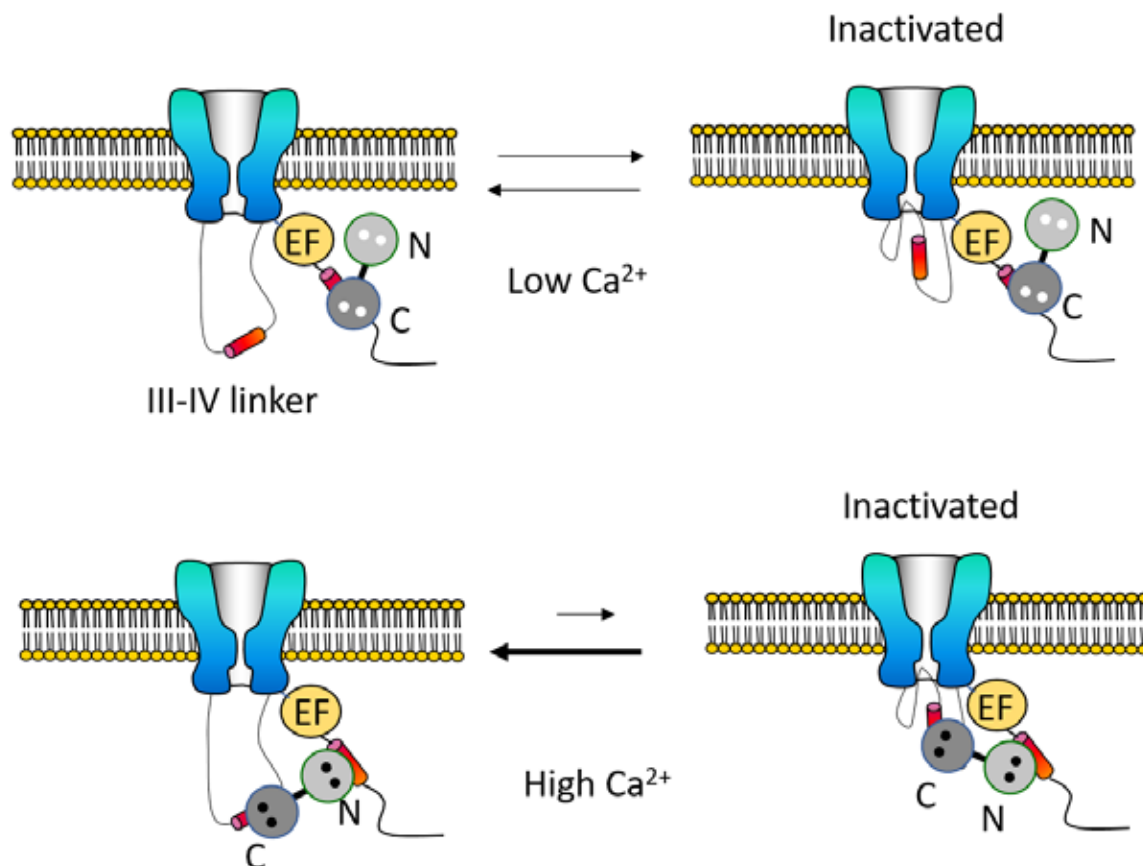


Figure 5. Working hypothesis for how CaM regulates sodium channel inactivation

In the presence of low Ca^{2+} , CaM associates with the IQ domain as a resident Ca^{2+} sensor. In high Ca^{2+} , the C-lobe can bind the III-IV linker and reduce the amount of inactivation. Since the Ca^{2+} -N-lobe can also bind the IQ domain, it may be possible for CaM to bridge the two cytosolic elements.

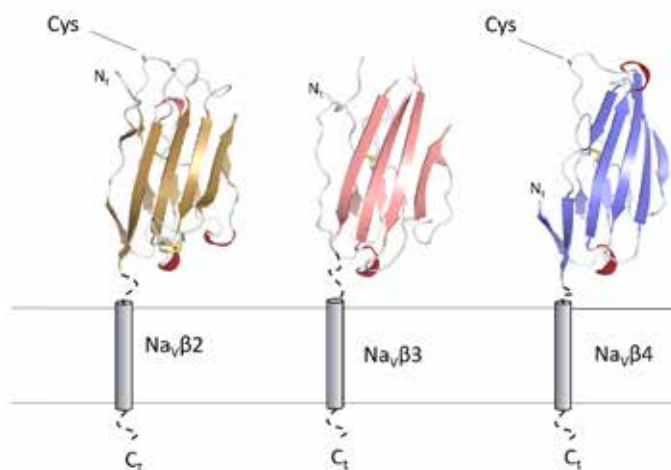


Figure 6. Crystal structures for the extracellular domains of three Na_v β isoforms

All display an immunoglobulin fold with a buried disulfide bond. Reactive cysteines on the surface of β2 and β4 are labelled.

changes the conformation of the loops surrounding the exposed cysteine. This mutant is also no longer able to protect neuronal sodium channels from protoxin II. The conserved disulfide bond therefore seems essential for maintaining the proper 3D structure to allow interaction with the α-subunit.

Future perspectives

Mammalian sodium channels are complex membrane proteins and only a small portion of their domains and subunits have been resolved at high resolution. A major hurdle towards structure determination of intact channels is the inability to obtain sufficient quantities from heterologous expression systems. However, the recent cryo-EM structure of a cockroach sodium channel⁸ now allows better homology models of the human channels to be built. In addition, chimeras can be used between prokaryotic and human sodium channels, a strategy that has previously allowed a voltage-sensing domain of Na_v1.7 to be resolved.²² The future for Na_v structure is bright.

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2016 Grant and Moens Award of Excellence in Genetics

How we use fruit flies to study cell growth, signal transduction and cancer pathways

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Abstract

In my lab we study Hipk proteins and their regulation of cell proliferation, organ growth and patterning. Hipks are found in many species including humans and fruit flies. *Drosophila* provides a powerful and rapid model system in which to genetically manipulate and study development and cellular growth. We generated a novel cancer model in flies caused by having too much Hipk protein. These flies have tumours, and their organs and limbs overgrow dramatically. In addition, cells bud off from these organs and move to new locations within the body, closely mimicking what occurs during metastasis of cancers in humans. Humans have four different HIPK proteins that are reported to have some similar functions to fly Hipk, but they may also have opposite functions in certain types of cells. We think that abnormal HIPK protein activity contributes to diseases, in particular cancer. We are using the power of *Drosophila* genetics to examine Hipk protein function to learn more about roles in tumour formation and metastasis.

For over a century, scientists have used the fruit fly *Drosophila melanogaster* to learn about fundamental evolutionarily conserved genetic and cellular processes. The pioneering work of Thomas Hunt Morgan, who in 1908 established the famous “fly room” at Columbia University, proved the chromosome theory of inheritance showing that genes are located on chromosomes and are sometimes co-inherited, or linked (Morgan, 1910). Morgan’s student Alfred Sturtevant constructed the first-ever genetic map of a chromosome using recombination to map distances between fly genes. More recently, in elegant genetic screens and studies of mutant phenotypes, Ed Lewis, Christiane Nüsslein-Vollhard and Eric Wieschaus showed that individual genes could be mutated to give characteristic embryonic patterning defects (Lewis, 1978; Nüsslein-Vollhard and Wieschaus,

1980). These studies revealed how complex patterned tissues arise from fertilized eggs and showed the precise roles that each gene played in that process, by studying the cellular effects of losing that gene product through mutation. For their discoveries, they were awarded the Nobel Prize in 1995, as was Morgan in 1933. Their genetic studies furthermore allowed them to order genes within linear pathways through epistasis analyses. The genes that they identified have subsequently been shown to have counterparts across species, and play key roles in embryonic patterning that are often conserved from flies to humans.

Given these parallels, the fruit fly has been used for decades to carry out basic research on developmental signalling pathways and the research has been

instrumental in revealing molecular functions of human disease and cancer-related genes due to two main reasons (reviewed in Gonzalez, 2013; Rudrapatna et al., 2012). First, 75% of all human disease genes have related sequences in *Drosophila*. Second, due to the low genetic redundancy in *Drosophila*, flies can be used to address specific questions about human disease that have been difficult to resolve in cell culture or in animals with a higher level of functional redundancy of genes (Bier, 2005). While anatomical differences exist, many of the cell behaviours observed in normal and malignant cells can easily be modelled in the fly (Herranz et al., 2014; Ninov et al., 2010). Tissue and organ growth is often studied using the larval imaginal discs. Discs are epithelial sacs that undergo extensive proliferation and subsequent patterning and differentiation to form adult structures. Disc development requires the same key signalling pathways needed for human development and growth. Indeed, for key signalling pathways such as Ras, Notch, Hedgehog, and Wnt much of the molecular circuitry was elucidated in *Drosophila* (e.g. creative names such as Hedgehog and Armadillo derive from the mutant embryo phenotypes).

In my lab we have been investigating how key signalling pathways are regulated during the patterning of tissues. We are interested in how cells control their proliferation, and how pattern formation and cell fate acquisition is controlled during development. Our focus has been on the reversible phosphorylation of key effector proteins by protein kinases and phosphatases. One of the proteins that we study is called Homeodomain-interacting protein kinase, or Hipk for short (Blaquiere and Verheyen, 2016). Hipk is a dual specificity tyrosine and serine/threonine kinase that is conserved across multicellular animals from flies and worms to humans. Humans and other vertebrates possess 4 paralogs, while *Drosophila* and *C. elegans* only have one Hipk gene. Most research in vertebrates has focused on Hipk2, and it shares the most sequence homology with *Drosophila* Hipk (Choi et al., 2005). Through mainly cell culture-based assays, Hipk2 was identified as a co-factor for numerous transcription factors that differentially regulate gene expression depending on the cellular context (Rinaldo et al., 2007). *hipk* in flies is an essential gene, meaning that animals lacking this gene product in embryos fail to develop and die. *In vivo* examination of murine Hipk2 protein function has thus far revealed a role in neurogenesis, specification of skeletal segment identity and cell

proliferation, although the mechanisms underlying these phenotypes remain to be elucidated (Isono et al., 2006; Zhang et al., 2007). Using genetically induced mitotic recombination, we can study the effect of *hipk* mutation in later developmental stages in patches, or clones, of mutant cells. Over the years, we have collected many reagents that let us manipulate the gene dosage of Hipk, and express kinase inactive Hipk or hyperactive forms, in addition to knocking down the gene using double stranded RNA (RNAi) in a temporally and spatially controlled manner using the Gal4-UAS misexpression system.

We have found that Hipk is required for proliferation, since tissues that have reduced *hipk* levels fail to grow adequately due to reduced proliferation. This is also seen in mouse mutants in which both *Hipk1* and *Hipk2* have been deleted (Isono et al., 2006; Trapasso et al., 2009). Conversely, elevated expression of Hipk in fly tissues has dramatic and severe consequences (Figure 1). Through genetic studies and biochemical experimentation we have found that Hipk proteins target and regulate the function of key effector molecules of numerous signalling pathways. We were able to show using *in vivo* and *in vitro* analyses that that fly and mouse Hipks promote the Wnt pathway by enhancing stabilization of the β -catenin protein (Lee et al., 2009a; Swarup and Verheyen, 2011). Thus in cells lacking *hipk* we observed reduced β -catenin and subsequently, reduced Wnt target genes, showing that normal levels of Hipk were required for robust Wnt signalling. A number of kinases involved in regulating Wnt signalling, such as GSK3 β and CK1, are also found to play distinct roles in other pathways (Verheyen and Gottardi, 2010). Hipk proteins have emerged to have additional targets during development, as we and others have found that Hipk can modulate the output of Notch, Hedgehog and Jnk signalling (Huang et al., 2011; Lee et al., 2009b; Swarup and Verheyen, 2011).

After observing massive overgrowths in discs overexpressing Hipk, we investigated whether it might interact with the Hippo tumour suppressor pathway. The kinase cascade of the Hippo pathway inhibits the transcription factor Yorkie (Yki)/YAP/TAZ, which promotes expression of genes that promote proliferation and block cell death. A mutant form of Yki that is resistant to this upstream inhibition, Yki^{S168A}, causes overgrowths. In this genetic context, loss of Hipk could suppress the dramatic overgrowths that resulted (Chen and Verheyen, 2012;

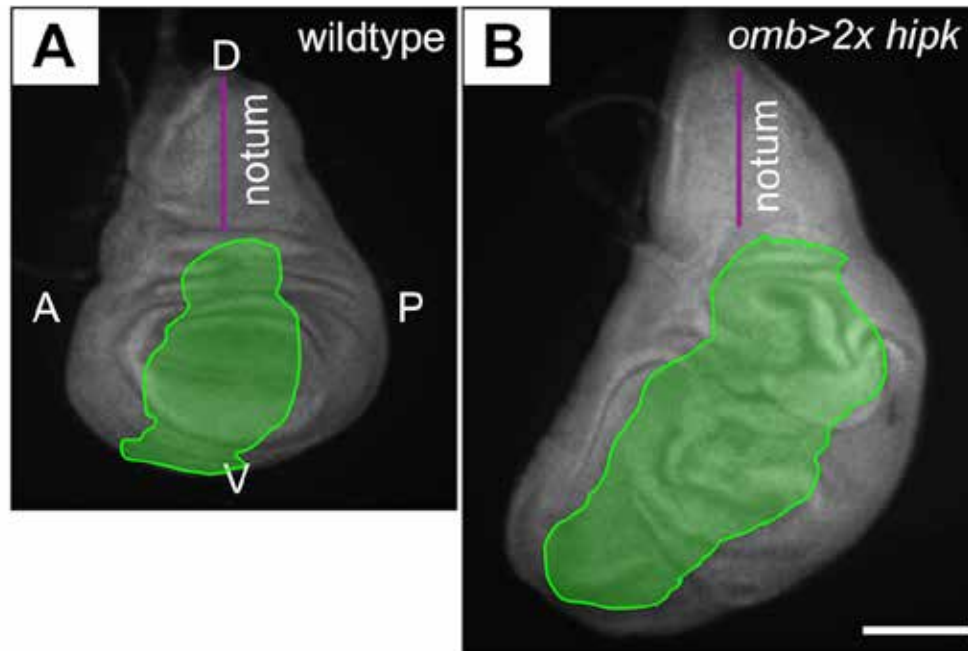


Figure 1. Overexpression of Hipk induces overgrowth and proliferation

(A) The fly imaginal wing disc contains tissue that will give rise to the thorax, or notum and to the wing blade and hinge. The *omb-Gal4* driver strain allows expression of transgenes in the central portion that gives rise to wing and hinge, as outlined in the wildtype control disc. (B) Using the *Gal4-UAS* system to express two copies of *Hipk* with *omb-Gal4* results in dramatic overgrowth of the disc due to proliferation of cells in which *Hipk* is overexpressed, as highlighted. The presumptive notum regions in both discs are normal since *Gal4* is not expressed in those cells.

Poon et al., 2012). Furthermore, overexpression of *Hipk* could trigger ectopic expression of Hippo targets. Since Yorkie/YAP/TAZ is an oncogene, we sought to investigate if *Hipk* also acts like an oncogene given their similar phenotypic effects. Tumorigenesis is a multifactorial process, which often begins with a genetic change that leads to uncontrolled growth of a particular tissue, followed by subsequent additional mutations. Since *Hipk* influences many of the major signalling pathways involved in the growth of imaginal discs we hypothesized that *Hipk*, if mis-regulated, could be a contributing factor in this process. Previous studies have described and validated assays for tumorous, metastatic and invasive behaviour in imaginal discs using the *GAL4-UAS* expression system (reviewed in Sonoshita and Cagan, 2017). These assays allow one to study tumour formation as well as follow the migration and invasiveness of individual cells.

When *Hipk* is expressed in the developing larva, in addition to elevated proliferation of imaginal discs, we also observed tumour-like masses in the abdomen (Figure 2). We also find that expression of *Hipk* just within

the developing blood cells using *hml-Gal4* causes similar tumours (Blaquiere et al., 2016). Such melanotic masses are hallmarks of Jak/Stat-induced lymphomas (Ekas et al., 2010). Jak/Stat signalling promotes tissue growth, and mutations causing hyper-activation of the pathway can lead to cancers in both humans and flies (Amoyel et al., 2014; Jones et al., 2005; Levine et al., 2005). Using genetic interaction studies we were able to show that reducing the dose of *hipk* in these animals could dramatically suppress this severe phenotype, suggesting that *hipk* is required for *hop^{Tum-L}*-induced phenotypes (Blaquiere et al., 2016). We also found that *hipk* regulates Jak/Stat activity under physiological conditions, since loss of *hipk* in somatic clones led to significant cell autonomous reductions in expression of a reporter for the Jak/Stat pathway in wing and eye-antennal imaginal discs. Together, these data support the hypothesis that *Hipk* promotes, and is normally required for, the Jak/Stat pathway activity.

Within imaginal discs, *Hipk* appears to induce cell migration in normally stationary cells. In a wildtype wing disc, using the *Gal4-UAS* system, we can express GFP

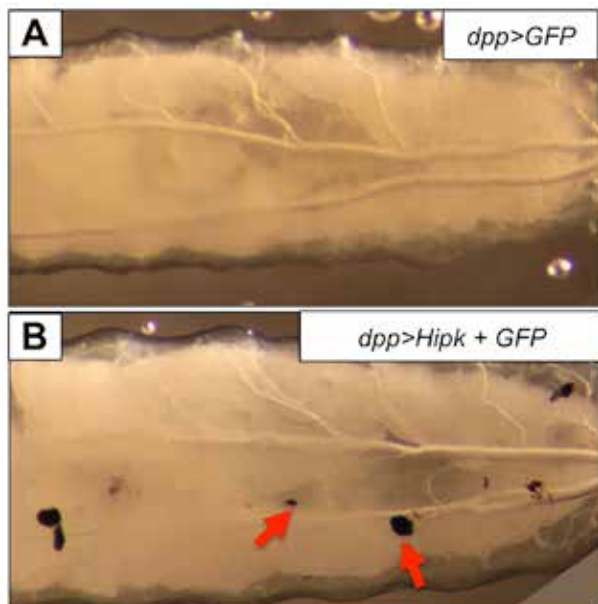


Figure 2. Hipk can induce tumours in immune cells

(A) A control third instar larva has no melanotic masses. Visible structures are the tube-like trachea that runs the length of the larva. (B) Expression of Hipk in larval tissues using *dpp-Gal4* (or *hml-Gal4*, not shown) causes enhanced proliferation and tumours in the blood cells (arrows).

(and other transgenes) with the *dpp-Gal4* driver strain in a defined stripe along the anterior/posterior boundary of the wing disc. Because of compartment boundaries that arise in development, a sharp division is seen between GFP+ cells expressed in the *dpp* domain and the neighbouring GFP- cells in the posterior compartment (Figure 3A, B). Normally, these boundaries are respected and cells do not migrate across them. In contrast, GFP-marked Hipk-expressing cells over-proliferate and also migrate into the posterior compartment (Figure 3C, D). Such boundary-crossing behaviour has been observed in other *Drosophila* metastasis models and is a hallmark of changes in cell behaviour and migration (Ferres-Marco et al., 2006; Pallavi et al., 2012). Another phenotype associated with migratory behaviour is movement of retinal tissue from the site of origin into the body of the fly (Pallavi et al., 2012; Palomero et al., 2007). When *hipk* is expressed in the eye-antennal disc with *eyeless-Gal4* or *dpp-Gal4*, clusters of retinal cells can easily be found in the thorax of the adult fly, due to their expression of pigment. Because the normal eyes are intact, we propose that this is a metastasis-like event in which retinal tissue migrated from the eye disc and lodged in the thorax.

All of these observations have led us to propose the model that Hipk acts an oncogene and that its roles in normal development are critical for proper tissue patterning. Thus, when Hipk is disrupted through mutation and hyperactivated or overexpressed, the consequences are severe. Consistent with such a model, elevated Hipk2 levels are seen in cervical cancers, colorectal cancer cells, pilocytic astrocytomas, and in several other proliferative diseases (Al-Beiti and Lu, 2008; Cheng et al., 2012; D'Orazi et al., 2006; Deshmukh et al., 2008). Overexpression of a wildtype Hipk2 in glioma cells confers a growth advantage (Al-Beiti and Lu, 2008). These findings point to an important potential oncogenic role for Hipk family members. Furthermore, Hipk2 expression in renal tubular epithelial cells triggers EMT, as shown by upregulation of the EMT marker vimentin and downregulation of the epithelial marker E-cadherin (Huang et al., 2015). These studies combined with the loss of function phenotypes in numerous animal models support the idea that elevated Hipk protein expression promotes cell proliferation and tissue growth.

While some studies validate our findings regarding Hipk's importance in promoting growth and patterning, other studies support a model that Hipk family members possess tumour suppressor activity. Most studied among these is the interaction of Hipk2 with p53 (Hofmann et al., 2002; Puca et al., 2009, 2010). p53 senses cellular stress and DNA damage, and initiates responses to maintain genomic stability. Dependent on the extent of stress, p53 either triggers cell cycle arrest and DNA repair, or destruction of the cell through apoptosis. Hipk2 can promote p53-induced apoptosis following lethal DNA damage (D'Orazi et al., 2002; Hofmann et al., 2002). When Hipk2 levels are reduced due to downregulation or mutation, cancer cells are capable of resisting apoptosis. Colon tumours with high levels of Hipk2 responded better to treatment than tumours with lower levels, suggesting that the presence of Hipk can suppress the cancer severity, independent of p53 status (Soubeyran et al., 2011). Interestingly, it has been proposed that the effects of Hipk2 on proliferation are independent of its role in sensing DNA damage (Iacovelli et al., 2009). Consistent with a tumour suppressor function, decreased expression of Hipk family members is found in several types of cancers including thyroid and breast carcinomas, thyroid carcinomas (Lavra et al., 2011; Pierantoni et al., 2002). Furthermore, Hipk2 deficiency has also been linked to chromosomal instability via cytokinesis failure,

increasing tumorigenicity in mouse embryonic fibroblasts (Valente et al., 2015).

It is likely that the various functions of Hipk proteins are context-dependent, thus our continued genetic and molecular studies in flies and in vertebrate cell culture will likely reveal the mechanisms at play. We are particularly interested in determining if the four vertebrate Hipks have evolved distinct, and perhaps opposing, functions. Given the diverse targets that have been identified for Hipks in numerous signalling pathways, it is likely that the phenotypes observed in model systems such as mice and flies will involve cross-regulation of signalling pathways. Our hope is that our studies will uncover important

context-dependent roles for this conserved kinase family that will provide insight into basic and conserved mechanisms of development as well as human disease.

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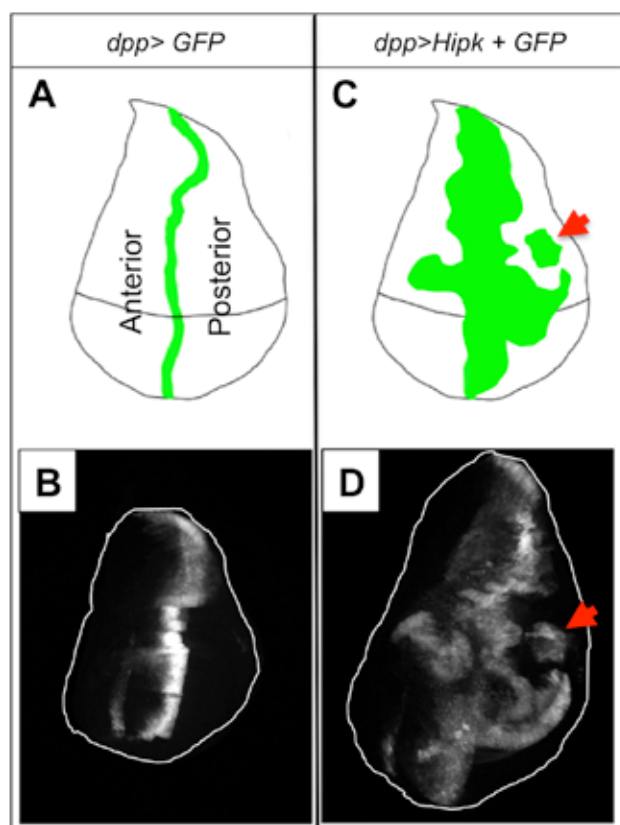


Figure 3. Cells expressing Hipk can migrate through tissues

(A, B) The *dpp-Gal4* driver is expressed along the anterior/posterior boundary of the wing imaginal disc, as seen through the expression of GFP. (C, D) Expressing *Hipk* together with GFP in this stripe allows us to visualize the enhanced proliferation of cells expressing *Hipk*, as seen by the expanse of GFP+ cells. Further we can follow their movement through the tissue and observe isolated clusters of cells that have migrated from their site of origin (arrow).

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2016 Robert H. Haynes Young Scientist Award in Genetics

Charting the centrosome landscape of human cells

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Circumventing scale and solubility to understand centrosome biology

Microtubules are dynamic filaments composed of polymerized tubulin and play diverse cellular roles, including the transport of protein complexes and chromosome segregation via the mitotic spindle apparatus. In most animal cells, the microtubule network is organized by the centrosome, whose core is composed of a pair of orthogonally oriented centrioles embedded in a complex, proteinaceous matrix known as pericentriolar material (PCM). Centrioles are submicron sized (0.5 μm x 0.2 μm), barrel-shaped organelles comprised of a symmetrical arrangement of nine triplet microtubules. The older, or 'mother', centriole duplicates to form a new 'daughter' centriole. The mother centriole has accessory structures called distal and sub-distal appendages which confer specialized microtubule anchoring capabilities [1-4]. The daughter centriole eventually matures into a mother centriole during the cell cycle. While centrosomes are found in actively cycling cells, centrioles form a 'non-motile' cilium in most differentiated cell types in animals, and specialized types like sperm and nodal cells have 'motile' cilia [5]. During ciliation, the mother centriole docks at the cell membrane and undergoes extensive structural modification to form the basal body, which provides a template for the formation of the microtubule-based axoneme, a structure critical for signal transduction via cilia and for cellular movement as flagella, respectively [6, 7]. In humans, primary microcephaly and ciliopathies (including ciliary dyskinesia, polycystic kidney disease, and Bardet-Biedl disease) are linked to defects caused by

mutations in genes that encode centrosomal proteins [4].

At the centrosome, centrioles appear to act as a structural scaffold to promote the organization of the PCM, while PCM acts to anchor microtubules directly or through microtubule-nucleating proteins (e.g. γ -tubulin ring complexes) [8]. At the onset of mitosis, in a process termed centrosome maturation, the PCM increases in size and microtubule-nucleation capacity so as to organize astral and spindle microtubules. Components of the PCM also play a role in the duplication of centrioles, and likely in cilia formation and disassembly [9-11]. Many questions remain regarding the dynamic changes in structure and function of the centrosome and PCM. For instance, the architecture of the PCM and its regulated expansion during mitosis so as to carry out spindle assembly has been a particularly challenging problem. Another long-standing problem is the paucity of information about the components and interactions involved, and how they are dynamically modulated during centrosome function. Indeed, studies of the centrosome are hindered by its biochemical complexity (hundreds of proteins, and numerous large coiled-coil containing proteins, the majority of which are completely uncharacterized structurally) and its dimensions at the boundary of the diffraction limit. Over the last few years, we have sought to use emerging techniques to solve centrosome complexity so as to understand its biology.

Structured illumination microscopy reveals centrosome substructure

In contrast to the centriole and basal body, our understanding of the architecture of the PCM has been lagging. The first description of the PCM (from Boveri in 1900) was ‘the unstructured region’ from which microtubules appeared to originate [12]. Gould and Borisy later demonstrated that microtubules indeed nucleated from the PCM, thus establishing its major cellular role [13]. The rather ‘featureless’ electron density of the PCM under the electron microscope (EM) may have limited early attempts to infer its organization. More detailed efforts using purified centrosomes and quantitative image analyses of EM or fluorescence micrographs have since provided indications of a higher order structure of the PCM [9, 14]. Specifically, the major PCM component pericentrin was found to be in a ‘lattice’ structure made of multiple interconnected rings by Doxsey et al. [15], while Rattner and colleagues reported a PCM circular ‘tube’ composed of centriolar proteins and pericentrin [16]. However, results derived from standard EM and light microscopy methods suffer from technical limitations of antigenicity preservation and relatively poor resolving power (given the size of the centrosome), respectively [9]. Without a consensus on a robust, alternative model with molecular details, the common perception of the PCM as an amorphous, electron-dense region has prevailed.

Subdiffraction resolution fluorescence microscopy has emerged as a powerful tool for the investigation of the architecture of protein complexes inside cells. Deterministic and stochastic super-resolution methods have been exploited so as to circumvent Abbe’s diffraction limit, and these advances were recently recognized by the Nobel Prize in chemistry (reviewed in [17]). Arguably the most practical implementation is three-dimensional structured illumination microscopy (3DSIM), which relies on modulation of the excitation light by spatial patterning. 3DSIM halves the resolution limit of traditional light microscopy (125 nm in the x/y plane and 250 nm in z), and readily accommodates multiple labellings and fluorophores without the need for special modifications to fixed or live samples [18]. Using 3DSIM, we and others analysed several centrosome components using positional mapping of domain-specific probes in multiple human cell lines. We demonstrated that they adopted a toroidal pattern with progressively larger, overlapping diameters around the proximal end of the mother centriole during interphase. On one side, the toroid was slightly opened in the area where the daughter centriole

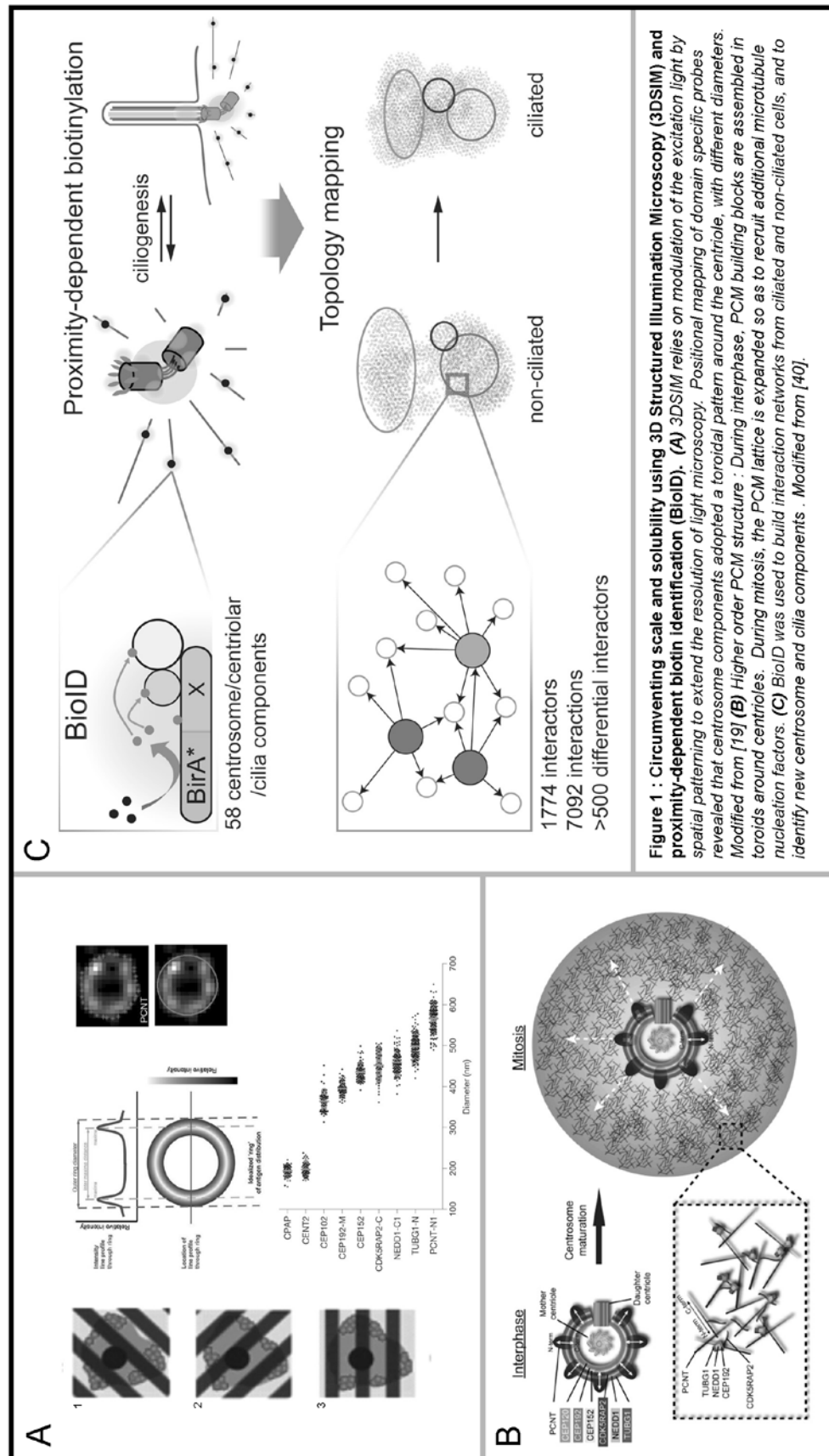
was positioned. Notably, pericentrin spanned the width of the PCM with a striking distribution. Targeting the N-terminal region of pericentrin yielded larger diameters than those from C terminal regions and probes targeting the middle region produced intermediate results. This suggested that pericentrin adopted an extended conformation and that it was anchored at the centriole wall region at its C-terminus, while the N-terminus projected outwards to the periphery [19]. Pericentrin molecules also formed spatial domains in the N-terminal PCM periphery, and their clustered appearance was reminiscent of the centriole 9-fold symmetry [9, 19]. Here, they were also found in close proximity to the microtubule nucleation-mediators NEDD1 and gamma-tubulin [19]. These findings were corroborated by parallel studies in different cell types and with other subdiffraction methods by Agard, Glover and Nigg [18, 20, 21], and together suggest that centriole symmetry may act as an organizing principle for the architecture of the PCM scaffold.

Another key finding was that the pericentrin-based toroid around the mother centriole was retained during mitosis, while the more peripheral spatial domains expanded and multiplied in number and size [19]. Dependency and recruitment analysis revealed that pericentrin was atop the hierarchy of components required to build the PCM scaffold during mitosis. We proposed a model whereby PCM building blocks are initially assembled in toroids around centrioles and released into the periphery where their organization is maintained during interphase. During mitosis, the PCM lattice is expanded so as to recruit additional microtubule nucleation factors in preparation for the generation of the spindle.

While these findings have provided a glimpse into the nano-architecture of the PCM, much work remains to be done to arrive at a more detailed structural map. The next steps that would advance the field would entail precise domain mapping of more PCM components, combined with fluorescent tagging at endogenous loci using clustered regularly interspaced short palindromic repeats (CRISPR) technology, as well as live 3DSIM to track the dynamics of PCM assembly.

Proximity labelling proteomics yields a network of centrosomal interactions

Shotgun proteomic, bioinformatic and genomic approaches have identified many centrosome proteins



[22]. We now seek to understand how this catalogue of proteins dynamically interacts with one another to drive centrosome form and function. However, due to the largely insoluble nature of the centrosome (presumably due to its high protein density and concentration of coiled-coil domains), generating detailed protein-protein interaction (PPI) networks for this organelle has remained challenging. The recent development of proximity labelling proteomic methods in living cells partially addresses this issue. Proximity-dependent biotin identification (BioID) is based on promiscuous biotinylation generated by the mutated form of the *E. coli* biotin-conjugating enzyme BirA* [23]. In a typical BioID experiment, a gene fusion encoding the protein of interest and BirA* is expressed *in vivo*. Once synthesized, the fusion protein of interest carries the BirA* tag on either its N- or C-terminus. Biotin is then added and after a typical 16-24 h labelling period, the cells are lysed, and biotinylated proteins are purified using streptavidin and identified using mass spectrometry. As labelling is proximity-dependent, potential interactors of the protein of interest must reside within the area reachable by the reactive biotinoyl-5'-AMP. This area (estimated to be ~10 nm) can be described as the practical labelling radius of BirA*. Although the exact value may vary depending on the protein complex under study, this radius is sufficient to allow detection of both direct interactors and non-interacting vicinal proteins, thus providing valuable information on the proteomic landscape surrounding the target. Crucially, the biotinylation modification will remain even after the interaction has ceased or the protein has moved out of range of the BirA* ligase, so BioID provides a 'history' of candidate PPIs under relatively physiological conditions. Also, unlike more conventional methods of affinity purification where stringent extraction buffers may disrupt protein-protein interactions, the strong affinity between biotinylated proteins and streptavidin allows cell lysis and protein isolation to be performed under harsher solubilization conditions [24]. For these reasons, BioID, which has been successfully implemented by the Raught and Gingras groups to investigate diverse cellular machinery and processes [25-39], is ideally suited for investigating the centrosome interactome.

We surveyed the interaction landscape of the centrosome by expressing 58 proteins as BirA* fusions in HEK293 cells for BioID. These fusions included proteins previously found to localize to the centriole, to centriolar appendages and to the centrosome-cilium interface. The resulting

interactome map contained 1405 unique components in a network with >4000 potential interactions [40]. We ensured the correct expression and localization of the fusion proteins, and validated a subset of these interactions using traditional affinity-purification and MS, as well as co-immunoprecipitation. The interactome was found to contain ~70% of the proteins identified in large scale proteomic studies, as well as to be enriched in genes associated with cilium and centriole formation, and those involved in ciliopathies and microcephalies. Critically, this 'known' space only amounted to ~5% of the interactions and 30% of interactors of the total BioID PPI complement, thus indicating that we revealed a very large, uncharted interaction space [40]. Systematic functional analysis of ~500 proteins (~30% of the interactome) using siRNA and automated high-resolution microscopy provided compelling evidence for novel roles for many of these in centriole duplication, ciliogenesis, and centriolar satellite formation. Further investigation of a number of previously uncharacterized proteins confirmed these as novel centrosome components, thus validating our gene discovery approach. An important additional facet of the study was the generation of BioID data from ciliated cells, which allowed us to examine how the centrosome interactome changed during ciliation. This yielded several observations: first, the most dramatic modulation of interactions during ciliation was observed for distal appendage bait proteins; second, gained interactors identified this way were likely to be enriched for ciliogenesis factors; and last, there was a 'surge' in interactors that were common to basal body and centrosome baits, particularly cytoskeletal and membrane trafficking components. These findings coincide well with existing models of the earliest steps of ciliogenesis involving vesicle trafficking of ciliary components to distal appendages of the mother centriole, followed by conversion to a basal body that docks at the plasma membrane [41]. The BioID centrosome-cilia interactome has thus provided a rich catalogue of candidate proteins and interactions which will enable us to understand centrosome function in exquisite detail [40].

The advent of newer proximity-labelling proteomic approaches with faster labelling times such as BioID2 and APEX [23] opens the possibility of deriving PPI networks with enhanced dynamic information. 3DSIM, proximity proteomics, and functional genomics have heralded an exciting era in centrosome biology. In the future, our

research program seeks to build upon these advances so as to increase the resolving power of our understanding of the centrosome and cilia function at all levels - cellular context, space, and time. This experimental approach can, of course, be applied to all cellular organelles.

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OPINION

Canadian science and the CSMB need to embrace Equity, Diversity and Inclusivity (EDI)

Imogen Coe

Dean, Faculty of Science, Ryerson University

Affiliate Scientist: Li Ka Shing Knowledge Institute,

Keenan Research Centre, and St. Michael's Hospital



The CSMB represents a major collective of research scientists in Canada and is therefore a significant voice for science in Canada, as has been evident in its advocacy in support of increased funding for the sciences at the federal level. As an organization that represents its community, it is the responsibility of CSMB, to advocate for the advancement, support, promotion and retention of all its members, regardless of sex, gender, ethnicity, sexuality, family status or disability. Science benefits from diversity, and diversity is a driver of innovation. We have heard a lot about innovation over the last few years – with relatively little understanding of what it really means. Indeed, Canada lags behind other jurisdictions in terms of general awareness, policy development and overall institutional commitments towards improved equity, diversity and inclusivity in science, technology, engineering and math (STEM). The current government has explicitly noted that diversity is a priority, and promoting diversity in science is part of the mandate of the Minister of Science. Increasing and embracing diversity is also an economic imperative for Canada, because we, like other G20 countries, are facing a shortage of skilled talent. As outlined by the Canadian Council of Academies in their [2015 report](#), “Canada is currently missing out on an important supply of skilled talent. Increasing the STEM participation of under-represented populations, including women and Aboriginal people, is an important strategy for diversifying the supply of STEM-skilled individuals. The recent federal budget was a heavily skills-based budget, aimed at feeding that STEM pipeline, while the recently released Fundamental Science Review spoke to

the need for enhance and embrace diversity within the scientific endeavour in Canada, and this is a clearly stated priority for [NSERC](#) and [CIHR](#). Academic science in Canada does not reflect the make-up of Canadian society and the recently reinstated [UCAS study](#) will almost certainly make this very apparent. The failure to engage significant proportions of the population in any enterprise is not good economic policy, and the failure to embrace EDI in STEM in Canada compromises creativity and suffocates innovation. A failure to leverage and engage all available intellectual capacity leads to lower quality outputs. For example, the failure to consider women’s body sizes in the development of air bags led to preventable fatalities when the technology was first introduced, and failures in voice-recognition software led to women’s voices literally being unheard (see “Unblocking the Clubhouse: Women in Computing” by Jane Margolis & Fisher, MIT Press). The tech industry continues to have a [well-documented problem](#) with diversity, which contributes to more [examples of technology](#) that is gender-biased, exclusionary and possibly dangerous. Ignoring 50% of the population in the development of your product or process would seem to be a significant oversight for any business and most G20 countries now recognize that diversity improves the bottom line by 15%. The wicked problems of the 21st century, like climate change, antibiotic resistance, water security and urban sustainability, will require all the brain power we can engage to find solutions. If we want to maintain our prosperity, our quality of life and our standard of living, Canada needs to address the lack of diversity and particularly, the low recruitment and

retention rates for women and other under-represented groups in STEM. Embracing EDI in STEM isn't just a good idea – it may be the only way we will find solutions that will solve some of the biggest challenges we face as a nation.

To achieve full and meaningful change in Canada, we need evidence-based policy changes that address organizational, institutional, structural and systemic barriers to full EDI in STEM. We need to collect data (both quantitative and qualitative) to inform policy and look to leading (best) practices in other jurisdictions. We need leadership by organizations such as CSMB, we need education, intentionality, accountability and, perhaps most of all, we need courage.

Every member of the CSMB has a role to play in improving science in Canada by embracing equity and diversity. Here are four steps (acknowledge, learn, act, build) that every member of CSMB can follow to help build a more inclusive and productive scientific community in Canada, which will benefit everyone:

1. Acknowledge that Canadian science is not currently equitable, diverse or inclusive

It still surprises me that Canadian scientists are unaware that there are barriers to full inclusion and access to participation in STEM in Canada. The voices that claim there is no problem or that any problem has been fixed are the voices of privilege and entitlement. And the privileged and entitled, who belong to the dominant group within a society, do not tend to see that there is anyone missing or disenfranchised when they look around them. They have not experienced bias, prejudice, exclusion, etc. and therefore cannot believe it exists. We need to acknowledge that there is a problem with equity and diversity in science and that we, collectively (men and women), need to improve access, engagement and participation for all under-represented groups.

So take a look at your student population in your school and/or university or your community. Canadian academic science is not reflective of our society and we must acknowledge that there are genders, colours, abilities and ethnicities missing in academic science and research. We must all start to ask questions about why that is – and then we must listen to the answers. I am often asked by [men in science what they can do to help support and advance under-represented groups in science](#) – and the

first thing I say is to listen and learn. Listen to the stories of the challenges they have experienced, and learn about the chilly climate or exclusionary culture many under-represented groups face. I have given more than 40 talks on EDI in STEM over the last 18 months or so and after each one, women and sometimes men share with me stories of exclusion (usually unintentional), marginalization (sometimes unconscious), and harassment (without consequences). I've heard from a graduate student who was told by male scientists that a panel discussion led by women was "just a bunch of vaginas talking"; the professor who says he always hires girls in the lab because they work harder and he can pay them less; the brilliant post-doctoral fellow at one of Canada's leading research institutes who had given up fighting the persistent harassment she experienced and was leaving science; the science student and elite athlete who began to doubt her abilities because she was asked, yet again, if she was "really sure she was a scientist because she sure didn't look like one"; the talented student who was told by a professor that she wouldn't last in the biomedical engineering program so perhaps she should drop out, enrol in Arts and find a rich husband; the junior scientist who was told by a senior scientist in her division to mind her own business when she raised the issue of an invited all-white male panel of speakers. Workshops for women in STEM and science camps for girls will not change participation rates of women and under-represented groups in STEM unless the culture and workplace also increase accessibility by removing systemic barriers and bringing in accountability and consequences. Everyone in science needs to acknowledge this and we all have a responsibility to contribute to finding solutions. These are not women's issues – these are human rights issues.

Many institutions now take stock of their own institutional diversity – which can be informative reading. Educate yourself about your own environment. Take a look around and be intentional about noticing who is there and who isn't. We cannot address inequity unless we first acknowledge that it exists, and yet this first step has been the hardest for some scientists in Canada. It is time to have courage and face this reality.

2. Learn the lexicon of EDI

We all need to be better educated in the [language and vocabulary of EDI](#). Academic leaders, hiring and review committees, graduate supervisors, professors – everyone involved in academic science should know what terms

like imposter syndrome and stereotype threat mean. Understand what intersectionalities are and why they are so important. Stop talking about the leaky pipeline (a derogatory and inaccurate metaphor) and start learning about [the glass obstacle course](#) and the invisible barriers that women and under-represented groups face. Find out how the Dunning-Kruger effect can manifest itself in science and how it can be experienced as exclusionary and hostile. Become aware of how language can be gendered. Understand that anyone – male or female – can experience imposter syndrome and that 100% of us have implicit or unconscious bias which affects all of our decisions and behaviours. Renowned German neuroscientist, Dr. Uta Frith, Chair of the Diversity Committee for the Royal Society (UK), commissioned [this animation](#) to explain bias. We should all be aware of our own implicit bias (by, for instance, taking the [Harvard Implicit Bias test](#)). We must be honest with how implicit bias colours our behaviours and decisions – and particularly, as scientists, we should accept the evolutionary biology and neuroscience that under-pin these irrational thought processes that all of us engage in. Being aware of our biases is the first step to disrupting them when we make decisions, so that we come closer to the objective scientists that we strive to be.

3. Act to correct inequity and promote diversity locally (and think globally)

We can all act to improve EDI in STEM. After acknowledging that it exists and learning to frame the issues using the appropriate language, then it is time to find ways to act in our local environments. This could mean ensuring that your local seminar series or regional conference panel is diverse. As Dean of Science, I am often asked for funding support for organizing conferences and I usually provide support with a clear expectation of a commitment to EDI by the organizers. I expect organizers to be intentional about [choosing a diverse slate of speakers](#) and I provide [resources to assist](#). Every scientific conference held in Canada should have a [code of conduct](#) and if conferences fail to meet minimum standards of equity, diversity and inclusivity, they should be called out.

Every CSMB member can promote EDI by speaking up about being aware of things like implicit bias and highlight the importance of EDI in any number of settings such as discussions about hiring, resource allocation, nominations etc. This is a reasonable expectation for more senior and secure members of the community (male and female)

but might be challenging for early career investigators. However, it is possible to engage in positive action in support of under-represented colleagues by amplifying the voices of the under-represented, repeating the good ideas put forward by minority colleagues, and sponsoring them for awards, presentations, nominations, committee panels, etc. Active participation by members of the dominant group (usually white males) in events that promote minorities – such as Ada Lovelace Day, Black History Month, International Women’s Day and similar – sends a clear message that these individuals are valued and recognized. Scientists can also ask for data to explain anomalies in allocations of resources – whether it be grants, assignments, workloads or space.

Holding individuals accountable for inappropriate behaviour and offensive statements is critically important and male scientists, in particular, must call out sexist and racist comments. It is not incumbent on the under-represented group to call out, name and fix systemic and structural barriers to inclusion and equity. This is known as the minority tax. Being one of the few women in a department inevitably leads to being asked to be the “diversity” representative on every committee. As if women were a single homogenous group that all speak with one voice for one another. They don’t. Middle-aged, white men, who have developed a strong EDI awareness and vocabulary, and who have a sincere intentionality to seek fairness and excellence, can be outstanding “diversity” representatives on many committees. It is time for members of the dominant group to step up in this way. [Be an ally to women](#) and under-represented groups in science. Remarkably, only 25% of science societies in Canada have statements that explicitly commit to EDI. If you have security and seniority, step up, speak out and commit to EDI in your society, department, division, institution or organization.

It is absolutely incumbent on academic leaders and scientists in positions of power and privilege to act to promote EDI in real and meaningful ways. Cultural change depends on modelling of appropriate behaviour by leaders, and articulating principles and values. Individuals or groups with authority and security have a special responsibility to call out inappropriate behaviour and to hold others accountable. This is the responsibility of leaders – regardless of gender or ethnicity. Act to call out inappropriate behaviour, as I did in 2015, when Science Careers posted offensive advice under their Ask Alice

column. [I wrote a letter to AAAS](#) that was shared around the world by social media and [which was subsequently used in a revised response in Science](#) describing appropriate advice for young women in science – notably quite different from that initially provided by Dr. Alice Huang. We currently have a dearth of male leaders in science who are willing or able to step up and speak to the inherent value of EDI in STEM. Academic science is one of the last remaining bastions of institutionalized misogyny and the power to change that rests with all of us. Regardless of your gender or ethnicity, it is the role of men and women to create an inclusive environment. A failure to act to advance EDI is a failure to be a leader these days.

4. Build initiatives for systemic change to achieve EDI in STEM

In contrast to Canada, other jurisdictions have implemented programs to advance EDI in STEM. In the UK, the [Athena SWAN program](#), which helps institutions implement policies that achieve EDI, have benefited from the concerns raised by professional scientific bodies about the lack of diversity in their own communities. While an Athena SWAN program would be difficult to copy in Canada (because of the provincial/federal division of responsibilities), the concept of scientific organizations (such as the CSMB) being key partners for national or provincial level EDI programming is clear. Moreover, since the idea that research funding might be linked to EDI metrics was raised as a potential incentivizing tool for Athena SWAN, the role of CSMB in working closely with provincial and/or federal agencies involved in a program of this sort is obvious.

We need programs and initiatives in Canada that are developed using an evidence-based approach to create a fabric of support across the country for a diverse workforce in science. What we do not need are specialized programs that target women or others (as the under-represented group) and focus on “fixing” them. There is no amount of mentoring or leadership workshops that will change the numbers of women (or under-represented groups) in science if we do not address the systemic, institutional, organizational and cultural barriers. The well-known NSERC-supported UFA awards for women were discontinued when data suggested that they were not effective in increasing retention of women in science. This is inevitable for any group-specific program that fails to address cultural barriers and systemic bias

in the environment that exists for that group in STEM. The Fundamental Science Review may provide an opportunity to re-investigate the benefits of a UFA-type program in support of EDI in STEM, but this should only be pursued in combination with programming modelled on best practices from elsewhere. In the UK, the [Daphne Jackson awards](#) appear to be helping science understand that there are many different types of pathways to a career in academic science. The Canadian version could be the Maud Menten awards or Harriet Brooks or Alice Wilson awards. Programs such as the Daphne Jackson awards, when combined with an Athena SWAN-like program, which addresses institutional systemic barriers and biases, bring both targeted and systemic approaches to achieve real impact. The Athena SWAN [program has also been rolled out to Australia](#), where it is known as [SAGE](#) pilot, and this might be a stronger model for Canada to adopt since Australia is a federation of semi-autonomous states much like Canada. The major scientific societies like the CSMB are critical advocates for systemic change and should be advocating for programs that will help to build a [national strategy around EDI in STEM](#). Remarkably, our data suggest that about 75% of Canadian scientific societies have no clear articulation in their mission to equity and diversity – suggesting that we still have a long way to go in terms of the scientific community recognizing this as being a priority.

Another avenue for advocacy is to work to bring government, business, industry, academia and education together to build systems that support a strong and diverse STEM workforce such as is seen in the UK with the [WISE Campaign](#).

The power of the Athena SWAN and the SAGE programs are that they hold the institution and the institutional culture and context responsible for EDI – and this is a strongly evidence-based approach that has been shown to work more effectively than programs that focus exclusively on girls or women and try to make them “fit” into a model that refuses to address structural, systemic, persistent and cultural barriers to inclusion and equity.

How do we achieve EDI in STEM? [Studies](#) support the efficacy of evidence-based policy changes that address organizational, institutional, structural and systemic barriers. We need data-driven approaches, using rigorous qualitative and quantitative data, which are informed by best (leading) practices in, for instance, [the UK](#) and

[Australia.](#)

I invite all members of CSMB, at all levels, in all disciplines, to acknowledge the systemic challenges to full equity, diversity and inclusivity in STEM in Canada, to learn more about EDI, to act in ways that support EDI at the individual, institutional, organizational level. Diversity drives innovation and improves outcomes and quality of product. Science tells us this. As scientists, we should all listen and act accordingly.

Parts of this article have been taken from various blog posts and other work which can be found at <https://imogencoe.blog.ryerson.ca/>

News from Member Departments

Dalhousie University

Department of Biochemistry and Molecular Biology

Correspondent: Stephen L. Bearne



Dr. David Langelaan,
Assistant Professor
(photo courtesy of Heidi McKinnon)

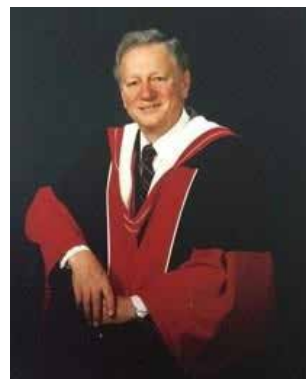
The 2016-17 academic year has been a time of renewal within the Department of Biochemistry and Molecular Biology at Dalhousie University. In July, we were very pleased to have **David Langelaan** join the Department as an Assistant Professor. David brings to the department his expertise in protein structure and function, specializing in both NMR spectroscopy and X-ray crystallography of biomolecules. David's research

will focus on protein self-assembly processes for biotechnological applications, and intermolecular interactions that transcription factors use to control cell differentiation, particularly as it relates to cancer. **Jan Rainey** is currently serving as the Treasurer for the CSMB and **Barbara Karten** was elected to a three-year term as a CSMB Councillor. **John Archibald** was inducted into the Royal Society of Canada's College of New Scholars, Artists, and Scientists. **Roger McLeod** stepped away from his teaching for the year to serve as Acting Associate Dean of Research within the Faculty of Medicine.

On a sad note, **Christopher W. Helleiner**, Professor Emeritus, passed away on October 18, 2016. Chris received his Ph.D. from the University of Toronto in 1955 ("Studies of the Structure of DNA"), which was followed by post-doctoral work at Oxford University. After serving as an Assistant Professor at the University of Toronto and a research scientist at the Ontario Cancer Institute, he joined the Department of Biochemistry at Dalhousie in 1963, serving as Department Head from 1965 to 1979. Chris opened the department in the Sir Charles Tupper Medical building in 1966 and oversaw its rapid growth

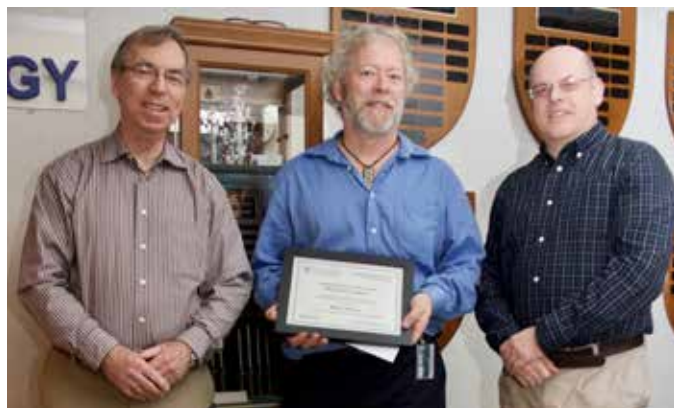
over the next decade. During his long career at Dalhousie, Chris maintained an active research program and distinguished himself as an inspirational teacher and mentor, not only for students but also for faculty. He played an instrumental role in developing many of the classes that the department still offers today. His superb teaching abilities were recognized in 1987

when he was awarded the Dalhousie Alumni Association Award for Excellence in Teaching. After retiring in 1995, Chris continued to teach students in nursing and biology until 2004. Subsequently, he was appointed to the rank of Professor Emeritus in recognition of his achievements and his exemplary service to the department, faculties of Medicine and Science, and Dalhousie University. He will be greatly missed.



Dr. Christopher W. Helleiner
(1930-2016)

During the past year, the department has continued to celebrate the success of its students, post-doctoral fellows, and research associates. **Bruce Stewart**, a long-time technician within the department and currently working in **Jan Rainey's** laboratory, received the 2016 Schnare-Spencer Prize, which was established by **Mike Gray** in honour of two long-time research associates in



Dr. Michael Gray, Bruce Stewart, and Dr. Stephen Bearne (left to right) and the presentation of the Schnare-Spencer Award (photo courtesy of Heidi McKinnon)

his lab. **Antonieta Pietrangelo**, a graduate student with **Neale Ridgway**, and **Kyungsoo Shin**, a graduate student with **Jan Rainey**, both received Beth Gourley Conference Awards, which were established by **Catherine Lazier** and her husband John Lazier.



Dr. Catherine Lazier presents the Beth Gourley Conference Award to Antonieta Pietrangelo (Ph.D. student) (photo courtesy of Heidi McKinnon)



Dr. Catherine Lazier and John Lazier present the Beth Gourley Conference Award to Kyungsoo Shin (Ph.D. student) (photo courtesy of Heidi McKinnon)

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 <http://www.biochem.dal.ca>.

Hospital for Sick Children Research Institute, Toronto

Correspondents: Charles Deber and Peter Kim

Cell Biology Program

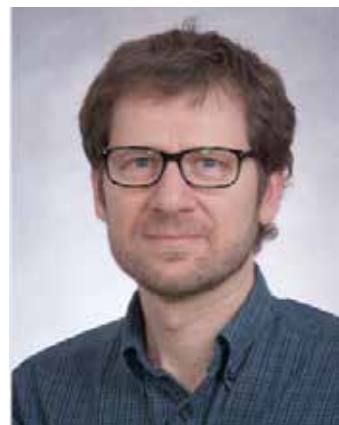


Dr. Cynthia Hawkins

Rubinstein Award from the American Association of Neuropathology:

Dr. Cynthia Hawkins, Senior Scientist, The Arthur and Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children, and Professor, Associate Professor, Departments of Laboratory Medicine & Pathobiology, University of Toronto, has been awarded the

2016 Lucien J. Rubinstein Award from the American Association of Neuropathology for her groundbreaking work on pediatric gliomas. Dr. Hawkins, together with Dr. Uri Tabori, characterized the morphologic and genetic features of low-grade gliomas in children. This work is the first to establish prognostic and predictive factors in this disease and has led to changes in clinical management of these children.



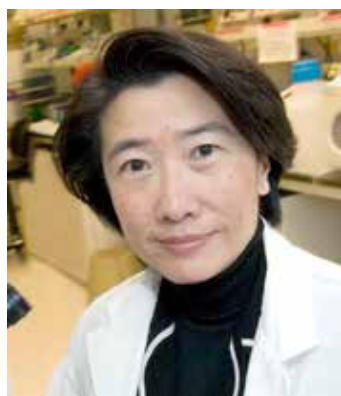
Dr. Ran Kafri

Early Researcher Award:

Dr. Ran Kafri, Scientist, Hospital for Sick Children, and Assistant Professor, Molecular Genetics, University of Toronto, was awarded an Early Researcher Award from the Ontario Ministry of Research and Innovation.

This award was for his research program in cell size regulation in animal cells. Dr. Kafri is an early career researcher whose research focuses on understanding the mechanisms that regulate cell size and how this dysregulation is linked to diseases.

Physician-Scientist Award:



Dr. Rae Yeung

Dr. Rae Yeung, Senior Scientist, Hospital for Sick Children, and Professor, Departments of Paediatrics and Immunology and Institute of Medical Science at University of Toronto, has been awarded the Physician-Scientist award from the Hospital for Sick Children/University of Toronto.

The award recognizes the accomplishments of a physician who has generated a body of research that is exerting a major impact in a field of study. Dr. Yeung received the award for her work in Kawasaki disease, childhood arthritis, and rheumatic diseases. Her research explores the molecular and cellular mechanisms governing autoimmunity towards discovery of molecular tools for improving disease diagnosis, treatment, outcome and prevention.

Society President:

Dr. Nicola Jones, Senior Scientist, Hospital for Sick Children, and Professor, Departments of Paediatrics and Physiology, University of Toronto, has been elected President of the Canadian Association of Gastroenterology for 2018-2020. Dr. Jones is also Principal Investigator of the Canadian Child



Dr. Nicola Jones

Health Clinician Scientist Program. Her research centres on cellular and molecular mechanisms by which infection and inflammation contribute to gastroenteric diseases such as *Helicobacter pylori* infection, inflammatory bowel disease, and inflammation-mediated cancers.

Banting Fellowship:

Dr. Spencer Freeman, Post-doctoral fellow, Hospital for Sick Children, has received a 2016 Post-doctoral Banting Fellowship award for his work in signalling in macrophages. After completing his Ph.D. at the University

of British Columbia in 2014 with a focus on Cellular Immunology, Dr. Freeman joined the laboratory of Dr. Sergio Grinstein at SickKids. His work focuses on biophysical mechanisms of receptor engagement and signalling; combining techniques like single particle tracking and micro-patterning to reveal how diffusion in membranes contributes to responses. These cutting-edge approaches have led to more than 25 publications, including articles in *Cell* and *PNAS*.



Dr. Spencer Freeman

Vanier Graduate Scholarship:



Ivette Valencia-Sama

Ms. Ivette Valencia-Sama, a PhD candidate in the laboratory of Drs. Meredith Irwin (Cell Biology, SickKids) and Michael Ohh (Laboratory Medicine and Pathobiology, University of Toronto), was awarded a CIHR Vanier Canada Graduate Scholarship (CGS). This scholarship is valued at \$50,000 per year for three years and considers three evaluation criteria:

research potential, academic excellence and leadership. Her project focuses on investigating the molecular mechanisms involved in neuroblastoma tumorigenesis and chemo- resistance, with particular interest in understanding the roles of the RAS-MAPK signalling pathway in neuroblastoma pathogenesis.

Molecular Medicine Program

Merrifield Award from the American Peptide Society:

Dr. Charles Deber, Senior Scientist in the Program in Molecular Medicine, Research Institute, Hospital for Sick Children, and Professor in the Department of



Dr. Charles Deber

Biochemistry, University of Toronto, has received the 2017 Bruce Merrifield Award of the American Peptide Society. The award was created in 1997 in honour of Dr. R. Bruce Merrifield, who won the Nobel Prize in Chemistry in 1984. The award is presented every two years to leaders in the field who have demonstrated outstanding career accomplishments in

peptide research, “recognizing the highest level of scientific creativity”. Dr. Deber’s research focuses on the hierarchy of forces that characterize the interactions of peptides and proteins with membranes, and how these forces produce membrane protein structure and function. The award is being presented to Dr. Deber and co-recipient Dr. Robert Hodges, University of Colorado, at the 25th American Peptide Symposium in Whistler, B.C. in June, 2017.

Election to the Royal Society of Canada:

Dr. Julie Forman-Kay (Senior Scientist, The Hospital for Sick Children; Professor, Department of Biochemistry, University of Toronto) has been elected as a Fellow of the Royal Society of Canada (FRSC). Dr. Forman-Kay is currently Program Head in Molecular Medicine at the SickKids Research Institute. Dr. Forman-Kay is a leading expert in the structural and functional analysis of molecular pathways, particularly by NMR spectroscopy, and has made internationally-recognized contributions to our understanding of intrinsically-disordered proteins.

McGill University

Department of Biochemistry

Correspondent: Martin Schmeing (with John Silvius and Marlene Gilhooly)

In the several years since the last report from McGill Biochemistry, **Sid Huang**, **Uri-David Akavia** and **Ian Watson** have been recruited as Assistant Professors. **Martin Schmeing** has been promoted to Associate Professor, and **Arnim Pause** and **Julie St. Pierre** have

been promoted to full Professor. **Albert Berghuis** was appointed chair of the department. **Phil Branton** retired in 2016 after many years in the department.

The department continues its strong contribution to teaching. Over the past year, the department has continued to introduce and refine new initiatives to improve our undergraduate program, and to introduce more ‘active learning’ approaches into our courses. The team project-based component of BIOC 404 (Protein Structure and Function), to which roughly 25% of total classroom time in the course is devoted, was introduced in 2014 and has now been refined. A second, new undergraduate course (BIOC 470, Lipids and Lipoproteins) devotes roughly 30% of class time to seminar-style discussions based on student oral presentations. These innovative features of both courses have been very well received by the students. Beginning in 2015-16, departmental instructors introduced more interactive elements into four other undergraduate lecture courses: BIOC 311 (Metabolic Biochemistry), BIOC 454 (Nucleic Acids), BIOC 404 (Biophysical Methods in Biochemistry) and ANAT/BIOC 458 (Membranes and Cellular Signaling). In each course, a portion of every lecture is devoted to questions presented by the instructor and specifically structured to stimulate in-class discussions, prompting (and guiding) students to apply the lecture material in novel contexts and directions. After two years, there is a consensus among faculty and students alike that this new, more systematic approach to promoting class discussion is proving very effective in enhancing student engagement. The new undergraduate laboratory course, BIOC 220, was offered this year for the second time. It provides students with an optimal first exposure to the laboratory practice of biochemistry and an optimal preparation for the follow-up laboratory course, BIOC 320. BIOC 220 is preparing students very well for BIOC 320, but will be refined in the coming years to concentrate more time on teaching the essential basic skills that are required to write high level laboratory reports.

The past year saw department members continue to publish exciting research results. Among the highlights are: **Thomas Duchaine** published studies which detail the dynamic interplay of mRNA 3'-untranslated regions with the miRNA machinery, including showing that miRISC interactions with the Ccr4-Not complex on target mRNAs nucleate mRNP assembly and leads to phase separation by intrinsically disordered region proteins

(*Nucleic Acids Res* 44 (12); *Nucleic Acids Res pii:gkw872*). **Kalle Gehring's** laboratory reported the involvement of phosphocysteine in mediating magnesium homeostasis through a newly discovered pathway involving a family of oncogenic phosphatases, PRLs (*EMBO Rep* 17 (12)). **Bill Muller** and colleagues described the role of tutor specific Stat3 in immunosuppression (*Cancer Research* 76 (6)). **Alain Nepveu's** studies demonstrated that proteins containing CUT domains function as auxiliary factors in DNA repair and increase the resistance of cancer cells to DNA damaging treatments (*J Biol Chem* 291 (43); *Oncotarget*, 8 (12)). **Martin Schmeing's** group visualized the entire catalytic cycle of the initiation of the nonribosomal protein synthetase that makes the antibiotic linear gramicidin, and used chemical biology tools to gain insight into nonribosomal peptide bond formation (*Nature* 529 (7585); *Cell Chem Bio* 23 (3)). **David Thomas'** research group described modulation of the unfolded protein response and protein quality control systems by ribosylation of the primary transducer IRE1, along with the development and characterization of latonduine and more potent analogues (*Mol Pharmacol* 90 (2)). **Arnim Pause's** lab established that the ESCRT component HD-PTP/PTPN23 is a prominent haploinsufficient human tumour suppressor gene which prevents tumour progression through control of integrin trafficking (*Cell Rep* 15 (9)).

Department of Biochemistry faculty were recognized with a variety of honours and awards in 2016. **Nicole Beauchemin** received the Limelight Award from the Goodman Cancer Research Centre for long standing commitment to cancer research and public education. **Maxime Bouchard** received the FRQS-Senior Research

Scholar Award. **Phil Branton** was named the Gilman Cheney Professor Emeritus in Biochemistry and received the McGill University Medal for Exceptional Academic Achievement. Notably, in 2014, Phil was appointed as an Officer of the Order of Canada, in recognition for his leadership in the development of a national cancer research framework, and for his contributions to our understanding of tumour viruses and cell division regulation. **Josée Dostie, Thomas Duchaine and Julie St. Pierre** won salary awards from the FRSQ. **Philippe Gros** was named to the Order of Canada for his pioneering use of molecular genetics to identify risk factors in a range of conditions, including infectious diseases and cancer, and for his leadership in the health sciences. **Rod McInnes** received the American Society of Human Genetics Arno Motulsky-Barton Childs Award for Excellence in Human Genetics Education. **Martin Schmeing** received the Joe Doupe Young Investigator Award from the Canadian Society for Clinical Investigation. **Nahum Sonenberg** was named a Distinguished Investigator of the Mental Health Research Association, received an honorary doctorate from Université Laval, the Leadership Impact Award from the Rosalind & Morris Goodman Cancer Research Centre and the IUBMB Lecture Medal and Certificate from the International Union of Biochemistry and Molecular Biology. Notably, in 2014, Nahum was awarded the Wolf Prize in Medicine, Wolf Foundation, 2014. **Ian Watson** received the Melanoma Research Alliance Young Investigator Award and the V Foundation Scholar Award.

The department also hosted many stimulating events for our undergraduate and graduate students. Of particular note are the BUGS (Biochemistry Undergraduate Society) Research Awareness Day, the BGSS (Biochemistry



Talk at Biochemistry Undergraduate Society Research Awareness Day



Lunch at Biochemistry Undergraduate Society Research Awareness Day

Graduate Student Society) Research Day, and the annual Pelletier lab/Biochemistry Department Christmas party (complete with piñata). More glimpses into departmental life can be found at <https://www.facebook.com/mcgillbioc> and <https://www.mcgill.ca/biochemistry/about-us/events/community>



Student group at Biochemistry Undergraduate Society Research Awareness Day



Group photo at Biochemistry Undergraduate Society Research Awareness Day

McMaster University

Department of Biochemistry and Biomedical Sciences

Correspondent: Alba Guarné

In 2016, the Stem Cell and Cancer Research Institute celebrated its 10th anniversary. There have been many discoveries over the past ten years, and this year was

no exception. **Kristin Hope** published a seminal article in *Nature* that represents an important step forward in overcoming the obstacles of stem cell transplants (*Nature* 532: 508-511); **Mick Bhatia's** team showed that accurate prediction of acute myeloid leukemia in MDS patients is possible (*Cancer Cell* 29:61-74); **Karun Singh** published his first senior author paper describing how DIXDC1 regulates the formation of brain connections (*Cell Reports* 17: 1892-1904). The rest of the department joined in the successes of our SCCRI investigators. Using a mouse model of Crohn's disease, **Brian Coombes** and his team discovered that acute infectious gastroenteritis caused by common food-poisoning bacteria accelerates the growth of adherent-invasive *E. coli* (*PLOS Pathog* 12: e1005907). **Gerry Wright** continued to bring members of the department together to fight antibiotic resistance. In collaboration with **Alba Guarné** and Alexei Savchenko (Toronto), the Wright lab discovered a novel mechanism of antibiotic resistance (*Nature Commun* 7:11343). In collaboration with **Andrew McArthur**, they characterized a diverse intrinsic antibiotic resistome from a cave bacterium (*Nature Commun* 7:13803). **Eric Brown**, in collaboration with **Brian Coombes**, discovered how pentamidine sensitizes gram-negative pathogens to antibiotics (*Nature Microbiol* 2:17028).

The excellence of BBS faculty is reflected in the level of research funding, with a total of \$15.5 M for 2015-16. **Eric Brown** was awarded one of the first 150 CIHR foundation grants for his work on identification of novel antibacterial targets. Teams lead by **Nathan Magarvey** and **Deborah Sloboda** were awarded a CIHR team grants to develop natural antibiotics for treating drug-resistant bacteria and to study how the microbiome of obese mothers influences the development of inflammation and obesity in their offspring, respectively. **Marie Elliot**,

associate member of the Department, renewed her NSERC Discovery grant and received an NSERC Discovery Accelerator Supplement. Our new recruits also made a splash on the funding competitions. **Lesley MacNeil** received NSERC funding and was also awarded an Accelerator Award.



Alba Guarné (2016 winner, right) and her nominator, Deborah Sloboda (left), celebrating at the 40th YWCA Women of Distinction awards ceremony

Matthew Miller had the highest ranked operating grant application in the 2015 CIHR transitional operating grant competition, garnering him the 2015 Bhagirath Singh Early Career Award from the Institute of Infection and Immunity. Our faculty were also successful in capturing infrastructure funds, with recent CFI awards to **Andrew McArthur** (for a new bioinformatics laboratory), **Joaquin**



2016 Karl Freeman Awardees: Jennifer Reid, Claudia Hung, Professor Karl Freeman, Tiffany Leighton and Fiona Wheelan



2016 Michael Kamin Hart Memorial Scholarships: From left to right, Gerry Wright (Director of the IIDR); Aaron Hart, Michael's brother; Jill Kamin, Michael's mother, Justin Nodwell (former IIDR member and Michael Hart MSc supervisor); Murray Hart, Michael's father; Fiona Wheelan (PhD student and recipient of the Michael Kamin Hart Memorial Scholarship); Savannah Colameco (scholarship recipient); Michael Ranieri (scholarship recipient); David Hart, Michael's grandfather

Ortega (for a cryo-EM microscope fitted with a direct electron detector) and **Gerry Wright** (for a platform for antibiotic discovery).

Alba Guarné won the prestigious 2016 Women of Distinction Award from the Hamilton YWCA, in recognition of her contributions to empowering women in science. **Eric Brown** was elected as a Fellow of the American Academy of Microbiology. **Gerry Wright** was named



Dr. Yu Lu

Distinguished University Professor and received the NRC Press Senior Investigator Award from the Canadian Society of Molecular Biosciences. **Lori Burrows** and **Jonathan Schertzer** were awarded Excellence in Graduate Supervision Awards from the Faculty of Health Sciences. **Brian Coombes** was designated a University Scholar, he joins past awardees from the Department **Marie Elliot** and **Greg Steinberg**. **Felicia Vulcu** was awarded with the MSU Teaching award for the Faculty of Health Science. Closing a strong year, **Deborah Sloboda** was honoured with the 2015 Nick Hale Award from the International Society from Developmental Origins and Health Disease.

Our graduate program welcomed 36 new students this year, including 25 in the MSc stream, 8 direct entry PhD



2016 Biochemistry Picnic: Our faculty team (Gerry Wright, Lori Burrows, Nathan Magarvey, Deb Sloboda and Matthew Miller) celebrating their 2nd place at the Biochemistry Olympics. Well done!

and 3 MD/PhD. Half of them came from our own undergraduate program and the other half from across Canada and abroad. Our students won 31 major scholarships in 2016, a record number, and an increase of eight awards from 2015. The Karl Freeman Awards, recognizing the best seminars in our graduate seminar series, were a women-only-affair this year, and were awarded to **Fiona Whelan** (1st PhD, Surette Lab), **Tiffany**

Leighton (2nd PhD, Burrows lab), **Jennifer Reid** (1st MSc, Bhatia lab) and **Claudia Hung** (2nd MSc, Truant lab). Through the continued and generous support of the Hart family, **Fiona Whelan** (PhD student) and **Sara Dizzell** (MSc student) won Michael Kamin Hart Memorial Scholarships, and **Michael Ranieri** and **Savannah Colameco** received summer undergraduate scholarships to continue their work in antimicrobial diseases.



Biochemistry Welcome BBQ 2016: Lori Burrows catching up with graduate and undergraduate students in our program



Biochemistry Halloween celebrations: Yingfu Li activating the professor factory machine

Our newest member, Dr. **Yu Lu** joined the Stem Cell and Cancer Research Institute in January. Yu obtained his PhD from the University of Washington, where he studied proteomics methodology development and biological applications. He then moved to the Dana Farber Cancer Institute for post-doctoral training, where he used proteomics and genomics to systematically study signalling networks involved in embryonic stem cell fate transition. **Alba Guarné** and **Joaquin Ortega**, our structural biology husband-and-wife duo, will move their laboratories to McGill University next year. Therefore,

the Department has spent a significant amount of time recruiting new faculty. Two new assistant professors, **John Whitney** (bacterial pathogenesis) and **Sara Andres** (DNA repair), as well as a mid-career medicinal chemist, **Jakob Magolan**, will join the Department during 2017.

Meagan Heirweigh, instructional assistant, left the department to pursue a new career opportunity in California. We are excited to welcome **Vivian Leong** to our teaching ensemble. Vivian has extensive research experience; she has worked as research associate for several laboratories in the Department since 2003 and is a talented laboratory instructor. Welcome Vivian!

As in previous years, the Biochemistry and Biomedical Sciences Graduate Association (BBSGA) helped us maintain a balanced -yet competitive- life style. We had a well-attended Biochemistry Picnic in June where we held once again the Biochemistry Olympics, and the Welcome Barbecue in September, where we welcomed new and returning Biochemistry and Biochemical Discovery and Commercialization students. The **Li** laboratory again ruled the Halloween costume contest, closely followed by the **Coombes** and **Burrows** laboratories.

Memorial University of Newfoundland

Department of Biochemistry

Correspondent: Mark D. Berry

This is the first report from the Department of Biochemistry, Memorial University in a couple of years and coincides with 2017 marking the 50th anniversary of the Department. To mark the occasion, preparations for an all years reunion of alumni, faculty and staff, from any of the programmes offered by the Department (Biochemistry, Nutrition, Food Science, and previously Dietetics) is planned. A committee of alumni spanning the 50 years of the Department has been established and they will be reaching out to fellow alumni over the next few weeks. While events are still being finalized, festivities will occur between September 7-11, 2017, in order to coincide with alumni events occurring in other units at Memorial University. All alumni are encouraged to set aside this timeframe and sign up for updates. Full details are available on the department's web and Facebook pages, and will be updated as things are finalized.

The few years have seen a period of turn-over in the Department. **Dr. Mark D. Berry** joined in July 2014 as the new Head of Department. Dr. Berry joined the Department from Brandon University, where he was a member of the Chemistry Department, including serving as the Department Chair. Prior to Brandon University, Dr. Berry had worked for several years at ALviva Biopharmaceuticals Inc., a University of Saskatchewan spin-off company based in Saskatoon. He brings extensive neurochemistry expertise to the department,

particularly in the area of Trace Amine-Associated Receptors, their endogenous ligands, and their roles in the modulation of central nervous system activity.



Ryan Mailloux

Dr. Ryan Mailloux joined the Department as an Assistant Professor in September 2015, coming from a Research Associate position at the University of Ottawa in

Dr. Laurie Chan's group. Dr. Mailloux supplements the existing and long-standing expertise in the Department in metabolic pathways, bringing a focus on mitochondrial bioenergetics and free radical signalling. Dr. Mailloux has rapidly established a functional laboratory, and we are excited to see his research and teaching career development over the coming years.

The last two years have also seen the retirement of a number of long-standing members of the Department. **Dr. Phil Davis** retired in December 2016; he joined the department as a faculty member in 1986, and held the distinction of also being an alumnus of both our undergraduate and graduate Biochemistry programmes. Dr. Davis also served multiple terms as Department Head, and his expertise in lipid metabolism will be sorely missed. **Dr. Gene Herzberg** will also be retiring at the end of the 2016/17 academic year after 40 years in the Department, again including a spell as Department Head. Dr. Herzberg was a major driving force in our Nutrition programme, a hugely popular lecturer, and leaves a very large pair of shoes to fill. **Dr. Sue Ghazala** departed in October 2015 after 24 years during which she was a mainstay of the

Food Science programme, and was a major shaping force in the Department for many years. All three individuals have made a lasting impact, and we wish them all a long and healthy retirement.

Two long-serving staff members have also recently retired. **Ms. Anne Sinnott** retired in June 2016 after 30 years of stellar service as an Administrative Assistant. Not only did Anne keep the department and research grant accounts in order, but she was one of the primary coordinators of the campus Food Bank and department social committees. We are delighted to welcome **Ms. Cathy Perry**, who joins the Department from ACENet, as Anne's replacement. **Ms. Donna Jackman** also retired in December 2016 after an amazing 36 years in the Department as a research technician. During that time Donna worked in the labs of a number of faculty members and her protein biochemistry expertise is going to be sorely missed.

The department was saddened to learn of the sudden and unexpected passing of **Dr. Ratnajothi (Jothi) Hoover** in August 2016. Jothi had been a member of the department for 28 years, and was a cornerstone of the Food Science programme. He obtained his Bachelor's degree (Honours) in Chemistry from the University of Ceylon (as it then was), followed by a Master's degree in Food Science from the University of Leeds, before coming to Canada. He received his PhD in Food Science at the University of Alberta, and was an Assistant Professor at the University of Ottawa before joining the faculty at Memorial University. Dr. Hoover had a lifelong interest in the chemical and physical properties of starches with a view to optimizing the use of starches from novel and different sources in the food industry. In this area he was internationally renowned and his research program was funded continuously by NSERC since 1988. Together with his students, he published close to 100 papers over his career. Dr. Hoover trained many students - including many from Sri Lanka - and some postdoctoral fellows over his career. They all benefitted from his diligence and the rigorous training he provided. He will be missed by all his trainees, past and present, and by all of us in the department of biochemistry. Our thoughts and condolences continue to be with Dr. Hoover's family, friends, and colleagues.

Congratulations go out to **Dr. Sean Brosnan** who in 2016 was inducted as a Fellow of the Texas Institute

for Advanced Studies. This highly prestigious award was established by Texas A&M University in 2010, and recognizes scholars for outstanding professional accomplishments. Election requires that nominees be a member of their home country's national academy (the Royal Society of Canada) and have an outstanding research programme. At the time of his induction there were only 35 fellows, including several Nobel laureates. Dr. Brosnan is internationally renowned for his pioneering work into the metabolism of amino acids and one-carbon units, including the mechanisms of amino acid conversion to glucose, hormonal regulation of amino acid metabolism, and more recently the role of folate in one-carbon metabolism. As part of this award Dr. Brosnan will spend 12 months over the next few years conducting collaborative research at Texas A&M.

Congratulations also go out to **Drs. Valerie Booth, Rob Brown** and **Sherri Christian**. Dr. Booth, a Canada Research Chair in Membrane Proteins was recently promoted to Full Professor. Dr. Booth's research examines lung surfactant peptides, antimicrobial peptides and structure-based design of new psoriasis therapeutics. Drs. Brown and Christian have both recently received tenure and promotion to Associate Professor. Dr. Brown's research examines the roles of lipids and lipoproteins in health and disease, while Dr. Christian's research focusses on cellular responses to changes in their environment, in particular the role of CD24 and microvesicles.

Ryerson University

Department of Chemistry and Biology

Correspondent: Roberto Botelho

The Department of Chemistry and Biology encompasses multi-disciplinary interests in research and education. Our Chemistry research programs are generally focused on macromolecular, synthetic and medicinal chemistry. The research interests in Biology enjoy strengths ranging from biochemistry, molecular and cell biology to genetics, microbiology and environmental biology. The breadth and variety of research interests creates an exceptional environment that permits cross-pollination of ideas and an open-concept milieu for learning and teaching. Last year, we had several notable events worth sharing with the CSMB community. Together with the Faculty of Science, now entering its fifth year of existence, we have seen continued growth in undergraduate and

graduate enrollment (60% and 20% increase over five years, respectively), 17% increase in science publications and 23% boost in tri-council funding. These numbers are accompanied by a growing participation by our faculty in teaching, research and service, including in our outreach activities for the lay public.

New leadership within our department:

Dr. Warren Wakarchuk is now the Chair of the Department of Chemistry and Biology. Dr. Wakarchuk is a biochemist studying glycosylation and glycosyltransferases in both bacteria and higher organisms. After years at the National Research Council, Dr. Wakarchuk joined our Department in 2012. He is funded by NSERC and by the Canadian Glycomics Network (GlycoNET) and has several ties to industry partners.

New infrastructure:

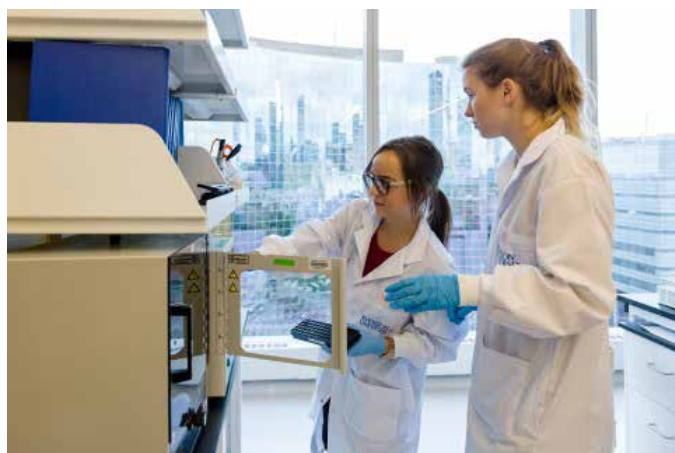
Ryerson leased 20,000 ft² of newly designed and equipped lab space within MaRS II Tower (<http://www.ryerson.ca/news-events/news/2016/10/new-science-lab-city>). Officially inaugurated in October 2016, eight labs transitioned into these state-of-the-art facilities including those headed individually by **Drs. Antonescu, Arts, Botelho, Fillingham, Foster, McPhee, Sabatinos** and **Wakarchuk**. The space will accommodate an additional four laboratories in the near future. The Ryerson MaRS Biomedical Research Facilities features an open-lab and modular concept, with designated rooms for cell culture, imaging and microscopy, radioisotope work, analytical instrumentation and other services. Importantly, the Ryerson MaRS facilities also feature abundant areas to encourage conversations and collaboration between trainees, staff and faculty. Ryerson MaRS comes on the heels of the Institute for Biomedical Engineering, Science and Technology (iBEST), a partnership between St. Michael's Hospital and the Faculties of Science and of Engineering and Architecture at Ryerson. iBEST is housed in the Keenan Research Centre and the Li Ka Shing Knowledge Institute at St. Michael's Hospital, and offers an opportunity to innovate and advance solutions for biomedical challenges:

<http://www.theglobeandmail.com/news/national/st-michaels-hospital-ryerson-unveil-venture-to-improve-health-care/article28390533>.

Awards, recognition and publications:

The Dean of the Faculty of Science, **Dr. Imogen Coe**, a molecular cell biologist who studies nucleoside

transporters, was recently recognized with a spot in Canada's Most Powerful Women: Top 100 for her work on Equity, Diversity and Inclusion in Science and Women in STEM (<https://www.wxnetwork.com/top-100/top-100-winners>). In addition, **Dr. Costin Antonescu**, a cell biologist investigating signal transduction and clathrin-mediated endocytosis, received several recognitions including an Early Researcher Award from the Government of Ontario, a New Investigator Award from CIHR and an award for Excellence in Graduate Education from Ryerson. We also continued to increase our research output with publications in *Current Biology*, *Molecular Biology of the Cell*, *Traffic*, *Cell Mol Life Sciences*, *Microbiology*, *PLoS One*, among others, with novel discoveries related to phagocytosis, endocytosis, receptor tyrosine kinase signalling, host-pathogen interactions, energy-dependent remodelling of the plasma membrane and phosphoinositide signaling.



View from the new Ryerson Biomedical Research Facilities at MaRS

Special events:

Ryerson hosted the 29th Ontario Biology Day (actually a two-day event) where undergraduate researchers in all fields of biology present their original research findings. This year we had close to 250 registrants from Universities across Ontario, with the event being held at the Mattamy Athletic Centre - the former Maple Leafs Gardens - now partly owned by Ryerson (<https://www.youtube.com/watch?v=92fmMb1dMIQ&feature=youtu.be>).

In addition, Ryerson University, and its subsidiaries, Department of Chemistry and Biology and the Faculty of Science, is a major sponsor of the 2017 Canadian Society for Molecular Biosciences taking place in Ottawa in May



Some of the over 250 students, representing most Ontario universities, registering for the 2016 Ontario Biology Day at Ryerson

16-20th. The CSMB meeting is entitled "Celebrating Canadian Molecular Biosciences: from organelles to systems biology" to follow the 150th Anniversary of Canada. **Drs. Roberto Botelho** and **Costin Antonescu** from Ryerson University are members of the organizing committee.

Ryerson was the first Canadian university to send an undergraduate-designed experiment to the International Space Station through the "Student SpaceFlight Exchange Program", a partnership with NASA. Led by undergraduate students in the Biomedical Sciences, Biology and Chemistry programs, the winning proposal was designed to study how fungi grow in microgravity (<http://www.ryerson.ca/science/newsevents/news/FOSgoesToSpace>).

Our Department was a key participant in Ryerson's Science Rendezvous that ran in May 2016. This was the 9th Science Rendezvous hosted at Yonge-Dundas Square, arguably the busiest intersection in Toronto. Open to the public, it easily attracts over 10,000 visitors and showcases research, hands-on activities, displays and stage shows that delighted, and demonstrated how science plays a part in our everyday lives. Our team built a 40-meter long DNA model, beating the Guinness world record for longest molecular model.

Additional milestones included the fifth anniversary of our Ph.D. program in Molecular Science. With that, our first Ph.D. graduates successfully defended their degrees, including **Dr. Amra Saric** and **Dr. Shannon Ho**, both from the Botelho lab, who are now post-doctoral fellows at the NIH and University of Toronto, respectively.

Lastly, we hosted our fifth Annual Research Symposium, with more than 80 poster presentations and more than 10 talks. These showcased our exciting and emerging research activities across various disciplines, and highlighted both undergraduate and graduate-based research activities. The keynote speaker was **Dr. Irena Creed** from Western University, a CRC on watershed processes and ecosystem health.

Simon Fraser University

Department of Molecular Biology and Biochemistry

Correspondent: Christopher Beh

The SFU/MBB 50/15 celebrations continue as Simon Fraser University looks beyond its 50th birthday and the SFU MBB Department is now 15 years old. Starting as an “Institute,” the Department of Molecular Biology and Biochemistry was spawned from faculty in the Departments of Chemistry and Biological Sciences. Our close affiliation with those Departments continues to this day, as well as our more recent associations with the BC Cancer Agency. Together with a number of other SFU Departments and Faculties, in 2016 the MBB and Biological Sciences Departments have in turn initiated the new SFU Centre for Cell Biology, Development, and Disease (C2D2). Its mission is to bring together the many SFU researchers working on cell and developmental biology to provide new opportunities for research collaboration and community outreach. The MBB Department continues with its mission to provide an undergraduate teaching program for a broad range of studies, including innovative joint programs uniting MBB and Business Administration, MBB and Chemistry, and MBB and Computer Science. Established in 2003, the latter program was in fact the first of its kind for bioinformatics training in Canada. From embryonic beginnings, SFU and MBB have moved on to firmly establish a reputation for innovative research and student training.

Department highlights:

We welcome our newest faculty member **Dr. Timothy**

Audas. Dr. Audas successfully initiated his research here at SFU last year. Dr. Audas continues his successful studies on non-coding RNAs (ncRNAs) that regulate the reversible conversion of proteins into amyloid-like aggregates. In the past year, **Dr. Nancy Hawkins** became our Departmental Chair, taking over from interim Chair **Dr. Esther Verheyen**, and we thank them for their efforts. We congratulate both **Drs. Lisa Craig** and **Sharon Gorski** who were promoted to full Professor. Dr. Craig’s research



Dr. Tim Audas, Assistant Professor

program investigates the structure of Type IV pili that extend from pathogens and mediate bacterial virulence. Dr. Gorski studies how cancer cells exploit mechanisms of autophagy for survival and proliferation.

For awards in recognition of research and professional excellence, 2016 was also a successful year for MBB faculty, staff and alumni.



Dr. Esther Verheyen, winner of the 2016 Grant and Moens Award of Excellence in Genetics

Dr. Esther Verheyen received the prestigious *Grant and Moens Award of Excellence in Genetics* from the Canadian Society for Molecular Biosciences in recognition of her groundbreaking work on the genetics of Wnt signalling, organ development and morphogenesis.

Dr. Christopher Beh would like to thank NSERC for its generous funding with the award of a *Discovery Accelerator Supplement (DAS)*. The award will help support his research on membrane trafficking and lipid signalling. MBB Department lecturer, **Dr. Irina Kovalyova**, continues to be honoured for “*Specimen*,” her collection of short story sci-fi tales; Dr. Kovalyova received the 2016 *Kobo Emerging Writer Prize* for literary fiction. Our alumni are also being honoured for their accomplishments. **Dr. Jennifer Gardy** (MBB PhD ‘06) was awarded the “Rising

Star” *SFU Outstanding Alumni award*. Dr. Gardy is current a senior scientist with the BC Centre for Disease Control, and a guest-host on CBC’s “The Nature of Things”. Another fiction author from the MBB Department, **Dr. Kristi Charish** (MBB BSc/MSc) has used her science training for the telling of her newest sci-fi novel, “The Voodoo Killings”. To all our MBB Department alumni, we welcome the opportunity to hear from you about the direction your careers have taken, so please contact us at mbbalumni@sfu.ca.

Several national and international infrastructure and network programs were initiated in 2016 at SFU, including the *iReceptor Data Integration System* for national health research and sequencing data sharing. With support from CFI, BCKDF, and SFU, associate MBB member **Dr. Felix Breden** and MBB professor **Dr. Jamie Scott** initiated this network for integrating immunogenetics data between its core partners: SFU, the BC Cancer Agency, and the University of Toronto. With NIH (US) funding, **Drs. Zabrina Brumme** of the Faculty of Health Sciences (FHS) and **Mark Brockman** (MBB and FHS) helped establish, with 18 international university centres and 2 private companies, the *Bench to Bed Enhanced Lymphocyte Infusions to Engineer Viral Eradication (BELIEVE)* initiative. The BELIEVE strategy aims to harness natural anti-HIV immunity and enhance mechanisms for clearing infected cells to combat HIV/AIDS.

Student awards and other news:

Among the many awards received by our graduate students, a few were especially significant. From Dr. Verheyen’s research group, **Mr. Eric Hall** received an NSERC Alexander Graham Bell doctoral scholarship. **Ms. Sarah Arthur**, an MSc student from **Dr. Ryan Morin’s** lab (MBB and Genome Sciences Centre, BC Cancer Agency) lab, received a CIHR Frederick Banting and Charles Best scholarship. As detailed in past reports, the MBB Department “sports” several remarkable undergraduate athletes. Apart from graduating as an “A” student in our Department, **Mr. Cameron Proceviat** (MBB BSc ‘16) earned the *Bill DeVries All-Around Athlete of the Year* for his wins as a middle distance runner; he hopes to represent Canada in the 2020 Olympics. From the champion SFU women’s golf team, senior undergraduate **Ms. Mackenzie Field** was selected to the *2015-16 Conference All-Academic Team* as a top student athlete in the Great Northwest Athletic Conference; Ms. Field earned straight “A’s” in her MBB studies.

Sunnybrook Research Institute

Biological Sciences Platform

Correspondent: David Andrews

Our scientists in the Biological Sciences Platform at Sunnybrook Research Institute (SRI) aim to understand how biological systems function in health and disease. Among our research areas are tumour biology, protein-protein interactions, immune system development, and neurodegeneration and regeneration. Areas of disease interest include cancer, cardiovascular disease, brain disorders like stroke and dementia, and traumatic injury, acute and acquired.

Under the leadership of **Dr. David Andrews**, director of Biological Sciences at SRI, there are 44 scientists



David Andrews

conducting research within the platform, including clinician-scientists who interact with patients and also run labs. Scientists in Biological Sciences work collaboratively with researchers in SRI’s two other platforms, Physical Sciences and Evaluative Clinical Sciences. Together, they are using interdisciplinary

approaches to translate basic science findings into improved diagnostic and therapeutic tools for clinical use.

New appointments:

In 2016, we welcomed two new researchers to our platform.

Dr. Carol Schuurmans is a senior scientist and the Dixon Family Chair in Ophthalmology. She studies how neurons are generated in the developing nervous system. As a neuroscientist, Dr. Schuurmans is particularly



Carol Schuurmans

interested in how different types of neurons form at distinct times in the developmental process and acquire their specialized functions. Her research focusses on two specific areas: the neocortex region of the brain and the retina.



Trung Le

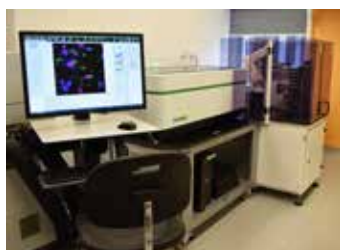
Dr. Trung Le joined SRI as an associate scientist in the Hurvitz Brain Sciences Research Program. His research focus is on developing therapeutic interventions to regenerate the auditory pathway and restore hearing to those affected by hearing loss. His lab is investigating different techniques of magnetic targeting as a therapeutic delivery method to

the cochlea, applying stem cell and gene therapy for regeneration of hair cells and auditory neurons, and studying the permeability of the blood-labyrinth barrier of the inner ear.

Research grants and awards:

Dr. Andrews, who holds the Canada Research Chair in Membrane Biogenesis, was awarded a grant through the John R. Evans Leaders Fund from the Canada Foundation for Innovation (CFI). The award, worth \$615,894, will support his research on high-content screening to identify and validate potential therapeutic targets for cancer chemotherapy. The Ontario Ministry of Research, Innovation and Science matched the award in full.

In December 2016, Dr. Andrews' high-content cellular analysis (HiCCA) lab installed the latest-generation Opera Phenix by PerkinElmer, which was purchased with funding from CFI. The Opera Phenix is designed for high-throughput, phenotypic screening and live cell assays for researchers to study complex disease models such as those in primary cells and microtissues. It can generate multi-colour,



The Opera Phenix in the HiCCA lab at SRI

high-resolution microscope images rapidly without compromising sensitivity. The instrument will enable the Andrews lab to develop further new approaches to understanding how proteins and small molecules function in cells. The Andrews lab seeks to understand and exploit protein-protein interactions and apoptosis toward identifying and validating potential therapeutic targets.

In 2016, five SRI scientists secured \$2.5 million from the Canadian Institutes of Health Research (CIHR) through the project scheme competition.

Dr. Robert Kerbel, a senior scientist, was awarded \$607,780 over five years to advance his preclinical work on improving testing of immune-oncology combination therapies for early- or late-stage metastatic disease.

Dr. JoAnne McLaurin, a senior scientist, was awarded \$898,289 over five years to further her research on promoting neurovascular recovery following stroke. **Dr. Diane Nam**, an associate scientist, was awarded one-year funding worth \$100,000 to conduct a randomized controlled trial on the effectiveness of lithium for fracture treatment. **Dr. Robert Screaton**, a senior scientist, received \$764,500 over five years to establish a comprehensive genetic roadmap for human pancreatic beta cell proliferation and function. **Dr. Burton Yang**, a senior scientist, was awarded a one-year grant worth \$100,000 to study the inhibitory effect of a circular RNA called circ-CCNB1 on ovarian cancer cell growth.

Senior scientist **Dr. Juan Carlos Zúñiga-Pflücker** received a Discovery Grant worth \$210,000 from the Natural Sciences and Engineering Research Council of Canada. The award will support his research on molecular mechanisms behind the expression of a gene called Delta-like 4 in thymic cells, and how the structure and organization of the thymus organ affects gene expression.

Abdikarim Abdullahi, a second-year PhD student in the lab of SRI senior scientist **Dr. Marc Jeschke**, was awarded a Vanier Canada Graduate Scholarship through CIHR. The award, worth \$150,000 over three years, recognizes academic excellence and leadership. He is studying glucose control and metabolic changes in liver and fat tissue after a burn injury to help improve quality of life for severely burned patients.

Researchers Profiled in SRI Magazine

Six scientists from the Biological Sciences platform

were profiled in the 2016 [SRI Magazine](#), the flagship publication of SRI. Here is a recap of their research with links to the stories.

Therapy can simply stop working to devastating end. **Dr. Robert Kerbel** studies how tumours become resistant to therapy, and how to thwart that resistance. Learn how in the story [Overcoming treatment resistance in cancer](#).

Dr. Arun Seth is a senior scientist working on the biology of prostate cancer. He has discovered biomarkers that predict disease recurrence. **Dr. Laurence Klotz**, an affiliate scientist and urologist, is the co-creator of active surveillance, a strategy that has changed the treatment landscape for men with prostate cancer. The story [“Bespoke” prostate cancer treatment](#) explains how they and others are cracking the tough nut of prostate cancer, exposing which patients are most likely to get worse, and where tumours might be concealed.

Dr. Rena Buckstein, an affiliate scientist and oncologist, specializes in blood cancers. Her research shows that when patient-related factors, such as frailty and the existence of other chronic health conditions, are taken into consideration, doctors are able to predict disease outcomes like survival more accurately. Learn how researchers are using a new score to improve risk assessment in the story [“Studies help blood cancer patients make treatment decisions”](#).

Dr. Georg Bjarnason, a senior scientist and oncologist working on kidney cancer, is testing an individualized approach to the oral cancer drug sunitinib. By adjusting the dose and schedule for each patient, he achieved one of the highest response rates for kidney cancer. Read [“A tapestry of clinical trials”](#), which highlights this and other high-impact findings hinting at what tomorrow’s cancer care might look like.

Dr. Bev Orser is an affiliate scientist and anesthesiologist. She is concerned with the effects of opioid use, but wants to ensure her patients get the pain relief they need. She explains how doctors are grappling with relieving acute pain while minimizing opioid use and averting descent into chronic pain in the story [“Is there still a place for opioids?”](#)

Trent University

Department of Biology

Correspondent: Carolyn Kapron



Robert Huber

In 2016, the Biology Department at Trent welcomed a new member, **Dr. Robert Huber** (PhD, University of Toronto), who joins us from a post-doctoral position at Harvard Medical School. Prof. Huber uses the social amoeba *Dictyostelium discoideum* as a model system for studying the functions of proteins linked to human disease,

and the structure and function of the extracellular matrix. His current research is focused on revealing the cellular mechanisms underlying neuronal ceroid lipofuscinosis (NCL, also known as Batten disease), and identifying proteins within the extracellular matrix that modulate cell motility and differentiation during *Dictyostelium* development. Prof. Huber will be teaching in the areas of cell and molecular biology.

We are also very fortunate to be joined by **Ms. Kelly Boadway** (MSc, University of New Brunswick), as a Lab Instructor/Demonstrator, as well as Stores and Account Manager. Ms. Boadway brings her expertise to assist in teaching Genetics and the Biology of Vertebrates.



Kelly Boadway

Dr. Craig Brunetti, who has been member of the Biology Department since 2003 and was former departmental chair and Director of the Environmental and Life Sciences Graduate Program, was appointed Dean of Graduate Studies for a 5-year term. We look forward to exploring new initiatives in graduate education with him.

The past year saw the inauguration of a new Biology department degree, the Bachelor of Biomedical Science. This program allows students to delve into aspects of health and disease, and culminates with an Internship course that places students in a variety of health-related settings in the Peterborough area. The new degree grew out of the Specialization in Health Sciences that has been offered to Biology majors since the 2000-2001 academic year.

Université de Montréal

Département de biochimie et médecine moléculaire

Correspondent: Luc DesGroseillers (Director)

New Canada Research Chair:



Sebastian Pechmann

Dr. Sebastian Pechmann was awarded a Tier 2 Canada Research Chair in Computational Systems Biology. Dr. Pechmann is an outstanding early-career researcher, and emerging leader in the development of integrated computational approaches to understand protein

homeostasis. Dr. Pechmann has acquired unique expertise in developing and applying computational and systems biology methods to study complex cellular systems that control proteome integrity. His research program focuses on understanding how proteins fold in the cell, and how the cell as a systems maintains protein homeostasis, which has important implications for understanding neurodegenerative diseases, cancer, and aging.

Faculty appointments:

Dr. Karim Benkirane, a clinical biochemist at Maisonneuve-Rosemont Hospital, was recently appointed as Assistant Clinical Professor in the Department. Dr. Benkirane is also chair of the committee for certification in the specialty of clinical biochemistry issued by the Ordre des Chimistes du



Karim Benkirane

Québec, and member of the committee for harmonization of academic and professional recognition in clinical biochemistry between Québec and other provinces.

Dr. James W. Coulton who is Professor Emeritus in the Department of Microbiology and Immunology at McGill University was appointed as Adjunct Professor in our Department. In collaboration with **Dr. John Pascal**, he works on structural biology of membrane protein complexes. Their research program emphasizes structural determinants of membrane proteins required for transport, including solving 3-D structures by X-ray crystallography.

Departmental activities:

For the fourth consecutive year, 16 members of the Department participated in the Movember fundraising effort as team "Biochimistes à la moustache" and raised \$4,335 for research on male health issues.



Department participants in Movember 2016

Université de Sherbrooke

Département de biochimie

Correspondent: Michelle Scott

Research:

It has been a busy year for our faculty members. **François Bachand** renewed his Canada research chair in Quality Control of Genetic Expression. The Bachand lab is focussing on understanding the surveillance systems that ensure genetic expression works properly. **Luigi Bouchard** received the prize Pierre-et-Danielle-Bourgau for his study of epigenetic links between gestational diabetes and child obesity, while **Eric Massé** received the institutional prize for research and creation for his discovery of a role for bacterial 3' external transcribed spacers of tRNA transcripts to prevent transcriptional noise.

Professors **Gilles Dupuis** and **Andrew Grant** retired in 2016. Professor Dupuis' group characterized mechanisms of lymphocytic activation and molecular mechanisms of inflammation. Professor Grant's research centred on biomedical informatics and on modelling patient data to support lab tests. Both have many projects in mind for their retirement.

2016 also saw the departure of Professor **Rafael Najmanovich** to the department of Pharmacology and Physiology of the Université de Montréal. While at the UdeS, Rafael's group created widely used servers for the detection of molecular similarities, docking simulations and the analysis of dynamic aspects of macromolecular structure. He was also a cornerstone in building the department's computational knowledge and expertise. We thank him for his contributions and wish him success in his new environment.



Top row from left: Jean-Pierre Perreault, Arnaud Droit, Jean-Michel, Martin Bisaillon. Bottom row from left: Guylain Boissonneault, Samir Rahman, Rachel Jodoin, Maxime Gagnon, Simon Boudreault, Michelle Scott.

Our 22nd annual graduate symposium held in March 2016 was a success. Professor **Arnaud Droit** from the Université Laval, our keynote speaker, discussed the challenges of integrating and analyzing genomic data, while Samir Rahman, invited PhD student from the Université de Montréal, presented on the localization and function of eRNA. 12 UdeS graduate students from the Biochemistry department presented their research. The finalists were the following: **Simon Boudreault** from the Bisaillon group won the first prize, **Maxime Gagnon** from the Roucou group won the second prize while **Rachel Jodoin** from the Perreault group won the third prize. **Marie-Claude Carrier** from the Massé lab won the Pierre-Chailler prize for best student of the year.

Teaching:

Over the past 3 years, the department has been

renewing its course offerings. At the BSc level, the course "Biochemistry applied to Health Sciences", which introduces clinical aspects of biochemistry, has quickly become a favorite, while the new Bioinformatics course promotes the use of computational tools and concepts through hands on practical modules, providing much needed experience in this field.

Université Laval

Department of Molecular Biology, Medical Biochemistry and Pathology

Correspondent: Jean-Yves Masson (Director)

Our department now comprises 36 professors working on medical biochemistry and pathology, and mostly on basic research and molecular and cellular biology. Congratulations to students and faculty for another year of exemplary achievements, only a few of which can be highlighted here. The Canadian Association of Pathologists rewarded **Bernard Têtu** for his contributions in pathology. **François Rousseau** was named chief of the medical biochemistry division in our department.

We are happy to welcome **Samer Hussein** as an Assistant Professor since May 2016. Samer's work focuses on how transcription factors define the epigenetic landscape of different pluripotent and cancer cell states. His overarching goal is to understand the mechanism of interactions between pluripotency transcription factors and chromatin regulators that lead to cell state changes, particularly in the context of cancer initiation. He completed his post-doctoral training under the



Samer Hussein

supervisions of Dr. Timo Otonkoski at the University of Helsinki, Finland, and Dr. Andras Nagy, a pioneering figure in the stem cell field, at the Lunenfeld-Tanenbaum Research Institute (LTRI) in Toronto in 2016, where he studied the genetic and epigenetic changes

occurring during reprogramming to induced pluripotent stem cells (iPSCs). Over the past 8 years, he has become an emerging figure in the field of cellular reprogramming to iPSCs as demonstrated by his publications in

Nature, *Nature Communications* and *J. Biol. Chem.* His first work, published in *Nature*, was among the first papers describing genetic abnormalities caused by the reprogramming of human somatic cells towards iPSCs. It was part of *ESTOOLS Consortium*, a European consortium that was dedicated to studying human ESC and iPSC biology. They showed that the reprogramming process compromises the genetic integrity of iPSCs, much like in cancer, and generates high levels of mutations in early passage of iPSCs. This work warned the field to the necessity of meticulous characterization of human iPSCs before their use for regenerative medicine or for disease modeling. His second major project, also published in *Nature*, was part of another international consortium to study genome-wide changes during reprogramming of mouse embryonic fibroblasts towards iPSCs. It relied on Samer's bioinformatics expertise in integration of multiple "omics" datasets to analyze transcriptional and epigenetic changes occurring during the reprogramming process. They were first to identify that reprogramming leads to multiple states of pluripotency, a concept that up to now was believed to be unique to early embryonic cells. This work also gave a deeper understanding of chromatin organization and its effect on transcriptional networks during reprogramming. Samer's expertise in molecular and cellular biology, bioinformatics and genomics data analysis will be a great asset to our department and Laval University.

As for the research highlights, **Jacques Côté** published a paper in *Molecular Cell*: "*The TIP60 Complex Regulates Bivalent Chromatin Recognition by 53BP1 through Direct H4K20me Binding and H2AK15 Acetylation*" in May 2016. **Marc-Etienne Huot** co-authored with Frédéric-Antoine Mallette of Université de Montréal a paper in *Nature Communications* entitled: "*The oncometabolite 2-hydroxyglutarate activates the mTOR signalling pathway*".

Michel Vincent, an expert in cell division and RNA-binding proteins, retired in April 2016. Michel devoted much time and was instrumental in establishing our Biomedical Sciences Baccalaureate program at Laval University. We organized a surprise party for Michel with departmental members including new retirees, such as **Jacques Landry**, former Canada Research Chair in Stress Signal Transduction (see picture).

Ron Hancock, whose research gave insights into the physics which underlies structures and functions in



Two retired BMBP professors: Jacques Landry, former Canada Research Chair in Stress Signal Transduction (left) and Michel Vincent, former director of the Biomedical Sciences Baccalaureate at Laval University (right)

the nucleus, retired from Laval University in 2016. Sadly, **Luc Bélanger**, died on September 9, 2016. Luc was a visionary colleague, known for his work on the transcriptional regulation of alpha-fetoprotein, but also as the director of *Centre de recherche de L'Hôtel-Dieu de Québec (CRHDQ)*, *Centre de Recherche sur le cancer de l'Université Laval*, and the Oncology Axis of the CHU de Québec. His interest in strategic oncology initiatives, led him to establish the *Centre de recherche clinique et évaluative en oncologie (CRCEO)* and also the *Consortium de recherche en oncologie clinique du Québec (Q-CROC)* with Gérald Batist. Luc will be missed deeply.

University of Alberta

Department of Biochemistry

Correspondent: Joe Casey

Appointments:



Olivier Julien

In September 2017, the Department of Biochemistry will welcome two new faculty members, **Dr. Olivier Julien** and **Dr. Sue-Ann Mok**, recruited from the University of California San Francisco (UCSF).

Dr. Julien obtained his

Ph.D. under the mentorship of Dr. Brian Sykes studying protein structure and dynamics using NMR spectroscopy. He then received a Banting Post-doctoral Fellowship to work with Dr. Jim Wells at UCSF, where he used systems biology to study the mechanisms of cell death in relation to cancer and neurodegeneration. Specifically, he has been using proteomics approaches to study the role of caspases and other proteases in health and disease.



Sue-Ann Mok

Dr. Mok completed her Ph.D. under the supervision of Dr. Robert Campenot where she studied mechanisms of long distance retrograde signalling in neurons. She went on to pursue her post-doctoral studies with Jason Gestwicki at UCSF before being promoted to Adjunct Assistant Professor. Dr. Mok's research utilizes a wide array of biochemical and cell biology approaches to

understand the protective roles of molecular chaperones against tau and other amyloidogenic proteins that are implicated in neurodegenerative diseases.

Retirements:

At the end of 2016, **Drs. Dennis Vance and Joel Weiner** began to transition toward retirement, changing their status to part-time Professors emeriti.

Events:

The Department of Biochemistry-based NSERC-CREATE-funded International Research Group in Membrane Biology hosted their German partners for a joint conference in September 2016. About 40 principal investigators and graduate students from Technical University Kaiserslautern and Saarland University shared two days of meetings, culminating in a picnic on the banks of the North Saskatchewan river.

The Department of Biochemistry held a research retreat at the Banff Centre for the Arts in November 2016, sharing scientific talks and relaxation in the mountain air.



Group photo taken at the department retreat 2016, at the Banff Centre for the Arts

Three graduate students, **Ms. Carmen Wong (Fliegel lab)**, **Mr. Darpan Malhotra (Casey lab)** and **Ms. Katie Badior (Casey lab)**, and two postdoctoral fellows, **Dr. Debajyoti Dutta (Fliegel lab)** and **Dr. Rashmi Panigrahi (Lemieux lab)**, visited partner labs in Germany for 1-3 months of research experience as part of their enrollment in the IRTG in Membrane Biology. The Department of Biochemistry also hosted visits by two German graduate students in 2016 as part of the same exchange program.

News:

Dr. Rachel Milner was elected Vice President of the Association of Academic Staff of the University of Alberta.

Awards:

Ms. Robyn Millott (Glover/Holmes) and **Mr. David Kramer (Fahlman)** won CIHR graduate studentship awards.

Dr. David Westaway, an adjunct member of Biochemistry, received a Tier 1 Canada Research Chair. **Dr. Joe Casey** won the 2016 Faculty of Medicine and Dentistry award for Excellence in Mentoring, which recognized his success in supervising 15 graduate students, 8 post-doctoral fellows and 24 summer students through his career.

University of Alberta

Department of Cell Biology

Correspondent: Andrew Simmonds

Cell Biology at the University of Alberta comprises 17 primary and cross-appointed investigators studying

the molecular and physiological aspects related to cell biology. Research in our department includes the cellular basis of development, organelle biogenesis and inheritance, protein folding, protein lipidation, mitochondrial biology and metabolism, protein and lipid transport, evolutionary cell biology, and virology. Our department has 20 graduate students; five of these individuals hold prestigious Vanier Scholarships and several others hold Dr. Fred Banting and Dr. Charles Best CIHR Graduate Fellowships. Cell Biology also hosts six research associates and six post-doctoral fellows.

In the past year, members of our department have also been successful in competing for research funding both nationally and provincially, with new grants from CHIR (**Drs. Tom Hobman, Michael Hendzel and Richard Lehner**) and NSERC (**Dr. Andrew Simmonds**) as well as provincial and other national funding bodies. This includes **Dr. Tom Hobman**, who was recently awarded a major grant to study the cell response to Zika virus. **Dr. Joel Dacks** was elected President of the International Society for Evolutionary Protistology. The faculty members in Cell Biology support the CSMB and their mandate to promote basic research across the country at the provincial and national levels.

University of British Columbia

Department of Biochemistry and Molecular Biology

Correspondent: Leonard Foster



Phil Hieter

in our department, throwing all his energy into making the department and its individuals as good as they could

Our department was saddened early in 2016 with the unexpected resignation and retirement of **Roger Brownsey**. Roger was well into his second term as our departmental Head but decided to retire at the end of June for personal reasons. Roger led the department through a period of great growth

be. His tireless efforts are already missed!

Around the same time, the new Dean of the Faculty of Medicine was putting the final touches to a strategic plan for the faculty. In order for the new plan to be rolled out in an orderly fashion, an internal search for



Bob Molday

an Interim Head was conducted, with the result being that **Leonard Foster** took over for one year. This is likely to be extended to two years, at which time we will be seeking to recruit a new Head.

In other news, several of our faculty members had outstanding years: **Phil Hieter** (also of the Michael Smith Laboratories) was elected to the National Academy of Sciences in the US. **Bob Molday** was awarded the Global Vision Award from the CNIB for outstanding achievements in vision



Vic Ling



Pieter Cullis

research. **Vic Ling** was awarded a Lifetime Achievement award by Life Sciences BC, as was **Pieter Cullis** by the Journal of Drug Targeting. **Natalie Strynadka** was awarded UBC's top research prize, the Jacob Biely Award, while **Leonard Foster** won a UBC Killam Research Prize.



Natalie Strynadka

On the practical front, perhaps the most significant news in our department was our securing of a Titan Kreos cryoTEM system. It was delivered in November 2016 and is still going through the installation and check-out process.



Leonard Foster

University of Calgary

Department of Biochemistry & Molecular Biology,
Cumming School of Medicine

Correspondent: Jonathan Lytton

The 2016 year was marked by lots of change in the Department of Biochemistry and Molecular Biology. We continue to recruit new faculty, and this year welcomed structural biologist **Gareth Williams** to our genome instability and aging group (dnascience.ca), and

Edwin Wang and **Quan Long** to our growing bioinformatics group.



Gareth Williams

Gareth joins us following a PhD from the University of St. Andrews in the UK and postdoctoral training with Prof. John Tainer at the Lawrence Berkeley National Labs in California. His research



Edwin Wang

focus will be on the structure of DNA repair complexes and their role in cancer.

Edwin moved to join us from a position as Senior Investigator in Bioinformatics and Systems Biology at the National Research Council's Montreal labs. Edwin's research focuses on systems biology approaches to cancer genomics.



Quan Long

Quan received his PhD from Peking University in Beijing and postdoctoral training in Austria, the UK and Mt Sinai School of Medicine in New York. His research program aims to develop and apply statistical models that link different 'omic' datasets to phenotype prediction in human disease.

Gareth, Edwin and Quan have all established their labs, recruited promising trainees, and are off to strong starts!

As well, **Ralf Paschke**, **Alexei Savchenko**, **Laura Sycuro**, and **Qingrun Zhang**, all joined the Department as joint or adjunct members.

The excitement of these new additions to our membership was offset by the bitter-sweet departures of long-time members **Mike Walsh**, **Julie Deans**, and **Carol Schuurmans**. Mike and Julie retired and, while they continue their scientific connection with the department, are glad to be pursuing their passions instead of writing grants! We congratulate Carol on her new job as Dixon Family Chair in the Sunnybrook Research Institute at the University of Toronto, and wish her well there. While we are happy that Mike, Julie and Carol are enjoying the next stages of their careers, we will badly miss their outstanding contributions to our Department.

We also received the sad news that **Gordon Dixon**, founding member of our Department, distinguished scholar, member of the Royal Societies of the UK and Canada, and Officer of the Order of Canada, passed away on July 24, 2016 at the age of 86.

Several members of our Department were recognized this year for their significant accomplishments. **Aaron Goodarzi** was chosen as one of the University's Peak Scholars for the outreach work he has done leading a province-wide study of household radon gas levels, raising awareness of risks and mitigation strategies. **Paul Mains** was a member of an interdisciplinary team of UofC scientists who were awarded a grant from the University's strategic priority in Infections, Inflammation and Chronic Diseases in the Changing Environment to study and manage drug resistance in human parasitic worms - a major global health issue. **Dave Schriemer's** innovative discovery research identifying novel natural proteases that can potentially be used to treat celiac and other human diseases, resulted in the launch of a spin-off company, Nepetx LLC. A team of undergraduate students, led and supervised by **Mayi Arcellana-Panlilio**, created a synthetic biology project that won a gold medal in Best Applied Design and a special award for Best Integrated Human practices at the International Genetically Engineered Machines (iGEM) Giant Jamboree in Boston.

While these achievements received public recognition, there are many unsung heroes among our diverse members whose daily commitment to academic excellence makes the Department of Biochemistry & Molecular Biology a special place for research and education.

BMB at the University of Calgary continues to recruit both new students and faculty. Please visit our website at UCalgary.ca/bmb for more information about our department.

University of Calgary

Department of Biological Sciences

Faculty of Science

Correspondent: Vanina Zaremborg

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, several colleagues from Biochemistry have been devoted to service in our Department. **Elmar**

Prenner continued in his role as Associate Department Head for Research and Planning. **Raymond Turner** finished a 4-year term as Associate Department Head for the Graduate Program, and **Greg Moorhead** has replaced him. This represents a strong contribution of biochemists to our departmental administration. We appreciate their tireless dedication and efficiency in helping our large Department run smoothly.

We are also very grateful to **Sergei Noskov** and **Marie Fraser** for their work as chairs of the Biochemistry cluster and Biochemistry program respectively. They have now passed the torch to **Ken Ng** and **Vanina Zaremborg**, who have agreed to step in to replace Sergei and Marie respectively. They will continue with the development and implementation of a five year vision plan focused on "quantitative biology".

Research in our cluster is thriving, and many of our members have been involved in the development of multidisciplinary initiatives, have secured important sources of funding, and have received prestigious recognitions. Our trainees are the mainspring of our Research programs and we are proud of their accomplishments. Several graduate students and post-docs have been recognized with distinctions/awards for their excellent research achievements.

These are the highlights of the year:

A fourth-year PhD student in Dr **Ken Ng's** group, **Miguel Torres**, won the PDB Poster Award at the 2016 American Crystallographic Association Annual Meeting and published his first paper in *JBC* in collaboration with **Peter Facchini's** lab. This was the first paper from a growing collaboration between these labs in the past couple of years, and the paper was highlighted with the cover image from the Nov 4 issue (*J. Biol. Chem.* 2016, 291:23403-23415).

The group led by **Ian Lewis** (AIHS Translational Health Chair) recently launched the Calgary Metabolomics Research Facility (CMRF), a state-of-the-art mass spectrometry facility specifically designed for unravelling the complex metabolic dynamics that occur during human infections. The CMRF was built with investments from the Canada Foundation for Innovation and the Western Canadian Microbiome Centre (WCMC). The CMRF houses two high-resolution mass spectrometers, a targeted mass spectrometer, and a high-performance computing

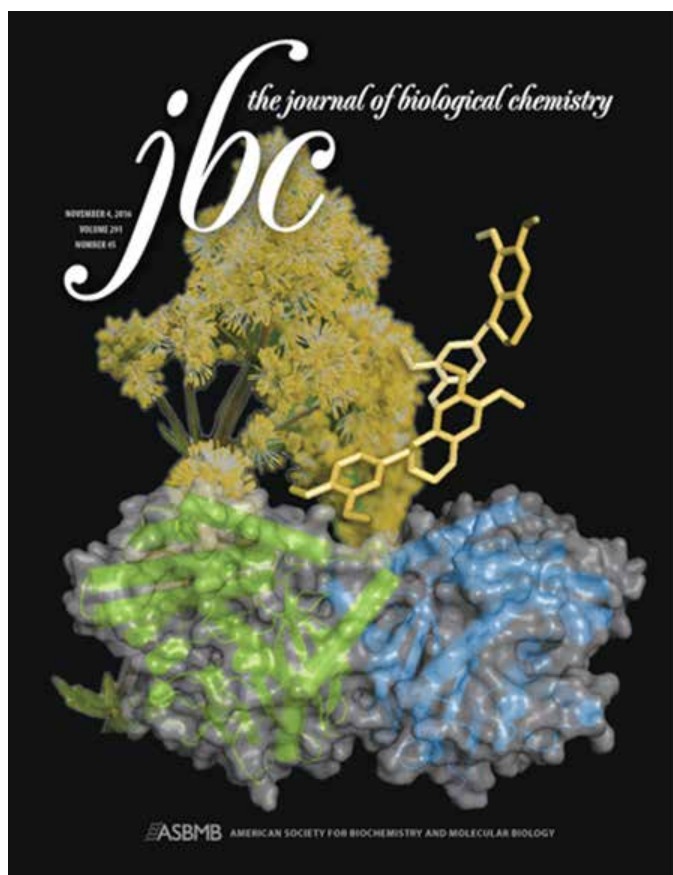


image from Miguel Torres' paper on the cover of the Nov 4 2016 issue of *J. Biol. Chem.*

server. The Lewis lab has grown over the last year and was pleased to welcome a new graduate student, Austin Nguyen, a postdoctoral fellow, Thomas Rydzak, two new technicians, Dominique Bihan and Ryan Groves, and also serve as the host lab for Dr. **Dan Gregson**, who is taking a sabbatical from Calgary Laboratory Services to learn metabolomics.

Glen Uhrig, former PhD student of **Greg Moorhead**, has been recruited back to Canada to start his own group at the University of Alberta. Glen has been doing a post-doc at the ETH Zurich using mass spectrometry to study large scale covalent modification of proteins. Glen starts his new position in the Department of Biological Sciences at the University of Alberta on July 1, 2017.

Sergei Noskov's group welcomed several graduate and undergraduate students this year. As well as graduating two PhD students, who accepted industry and academic appointments, the Noskov lab continued research on the developing of integrative platforms allowing modelling of ion channels in the heart from protein function to cellular

and tissue dynamics levels. Noskov and his collaborators from UC Davis (Colleen E. Clancy is the grant PI) were awarded a team R01 grant from the National Institutes of Health to work on the rapidly emerging field of predictive cardio-toxicology. Together with researchers at the National Institutes of Health and National Institutes of Standard and Technology (USA), the Noskov lab created and expanded a network of researchers working on transport phenomena in mitochondria and mitochondrial disease profiling. The first joint paper from this project was published in *PNAS*. Sergei recently joined the editorial boards of *BBA-Biomembranes* and the *European Journal of Biophysics*. Several members of this group have been awarded provincial and national scholarships, including the recent announcement of a Vanier award to **Williams Miranda** (also recipient of Alberta Innovates Health Solution graduate scholarship), a QE-II graduate scholarship to **John Keenan** Fanning and an Alberta Innovates Post-doctoral Fellowship to Dr. **Hristina Zhekova**.

Elmar Prenner continued teaching in the Nanoscience minor and Biochemistry programs. His basic science research focusses on lipid-metal interactions, lipid-based anticancer drugs and nanoparticle-based drug delivery and tear film architecture. His applied research deals with the design of fluorescence instruments and bioanalytical assays. Elmar received a "Great Supervisor Award" from the Faculty of Graduate Studies.

The Centre for Molecular Simulation, directed by **Peter Tieleman**, organized several well-attended seminars given by visiting speakers. The **Tieleman** group develops computer models to study lipids and membrane proteins, at both atomistic detail and at a slightly coarser level of detail, in the now widely-used MARTINI force field for biomolecular simulation. Working towards high-throughput computational screening of interactions between lipids and membrane proteins, they continue to develop new tools for membrane protein simulations and applications to ABC transporters and other membrane proteins. Peter was the recipient of the Thomas E. Thompson award from the Membrane Structure and Assembly subgroup of the Biophysical Society. **Anastassiia Moussatova**, from the Tieleman's group, successfully defended her PhD Thesis on signal sensing mechanism by bacterial thermosensor DesK.

Raymond Turner took a 6-month leave in the fall to catch

up on research, where he also dedicated time to rework our new Biochemical Toxicology course. PhD student **Sean Booth** from the Turner lab won the JB Hyne university thesis award, and PhD candidate **Elena Piacenza** from the same group won the top young woman in nanoscience award at an international conference.

Three graduate students in the laboratory of **Hans Vogel** recently successfully defended their PhD degrees. **Marie Palmnäs** and **Nusrat Shommu** both worked on various clinically relevant metabolomics projects, while **Subrata Paul** performed structural work on a number of bacterial proteins that could potentially be used to address antibiotic resistance. All three have been very productive and they have produced numerous manuscripts that are now making their way into the scientific literature. Congratulations on a job well done!

Vanina Zaremborg was the recipient of an NSERC Discovery Accelerator Supplement as an add-on to her renewed NSERC Discovery grant to study lipid metabolism and signalling. PhD candidate **Suria Ganesan** from the Zaremborg's lab, was invited to give an oral presentation at the Experimental Biology meeting held in San Diego, USA, and was the recipient of an Eyes High International Doctoral Scholarship awarded by the University of Calgary. **Brittney Shabits** from the same group received a QE-II graduate scholarship to support her MSc studies.

University of Guelph

Department of Molecular and Cellular Biology

Correspondent: Frances Sharom

Dr. Marc Coppolino began a 5-year term as department Chair on May 1, 2016, taking over from outgoing Chair, **Dr. Rob Mullen**, who we thank for his hard work and dedication.

The College of Biological Science (CBS) Office of Educational Scholarship and Practice (COESP) officially came into being on March 1, 2016, when **Dr. John Dawson** of MCB took on the role of its faculty Director. Since that time, they have been very busy behind the scenes discussing who they are and what they will do. Meetings were held every morning for a week with Dr. Keith Trigwell, a teaching and learning expert from Sydney, Australia, to discuss the COESP and where it is going. The COESP Kick-off event on May 10 2016 included a plenary



John Dawson , Director of COESP

lecture from Dr. Trigwell, and presentations and participatory sessions for the CBS community. COESP has collected information about the challenges and needs in biology higher education, and plan to report their findings back to the community, and address some of the challenges through information releases, seminars and resources. The COESP website is up

and running with lots of information (www.uoguelph.ca/ada-cbs/coesp) and you can follow them through Twitter, Facebook and Insta feeds for news, announcements, and highlights from the literature and meetings.

New staff members:

We extend a warm welcome to **Elsbeth Smith**, our new Undergraduate Teaching Coordinator, and **Vanessa Breton**, our new Administrative Service Assistant, who joined us in 2016.

Faculty and research news:



Nina Jones

Dr. Nina Jones received the prestigious honour of being elected to the College of New Scholars, Artists and Scientists, joining the "emerging generation of Canadian intellectual leadership." Created by the Royal Society of Canada in 2014, the College recognizes academics who have made exceptional achievements within 15 years of completing their doctoral degrees.

Dr. Jones, who holds the Canada Research Chair in Eukaryotic Cellular Signalling, studies fundamental mechanisms of cell communications. Her work has helped in understanding molecular processes involved

in kidney disease, cardiovascular disease and cancer. She also received a \$750,000 grant from CIHR to support kidney disease research, and was presented with an "Award of Merit for Outstanding Community Partner" from the Kidney Foundation of Canada, in recognition of her outreach activities.

Dr. Chris Whitfield, received a 7-year CIHR Foundation Grant for studies of drug-resistant pathogens that increasingly threaten human health.

Dr. Peter Krell received funding from Genome Canada's "Disruptive Innovation in Genomics" program, together with collaborators from the Great Lakes Forestry Centre (GLFC) in Sault Ste. Marie. They aim to use a new genomics approach to develop a simple diagnostic test for the emerald ash borer, which lacks natural predators and parasites. The invasive pest has swept through numerous ash stands, threatening to devastate parts of Canada's multibillion-dollar forestry sector, and is already wreaking havoc in cityscapes in southern Ontario since its arrival in 2002.

Congratulations go out to **Drs. Mark Baker, Anthony Clarke, Steffen Graether, Cezar Khursigara, Dick Mosser and Terry Van Raay**, whose NSERC Discovery grants were renewed.

Cezar Khursigara was the recipient of the 2016 Canadian Society of Microbiology Fisher Scientific Award, which is given to stimulate and recognize new researchers in the microbiological sciences.

Canadian Oxidative Stress Consortium Meeting



Scott Ryan

stress. This year's meeting boasted an outstanding

The 9th Meeting of the Canadian Oxidative Stress Consortium (COSC) was held at the University of Guelph from June 1-3, 2016, with **Drs. Scott Ryan and Jim Uniacke** acting as the meeting Co-Chairs. This is a national conference held every two years in locations across Canada to support excellence in research in the field of oxidative



Jim Uniacke

trainees, and highlighted the work of graduate and post-doctoral trainees in dedicated symposia. Ties between academia and industry partners were showcased in workshops featuring new biotechnology approaches to encourage attendee networking. The two international keynote speakers were Alicia Kowaltowski from Sao Paulo, Brazil and Christine Foyer from Leeds, United Kingdom.

scientific program that brought together Canada's leading researchers in the field, with 10 symposia focussed in areas including metabolism, plants, cancer, neuroscience, DNA repair, kidney disease, and transcriptional regulation. This three day meeting had 100 attendees including 40

Drs. Steffen Graether and Matt Kimber organized the Guelph Protein Symposium 2016. This is a continuation of the tri-university (Laurier, Guelph, Waterloo) Protein Symposium started last year. The one-day symposium had over 100 attendees, including 46 graduate students and 23 undergraduate students, and there were talks from PIs and students, as well as a keynote address given by Julie Forman-Kay from Sick Kids.

Staff retirements:

The department celebrated the retirement of our long-serving Administrative Officer, **Sandra Good**, after an amazing 46 years at the University of Guelph! Her position was taken over by **Cate Mennega**. Our Graduate Program Assistant, **Carol Schlaht**, retired after 27 years at the university, and was replaced by **Bertilla Moroni**, whose position as Administrative Service Assistant was filled by **Vanessa Breton**. We wish Sandra and Carol all the best on their well-deserved retirement, and welcome Cate and Vanessa to our department.

Graduate and post-doctoral news:

Molecular & Cellular Biology joined forces with the Department of Management to offer a new Master of Biotechnology program, which accepted its first students in Sept 2016. This 3- or 4-semester program combines

courses and hands-on research in molecular approaches to biotechnology, with business skills in various aspects of commercializing innovations. It aims to prepare students for work in the agribusiness and food industries, plant biotechnology, pharmaceuticals, health management and environmental management and research. For more details, see the program web page at: <http://www.uoguelph.ca/mbiotech>

Melanie Wills (Jones lab) was the 2016 recipient of the Forster Medal (PhD), the most prestigious University of Guelph graduate award. The medal is awarded to a convocating PhD student who excels both academically and in extracurricular activities. MSc graduate **Brandon Wyse** (Yankulov lab) was awarded the College of Biological Science silver medal.

Michal Pyc (Mullen lab) won an award for the best student oral presentation for his talk at the Canadian Society of Plant Biologists (CSPB) Eastern Regional Meeting. **Dr. Olga Ovchinnikova** (Whitfield lab), won a poster award at the Canadian Glycomics Symposium (held in Banff Alberta), and **Liam Doyle** (Whitfield lab), won an award for his poster at the Guelph-Laurier-Waterloo Protein Symposium.

University of Lethbridge

Correspondent: Ute Kothe

Three new researchers in the molecular biosciences at the University of Lethbridge



Trushar Patel

Dr. Trushar R. Patel is a recent addition to the Alberta RNA Research and Training Institute and the Department of Chemistry and Biochemistry. Dr. Patel graduated with BSc and MSc degrees in Biotechnology from the Sardar Patel University, India followed by PhD studies at the University of Nottingham (UK), where he performed biophysical characterizations of therapeutically important polysaccharides. In 2007, he joined the laboratory of

Dr. Jörg Stetefeld (University of Manitoba) where he characterised extracellular matrix proteins to establish a link between their structures and functions, with the support of post-doctoral fellowships from the Manitoba Institute of Child Health (2008-2010) and CIHR (2010-2012). Dr. Patel also worked in the McKenna Laboratory (2012-2013), where he studied interactions between host proteins and viral RNA molecules to understand how the terminal regions of viral RNAs recognize host proteins. In 2013, Dr. Patel was successful in receiving a distinguished Marie Skłodowska-Curie International Incoming Fellowship to understand the role of a focal adhesion protein in cancer cell signalling using cell biology techniques at the Hotchin Laboratory (the University of Birmingham, United Kingdom).

Dr. Patel returned to Canada in 2015 to establish a Medicinal Biophysics Laboratory as part of ARRTI at the University of Lethbridge. His current research is focussed on studying multi-domain proteins, RNA-protein and protein-protein complexes that affect various cellular processes and diseases. His background working with molecules from polysaccharides to nucleic acids and experience in techniques from cell biology to structure biology allows him to connect dots from genes to function. Such information can lead to the development of novel inhibitors that interfere with host-viral component interactions and therefore inhibit viral replication. Dr. Patel is also associated as a co-Director with the DiscoveryLab (the University of Alberta) that supports collaborative efforts from researchers with a wide range of background to discover and develop novel therapeutic agents.

Dr. Athanasios Zovoilis is a Principal Investigator at the Alberta RNA Research and Training Institute (ARRTI) and an Assistant Professor of Bioinformatics at the University of Lethbridge. Dr. Zovoilis joined ARRTI from Harvard Medical School (USA), after his nomination as a Canada Research Chair in RNA Bioinformatics and Genomics. Dr. Zovoilis' research in



Athanasios Zovoilis

RNA Bioinformatics and Genomics is inspired by the convergence of human genetics with recent advances in RNA biochemistry and computational sciences. It is at the intersection of these fields that Dr. Zovoilis tackles complex research challenges to elucidate the complexity of the human non-coding genome, and the role of non-coding RNAs in cancer and dementia. Dr. Zovoilis is a physician with a background in Medical Genetics, a PhD in Molecular Genetics from the University of Goettingen (Germany), post-graduate training in bioinformatics from the University of Manchester (UK), and expertise in bioinformatics of next generation sequencing from his time as research fellow at Vancouver Genome Sciences Centre (Canada) and Harvard Medical School (USA). He has also been a fellow of the European Molecular Biology Organization, a fellow of the German Research Foundation and member of The Cancer Genome Atlas Research Network. Dr. Zovoilis has contributed significantly to our understanding of the role of non-coding genome in cell function and human disease and his studies include leading author publications in Journals such as *Science* and *Cell* that have been highly influential and widely cited in the field of RNA Genomics and Epigenomics.

Dr. Steve Wiseman joined the Department of Biological Sciences at the University of Lethbridge in June 2016 as an Associate Professor and a Canada Research Chair (Tier II) in Aquatic and Mechanistic Toxicology. Dr. Wiseman earned his PhD in Biology from the University of Waterloo and did his post-doctoral work at the University of



Steve Wiseman

Saskatchewan. His research program is investigating the molecular and biochemical mechanisms of both adaptive and maladaptive responses in aquatic organisms, particularly fishes, exposed acutely or chronically to natural and anthropogenic chemical stressors. A major focus of Dr. Wiseman's research at the University of Lethbridge will be determining whether exposures to chemical stressors during sensitive early life-stages of development triggers molecular reprogramming that results in life-long and even multi-generational effects on physiological functions, including changes in sensitivity of physiological systems to re-exposure.

Three U of L professors elected to the Fellowship of the Royal Society of Canada

A renowned neuroscientist, an accomplished anthropologist and a leading biologist from the University of Lethbridge have been elected to the Fellowship of the Royal Society of Canada (FRSC). Their election acknowledges the remarkable accomplishments of **Drs. Louise Barrett, Bruce McNaughton and Joe Rasmussen** in advancing knowledge and scholarship.

Dr. Barrett, a U of L psychology professor, applies innovative approaches to evolutionary anthropology and psychology that have contributed to an exciting and fruitful interdisciplinary research program. Her training in ecology and anthropology led her to accept a Canada Research Chair in Evolution, Cognition, and Behaviour, and she has also published influential books and articles on the social nature of cognition. Her research is firmly grounded in world-class empirical field study of social interaction in primate populations.

Dr. Rasmussen, a biology professor, has contributed significantly to the development of tracer approaches to modelling energy flow in food webs, based on fractionation and kinetics of naturally occurring isotopes. These approaches have yielded fresh insights and technical inroads into important ecological problems such as the biomagnification of persistent contaminants and the impacts of heavy metals and mining practices. Dr. Rasmussen's research has important applications to conservation problems, including invasive species, habitat modelling and fragmentation.

Dr. McNaughton, a neuroscience professor, has made ground-breaking discoveries in systems neuroscience that have been the basis for thousands of studies and publications focused on how the world thinks about synaptic plasticity, spatial cognition and long-term memory. His research has dramatically impacted neuroscience theory and his experimental and conceptual work contributed significantly to the work upon which the shared 2014 Nobel Prize in Physiology and Medicine was awarded.

Leading RNA researchers gathered at U of Lethbridge for RiboWest Conference 2016

Investigators in the field of Ribonucleic acid (RNA) research met at the University of Lethbridge, June 5-8, 2016, to attend the 12th Annual RiboWest Conference.

The RiboWest Conference is an annual meeting of RNA researchers from western Canada and beyond. “This meeting is an excellent opportunity for networking, establishing new collaborations and having fun in sharing our enthusiasm for RNA,” said Dr. Ute Kothe, professor of chemistry & biochemistry at the UofL and a main conference organizer. “The focus this year has been on RNA and synthetic biology: new RNA technologies, as well as RNA in health & disease. We have welcomed over 80 attendees from 10 universities and five business enterprises.” A pair of keynote speakers represented the highlight of this year’s conference. **Dr. Adam Arkin**, a professor at the University of California Berkeley and co-director of BIOFAB: International Open Facility Advancing Biotechnology, presented on “Discovery and Design of mRNA Determinants of Expression Control.” **Dr. Paul Lasko**, a professor at McGill University and a founding member of the Developmental Biology Research Institute (DBRI), talked about “Translational Control in the *Drosophila* Germ Line”.

Alberta RNA Research and Training Institute welcomes Gairdner Award winner 2016

The Alberta RNA Research and Training Institute (ARRTI) was delighted to host **Dr. Rodolphe Barrangou**, recipient of the 2016 Canada Gairdner International Award, in November 2016. Dr. Barrangou, an Associate Professor in the Department of Food, Bioprocessing and Nutrition Sciences at North Carolina State University, is renowned for his work in establishing and characterizing the CRISPR-Cas bacterial immune defense system. During his two-day visit to southern Alberta, Dr. Barrangou shared his scientific insight through lectures at the University of Lethbridge and the Agriculture and Agri-Food Research Centre. He explained his research, as well as the far-reaching implications of these CRISPR-Cas systems, or gene scissors, for society. Dr. Barrangou also inspired the next generation of young scientists by presenting lectures at two local high schools in English and French, respectively. Last but not least, Dr. Barrangou joined ARRTI researchers for a one-day scientific symposium where he shared his expertise and career advice with U of L students

U of L iGEM team wins gold medal for project with Lethbridge Fire and EMS

The University of Lethbridge’s International Genetically Engineered Machine (iGEM) team’s project this year involved creating an easy-to-use and cost-effective kit for

the rapid detection and monitoring of newly emerging germs in ambulances and health-care facilities. “Our presentation went really well, we had a lot of positive feedback and a lot of interest around how feasible it would be for EMS to actually implement the system,” says first-year PhD student Taylor Sheahan after her team returned from the International Genetically Engineered Machines (iGEM) World Jamboree in Boston, Mass. with a gold medal in tow.

Lethbridge Fire and Emergency Medical Services contacted the U of L iGEM team to determine if their current cleaning practices were adequate. The team met with paramedics, surveyed them about areas of concern and participated in ride-alongs with emergency medical workers to better appreciate the situations faced daily by first responders. These steps helped shape the project and determine its scope, with the goal of determining if emergency medical vehicles are indeed reservoirs for pathogens. Using cutting-edge, in-house DNA sequencing technology to aid in identifying pathogens present in the emergency medical vehicles, the U of L team conducted experiments to identify different bacterial species present in each ambulance by investigating a region of DNA unique to each organism.

The fact the project was community-driven and seeks to solve a real problem garnered praise from the judges in Boston. This aspect has been a focus of iGEM in recent years and something the U of L has excelled at, winning gold at each of the last four competitions. In particular, the Federal Bureau of Investigation and the Public Health Agency of Canada expressed interest in following the project as it continues. In addition to the U of L iGEM team, the Lethbridge High School iGEM team was awarded a bronze medal for their work on a rapid wound treatment system.

University of Manitoba

Department of Biochemistry and Medical Genetics

Correspondent: Louise Simard

After years of diligent efforts by **Dr. Louise Simard** and Genetic Counsellors **Jessica Hartley**, **Sherri Burnett** and **Shannon Chin**, the University of Manitoba and the Provincial Government of Manitoba approved our proposal to implement a MSc degree program in Genetic Counselling. This accomplishment would not have been



*Jessica Hartley, Interim
Program Director of the MSc in
Genetic Counselling*

possible without the hard work of **Dr. Alison Elliott** (now at the University of British Columbia) who had the vision to seek support from the College of Medicine to create this program, Genetic Counsellor **Erin Dola** (now at the University of Utah) who was among the initial drivers of

this proposal and **Dean Brian Postl** who was extremely supportive of this professional program. Importantly, we were granted New Program Accreditation status from the Accreditation Council for Genetic Counseling (ACGC). Genetic Counsellor **Jessica Hartley** is Acting Program Director and the application deadline for 2017 was February 1. We will commence training our first cohort of three students on September 2017. For more information, you are directed to our website (http://umanitoba.ca/faculties/health_sciences/medicine/units/biochem/10437.html) under the link, Prospective and Current Students.

Tri-Council funding has become increasingly difficult to acquire; this year, NSERC awards went to **Dr. Jim Davie** for research on "Protein arginine methyltransferases and transcriptionally active chromosomal domains", **Dr. Hao Ding** to study the "Function of RTEL1 in protecting the heritable genome in spermatogonial stem cells", and **Dr. Mojgan Rastegar** to study "Gene regulatory network of neural stem cells: Implicating the role of MeCP2 isoforms". **Dr. Jim Davie** was a Co-investigator on a CIHR Team Operating grant entitled "The developmental origins of obesity and obesity-related complications in children, while **Dr. Spencer Gibson** was the recipient of a CIHR Bridge Grant to pursue his work on "Targeting the regulation of subtypes of autophagy in cell survival and death to develop novel treatment strategies in glioblastoma". **Dr. Mojgan Rastegar** also received funding from the International Rett Syndrome Foundation, and the Ontario Rett Syndrome Association. **Dr. Barbara Triggs-Raine** was awarded an operating grant from Glyconet to study the "Pathogenesis of, and therapeutic approaches for, hyaluronidase 2 (HYAL2) deficiency".

Our faculty were recognized by a number of significant awards in 2016. The most prestigious was the Rx&D's

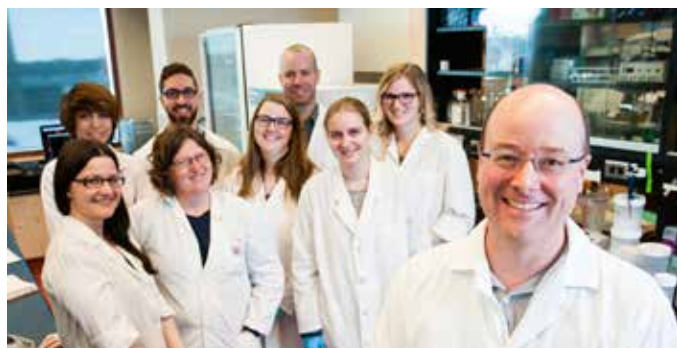


*Distinguished Professor Cheryl
Rockman-Greenberg*

Health Research Foundation Medal of Honour awarded to **Distinguished Professor Cheryl Rockman-Greenberg** in recognition of her outstanding contributions as a pediatrician, geneticist, and clinician scientist. Congratulations go to **Dr. Kirk McManus** for his

University of Manitoba Merit Award for a Combination of Teaching, Service, and Research, as well as the 2016 Graduate Student's Association Teaching Award; it is especially rewarding when one is recognized by one's own students! Consistent with his outstanding mentorship, Dr. McManus' students have received many distinctions; most notably, **Laura Thompson** obtained both the University of Manitoba Emerging Leader Award and the Most Promising Life Sciences Student Award. We are also pleased to announce that Clinician Scientist **Dr. Versha Banerji** was the recipient of a New Investigator Award from Research Manitoba, the premier funding body of the Province. Lastly, **Dr. Mark Nachtigal** was appointed as Director of the Interdisciplinary Health Program (IHP), a joint program of the Rady Faculty of Health Sciences and the faculties of Arts and Science. The IHP offers two undergraduate degrees, a Bachelor of Health Sciences, and a Bachelor of Health Studies; IHP aims to provide a strong foundation for students seeking entry into professional healthcare programs. More information can be obtained at http://umanitoba.ca/faculties/health_sciences/ihp/program.html.

This was a busy year and many of our graduate students successfully defended their thesis work. MSc degrees were awarded to **Eric Bouchard** (Dr. Versha Banerji), **Fahmida Jahan** (Dr. Jeff Wigle), **Angela Krutish** (Drs. Michelle Liu and Louise Simard), **Erin McAndrew** (Dr. Kirk McManus), **Niaz Mahmood** (Dr. Jiuyong Xie), **Amani Moraya** (Dr. Mark Nachtigal), **Megha Murali** (Dr. Jeff Wigle), and **Kate Zhao** (Dr. Pingzhao Hu). PhD recipients included **Biswajit Chowdhury** (Dr. Barbara Triggs-Raine), **Brent Guppy** (Dr. Kirk McManus), **Ravinder Kaur** (Dr. Tamra Werbowetski-Ogilvie), **Peter McQueen** (Dr. John Wilkins), **Samantha Pauls** (Dr. Aaron Marshall), **Yi Yan** (Dr. Etienne Leygue), and **Robby Zachariah** (Dr. Mojgan Rastegar). They are to be congratulated for their hard



Members of the McManus lab, left to right: Laura Thompson, Yasamin Asbaghi, Zeldá Lichtensztejn, Tarik Leylek, Nicole Wilkinson, Brent Guppy, Lucile Jeusset, Erin McAndrew, and Dr. Kirk McManus

work in disseminating their research, and passing their oral thesis examinations.

On the awards front, our students were even busier than our Faculty and received numerous recognitions at local, provincial, and national levels; here is a snapshot of a few of these distinctions. **Anna Blankstein** (MSc student with Dr. Spencer Gibson) was awarded a Canada Graduate Scholarship – Master’s, while NSERC Postgraduate Doctoral Scholarships went to **Sasha Blant** (PhD student with Dr. Trevor Pemberton), and **Laura Thompson** (PhD student with Dr. Kirk McManus). **Lisa Liang** (PhD student with Dr. Tamra Werbowetski-Ogilvie) was among the CBC Manitoba Top 40 under 40, and she also received the Carolyn Cope Oncology Award. Research Manitoba Studentships went to **Ifeoluwa Adewumi**, **Shayan Amiri**, **Anna Blankstein**, **Lucile Jeusset**, and **Nicole Wilkinson** at the MSc level, and to **Lisa Liang**, and **Laura Thompson** to complete their PhD studies. **Yasamin Asbaghi** (MSc student with Dr. Kirk McManus) received the President’s Graduate Scholarship in Human Genetics. We have three departmental awards that are part of yearly competitions; this year, **Lisa Liang** was the recipient of the Human Genetics Endowment Fund, **Laura Thompson** received the Mindel Rady Olenick Fellowship in Human Genetics, and **Sasha Blant** and **Chen Chi** shared the Phyllis J. McAlpine Graduate Fellowship. Go to our website for a more fulsome list and more pictures!



Lisa Liang

Lisa Liang (PhD student with Dr. Tamra Werbowetski-Ogilvie) was among the CBC Manitoba Top 40 under 40, and she also received the Carolyn Cope Oncology Award. Research Manitoba Studentships went to **Ifeoluwa Adewumi**, **Shayan Amiri**, **Anna Blankstein**, **Lucile Jeusset**, and **Nicole Wilkinson** at the MSc level, and to **Lisa Liang**, and **Laura Thompson** to complete their PhD studies. **Yasamin Asbaghi** (MSc student with Dr. Kirk McManus) received the President’s Graduate Scholarship in Human Genetics. We have three departmental awards that are part of yearly competitions; this year, **Lisa Liang** was the recipient of the Human Genetics Endowment Fund, **Laura Thompson** received the Mindel Rady Olenick Fellowship in Human Genetics, and **Sasha Blant** and **Chen Chi** shared the Phyllis J. McAlpine Graduate Fellowship. Go to our website for a more fulsome list and more pictures!

This is the second year that the University of Manitoba held a Three Minute Thesis (3MT®) competition that challenges graduate students to describe their thesis work in a mere three minutes or less. Originating in the University of Queensland, there are now at least 43 participating universities with regional events held in Canada, Hong Kong, United Kingdom, and the United States. The first place university recipient moves on to the Western Regional 3MT® Competition. Congratulations to **Lisa Liang** (PhD candidate under the supervision of Dr. Tamra Werbowetski-Ogilvie) for being chosen as one of 2016’s Top 10 Challengers.

University of Ottawa

Department of Biochemistry, Microbiology and Immunology

Correspondent: Daniel Figeys

We are pleased to introduce our newest members of the Department:



Benjamin Rotstein

Dr. Benjamin Rotstein joined the department as an Assistant Professor in July 2016. He is located at the University of Ottawa Heart Institute. He received his Ph.D. in chemistry from the University of Toronto and pursued a post-doctoral fellowship at Harvard Medical School and

Massachusetts General Hospital. His research program aims to develop medical imaging to use in clinical diagnosis and in nuclear molecular imaging research.

Dr. Kin Chan joined our department in July 2016 as well. He earned a doctorate in molecular and cellular biology from the University of Washington, based on dissertation research carried out at the Fred Hutchinson Cancer Research Center. His



Kin Chan

post-doctoral training was at the National Institute of Environmental Health Sciences in North Carolina. His research is focused on elucidating the molecular origins of cancer and the molecular basis of mutations caused by carcinogens, to devise better cancer prevention, diagnosis, and treatment strategies.



Carolina Ilkow

Dr. Carolina Ilkow completed her graduate studies at the University of Alberta, under the supervision of Dr. Tom Hobman. She pursued her research training as a post-doctoral fellow in Dr. John Bell's lab, at the Ottawa Hospital Research Institute. She joined the Department

of Biochemistry, Microbiology and Immunology as an Assistant Professor in July 2016, and her research is focused on oncolytic viruses and the impact of tumour microenvironment on the therapeutic outcome of viroimmunotherapy. She is also interested in learning how the metabolic diseases (such as obesity) or aging can affect the response to the virotherapy.

Dr. Mathieu Lavallée-Adam joined the Department in September 2016, and the main objective of his lab is to develop computational methods that will lead to a better understanding of cellular mechanisms and diseases processes, by using proteomics



Mathieu Lavallée-Adam

technologies in the context of systems biology. He completed his graduate studies in Computer Science, with Bioinformatics option, at the McGill University. He expanded his knowledge in proteomics and mass spectrometry technologies by pursuing a post-doctoral fellowship in the John R. Yates proteomics lab at the Scripps Research Institute in San Diego, California.

Dr. Michele Ardolino is an immunologist whose aim is to fight cancer by using the immune system. He started his



Michele Ardolino

laboratory at the Ottawa Hospital Research Institute in November 2016 and is a member of the department of Biochemistry, Microbiology and Immunology. Dr. Ardolino obtained his Ph.D. in Immunology at the University of Rome. He then moved

to Berkeley in California to work with David Raulet as a post-doctoral fellow, where he spent six years studying how a population of immune cells called Natural Killer cells respond to cancer.

New undergraduate program, Translational and Molecular Medicine (TMM):

In 2016, we launched our new undergraduate program in Translational and Molecular Medicine (TMM), a collaborative effort between the researchers at the University of Ottawa, Faculty of Medicine and its affiliate health care institutes, under the supervision of the Director of the programme and Assistant Professor in the Department of Biochemistry, Microbiology and Immunology, **Dr. Jean-Francois Couture**. TMM is truly revolutionary in integrating theoretical and practical courses with e-learning techniques to offer students the most advanced and innovative learning experience in Canada. In TMM, students not only learn about biologically relevant medical issues in the largest health network in Eastern Ontario, but they also acquire the technical knowledge to confront the complex biomedical challenges of tomorrow.

Awards and honours:

The Vice-President, Research, **Dr. Mona Nemer**, a member of our department, has been elected a fellow of the American Association for the Advancement of Science (AAAS), the world's largest general scientific society and publisher of the esteemed journal, *Science*.

University of Ottawa

Department of Cellular and Molecular Medicine

Correspondent: David Lohnes

The Department of Cellular and Molecular Medicine

(CMM) is home to 40 regular faculty members and over 100 cross appointees and adjunct members. Departmental members conduct basic research in the biomedical sciences, including regenerative medicine, neuromuscular and neurodegenerative disorders, cancer, kidney disease, stroke recovery, congenital defects, and other areas of relevance to human health. The department is actively engaged in undergraduate education in areas including physiology, anatomy, reproductive biology and pharmacology, the undergraduate medical education curriculum, and the honours program in Translational and Molecular Medicine. CMM also offers MSc and PhD degrees through the Cellular and Molecular Medicine and Neuroscience Graduate Programs, with over 200 students currently registered. In addition to offering a wide range of contemporary graduate courses in support of this training, both of the graduate programs host seminar programs feature prominent local, national and international guest speakers.

New faculty members: CMM continues to benefit from an aggressive recruitment effort that has brought some outstanding young talent to the department. Our most recent recruits are highlighted below.

Richard Naud:



Richard Naud

Richard Naud is the first Canadian scientist to be elected as a member of the prestigious Next Generation Leaders of the Allen Institute for Brain Science. This is a group of six esteemed young scientists who will provide feedback in both formal and informal settings to researchers at

the Allen Institute. The program recognizes distinguished and innovative contributions from early-career scientific leaders, nurtures professional growth and provides informal training on serving as a scientific advisor.

Richard's research encompasses three areas:

Understanding the neural code: If an electrode is implanted in the brain and connected to a loudspeaker, one would hear a rough and unstructured sound. This noise can be the manifestation of imprecision intrinsic to biological signal processing, or it can be the reflection of a highly optimized algorithm. Using mathematical models,

the Naud group researches the structure of the neural code in order to develop efficient information algorithms and improve brain machine interfaces.

Statistics of neuroscience data: To arrive at compact and accurate description of neurons and how they interact, the Naud group designs statistical methods that can be used on multiple types of biomedical data: electrophysiology, multi-electrode arrays, and fluorescence imaging.

Computer simulation of neural systems in health and disease: Using simulation of neural systems, the Naud group can screen hypotheses at a rate unachievable with experimental methods. They use simulation to test recovery protocols in demyelinating diseases and stroke.

Greg Silasi:



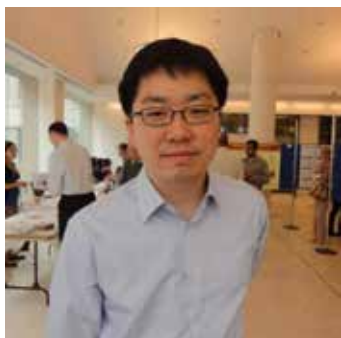
Greg Silasi

The Silasi laboratory utilizes pre-clinical models of stroke to identify informed targets for therapeutic brain stimulation, and to evaluate the safety and efficacy of this intervention following various forms of stroke. It is now becoming clear that the majority of stroke sufferers also have

a number of smaller, "silent" strokes that frequently go unnoticed, but may impact recovery after a major stroke. The Silasi group systematically assesses the effects of diffuse microinfarcts on recovery after a focal stroke using behavioural tests and cortical mapping techniques. Their experiments will focus on forelimb function through automated, home-cage assessment, while cortical reorganization will be followed longitudinally through widefield mapping of both evoked and spontaneous activity in sensorimotor cortex. These studies address how microinfarcts influence re-mapping of lost function after stroke, and thus identify potential targets for future brain stimulation.

Han Kim:

The Kim laboratory focuses on genetic and metabolic regulation of heart development, function and disease, with emphasis on obesity, diabetes and heart failure. First, they are interested in the molecular function and mechanism of *Iroquois* transcription factors in the heart, which are not only implicated in organ development,



Han Kim

but also in energy homeostasis regulation. Second, they are investigating metabolism of the heart and its communications with other core metabolic tissues/organs (e.g. adipose tissue and liver). Using genetically engineered mice as their principal models,

the Kim lab integrates physiology with molecular and systems biology approaches to address the fundamental questions about cardiac metabolism in heart function and diseases.

Pierre Mattar:

Dr. Mattar's research is primarily focused on understanding how the cellular diversity of the nervous system is generated, focusing on the retina as a model system. His lab is trying to decipher how retinal progenitors undergo progressive changes in their developmental potential as development proceeds. He studies a group of transcription factors originally identified in the *Drosophila* CNS that he previously found to regulate the potential of retinal progenitors. He is interested in how these transcription factors function at the epigenomic and transcriptomic levels to expand or contract progenitor multipotency. His group is also interested in post-developmental roles for these transcription factors. In particular, they study the requirement for these transcription factors in retinal photoreceptor survival and homeostasis, with a focus on their effects on photoreceptor genome organization and function.



Pierre Mattar

Honours and awards:

Dr. Leonard Maler, Professor in the Department of Cellular and Molecular Medicine, and **Dr. André Longtin** from the Department of Physics, together have won the Natural Sciences and Engineering Council of Canada (NSERC) Brockhouse Canada Prize for Interdisciplinary

Research in Science and Engineering. The distinguished accolade is accompanied by a \$250,000 research grant. The two are highly deserving of this award that recognizes Canadian researchers turning shared knowledge and skills into excellent achievements. Dr. Maler and Dr. Longtin combine expertise in neurobiology, mathematics and physics. Together they decipher the neural code underlying the brain's activity in efforts to map the mind and its functions. The pair's important discoveries in basic research are part of a growing number of exciting initiatives casting uOBMRI (uOttawa Brain and Mind Research Institute) as a hub of neural research in Canada.

University of Toronto

Department of Biochemistry

Correspondent: David Williams

Faculty news:



The MaRS West Tower

In a major development, 14 of the core faculty members have moved from the Medical Sciences Building to the 15th and 16th floors of the MaRS West Tower, located on the south east corner of University Avenue and College Street. The move was spearheaded by the joint efforts of **Chair Justin Nodwell**, Leah Cohen, Chair of Molecular

Genetics and Avrum Gotlieb, Chair of Laboratory Medicine and Pathobiology. The two modern open-concept floors, which are also occupied by labs from the Molecular Genetics and Laboratory Medicine and Pathobiology Departments, have already fostered new collaborations and closer ties between the various research groups. The floors were organized thematically rather than by department with the 16th floor housing labs with a focus on "Infectious Disease", while those of 15th floor focused on "Genetic Models of Disease". In addition to labs that have already moved, the space will also be the new home of 4 future faculty members. The first of them, **Dr. Haley Wyatt** (<http://biochemistry.utoronto.ca/person/haley-wyatt>) arrived at the University on April 1, 2017.

The Department was delighted to learn that **Lewis Kay** has won the **Gairdner International Award**, Canada's highest science prize. Lewis' work on the development and use of nuclear magnetic resonance (NMR) techniques for investigating molecular motion and short lived conformations in large multiprotein complexes, or 'seeing the unseeable' to use the vernacular,



Lewis Kay

has pushed boundaries and opened up new paradigms in macromolecular structure and function. The award will be presented in Toronto next October, 2017. This has been a banner year for Lewis since he was also named an **Officer of the Order of Canada** for "his pioneering research in biochemistry and medical imaging science which explores the structure and behaviour of proteins." Our warmest congratulations to Lewis!

Julie Forman-Kay was elected as a **Fellow of the Royal Society of Canada**. Julie studies the structure, interactions and functions of disordered proteins of significant biomedical relevance. Her work has led to scientific understanding of the importance of disordered proteins and links their dynamic properties and biological function, providing a foundation for novel therapeutic approaches.



Greg Fairn

We were pleased to learn that **Greg Fairn** has won the **Walter A. Shaw Young Investigator Award in Lipid Research** from the American Society for Biochemistry and Molecular Biology. Greg is the first Canadian to win this award, which recognizes outstanding research contributions in the area of lipids by young investigators who are an Assistant

Professor or equivalent, and with no more than 10 years of experience post M.D. or Ph.D. The award consists of a plaque, cash prize, transportation and expenses to present a lecture at the 2017 ASBMB Annual Meeting to be held in Chicago.

Khosrow Adeli received the **2016 Senior Investigator Award, Canadian Lipoprotein Conference**, which was presented in St. Johns, Newfoundland, in September 2016. He also established the **CALIPER database** of healthy reference values for biochemical markers in children and adolescents (<http://www.sickkids.ca/Caliperproject/About>). The database is now accessed by thousands of scientists/physicians in hospitals and universities around the world to help with diagnosis and monitoring of pediatric disease. It is the most comprehensive biochemical marker database in children worldwide.

Our **Graduate Professional Development program**



Khosrow Adeli

continues to gain recognition as it was recently featured in a 2017 report by the Council of Graduate School, funded by the National Science Foundation, about Graduate Professional Development in STEM disciplines in North America. GPD Director, **Nana Lee**, currently consults with other departments and universities across North

America to start their own GPD courses and programs. She is also spearheading a faculty development workshop series (GFD) through Graduate and Life Science Education, Faculty of Medicine, U of Toronto, to provide training to other faculty members wishing to instruct their own graduate students in professional development. Nana's many speaking engagements this past academic year include workshops and trainee sessions for the Canadian Society of Immunology, Canadian Society of Microbiologists, University of Guelph, Canadian Society of Pharmaceutical Sciences, North American Graduate Career Consortium at Berkeley and University of Toronto's 10th Annual Teaching and

Learning Symposium. She makes her CSMB speaking debut at their 2017 conference.

Keeping with the theme of professional development, **Reinhart Reithmeier** has been busy in his role as Special Advisor to the Dean of the School of Graduate Studies, where he completed a major report on "Graduate Professional Development at the University of Toronto". He is currently finishing work on "The 10,000 Ph.D.s Project". This project has determined the current employment positions of all Ph.D.s who graduated from the University of Toronto from 2000 to 2015. In the biomedical sciences, about 15% of Ph.D.s are currently employed as tenure-track professors. Increasingly, more Ph.D.s are finding employment in the private and public sectors. This highlights the importance of providing professional development training as an integral part of a graduate education, which is a major recommendation of the report.

Nana Lee and **Reinhart Reithmeier** also launched their new guidebook for graduate professional development titled "**Success after Graduate School**". It was designed to help create the pathway to students' dream careers. Special thanks to Ph.D. student **Nikko Torres** for his illustrations and book design work. The book can be obtained online at the UofT Bookstore: <http://uoftbookstore.com>

On June 12-15, the **66th Conference of the Canadian Society of Microbiologists**, led by co-chairs **Trevor Moraes** and **Alex Ensminger**, was held at the University of Toronto. CSM 2016 was a resounding success with over 525 registrants, the most ever recorded at a CSM conference. The conference was held on campus with more than 45 talks and 300 posters. A gala closing reception was held at the art deco gem, the Carlu. Betty Zou, an aspiring science journalist, was invited to cover the conference for Science Borealis.

Oliver Ernst with post-doc **Jana Broecker** and **Michael Overduin (U Alberta)** organized the 2016 North American SMALP Conference which was held April 29th at the University of Toronto. This conference focused on the applications of polymer nanodiscs in membrane protein research. Oliver and his group also ventured into the world of virtual reality, conducting presentations in Potsdam and Shanghai using the Autodesk virtual reality viewing system.

Stavroula Andreopoulos and **Derek Ng** were awarded an Elevation Grant from the Advancing Teaching and Learning in Arts & Science (ATLAS) initiatives fund. The proposal "Visual and Interactive Media for Deeper Molecular Understanding of Enzyme Kinetics" represents the start of a long-term mutually beneficial collaboration between the Department of Biochemistry and UT Mississauga's Biomedical Communications (BMC) program. MSc BMC students will design and develop a series of 3D animations and an interactive simulation tool to help undergraduate students better visualize the relationship between abstract mathematical models and the molecular behaviours, interactions, and dynamics that produce kinetic phenomena.

Congratulations to **Khosrow Adeli**, **Liliana Attisano**, **Julie Forman-Kay** and **Shana Kelley** who were awarded Foundation Grants from the Canadian Institutes for Health Research. Congratulations also to **Penney Gilbert**, who was named a Tier II Canada Research Chair in Endogenous Repair for her work on understanding the mechanisms that control muscle stem cell fate during skeletal muscle homeostasis and regeneration.



Gordon Dixon

The Department was saddened by the news of the passing of **Gordon Dixon** on July 24th, 2016. Gordon, a very accomplished biochemist, was Associate Professor in our Department for the period 1960-63. Gordon was most recently Professor Emeritus of Medical Biochemistry at the University of Calgary. He served as Department Chair there from 1983-88. As noted in the

University of Calgary's In Memoriam message, he had an illustrious career during which he received "numerous accolades and international recognition. He served as President of the Canadian Biochemical Society (1982-83); Pan-American Biochemical Society (1987-90); and was a member of the Executive of the International Union of Biochemistry (1988-94). He received the Ayerst Award (1966), the Steacie Prize (1966), the Flavelle Medal of the

RSC (1980), and the Izaak Walton Killam Memorial Prize (1991). He was inducted as a Fellow of the Royal Society of Canada and a Fellow of the Royal Society (London) in 1978. He was made an Officer of the Order of Canada in 1993 in recognition of his long and distinguished research career.”

Research highlights:

Moraes lab identifies a novel protein required for the proper display of virulence factors in bacteria. (Nature Micro. 2016, 1:16009)

Bacterial pathogens that cause gonorrhea and meningitis have developed a number of virulence factors to survive inside our body. One of the most well characterized virulence factors is the class of proteins called surface lipoproteins or SLPs. The Moraes lab showed that movement of these SLPs across the outer membrane requires a previously uncharacterized family of proteins named Slam for Surface lipoprotein assembly modulator. They also showed that the addition of Slam allowed for the delivery of SLPs to the surface of laboratory strains of *E. coli*. In the future, the display of SLPs by Slam has applications in development of SLP-based vaccines against bacterial pathogens.

Banting Fellow in Julien lab contributes structure of immune hook that sets a paradigm for HIV-1 vaccine testing in humans (Science 2016, 351:1458)

June Ereño-Orbea solved the crystal structure of an engineered HIV-1 immunogen, which brings the field one step closer to inducing broadly neutralizing antibodies (bnAbs) as a major HIV vaccine goal. This study resolves a critical unmet challenge: to design a molecule that binds naïve B cell precursors of bnAbs at sufficient frequency in humans for reliable vaccine responses. As a proof-of-concept, the engineered immunogen was successful in isolating naïve B cell precursors of bnAbs in 96% of HIV-uninfected donors. Structures of antibodies isolated from HIV-uninfected donors and their affinities to the immunogen support its testing as a candidate human vaccine.

Rubinstein lab finds one of the missing puzzle pieces in the structure of the vacuolar type ATPase (PNAS 2016, 113:3245)

Vacuolar-type ATPases (V-ATPases) are ATP-powered proton pumps involved in numerous essential processes in the cell. In this paper, cryo-EM studies are combined with the use of information from evolutionary covariance

to build a first atomic model for the membrane-embedded subunits from a bacterial V/A-ATPase and the eukaryotic V-ATPase. The models show a surprising conservation of architecture in all rotary ATPases.

Understanding the molecular underpinnings of cell signalling through GPCRs (Nature 2016, 533:265)

There is a great deal of interest in understanding the broad class of cell signalling receptors called GPCRs (G-protein-coupled receptors), which are responsible for basic processes such as vision, taste, smell, chemical and hormonal signalling in the brain and whole body, cell homeostasis, and immune defence. 30-40% of current pharmaceuticals target these membrane receptors, which essentially serve as gate-keepers for cell signalling. New findings by the Prosser and Ernst labs allow the design of the next generation of GPCR drugs that stabilize specific receptor conformations to exert specific pharmacological effects. This work represents the beginning of several key collaborative projects that use NMR, pulsed EPR (DEER spectroscopy) and crystallography to better understand the activation process of GPCRs and interpret pharmacological phenomena in terms of protein structural and dynamic information.

Howell lab develops novel ways to treat chronic bacterial infections (Science Adv. 2016, 2:e1501632)

Bacterial biofilms represent a significant medical challenge due to the inability of therapeutics and the immune system to penetrate this protective coating. The Howell lab identified and produced two enzymes to degrade this critical component of the biofilm. The enzymes, known as glycoside hydrolases, do not kill the bacteria directly but instead remove the protective coating allowing antibiotics and the innate immune system to function more efficiently. The next step in the project involves showing the efficacy of these enzymes in an animal model of infection.

Kelley lab screens for new pathways involved in the maintenance of mitochondrial DNA (Nature Chem. Biol. 2016, 12:567)

Ph.D. student Simon Wisnovsky undertook a high-throughput screening study that leverages small-molecule probes to look for new DNA repair and replication factors in human mitochondria. The study uncovered a novel DNA polymerase that is essential for mitochondrial function. Given the importance of mitochondria as cellular energy generators and trigger points for programmed cell death,

this discovery may provide new ways to probe or perturb essential cellular functions.

Andrews' lab identifies potential new drug combinations for chronic lymphocytic leukemia (Blood 2016, 128:934)

The Andrews group used high-content screening to test 320 kinase inhibitors and identify ones that, when given in combination with venetoclax, can overcome resistance to the drug. Venetoclax inhibits the anti-apoptotic protein Bcl-2 and is available in the U.S. to treat patients with chronic lymphocytic leukemia (CLL). Using cells from patients with CLL, Andrews and oncologist Dr. David Spaner found that for approximately half of the CLL patient samples, the kinase inhibitor sunitinib enhanced venetoclax-mediated cell killing dramatically compared to venetoclax alone. This proof-of-principle study demonstrates the feasibility of using high-content screening to individualize treatment regimens for patients.

Seeing the first steps of DNA repair (Nature 2016, 536:100)

The laboratories of John Rubinstein, Frank Sicheri and Dan Durocher used electron cryomicroscopy (cryo-EM) to determine the structure of the DNA-damage recognizing protein 53BP1 bound to modified nucleosome core particles. The work was led by post-doctoral fellow Marcus Wilson and research associate Samir Benlekhir, and provides the first structural insight into how dimethylation and ubiquitination of nucleosomes in response to DNA damage recruits 53BP1, initiating repair of the damage. The structure was determined by cryo-EM at 4.5 Å resolution, which approaches the resolutions that can be determined by X-ray crystallography.

Protein unfolding machinery visualized (PNAS 2016, 113:E4190)

Using a combined cryo-EM and solution NMR approach, the laboratories of John Rubinstein and Lewis Kay have determined the structure and equilibrium distribution of two unique conformers along the ATP hydrolysis cycle of the AAA⁺ unfoldase VAT. This work provides insight into how this class of molecular machines is able to convert the chemical energy of ATP hydrolysis into the mechanical force required to unfold client proteins. The study was led by Rui Huang and Zev Ripstein.

Malnutrition in children may lead to severe impairments in liver function (J Cell Biol 2016, 214:677)

Malnourished children living in the same household who are given the same food to eat sometimes have stark differences in health, leading researchers to query why some severely malnourished children face death while others don't. Peter Kim and Robert Bandsma, together with international collaborators, found in an animal model that severe malnutrition could lead to dysfunctional liver mitochondria, which are essential for energy production, and a loss of peroxisomes, which are important for normal liver metabolic function. They identified the gene PEX2, which, when turned on by malnutrition, causes the loss of peroxisomes. This is the first study to demonstrate a diet-induced loss of peroxisomes in vivo.

Proton pumping region of rotary ATPases revealed (Nature 2016, 539:118)

In work led by postdoctoral fellow Mohammad T. Mazhab-Jafari, the Rubinstein laboratory used electron cryomicroscopy to determine the atomic structure of the membrane-bound region of a eukaryotic V-ATPase. This study provides the first high-resolution structure for the membrane region of any rotary ATPase, a family of enzymes that includes proton pumping V-ATPases and proton-driven ATP synthases. The structure reveals several surprising features of the enzyme, locates the cytoplasmic half-channel for protons, suggests a mechanism for proton translocation, and identifies a novel subunit of the V-ATPase.

Davidson and Maxwell help discover off-switches for CRISPR (Cell 2016, 167:1829)

Scientists are developing CRISPR to target specific cell types, tissues or organs where a disease occurs. But sometimes, CRISPR hits the wrong target, causing unintended damage. But if you could build an off-switch that keeps Cas9 (the enzyme that cuts the DNA for editing) inactive everywhere except the intended target tissue, then the tissue specificity will be improved. This paper, featured on the cover of the Dec 15 issue of Cell, not only identifies that "off switch" but it shows that CRISPR inhibitors have evolved naturally and can be identified and exploited. The "off switch" will allow researchers to be more precise in their use of CRISPR.

One of our resident physical biochemists, **Scott Prosser**, is working closely with Patrick Gunning's group on some new drug delivery and drug screening projects that will use

both ^{19}F NMR and MRI imaging. Scott confesses to having a love affair with all things related to fluorine chemistry and Patrick Gunning's chemistry. New experiments with live animals at the National Magnet Lab (Gainesville, FL, USA) will test their capacity to monitor drug delivery system partitioning and targeting in real time, using MRI. Much of Scott's recent work has been focussed on the inner workings of GPCRs by ^{19}F NMR. Building upon their published work in *Cell* (161(5), 1101-1111), co-authored with Nobel laureate Brian Kobilka, their most recent GPCR work was recently published with Oliver Ernst in *Nature* (*Nature* 2016, 533: 265) followed by a second *Nature* paper with Robert Lefkowitz (*Nature* 2016, 535: 448). Scott and co-author Emil Pai have finally published their first joint paper on a dimeric enzyme and the role of enzyme dynamics in catalysis. This was just published by *Science* as a full article (*Science* 2017, 355: Jan 20) though you can get the gist of the paper in this YouTube video <https://www.youtube.com/watch?v=db5gaE-c6aw>.

Faculty appointments:

The Department was pleased to welcome four new faculty members in 2016.

Dr. Haley Wyatt joined the Department with a primary appointment as Assistant Professor. Her research interests are focussed on understanding the mechanistic details of macromolecular complexes that safeguard genome integrity and how mutations in these complexes contribute to human disease. Haley completed her Ph.D. studies in 2009 in the laboratory of Dr. Tara Beattie (U of Calgary) where she studied the human telomerase reverse transcriptase. As a post-doctoral fellow with Dr. Stephen West at the Francis Crick Institute, her research centred on the biochemical and cellular functions of

the SLX4 protein and its role as a scaffold for an endonuclease DNA repair complex. This research is of particular relevance to human health because mutations in SLX4 (and its associated nucleases) are linked to Fanconi anemia, a complex disorder characterized by bone marrow failure, chromosomal instability, and cancer susceptibility.

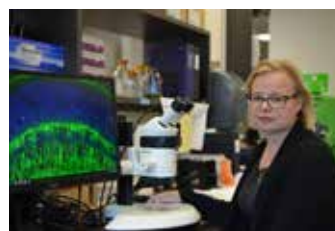


Haley Wyatt

Dr. Karen Maxwell also joined the Department with a primary appointment as Assistant Professor. Karen did her doctoral work at the University of Toronto studying the virion assembly process of *E. coli* phage λ . She subsequently conducted postdoctoral studies in the laboratory of Dr. Aled Edwards in the area of phage structural genomics. Since 2007, Karen has led her own research group at the Donnelly Centre at U. of T. Her current focus is on the molecular mechanisms by which phages contribute to bacterial virulence in the human pathogens *E. coli* and *P. aeruginosa*, and identifying small molecules that inhibit these activities.



Karen Maxwell



Carol Schuurmans

Dr. Carol Schuurmans, the Dixon Family Chair in Ophthalmology Research and Senior Scientist at the Sunnybrook Research Institute, joined our Department with a primary appointment as full Professor. She

completed her Ph.D. degree in Medical Genetics at the University of Toronto. She then undertook post-doctoral studies at the Institut de Génétique et de Biologie Moléculaire et Cellulaire in Strasbourg. Carol joined the Department of Biochemistry and Molecular Biology at the University of Calgary as an Assistant Professor in 2001, and became full Professor in 2014. In July, 2016, she joined the Sunnybrook Research Institute. Her research is focused on the specification of neural cell fates and the control of tissue morphogenesis in the developing central nervous system, in particular in the retina and neocortex. She is now applying her knowledge of neural development to understand the injury response, and to create lineage conversion strategies for cell replacement therapies.

Dr. Andreas Schultze, Associate Scientist and Head of Clinical and Metabolic Genetics at the Hospital for

Sick Children, was cross-appointed to the Department as an Associate Professor. Andreas obtained his M.D. and Ph.D. degrees at the University of Leipzig and undertook post-doctoral work at the Ruprecht-Karls University on the use of electrospray ionization tandem mass spectrometry for neonatal screening of inborn errors of metabolism.



Andreas Schultz

He also holds specialist certification in pediatrics and biochemistry. His current research is focussed on improving strategies for early diagnosis and treatment in genetic defects of guanidinoacetate methyltransferase, arginine:glycine amidinotransferase and the creatine transporter. He also uses magnetic resonance spectroscopy for in vivo metabolic profiling in brain and ESI- tandem MS for comprehensive metabolome description.

Retirements (written by Peter Lewis and Reinhart Reithmeier):



Larry Moran

Laurence (Larry) A. Moran will become Professor Emeritus effective July 1, 2017. Larry joined our department in 1978 following a post-doctoral stint with Alfred Tissieres at the Université de Genève and a Ph.D. with Bruce Alberts at Princeton. Larry's research has been focussed on a variety of topics

including molecular evolution. He is passionate about undergraduate education and science education in general. Larry has educated legions of undergraduates and mentored many graduate students. He is co-author of a very popular textbook - Principles of Biochemistry - now in its 5th edition. Larry actively contributes to

the blog Sandwalk, which encourages discussions on a variety of science topics including molecular evolution. We wish Larry and his wife Leslie every happiness in this new phase of their lives. We will miss him.



David Williams

David Williams has decided to pack up his pipettes, recycle a mountain of X-ray films and bid a fond farewell to the Department of Biochemistry that has been his academic home for 33 years. David is known internationally for the discovery of the calnexin chaperone system and how class I histocompatibility molecules assemble with antigenic peptides in the

endoplasmic reticulum, a process necessary for antigen presentation. Recent research has focussed on the roles of molecular chaperones, protein disulfide isomerases and peptidyl prolyl isomerases in protein folding as well as in the quality control system of the endoplasmic reticulum. This work has been continuously funded by NCIC and CIHR and has led to influential publications in Nature, Science, Mol. Cell, PNAS, EMBO J. and J. Cell Biol.

An excellent mentor and teacher, David's many graduate students and post-docs have gone on to a variety of positions in academia, industry and medicine-related fields. David's enthusiasm has also made him a popular lecturer at both the undergraduate and graduate levels in his courses on the eukaryotic secretory pathway. David's lectures always featured the presentation of "real" data and helped develop his students' critical thinking and analysis skills.

David held several administrative positions within the Biochemistry Department including Acting Chair (1996-1997) and Graduate Coordinator (2001-2005). His many contributions were recognized in 2014 when he won the Department of Biochemistry Citizenship Award. David was elected President of the Canadian Society of Biochemistry, Molecular and Cellular Biology in 2009, and received the Society's Merck-Frosst Award in 1994.

But the Biochemistry Department may remember David most fondly for his science parody songs, jointly penned and performed with fellow guitarist and biochemist John Glover and several grad students who passed through the lab over the years. Indeed, rumour has it that one of his top questions posed to prospective grad students during interviews was “But can you sing?” <https://www.youtube.com/watch?v=ihsI9ZfcCHc>

An avid street photographer, David could also be seen documenting departmental events and keeping the website filled with images of the latest happenings. Indeed, David is eagerly looking forward to having enough time to devote to his photographic pursuits, a passion he’s had since his teen years. The past year has seen two solo exhibitions as well as a joint documentary photography exhibition on the Little India area of Toronto that attracted interviews on CBC Radio, CBC TV News and Ryerson TV. For more information on David’s street photography check out: <http://www.davidwilliamsphotography.ca>. David is also a skilled wine maker and wine drinker, and he enjoys working on his many carpentry projects. It seems like David will have little trouble transitioning to an active retirement and we wish him the very best in his future endeavours!

The Department will be celebrating David’s many contributions to research, teaching and service at the University of Toronto at a retirement celebration at the Faculty Club, June 8th, 2017.

Departmental events:

Research Day

On August 25 and 26, the Biochemistry Department held its first Retreat outside of Toronto at the Geneva Park Conference Centre near Orillia. The turnout was terrific, with 140 trainees, staff and faculty gathering for two days to celebrate the science that we do, and to enjoy each other’s company in a beautiful lakeside setting. The Retreat featured cutting-edge talks by trainees and Faculty members as well as an evening poster session that showcased the excellent research being carried out by more than 60 students and post-docs. We also enjoyed an excellent presentation from this year’s **Theo Hofmann Lecturer, Dr. Molly Shoichet**, who gave a superb presentation on the use novel injectable hydrogels for localized drug delivery.



It's all smiles for the 2016 Research Day

But it wasn’t all about science - the Biochemistry Graduate Students Union organized an entertaining (and often hilarious) photo scavenger hunt that had people from different nodes of the Department working together to find arcane items and to create unusual photos and videos. The evening bonfire with songs, glowsticks, s’mores and conversation into the very wee hours, was also a big hit. The free afternoon on the second day saw many taking the opportunity to hike, swim, paddle, or play volleyball and baseball.

For some additional photos of the event, please go to: <http://biochemistry.utoronto.ca/2016/08/2016-biochemistry-retreat-at-geneva-park/>



Molly Shoichet with Theo Hofmann and Chair, Justin Nodwell

Golf Day

August 9 dawned hot and steamy, but that didn’t deter our hardy biochemists from heading out to Flemingdon



The Dead Ringers hoist the coveted Biochemistry Cup at our Annual Golf Day

Park 9-hole Golf Course in midtown Toronto for our annual Golf Day. Each team had its share of beginners and ringers playing a “best ball” format that allowed everyone to contribute to their team. Despite the 32 C heat and sticky humidity the competition was fierce, with the Dead Ringers pulling out the win, just ahead of the The Right Lefties and ERADicals.

More pics at: <http://biochemistry.utoronto.ca/2016/08/2016-biochemistry-golf-day/>

Graduate student news:

Benjamin Schachter Memorial Lecture

From 1934-1939 Dr. Benjamin (Benny) Schachter worked in the Department of Biochemistry conducting research on female sex hormones, isolating and identifying conjugated estrone sulfate (Premarin). To honour Benny Schachter’s memory, an annual lectureship is held in which our graduate students select and host the speaker who is a graduate from our Department and who has followed a non-academic career path. This year featured our first alumni appreciation reception during which students had the opportunity to network with Biochemistry alumni from different fields including biotech, education, business, government/policy and communication.

The 2016 Schachter Lecturer was **Josephine Marks**, a Principal at the Toronto Financial Services practice of Eckler Ltd. She completed her M.Sc. from the Department of Biochemistry in 1981. Since then, she gained over thirty years of financial sector experience, with previous employment with two major Canadian

insurance companies, a major public sector pension plan and, most recently, with a major Canadian bank. Her expertise encompasses various financial aspects of insurance and pension operations, with a focus on asset-liability management, risk management, product design and development, financial reporting and governance.

Annual poster competition

One of the highlights of the Department’s Annual Research Day is the student and post-doc poster competition. This year it was particularly enjoyable within the lakeside setting of Geneva Park. As usual, the quality was high and the decisions tough but, in the end, the following students were chosen as poster winners:

Ph.D. category

Anan Chen (Wilde Lab) *“Determining the roles of anillin-DIAPH3 interaction in organizing the actin cytoskeleton”*

Olesia Ivantsiv (Davidson Lab) *“This chaperone can dance - a new role for phage tail fibre assembly proteins”*

Marios Mejdani (Davidson Lab) *“ Structure and function of an anti-CRISPR that converts CRISPR-Cas into a transcriptional regulator”*



Winners of the 2016 Poster Awards, (left to right) Thiago Seraphim, Anan Chen, Marios Mejdani, Olesia Ivantsiv, Julianne Burcoglu, Samantha Wasserman, Tom Bateman with Grad. Coordinator Angus McQuibban

M.Sc. category

Thomas Bateman (Moraes lab) *“A novel slam-dependent heme acquisition system in the bacterial pathogen Acinetobacter baumannii”*

Samantha Wasserman (Rotin Lab) *“Investigating the*

interaction of SH3PX1 and dNedd4-long in Drosophila melanogaster

Julianne Burcoglu (Enenkel Lab) "*Nuclear export of yeast proteasomes*"

Post-doctoral category

Thiago Seraphim (Houry Lab) "*Mapping the subunit assembly of the R2TP complex*"

Graduate awards

Connell Award for Paper of the Year



Attila Balint presents his Paper of the Year (2015) Award talk

This year's winner of the Paper of the Year was **Attila Balint** (Brown lab) for his paper entitled: "Assembly of Slx4 signaling complexes behind DNA replication

forks". A. Balint, T.H. Kim, D. Gallo, J.R. Cussiol, F.M. Bastos de Oliveira, A. Yimit, J. Ou, R. Nakato, A. Gurevich, K. Shirahige, M.B. Smolka, Z. Zhang and G.W. Brown. *EMBO J.* (2015) 34(16):2182-2197.

Centennial Award

Created in memory of alumna **Sela Cheifetz**, this award was presented to **Simon Wisnovsky** (Kelley lab) who received the honour as our top Ph.D. student beyond year 3.

David Scott Prize

The annual prize for outstanding all-round graduate student was awarded to **Shawn Xiong** (Sicheri lab). Award winners are selected



Simon Wisnovsky receives the Centennial Award from Angus McQuibban



Angus McQuibban presents the Scott Award to Shawn Xiong

on the basis of research and teaching excellence, and outstanding contributions to the Department and to fellow students.

Congratulations to all winners on their achievements!

More graduate news

Natalie Bamford, Ph.D. student in the **Howell lab**, was recently awarded a prestigious **Vanier Canada Graduate Scholarship** from the Natural Sciences and Engineering Research Council of Canada (NSERC) to continue her research focussing on understanding the biosynthesis of the fungal biofilm exopolysaccharide galactosaminogalactan. She was lead author on a paper, published in the *Journal of Biological Chemistry*, entitled "Sph3 is a glycoside hydrolase required for the biosynthesis of galactosaminogalactan in *Aspergillus fumigatus*." The paper was featured on the front cover and named as "Paper of the Week".

Undergraduate news:

Congratulations to **Zaid Al-Azzawi** for winning the Roy Baker Award, which honours the top Biochemistry Major student in the 1200-strong introductory BCH210 course. Congratulations also to **Adrian Loe**, winner of the Anderson/Giles award, for top marks in our 3rd year Introductory Laboratory Course, BCH377, and to **Ida Szarics** for winning the Bronskill/Painter award for the top BCH Specialist in our BCH478 advanced laboratory course.

University of Toronto

Department of Cell and Systems Biology

Correspondent: Tony Harris

We are 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*, *C. elegans*, *Drosophila*, mouse, *Xenopus*, zebrafish and cell culture) and non-model organisms. The department's major strengths include its groups studying plant molecular biology, its labs focussed 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



John Calarco

centre for genomics and proteomics research, in addition to a state-of-the-art CFI-funded microscopy centre.

Two new faculty members started this year. Dr. **John Calarco** studies the mechanisms and function of alternative pre-mRNA splicing in generating physiologically diverse neurons in *C. elegans*. Dr. **Shelley Lumba** studies abscisic acid signalling networks and their function under abiotic stress in *Arabidopsis* and *Striga*.

Drs. **Vince Tropepe**, **Darrell Desveaux** and **Tony Harris** were promoted to Full Professor.



Shelley Lumba

Dr. **Peter McCourt** was named the Jack Dainty Distinguished Professor at the University of Toronto. The purpose of the Distinguished Professor program is to advance and recognize individuals with highly distinguished accomplishments and those who display exceptional promise, who maintain an extraordinary level of activity in their research and scholarly work and have achieved pre-eminence in their field in line with the University's stated objectives and emerging priorities.

Dr. **Jennifer Mitchell** was the recipient of the inaugural Dorothy Shoichet Women Faculty in Science Award of Excellence. Dr. Molly S. Shoichet, PhD, FRSC, O. Ont. has established this award in honour of her mother, an honorary degree recipient, for female faculty in any of the physical or life sciences, computer sciences or mathematics within the Faculty of Arts and Science at any of our three campuses.

Dr. **Ashley Bruce** was awarded the Faculty of Arts and Science Outstanding Teaching Award for 2016-2017. In

addition to her achievements in curricular development and co-curricular initiatives (e.g., POP), this award recognizes Ashley's excellence in course instruction as well as supervision and mentorship in student research at both the undergraduate and graduate levels. Additionally, Dr. **Kenneth Yip** was the recipient of the Faculty of Arts and Science Superior Sessional Instructor Teaching Award for 2016-2017. Ken is well-known for his teaching contributions to several of our undergraduate courses, especially BIO130 and BIO230 and as his course evaluations attest, has been an outstanding Sessional Lecturer for CSB for many years.

Peggy Salmon and **Jim Dix** were recipients of two of the Dean's Outstanding Staff Awards. We are very fortunate to have fantastic staff members in CSB that help us fulfill our potential for research and teaching excellence.

Congratulations to Dr. **Alan Moses** on the publication of his book *Statistical Modeling and Machine Learning for Molecular Biology* with CRC Press. Molecular biologists are performing increasingly large and complicated experiments, but often have little background in data analysis. The book is devoted to teaching the statistical and computational techniques molecular biologists need to analyze their data. It explains the big-picture concepts in data analysis using a wide variety of real-world molecular biological examples such as eQTLs, ortholog identification, motif finding, inference of population structure, protein fold prediction and many more. The book takes a pragmatic approach, focussing on techniques that are based on elegant mathematics yet are the simplest to explain to scientists with little background in computers and statistics.

Notable publications in 2016 included:

NIN-like protein 8 is a master regulator of nitrate-promoted seed germination in *Arabidopsis*.

Yan D, Easwaran V, Chau V, Okamoto M, Ierullo M, Kimura M, Endo A, Yano R, Pasha A, Gong Y, Bi YM, Provart N, Guttman D, Krapp A, Rothstein SJ, Nambara E.

Nature Commun 2016 7:13179.

G9a and ZNF644 physically associate to suppress progenitor gene expression during neurogenesis.

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Sakthi D Moorthy, Scott Davidson, Virlana M Shchuka, Gurdeep Singh, Nakisa Malek-Gilani, Lida Langroudi, Alexandre Martchenko, Vincent So, Neil N Macpherson and Jennifer A Mitchell

Genome Res 2016 Nov; PMID:27895109

University of Toronto

Department of Molecular Genetics

Correspondent: Barbara Funnell



Leah Cowen

In 2016 Molecular Genetics experienced a big year of both change and growth. We welcomed Leah Cowen as the new Chair of Molecular Genetics, appointed on July 1, 2016. Howard Lipshitz concluded over 10 years as Chair (since 2005) and is enjoying a year of well-deserved administrative

leave. We welcomed our largest graduate class ever in September, with 80 bright young minds, and we have witnessed phenomenal growth in our undergraduate program with two new online courses that are engaging well over 1,000 students. A large cohort of colleagues from the Medical Sciences Building moved to brand new research space on the 15th and 16th floors of the MaRS2 tower, and preparations are underway for major renovations to improve the research space in the Medical Sciences Building. Finally, we are actively recruiting for two new faculty members; one in Molecular Microbiology & Infectious Disease and the second in Genetic Models of Development and Disease, who will join us in the MaRS research space. We hope that you will enjoy our update of 2016 events, achievements and initiatives.

Faculty highlights and awards:

Dr. Monica Justice has been elected a Fellow of the American Association for the Advancement of Science. She was recognized for her contributions to genetics, and in particular for the development of the mouse as a model for identifying disease genes and elucidating therapies for human diseases.



Monica Justice

Dr. Lewis Kay was named an Officer of the Order



Lewis Kay

of Canada, the second highest level of this honour. He is recognized "for his pioneering research in biochemistry and medical imaging science which explores the structure and behaviour of proteins".

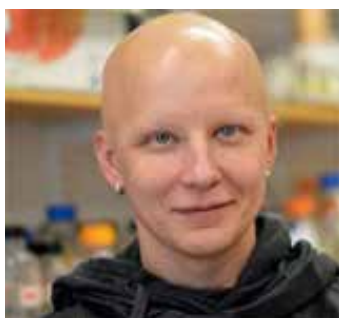
Dr. Anne-Claude Gingras has been appointed a Tier 1 Canada Research Chair in Functional Proteomics. Her research develops



Anne-Claude Gingras

and uses sophisticated systems biology tools to map the protein-protein interaction networks inside cells, and to better understand how these networks are altered as a consequence of disease.

Dr. Mikko Taipale has won an inaugural \$100,000 Canadian Institute for Advanced Research (CIFAR) Azrieli Fellowship, and has been appointed a Tier 2 Canada Research Chair in Functional Proteomics and Protein Homeostasis. His research examines how protein quality control networks are organized in cells and how they contribute to human disease, with particular focus on deciphering the Hsp70 chaperone and its co-chaperones. Dr. Taipale is one of 18 recipients of the CIFAR award, given to scholars who are less than 5 years into their first academic appointments.



Mikko Taipale



Sabine Cordes

Dr. Sabine Cordes is the recipient of the Lloyd S.D. Fogler, QC, Award of Excellence for her work on mood disorders.

Dr. Cordes studies the molecular mechanisms that govern neurodevelopment, neuronal function and angiogenesis. Established in 1997, the award is presented annually to an investigator or group of investigators within Sinai Health System whose recent research contributions have had a significant impact at the highest level of international excellence.

Dr. Laurence Pelletier is the 2016 recipient of the Robert H. Haynes Young Scientist Award in Genetics, awarded by the Canadian Society for Molecular Biosciences (CSMB). His research studies the biogenesis and function of centrosomes, and how damage to these functions can lead to genome instability, developmental diseases and cancer.



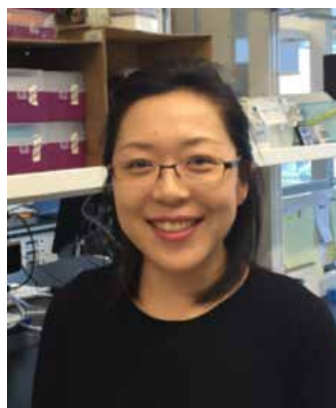
Laurence Pelletier



Julie Claycomb

Dr. Julie Claycomb is the 2016-2017 recipient of the Early Career Excellence in Graduate Teaching and Mentorship Award at the University of Toronto. The award recognizes her outstanding contribution to the training of graduate students through teaching, supervision and mentorship.

Welcome to new faculty:



Jeehye Park

Dr. Jeehye Park is a Scientist in the Genetics and Genome Biology Program at the Hospital for Sick Children, and was appointed to the department as an Assistant Professor in March 2016. She completed her PhD at the Korea Advanced Institute of Science and Technology, and her postdoctoral

training at Baylor College of Medicine in the US. Her research investigates the molecular mechanisms of neurodegenerative diseases with the aim of identifying targetable pathways for therapeutic interventions.

Dr. Jessica Hill was appointed an Assistant Professor, Teaching Stream, in Molecular Genetics Online & Undergraduate Education, in November 2016. Her current research is focused on improving on-line education in medical genetics and microbiology. In particular, she is interested in evaluating the effectiveness of on-line educational tools, improving student engagement in on-line courses, and adapting modules for teaching medical genetics and microbiology in various settings.



Jessica Hill

Trainee awards:

Molecular Genetics has several competitive awards and fellowships, which are given annually to our graduate students. Congratulations to all recipients!! They are:

Elizabeth Polvi (Cowen lab): L.W. Macpherson Award

Ashrut Narula (Rissland Lab): Roman Pakula Award

Boris Dyakov (Gingras Lab): Norman Bethune Award

Tavia Kaplan (Cowen lab): Eric Hani Fellowship

Cassandra Wong (Gingras Lab): Hannah Farkas-Himsley and Alexander Himsley Memorial Prize

Justin Belair-Hickey (van der Kooy lab): David Stephen Cant Graduate Scholarship in Stem Cell Research

Samuel Lambert (Hughes lab): Jennifer Dorrington Graduate Research Award

Departmental and community events:

2nd Annual MoGen Career Development Symposium.

Empowering trainees and engaging alumni are among our goals for the Career Development symposia series started in 2015. The 2nd Annual MoGen Career Development Symposium was held on June 10, 2016, at the Chestnut Residence and Conference Centre. Dr. Leah Cowen and Dr. Julie Claycomb spear-headed the event and organized a day in which trainees could interact and seek mentorship from the breadth of extraordinary alumni in the Department of Molecular Genetics. We are building on the success of the first two symposia, and have scheduled the 3rd Annual Career Development Symposium for June 9, 2017. Please join us!

66th Annual Canadian Society of Microbiologists Meeting. On June 12-15, 2016, the University of



Career Development Symposium 2016

Toronto hosted the 66th Annual Canadian Society of Microbiologists Meeting for the first time in 30 years, co-chaired by Dr. Alex Ensminger (Molecular Genetics & Biochemistry) and Dr. Trevor Moraes (Biochemistry). With 525 registrants, the conference was a huge success, and faculty and trainees from the Department of Molecular Genetics were well represented among the speakers and presenters at the conference.

Toronto RNA Enthusiasts' Day. On August 2, 2016, the very first annual Toronto RNA Enthusiasts' Day (TREnD) was held at the Peter Gilgan Centre for Research and Learning, Hospital for Sick Children. The Symposium was a student-led and trainee-focussed event and was spear-headed by five graduate students in the Department of Molecular Genetics: Amanda Charlesworth, Ashrut Narula, Christopher Wedeles, Miranda Wang and Monica Wu. With guidance from their faculty advisors, Dr. Julie Claycomb and Dr. Olivia Rissland, the organizing group aimed to take advantage of the vibrant and diverse RNA biology community in the Greater Toronto Area, and create a platform that will bring together researchers of every level for a day of RNA-related discussions.

Science Rendezvous. On Saturday, May 7, the University of Toronto (St. George Campus) opened its door to the general public to showcase the important discoveries and innovations in science, engineering and medicine. The event, Science Rendezvous, allows visitors of all ages the opportunity to interact with world-class researchers, gain hands-on experience in conducting experiments and experience science in new and creative ways. The Department of Molecular Genetics came out in full force

this year and had one of the largest displays of the day, spanning multiple tables and rooms. Led by GSA vice-president Elizabeth Polvi, over 30 volunteer students and professors gathered bright and early to show members of the public (both young and young-at-heart) how to extract DNA from a banana, analyze unique genetic traits, craft superhero bacteria and introduce various model organisms, such as flies, worms, yeast, and much more!

MoGen Retreat 2016. We gathered for our 2016 Molecular Genetics Retreat at Geneva Park YMCA, on September 21-23. The retreat was organized by Julie Lefebvre, Jim Rini and Leah Cowen, with the assistance of Amanda Veri, Sabrina Stanley and their GSA team. Our new Department Chair, Leah Cowen, organized an excellent scientific program of 15 faculty talks that captured the diversity and excellence of the research ongoing in MoGen. The retreat kicked off on Wednesday evening for first-year students and faculty members with a faculty-student mixer dinner and the always entertaining Power Hour. On Thursday, the remaining attendees arrived for our largest turn-out yet: 42 Pls, 74 rotation students, 114 graduate students, 12 post-docs/staff, and 17 undergraduate MoGen specialists. The day began with opening remarks from Leah Cowen followed by 2 sessions of talks, a soggy faculty-student soccer showdown, and a poster session boasting a record 110 presentations. We capped a great day off with an entertaining evening of comedy and games, music and dancing, and a campfire by the beach!

Summer BBQ and MoGen Camping Trip. In the summer, the GSA sponsored the annual BBQ (July 28) and a brand new event, a MoGen camping trip (Aug 26-28). Capitalizing on some beautiful weather, the annual GSA BBQ was held on the front lawn of the Centre for International Experience. Students, staff and faculty gathered in the shade and enjoyed some perfectly grilled hotdogs and hamburgers, watermelon and freezies. The food kept on flowing, thanks to Vice-President Eric Chapman who diligently manned the grill, and the day concluded with a Pub Night at the Maddy.

Thanks to the immense hard work of the GSA Event Coordinators, Lauren Tracey and Samantha Esteves, the camping trip was a huge success! Over 13 graduate students made the trek up to Six Mile Lake Provincial Park, and for some of them, it was their very first camping trip! There was much hiking, swimming and roasting s'mores



MoGen Camping Trip 2016

by the campfire. Samantha Esteves commented, “the MoGen Camping Trip went very well! Everyone did their part to keep the camp running and I think these simple activities really bring people together”. There really is nothing like roughing it in the great out-doors to bring people together and help form lifelong friendships.

Halloween Pub Night. On October 26, the GSA held its annual Halloween Pub Night at Prenup Pub. An incredible number of students attended the event and filled the entire upstairs, demonstrating that no matter how young or old, everyone loves celebrating Halloween and getting free candy. As always, awards were given for best individual and group costumes. Competition was fierce this year as students showed off their creativity. First place for best group costume was awarded to members of the Claycomb lab (Amanda Charlesworth, Amy Nabih, Monica Wu, Melissa Wong and Allison Jandura) who



Halloween Pub Night 2016

dressed up as “spice” girls. The best individual costume was awarded to a first year rotation student, Boyang Qiu, whose costume appealed to all Toronto Jays fans. Runner-up for best group costume went to a pair of first year students, Dustin Ammendolia and Krista Schleicher, who showed off their scientific knowledge through their very accurate depictions of DMEM and FBS bottles.

MoGen Holiday Party. On December 9, we gathered together for the annual MoGen Holiday Party held at the U of T Faculty Club. Students, post-docs and faculty shed their lab coats and jeans in favour of their fanciest clothes for a night of socializing and dancing into the wee hours of the next morning. Attendance was outstanding from all nodes of the Department, and holiday cheer was enjoyed by all!

University of Toronto Mississauga

Department of Chemical and Physical Sciences

Correspondent: Scott Prosser

New faculty member **Andrew Beharry** joined the department in September 2016, and is part of a nucleus of researchers interested in Biochemistry and Medicinal Chemistry. Andrew’s lab has started to synthesize small molecule probes for fluorescence-guided photodynamic therapy - a field that combines a robust signal for imaging cancer while providing a cancer-killing “right hook”, through the generation of reactive oxygen species. More information can be found on his website, <http://www.beharrylab.com>

We will be adding a computational chemist/biophysicist to the mix in a few short months. **Sarah Rauscher** (Theoretical and Computational Biophysics, Max Planck Institute for Biophysical Chemistry) will be joining our faculty ranks and working largely on protein allostery and disordered systems. We are really excited about the possibilities of working with Sarah.

Andrew will be a welcome addition to the Medicinal Chemistry Group at UTM, which is led by **Patrick Gunning**. Patrick’s group is focussed on a host of cancers, through the development of novel inhibitors of ubiquitination enzymes and Signal Transducers and Activators of Transcription (STAT) proteins. Patrick has recently



Kanelis lab selfie with Sasha Weiditch shown lower right

completed renovations to a brand spanking new research facility which features state-of-the-art organic hoods and cell culture facilities. Thanks to private benefactors and effort on the part of the University administration, work will soon begin on a new Medicinal Chemistry Research Building and Animal Facility, spear-headed by Patrick. See <http://www.gunninggroup.ca> for the latest!

Voula Kanelis is doing great things with ABC transporters and phage proteins and structural biology studies by NMR <https://sites.google.com/site/kanelislaboratory>. Congratulations to PhD student **Sasha Weiditch** for winning the prize for best talk at the Cell and Systems Biology Research Day, and also for winning the Kenneth C. Fisher Fellowship for 2016 from the CSB Department.

Jumi Shin is continuing to make great research strides in DNA-protein interactions. Details of her work can be found at <http://www.utm.utoronto.ca/~shinjumi/People/People.html>. Recently, she and her post-doc **Ichiro Inamoto** published an article in Molecular BioSystems entitled “Protein dimerization partners are dictated by the DNA target, not protein target”. The article was selected as “hot” and featured on the cover of that issue. They found that many genes are regulated by protein hetero- or homodimers, and DNA bases outside the protein-DNA recognition target determine the protein dimerization partner.

David McMillen’s group is busy with their own model systems, studying synthetic biology and systems biology in cells. You can find their latest publication in: Edouard A. Harris, Alla Buzina, Jason Moffat, and David R.

McMillen (2016). Design and experimental validation of small activating RNAs targeting an exogenous promoter in human cells. ACS Synthetic Biology. DOI: 10.1021/acssynbio.6b00125.

In this paper, the McMillen group reports the first example of targeting exogenous promoters in human cells with small activating RNAs (saRNAs), laying the groundwork for using RNA activation as a tool in synthetic biology. Their selection of activating RNA candidates was informed by a custom-written computer program designed to choose target sites in the promoter of interest according to a set of empirical optimality criteria drawn from prior research. Activating RNA candidates were assessed for activity against two exogenously derived target promoters, with successful candidates being subjected to further rounds of validation as a precaution against potential off-target effects. A genetic platform was assembled that allowed activating RNA candidates to be simultaneously screened both for positive activity on the target reporter gene and for possible nonspecific effects on cell metabolism.

Our resident physical biochemist, **Scott Prosser** (<http://sites.utm.utoronto.ca/prosserlab>)



Scott Prosser

is working closely with Patrick Gunning and his minions on some new drug delivery and drug screening projects that will use both ¹⁹F NMR and MRI imaging. Scott confesses to having a love affair with all things related to fluorine chemistry and

Patrick Gunning's chemistry. New experiments with live animals at the National Magnet Lab (Gainesville, FL, USA) will test their capacity to monitor drug delivery system partitioning and targeting in real time, using MRI.

Much of Scott's recent work has been focused on the inner workings of GPCRs by ¹⁹F NMR. Building upon their published work in Cell (161, 1101-1111), co-authored with Nobel laureate Brian Kobilka, their most recent GPCR work was recently published in Nature <http://www.nature.com/nature/journal/v533/n7602/full/nature17668.html> This was followed by a second Nature paper with Robert Lefkowitz <http://www.nature.com/>

nature/journal/v535/n7612/abs/nature18636.html. Scott and co-author Emil Pai have finally published their first joint paper on a dimeric enzyme and the role of enzyme dynamics in catalysis. This was just published by Science as a full article <http://science.sciencemag.org/content/355/6322/eaag2355>, though you can get the gist of the paper in this YouTube video <https://www.youtube.com/watch?v=db5gaE-c6aw>.

Everyone is looking forward to celebrating the 100th anniversary of the Canadian Society of Chemistry and the annual meeting in Toronto this summer (<http://www.csc2017.ca>).

University of Toronto at Scarborough

Department of Biological Sciences

Correspondent: Rongmin Zhao

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



Dr. Clare Hasenkampf, who is the director of Centre for Teaching and Learning; her research focusses on the mechanisms of homologous chromosome interactions

The Department currently has 34 full time faculty

members and is still rapidly growing, with two new faculty searches currently in progress. In the past year, **Drs. Nick Mandrak, Patrick McGowan, and Jason Weir** were granted tenure. **Dr. Clare Hasenkampf** who studies meiosis in *Arabidopsis* using immunocytochemistry, light and electron microscopy, was promoted to full Professor. Additionally, **Dr. Maydianne Andrade** received the Principal's Research Award for the year 2016.

The Department was very successful in attracting external research funding in 2016. Six PIs (**Drs. Boonstra, Cadotte, Lovejoy, Weir, Molnar and Thiele**) secured their NSERC Discovery Grant as renewals or new applicants. **Dr. Kenneth Welch** was awarded a research grant from the Human Frontier Science Program. Three NSERC RTI applications (**Drs. Harrison, Vanlerberghe and Welch**) were successful, and brought in novel and upgraded research facilities to the department. Additionally, **Dr. Rene Harrison** who studies how the microtubule cytoskeleton is modulated during invasion of pathogens and in bone-wasting disorders, was awarded a major grant from the Canadian Space Agency.

Particularly, **Dr. Bebhinn Treanor** has been awarded a Canada Research Chair in Spatially-Resolved Biochemistry. Dr. Treanor's research focusses on the biochemical processes that drive immune cell activation, specifically the role of B cells, and her research aims to fundamentally understand immune response, how it's regulated, and how it can be controlled to develop therapies for lymphomas and autoimmune diseases. In addition to our faculty, graduate students in the Department also made significant achievement in the past year. **Devrim Coskun** (Kronzucker lab) received the Principal's Graduate Research Award. **Matt Kolmann** (Lovejoy lab) and **Kewei Xu** (Harrison Lab) won the best publication awards. Additionally, **Nikki Alber** (Vanlerberghe lab) won the UTSC Graduate Student TA Teaching Award.

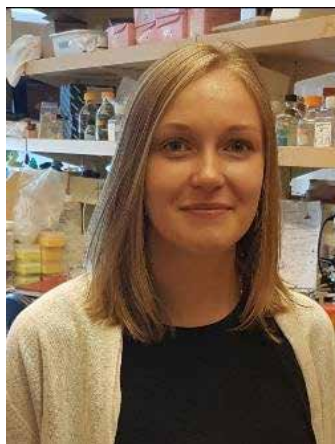
University of Victoria

Department of Biochemistry and Microbiology

Correspondent: Perry Howard

New faculty member:

In our last report the department was in the middle of recruiting a molecular microbiologist/immunologist. We are very pleased to announce that **Dr. Lisa Reynolds**



Lisa Reynolds

will join us as Assistant Professor on March 1, 2017. Dr. Reynolds completed her BSc at the University of Manchester and her PhD at the University of Edinburgh. She studies interactions between the bacterial microbiota, parasites, and mammalian immune cells at mucosal surfaces, particularly in the intestinal tract. Both the microbiota and parasites

must avoid expulsion by the host immune system, and she examines how they manipulate the host immune system and intestinal environment to do so. She is particularly interested in how immunomodulation by the microbiota and parasites can also alter host susceptibility to pathogenic infections and allergic inflammation.

Faculty news:

Dr. Christoph Borchers and the **UVic Genome BC Proteomics Centre** were invited to join the Moonshot initiative, a US-led international collaboration created by former Vice-President Joe Biden to spur cures for cancer.

Drs. Martin Boulanger and Brad Nelson, together with their industrial partner **Zymeworks**, were awarded the largest NSERC CRD grant that UVic has ever received (\$800,000), to develop engineered cytokine/cytokine receptor pairs for engineering of T cells for autologous T cell therapy.

Dr. John Burke, Gillian Dornan, Braden Siempelkamp and Meredith Jenkins together with international collaborators, have coauthored a paper recently published in the [Proceedings of the National Academy of Sciences](#), the results of which provide hope for people afflicted with the primary autoimmune disease, Activated PI3K Delta Syndrome (APDS). "We were able to determine the molecular basis for how the PI3K enzyme is being disrupted by APDS-promoting mutations," says Burke. "This allowed us to screen clinically approved PI3K inhibitors against these mutated versions, and we found that all of them potently inhibited enzyme activity. The result reveals a promising therapeutic strategy for treating APDS patients."

Dr. Caroline Cameron, together with **Dr. Sheila Lukehart** at the University of Washington, have received almost \$3 million in funding from the US National Institute of Allergy and Infectious Diseases at NIH towards developing a vaccine against syphilis. Dr. Lukehart's studies focus on the initial stages of the disease; Dr. Cameron's look at on how *Treponema pallidum* subsp pallidum spreads throughout the body.

Student news:

Congratulations to biochemistry student **Paul Kim**, who was recently named the Association for Co-operative Education (ACE) British Columbia and Yukon Co-op Student of the Year for the University Category. Paul also won a 3M National Student Fellowship in 2016, of which there are 10 awarded across Canada.



Paul Kim

University of Waterloo

Department of Biology

Correspondent: Bernie Duncker



Dr. David Rose

2016 marked the end of an era at the University of Waterloo as **Dr. David Rose** completed his second term as Chair of Biology, and will soon be starting a much deserved sabbatical leave. Our new Chair is **Dr. Hugh Broders**, an animal population biologist specializing in the study of bats, who joins us from Saint Mary's University, where he previously also served

as Chair of Biology. Still on the topic of Chairs of Biology, **Dr. Bernie Glick**, who served in this role from 2001-2007, recently retired.

Numerous Biology Department members were recognized with prestigious awards over the past year, including **Dr. Andrew Doxey**, who was given an Ontario Early Researcher Award, and **Dr. Laura Hug**, whose

recent *Nature Microbiology* paper detailing a new Tree of Life was named one of Altmetric's top 100 articles of 2016. Our graduate students also did us proud in 2016. **Gah-Jone Won** was the national winner of the Three Minute Thesis (3MT) competition for his presentation "The Development of an Antibody-Drug Conjugate to Specifically Target and Soften the Crystalline Lens", **Casey Remmer** and **Samantha Burke** were each awarded a prestigious W. Garfield Weston Award for Northern Research, and **Laura Sauder** won the 2016 Amit and Meena Chakma Award for exceptional teaching. As for our undergraduate students, the Waterloo iGEM (International Genetically Engineered Machine) team

attained Gold Medal standing at the 2016 International Jamboree for the fourth straight year.

Finally, we continued our series of highly successful, well attended public lectures, this time focussing on the Science behind the Zika virus spread, featuring Dr. Christine Dupont among other speakers.



Dr. Andrew Doxey



Dr. Laura Hug

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.

*The society will support **up to six** events each year, to a **maximum of \$500** per event, on a competitive basis. Student organizations seeking financial support under this program should contact the society Secretary with a short description of the planned event, and the amount of funding requested. The request should also include a Regular Member of the Society as a Sponsor/Coordinator, working with the Student Organization. Requests will be accepted twice each year (up to 3 possible awards for each competition), with deadlines of **February 15** and **September 15**.*

James Lepock Memorial Student Symposium 2016 **Department of Medical Biophysics, University of Toronto**

Correspondent: Diana Resetca

The James Lepock Memorial (JLM) Symposium is organized by students in the Medical Biophysics Graduate Student Association. The goal of the JLM Symposium is to offer a forum for graduate students in the Department of Medical Biophysics. At the JLM Symposium, students and faculty are engaged in discussing the latest technology and research in our varied affiliated institutes, including the Princess Margaret Cancer Centre, the Ontario Institute of Cancer Research, SickKids Hospital, Sunnybrook Health Sciences Centre, the Lunenfeld-Tanenbaum Research Institute, and the Donnelly Centre.

This year's event took place in the Medical Science Building at the University of Toronto, and consisted of a keynote talk and a keynote panel, 2 poster sessions, and oral presentations by M.Sc. and Ph.D. students. Approximately 160 graduate students, post-docs, research technicians and faculty participated. This year, our event featured a keynote talk by Dr. Mikhail G.



Poster session at the JLM Symposium 2016



Winners of the best MSc and PhD student talk awards at the JLM Symposium 2016

Shapiro, Assistant Professor of Chemical Engineering at the California Institute of Technology. The keynote panel was focussed on Science Policy and Innovation in Canada, and consisted of Dr. Jim Woodgett, Senior Investigator and Director, the Lunenfeld-Tanenbaum Research Institute, Ms. Gail Garland, CEO, Ontario Bioscience Innovation Organization (OBIO), and Dr. Mehrdad Hariri, Founder and CEO, Canadian Science Policy Centre (CSPC).

La Journée Scientifique des Étudiants du Centre de Recherche sur le Cancer de Québec et l'Axe Oncologie du CHU de Québec 2016

Correspondent: Claire Dziengelewski

La 20ème 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 18 et 19 août 2016 au Centre de Recherche sur le Cancer de l'Université Laval. Organisée par les étudiants du Centre de Recherche, cette journée a rassemblé environ 150 participants provenant des diverses équipes de recherche en cancérologie fondamentale et clinique, en radio-oncologie ainsi qu'en néphrologie. Plus de 110 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.

Cette participation record fait de cette 20ème édition une des plus réussies des dernières années. Les meilleures présentations ont été récompensées par l'octroi de plus de \$9,000 en bourses de congrès et de \$2,000 en prix.

Chaque année, les étudiants invitent pour l'évènement un ou plusieurs chercheurs de renommée internationale qui présentent leurs travaux. Pour la 20ème édition, nous avons eu le plaisir d'accueillir les Dr. Pierre Thibault de l'Université de Montréal et Dr. Jerry Battista de l'University of Western Ontario. Ils ont présenté leurs travaux de recherche portant sur la dynamique des modifications post-traductionnelles des protéines, et sur les dangers potentiels dus aux radiations lors d'un éventuel voyage vers Mars, respectivement. Ces deux conférences de très grande qualité ont été appréciées à la fois par les étudiants des différents axes de recherche, mais également par les chercheurs. La disponibilité et la facilité d'approche des conférenciers ont aussi été soulignées par les étudiants.

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



Présentations d'affiches à la Journée Scientifique Université Laval 2016; Poster session at the Journée Scientifique Université Laval 2016

McGill University Annual McGill Biomedical Graduate Conference (AMBGC)

Correspondent: Rachel La Selva

For the past 15 consecutive years, the Experimental Medicine Graduate Student Society (EMGSS) of McGill University has hosted the Annual McGill Biomedical Graduate Conference (AMBGC). The EMGSS is a nonprofit, studentrun, academic organization that represents graduate students registered in the Division of Experimental Medicine at McGill University.

The AMBGC is a oneday symposium which allows outstanding graduate and undergraduate students the opportunity to present their research. Students from universities across Canada participate in the conference, and participation is open to any student around the world. Attendees are given an opportunity to interact, present their work, and learn from fellow members of the scientific community. Postdoctoral fellows from the aforementioned programs volunteer as judges to award prizes to attendees based on the merit of their presentations. The goal of this conference is to provide training opportunities for graduate students from all labs, regardless of budgetary restrictions. In this vein, the AMBGC does not charge a registration fee. We rely for the most part on the generosity of academic and corporate sponsors to finance our conference.

The 16th AMBGC took place on Thursday, March 17th, 2016 at La Plaza Conference Centre, 420 Sherbrooke Street, Montreal, QC. In recent years, the number of attendees has ranged from 150200. Participants include

undergraduate and graduate students, postdoctoral fellows, university faculty, corporate representatives and community members.

Themes for the conference included:

- Cell Signalling and Gene Expression
- Clinical and Experimental Oncology
- Central and Peripheral Neuroscience
- Endocrinology and Metabolism
- Microbiology and Immunology
- Cell Biology, Polarity and Localization
- Epidemiology, Bioethics and Medical Genetics
- Cardiovascular and Respiratory Disease
- Musculoskeletal and Developmental Disorders

The keynote address this year was given by Dr. Xiaoyan Jiang from the Terry Fox Laboratory at the University of British Columbia. Dr. Jiang received her MD from Shanghai Second Medical University and her PhD with Dr. Paul Jolicoeur in the Division of Experimental Medicine at McGill University. She undertook post-doctoral training with Dr. Connie Eaves at the BC Cancer Agency. She is a Distinguished Scientist at the Terry Fox Laboratory of the BC Cancer Agency and an Associate Member of the Department of Medicine at the University of British Columbia. She is also an Adjunct Professor at the Shanghai Institute of Medical Genetics. Dr. Jiang's research interests are focussed on basic and translational research of molecular properties of cancer stem cells that contribute to the development of leukemia and drug resistance. In particular, she discovered the AHI-1 oncogene in a mouse model of human leukemia during her PhD studies at McGill University; it has been widely recognized as a critical therapeutic target in several diseases. She has published more than 80 peer-reviewed publications,



AMBGC oral presentation session



AMBGC poster session



The Experimental Medicine Graduate Student Society of McGill University celebrating another successful year of organizing the AMBGC for student research trainees

review articles and book chapters and received several prestigious awards, including an MSFHR (Michael Smith Foundation for Health Research) Investigator Award, CFI Award and UBC Merit Awards. Dr. Jiang also plays lead roles in several national and international collaborative translational research projects to develop improved prognostics and treatments for human hematologic disorders. Her current translational studies on cancer stem cells are funded by CIHR, CCSRI, LLSC, CRS, and by industrial research grants from Novartis, Bristol-Myers Squibb and Pfizer.

Ontario Biology Day 2016 Ryerson University

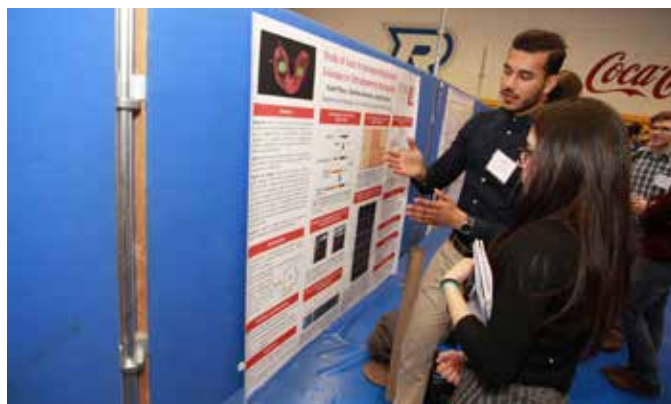
Correspondent: Aju-sue Francis

The goal of Ontario Biology Day is to foster and provide a venue to showcase biological research carried out by undergraduate students in Ontario universities. In 2016, Ontario Biology Day was held at Ryerson University; the event was organized by graduate and undergraduate Biology Students at Ryerson University.

About 270 students participated in an active day, which included the invited speakers Dr. Hendrik Poinar (Department of Anthropology, McMaster University), Dr. Zayna Khayat (Senior Advisor, Health System Innovation and Director, MaRS EXCITE), Dr. Burton Lim (Assistant Curator of Mammalogy at the Royal Ontario Museum) and Dr. Lynda McCarthy (Department of Chemistry and Biology, Ryerson University). Participants had the opportunity to present their research in poster sessions and student talks.



Students registering for Ontario Biology Day



A student presenting his poster to one of the graduate student judges

Ottawa-Carleton Institute of Biology 12th Annual Symposium 2016

Correspondents: Michael Country, Carl Farah, and Lauren Gallant (University of Ottawa); Kama Szereszewski, Sanoji Wijenayake, and Chanchal Yadav (Carleton University)

Each spring, the Ottawa-Carleton Institute of Biology (OCIB) Symposium brings together students from the biology departments of both Carleton University and the University of Ottawa to engage in exciting discussions related to current developments in biology with leaders in the field. The OCIB Symposium has become an integral part of the biology community at both universities and is an important opportunity to showcase the high calibre research being performed there.

The 2016 OCIB Symposium, which is the biggest event held by the OCIB, took place in the SITE building at the University of Ottawa, and was a great success. We had nearly 200 registrants over our 2-day conference, the theme of which was Research with Impact. Our goal was to emphasize the power of biology by having speakers discuss their research with an emphasis on highlighting novelty, applications, and/or contributions to a field of study.

Keynote speakers were Dr. Stephen Archer from the Department of Medicine at Queen's University, and Dr. Moshe Szyf from the Department of Pharmacology and Therapeutics at McGill University. The day's activities included a careers session, where attendees



Keynote speaker, Dr. Moshe Szyf

were invited to meet industry/government professionals Phil Thomas (Environment Canada), Clark Holden (Registered Patent Agent with the Canadian Intellectual Property Office), Kristen

Mattison (Director for Health Canada), and Stacey Mantha (Director of the Public Health Agency). A poster session included over 60 graduate, post-doc, and undergraduate research posters. Participants also heard guest speakers from industry (Paul Lem; CEO of Spartan Bioscience) and from a patent office (Clark Holden; Registered Patent Agent with the Canadian Intellectual Property Office). There was a well-attended pub talk by Dr. Jack Cornett (Canada Research Chair in Radiochemistry and Environmental Health, and a member of the University of Ottawa Departments of Chemistry and Earth Sciences), and Speed Rounds - one with graduate presentations,



Participants attending one of the talks



OCIB organizers



Participants attending one of the talks



Poster session

one featuring professors - which challenged researchers to summarize their work in mere minutes.

Simon Fraser University Molecular Biology and Biochemistry (MBB) Graduate Colloquium 2016

Correspondent: Kaylee Magee



Colloquium presentation by PhD student Bhav Dhillon (taken by Kevin Rey)

For our event, which took place on April 28th 2016 at the Diamond Family Auditorium at Simon Fraser University, the MBB department was celebrating “50/15”: the 50th anniversary of SFU and the 15th anniversary of the MBB department. We held our annual graduate student colloquium during the day, with talks and poster presentations from students on their

recent research, and held an alumni mixer in the evening. The aim of this event, in addition to celebrating our 50th and 15th anniversaries, was to foster relations between all members of the MBB community and provide an opportunity for our past and present students to reunite and discuss their career paths and scientific interests.

The colloquium was planned by students in the MBB Graduate Caucus. Students, faculty, and staff all worked together to organize and advertise the alumni mixer. Over 130 people attended the event. The colloquium had presentations from over 15 graduate students, and a poster session with 20 undergraduate and graduate participants. The sessions were judged by faculty and over \$800 in prize money was awarded to graduate students. The mixer had presentations from two alumni, Brian Kwok of Fusion Genomics and Lorena Braid of Aurora BioSolutions, on their career progression after graduating from the MBB department. The mixer also had “Then and Now” presentations from current MBB faculty on the changes that have occurred in their respective scientific disciplines since SFU opened in 1965.

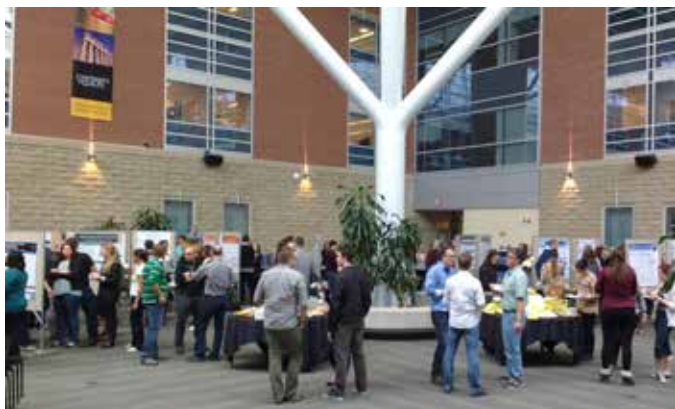


The MBB poster session (taken by Kevin Rey)

University of Guelph, College of Biological Sciences Graduate Student Symposium 2016

Correspondent: Dita Moravek

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 the college. The Graduate Student Symposium took place on April 25 2016 at the University of Guelph. Over 200 people attended, including graduate students and faculty from the departments of Molecular and Cellular Biology, Integrative Biology and Human Health and Nutritional Sciences.



Student poster presentations

The overall theme of the Graduate Student Symposium is sharing science! Every year the event includes oral and poster presentations by graduate students regarding their current research. Many of the students have never had an opportunity to present their research and this event gives them the chance to do so. This year, there were around 50 presenters in both the oral and poster presentations, which means 100 students had the opportunity to share their research.

The event also includes a presentation from a keynote speaker about their research, and they often share much more great insight into the life of a senior scientist. This year we were delighted to hear from Dr. Jessica Grahn, who is a cognitive neuroscientist from Western University, about the research she conducts regarding music rhythm and the motor areas of the brain.

Our organizing committee consisted of 12 enthusiastic individuals (students and faculty) from the three departments including Shawn Beaudette, Alison Berezuk, Francesca Herlihey, Liz Johnston, Sahar Mehrpooyan, Dita Moravek, Lily Nasanovsky, Trevor Partch, Katie Sutor, Glen Van Der Kraak, Karen White and Derek Zwambag.

University of Victoria Department of Biochemistry and Microbiology Graduate Research Symposium

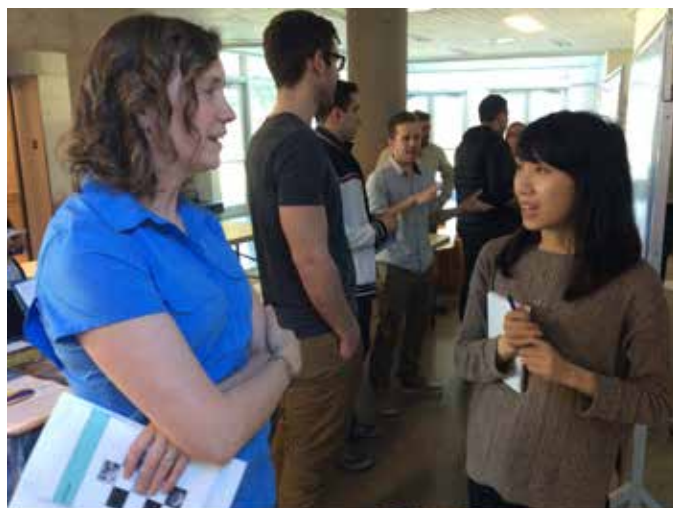
Correspondent: Gillian Leigh Dornan

The Biochemistry and Microbiology Graduate Student Research Symposium is an annual event, which allows graduate students a chance to showcase their research

to their peers in either an oral or poster presentation format. This event is vital in the development of graduate students' careers in that it allows them to practice key skills such as abstract writing, science communication, and discussion in a comfortable environment.

The organizing committee consisted of 5 key members this year: Gillian Dornan, Karen Lithgow, Neda Savic, Karl Makepeace, and Teesha Baker. In addition we had wonderful support from the entire department including our department Chair, Dr. Perry Howard, and our administrative team Margaret Blake, Melinda Powell and Deb Penner.

The event was held at the University of Victoria in the Bob Wright Building on February 12 2016, from 9:00 am to 4:00 pm. Approximately 30 students, 2 post-docs, and 11 faculty members attended for the entire day with many



Scenes from the UVic Biochemistry and Microbiology Graduate Research Symposium



Scenes from the UVic Biochemistry and Microbiology Graduate Research Symposium

post-docs, research assistants and external members of the university popping in for different sessions.

This year we hosted two keynote speakers: Dr. Leonard Foster, from UBC, and Dr. Craig Brown, from the UVic Division of Medical Sciences. From our departmental advertisement of the keynote speakers, "Dr. Leonard Foster is coming from UBC to give us the buzz on applying proteomics to honey bees. Dr. Craig Brown from UVic DMS will shine the light on vascular repair in the brain."

In addition to our keynote speakers, there were 7 highlighted student speakers this year, covering our department's broad range of research including structural studies, cellular signalling, and studies of microbial pathogenesis. Another special feature was our poster session highlighting the research of students from a variety of stages in our program. There were two

separate poster sessions, and we had the opportunity to invite senior members of our department to judge students and provide feedback. These judges included Dr. Jo Hobbs, Charmaine Wetherell, Dr. Ellen Busby, and Dr. Omid Haji-Ghassemi.

The Graduate Research Symposium was a great success this year, with many students expressing a high level of satisfaction and enjoyment in the feedback we collected. It is with the continued support from our sponsors that we can provide our graduate students the opportunity to communicate their research and hear from outstanding senior members of the greater scientific community.

Vins et Fromages 2016 **Institut de recherches cliniques de** **Montréal (IRCM)**

Correspondents: IRCM Student and Post-doc Association, Wine and Cheese Committee: Tiphaine Dolique, Michael Housset, Marine Roux, Shannon Swikert

Le 7 avril 2016, comme chaque année depuis sa création il y a 23 ans, l'Association étudiante de l'Institut de Recherches Cliniques de Montréal (IRCM) avait pour mission d'organiser son "Vins et Fromages". Un événement annuel d'importance puisque tous les membres de la communauté interne l'institut, incluant chercheurs, cliniciens, membres de la Fondation de l'IRCM, ainsi que des étudiants internationaux sont invités à se réunir. Les étudiants sont affiliés aux différents programmes de Biochimie, Biologie Cellulaire, Biologie Moléculaire de l'Université de Montréal, et au programme de Médecine



Le comité organisateur autour de l'affiche de l'évènement; The organizing committee around the event posters



Forte affluence autour du buffet; Rush hour at the buffet



Les participants se sont regroupés par équipes pour tenter de répondre aux questions du quiz; Participants formed teams to try and answer the quiz questions



Une occasion pour les scientifiques de se retrouver ou de se rencontrer dans un cadre convivial; An opportunity for scientists to meet in a convivial setting

expérimentale de l'Université McGill. Ce regroupement permet aux étudiants d'échanger de manière informelle avec les chercheurs et directeurs de laboratoire dans une ambiance décontractée et conviviale.

Cette année, le soutien financier de la SCBM a grandement contribué à faire de cette soirée un succès! Entre 150 et 200 participants ont pu se retrouver dans l'atrium de l'Institut au milieu d'un décor sur le thème d'un marché fermier et déguster des fromages canadiens et des vins du monde entier dans une ambiance musicale. L'organisation de séances de "quiz" par équipes tout au long de la soirée autour du thème de la science de la fabrication du vin et du fromage fut un divertissement très apprécié qui a réveillé l'esprit de compétition de bon

nombre de nos collègues scientifiques et amateurs de ces produits et fut également l'occasion pour les novices d'en apprendre plus sur le sujet.

On April 7, 2016, as in every year since its creation 23 years ago, the student association of the Montreal Institute of Clinical Research (IRCM) had the mission to organize its "Wine and Cheese". This is an anticipated annual event as all the members of the internal community, including researchers, clinicians, members of the IRCM Foundation, as well as international students are invited to join. The students here are affiliated with the different programs of Biochemistry, Cell Biology and Molecular Biology of the University of Montreal, and with the Experimental Medicine program of McGill University. This gathering allows students to meet and exchange in an informal manner and a convivial setting with researchers and laboratory directors.

This year, the financial support of the CSBM largely contributed to make a success of this event! Between 150 and 200 participants met in the Institute's atrium in a decor on the theme of a farmer's market and tasted Canadian cheeses as well as wines from all over the world, while enjoying live music. A big hit of the evening was the organization of quiz sessions around the theme of the science of wine and cheese making, revealing the competitive nature of some of our scientists and enthusiastic colleagues, and the opportunity for the beginners to learn more on the subject.

