Bulletin

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

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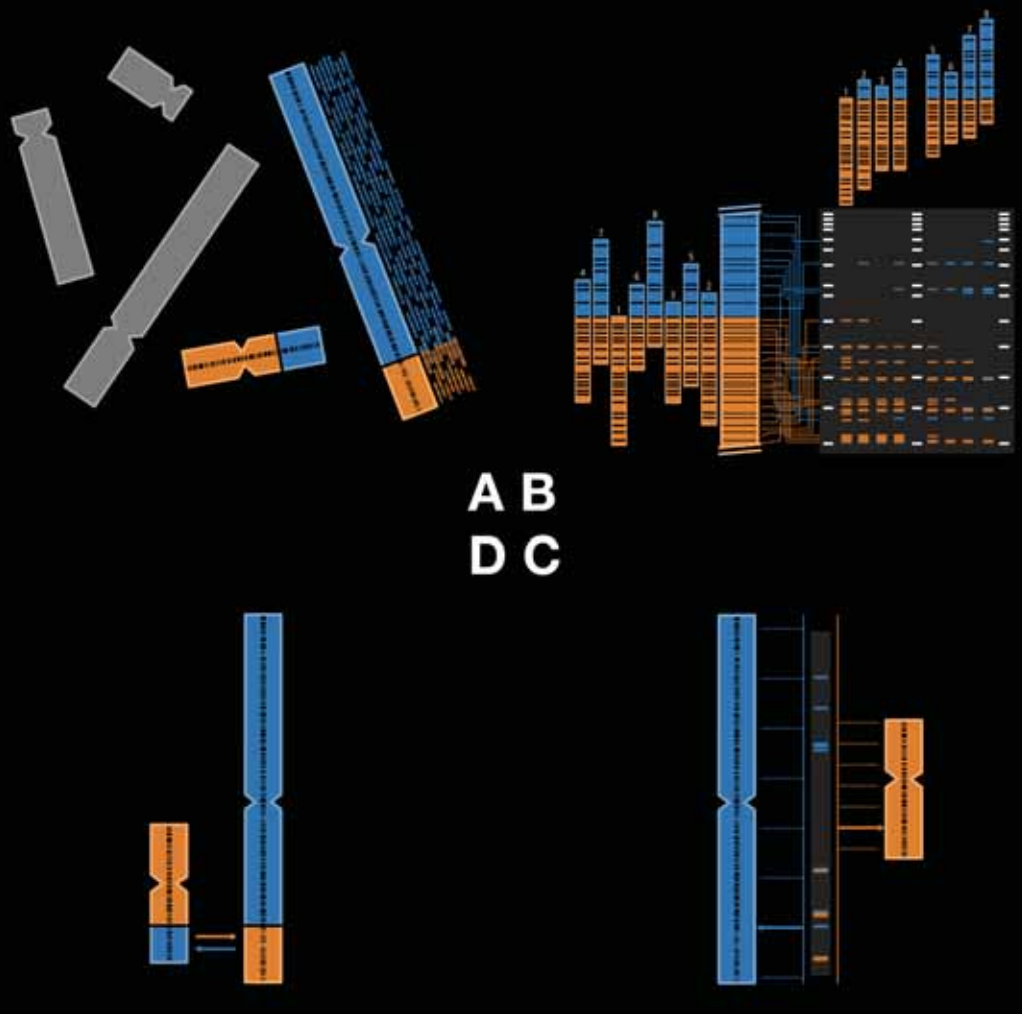

2007

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FRONT COVER IMAGES:

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CSBMCB President's Report

Reinhart Reithmeier

Preamble

In 2007, the CSBMCB celebrated its 50th Anniversary – and we have a lot to celebrate. The disciplines of biochemistry, molecular and cellular biology have assumed a central place in biology and medicine. The CSBMCB has embraced emerging areas such as systems and chemical biology, the theme of this year's Annual Meeting and Conference. We have seen new investments in research by federal and provincial governments through increases to the base budgets of the granting agencies, Canada Graduate Scholarships, the Canada Research Chairs Program and the Canada Foundation for Innovation – investments that have been of great benefit to our members. The resulting expansion in the research enterprise has, however, put incredible strain on the granting councils, causing success rates to plummet, with many grants rated in the excellent range not funded. This funding gap needs to be addressed quickly by increases to the base budgets of the granting councils. Governments however prefer to create new programs, with which they can be identified. Universities and hospitals in turn are interested in the funding of indirect costs. Clearly, the CSBMCB can play an advocacy role by voicing the concerns and priorities of the "scientist in the lab". Our voice needs be a chorus by ensuring that the membership continues to grow, and that our members are active in the affairs of the Society.

Annual CSBMCB Meetings

The highlight of 2007 was the 50th Annual Meeting and Conference of CSBMCB on "Systems and Chemical Biology", which was held at McGill University in July. The CSBMCB has organized first-rate meetings on topics of interest to our members for many years and 2007 was no exception. David Thomas (McGill) and Eric Brown (McMaster), along with administrator Nancy Dufour, organized an exceptional meeting on the occasion of the 50th Anniversary of the Society. Once again, top Canadian and international scientists presented their latest results at our Annual Meeting, which attracted over 200 registrants. The 50th Anniversary Banquet and Awards Presentation took place at the venerable McGill Faculty Club, with a festive atmosphere provided by a Dixieland Band. A number of our long-time members were in attendance, with reminiscences provided by the equally venerable Rose Johnstone.

The 51st Annual Meeting on "Epigenetics and Chromatin Dynamics" organized by Jim Davie (Manitoba) was held March 6-9, 2008 at the Banff Centre in Banff, Alberta. For 2009, the Annual Meeting moves to Ontario, organized by David Williams and Hue-Sun Chan (Toronto), on "Protein Folding: Principles and Disease". We return to Banff for the 2010 meeting on "Membrane Proteins", organized by Joseph Casey (Alberta) and the Membrane Protein Group. The 2011 Meeting is in Québec on the topic "The RNA World/La monde ARN", and will be organized by Jean-Pierre Perreault (Sherbrooke).

CSBMCB Awards Recognize Excellence

The 2007 Merck-Frosst Prize to a junior investigator with less than 10 years independent experience was won by Marco Marra (UBC) for his work on genome rearrangements in lymphoma. The Roche Diagnostics Award went to Nahum Sonenberg (McGill) for his outstanding work on protein translational control. The award winners gave excellent presentations during the Annual Meeting in Montréal and provided articles that are

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included in the Bulletin. Merck-Frosst and Roche Diagnostics are thanked for their continued and generous support of these major awards.

To celebrate the 50th Anniversary of CSBMCB, the Executive created the Arthur Wynne Gold Medal Award. This life-time achievement award is presented to an individual who has attained an international reputation for research in biochemistry, molecular and cellular biology, played a role in the development of the discipline, and provided outstanding service to our community. Arthur Wynne, Chair of Biochemistry at the University of Toronto from 1951-60, was the first President of the Canadian Biochemical Society (CBS), which was created in 1957. The first recipient of the Arthur Wynne Gold Medal is Alan Bernstein, best known in his role as President of CIHR.

There is a lot of talent in Canada. Be sure to nominate your colleagues for CSBMCB Awards!

CSBMCB Supports Graduate Student Activities

The CSBMCB provides small grants ($250) to support graduate student activities, such as career development seminars and symposia. Requests should be made in a letter, counter-signed by the Chair of the Department, to Albert Clark, Secretary of CSBMCB. Please encourage your graduate students to apply.

Advocacy Remains a Priority

A focus of the President over the past year has been on advocacy, and increasing the public's awareness of issues facing biomedical scientists in Canada.

An Op-Ed piece on research funding was published in the Toronto Star during the International AIDS Conference in Toronto. Letters to the Editor were published on the essential role of health charities in funding research, on how Canada lags behind other countries in research funding, and on the federal government's new science and technology strategy and the role of industry in supporting research. Many other articles have appeared on research funding by journalists and other interested parties in newspapers across the country.

A new advocacy strategy was needed in light of resignation of lobbyist Art Olson from CFBS. CSBMCB has joined Research Canada (http://www.rc-rc.ca/) and we are continually informed as to their activities. Research Canada's focus is on funding of health research and should serve our interests well. They are however not seen as a neutral arm's length group by government but rather a representing the interests of their members (hospitals, Faculties of Medicine, etc).

CSBMCB supports Friends of CIHR and their Dr. Henry Friesen Prize. The first recipient was Dr. Joe Martin, an Albertan who was Dean of Medicine at Harvard. There was a lecture and celebration in Ottawa that the President attended. The second recipient is Dr. John Evans, creator of Allelix, and the first Dean of the Medical School at McMaster. The award ceremony was held in Montreal in September 2007. The profile of CSBMCB is enhanced due to our involvement in the Henry Friesen Prize. Consider joining the Friends of CIHR (http://www.fcihr.ca/)

A national post card campaign to encourage the federal government to move forward on the budget committee recommendation to increase CIHR budget was successful in engaging the research community from coast-to-coast. Thousands of cards from across Canada landed on the desks of politicians in Ottawa, apparently to the chagrin of some. The CIHR budget was increased modestly. Rather, new funds were directed to implementing the government's commercialization strategy, through a process without application, or peer-review.

The CSBMCB has been active in selection of a new CIHR President. A letter was sent to Alan Bernstein thanking him for his years of service and support of health research, and copied to Health Minister Clement.

The Council of Canadian Biomedical Chairs (CCBC) was created with David Thomas as its first Chair, and an organizational meeting was held during CSBMCB Conference in Montreal. This group provides a mechanism to enhance communication among departmental heads from across the country.

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Many of our members have been active locally and on the national scene in advocating for health research. Clearly, simply asking for more money for existing programs is not a viable strategy. Rather, we need to come up with new ideas that would benefit health research, and align with the federal government's priorities and Science & Technology strategy. We also need "champions" for our cause. The closer our champions are to key decision makers, the more influence we will have.

National Health Research Week

One idea to better inform the public and politicians as to the importance and benefits of health research is to launch a National Health Research Week. This event would take place in the Fall at the time of pre-budget consultations. Advocacy activities in Ottawa in partnership with other groups could be coordinated by Research Canada. Events to engage the public would take place across the country, which could involve groups like Canadians for Health Research (http://www.chr.org). Support for this idea is growing.

CFBS

At the last board meeting, the Executive decided to sever our ties with CFBS. CSBMCB will no longer provide funding to CFBS for advocacy, rather we will use Research Canada as our voice in Ottawa. The CSBMCB Office will be moved to Toronto with Rob Reedijk providing administrative support one day per week. Rob worked for PENCE for many years, and he has helped in the organization of recent CSBMCB meetings. We thank Wafaa H. Antonious in the CFBS Office for providing a high level of administrative support to CSBMCB over the past few years.

There is a view that a powerful new national umbrella bioscience organization is required, perhaps one that can organize the annual meetings of its constituents' societies, and be involved in liaison and coordination with other advocacy groups such as Research Canada. Perhaps a new CFBS, the Canadian Federation of Biomedical Societies, or Biosciences Canada is needed.

A Membership Challenge

If each member of CSBMCB convinces just one colleague to join, we would double our membership. Membership in CSBMCB cost only $100 per year and provides many benefits. The funding goes to providing administrative support, running our web-site, supporting our Annual Meeting and awards, funding membership in Research Canada and Friends of CIHR, and other advocacy efforts. Members get a $75 reduction in the registration fee to our Annual Meeting and their trainees qualify for generous travel awards to attend the meeting. CSBCMB will continue to be a strong voice in advocating for increased research funding. This voice is strengthened by speaking for more members. So talk to a colleague about CSBMCB today and get them to join. Watch for the new recruitment flyer.

CSBMCB Executive

The CSBMCB Executive Board is a great team. Past-President Eric Brown served double duty as President and Co-organizer of the 50th Annual Meeting. Finances are ably managed by the ever-prudent Vince Duronio (UBC). Our Secretary, Albert Clark (Queen's), organizes the CSBMCB Awards and the Board and General Meetings. Frances Sharom (Guelph) continues to do a brilliant job as Bulletin Editor and looking after the abstract submission, poster sessions and awards at our annual meeting. Linda Penn took the initiative to launch a membership recruitment drive with a compelling colour flyer sent out to all members for distribution. Councillor John Orlowski undertook a project to collect all CBS/CSBMCB Bulletins in CD format as part of our 50th Anniversary celebration. We welcome Laura Frost (Alberta) to the office of Vice-President and David Williams (Toronto) and Jean-Pierre Perreault (Sherbrooke) as a new Councillors. Former Councillors Guy Poirier (Laval), George Chaconas (Calgary) and Dev Mangroo (Guelph) are thanked for their contributions. A special thanks to David Thomas (McGill) as he has completed his term on the Executive as Past-President. Please consider getting involved in the CSBMCB Executive – we are always looking for new members dedicated to promoting the interests of CSBMCB.

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Incoming Member of the CSBMCB Executive Board 2006-2007

Laura Frost, Vice-President

My personal history reflects the many opportunities afforded to immigrants to the New World. Both my parents were the only children in their respective families to receive a university education and both received their PhDs in Chemistry in the 1940's. My father, Raymond U. Lemieux, came from a large French-Canadian family and his father was a carpenter and coal miner in Lac la Biche and Edmonton. My mother's parents emigrated from England and entered the United States through Ellis Island in New York in 1919. My parents met on the tennis court at Ohio State University where my father was a postdoctoral fellow in carbohydrate chemistry and my mother, Virginia McConachie, was working on her PhD in physical chemistry.

Dad's first job was at the Prairie Regional Lab in Saskatoon where I was born many, many years ago. I remember cold winters and hot summers that could not be relieved by going to the swimming pool because of fears of contracting polio. Dad moved my family (5 girls and a boy) twice, first to Ottawa where I attended elementary school and then to Edmonton where he joined the Chemistry department at the University of Alberta in 1961. During high school I suffered the usual bouts of indecision about my future direction in life. Although I was greatly drawn to the Arts, I didn't feel part of the then hippie scene and I didn't share my Dad's enthusiasm for organic chemistry, much to his distress. One day a poster appeared outside the career counselor's office from the Biochemistry department at the U of A. It had a full colour model of the structure of chymotrypsin, I think, painstakingly put together with bits of metal and screws. I was intrigued by the beauty and intricacy of this molecule, which appealed to both my scientific and artistic interests. Little did I know that it would take 30 years for me to obtain the structure of my first protein.

I received my PhD in 1978 and decided to stay in the Biochemistry department with my PhD supervisor Bill Paranchych because it was such a happening place. I had married Ed Frost, a lawyer, in 1970 and we had three children during my PhD. This made it nigh impossible to take up a postdoctoral position elsewhere and no other department on campus seemed as lively or successful. The Alberta Heritage Foundation for Medical Research was founded around them, and a host of talented graduate students, including Brett Finlay, Randy Read, Betty Worobec, Tania Watts and Natalie Strynadka, joined the department. Everyone had money in their pockets and staff and students joined in hiking and skiing trips and many great parties. In 1981 and again in 1983, I went to the University of Edinburgh for a mini-postdoc in Neil Willett's lab where I learned how to do bacterial genetics and DNA sequencing. I was intrigued by the power of these techniques to reveal the orchestration of life processes and I enjoyed designing experimental controls, especially negative controls, a concept foreign to chemistry or at least to my father!

My initial PhD project was to try to sequence the protein subunits of conjugative pili of the F-like plasmids. Larry Smillie suggested that if I could get 3 grams of material I should be able to complete the project. Unfortunately, I was about 1000-fold off the mark! After reading Peter Medawar's "The Art of the Soluble", I looked for another project and ended up characterizing the pili of the multi-piliated organism, Pseudomonas aeruginosa, although conjugation was always my first love. During the 80's, Brett Finlay and I had a great time sequencing the F-like plasmid transfer

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regions, revealing the components of a complex structure for conjugative DNA transfer that now belongs to the type IV secretion family. The sequence of the F plasmid transfer region also revealed a tightly knit regulatory network of transcriptional and post-transcriptional control elements that acted at multiple levels. This burst of success made it possible for me to be taken seriously by the Microbiology department at the U of A where I became an Associate Professor in 1990. My research program has centred around two aspects of conjugative DNA transfer: how does the conjugative pilus, a primitive touch system, know it has contacted a suitable recipient cell, a process that initiates DNA transfer; secondly, how does the plasmid regulate transfer region gene expression in harmony with its host? These two questions have led me into protein biochemistry and structural biology, as well as the mechanisms of regulating gene expression through antisense RNA, RNA and DNA binding proteins, protein and RNA degradation and DNA silencing. Taken all together, it appears I have become a systems biologist through sheer serendipity.

I owe a debt of gratitude to the members of the Biochemistry department at the U of A, and to Karen-Ippen Ihler, Erich Lanka and Brian Wilkins, who allowed me to work in their labs during mini-sabbaticals. I also want to acknowledge Mark Glover and Bart Hazes at the U of A who have been exceptional collaborators. Starting in 2000, I began a career as an administrator, first as Associate Chair, Research, and then as Chair of Biological Sciences in the Faculty of Science at the U of A. Biological Sciences is a treasure trove of talented people, amazing collections and diverse research interests that have greatly broadened my understanding of biology. Since my tenure as Chair draws to an end in 2008, I have been looking for a way to contribute to science on the national stage. I look forward to working with the executive of the CSBMCB, which embodies the key research interests in my career and which has provided a lively forum for the politics of science in the past few years.

Jean-Pierre Perreault, Councillor

During my last year in the B. Sc. Program in Biochemistry at the Université de Montréal, I had a class called “Research Seminar” in which I presented a review paper on catalytic RNA. We were in the fall of 1985, three years after the publications of Thomas Cech and Sidney Altman presenting the original description of catalytic RNA, a novel class of RNA. My mentor for the preparation of the paper was the late Bob (Robert J.) Cedergren. The paper that I had selected among a multitude of others was the launching pad for my career. Following my critique of the paper, which focussed mainly on the features that could explain the catalytic ability of the RNA molecules, Bob invited me to join his research group in May of 1986 where I endeavoured to validate my hypothesis that the 2□-hydroxyl group of ribonucleotides is central for the catalytic properties of RNA.

During my Masters degree studies (1986-1988), I synthesized chimeric tRNAMet and the corresponding tDNAMet, including only one ribonucleotide as terminal nucleotide to allow aminoacetylation of the 2□-hydroxyl group. This project was my initiative, as were RNA chemical synthesis and the chemistry and biochemistry of nucleic acids. More importantly, Bob was very inspiring and he stimulated us with a creative environment that led me to continue with a Ph. D. instead of accepting a job that was offered to me. During my doctoral studies (1988-1990), I contributed to the original synthesis of RNA-DNA mixed polymers having catalytic properties. This permitted us to address some aspects of the molecular mechanisms of the hammerhead ribozyme and initiated me to the enzymology of catalytic RNA.

Afterwards, I moved on and joined the laboratory

of Professor Sidney Altman at Yale University. I spent almost three years there (1990-1993) studying how the catalytic RNA subunit of E. Coli ribonuclease P recognizes a model substrate derived from the precursor tRNA. The time I spent in Altman's lab was very pleasant and I met many post-doctoral trainees from all over the world. Moreover, the environment of Yale Campus and New Haven really inspired my research, and gave me the drive to start my own lab in the spring of 1993 at Université de Sherbrooke.

There, I established a relatively well-funded research program on the study of the RNA structure-function relationship. Specifically, my lab has three lines of research: (i) the biochemistry and molecular biology of a model RNA viroid; (ii) the elucidation of the molecular mechanism of the hepatitis delta virus ribozyme; and (iii) the use of the latest ribozyme to develop gene-inactivation systems. Moreover, several colleagues and I founded a Research Centre on RNA biology, as well as the national RiboClub, two organizations whose goals are to promote RNA Science and sponsor the training of graduate programs. I must confess that good student training is what I believe to be the most important issue and objective of my career.

I joined the Board of the CSBMCB in July 2007 as councillor with the feeling that this organization should do more to promote the excellence of student training at the graduate level across the country.

Dr. David Williams, Councillor

I was born and raised in Winnipeg and, from an early age, had an interest in chemistry. In fact I was the only one of my elementary school friends to own and actually use (for what purposes I can't quite recall now) a chemistry set. Those were the days when it was considered character-building to leave 10-year olds alone with a collection of toxic chemicals. Somehow I survived to adulthood and my undergrad training was an indecisive mix of engineering, chemical engineering and ultimately chemistry at the Universities of Saskatchewan and Manitoba.

It wasn't until my late undergrad years that I had some serious exposure to biochemistry, and it was several lectures from Jim Jamieson at U. of M. that piqued my interest in the area of glycoproteins. This motivated me to do a Master's degree at the University of Toronto with Harry Schachter, where I learned about the complexities of Asn-linked glycoproteins with their dizzying array of oligosaccharide structures. Following my M.Sc. I decided to try my hand at industrial research, and I worked for two years in the Research Centre at Canada Packers. Although I learned a great deal about how industry operates, my greatest lesson was how sorely I missed both academic life and curiosity-driven research. I returned to Harry Schachter's lab as a far more motivated Ph.D. student than I'd ever been as a Master's student. During my Ph.D., I became immersed in mucus, which gets its viscous properties from the characteristic oligosaccharides present on mucous glycoproteins. Despite the challenges of working with such material I was able to discover two new enzymes involved in the glycosylation process, and I became completely hooked on research. Harry was a superb mentor and his enthusiasm for science, his integrity, warmth and easy rapport with trainees still serves as a model for how I try to run my lab to this day.

Following my Ph.D. in 1981, I traveled to Baltimore to do postdoctoral work, first with William Lennarz, and then with Gerald Hart at the Johns Hopkins Medical School. Although I initially worked in the area of Asn-linked glycosylation, I became less enchanted with sugars and more interested in how proteins fold within the endoplasmic reticulum and subsequently are exported from this organelle along the secretory pathway. A chance conversation with another postdoc at Hopkins led to the adoption of the class I histocompatibility molecule as a model protein to study. This provided access to an array of folding mutants and conformation-sensitive antibodies generated by the immunological community that are still proving invaluable 25 years later.

In 1984, I returned to Canada as an MRC Scholar and started an independent research program in the Department of Biochemistry at the University of Toronto. Although I had sworn I was finished with sugars, my first cross-linking experiment aimed at identifying a receptor that exports class I

molecules from the ER led to the discovery of calnexin, a molecular chaperone of the ER that is also, ironically, a lectin that binds to Asn-linked oligosaccharide chains. In 1994, I was fortunate to win the CSBMCB Merck Frosst Prize in recognition of this discovery and related work. So, drawn back to my roots, I've spent much of my independent career studying how calnexin and its homolog calreticulin use oligosaccharide binding as well as other modes of substrate interaction to promote the folding and quality control of nascent glycoproteins in the ER. We also have an ongoing interest in the protein disulfide isomerase family of thiol oxidoreductases that catalyze disulfide formation, reduction and isomerization in this organelle. We are trying to understand why the mammalian ER possesses as many as 17 members of this family of enzymes. Finally, our use of class I molecules to study ER protein folding has also focused our attention on the immunological function of these proteins as molecules that present antigenic peptides to cytotoxic T cells. This has been a very fruitful area of research that has important implications in the design of vaccines to exploit T cell responses against tumours and viruses.

Over the years I've enjoyed administrative posts as graduate coordinator of the Biochemistry Department and also Acting Chair. I look forward to working with the CSBMCB in its role as a national advocate to promote the life science research enterprise in Canada and in its mission to host scientific conferences of exceptional calibre. I'll be heavily involved in the latter aspect in 2009 as co-organizer of the 52nd Annual Meeting of the Society on the topic of "Protein Folding: Principles and Diseases". On a personal note, I'm an avid cyclist who routinely, and perhaps ill-advisedly, braves Toronto traffic for my daily 10 km commute. I'm also a passionate winemaker and woodworker and, along with my artist wife Teri, a lover of the Toronto visual arts scene.

Minutes of the 50th Canadian Society of Biochemistry, Molecular and Cellular Biology Annual General Meeting

McGill University, Montreal
Monday July 9, 2007

Chair: Dr. Eric Brown, President CSBMCB

Board Members Present: David Thomas, John Orlowski, Eric Brown, Vincent Duronio, Linda Penn, Guy Poirier, Reinhart Reithmeier, Albert Clark

Seven members present

808. Approval of the Agenda

The agenda was approved as circulated (motion by Dr. Reithmeier, seconded by Dr. Orlowski)

809. Approval of the Minutes of the 49th Annual General Meeting

The minutes of the 49th Annual General Meeting held at Niagara-on-the-Lake, June 3, 2006 were approved as circulated (motion by Dr. Reithmeier, seconded by Dr. Orlowski)

810. Business Arising from Minutes

Any items arising from the minutes will be discussed under later agenda items.

811. President's Report

The President's report dealt primarily with advocacy issues. There was concern with the low success rate at CIHR. The letter writing on the WEB site and the post card campaign was followed by a small increase in budget. There was an indication that this was not well received by the politicians and they did not like all the post cards. There was criticism that the campaign was not focused on the health of Canadians. The budget increase was 37 million as opposed to an expected 20 million. Thirty thousand people liked the post card campaign approach. Drs. Casey and Brown wrote a position paper on advocacy.

Progress had been made with the new web-site which should help with advocacy. A contribution of $1000 was made to Research Canada which is considered a good conduit for advocacy. The slide show prepared by Art Carty was not considered a good reflection of the problems facing science. CSBMCB could become a supporter of Science Convergence with the university presidents. This will require further investigation.

Dr. Brown closed his report by thanking Drs. Thomas and Reithmeier for their efforts in the advocacy arena. The contributions of Dr. Casey to the Society have been significant.

812. Past-President's Report

Dr. Thomas reported on the review of Genome Canada, which was part of a larger review of all R and D funding by the federal government. Drs. Thomas and Shrier lobbied in Ottawa for science support with members of parliament.

813. Treasurer's Report

Dr. Duronio presented the Treasurer's Report. The audit had been completed one week earlier. The Society Special Fund had $440,000 at the end of 2006 and was increasing at the rate of approximately 10% per year. The $150,000 in the bank includes revenue for the meeting. The statement also includes the $76,000 plus $10,000

originally transferred from PENCE. There is now $70,000 remaining in the PENCE line item. Of the 100 PENCE members, 25 belong to CSBMCB. There has been a problem with members not being reminded regularly about renewing membership.

814. Membership Report

Dr. Penn reported that there are currently 446 regular members in CSBMCB. There was a brief discussion on ways of increasing the membership and retaining stability i.e. encouraging longer term memberships.

815. Communications Report

Dr. Sharom was thanked for her tremendous efforts in preparing the Bulletin and having it put on the website. All available past Bulletins are being put on a CD for the meeting attendees. It is proving difficult to get articles for the LINK. It was suggested that an electronic LINK might be the better way to proceed. A possibility of using news from CIHR as a component of the LINK was suggested.

816. CSBMCB and CFBS

Our relationship with CFBS has been a topic of discussion at meetings for a number of years. CSBMCB is an associate member as opposed to being a full member of CFBS. Our society runs our own conferences and does not actively participate in the Northern Lights Conferences run by CFBS. Dr. Thomas has attended the CFBS Board meetings. With the resignation of Dr. Olson, the future of the office of CFBS is uncertain. The CFBS office looks after our web-site in collaboration with S. Lau. It has been frustrating working with the CFBS office because of their many competing activities. CSBMCB has a contract with CFBS for office services.

It was agreed that the relationship with CFBS should cease (motion by Dr. Thomas, seconded by Dr. Reithmeier). Carried unanimously. The contract will not be renewed when it expires at the end of 2007. CFBS will be notified within 30 days. Dr. Reithmeier will communicate with Dr. Ratcliffe, President of CFBS.

817. Advocacy Activities

There was a brief discussion of and reporting on advocacy activities. Media articles and letters had been written on behalf of charities supporting research. CSBMCB has joined Research Canada. CSBMCB contributes to the Henry Friesen Prize which is sponsored by Friends of CIHR. A significant role was played in organizing the Council of Canadian Biomedical Chairs. There was agreement for being active in supporting the new CIHR president. Advocacy is seen as a significant task for the Society Vice-President.

It was agreed that CSBMCB should financially support the development of the Canadian Council of Biomedical Chairs to a maximum of $10,000 (Motion by Dr. Reithmeier, seconded by Dr. Brown).

818. Administrative Changes at CSBMCB

It was agreed that Mr. Rob Reedijk will be hired as Administrator Coordinator of CSBMCB to run the office functions of the society from the University of Toronto. He will work one day per week for the Society beginning July 1 2007, and the transition will occur over the fall period. He will take over administration of the website.

819. CSBMCB Funding of "2007 Biochemistry Roadshow"

Dr. Reithmeier spoke to an idea of visiting several universities each year to promote Biochemistry as a career and increase the pool of qualified graduate students. The visits would include Graduate Coordinators. This could be done in collaboration with the Canadian Council of Biomedical Chairs. Dr. Reithmeier will develop a proposal.

820. Engaging Trainees in CSBMCB Activities

There was a brief discussion on expansion of support for student sponsored activities. There was agreement to supporting the attendance of two graduate students at the next conference.

821. Report on Nominations

The nominations presented by Dr. Thomas (Chair of Nomination Committee) to the meeting were Dr. Laura Frost for Vice-President and Drs. David Williams and Jean-Pierre Perreault for Councillor. There were no further nominations and the ones presented were accepted (motion by Dr. Brown, seconded by Dr. Reithmeier).

822. Awards

There was a discussion on developing a 50th Anniversary Medal in memory of the first President of the Society, Dr. A M Wynne.

823. Name Change for Society

There was a brief discussion regarding the possibility of changing the name of the Society. There were perceived problems with the suggestions of a shorter name not reflecting the scope of the interests of the membership. No consensus was reached.

824. Adjournment

The meeting adjourned at 15:40 hours (motion by Dr. Reithmeier, seconded by Dr. Brown).

CSBMCB/SCBBMC Audit

Statement of Financial Position

December 31	2006	2005
ASSETS		
Current assets		
Bank	$9,729	$2,442
GST receivable	1,892	1,103
Sponsorships & accounts receivable	7,081	26,693
Meeting deposit	17,000	5,000
	35,702	38,218
Meeting deposit 2008	14,000	7,000
Investments – at market value (Note 3)	441,001	4000,480
	$490,703	$445,698
LIABILITIES AND SURPLUS		
Current liabilities		
Accounts payable & accrued liabilities	$12,232	$7,407
Deferred sponsorship	-	7,500
Deferred membership fees	2,710	2,056
	14,942	16,963
Deferred membership fees	4,487	4,672
	19,429	21,635
Net assets	471,274	424,063
	$490,703	$445,698

STATEMENT OF CHANGES IN NET ASSETS

December 31	2006	2005
Net assets, beginning of year	$424,063	$382,533
Excess of revenues over expenses for the year	47,211	41,530
Net assets, end of year	$471,274	$424,063

STATEMENT OF REVENUE AND EXPENSES

December 31	2006	2005
Revenue from operations		
Memberships	$19,963	$17,107
Corporate contributions	28,254	15,500
Annual meeting & other	23,995	30,706
	72,212	63,314
Investment revenue	45,521	31,930
Total Revenue	117,733	95,244
Expenses		
Annual Meeting	35,118	17,593
Audit	2,506	3,000
Bank & credit card fees	830	914
Board meetings	6,461	6,848
Bulletin	6,039	6,093
Dues & subscriptions	795	379
Funding & other sponsorship	6,082	1,750
Management fees	8,091	9,627
Printing	-	2,575
Publicity	-	385
Website	4,600	4,550
	70,522	53,714
Excess of revenues over expenses for the year	$47,211	$41,530

Canadian Society of Biochemistry and Molecular & Cellular Biology
Statement of Cash Flows

December 31	2006	2005
Cash flows from operating activities		
Cash received from members and events	$88,676	$48,657
Cash paid to suppliers	(84,697)	(70,463)
Cash flows from operating activities	(3,979)	(21,806)
Cash flows from investing activities		
Net flows from investing activities	(16,269)	35,292
Net change in cash and cash equivalents	(12,290)	13,486
Cash and cash equivalents, beginning of year	57,604	44,118
Cash and cash equivalents, end of year	$45,314	$57,604
Cash and equivalents is made up of:		
Bank account	9,729	$2,422
Cash held with investment broker	35,585	55,182
	$45,314	$57,604

Income Statement (Cash basis) 01/01/2007 to 12/31/2007 (Incomplete)

REVENUE		
Membership Revenue		
CSBMCB Membership Fees		13,082.61
CFBS Membership Fees		9,880.00
Membership Total		22,962.61
Annual Meeting Registration		
Meeting Sponsors		31,460.57
Annual Meeting Registration		54,440.60
Exhibits Revenue		11,537.74
Meeting Miscellaneous Revenue		5.00
Meeting Revenue Total		97,443.91
PENCE Revenue		
PENCE Transferred Funds		77,447.55
PENCE Revenue Total		77,447.55
Total Other Revenue		397.61
TOTAL REVENUE		198,251.68
EXPENSE		
Bulletin Expenses		
Bulletin Printing		7,163.13
Total Bulletin		7,163.13
Annual Meeting Expenses		
Exhibit & Facility Expenses		57,831.84
Receptions & Banquets		2,359.51
Speakers Travel & Expenses		20,208.46
Merck Frosst Awards	9,000.00	
Roche Award	1,500.00	
Platform and Travel Awards	9,400	
Awards Total		19,900.00
Meeting Organizer Fees		7,124.00
Meeting Supplies		13,999.19
Board Travel To AGM		4,974.38
Other Meeting Expenses		3,083.26
Meeting Total Expenses		129,480.64
Other Expenses		
CFBS Fees		7,171.32
Admin Printing		135.44
Other Meetings Sponsorship		3,000.00
Other Org. Mmb. Fees (IFCB & PABMB)		1,691.63
Board Meetings & Travel Expenses		8,996.68
CFBS Admin Contract		9,300.00
Other Expenses Total		30,295.07
General & Administrative Expenses		
Courier & Postage		24.31
Credit Card Sales Discount Fees		2,351.35
Credit Card Interest and Fees		31.25
Interest & Bank Charges		172.54
Website Expenses		4,760.00
Total General & Admin. Expenses		7,339.45
TOTAL EXPENSE		174,278.29
NET INCOME		23,973.39

50th Annual Meeting of the CSBMCB

A report on a celebration of great science and a CSBMCB milestone

Eric Brown, Department of Biochemistry and Biomedical Sciences, McMaster University, Past President CSBMCB

It is my pleasure to declare the 50th Annual Meeting and Conference of the Canadian Society of Biochemistry, Molecular and Cellular Biology (CSBMCB) in Montreal at McGill University a roaring success. This year's program included an extraordinary collection of talks and poster presentations in "Systems and Chemical Biology". We had participants from the United States, Europe and Asia, so it was a real privilege to extend our welcome in particular to these international travelers.

The meeting encompassed a very high quality and diverse assortment of science that was crafted by an enthusiastic organizing committee. So let me thank in particular all of these folks: Benoit Coulombe, Dan Figueys, Michael Hallet, Martin Latterich, Yingfu Li, Guy Poirier, Reinhart Reithmeier, Ray Truant, Gerry Wright and David Thomas (my co-chair). But most of all we owe a debt of gratitude to Nancy Dufour, who did just a smashing job as our Event Coordinator. As always, we are also grateful to our sponsors who came out in force this year to help us celebrate the 50th.

The meeting began strongly with two keynote presentations, the first by Ron Breaker from Yale on ribo-switches, followed by a talk on biological systems design by Pam Silver of Harvard Medical School. These presentations were an extraordinary start to a terrific scientific program that spanned systems and small molecule approaches in biology. As such, the meeting combined two emerging disciplines that have a growing interface and I, for one, was delighted by the response of the two communities in coming together for this meeting.

The Annual Meeting had a busy scientific program that included a trainee symposium, poster sessions and CSBMCB awards lectures. The award lecture for the Roche Diagnostics Prize for outstanding achievement in research was delivered by Nahum Sonenberg from McGill University. It was a tour de force of Dr. Sonenberg's life's work in the regulation of protein synthesis. The 2007 Merck Frosst Prize for meritorious research by a young Canadian went to Marco Marra, who presented a lovely talk on mapping the human genome.

In addition to the science at this meeting, we had the pleasure of participating in the 50th birthday party for the CSBMCB. This made the Banquet and Awards presentation dinner a particularly exciting and fun evening that was chock full of memories of CSBMCB meetings past.

The Canadian Biochemical Society (CBS), as it was first called, was created by a group of renegade biochemists from within the Canadian Physiological Society in a meeting held at the University of Ottawa in October of 1957. The first President was Professor A.M. Wynne, head of the Department of Biochemistry at the University of Toronto, and the first meeting was held at Queen's University in 1958. In 1992 the Society changed its name to the Canadian Society for Biochemistry and Molecular Biology, and merged with the

Canadian Society of Cellular and Molecular Biology in 1995, resulting in the tongue-twisting name of today, the Canadian Society for Biochemistry and Molecular & Cellular Biology, and the beloved acronym CSBMCB.

The 50th Annual Meeting was a great opportunity for reflection on the history of the CSBMCB, and presented a welcome chance to embrace the emerging fields of systems and chemical biology. We look forward to the 2008 Annual Meeting, and another 50 years of great meetings hosted by the CSBMCB!

Travel and Poster Award Recipients for the 2007 CSBMCB Annual Scientific Meeting

Montreal, Quebec

POSTER PRIZES

AWARDEE	UNIVERSITY	SUPERVISOR
Roche Diagnostics Poster Prizes		
Michael D'Elia	McMaster University	Dr. Eric Brown
Long Nyguyen	McGill University	Dr. Kalle Gehring
Jake Duerckson Poster Prize in Cell Biology		
Kento Onishi	University of Toronto	Dr. Peter Zandstra
CSBMCB Poster Prizes		
Keith Stubb	Simon Fraser University	Dr. David Vocadlo
Dimitri Rodionov	McGill University	Dr. Annette Herscovics
Daniil Zhuravel	University of Ottawa	Dr. Mads Kaerns
Lee Freiberger	McGill University	Dr. Karine Auclair
Wendy Mok	McMaster University	Dr. Yingfu Li
Kristin Horton	University of Toronto	Dr. Shana Kelley
Pekka Maatanen	McGill University	Dr. David Thomas
CSBMCB Platform Presentation Prizes		
Ranjana Pathania	McMaster University	Dr. Eric Brown
Jena-Philippe Lambert	Ottawa Institute for Systems Biology, University of Ottawa	Dr. Daniel Figeys

TRAVEL AWARDS

AWARDEE	UNIVERSITY	SUPERVISOR
Merck Frosst 10 x $750 awards		
Md Alamgir	Carleton University	Dr. Ashkan Golshani
Ginny Chen	Samuel Lunenfeld Research Institute	Dr. Anne-Claude Gingras
Jean-Philippe Lambert	University of Ottawa	Dr. Daniel Figeys
Dr. Michael Prakesch	SIMS	Dr. Prabhat Arya
Gina Rossi	UBC	Dr. Michael Cox
Tushar Shakya	McMaster University	Dr. Gerry Wright
Dr. Keith Stubbs	Simon Fraser University	Dr. David Vocadlo
Dr. Yuen Yi Chris Tam	University of British Columbia	Dr. Elizabeth Conibear
Garrett Whitworth	Simon Fraser University	Dr. David Vocadlo
Dr. Barry Young	LSI, University of British Columbia	Dr. Chris Loewen

Amgen 11 x $700 awards

Casey Fowler	McMaster University	Dr. Yingfu Li
Julie Gauley	University of Waterloo	Dr. John Heikkila
Chand Mangat	McMaster University	Dr. Eric Brown
Kento Onishi	University of Toronto	Dr. Peter Zandstra
Jaeok Park	McMaster University	Dr. Radhey Gupta
Dr. Paschos Athanasios	McMaster University	Dr. Christian Baron
Ken Schlosser	McMaster University	Dr. Yingfu Li
Jessica Woolfson	University of Waterloo	Dr. John Heikkila
Daniil Zhuravel	University of Ottawa	Dr. Mads Kaern

Nunc and Nalgene $600 award

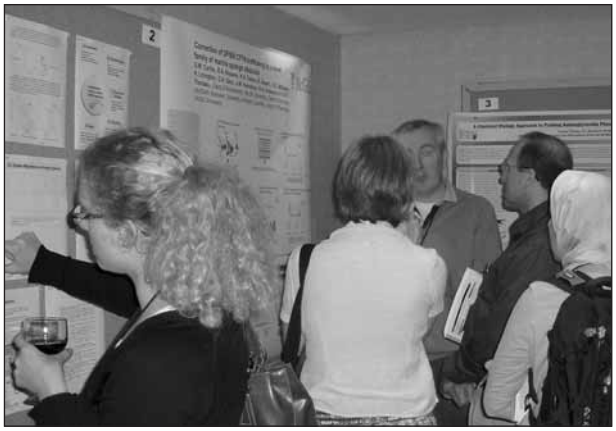
William Chiuman	McMaster University	Dr. Yingfu Li

Scenes from the 2007 CSBMCB Annual Meeting

The Registration Desk was run by Nancy Dufour and her assistants

Exhibitors from Dionex, Beckman and MDS labs

Lecture hall



Poster Pub I

Poster Pub I

Poster Pub I

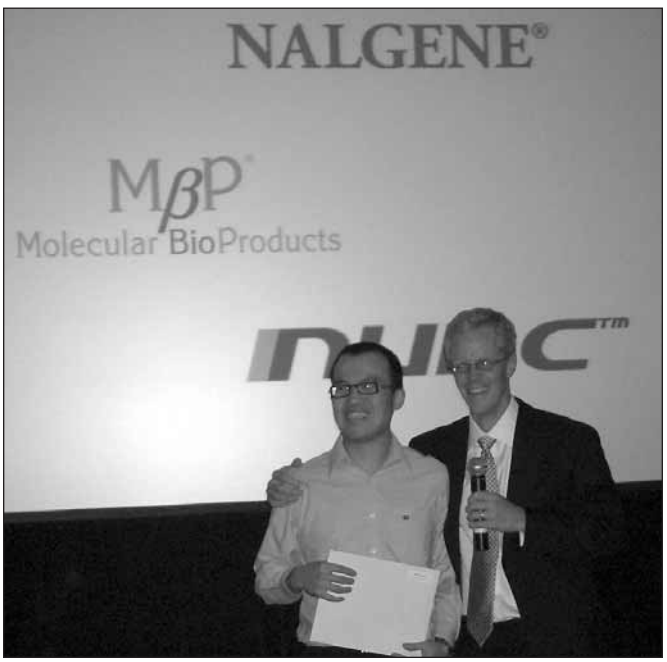
Judging at Poster Pub I

Cheers to the two Presidents, Dr. Eric Brown (outgoing President, right) and Dr. Reinhart Reithmeier (incoming President, left)

Members of the Local Organizing Committee

Exhibitor's hall

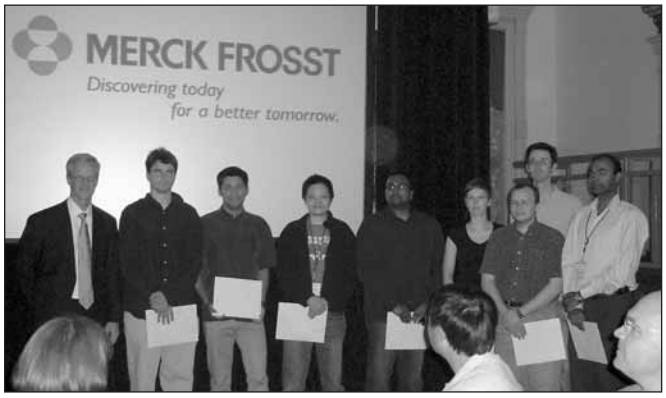
Dr. Nahum Sonenberg of McGill University prepares to deliver his CSBMCB Roche Diagnostics Prize lecture



Dr. Eric Brown, President of the CSBMCB (right) with the Nunc and Nalgene Travel Award winner

The 2007 winner of the CSBMCB Roche Diagnostics Prize, Dr. Nahum Sonenberg of McGill University, receives his award plaque from Dr. Eric Brown and a representative of Merck Frosst Canada

The 2007 winner of the CSBMCB Merck Frosst Prize, Dr. Marco Marra of the BC Cancer Agency Genome Sciences Centre, receives his award plaque from Dr. Eric Brown



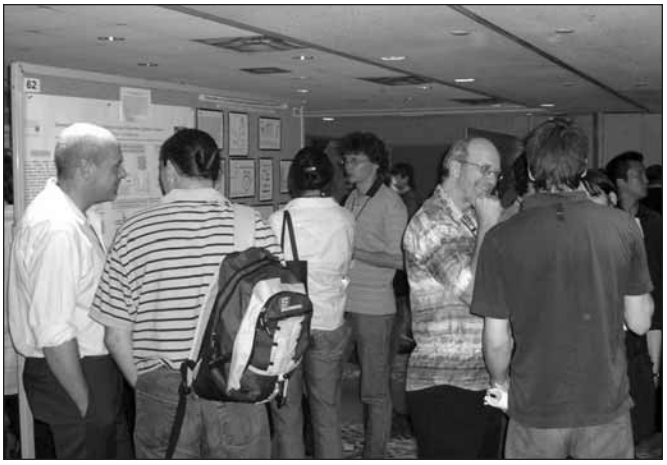
Dr. Eric Brown, President of the CSBMCB (left) with the Merck Frosst Travel Award winners

The Amgen Travel Award winners

Dr. Eric Brown congratulates the winners of the Roche Diagnostics Poster Prizes

Dr. David Thomas, co-Chair of the Conference Organizing Committee, is presented with a set of bongo drums in appreciation for all his hard work

Poster Pub 2

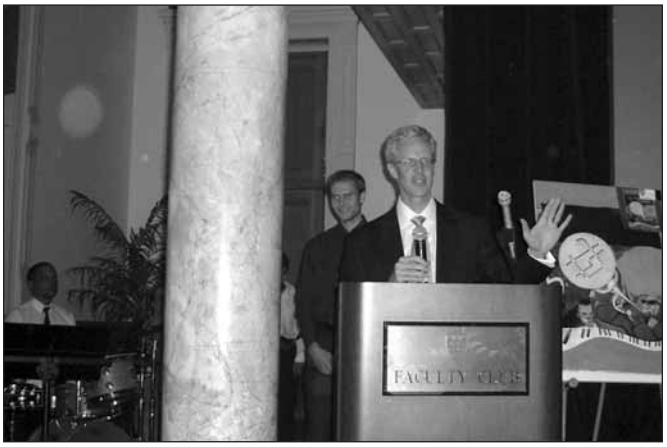


Poster Pub 2

Speakers enjoying breakfast

Graduate students and exhibitors

Former CSBMCB Secretary, Dr. Eugene Tustanoff, with the current Secretary, Dr. Albert Clark



Dr. Eric Brown kicks off the formal ceremonies at the 50th Anniversary Gala Dinner, held at the McGill University Faculty Club

The jazz band tuning up at the Gala Dinner

Gala dinner table

Gala dinner table

Gala dinner table

Graduate students enjoying the Gala dinner

Emeritus member Dr. Rose Johnstone raising a toast to the CSBMCB's 50th anniversary at the Gala Dinner

Emeritus members Dr. Marion Packham (University of Toronto, left) and Dr. Rose Johnstone (McGill University, right)

Gala dinner table

Gala dinner table

51st Annual Meeting and Conference of the CSBMCB "Epigenetics and Chromatin Dynamics"

Thursday March 6 - Monday March 9, 2008

The Banff Centre, Banff, Alberta, Canada

Scientific Program

Thursday, March 6, 2008

Session I **Plenary and Awards Lecture**

Session Chair: Jim Davie, University of Manitoba

7:00 pm	Keynote Speaker: Shelley Berger (The Wistar Institute) The complex language of histone and factor post-translational modifications in genome regulation
7:45 pm	Merck Frosst Award Lecture
8:30 pm	Jeanne Manery Fisher Memorial Lecture
9:15 pm	Welcome Reception

Friday March 7, 2008

Session II **Session II Epigenetics and Genome Integrity**

Session Chair: Linda Penn, University of Toronto

8:15 am	Anja Groth, Institut Curie-Recherche, France Histone dynamics and DNA replication
8:50 am	Alain Verreault, University of Montreal Histone H3 lysine 56 acetylation: A new twist in the chromosome cycle
9:25 am	Jacques Côté, Université Laval Roles of histone acetyltransferases complexes in genome stability and maintenance
10:00 am	Coffee Break
10:30 am	Karolin Luger, Colorado State University Nucleosomes and their chaperones
11:05 am	Carolyn J. Brown, University of British Columbia Human X chromosome inactivation: establishment of facultative heterochromatin by the XIST RNA
11:40 am	Hugh Brock, The University of British Columbia Do long non-coding RNAs of the bithorax complex repress by transcriptional interference?
12:00 pm	Lunch/CSBMCB Board Meeting
1:30 pm	Poster Session I or Free Time
3:00 pm	Poster Pub & Judging
5:00 pm	CSBMCB Annual General Meeting

Session III **Nuclear Architecture and Function**

Session Chair: Michael Hendzel, Alberta Cancer Board

7:30 pm Gary Stein, University of Massachusetts
Organization and assembly of transcriptional regulatory machinery in nuclear microenvironments: Implications for biological control and cancer

8:05 pm Roel van Driel, University of Amsterdam
Principles of large-scale chromatin folding of the human genome inside the interphase nucleus

8:40 pm Coffee Break

9:10 pm David P. Bazett-Jones, The Hospital for Sick Children
Functional interactions between chromatin and PML nuclear bodies

9:40 pm Thomas Cremer, Ludwig-Maximilians-Universität München
Chromosome territories and nuclear organization: structural, functional and evolutionary aspects

10:15 pm Evening Reception

Saturday March 8th, 2008

Session IV **Chromatin Remodeling and Gene Regulation**

Session Chair: Daniel Figeys, University of Ottawa

8:15 am LeAnn Howe, University of British Columbia
Novel mechanisms of targeting chromatin-modifying complexes

8:50 am Jerry L. Workman, Stowers Institute for Medical Research
Protein complexes that modify chromatin for transcription

9:25 am Mike Schultz, University of Alberta
Metabolic regulation of global Histone acetylation in yeast

10:00 am Coffee Break

10:30 am Craig Peterson, University of Massachusetts Medical School
Chromatin remodeling machines

11:05 am Luc Gaudreau, Université de Sherbrooke
Regulation of gene expression by Histone H2A.Z

11:40 am Rod Bremner, University of Toronto
Lessons on remote control from the interferon transcriptional cascade

1:30 pm Poster Session II or Free Time

3:00 pm Poster Pub & Judging

Session V **Chromatin Networks, Epigenetics and Oncogenesis**

Session Chair: Mark Glover, University of Alberta

5:15 pm Danesh Moazed, Harvard Medical School
Role of RNAi in heterochromatin assembly and function

5:50 pm Peter Cheung, Ontario Cancer Institute
The epigenetic functions of mono-ubiquitylated H2A.Z

6:25 pm Coffee Break

6:55 pm Trevor Archer, National Institute of Environmental Health Sciences, North Carolina
Regulating hormone activated transcription via chromatin and epigenetics

7:30 pm Ali Shilatifard, Stowers Institute for Medical Research, Missouri
Translating histone crosstalk

8:30 CSBMCB Banquet and Awards Presentations

Sunday March 9th, 2008

Session VI **Chromatin Modifications, Associated Proteins and Disease**

Session Chair: Xiang-Jiao Yang, McGill University

8:15 am	Karl Riabowol, University of Calgary ING tumour suppressor proteins target and regulate chromatin modifying complexes
8:50 am	Vicky Richon, Merck Research Laboratories, Boston Progress in the development of HDAC inhibitors for the treatment of cancer
9:25 am	Craig Mizzen, University of Illinois Certain and progressive methylation of H4 at lysine 20
10:00 am	Coffee Break
10:30 am	Jinrong Min, University of Toronto Division of labor among human MBT repeat proteins
11:05 am	Christopher Wynder, McMaster University The role of histone demethylation on stem cell properties
11:40 am	Michael Bustin, National Cancer Institute, Maryland The epigenetic function of chromatin architectural proteins
12:00 pm	Departure

100 Years of Biochemistry at the University of Toronto

Marian A. Packham
University Professor Emeritus

The Department of Biochemistry at the University of Toronto celebrates its 100th anniversary in 2007/08. This article provides a review of some of the contributions of its members and graduates to biochemistry in Canada and internationally.

It would be impossible to mention or even list all the contributions that members and graduates of the Toronto Biochemistry Department have made scientifically, administratively, and to teaching, so only a few individuals, particularly the early ones, have been chosen for comment. The many awards and honours bestowed on them are impressive, but space limits a comprehensive description of them.

Since the biochemistry department at Toronto was established 12 years before any other of the biochemistry departments in Canada, it is not surprising that its graduates populated the departments of biochemistry that began to be formed at universities throughout the country in the 1920s and 1930s; at least 20 of our graduates went on to chair departments of biochemistry and 5 chaired related departments (Table 1).

Role of the Department in CSBMCB

Members of our professorial staff, particularly Gordon Butler, played a major role in the formation of the Canadian Biochemical Society in 1957, and the Chair of our department at that time, Arthur Wynne, was its first president. Seventeen presidents of the Society that is now called The Canadian Society of Biochemistry, Molecular & Cellular Biology (CSBMCB) were either graduates of our department or on its professorial staff (Table 2). One of our graduates, David Tinker (Ph.D.1965) who was also a member of our professorial staff (1966-1997), was editor of the Society's Bulletin for 5 years after retirement. Currently, our Chair, Professor Reinhart Reithmeier, is CSBMCB/SCBBMC President. Twelve of our staff members or graduates have received the Merck-Frosst Award of the CSBMCB (Table 3). It is given for "meritorious research in biochemistry in Canada" and was at first limited to investigators who had not reached their 40th birthday. The criterion is now "someone who has been an independent investigator for 10 years or less".

A.B. Macallum – Founder of the department

The founder of the department, Archibald Byron Macallum is acknowledged as the "father of biochemistry in Canada". He was a graduate of the University of Toronto where he obtained his B.A. and M.B. degrees, and he also had a Ph.D. from Johns Hopkins University. He had been chair of the Physiology Department in Toronto before setting up the Department of Biochemistry. His research comparing the concentration of the inorganic elements in seawater with those in the body fluids of many animals supported the concept of the origin of land animals from the sea. His work was recognized by his election to a Fellowship in the Royal Society of London, an unusual honour for a Canadian at that time. At the opening of the newly built medical building in Toronto in 1903, Dr. William Osler praised Prof. Macallum saying "He has carried the name of this university to every nook and corner of the globe".

One of Prof. Macallum's most notable contributions was establishing research and scholarship as essential functions of a university. He was instrumental in establishing the Ph.D. degree as a research degree requiring a thesis and in the formation of a separate Board of Graduate Studies. Undoubtedly his concept that a university should be involved not only in the preservation and dissemination of knowledge, but also in its advancement through research, had a far-reaching influence on other universities.

In 1917 Prof. Macallum left the University of Toronto to chair a government Advisory Council for Science and Industrial Research that became the National Research Council of Canada. In 1920 he accepted a professorship at McGill and in 1922 he founded the Biochemistry Department there. Meanwhile, he had been in China where he assisted in the organization of the Peking Medical School.

Clara Benson breaks the gender barrier

Prof. Macallum arranged the appointment of Clara Cynthia Benson (Ph.D. 1903 in Chemistry at the University of Toronto) to the Faculty of Household Science that was being established. She was one of the first two women to enter the professorial ranks at the University of Toronto and was the first cross-appointee to the Department of Biochemistry. She and Prof. Macallum were in the small group that organized the American Society of Biological Chemistry and they both presented papers at its first meeting. Prof. Macallum served as its president from 1911 to 1913 and when the Journal of Biological Chemistry was founded, he was a member of its editorial board. Prof. Benson carried out research and taught until her retirement in 1945. During the 1st World War she initiated the application to munitions of the analytical techniques she had developed for foods, and she was listed in 1920 in American Men of Science. Prof. Benson also played a major part in developing women's athletics at the University of Toronto where the Women's Athletic facility bears her name.

J.B. Collip and the insulin connection

In Toronto, one of Prof. Macallum's early graduate students was James B. Collip (Ph.D. 1916) who then spent 13 years at the University of Alberta, becoming the first chair of its new Department of Biochemistry in 1920. During the first 5 years at U. of A., Collip's research was focused on blood chemistry, including the acid-base exchange between plasma and red blood cells, osmotic pressure of serum and red blood cells, the syndrome of hyperventilation alkalosis and tetany, and the effects of adrenaline. In 1921 a sabbatical leave in Prof. J.J.R. Macleod's laboratory in Toronto resulted in his involvement in Banting and Best's insulin work. Collip showed that a purer preparation, suitable for therapeutic administration, could be obtained by increasing the alcohol concentration used for extraction. Working with rabbits, Collip went on to recognize insulin-induced hypoglycemia and to develop a biological assay of insulin. Macleod shared his half of the Nobel Prize with Collip while Banting shared his with Best. Collip's research interests turned to the identification, purification and study of hormones; the first he isolated was the parathyroid hormone which he and his research assistant showed regulates the calcium concentration of blood. Collip's method for measuring serum calcium was used in clinical laboratories for many years. He left Alberta to take the Chair at McGill when Macallum retired.

There he continued his research in the rapidly developing field of endocrinology. His group carried out isolation and chemical identification of estriol from the placenta; and preparation of "Emmenin" from the placental or from pregnancy urine that later led to the development of the related drug Premarin. They also studied chorionic gonadotrophin; growth hormone; thyroid stimulating hormone; and, most noteworthy, adrenocorticotrophic hormone (ACTH). Beginning in 1938 he was a member and in 1941 he became Chair for 16 years of an Associate Committee on Medical Research of the NRC that eventually (1960) became the MRC. During World War II, Collip's involvement in medical war research and his role as Medical Liaison Officer in Washington led to his C.B.E. in 1943, and Medal of Freedom, Silver Palm (USA) in 1947. In 1947 Collip accepted the positions of Dean of Medicine at the University of Western Ontario and Head of the Department of Medical Research. In the book "The Development of Biochemistry in Canada" written in 1976 by E. Gordon Young, Prof. Collip was said to be "our most eminent Canadian biochemist".

Henry Borsook – Chair at Caltech

Among other graduates of biochemistry in Toronto in the very early years was Henry Borsook (Ph.D. 1924) who twice became chair of the Department of Biochemistry at Caltech where he taught biochemistry and carried out research for 35 years. He showed that energy is required for protein synthesis from amino acids, disproving a theory that was prevalent at the time that proteins were synthesized by a reversal of the action of proteolytic enzymes. His work on nutrition, particularly the effects of the B vitamins, led to his appointments on boards and commissions advising federal and state governments on nutritional questions. He became the research director of the Meals for Millions Foundation set up to distribute to impoverished populations a low-cost enriched food based on soybeans that he had been instrumental in devising.

David A. Scott Award

David Aylmer Scott (Ph.D. 1925) discovered that the addition of zinc led to the formation of insulin crystals and this method became one of the basic steps in the purification of insulin. He was also involved in devising an economical way of purifying heparin. His contributions were recognized throughout the world by many awards. After his death, the "David A. Scott, F.R.S. Award" was established by his family for the best all-round graduate student each year in the Biochemistry Department in Toronto.

Bruce Collier – Prairie pioneer

Prof. H. Bruce Collier (Ph.D.1930) spent the first 7 years of his career in China where he set up (and was the sole member) of the Biochemistry Department at the West China Union College of Medicine. In 1946 he established the Biochemistry Department in the College of Medical Sciences at the University of Saskatchewan and later moved to chair the Biochemistry Department at the University of Alberta in 1949. He enjoyed teaching and regretted the lack of time for his research on hemoglobin and hemolytic anemia. He was amused that the most popular paper he ever wrote "A punched card for biochemical references" attracted 400 reprint requests in 1964. The appointments to the professorial staff that he made at the University of Alberta resulted in a program of graduate teaching and research that (in his words) were "about as good as anywhere in Canada".

Thomas Jukes – Vitamins, cancer and myths

Thomas Hughes Jukes graduated from the Ontario Agricultural College in Guelph and then completed a Ph.D. in biochemistry at the University of Toronto in 1933. He continued his interest in the components of an adequate synthetic diet for baby chicks when he became a nutritionist at the University of California, Berkeley, and later in very inadequate facilities at

Davis. His feeding experiments with chickens determined the components and effects of the B-vitamin complex, and of pantothenic acid and choline. His work led to the finding that nicotinic acid (niacin) cured pellagra. Next, as a research scientist at the Lederle laboratories in New Jersey, he showed that folic acid was a vitamin, suggested the use of antibiotics as growth promoters in animals, and developed the use of methotrexate as a chemotherapeutic agent. Essentially, he participated in and was one of the winners of the world-wide contest to identify the vitamins that took place between 1933 and 1948. Back at Berkeley he switched his interests to DNA replication and was the first advocate of the idea that most genetic mutations are neutral. His regular column in Nature between 1975 and 1980 debunked a number of controversial topics such as the quack cancer cure 'Laetrile' from peach stones, and Linus Pauling's advocacy of massive doses of Vitamin C. "Tommy" Jukes was the keynote speaker at our 75th anniversary celebration in 1983.

Bradley Pett recognized by award

Dr. L. Bradley Pett (Ph.D.1934) played a major role in the early development of nutrition research in Canada. In 1941 he became the Director of Nutrition Services for the Department of National Health and Welfare and personally wrote the first draft of Canada's Official Food Rules. He eventually became Deputy Director General of Health Services and was an Advisor to the UN Relief and Rehabilitation Mission. In 1998 his gift of $50,000 established an endowment for graduate awards in biological chemistry and biochemistry at the University of Toronto.

Ignatieff royalty

Count Vladimir Ignatieff fled to Britain from Russia after the revolution and reached Canada in 1927. After homesteading in Alberta he obtained a master's degree in soil science from the University of Alberta and then a Ph.D. in Biochemistry from the University of Toronto in 1935. His few years of teaching and research in the Department of Soil Science, University of Alberta, were interrupted by World War II. He joined the Calgary Highlanders and rose to the rank of major during the 6 years of the war, serving in Germany and Italy. He was repeatedly decorated. In October of 1945 he was seconded to the Department of External Affairs to assist in the organization of the first Conference of the Food and Agricultural Organization (FAO) of the United Nations. He remained with FAO for 25 years and was one of the architects of the UN program, the Green Revolution, which greatly increased Third World food production through the introduction of modern farming techniques.

Guy Marrian – Steroid star

While Guy F. Marrian was a professor in our department for the five years beginning in 1933, he supervised several graduate students whose future careers became well known. When he came to Toronto from University College, London, England, he was already a star researcher – a co-discoverer of estrogenic steroids and one of the investigators who determined the four-ring structure of the steroid hormones. Several of his graduate students went on to noteworthy careers.

Saul Cohen – Being a scientist can be fun

One of Guy Marrian's first graduate students in Toronto was Saul L. Cohen (Ph.D.1936). They developed the Kober reaction to measure urinary estrogen and isolated estriol glucuronide from many gallons of late pregnancy urine. Saul Cohen joked that he never lacked a seat on a street car because of the odour of the urine concentrates that permeated his clothing. Acknowledging that he is considered a pioneer in the field of reproductive endocrinology, Cohen pointed out that he was in the right place (Guy Marrian's laboratory in Toronto) at the right time (the early thirties) so that everything he did yielded new information. During his career in Columbus, OH, Ann Arbor, MI, Minneapolis MN, and finally back in Toronto in the Department of Obstetrics and Gynaecology,

he developed assay methods for estrogens and pregnanediol, and methods for the isolation of conjugated steroids and their hydrolysis. In 1985, the Bulletin of the British Biochemical Society noted that "There has been a stream of hundreds of useful papers from Cohen's laboratory in the past 50 years, despite the fact that for half of this time he has been suffering from Wilson's disease". Originally diagnosed as having Parkinson's disease, he was unable to work for 10 years until it was recognized that a defect in copper metabolism was responsible for its accumulation and his resulting neuromuscular problems. Despite his medical condition, Saul Cohen never lost the sense of humour for which he was also famous. His memoirs "Being a Scientist Can Be fun" are full of amusing anecdotes.

Gordon Butler – Surviving the depression and WWII

Our archives from the 1930s contain descriptions of the performances of some of our graduate students at their Ph.D. oral examinations in which questions about the entire field of biochemistry could be asked. The note about Gordon Butler (Ph.D.1938) reads, "The candidate not only exhibited a broad knowledge of biochemistry but also marked ability to reason out answers when the detailed facts had not been recalled and to correlate facts from different fields. We consider that he passed the examination with exceptional brilliance." The examiners who signed this note were Prof. Hardolf Wasteneys, the chairman of the department, Prof. Arthur Wynne who succeeded him as chairman, and Prof. Guy Marrian who had supervised Gordon Butler's graduate research on the isolation and characterization of steroids. After a post doctoral fellowship in London, England, and employment in industry as a research chemist, Gordon Butler joined the Canadian Army and carried out research in the Chemical Warfare Laboratory, retiring at the end of World War II with the rank of major. During the next 2 years with the Atomic Energy Project at Chalk River, Ontario (part of the National Research Council of Canada) his work was a key factor in the derivation of maximum permissible concentrations for occupational exposure to a number of radionuclides. This contribution was timely because of the development of the atomic bomb that ended the war and the fear of its use in future warfare. In addition, the use of radioisotopes in industry and in medicine was just beginning, as well as in biochemical studies of metabolic pathways. In 1947 Gordon Butler joined the professorial staff of the Department of Biochemistry at the University of Toronto and during the next 10 years he supervised 19 graduate students. Most of them had research projects on nucleic acids at a time when the notion of a protein nature for the genetic material was just losing credibility and 6 years before Watson and Crick's double helix of DNA. In addition to daily interactions with his graduate students and his undergraduate teaching in lectures and laboratory classes, he added new research equipment that was sorely needed after the privations of the depression and the war years. Among the additions were a Beckman DU spectrophotometer, fraction collectors that he designed to facilitate separations by column chromatography, and a radioisotope laboratory with the facilities for counting beta-particles with a Geiger tube. In 1957 he returned to Chalk River as Director of the Biology and Health Sciences Division and later became Director, Radiation Biology Division, NRC, in Ottawa. After 1968 he was Director of Biological Sciences, NRC, continuing as a Consultant after retirement in 1978. From 1982 to 1987 he was President of the International Foundation for Science.

Bill Fishman – Founder of the LaJolla Cancer Research Foundation

Another graduate student of Guy Marrian was

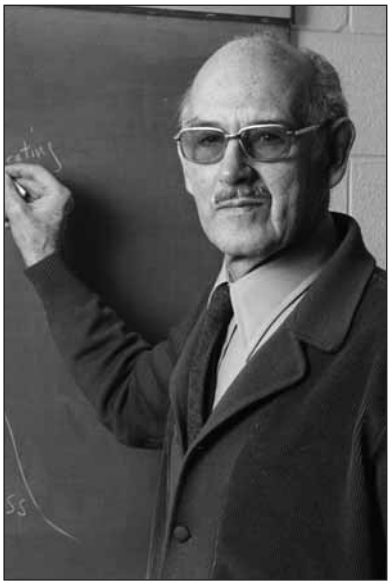
William (Bill) H. Fishman (Ph.D.1939) who prepared and studied beta-glucuronidase because it could hydrolyse urinary estrogen glucuronides. Fishman went on for 37 years with investigations of the role of this enzyme in vivo, exploring the hormonally-induced changes in its activity. At the University of Chicago in 1946, with Dr. A. John Anlyan, he discovered that high levels of beta-glucuronidase are present in cancer tissue and turned his attention to cancer research. He joined Tufts University in 1948 where the discovery of a placental protein in a man's lung cancer led to Fishman's belief in the relationship between developmental biology and oncology. In 1974 he created the Tufts Cancer Research Center and in 1976 the La Jolla Cancer Research Foundation on Torrey Pines Mesa where he remained its president until 1989. In the 1990s this foundation was described as "one of the world's premier bioresearch institutions" by Sidney Weinhouse, a former president of the American Association for Cancer Research. A class-mate of Bill Fishman, Benjamin Schachter is remembered through an endowed annual lectureship organized by our graduate students.Ï

Tony Young and "W"

During World War II, one of the professors in our department, Leslie (Tony) Young, held a contract with the Department of National Defence (DND) to investigate chemical warfare agents (secretly known as "W") – sulfur mustard gas, Lewisite, the nitrogen mustards, and BAL (British Anti Lewisite). Among others, three of our graduate students were recruited to work on these projects – John Alexander (Alec) McCarter, Sidney Zbarsky (Ph.D. 1942) and Lung-Hsien Chang (Ph.D. 1942). Their main contact with DND was through Major Gordon Butler. Alec McCarter's thesis title in 1945 was "Biological aspects of mustard gas poisoning". After the war, he was one of the biochemistry graduates from the University of Toronto who worked with Gordon Butler at Chalk River on the NRC Atomic Energy Project. McCarter joined the Department of Biochemistry at Dalhousie in 1948, became its head in 1950 and is credited with having a profound influence on its development in the next 15 years. From 1965 to 1980 he was a professor of biochemistry and Director of the NCI Cancer Research Laboratory at the University of Western Ontario where he focused on RNA tumour virus research. Upon moving to Victoria University in 1983, he turned his attention to analysing trout for metallothionein.

Charles Hanes – Graduate mentor

Prof. Charles Hanes who joined the Department in 1951 and chaired it from 1960 to 1965 had several graduate students whose names have featured prominently in this Bulletin. Among them are George Connell (Ph.D.1955) and Gordon Dixon (Ph.D.1956). Prof. Hanes graduated with a B.A. in 1925 from the University of Toronto having specialized in biology and biochemistry. His Ph.D. project at Cambridge University, U.K., focused on amylases and the interconversions of starch and soluble sugars in plant tissues. He remained at Cambridge for 25 years where he made the first suggestion of a helical conformation for a macromolecule, starch, on the basis of its iodine-colouring property. He became well known for his discovery and initial characterization of the plant phosphorylases. This work was completed just before he took up wartime duties, working on technical problems of production and handling of wartime food supplies. After the war, at Cambridge, he used the new tool, paper chromatography, to separate phosphoric acid esters and he was involved in the discovery of a number of transpeptidases. George Connell wrote an appreciation of Prof. Hanes for the Bulletin of the Canadian Biochemistry Society in 1979 in which he described the "profound influence that Prof. Hanes had not only on his students and colleagues, but in the councils of the University of



Toronto and in Canadian biochemistry. Prof. Hanes was capable of remarkable leaps of intellect, from polysaccharides to proteins, from simple kinetics to matrix algebra, as well as grasping the significance of his work in the context of the whole organism." He was elected a Fellow of the Royal Society of London in 1942 and of Canada in 1956, and he was the Flavelle Medallist in 1955.

George Connell – Graduate student, Professor, Chair, President

George Connell was appointed to our professorial staff in 1957 and began a successful research career on the chemistry of immunoglobulins and haptoglobulins. He chaired the department from 1965 to 1970, beginning a series of administrative posts that eventually took him away from active involvement in research: Associate Dean of Medicine (1972-74), Vice President for Research and Planning at the University of Toronto (1974-77), President of the University of Western Ontario (1977-84), and then President of the University of Toronto (1984-90). He is an Officer of the Order of Canada and one of the 10 "Giants of Biomedical Science" for whom the floors of the newly built Terrence Donnelly Centre for Cellular and Biomolecular Research in Toronto are named. The contributions made upon his retirement support the George Connell Biochemistry Lectureship that enables the department to fund a visiting lecturer each month.

Gordon Dixon – Protein research and regulation of protamine gene expression

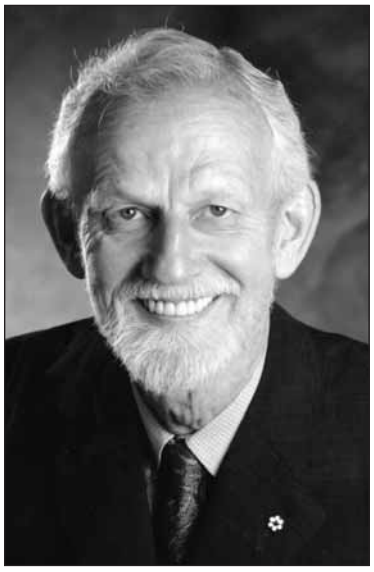
Gordon Dixon has had an impressive research career at universities in Toronto, British Columbia, Sussex U.K. and Calgary. His Ph.D. thesis on transpeptidation reactions in biological systems was followed by post doctoral work on the structure and active sites and mechanisms of action of trypsin and chymotrypsin. Returning to Toronto in 1960, he took a position at the Connaught Laboratories and was appointed to the staff of the Department of Biochemistry. He and George Connell and Oliver Smithies developed the technique of starch gel electrophoresis that at one time was used in protein research throughout the world. Oliver Smithies won the Nobel Prize in Physiology or Medicine in 2007 for his work on mouse stem cells. In collaboration with A.C. Wardlaw, Gordon Dixon achieved the first recombination of the separated A & B chains of insulin. In 1963 he moved to the Department of Biochemistry at the University of British Columbia and began his studies of the regulation of protamine gene expression, largely concentrating on the trout testis. He was elected to the Royal Society of Canada in 1970 and of London in 1978. His many other honours and awards include a Killam Award in 1991. One of his first graduate students in Toronto was Harry Schachter.

Banting and Best Department of Medical Research appointments

With the exception of Clara Benson from 1908 to 1928, the practice of giving members of other departments cross appointments to the Department of Biochemistry did not begin until 1965 when Arnis Kuksis of the Banting and Best Department of Medical Research (BBDMR) joined our staff and brought his expertise in lipid biochemistry. He became one of the 23 members of our staff who have been chosen to be Fellows of the Royal Society of Canada. The members of the department who are outside the "core" have always made major contributions to both undergraduate and graduate education. International recognition of their research has come to many of them, including Gairdner Foundation International Awards to Irving Fritz (1980) and David MacLennan (1991), both based at BBDMR, and John Riordan (1990) in the Research Institute of the Hospital for Sick Children.

Irving Fritz came to Toronto in 1968 to be chair of BBDMR for 10 years during which he recruited a number of outstanding researchers for that department including David MacLennan. Before coming to Toronto, Prof. Fritz had discovered the role of carnitine in fatty acid oxidation and had

made several other important discoveries about metabolism. His interest in cell differentiation led him to develop cell culture techniques that were essential for his investigations of the hormonal regulation of spermatogenesis. While he was in Toronto he was cross-appointed to the Department of Biochemistry, became a University Professor and a Fellow of the Royal Society of Canada. Faced by imminent mandatory retirement, he left Toronto in 1992 to become a Visiting Senior Research Fellow at the AFRC Laboratories in Babraham in the Cambridge UK area where he died 4 years later.



David MacLennan is recognized as the leading authority on the structure and function of the proteins of the sarcoplasmic reticulum, which regulates muscle contraction by controlling calcium ion concentrations. The theory he developed about the mode of action of this ATP-dependent calcium pump has been confirmed experimentally. His group has defined the genetic basis for three muscle diseases: malignant hyperthermia, central core disease and Brody disease. His finding that mutations in phospholamban, a regulator of the calcium pump, can cause cardiomyopathy and is also responsible for a related disorder in swine, has led to a diagnostic test that will eventually eliminate it from swine populations. In 1992 he received the distinction of University Professor at the University of Toronto. Prof. MacLennan has served on advisory boards and editorial boards and received many prestigious awards including being appointed an Officer of the Order of Canada in 2001.

Perfect partnership with Sick Kids

The Department of Biochemistry enjoys a long-standing partnership with the Research Institute at the Hospital for Sick Children. In 1967, Bibudhendra (Amu) Sarkar was our first professorial appointee from the Research Institute of the Hospital for Sick Children where he eventually became the Head of Biochemistry Research from 1990 to 1997, and then Director of the Advanced Protein Technology Centre (1999-2002). His research centred on metals and metal-related diseases and resulted in many visiting professorships and honours, including the Nuffield Foundation Award (U.K.) in 1977, and prestigious awards in 2005 and 2006 in India. He edited 5 books and authored approximately 200 publications. His discovery of the drug treatment of Menkes disease, a fatal neurodegenerative disease of genetic origin, is saving children around the world. In 1998 his research expertise received national and international attention in connection with a health crisis in Bangladesh and India caused by arsenic in ground water.

John Riordan (Ph.D.1970 in Biochemistry at U. of T.) and a member of our professorial staff from 1979 to 1995, gained fame and was appointed an Officer of the Order of Canada for his participation in the identification and analysis of the cystic fibrosis gene at the Hospital for Sick Children.

In 1969, Mario Moscarello was one of our first appointees from the Research Institute of the Hospital for Sick Children where he went on to head the Biochemistry Department from 1989 to 1992. His research interests centred on myelin basic proteins, resulting in more than 270 publications describing his research work that involved 19 graduate students registered in our department.

Harry Schachter was Gordon Dixon's first graduate student when Gordon was briefly a professor of biochemistry at Toronto. Immediately after the award of his Ph.D. in 1964, Harry joined the core staff in our department. In 1976 he transferred to

the Hospital for Sick Children in Toronto where he became the head of the Division of Biochemical Research until 1989. He was also Chair of our Department from 1984 to 1989. The importance of his research that is focused on the biochemistry of glycoproteins and other glycoconjugates has been recognized by numerous medals, awards, visiting professorships, a Fellowship in the Royal Society of Canada, and the presidency of the International Glycoconjugate Organization. But most noteworthy is Harry Schachter's enthusiasm and his lucid and compelling style of presenting his ideas, as well as his superb grasp of his subject. He has been a favourite as a lecturer locally, nationally and internationally. Among his graduate students is David B. Williams (Ph.D.1981) who joined our core staff in 1984. He was the recipient of the CSBMCB Merck-Frosst Award in 1994 and the U. of T. Dales Award in 2002 for his research on protein folding and quality control within the endoplasmic reticulum (ER). His recent work has focused on the characterization of a membrane-bound molecular chaperone of the ER termed calnexin and its soluble homologue, calreticulin.

Janet Forstner was based at the Hospital for Sick Children from 1974 until her retirement in 2003. She received awards from the Canadian Cystic Foundation and from the Governor General of Canada for her "significant contributions to Canada". Other members of the Research Institute continue to make major contributions to biochemistry through their splendid research and teaching activities.

The medical/dental connection

Many students who received B.Sc. or M.Sc. degrees in our department went on to medical school, but little is known about their subsequent careers. One who was prominent in the news during the SARS crisis in 2003 is Dr. Allison McGeer (M.Sc.1976), now a University of Toronto professor in Laboratory Medicine and Pathobiology and Public Health Sciences based at Mount Sinai Hospital. She has become one of Canada's foremost infectious disease specialists.

At least four of our professorial staff with medical degrees and with Ph.D. degrees from our department have combined their knowledge of medicine with their biochemical expertise – Mario Moscarello (M.D.1955, Ph.D.1962), Harry Schachter (M.D. 1959, Ph.D.1964), Robert Murray (M.B. Glasgow, 1956, Ph.D.1961) and Janet Forstner (M.D.1962, UBC, Ph.D. 1971).

Robert Murray, who became a member of our core staff in 1961, has repeatedly won prestigious awards from the Faculty of Medicine for his teaching prowess. He was co-author of the 21st to 26th edition of Harper's Biochemistry (1988-2003) and co-author with R. Roy Baker of PDQ Biochemistry (2001). Other members of the Department, notably Larry Moran and Gray Scrimgeour, have dedicated a large part of their efforts to production of biochemistry textbooks.

Degrees in dentistry also preceded an interest in biochemistry and physiology for Irving Fritz and Anders Bennick. The latter went on from his M.Sc. degree in Dentistry in Denmark in 1965 to a Ph.D. in Biochemistry at Toronto in 1970. As well as his invaluable assistance in teaching our dental students, Prof. Bennick carried out research that resulted in many prestigious awards, including the Spitton Award ("Salivary researcher of the year") in 1985 and the "Distinguished Scientist Award" in 2003 from the International Association for Dental Research.

More on biochemistry partnerships

A shared interest in biochemistry has led to a number of marriages between graduate students. Again, records are incomplete, but we know that in the early days, Prof. Blythe Eagles (Ph.D.1926 in Pathological Chemistry) met Violet Dunbar (Ph.D. 1929 in Biochemistry) in our department. He later joined the professorial staff at the University of British Columbia. Vladimir Ignatieff (Ph.D.1935) and Florence Hargreaves (M.A.1934) met while they were both our graduate students. These marriages occurred at a time that when

women married they were prevented by regulations from continuing their careers, but these capable women undoubtedly contributed without pay or formal recognition to the future accomplishments of their husbands.

In our department, one of the first women for whom this regulation was broken was Jeanne Manery Fisher, whom the chairman, Hardolf Wasteneys, connived to appoint as a demonstrator in 1939 because (in her words) the position was so unimportant. Jeanne Manery had obtained her B.Sc. in Biology and Medicine and then her Ph.D. (1935) in Physiology at Toronto. After post-doctoral work at the University of Rochester and Harvard University and marriage to Kenneth Fisher in 1938, she returned with him to Toronto where he had joined the Zoology Department. Because of her marriage she found her career path almost blocked and it was not until 1948 that she was finally appointed as an assistant professor in our department, although she had been supervising graduate students, carrying out research and lecturing not only in biochemistry but also to her husband's Zoology students while he was away from the university during World War II. She went on to become the first woman to hold a full professorial appointment in our department. With her graduate students and research assistants she investigated the plasma membrane of cells at a time when it was generally considered to be just an inert wrapping. Her research projects included the control of Na+ and K+ concentrations in cells, the effect of insulin on electrolytes in muscle and the role of Ca2+ in the structure and function of membranes. Her group was one of the first to recognize the nucleotide-converting ectoenzymes. She was honoured in 1977 for her contributions to science by the award of the Queen's Jubilee Medal. As a charter member of the Canadian Biochemical Society, she was acutely aware of the lack of involvement of women scientists in its affairs. Not surprisingly, she was one of the instigators and the first chair of the Equal Opportunities Committee of the Canadian Biochemistry Society in 1980. After her death in 1986, the Society established the Jeanne Manery Fisher Memorial Lectureship that is given on alternate years by an eminent Canadian woman scientist associated with the fields of biochemistry and molecular or cellular biology.

Times have changed, and several husband and wife teams are associated with the department. Prof. Robert Painter joined our core staff in 1968 where his wife, Dorothy, had already been a lecturer since 1964. Over the next 33 years, Dorothy made major contributions to the laboratory courses in biochemistry, resulting in sharing a prestigious W.T. Aikins Award with Prof. David Isenman in 1996 for course development and coordination. Prof. Painter's research was directed at elucidating the structure and function of immunoglobulins, complement, plasminogen, and albumin in human blood and the use of hemoglobin as an alternative to the transfusion of whole blood. In addition to research, teaching, and service on many scientific advisory committees, Prof. Painter was Provost and Vice-Chancellor of the University of Trinity College, University of Toronto, from 1986 to 1996, with Dorothy functioning as his helpmate and hostess of the obligatory events associated with this responsibility. David Isenman was one of Professor Painter's graduate students, and he and his wife Jacqueline Segall have been faculty members in the Department since 1977 and 1980.

We have two other husband and wife teams on our professorial staff. Sergio Grinstein and Amira Klip came to the Hospital for Sick Children in 1979 and were appointed to the Department of Biochemistry in 1984. Both of them were elected as Fellows of the Royal Society of Canada in 2000. Prof. Grinstein is recognized as an international

authority on ion pumps and their roles in intracellular homeostasis, and his group has devised methods to measure pH in subcellular compartments in living cells. He has also furthered the understanding of how white blood cells are activated to destroy microbial invaders. His numerous awards and honours include the McLaughlin Medal of the Royal Society of Canada (2002), and the Michael Smith Prize in Health Research (2004). Prof. Klip's group has pioneered studies of the mechanism of glucose uptake into muscle cells through glucose transporters or GLUTs. Their work focuses on how a series of signal transduction pathways activated by insulin impinge on intracellularly stored GLUT4 to move to the cell surface and become activated with the participation of the actin cytoskeleton. Among her many awards are the CBS Pharmacia Award (1992), the Jeanne Manery Fisher Memorial Lectureship (2000) and the U. of T. Dales Award for Medical Research (2002).

With Ph.D.s from Yale University and after post-doctoral work at NIH, both Julie Forman-Kay and Lewis Kay joined our Department in 1992. Prof. Julie Forman-Kay is based at the Hospital for Sick Children where she studies protein structure, interactions, dynamics and folding. Since coming to Toronto, Prof. Lewis Kay has become probably the world's greatest authority on NMR in the study of biological molecules and complexes. He has developed and applied NMR methods to the study of protein structure and dynamics. He credits part of his success to the resources available at the University of Toronto where the research facilities are among the best for NMR research. His many awards include the Steacie Prize (1999) which is Canada's most prestigious award for a researcher under 40, and the Flavelle Medal (2002) of the Royal Society of Canada. He was elected to the Society in 2006.

Even if the information were complete, it would not be realistic to list all the marriages between students who obtained graduate degrees in our Department. In recent years, Liliana Attisano (Ph.D.1990) and Jeffrey Wrana (Ph.D.1991) have both joined the professorial staff at the University of Toronto and are receiving international recognition. Since 2001, Prof. Attisano has been a member of our department, and in 2002 she was one of the 100 most-cited researchers in the field of Molecular Biology and Genetics for the last decade (ISI Essential Science Indicators). Jeffrey Wrana is based at the Samuel Lunenfeld Research Institute with a professorial appointment in Medical Genetics and Microbiology. In 2005 he was awarded the Paul Marks Prize for Cancer Research given by the Memorial Sloan-Kettering Cancer Center. They have published jointly on the transforming growth factor-beta family of cell signalling proteins that regulate cell growth and function. One of our most recent faculty appointments, Angus McQuibban met his wife Erin Mitchell while they were graduate students in the department, so the tradition continues.

Biochemistry and leadership

A number of our graduates and professorial staff eventually pursued noteworthy careers that took them beyond research. Some of these have already been mentioned – L. Bradley Pett, Vladimir Ignatieff, Gordon Butler, George Connell, and Robert Painter. Chairs of our Department who have gone on to take heavier administrative loads at the University of Toronto include G. Ronald Williams (famous, with Britton Chance, for measurements of the oxidation-reduction state of the individual electron carriers as they function in intact mitochondria). He became principal at the Scarborough Campus of the University of Toronto (1984-1989). Peter Lewis (who carried out research on chromatin structure and function) began his second five-year term in 2007 as Vice Dean, Research, in the Faculty of Medicine.

Keith Dorrington – Chair and administrator

Keith J. Dorrington came from England to the Department of Biochemistry in Toronto in 1970 and quickly established an active research group focused on molecular immunology. Their work involved setting up laboratory models for studying the physical and chemical facets of antibody

biosynthesis, and examining the various roles of antibodies. The importance of their findings was recognized by the Ayerst Award of the Canadian Biochemical Society to Prof. Dorrington in 1977. By this time, however, his administrative talents had already led to his appointment as Vice-Provost for Health Sciences (1976) and Chair of the Department of Biochemistry (1977). In 1978 he became Associate Dean, Basic Sciences, in the Faculty of Medicine. He resigned the Chairmanship of the Department in 1982 to become the Director of the Connaught Research Institute and Vice-President of Research and Technology, but he maintained his research laboratory in the university until 1989 when he left Canada to take up the position of Managing Director, Wellcome Biotechnology Ltd. in the U.K. He eventually returned to Canada to be the Senior Vice-President of MDS Capital Corp. until his untimely death from hereditary hemochromatosis in 2002.

Rose Sheinin – Woman scientist

Rose Sheinin (Ph.D.1956) became a Research Associate in Tumour Virology at the Ontario Cancer Institute (1958-76) with a professorial appointment in Medical Biophysics. After moving to the Department of Microbiology and Parasitology in 1975, she chaired the department from 1976 to 1982. Always a strong promoter of women's issues, she has authored several books about early women scientists. She was the first woman to be President of the Canadian Biochemical Society (1975-76). Rose was elected a Fellow of the Royal Society of Canada in 1981 and has received a number of honorary degrees. At the University of Toronto, she became the Vice-Dean of Graduate Studies (1984-89), but left Toronto to become the Vice-Rector, Academic, at Concordia University from 1989 to 1994.

Diana Michener Schatz and medical technology

Immediately after graduation, Diana Michener Schatz (Ph.D.1958) was instrumental in founding the Toronto Institute of Medical Technology that is now known as The Michener Institute for Applied Health Science (or just "The Michener"), named for her father who was Governor General of Canada from 1967 to 1972. Currently it educates 800 full-time and 3,300 part-time and continuing education students each year in medical laboratory science, medical radiation sciences, respiratory therapy, diagnostic cytology, genetics technology, ultrasound, MRI and computed tomography.

Kevin Keough – Scientist and administrator

After post-doctoral studies, Kevin Keough (Ph.D.1971) joined the Biochemistry Department at Memorial University, became its chair in 1986 and then Vice President Research in 1992. Following his presidency of the CBS in 1988-89, he served as president of the Canadian Federation of Biological Societies in 1990-91. His research interests focused on lipid-lipid and lipid-protein interactions in biological membranes and pulmonary surfactant. He founded a company called NovaLipids Incorporated based on his research innovations in the research laboratory that he maintained for over 30 years.

He has taken an active role in science policy matters and in 2001 the Liberal government appointed him as Canada's first Chief Scientist for Health. In 2004 he was appointed as President and CEO of the Alberta Foundation for Medical Research. At the time of this appointment, the Globe and Mail noted that, "As a former member of the Medical Research Council, Dr. Keough was involved in the creation of the Canadian Institutes of Health Research (CIHR) and is now a member of its Governing Council. He is a member of the Council of Science and Technology Advisors, the Canadian Co-Chair of the Canada-European Union Science and Technology Agreement, and a founding member of the Board of Directors of Genome Canada".

The Department today

At the present time, the Department has 56 individuals on its professorial staff, 27 in the

Medical Sciences Building and the adjoining Donnelly Centre for Cellular and Biomedical Research (CCBR), and the rest in other departments and the research institutes of the hospitals. A research powerhouse, members of the Department have published over 1,000 papers in the last five years. We teach thousands of undergraduate and medical students every year, and many of our faculty have won teaching awards. Over the past 100 years the Department has graduated over 360 Ph.D. and 380 M.Sc. students and we currently have about 200 graduate students and post-doctoral fellows. Our new faculty members and recent graduates who are now carving out research and administrative careers will undoubtedly be featured in further historical records about the Department of Biochemistry at the University of Toronto. To celebrate its many achievements in research and education over the years, the Department is holding a 100th Anniversary Symposium May 28-30, 2008 at the University of Toronto, which we hope our many colleagues from across Canada and around the world will attend.

Marian A. Packham University Professor Emeritus

Marian Packham is one of the world's leading authorities on the biochemistry and physiology of blood platelets and is credited with major contributions to the understanding of platelets and their role in heart attacks and strokes. She is the official historian of the Department of Biochemistry.

Table 1

Graduate Students who later became Chairs of Departments of Biochemistry

	Date of Chairmanship	University
James Bertram Collip (Ph.D.1916)	1922-28	Alberta
James Bertram Collip	1928-41	McGill
Henry Borsook (Ph.D.1924)		Cal.Tech. USA
Arthur Marshall Wynne (Ph.D.1925)	1951-60	Toronto
Herbert Bruce Collier (Ph.D.1930)	1946-49	Saskatchewan
Herbert Bruce Collier	950-61	Alberta
Marvin Don Darrach (Ph.D.1941)	1950-?	Brit. Columbia
John Alexander McCarter (Ph.D.1945)	1950-65	Dalhousie
Harold Brown Stewart (Ph.D.1950)	1965-70	Western Ont.
Christopher Walter Helleiner (Ph.D.1955)	1965-78	Dalhousie
George Edward Connell (Ph.D.1955)	1965-70	Toronto
Gordon Henry Dixon (Ph.D.1956)	1972-74	ussex, UK
Gordon Henry Dixon	1983-93	Calgary
Alastair Taylor Matheson (Ph.D.1957)	1977-85	Victoria
James Michael Neelin (Ph.D.1958)	1978-85	Carleton
Karl Boruch Freeman (Ph.D.1959)	1973-79	McMaster
Harry Schachter (Ph.D.1964)	1984-89	Toronto
William Carl Breckenridge (Ph.D.1970)	1993-?	Dalhousie
Kevin Michael Keough (Ph.D.1971)	1986-93	Memorial
Gerhard Ernst Gerber (Ph.D.1975)	1991-96	McMaster
Jeffrey Tze-Fei Wong (Ph.D.1963)	1990-	Hong Kong Univ. of Sci. & Tech.

Chairs of Departments other than Biochemistry

James Arnold Dauphinee (Ph.D.1929) Dept. of Pathological Chemistry	1947-66	Toronto
Hugh D. Branion (Ph.D.1933) Dept. of Nutrition	1938-64	OAC, Guelph
Joseph Francis Morgan (Ph.D.1945) Dept. of Cancer Research	1962-76	Saskatchewan
Rose Sheinin (Ph.D.1956) Dept. of Microbiology and Parasitology	1976-82	Toronto
Michael Christopher Archer (Ph.D.1970) Dept. of Nutritional Sciences	1999-	Toronto

Table 2

Faculty and graduate students who became Presidents of the Canadian Biochemical Society/ Canadian Society of Biochemistry, Molecular & Cellular Biology

Arthur M. Wynne	1957-58
Marvin D. Darrach	1960-61
Gordon C. Butler	1961-62
J. Alexander McCarter	1966-67
Sidney Zbarsky	1967-68
G. Ronald Williams	1971-72
George E. Connell	1973-74
Lawrence B. Smillie	1974-75
Rose Sheinin	1975-76
Alastair T. Matheson	1980-81
Gordon H. Dixon	1982-83
Kevin M. Keough	1988-89
Harry Schachter	1993-94
Peter N. Lewis	1999-00
Joseph R. Casey	2004-05
Reinhart A.F. Reithmeier	2007-08

Presidents of other societies of the CFBS

Rose Sheinin	1973-74
Can. Soc. Cell Biology	
Bruce Holub	1974-75
Can. Soc. for Nutritional Sciences	
James M. Neelin	1983-84
Can. Soc. for Cell Biology	

Presidents of the Canadian Federation of Biological Societies

Gordon C. Butler	1967-69
G. Ronald Williams	1974-75
Kevin M. Keough	1990-91

Table 3

Graduate students and staff members who were recipients of the Ayerst/Pharmacia/Merck-Frosst Award of the Canadian Society of Biochemistry, Molecular & Cellular Biology

Year	Recipient	Staff Member
1966	Gordon H. Dixon (Ph.D.1956)	1960-63
1971	Byron G. Lane (Ph.D.1959)	1968-98
1974	David H. MacLennan	1980-
1977	Keith J. Dorrington	1970-89
1984	Ross N. Nazar (Ph.D.1970)	
1987	Sergio Grinstein	1984-
1992	Amira Klip	1984-
1994	David B. Williams (Ph.D.1981)	1984-
1996	Lewis E. Kay	1992-
1998	David M. Clarke	1992-
2002	Jeffrey L. Wrana (Ph.D.1991)	
2005	J. N. Mark Glover (Ph.D.1991)	
2006	Joseph R. Casey Ph.D.1992)	

eIF4E, the mRNA cap-binding protein: from basic discovery to translational research

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Abstract

Translational control is an important strategy by which eukaryotic cells regulate gene expression. Translation is the last step in the flow of genetic information, and regulation at this level allows for an immediate and rapid response to changes under physiological conditions. Because mRNA biogenesis including transcription, splicing, and export to the cytoplasm are time consuming, the use of pre-existing mRNAs by controlling translation is of advantage in many circumstances. A prime target of translational control is the initiation factor eIF4E, which recognizes the m7GpppN, cap structure present at the 5'end of all nuclear transcribed eukaryotic mRNAs. In this article I describe the discovery of eIF4E, its mechanism of action in translation initiation and its role in the control of cancer and innate immunity.

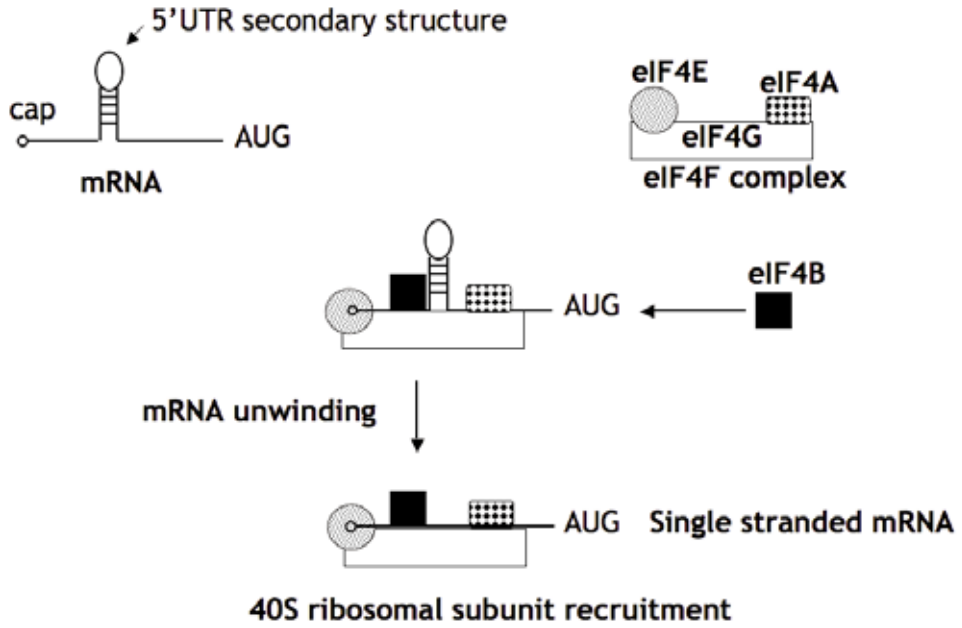

Figure 1. Mechanism of action of eIF4F in translation initiation. eIF4F binds to the mRNA cap-structure via the cap-binding subunit, eIF4E. The helicase eIF4A subunit with the assistance of the RNA-binding protein, eIF4B, is thought to unwind the mRNA 5'UTR secondary structure to create a landing pad for the ribosome.

Translation is divided into three distinct phases – initiation, elongation, and termination (Mathews et al., 2007). Translation initiation is under most circumstances the rate-limiting step in translation. Translation initiation is a complex, ordered process, which commences with the binding of eIF4F, a three-subunit protein complex, with the mRNA 5' end cap (m7GpppN, where N is any nucleotide and m is a methyl group) structure, which facilitates the recruitment of the ribosome to the mRNA (Pestova et al., 2007) . The cap is present on all nuclear transcribed cellular eukaryotic mRNAs (Shatkin, 1985). eIF4F is comprised of three subunits (Fig. 1): eIF4E, the cap binding protein; eIF4A, an ATPase and RNA helicase; and eIF4G – a scaffolding protein that bridges the mRNA and the ribosome through eIF3, which binds the ribosome directly (Gingras et al., 1999b). eIF4F binds the cap structure via the eIF4E subunit, and is thought subsequently to unwind the mRNA 5'UTR secondary structure to facilitate the binding of the 40S ribosomal subunit. The 40S ribosome complex then traverses the 5' UTR until it recognizes the initiation codon AUG following by binding of the 60S large ribosomal subunit to form the 80S initiation complex, which is competent to enter the elongation cycle. Entry through the 5'-cap is not the only mechanism by which ribosomes can access the mRNA and proceed to an initiation codon. Some mRNAs contain internal entry sites to which ribosomes can bind directly (Doudna and Sarnow, 2007; Elroy-Stein and Merrick, 2007). This essay describes the discovery of the mRNA cap binding protein, eIF4E, three decades ago, and the following studies demonstrating its importance in controlling gene expression and thereby cells physiology under normal conditions and in disease.

I chose to join Aaron Shatkin's research group at the Roche Institute in Nutley, New Jersey, in 1976, as a post-doctoral fellow, because his group was the first to show that a eukaryotic mRNA (that of reovirus mRNA), in stark contrast to the prokaryotic mRNAs, harbors a cap structure at its 5' end (Furuichi and Shatkin, 1976; Shatkin, 1976). When I joined Shatkin's lab it was already known that the cap-structure facilitates the recruitment of ribosomes to the mRNA and thus activates translation (Muthukrishnan et al., 1975). My project was to identify the putative protein(s), which was postulated to interact with the cap structure and mediate the stimulatory effect of the cap on translation. The strategy, which was rather straightforward, was to generate a reactive group on the cap structure, which could form a stable covalent bond with amino acids of proteins, which interact with the cap; in other words, the protein would become cross-linked to the mRNA via the cap. If the cap is made radioactively labeled the label will then be transferred to the cross-linked protein(s), whose molecular mass could be determined by using SDS-polyacrylamide gel electrophoresis. The method, which I used for cross-linking was a well-known one (Sonenberg and Shatkin, 1977), whereby the ribose of the m7G-cap was oxidized with periodate to convert the 2',3' cis-diol to the reactive dialdehyde. The dialdehyde group could then form a Schiff base with -amino groups of lysine residues in their vicinity. However, a Schiff base is unstable, but can be converted to a stable covalent bond with a reducing agent such as sodium borohydride (Kenner, 1973). As mentioned above, this was a rather standard technique, but disappointingly did not work for me, as I failed to cross-link any protein to the cap. Shatkin then suggested asking for advice from Charles Cantor, a well known chemist at Columbia University in New York, who promptly told us to use sodium cyanoborohydride, which is much more potent in stabilizing the Schiff base (Borch et al., 1971). And, indeed, it worked like a charm. Only one polypeptide of a molecular mass of 24 kDa cross-linked specifically to the cap, inasmuch as the cross-linking was inhibited only by cap analogues, such as m7GMP, m7GDP, but not GMP or GDP (Fig. 2) (Sonenberg et al., 1978). Subsequently, the 24 kDa polypeptide was purified to homogeneity using affinity chromatography (Sonenberg et al., 1979). I had

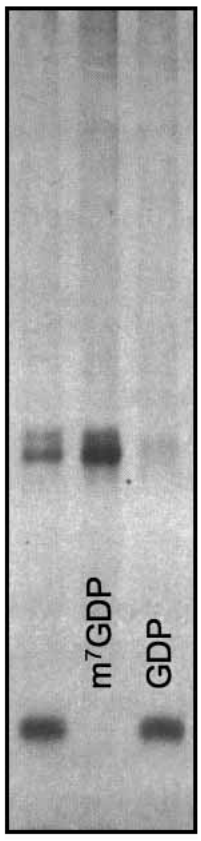

Figure 2. Identification of the eIF4E, cap-binding protein by chemical cross-linking of reovirus mRNA to proteins in fractionated cell extract. The experiment shows that eIF4E cross-links to eIF4E and that this cross-linking is inhibited by the cap-analog m7GDP, but not by GDP.

shown that the 24 kDa polypeptide, which was later termed, eIF4E, could stimulate the translation of capped mRNAs, but not uncapped mRNA(Sonenberg et al., 1980), as expected from a protein that mediates the effect of the cap-structure on translation (Sonenberg et al., 1979). Follow-up workby Stanley Tahara in Shatkin's group showed that eIF4E functions as a complex with eIF4A and eIF4G, as described above to stimulate translation (Tahara et al., 1981).

eIF4E and cancer

The importance of eIF4E in controlling translation and cell physiology became evident after the cloning of the eIF4E cDNA of Saccharomyces cerevisiae and human (Altmann et al., 1987; Rychlik et al., 1987). Later, after we cloned in our lab at McGill university the mouse cDNA (Jaramillo et al., 1991), we were keen to explore the effect of overexpression of eIF4E on cell growth and proliferation, because some reports documented that eIF4E is present in the cell in limiting amounts relative to other initiation factors (Duncan et al., 1987), suggesting that eIF4E might function as the rate limiting factor in translation. Anthoula Lazaris-Karatzas who performed these experiments in NIH-3T3 cells made the seminal discovery that eIF4E causes their malignant transformation when overexpressed (Lazaris-Karatzas et al., 1990). The same experiments were repeated in rat primary embryo fibroblasts in which two oncogenes are required for transformation. eIF4E could transform these cells in collaboration with "immortalizing" genes such as the adenovirus E1A or cellular myc (Lazaris-Karatzas and Sonenberg, 1992). Thus, eIF4E behaves as a classical proto-oncogene. This conclusion was reinforced more recently through experiments in transgenic mice. Overexpression of eIF4E via the -actin promoter engendered tumors in many different tissues (Ruggero et al., 2004). In another system in which -myc causes lymphomas in the spleen, eIF4E dramatically accelerated tumor formation (Wendel et al., 2004). The amounts of eIF4E, which are required to transform cell in culture are not highly excessive as 2.5 excess is sufficient to cause transformation (Rousseau et al., 1996). This is an important observation vis-à-vis cancer in humans, because in a sizable number (~30%) of major cancers this is the magnitude of increase in the amounts of eIF4E (Ruggero and Pandolfi, 2003). In light of these findings different approaches are currently developed to treat cancer by interfering with eIF4E function. One approach taken by Eli Lilly Co. has been to use anti-sense DNA against eIF4E. Graff et al., (Graff et al., 2007) reported that eIF4E anti-sense DNA inhibited tumor growth in mice without general deleterious effects and that they are conducting Phase I clinical trials in humans. In a different approach the group of Gerhard Wagner screened for chemical compounds that inhibit the eIF4E-eIF4G interaction and subsequently binding of the 40S ribosome subunit to the 5'end of the mRNA. They discovered two compounds, which inhibit cap-dependent, but not cap-independent translation and demonstrated that the compounds inhibit cancer cell growth, albeit at high concentrations (Moerke et al., 2007).

A critical question that has not been fully answered concerns the mechanism by which eIF4E induces cancer. Numerous studies demonstrated that eIF4E preferentially stimulates the translation of a subset of mRNAs which contain a highly structured 5'UTR and encode proteins playing important roles in cell growth, proliferation, and apoptosis. Such studies were also carried out on a genome-wide scale (Larsson et al., 2007; Mamane et al., 2007). The translation of many mRNAs with extensive 5'UTR secondary structure is preferentially stimulated by eIF4E (Gingras et al., 1999c; Koromilas et al., 1992). Thus, the molecular mechanism that would explain the differential effect of eIF4E on mRNA translation is based on the findings that mRNAs, which contain extensive secondary structure in their 5'UTR require more unwinding by eIF4F, and therefore elevated eIF4E activity.

A major signaling pathway through which eIF4E activity controls cancer is the PI3K/Akt/mTOR via the phosphorylation of 4E-binding proteins (4E-BPs). The 4E-BPs, of which there are three isoforms in mammalian cells, are suppressors of eIF4E activity. They exert their inhibitory activity by binding to eIF4E and preventing its interaction with eIF4G to form the eIF4F complex(Pause et

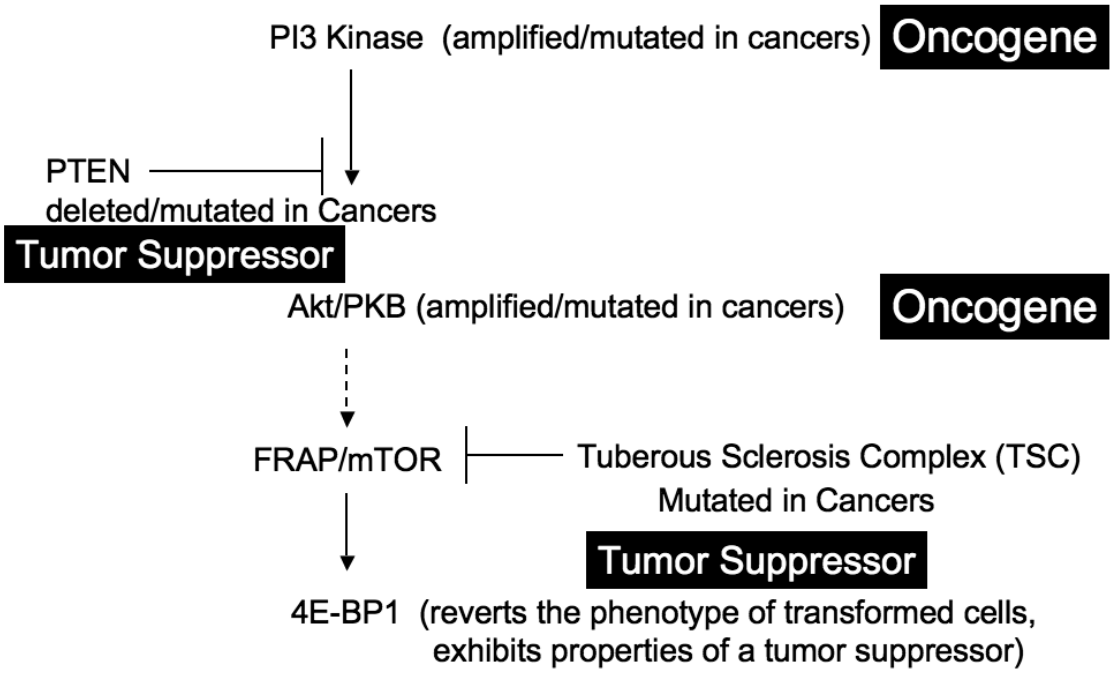

Figure 3 Changes in components of the PI3K/Akt/mTOR pathway are associated with cancer. Mutations and overexpression in PI3K and Akt proto-oncogenes were demonstrated in several kinds of cancers, while mutations and deletions of the tumor suppressor genes were documented in other cancers. Changes in 4E-BP1 were shown to correlate with cancer outcome.

al., 1994; Poulin et al., 1998). The binding of 4E-BPs to eIF4E is controlled by phosphorylation of 4E-BPs downstream of the PI3K/Akt/mTOR signaling pathway (Gingras et al., 1999b; Hay and Sonenberg, 2004). When phosphorylated the 4E-BPs can no longer interact with eIF4E. 4E-BPs become phosphorylated on several sites (e.g. 4E-BP1 is phosphorylated on at least 6 sites) in response to many extracellular stimuli and intracellular cues that activate the mTOR (mammalian Target Of Rapamycin) kinase, including growth factors, energy status, amino acid availability and oxygen tension. mTOR phosphorylates directly several sites on 4E-BPs (Gingras et al., 1999a).

The upstream components of the PI3K/Akt/mTOR signaling pathway (Fig. 3) are all strongly implicated in cancer development and progression. In particular, activating mutations in the proto-oncogene products, PI3K and Akt have been documented in different types of cancers (Petroulakis et al., 2006). In addition, inactivating mutations in the tumor suppressor gene products, Pten and Tsc2 are common in many cancers. All these mutations result in the activation of mTOR and subsequently phosphorylation of 4E-BPs and their release from eIF4E. Thus, constitutive activation of the PI3K/Akt/mTOR signaling pathway is expected to inactivate the tumor suppressor activity of 4E-BPs, and in turn to contribute to cancer development. In this regard it is striking that the phosphorylation status and amounts of 4E-BP1 strongly correlate with survival of patients with ovarian, breast, prostate cancers and rhabdomyosarcoma (Armengol et al., 2007). Thus, patients in which 4E-BP1 is highly phosphorylated or expressed at low amounts exhibit poor survival. This raises the intriguing possibility that 4E-BP1 could be used as a prognostic marker for survival in many cancers.

There are several candidate anti-cancer drugs in advanced phase clinical trials, which target components of the PI3K/Akt/mTOR pathway. These include chemically synthesized inhibitors of PI3K and Akt, and the natural product rapamycin, which is a highly potent and specific inhibitor of TOR (Easton and Houghton, 2006; Tokunaga et al., 2008). All of these candidate anti-cancer drugs

inhibit as expected the phosphorylation of 4E-BPs. In the light of the role that 4E-BPs play as tumor suppressors it is conceivable that at least some of the anti-tumorigenic effects of these drugs are due to inhibition of 4E-BP's phosphorylation.

eIF4E and innate immunity

Because eIF4E controls gene expression in a variety of biological processes it was expected that mice in which 4E-BP1 and/or 4E-BP2 was deleted exhibit certain phenotypes. For example, the 4E-BP1/4E-BP2 knock out mice become more obese than wild-type mice when fed a high-fat diet (Le Bacquer et al., 2007) whereas 4E-BP2 knockout mice exhibit an impaired long-lasting synaptic plasticity and memory formation (Banko et al., 2006; Banko et al., 2005). A very striking phenotype of these mice concerns virus infections, as embryo fibroblasts derived from the 4E-BP1/2 deficient mice were resistant to infections by a wide range of viruses, including influenza, vesicular stomatitis virus, and Sindbis virus, and mice were resistant to vesicular stomatitis virus infections (Colina et al., 2008). 4E-BP1/2 deficient mice produced more Interferon (IFN)-I (and IFN), as compared to wild-type mice which explains why these mice are resistant to infections by diverse viruses. The molecular basis of the increased production of IFN-I is based on the fact that elimination of 4E-BP1/2 results in the increased of translation of a subset of mRNAs in particular that encoding for the interferon regulatory factor 7, IRF-7, which is critical for the transcriptional activation of IFN-I genes (Honda et al., 2005). The mRNA 5'UTR of irf-7 is highly structured and thus is expected to be translated better when eIF4E activity is increased, as is the case when the 4E-BPs are deleted. These findings raise the interesting possibility that chemical compounds which inhibit the activity of 4E-BPs can be discovered and used to prevent and even treat serious virus outbreaks such as a new influenza epidemic, Ebola or SARS infections.

In summary, I described here the paramount role that a well-known structure of the eukaryotic mRNA, the cap, and its binding protein, eIF4E, play at the cellular and organismal level. The advances made by this work reinforce the tenet that classical basic research often leads to better understanding of major human disease and consequently to the development of cures.

Acknowledgements

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From cytogenetics to next-generation sequencing technologies: advances in detecting genome rearrangements in tumors

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Abstract

Genome rearrangements have long been recognized as hallmarks of human tumors and have been used to diagnose cancer. Techniques for the detection of genome rearrangements have evolved from microscopic examinations of chromosomes to, more recently, microarray-based approaches. The availability of next-generation sequencing technologies may provide a means for scrutinizing entire cancer genomes and transcriptomes at unparalleled resolution. Here, we review the methods that have been used to detect genome rearrangements and discuss the scope and limitations of each approach. We end with a discussion on the potential that next-generation sequencing technologies may offer to the field.

Introduction

Cancer is a genetic disease caused by an accumulation of mutations leading to uncontrolled cell growth and proliferation (Vogelstein 2004). Genetic changes in cancer can be either inherited through the germ line, resulting in cancer susceptibility, or acquired as somatic mutations (Futreal et al. 2004). Aberrations implicated in tumorigenesis include point mutations and extended genome rearrangements, such as translocations, inversions, small insertions/deletions (indels), and copy number variants (CNVs). Throughout this review, indels are defined as duplications or deletions involving <1 kb of DNA while CNVs are similar events involving >1 kb DNA (Freeman et al. 2006).

Extended genome rearrangements are hallmarks of cancer. In fact, chromosomal translocations that result in either chimeric protein products or misregulation of gene expression due to the apposition of coding sequences to regulatory regions of other genes are common types of mutations associated with known cancer genes (Futreal et al. 2004). Translocations had originally been thought to be characteristic of hematopoietic neoplasias, such as lymphomas and leukemias, but have recently been shown to be common in solid tumours as well (Futreal et al. 2004; Teixeira 2006). The importance of structural genomic variation in health and disease has been further underscored by the recent realization of the abundance of copy number variation in human genomes (Freeman et al. 2006). This discovery was largely the result of genome-wide approaches that enabled scanning the entire genome at higher resolutions than had previously been possible. Although large-scale CNV characterization is still in its infancy, genetic association studies have already implicated some copy number variants in cancer (Frank et al. 2007).

The prevalence of extended rearrangements in cancers and their apparent significance in disease pathogenesis have led to the development of

numerous methods for their detection. The earliest methods for detecting chromosomal and genomic aberrations involved microscopic examinations of chromosomes (Tjio and Levan 1956) and chromosome banding patterns (Caspersson et al. 1970). Application of these approaches led to the discovery of the Philadelphia chromosome, which results from an exchange of DNA between chromosomes 9 and 22 in chronic myeologenous leukemia (CML) (Nowell and Hungerford 1960; Rowley 1973). While chromosome banding, most commonly using the Giemsa stain-based G banding protocol, is still widely used today for diagnoses (Speicher and Carter 2005; de Jong 2003), cytogenetic techniques of much higher resolution, as well as PCR, microarrays, and most recently clone-based methods have been developed. Here, we provide a review of these approaches and discuss the strengths and limitations of each one.

PCR approaches

Real-time quantitative PCR

PCR-based methods have been used to detect known genome rearrangements, particularly alterations in gene copy number. In real-time quantitative PCR, the accumulation of amplified products is monitored by measuring the fluorescence of probes or intercalating dyes introduced into the reaction. The number of cycles necessary to attain a particular DNA concentration (estimated from fluorescence intensity) is measured. Starting DNA concentrations are determined using the amplification efficiency of each cycle (Higuchi et al. 1992). Real-time PCR has been applied to the detection of specific copy number changes, for example, MYCN amplifications in neuroblastoma (De Preter et al. 2002; Boensch et al. 2005). While this method is rapid and does not require a large amount of starting material, it has a very limited throughput, is quite costly, and is unsuitable for the detection of translocations or inversions (Armour et al. 2002). In addition, it is unsuitable for genome-wide screens for rearrangements (De Lellis et al. 2007).

Multiplex PCR

Multiplex PCR methods, including multiplex ligation-dependent probe amplification (MLPA) (Schouten et al. 2002), multiplex amplifiable probe hybridization (MAPH) (Armour et al. 2000), and more recently, nonfluorescent multiplex PCR coupled to high performance liquid chromatography (NFMP-HPLC) (De Lellis et al. 2006), have been designed to screen for copy number changes at multiple loci simultaneously. These methods are more efficient than standard PCR as they allow concurrent screening for rearrangements at multiple loci; however, they are still limited to detecting known unbalanced rearrangements at a few loci at a time.

Other PCR methods

Several techniques allow detection of larger genomic rearrangements than those detectable by traditional PCR. For instance, Long PCR uses a mixture of two polymerases, a proofreading and a non-proofreading one, thus increasing the product size to 35 kb (Barnes, 1994). The method is useful for identifying specific large aberrations, including intragenic deletions, insertions and duplications (Vasickova et al. 2007). In contrast, competitive genomic PCR (CGP) is a combination of restriction digestion of genomic DNA and a competitive PCR procedure (Becker-Andre and Hahlbrock 1989). The technique provides a moderate throughput and is particularly useful for high resolution analysis of a specific genomic region (Iwao-Koizumi 2007).

All of the above PCR methods were designed to detect gene copy number changes rather than translocations or inversions. Recently, a single-molecule haplotyping assay has been developed for the genome-wide detection of inversions. The method uses fusion PCR performed on single molecules of genomic DNA. The fusion PCR procedure juxtaposes single-copy sequences on either side of putative inversions in an orientation-specific manner and inversions are then detected from the haplotypes of these sequences (Turner et al. 2006). The technique can be used for genotyping known inversions and identifying novel inversions flanked by known inverted repeats.

Overall, PCR methods are prompt, require little starting material, and are excellent for locus-

specific identification of known rearrangements. These features render them ideal for diagnostic purposes. However, they suffer from low throughput and are unable to provide a genome-wide view of rearrangements; in addition, for the most part these methods are limited to detecting CNVs and indels.

Hybridization approaches

FISH and its derivatives

An important milestone in molecular cytogenetics was the development of the concept of in situ hybridization. This procedure is based on the principle of the hybridization of a labeled probe, containing genomic DNA of interest, to a complementary target; probe copy number is assessed by means of microscopic visualization. Since the first report of the method in 1969 (Buongiorno-Nardelli and Amaldi 1969), in situ hybridization methods have undergone extensive advancement with regards to both the target and the probe (Speicher and Carter 2005; de Jong 2003).

Probe labeling techniques have evolved from the original radiographic labeling to fluorescent and chromogenic-based detection as in fluorescence (Pinkel et al. 1986) and chromogenic (Mullink et al. 1989) in situ hybridization, FISH and CISH, respectively. Currently, the most commonly used conventional in situ hybridization protocol in cancer research is dual-color fluorescence in situ hybridization (FISH). This method involves labeling centromeres and the DNA region of interest with different colors and estimating probe copy number from the ratio of the centromeric and non-centromeric signal. Dual-color FISH is used for the detection of chromosomal gains or losses (aneuploidy); intrachromosomal insertions, deletions, inversions, amplifications; and chromosomal translocations in both solid and hematopoeitic cancers (Henderson et al. 2004; Karenko et al. 2005; Elnenaei et al. 2003; La Starza et al. 2007; Mancini et al. 2000; Fejzo et al. 1998). An important extension of conventional FISH methods is the development of multi-fluorochrome techniques such as multiplex FISH (M-FISH) (Speicher et al. 1996), spectral karyotyping (SKY) (Schröck et al. 1996) and combined binary ratio labeling (COBRA) (Tanke et al. 1999) which allow the simultaneous visualization of all chromosomes in 24 colors. While these techniques provide a genome-wide comprehensive view of interchromosomal aberrations such as translocations, they are not suitable for the detection of intrachromosomal rearrangements, including deletions and amplifications, due to poor resolution (Kearney 2006).

Improvements in target resolution have been achieved through the use of different probe substrates, including metaphase chromosomes (~5 Mb resolution), interphase nuclei (50 kb – 2 Mb resolution), and extended chromatin or DNA fibers (5—500 kb resolution) (Speicher and Carter 2005). Mapped genomic clones such as bacterial artificial chromosomes (BACs), P1-derived artificial chromosomes (PACs), and yeast artificial chromosomes (YACs) have also been used as FISH probes to achieve a higher resolution mapping of genome rearrangements to the human genome sequence than that achievable by chromosome FISH (Henderson et al. 2004; Fujiwara et al. 2001; Huang et al. 2003). For instance, fingerprinted BAC clones spanning the 6q16.2—q21 region on human chromosome 6 have been successfully used as FISH probes to delineate a region at 6q16.3 frequently deleted in follicular lymphoma (Henderson et al. 2004). The importance of linking cytogenetic aberration data to the human genome sequence has been recognized by the Cancer Chromosome Aberration Project (CCAP). This initiative has reported a collection of mapped clones for relating chromosomal aberrations detected microscopically to the human genome sequence (Jang et al. 2006). Mapped genomic clones have also been widely used in higher resolution and higher throughput cytogenetic approaches such as array comparative genomic hybridization (aCGH), described below.

Overall, FISH is an important tool, with advantages including the ability to analyse single cells, applicability to a wide range of substrates including fixed samples, and relative simplicity of use. The method cannot provide a genome-wide assessment of DNA rearrangements with the exception of gross chromosomal aberrations

detected by multifluor-based techniques, and is thus of limited value for genome-wide discovery of smaller-scale chromosomal aberrations. Nevertheless, it has proven to be extremely useful for validating the finding of other, higher throughput methods described below (Bayani and Squire 2007).

Comparative genomic hybridization on chromosomes (CGH)

Comparative genomic hybridization (CGH) is a molecular cytogenetic method for detecting relative differences in copy number between two genomes. In its original form, DNA from reference and test samples was labeled with different colors and hybridized to metaphase chromosomes. The ratios of test to reference fluorescence intensities were quantified using digital image analysis, and were used to identify genomic losses or gains in the test sample (e.g. a tumor sample) with respect to the reference sample (Kallioniemi et al. 1992). Conventional CGH is labor intensive, providing relatively low resolution of 5—10 Mb for deletions and 2 Mb for amplifications (Mantripragada et al. 2004); moreover, it is unsuitable for the detection of balanced rearrangements (e.g. balanced translocations and inversions) as well as whole genome copy number changes (ploidy) (Carter 2007). However, CGH can be used as a discovery tool as it requires no prior knowledge of chromosomal imbalances (Speicher and Carter 2005).

Comparative genomic hybridization on arrays (array CGH, aCGH)

To overcome the low resolution limitation of CGH, array CGH (aCGH) was developed (Pinkel et al. 1998; Solinas-Toldo et al. 1997). In aCGH, the differentially labeled test and reference DNA is hybridized to a glass slide containing arrayed DNA probes rather than metaphase chromosomes (Pinkel et al. 1998; Pollack et al. 1999). The resolution of aCGH depends on the density and sizes of DNA probes on the array. While a number of probe substrates have been used in aCGH to date, including large-insert clones (40—200 kb), small insert clones (1.5—2.5 kb), cDNA clones (0.5—2 kb), PCR products (0.1—1.5 kb) and oligonucleotides (25—85 bp) (Carter 2007), large-insert clones and more recently oligonucleotides have been the most popular. With the recent development of arrays of mapped clones spanning whole chromosomes (Buckley et al. 2002; Buckley et al. 2005a) and the whole human genome (Krzywinski et al. 2004), large-scale aCGH experiments are feasible. For instance, 79 kb resolution has been achieved using a genome-wide array of BACs (Ishkanian et al. 2004); 75 and 110 kb resolutions have been reported with chromosomal arrays containing a mix of BACs/PACs and fosmids/cosmids, and BACs only, respectively (Buckley et al. 2002 and Buckley et al. 2005a, respectively). Arrays of mapped genomic clones are robust, provide the most comprehensive coverage of the genome with a high signal to noise ratio (Carter 2007), and have been applied to the detection of copy number changes in tumors on a genome-wide and chromosome-wide scale (e.g. Mosse et al. 2007; Kim et al. 2007; Buffart et al. 2007; de Ståhl et al. 2005). However, a limitation of large-insert clone probes is the inability to pre-select the sequence present in the clones, which results in an overrepresentation of common repeated elements in the array, potentially complicating downstream analysis (Mantripragada et al. 2004).

In contrast, oligonucleotide arrays can provide a higher resolution (generally 5—50 kb) but have been reported to suffer from lower sensitivity. This can result in failure to reliably detect low-copy number changes due to a poorer signal to noise ratio (Carter, 2007; De Lellis et al. 2007). Oligonucleotide array CGH can potentially provide even higher resolution than 5 kb as overlapping nucleotides can be synthesized with as little as a single base off-set (Carter, 2007). While such high resolution cannot currently be achieved on a genome-wide level in a cost-effective manner, it is practical for the study of CNVs in specific regions (Gribble et al. 2007). For a more detailed discussion of the advantages and disadvantages of the different aCGH platforms the reader is referred to Ylstra et al. (2006) and Mantripragada et al. (2004).

In summary, array CGH methods have been widely used for the detection of genome rearrangements in tumors. Despite their increasing popularity, the main technological limitation of these methods is

the restricted applicability to detection of genome rearrangements that involve a change in copy numbers.

Representational oligonucleotide microarray analysis (ROMA)

Another microarray-based technique, representational oligonucleotide microarray analysis (ROMA), has been developed to address the low signal to noise ratio problem of oligonucleotide aCGH (Lucito et al. 2003). ROMA uses restriction digestion of genomic DNA followed by the selection of shorter fragments that are then amplified by PCR. DNA obtained from reference and test samples is differentially labeled and hybridized to an oligonucleotide array as in array CGH. In this manner, the complexity of the genomic sequence is reduced as only representative fragments are analyzed by hybridization thus increasing the signal to noise ratio. ROMA achieves an average resolution of 30 kb, which is comparable to that of oligonucleotide aCGH. However, several challenges have prevented this method from becoming widely adopted. First, the signal to noise ratio is still lower than that of BAC arrays, and typically signals from several probes are averaged to reduce noise-induced variance in the data. Second, the complexity reduction may lead to unequal representation of different parts of the genome potentially leading to erroneous CNV calls. Third, restriction digestion patterns may vary among different individuals due to restriction fragment length polymorphisms, which ROMA may misinterpret as CNVs (Carter 2007). Further, the PCR amplification step has the potential of introducing additional biases.

SNP arrays

SNP arrays, originally designed for genotyping, are oligonucleotide arrays that detect the two different alleles of biallelic SNPs (Gunderson et al. 2005). Probe signal intensities can be used to determine SNP genotypes and to detect copy number changes (Bignell et al. 2004). In contrast to array CGH, in which samples are differentially labeled and co-hybridized, only one labeled sample is hybridized to the SNP array at a time; CNVs are detected by comparison with one or several reference samples analyzed in separate hybridizations. Currently SNP arrays capable of genotyping more than 900k SNPs are available from companies such as Illumina and Affymetrix, providing a resolution that matches or exceeds that of most state-of-the-art aCGH platforms. An important advantage of SNP arrays is the ability, unique among genomic methods discussed thus far, to detect copy number neutral losses of heterozygosity (Heinrichs and Look 2007). Further, SNP arrays have been used to detect allele-specific copy number variants (LaFramboise et al. 2005). A disadvantage of the technology is the requirement of a PCR amplification step to increase the signal to noise ratio; as a result, amplification biases may be introduced giving rise to spurious CNVs (Carter 2007). Moreover, CNV predictions by SNP arrays vary depending on the reference set and computational approach used (Baross et al. 2007). Even so, SNP arrays have been widely applied to the analysis of tumor genomes, including ovarian cancer (Park et al. 2006; Gorringe et al. 2007), prostate cancer (Rubin et al. 2004; Koochekpour et al. 2005), colorectal cancer (Tsafrir et al. 2006), malignant melanoma (Garraway et al. 2005), and pancreatic cancer (Harada et al. 2007); also see reviews by Heinrichs and Look (2007) and Dutt and Beroukhim (2007).

Array painting

While array CGH and SNP arrays have been used successfully to detect copy number changes in tumors, they are incapable of detecting balanced rearrangements, such as reciprocal translocations or inversions. Array painting has been developed to map such rearrangements at a high resolution on a genome-wide scale (Fiegler et al. 2003). Briefly, in array painting, the two derivative chromosomes from a balanced translocation are separated by flow sorting, and are then PCR amplified, differentially labeled, and hybridized to an array of genomic clones. Only clones corresponding to the sorted chromosomes will show fluorescence above background. Fluorescence ratios of the signals from the two derivatives can be used to identify clones that span a rearrangement breakpoint; as such clones will have intermediate ratios representing the hybridization of both derivatives (Fiegler et al. 2003).

Sequencing approaches

Digital karyotyping (DK)

Digital karyotyping (DK) is a high resolution method for genome-wide analysis of copy number changes and other genome rearrangements (Wang et al. 2002). The method can be regarded as a "genomic version" of the serial analysis of gene expression (SAGE) technique (Velculescu, et al. 1995). In DK, genomic DNA is digested with a "mapping" restriction enzyme, originally SacI (6 bp recognition sequence) followed by the ligation of biotinylated linkers and a second digestion using a "fragmenting" restriction enzyme with a 4 bp recognition sequence. The biotinylated sequences are isolated by binding to streptavidin and the DNA tags are released using a tagging enzyme with a 6 bp recognition sequence. The isolated sequence tags are concatenated, cloned, sequenced, and aligned to a reference genome assembly, providing a copy number estimate at the particular locus. The combination of the mapping and fragmenting enzymes used determines the size of detectable rearrangements, and the genome-wide occurrence of mapping enzyme recognition sites defines genomic areas represented in DK analysis. In the case of SacI, recognition sites are abundant and expected to occur every 4 kb; however, some areas of the human genome (<5%) have lower density of SacI sites and thus would be analyzed at a lower resolution (Wang et al. 2002). To date, DK has been successfully applied to the analysis of human ovarian (Nakayama et al. 2006; Shih et al. 2005) and colorectal cancers (Wang et al. 2004) as well as human cancer cell lines from melanoma (Körner et al. 2007) and medulloblastoma (Di et al. 2005). The method is promising and has been used to detect genome rearrangements, particularly small amplicons of less than 1 Mb and homozygous deletions, previously missed by studies using SKY and CGH (Shih and Wang 2004). The original version of DK has a theoretical resolution of 4 kb defined by the genomic spacing of SacI sites, which is higher than the available array-based methods. However, DK provides more robust readouts of copy numbers as it depends on digital sequence tag counts rather than hybridization signal intensities produced by array technologies. A partial limitation of DK imposed by the use of restriction enzymes is the uneven coverage of the genome, which may be addressed by using different combinations of mapping and fragmenting enzymes. Another current limitation is the cost of sequencing, which will be improved with the advent of next-generation sequencing technologies.

Clone-based approaches for rearrangement detection

Clone-based methods have been recently developed to detect both balanced and unbalanced genome rearrangements. Tuzun et al. (2005) mapped paired-end sequence reads generated from a human fosmid library to the human reference genome sequence to discover and catalogue structural genomic variants. The basis for this analysis was the tight regulation of insert sizes of fosmid clones imposed by lambda phage packaging machinery; if no rearrangement was present in a clone, the pair of its end sequences would align to the reference sequence with ~40 kb spacing. Significant deviations of the spacing were indicative of a rearrangement in the clone. In this manner, the investigators were capable of detecting finer-scale structural variants, such as small indels and inversions, which would not have been detected using conventional array methods. The resolution of this analysis, determined by the insert size of fosmid clones as well as the level of read coverage, ranged between 8 kb and 40 kb (Tuzun et al. 2005; Freeman et al. 2007).

A conceptually similar approach, named end sequence profiling (ESP), has been developed and successfully applied to the genome-wide analysis of rearrangements of the MCF7 breast cancer cell line (Volik et al. 2003; Volik et al. 2006). In ESP, a BAC library is constructed for the tumor genome of interest, both ends of BAC clones are sequenced, and the paired-end sequences are mapped back to a reference genome assembly. Structural genomic variants are discovered by identifying clones whose paired-end sequences map to the reference genome in orientations that suggest the clone was derived from rearranged DNA. The ESP approach is potentially applicable to the detection of all types of genome rearrangements which could be inferred from different types of "ESP signatures" (Volik et al. 2006).

While powerful, paired-end sequencing of clones has several limitations. First, the approach is dependent on the construction of clone libraries, which can be a slow and costly process. Second, the resolution of paired-end sequencing methods is determined by the clone properties and the redundancy of genome coverage. While insert sizes of cosmid and fosmid clones are tightly bounded by the lambda packaging limits of 32–48 kb, BAC insert sizes are less constrained. This feature of fosmid clones, exploited by Tuzun et al. (2005), may facilitate rearrangement detection; however, a larger number of fosmid clones than BAC clones would be required to achieve a similar degree of genome coverage. Also, with both clone types, since the sampling occurs only from the ends, large numbers of clones would be necessary to achieve genome-wide high resolution coverage of rearrangements.

To address this limitation we have recently developed a BAC clone fingerprint profiling (FPP) approach for high resolution detection of genome rearrangements that achieves redundancy of genome coverage with fewer BACs than would be required by end sequencing (Krzywinski et al. 2007). The method includes the digestion of genomic BAC clones prepared from tumor DNA with five restriction enzymes, HindIII, EcoRI, BglII, NcoII, and PvuII to generate clone fingerprints that are then aligned against the in silico digests of the reference genome sequence using the FPP alignment algorithm. The restriction enzymes were selected to achieve frequent cutting and restriction site location complementation (restriction site-poor areas of one enzyme corresponding to restriction site-rich areas of another enzyme). The FPP alignment algorithm consists of four steps that are detailed in Krzywinski et al. (2007). Briefly, the steps for aligning each BAC fingerprint to the reference genome sequence include: a global search of the reference genome sequence to identify BAC-sized or smaller genomic regions that yield similar digest patterns to that of the query clone; a local search that further delineates the local correspondence between the fingerprint of the query clone and that of the in silico digested genomic region(s) identified in step 1; an edge detection algorithm that precisely identifies the extent of the alignment; and the final partitioning step that selects an optimal solution, whereby a minimal set of alignments maximally accounts for all clone fragments on the genome. Differences between the experimental and in silico digestion patterns are indicative of genomic differences including genome rearrangements in the clone versus the reference genome. For instance, an alignment in which the clone maps to one genomic region but where there are internal gaps in fragment alignments, indicates the presence of a localized rearrangement confined to the clone; on the other hand, an alignment where the clone fingerprint is partitioned over several regions in the genome suggests the presence of a translocation, inversion or a large deletion.

We used simulations and experimental data to demonstrate the potential of the FPP approach as a whole-genome method for the detection and characterization of genome rearrangements. Krzywinski et al. (2007) fingerprinted 493 BAC clones from the MCF7 ESP study (Volik et al. 2006) and were able to map the positions of 51 rearrangement breakpoints and 17 micro rearrangements. In addition, novel rearrangements missed by the ESP approach were identified. Encouraged by these findings, we have now initiated a large-scale FPP effort to characterize genome rearrangements in at least 24 follicular lymphoma genomes. Our preliminary findings indicate that the approach is fruitful and will identify novel genome rearrangements in this tumor type (unpublished).

The FPP approach provides several important advantages over ESP and other genome-wide methods for rearrangement detection. First, the method samples the entire clone insert and not just the clone ends, as in ESP. Therefore, rearrangement coordinates mapping within the clone will be more precisely localized with FPP than ESP, given the same number of clones sampled (Krzywinski et al. 2007). Second, FPP is relatively tolerant of repeats compared to ESP and oligonucleotide microarrays, since only 7% of human repeats are found in contiguous regions of 3.9 kb (the average sizeable HindIII restriction fragment) (Krzywinski et al. 2007). This is an important advantage considering that a significant portion of the human genome is composed of

repeated sequence. Third, both balanced and unbalanced rearrangements are potentially detectable. Fourth, clones harboring rearrangements can be directly selected for functional analyses and sequencing (as in ESP). Some of the disadvantages include the cost and speed of library production, the cost of clone characterization, and the requirement of a large amount of starting DNA material. Consequently, although the FPP approach is potentially very powerful, the reliance on clones currently limits its widespread application. In addition, just as it is the case with other methods that rely on restriction enzyme digestion, FPP may erroneously interpret restriction fragment length polymorphisms as genomic rearrangements. This limitation may be partially addressed in the future as more complete catalogues of normal genomic variation are compiled.

Cancer genome and transcriptome re-sequencing for rearrangement discovery and detection

Recently, several studies involving re-sequencing of exons in cancers using capillary technologies have demonstrated the potential of large-scale sequencing approaches for identifying DNA aberrations, including genome rearrangements, in cancer cells (Greenman et al. 2007; Sjoblom et al. 2006; Wood et al. 2007). Greenman et al. (2007) systematically re-sequenced the PCR-amplified coding exons of 518 protein kinase genes in 210 diverse human cancers and identified 78 indels, 2/3 of which had previously been uncharacterized (Greenman et al. 2007). Two other studies re-sequenced the coding regions of RefSeq and Consensus Coding Sequence (CCDS) genes from 11 breast and 11 colorectal cancers (Sjoblom et al. 2006; Wood et al. 2007) and identified somatic mutations in 1718 genes (9.4% of the genes analyzed); 7.3% of all identified mutations were insertions, deletions or duplications (Wood et al. 2007). It is worth noting that prior to these studies approximately 1% of human genes had been shown to be mutated in cancers by other techniques (Futreal et al. 2004) implying that our current list of cancer genes is a gross underestimate of the total number of genes that can be mutated to produce cellular growth advantage.

With the advent of next-generation sequencing technologies, which do not require clones, genome and transcriptome re-sequencing studies are becoming more and more cost-effective rendering the prospect of a $1,000 genome a definite possibility in the future (Mardis 2006). A recent study using the 454/Roche sequencing technology showed the potential of next-generation sequencers to detect rare variants present in specific subpopulations of cells that elude cost-effective detection by capillary sequencing approaches (Thomas et al. 2006). The ability to detect cancer genome heterogeneity is due to the use of sequencing templates that have been clonally derived from a single molecule; in this manner, a variant present in a few cells can be detected if sufficient sequencing depth is applied. This feature is particularly important in cancer research in light of multiple reports describing cancer stem cells or tumor subpopulations with enhanced tumorigenic potential (Al-Hajj, 2007). The detection of genomic variation in these rare subpopulations is particularly important as it may shed light on the malignant phenotype of the tumor.

A current limitation of next-generation sequencing technologies is the production of short sequence reads that are not readily assembled de novo and that do not accurately represent genome structure in repeated segments of the genome. This shortcoming may be especially problematic for those studies seeking to comprehensively map human genome variation, as much of it resides within sequence repeats. The use of paired-end sequencing methodologies, whereby sequence alignment is facilitated by the availability of sequence reads from both ends of the same fragment of a defined length can provide a potential solution to this problem. Although DNA paired-end strategies have been a mainstage of genome analysis using capillary sequencing, development of paired-end approaches for next-generation sequencing is still at its in early stages of development. For example, a paired-end sequencing approach has recently been applied to the sequencing of a bacterial genome (Shendure et al. 2005); and a recent study reported the development of a paired-end approach for mapping rearrangements in the human genome (Korbel et

al. 2007). One paired-end mapping (PEM) procedure for the analysis of the human genome included the isolation of 3 kb sequence fragments, and end sequencing with 454/Roche technology, followed by mapping of paired-end reads back to the reference sequence using a computational algorithm developed by the authors (Korbel et al. 2007). Korbel et al. (2007) reported the analysis of two human genomes that had been previously analyzed to detect genome rearrangements using other approaches. The production of 10 and 21 million paired ends resulted in the 2.1- and 4.3-fold genome coverage and the detection of 62% and 93% of structural variants previously identified by fosmid paired-end sequencing and the HapMap project in the two genomes, respectively.

Despite the attractiveness of next-generation sequencing technologies for the detection of all types of DNA variation, including genome rearrangements, the current state of the field does not yet allow for routine genome re-sequencing studies due to the associated cost (Mardis 2006). The short read length and sequencing error rates are some factors that contribute to the requirement of a rather high read coverage required to call a DNA polymorphism or a rearrangement in the sample versus reference sequence. Thomas et al (2006) estimated that 10-fold read coverage was required to detect a mutation present in 50% of DNA molecules in a sample (i.e. a heterozygous mutation in a PCR-amplified genomic region) using 454/Roche technology. Given the aforementioned heterogeneity of tumor populations, mutations or rearrangements that occur in tumor cell subpopulations would require a significantly higher read coverage to be reliably detected. Overall, it has been estimated that at present accuracy, read length, and cost per run, the sequencing of one human genome would cost more than $100,000 (Mardis, 2006).

The sequencing of cancer transcriptomes rather than genomes to detect rearrangements in coding regions of the genome can in principle reduce the sequencing cost and increase the depth of coverage that can be achieved with the same amount of sequence data. We have investigated the utility of next-generation sequencing for large-scale profiling of cancer transcriptomes using the 454/Roche and Illumina sequencers (Bainbridge et al. 2006; Bainbridge et al. unpublished). The Illumina sequencing technology is similar to the 454/Roche in that is also uses DNA templates clonally-derived from a single molecule, and thus would also detect cell-specific variants. These studies have shown that the current capacities of next-generation sequencers are well aligned to the size of the human transcriptome, and that such approaches are capable of detecting both single base variants and structural variants in the coding part of genomes; the technologies are also amenable to the detection of variants that affect alternative splicing, and can be used to discover novel genes (Bainbridge et al. 2006; Bainbridge et al. unpublished).

In summary, sequencing approaches including large-scale re-sequencing of genomes and transcriptomes appear promising for the large-scale comprehensive detection of structural variation in cancers. These approaches are able to detect absolute rather than relative changes in copy numbers and have a high resolution, potentially down to a single nucleotide, that would allow the detection of all types of genome rearrangements. The use of next-generation sequencers for whole-genome and transcriptome analysis does not require the construction of clone libraries and thus provides an advantage over clone-based approaches. These technologies also offer the additional benefit of being able to detect cell-specific variants. Current limitations of such sequencing approaches are the reliance on the reference genomic data for identification of structural polymorphisms, which may be overcome in the future by data from large-scale human genome re-sequencing efforts, as well as the associated cost.

Concluding remarks

Cytogenetic methods such as chromosome banding and FISH have long been used to detect chromosomal rearrangements. Historically, these methods have had a significant impact on our understanding of cancer and ultimately led to the development of an effective treatment for chronic myeologenous leukemia (Rowley 2001). Cytogenetic analyses, as well as the more recent

locus-specific PCR approaches, are still widely used in diagnostics and are important for validating the results of high throughput studies (De Lellis et al. 2007). These approaches are very reliable but limited to the identification of known rearrangements and by low throughput. Nevertheless, some FISH methods, particularly SKY and M-FISH, have been extended to provide a genome-wide view of structural rearrangement albeit at a low resolution.

The development of array CGH methods and other microarray-based approaches has revolutionized research into structural genomic variation in cancer cells as such methods enabled high throughput interrogations of cancer genomes at higher resolution. Array platforms are being continuously improved to achieve even higher resolutions, increased robustness and more complete coverage of the genome. However, their application is inherently limited in that they are used to detect relative rather than absolute changes in copy numbers in a test sample with respect to a reference. Another important issue is the reproducibility of microarray results and their transferability from one platform to another (Buckley et al. 2005b). Moreover, with very few exceptions, these technologies are suitable for the detection of specific types of variation, such as CNVs, rather than other types, such as inversions or translocations (Fiegler et al. 2003).

Sequencing methods have been developed to achieve better resolution and allow the detection of absolute copy number changes including ploidy. These methods are currently limited by cost, and the availability and quality of reference sequence data. In addition, DK has many of the same limitations as SAGE and may not provide uniform coverage of the genome (Wang et al. 2002). Recent advancements in next-generation sequencing technologies speak to the promise of cost-effective re-sequencing of cancer genomes and transcriptomes at an unprecedented depth allowing the simultaneous detection and quantification of multiple molecular events on a genome-wide scale. It has become evident that tumor genomes contain a vast spectrum of aberrations; these include a small number of characterized mutational hot spots and a large number of rare changes most of which had previously been undetected by conventional experimental methods (Wood et al. 2007). Since both of these classes likely harbor cancer driving mutations, the need for more re-sequencing studies is unquestionable if we are to approach a comprehensive view of cancer genomes (Wood et al. 2007; Thomas et al. 2006). Another emerging feature of cancers is their heterogeneity, whereby the genomes of individual tumors as well as cell subpopulations within the same tumor show sequence variation. Studies of such variation will be enabled by single-molecule sequencing technologies.

However, before large-scale re-sequencing studies for the discovery of genome rearrangements using next-generation sequencers are widely-adopted, computationally-efficient methods for the analysis of short read data and the effective handling of repeats need to be developed and implemented. FPP of large genomic clones may provide a more feasible method for the discovery and cataloging of genome rearrangements, and in any event will produce an excellent set of test cases for subsequent analyses using next-generation sequencers. It seems feasible and desirable to subject clones bearing structural rearrangements to next-generation sequencing, as such efforts should provide focused tests of “true positives” and allow method development on small genomic intervals rather than the entire genome.

Perspectives on genome rearrangements and cancer susceptibility

Most of the work in the field of structural genomics in cancer has focused on the analysis of somatic mutations that are presumably acquired throughout the lifetime of an individual (Weir et al. 2004). This is reflective of the current view of cancer as a gradual process of accumulating genetic alterations that drive the transformation of normal cells into highly proliferative cancer cell types (Hanahan and Weinberg 2000). However, the genetic background of individuals in which tumorigenesis occurs has been given comparatively little attention. We suggest that the genetic background of the “host” may in fact impact and perhaps partially govern the course of

tumorigenesis. This may at least in part account for the genetic predisposition of certain individuals to cancers.

With the recent discovery of the abundance of CNVs in the human genome, a number of studies have reported associations of particular CNVs with the susceptibility to complex disorders, including systemic lupus erythematosus (Yang et al. 2007) and autism (Autism Genome Project Consortium 2007). Moreover, two recent studies have found that particular copy number variants may account for the increased risk of gastrointestinal cancer (Fan et al. 2006) and familial breast cancer (Frank et al. 2007) in certain populations. It has also been reported that structural genomic rearrangements may determine the degree of susceptibility to infectious diseases (Turner et al. 2006). Given the abundance of structural variation in the genome and the rudimentary stages of the research in the field, it is reasonable to expect that an unknown proportion of genetic risk of cancer will also be partially determined by genomic rearrangements. Tests of this idea may require large-scale re-sequencing studies, a trend that we eagerly anticipate in the next few years.

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2008 Society Award Designates

The 2008 CSBMCB Merck Frosst Prize

Dr. Frank Sicheri

Dr. Frank Sicheri obtained his B.Sc. and Ph.D. degrees from McMaster University, the latter under the supervision of Dr. Daniel Yang. He then spent 2 years as a post-doctoral fellow with Dr. John Kuriyan at Rockefeller University in New York. In 1998 he returned to Canada, joining the Samuel Lunenfeld Research Institute at the Mount Sinai Hospital in Toronto, and the Department of Medical Genetics and Microbiology and Graduate Department of Molecular and Medical Genetics at the University of Toronto. He is currently a Senior Investigator in the Program in Systems Biology at the Samuel Lunenfeld Research Institute and Professor in the University Departments.

Dr. Sicheri has established himself at a relatively early stage in his career as a highly regarded structural biologist specializing in protein structure determination. He has over 40 publications, many in the highest impact peer reviewed journals. These studies began with antifreeze proteins during his Ph.D. studies, continued with the Src family tyrosine kinase Hck during his postdoctoral period in New York, and continued with proteins in the large regulatory protein kinase family when he initiated his independent research program at the Samuel Lunenfeld Research Institute in Toronto. He is currently focussing on protein kinase function, looking at substrate recognition and catalytic switching. His work has been presented at a number of international meetings, and he has given invited seminars at a number of institutions across North America. His research is supported by the Canadian Institutes for Health Research, the National Cancer Institutes of Canada, and Celgene Pharmaceutical Company. He has served on several grant review panels and supervised a number of graduate students in his laboratory.

Recently, Dr. Sicheri was selected as co-chair of the Centre of Excellence in Acute and Chronic Medicine within the Mount Sinai Hospital. His specific role in this new position is to facilitate the cross-fertilization of research and science between the hospital and the research institute. Dr. Sicheri is a high achieving young Canadian scientist, who is highly deserving of this award.

The 2008 Jeanne Manery Fisher Memorial Lectureship

Dr. Katherine Siminovitch

Katherine Siminovitch, known to her colleagues as Kathy, is a Professor in the Departments of Medicine, Immunology, Medical Genetics and Microbiology at the University of Toronto and the Mount Sinai Hospital. She is very involved in genetics research and service, and is currently Director of the Genomic Medicine Division at the Toronto General Research Institute, the Adult Clinical Genetics Service of the University Health Network, the Molecular Therapeutics Immunogenetics Program of the McLaughlin Centre for Molecular Medicine, and the Genomic Medicine Centre at the Samuel Lunenfeld Research Institute.

Dr. Siminovitch's education started with two years of general science at the University of Toronto, followed by four years of Medical school. After receiving her MD degree she did residency training, becoming certified by the Royal College of Physicians and Surgeons of Canada in both Internal Medicine and Rheumatology. Following her clinical training, she spent three years as a Centennial Fellow of the Medical Research Council of Canada at the National Institutes of Health in Bethesda, Maryland, doing research on

the mechanisms of control of immune regulation with Drs. Steinberg and Korsmeyer.

Her research focuses on the molecular and genetic aspects of arthritis and autoimmunity. Two examples of areas where she has made significant contributions are Wiskott-Aldrich Syndrome and IBD/Crohn's Disease. She is recognized as an international leader in the former, and has taken her work from identification of the location of the debilitating causative gene, to the genetics of the disease, to the involvement of the WASP1 protein, including investigations of how it functions, and the development of a clinically relevant prenatal test for the disease. Her laboratory is now a referral centre for all of North America. She has literally gone from DNA to protein to disease to patient. The remaining target is a molecularly designed therapeutic.

Dr. Siminovitch's experiences with the WASP gene and Wiskott-Aldrich syndrome, together with the new technologies and knowledge gained from the human genome project, have allowed her to investigate the genetic aspects of inflammatory bowel disease and Crohn's disease. These studies have allowed her to identify variants of OCTN cation transporters as being associated with Crohn's disease.

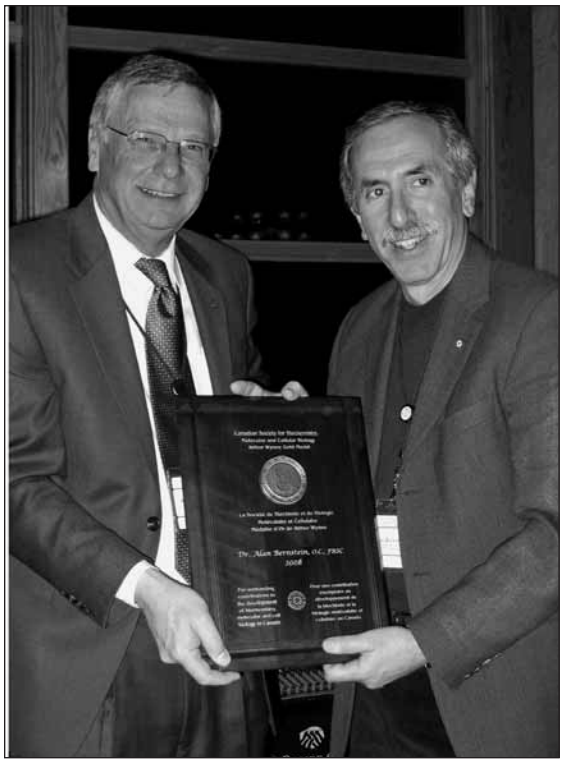
Dr. Siminovitch's work has led to over 200 publications in peer reviewed journals. As well, she has 70 abstracts on her work, has presented lectures at many institutions, and has served on a number of grant panels and many committees. Her grant support has come from the Canadian Institutes of Health Research, the Canadian Foundation for Innovation, and the Crohn`s and Colitis Foundation of Canada. She holds a Tier 1 Canada Research Chair.

She is a serious teacher of graduate students, fellows and her colleagues on the potential of the genomic and molecular sciences. She supports and assists her fellow women scientists. Along with her many scientific and professional achievements, she has also found time to be a mother for two young daughters (8 and 9 years of age). Dr. Siminovitch without doubt sets a high standard for women scientists.

The CSBMCB Arthur Wynne Gold Medal

Dr. Alan Bernstein

The CSBMCB Arthur Wynne Gold Medal is presented by the Canadian Society of Biochemistry, Molecular and Cellular Biology (CSBMCB) to an individual who has made a major contribution to biochemistry, molecular and cell biology in Canada over their career. The recipient of this life-time achievement award typically has attained an international profile in research, has played a major role in the development and promotion of the discipline in Canada, and has a long-standing record of service to the academic community. The Medal is named in honour of Professor Arthur M. Wynne, the first President of the Society, and was initiated in 2007 to celebrate the 50th Anniversary of CSBMCB. The recipient is presented with a plaque depicting the likeness of Professor Wynne and a cash award funded by the Society. The awardee will be invited to attend the Annual Meeting and Conference at the Society's expense to receive the award and to make some brief remarks at the Banquet. He/she will also be invited to submit a manuscript summarizing their career for publication in the Bulletin of the Society.



The inaugural winner of the award for 2008 is Dr. Alan Bernstein, OC, FRSC, and former President of the Canadian Institutes for Health Research from 2000-2007. Dr. Bernstein received his Ph.D. in Medical Biophysics at the University of Toronto. He first began working on retroviruses during his postdoctoral work, and returned to Canada to join the faculty of the Ontario Cancer Institute in Toronto. Dr. Bernstein was subsequently appointed head of the Division of Molecular and Developmental Biology at the Samuel Lunenfeld Research Institute at Mount Sinai Hospital in Toronto, and then its director of research. He is an internationally renowned researcher who has made extensive contributions to the study of embryonic development, hematopoiesis and cancer. Dr. Bernstein has received a number of national and international awards for his research, and has served on a large number of international scientific bodies, including the scientific board of the Grand Challenges in Global Health initiative. He was the appointed founding president of the Canadian Institutes of Health Research in 2000. Over the seven years Dr. Bernstein held this office, he built CIHR into one of the world's leading research agencies, supporting more than 11,000 health researchers with an annual budget of $1 billion.

In 2007, Dr. Bernstein was appointed the inaugural executive director of the Global HIV Vaccine Enterprise, an international alliance of researchers, funders and advocates committed to hastening the development of an HIV vaccine. The Global HIV Vaccine Enterprise is charged by its founders with setting scientific priorities, mobilizing resources, and improving collaboration in the HIV vaccine field. Originally proposed by 24 leading HIV vaccine researchers in 2003, the Enterprise has mobilized more than US$750 million to date in support of its scientific plan.

Arthur Wynne Gold Medal Address

Health Research in the 21st Century: New Approaches to New Problems

Alan Bernstein, OC, PhD, FRSC, LLD (Hons)
Executive Director, Global HIV Vaccine Enterprise, New York, NY

I am deeply honoured to be the inaugural recipient of the Arthur Wynne Gold Medal from the Canadian Society of Biochemistry, Molecular and Cell Biology. When one receives such a prestigious award, in this case from Canada's national body representing some of the most exciting and important areas of biological sciences today, it is customary and appropriate to refer to the constellation of stars who have preceded you in receiving the award and to humbly acknowledge that you don't belong in such illustrious company. In my case, being the first awardee, I am unable, of course, to do that. All I can do is hope that future awardees will behave appropriately and adhere to the rules.

In my address to you tonight, surrounded by the magnificent Canadian Rockies and inspiring surroundings of the Banff Centre, I would like to discuss two issues that have interested me, first as a scientist, then as president of CIHR, and now as the executive director of the Global HIV Vaccine Enterprise. The first issue stems from the profound revolution that is going on the biological sciences today and the second, a direct consequence of this revolution, is the increasing opportunities to harness science as a global enterprise to tackle some of the most important health challenges facing humanity today. I am very pleased that there are so many graduate students and postdoctoral fellows at this meeting as my remarks I hope will be especially relevant to young people.

The Revolution in Health Research

The decision to determine the sequence of the human and other genomes unleashed a profound revolution in the biological sciences. This revolution goes far beyond simply knowing the sequence. It has changed how we go about doing biology. It is a revolution fuelled by two powerful engines: new technologies and new ways of thinking. The 'omics' means that we no longer have to tease apart individual components of a complex, interacting system. It is now feasible to interrogate the logic of an entire pathway. Of course, systems engineers have thought like this for a long time. Like the revolution in physics in the 1920s, the enablers in this revolution are transformative new technologies and a profoundly multidisciplinary approach to problems in biology. The origins of this new approach to biology started back in the 1940s and 1950s; indeed, the landmark 1953 paper by Watson and Crick encapsulates this new world: a young physicist-crystallographer who knew no genetics and an even younger geneticist who knew no X-ray crystallography combined forces to solve the structure of DNA. Indeed, at this meeting of the CSCMB, we've heard many talks that were the result of collaborations between biochemists, engineers, theoretical and polymer physicists, and geneticists.

There are many implications of this new style of science for how we organize ourselves as a community. And I think it's correct to say that the pace of the science has far outstripped changes in the way we think about science. And that's a problem, especially for young people. Promotion and tenure, peer review of grants, the departmental structure of our universities, the alarming increase in the training period, national funding policies and the concomitant increase in the costs of doing leading edge biomedical research, are still all

largely based on a model of doing science that was relevant 35 years ago when I first began doing research. But it no longer describes how science is now carried out. Today, leading edge health sciences frequently demands multidisciplinary teams that are made up of collaborators from multiple institutions from different countries. How does a young scientist gain recognition, receive grant support, promotion or tenure when the system dictates that you must first demonstrate that you are capable of independent research? And yet, the best research today frequently demands large team efforts.

Recent data suggests that the average age for obtaining a first grant from the US NIH is 43! That is simply unacceptable, as noted by Dr. Elias Zerhouni, director of the NIH. (the average age in Canada for obtaining a CIHR grant is at least 5 years younger. But we should not be complacent: that age is also creeping up.) It is unacceptable not only because it is depriving young people of the opportunity to pursue their own ideas. It is also unacceptable for at least two other reasons: first, this revolution is driven by new ideas and new technologies. In other words, it is being driven by young people. And second, arguably this disconnect between how we actually do science today and how are community is structured is turning off young people from even contemplating a career in biomedical research.

Institutions involved in the support of science-our universities, public funders, professional associations-all have the responsibility and the opportunity to start a conversation about how to fix the current situation. I believe that Canada is well positioned to experiment with new models that respect the historic strengths and culture of universities while at the same time explore new ways of self-organizing.

Global Science for Global Challenges: The Global HIV Vaccine Enterprise

We live in an age dominated by science, one in which our ability to understand the natural and living worlds has transformed the world we live in. We live in an age in which, when the Spanish flu broke out in 1917 and killed between 25-40 million people before it disappeared on its own, it took 16 years to isolate the virus. Its sequence was only determined another 60 years later. In contrast, when SARS broke out in this country in 2003, the virus was isolated and sequenced by a team of Canadian clinicians and scientists in Toronto, Winnipeg and Vancouver in 16 weeks. And our ability to track how the SARS virus was transmitted from person to person was key to controlling its spread and ultimately containing the outburst.

Without giving away any political secrets, I can tell you that the federal-provincial politics around SARS was more challenging than getting CIHR funding out the door to do the science. As I look at the world, I am struck by several great unmet human and scientific challenges that face us today: climate change, the need for non-carbon based energy, HIV/AIDS, and mental illness. In my view, the solutions to all of these great challenges lie in science and its applications.

HIV/AIDS is one of the most urgent challenges facing our planet. Over 60 million people have been infected with HIV since its discovery about 25 years ago. Of these, over 20 million people have died. This year alone, about 2.5 million people-men, women, and children-will become newly infected with the virus. The toll of human suffering, the destabilizing effects of the virus on civil society, and the impact on the economies of countries most affected, has created a humanitarian crisis of enormous proportions. Resolution of this seemingly intractable challenge requires a level of global cooperation far beyond what is normal even for the naturally international scientific community. While social interventions, including circumcision, condoms, and clean needles, all have critical roles to play, we know from other infectious diseases that a safe and effective vaccine is the best way to stop HIV. And yet, after billions of dollars invested in research, there still is not a safe and effective vaccine. Why is this?

The answer lies at least partially in the biology of the virus and at least partially how we organize ourselves as a global scientific community. The tremendous sequence and hence antigenic

diversity of HIV makes the development of an effective vaccine particularly challenging. The dormancy of the virus as a natural part of its replicative life cycle and the destruction of T cells by the virus that are involved in mounting effective immune responses also conspire together to increase further the challenge. Resolution of these challenges requires a level of global cooperation far beyond what is normal for the scientific community and for national funding bodies. The Global HIV Vaccine Enterprise (http://www.hivvaccineenterprise.org/) represents an imaginative response to these challenges. It rests on the belief that a coordinated and better integrated approach globally is the best hope of defeating HIV. The Enterprise is not a funder of the research but rather an honest broker that serves as an intellectual compass that fosters discussion and debate, identifies gaps and redundancies, and encourages collaboration, transparency and open sharing of data.

Since I agreed to serve as the inaugural Executive Director of the Enterprise, I have been very impressed with the commitment and passion of all those associated with trying to develop a vaccine-researchers, clinicians, funders, advocates. Science brings to the table a universal culture that transcends individual cultures and a language that transcends linguistic divides. By focusing on pressing human problems, science creates an opportunity to bring together people of diverse languages and culture to solve important challenges. As Louis Pasteur, the great French microbiologist said over 100 years ago: “Science knows no country for science is the light that illuminates the darkness in the world”. The development of a safe and effective vaccine against HIV is but one example of the broader challenges and opportunities that face the planet today: how to forge strong partnerships across nations and the academic, industrial and government sectors to harness science effectively to eradicate disease, feed the hungry, and stop global warming.

In closing, I want again to thank the Canadian Society for Biochemistry, Molecular and Cell Biology for this honour and, in so doing, providing me with the opportunity hear some great science by exceptionally talented scientists in such wonderful surroundings.

Why Join the CSBMCB?

An Open Invitation from Dr. Rose Johnstone

Dear Colleague,

The biochemists of Canada have just celebrated 50 years in the life of our professional society, the Canadian Society of Biochemistry, Molecular and Cellular Biology (CSBMCB). In the course of this time there have been profound changes in our discipline. Areas of activity hardly dreamed of half a century ago are now a natural part of biochemistry, even to our undergraduate students. So successful have been the tools used by biochemists that sister disciplines like molecular and cellular biology have adopted similar approaches to tackle important problems, thus leading to a blurring of the edges between disciplines.

Despite the blur, those of us who are biochemists by virtue of training or the nature of the work we pursue, know well which professional association should be our home base.

As a rough estimate, the number of practicing biochemists in Canada likely exceeds 2000 individuals, given the number of biochemistry departments, the number of medical schools and the number of biochemistry-based research laboratories. Cell and molecular biologists swell those numbers if the universities lacking medical schools, without official “biochemistry" departments, are included. We have yet to do a census to get a realistic estimate of our numbers.

What we do know is that the number of adhering members of our professional society, the CSBMC is under 500, a sad reflection of our true strength.

A strong Society provides an important voice to address our governments at both levels to commit adequate resources for improved research, teaching and student development. Acting as individuals, our voices hardly form a whisper. A collective voice representing most of the practitioners of our profession could be much louder and clearer across our country.

By virtue of our geography and friendly cross-border relationships, we Canadians tend think in North/South rather than East/West terms. Perhaps more of us are members of American societies representing our discipline than of the Canadian societies. However, no “external” society shares the specific problems we all face in our wide-spread country. To be effective, we need a strong and vocal society, which includes you.

If you are not a member of CSBMB, please reconsider and join. If you are a member, convince a colleague to join. Get involved. Make the society more effective and more able to tackle the problems that confront us as researchers and instructors of the profession we practice. I believe we all want to advance our profession. We chose this profession in the belief the work was worthwhile both personally and socially. The CSBMCB represents all of us. Become a member and make the Society better.

With best wishes for your continued success,

Rose M. Johnstone, Ph.D. FRSC
Emeritus Gilman Chair of Biochemistry
McGill University

NEWS FROM MEMBER DEPARTMENTS

Dalhousie University

Department of Biochemistry and Molecular Biology

Correspondent: David Byers

On July 1, 2007, David Byers was appointed to a five year term as Head of the Department of Biochemistry & Molecular Biology, replacing Michael Gray who stepped down after providing three years of strong leadership. Apparently, the role of CSBMCB correspondent comes with the job. I am no stranger to the Department, having graduated (B.Sc., M.Sc.) from here in the late '70s, and I have been cross-appointed for the last two decades as a member of the affiliated Atlantic Research Centre (ARC) in the Department of Pediatrics. My research group remains a short elevator ride away at the ARC, which has been left in Neale Ridgway's capable hands as its new Director.

Last year also saw the retirement of Ford Doolittle, one of Dalhousie's most renowned professors and a giant in the field of molecular evolution. Together with Mike Gray, Ford has established our Department as one of the leading centres in the world for molecular evolution research, and they have populated much of the international research community in this field with their graduates. Meanwhile, the leadership torch is being passed to one of these former graduates, Andrew Roger, who has spearheaded creation of the Dalhousie Centre for Comparative Genomics and Evolutionary Bioinformatics, with generous support from the Canadian Institute for Advanced Research (CIFAR) and the Tula Foundation. The Centre will provide long overdue formal recognition of our strength in this area at Dalhousie and will also be home to John Archibald, Christian Blouin and several other researchers in Computer Science, Mathematics and Statistics, and Biology. CIFAR and the Tula Foundation are currently supporting recruitment of an additional faculty member in the area of integrated microbial diversity to join this stellar group in our Department. We are delighted that Ford will remain associated with the group in a post-retirement capacity.

We also said goodbye last year to Ted Palmer and Cathy Lazier, lifelong members of the Department who contributed so much to our research, education and administration. Like Professor Emeritus Chris Helleiner before them, Ted and Cathy continued to participate in teaching activities well past their official retirement dates. Their knowledge and experience will be particularly missed in the area of physiological biochemistry, e.g., the undergraduate medical program, but fortunately others in the Department have stepped in and done a great job to fill this gap.

Members of our Department were recipients of several notable awards and prizes in the past year. We are extremely proud that Andrew Roger was awarded a prestigious NSERC E.W.R. Steacie Memorial Fellowship, given to Canada's most promising and outstanding scientists. Barbara Karten received the Young Investigator award at the Canadian Lipoprotein Conference last summer. Congratulations also to Melanie Dobson, who received a Dalhousie University Award for Outstanding Academic Advisor, and to Chris McMaster, who won a Dal Student Union award for Teaching Excellence.

In other faculty news, Paul Briggs has just been appointed as an Instructor in our Department. Highly respected by faculty and students alike, Paul has developed many of our undergraduate science lab courses over the past two decades and looks forward to new activities and challenges in education. Last year, Cathy Too and Kirill Rosen were promoted to Full and Associate Professor, respectively, while Graham Dellaire (a new faculty member in Pathology) was cross-appointed to our Department. Stephen Bearne and Jan Rainey were cross-appointed to the Dept. of Chemistry. Both Graham and Jan were recipients of major CFI

awards to provide research infrastructure and renovations.

Our graduate students also received a variety of scholarships and awards, including Killam Predoctoral Scholarship and Dalhousie President's Awards to Ryan Gawryluk and Jordan Pinder. New studentships were also received from the IWK Health Centre (Peter Murphy), the Nova Scotia Health Research Foundation (Salma Abdelmagid, Craig Morton, Meghan Agnew), and the Dalhousie Cancer Research Training Program (Paul O'Connell, Craig Morton). Meghan Agnew and Adrian Sharma were recipients of CIHR Graduate Scholarships, and Jordan Pinder was awarded an NSERC PGSD. Greg Fairn was the winner of our Department's Patrick Prize for excellence in graduate student research, while Faylene Lunn received the Doug Hogue Award for persistence and dedication to research.

The role of Department Head comes with new rewards and challenges, but the experience is made so much more enjoyable with the collegiality and support shown by our faculty, staff, and students...let's see how they feel in four years!

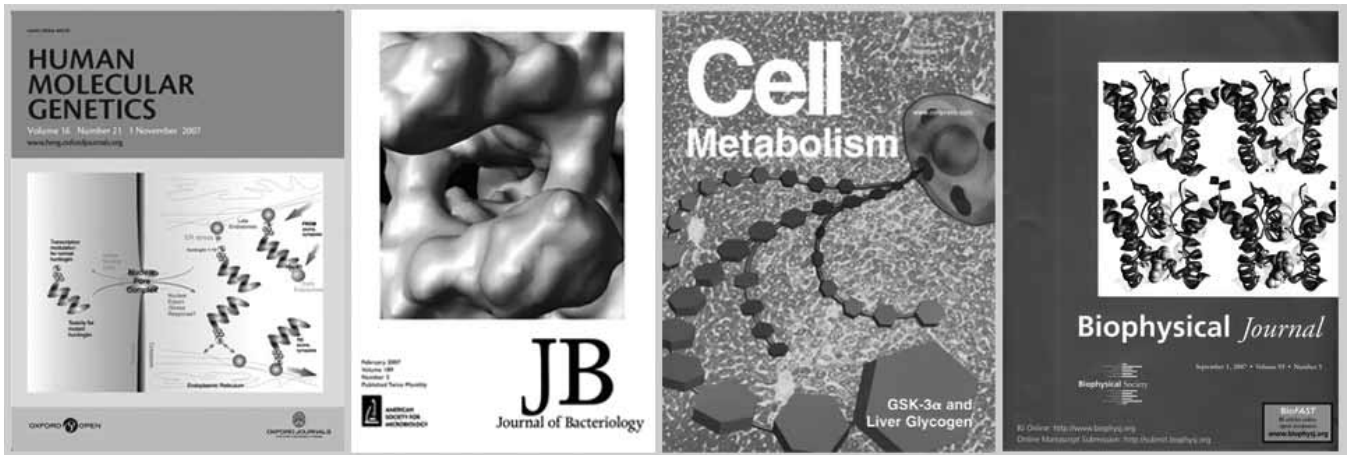
McMaster University

Department of Biochemistry and Biomedical Sciences

Correspondent: Alba Guarné

In 2007, our Department celebrated its 40th anniversary, which we commemorated with a Scientific Symposium and a Gala Dinner on October 13th. The celebration had something for everyone: science, sports, good food, and above all a great alumni reunion where we met old and new friends.

Over the last 40 years, the Department has grown tremendously and our research programs continue to thrive. The great run of important papers this past year is a testament to it. To name a couple, Mick Bhatia's work on stem cell environments in Nature Medicine garnered international attention in the press, and Murray Junop's work in Molecular Cell stirred the DNA repair field. The work from several labs was also featured in the cover of prestigious journals in the field such as Cell Metabolism (Brad Doble), Human Molecular Genetics (Ray Truant), Journal of Bacteriology (Joaquin Ortega) and Biophysical Journal (Boris Zhorov). Our faculty members also succeed at securing research dollars in this difficult funding climate. Brian Coombes was awarded operating funds and a new investigator award from CIHR. Russell Bishop, Alba Guarné, Giuseppe Melacini, Joaquin Ortega and Ray Truant renewed their CIHR grants. Radhey Gupta, Yingfu Li, Justin Nodwell and Joaquin Ortega secured funds from NSERC. Richard Epand, Radhey Gupta and Geoff Werstuck obtained grants from the Heart and Stroke Foundation of Canada. David Andrews received grants from the CBCRA, US DoD Breast Cancer Initiative, the Ontario Institute for Cancer Research and the Canadian Foundation for Innovation. Mick



Bhatia and Brad Doble were awarded Canada Research Chairs in Human Stem Cell Biology (Tiers 1 and 2, respectively) and Christopher Wynder in Epigenetic Control of Stem Cells (Tier 2). Through a generous donation to McMaster University from Mr. David Bradley, Mick Bhatia and David Andrews will establish the first stem cell library.

During the year we also saw some familiar faces move onto different endeavours. Gerhard E. Gerber retired this summer. Colleagues, family and friends gathered on September 28 to celebrate his many contributions to the Department and the University. Sujata Persad, assistant professor, took a new position in the Department of Pediatrics at the University of Alberta. Graham McGibbon, assistant professor, returned to the private sector after four years as a joint appointment between Chemistry and Biochemistry. Jonathan Cechetto, Manager of the High-Throughput Screening Lab, started a new position in Seoul, Korea. Paulina Duglosz, Lecturer, headed south to Texas to take a new position as a research project manager. On the other side of the coin, we have welcomed Andrew Willems, Assistant Professor, who will continue Paulina's work in our undergraduate program, and Mark Larché, who became associate member of our Department in July. Mark has his primary appointment in the Department of Pathology and Molecular Medicine and is a New Canada Research Chair (Tier 1) in Allergy and Immune Regulation.

After six years as Chair of our Department, Gerry Wright stepped down to take on a new role as Director of the new M.G. DeGroote Institute for Infectious Disease Research here at McMaster University. We wish him the best in his new role. We welcome Eric Brown as the new Chair of our Department, and we are all looking forward to working with our "new boss!" The Chair will continue to have three Assistant Chairs in Undergraduate Education (Michelle MacDonald), Graduate Education (Justin Nodwell), and Research (Lori Burrows).

Graduate education highlights

2007 was a watershed year for the Biochemistry and Biomedical Sciences graduate program. 35 new students enrolled in our program and our total graduate student population is now 115 students, more than twice what it was 6 years ago. A total of 25% of our graduate students were funded by rather competitive scholarships from NSERC, CIHR, Canadian Cystic Fibrosis Foundation and OGS, a testament to the exceptional quality of our students. Patricia Taylor received the 2007 Thomas Neilson Award, the highest award offered by our Department. Anna Bowes (PhD), Ken Schlosser (PhD), Ricky Cheng (MSc) and Margaret Sulek (MSc) were the recipients of the 2006-07 Karl B. Freeman Awards that recognize students deemed to have presented the most outstanding graduate seminars of the year. Three Ph.D. candidates successfully defended their theses: Tracey Campbell (Brown lab), Jeff Schertzer (Brown lab) and Sherry Lamb (Wright lab). Two of them continue in academia and now have post-doctoral positions at Princeton University (Tracey) and University of Texas (Jeff). Eleven more students graduated with a MSc degree.

Undergraduate education highlights

In September, we hosted the traditional "Welcome Barbecue" to welcome back all of our students including 145 new students to level II of our program. In October, the Department hosted a "Twist and Turns" event for the sixth year, as part of the Engineering and Science Olympics. Over 900 high school students converged on the campus to participate in a variety of events to compete for McMaster University entrance awards. This year, we added two new courses to our undergraduate curriculum: a Molecular Membrane Biology course taught by Russell Bishop and Richard Epand in fourth year, and a new elective course that expands our offerings in structural biology. Biochem 3X03 (taught by Alba Guarné and Joaquin Ortega) investigates the structure and function of macromolecules.

Facilities

The Canadian Centre for Electron Microscopy (CCEM) at McMaster, a $20M investment of the Canadian Foundation for Innovation and the Ontario government, became operational in 2007. The CCEM's mission is to lead the Canadian nanotechnology research in all fields from biology to materials research. The facility houses seven different electron microscopes. Especially relevant for research with biological specimens is the FEI Titan 80-300 electron microscope. This instrument is a unique ultrahigh-resolution electron microscope that constitutes the world's first commercial system capable of delivering sub-Angstrom resolution, and hence makes McMaster University a unique place in North America for research in structural biology.

Simon Fraser University

Department of Molecular Biology and Biochemistry

Correspondent: Christopher Beh

After years of tumultuous change and large projects, 2007 was relatively quiet for our Department and SFU as a whole – though the past year was punctuated with several notable events and successes. This period of calm is a welcome respite, and precedes an expected flurry of initiatives on the horizon for the coming year.

Department highlights. Much-deserved awards were bestowed on new and senior faculty members. Dr. Jack Chen, who recently joined our Department, received a Michael Smith Foundation for Health Research (MSFHR) Scholarship for his work on C. elegans bioinformatics and genomics. Drs. Fiona Brinkman and Mark Paetzel both received MSFHR Senior Investigator Awards. Among Dr. Brinkman's many research interests, she has developed computer programs to analyze subcellular localization of bacterial proteins, and has successfully applied bioinformatics to investigations of bacterial pathogenesis. Dr. Paetzel's research applies X-ray crystallography to the structural understanding of protein targeting and translocation across bacterial membranes. These awards complement the many other awards received by the MBB Department's faculty.

Research highlights. Earlier this year, Drs. David Baillie and Bob Johnsen gained international attention for their "extraterrestrial" project in which *Caenorhabditis elegans* (worms) were sent into Earth's orbit on the space shuttle Atlantis. One goal of the project was to analyze the effects of space radiation on *C. elegans* growth and development as a model for human radiation exposure in outer space. Closer to planet Earth, a generous endowment has been established to support graduate student research in our Department. Drs. Terry Snutch and Mary Gilbert founded the David L. Baillie Graduate Endowment Fund in tribute to Dr. Baillie's achievements during his long career at SFU. Under Dr. Baillie's mentorship, Dr. Snutch obtained his PhD at SFU in 1984 and is currently a faculty member at UBC. In addition to his many academic awards for excellence, Dr. Snutch is the founder Neuromed Pharmaceuticals. Dr. Baillie holds a Canada Research Chair Tier 1 in Genomics in our Department.

In other matters, a broad and urgent need for microscopy infrastructure has been recognized, and the SFU Faculty of Science, Office of Research Services, and the MBB Department have made commitments to the acquisition of new confocal microscopes and sophisticated imaging equipment. This essential infrastructure will directly contribute to the research efforts of many SFU investigators from multiple faculties and departments.

New faculty and staff. In the past year we said good-bye to Dr. Christine Carson who served as the SFU and MBB Department microscopy and imaging consultant. Dr. Carson spearheaded several initiatives to improve services and microscopy infrastructure available for cell biology research at SFU. She has taken a position with Quorum Technologies Inc., and we wish her much success. Dr. Tim Heslip was appointed earlier this year as the SFU and MBB Department's new microscopy consultant. Dr. Heslip joins us from

the University of Calgary, and he brings considerable research and microscopy experience to his position at SFU. His position at SFU is funded by the MSFHR.

Teaching accomplishments. In addition to new faculty awards, our graduate students continue to receive many awards for research, and for their contributions to the Department's teaching mission. The MBB Department provides the largest undergraduate majors program in the SFU Faculty of Science and our teaching assistants are integral to our success. In recognition of their teaching excellence, Ms. Kelly Kim and Nadine Wicks were awarded two of the four "Teaching Assistants of the Year Awards" in the SFU Faculty of Science. These graduate students exemplify the talent and dedication that our students bring to teaching and research.

Université de Sherbrooke

Department of Biochemistry

Correspondent: Marcel Bastin

Université de Sherbrooke's Department of Biochemistry (http://www.usherbrooke.ca/biochimie/) has experienced rapid growth in the last several years. Today, it has 14 full-time professors of various academic ranks and 16 minor appointments.

All this new blood has brought about several initiatives, including the revision of the Bachelor's Degree in Biochemistry (a B.Sc. Degree). The bachelor program now offers three different study possibilities: medical genetics, genomics and proteomics, and organic synthesis. These different paths allow the undergraduates to design the final year of their program of studies.

As for the graduate program (coordinated by Dr. Martin Bisaillon), Guylain Boissonneault and Jean-Pierre Perreault are currently developing a program whose goal is the long-distance training of graduate students. The program is being tried out with the Atlantic Cancer Research Institute and Université de Moncton, both organizations in New Brunswick, and Agrifood and Agriculture Canada in Lennoxville, Quebec. Several activities, including seminars using web tools, graduate classes by videoconferencing, exchanges using Web cams, etc. are being offered and the best means of communication identified. This research is sponsored by the Université de Sherbrooke. The result of the trials should be available by the end of 2008.

Université Laval

Correspondent: Guy Poirier

Our Department (Biologie médicale) is undergoing major changes to again become a fully fledged Biochemistry Department. At CHUL Research Centre, some members of the department are moving in a new Genomics Center; a 6 000 square meters expansion. A group led by Guy Poirier has just been awarded a CFI for two mass spectrometers: a FT MS and a TOF-TOF. This will increase the capacity of the Proteomics Centre at CHUQ to 9 mass spectrometers. L'Hotel-Dieu Research Centre has recruited three outstanding young scientists: Patrick Laprise, Mohsen Agharaxi, and Martin Simard. In addition, Jacques Côté has been awarded a senior CRC plus a CFI grant for major equipment, which includes a confocal microscopy system to upgrade the Cell Imaging Unit.

Programs in Molecular Medicine and Medical Sciences are being started and will increase enrolments at both the undergraduate and graduate levels. Finally the Pavillon Vandry (Faculty of Medicine) on the main campus is being completely rebuilt and expanded to become an integrated teaching building for Health Sciences; its inauguration will coincide with the 400th anniversary of Quebec City. New researchers have also been recruited in the Biochemistry Department on campus, including Patrick Lague, a structural biologist, Lisa Topolnik, a neurobiologist and Steve Charette, a cell biologist.

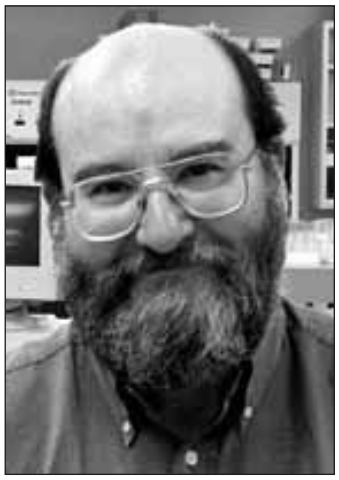
University of Alberta

Department of Biochemistry

Correspondent: Bernard Lemire

The Department welcomed two new Assistant Professors in 2007. Nicolas Touret received his Ph.D. under the supervision of Dr. L. Counillon at the Université de Nice Sophia-Antipolis in France. In 2001, he joined Dr. Sergio Grinstein in the Cell Biology Department at the Hospital for Sick Children in Toronto for postdoctoral training. Nicolas uses advanced imaging and biophysical technologies capable of resolving the behaviors of single molecules to better understand the molecular mechanisms involved in the initiation of immune responses when the organism is challenged with pathogens. Joanne Lemieux received her Ph.D. from the Structural Biology Program at the New York University School of Medicine under the supervision of Dr. Da Neng Wang. Since 2003, she has continued her training in structural biology with Dr. Michael James of this department. Joanne employs a variety of structural and biophysical approaches to investigate the structure and mechanism of the rhomboid intramembrane proteases and of other membrane proteins. We welcome them of both and wish them flourishing research programs.

Past and present department members garnered a number of awards in 2007. Cyril Kay was promoted to Officer of the Order of Canada by the Right Honorable Michaëlle Jean in a ceremony at Rideau Hall. Cyril is currently vice-president of research for the Alberta Cancer Board, where he is developing a new comprehensive cancer research institute. Ronald McElhaney and Marek Michalak were elected to the Royal Society of Canada, the Academies of Arts, Humanities and Sciences of Canada. Michael James was awarded the Killam Award for Excellence in Mentoring. Luis Schang received a McCalla Research Professorship to recognize significant contributions to research, teaching and learning. Joel Weiner was recognized by the AHFMR for 25 years of continuous funding by the Foundation while David Brindley, Larry Fliegel and Marek Michalak were recognized for 20 years.



The Department sponsored a symposium and dinner honoring Paul Scott upon his retirement. Paul first joined the Department of Oral Biology in 1981. He served as Chair of that department from 1993-1995. He also served a short term as Associate Dean of Dentistry before transferring to Biochemistry in 1996. Paul is now spending most of his time on his boat and is planning to circumnavigate the globe. We look forward to Paul's reports and to traveling vicariously with him.

The Department would also like to congratulate the following individuals for their years of service: Roger Bradley and Perry d'Obrenan, 40 yrs; Ruthven Lewis, 25 years.

Two of our most notable visitors last year were Dr. Bruce Spiegelman from Harvard Medical School in Boston. Dr. Spiegelman delivered an exciting presentation entitled "Transcriptional Control of Energy Homeostasis" as the 20th John S. Colter Lecturer in Biochemistry. We were also honored by the visit of Dr. Chris Rochet of the Department of Medicinal Chemistry and Molecular Pharmacology at Purdue University. He delivered the 3rd W.A. Bridger Lecture in Biochemistry on "Alpha-synuclein and DJ-1: two proteins with opposing roles in Parkinson's disease".

University of British Columbia

Department of Biochemistry and Molecular Biology

Correspondent: Christopher G. Proud

During the last year, we have welcomed two new Faculty members to our Department, and marked the retirement of our longest serving colleague.

Dr. Thibault Mayor joined this Department from CalTech (with Ray Deshaies) as part of UBC's 'Proteomics Initiative'. His research focuses on proteomic analysis of the ubiquitin system, and he also has a strong interest in neurodegenerative disorders. Dr. Filip Van Petegem was previously at UCSF in Dan Minor's group. Filip's research centres on the crystallographic and electrophysiological investigation of calcium channels.

Dr. Richard Barton, who ran our very successful fourth year laboratory courses (and contributed to the Department in too many other ways to mention!), retired in June 2007, having been in this Department for 37 years. During an exceptionally pleasant evening spent at the Royal Vancouver Yacht Club, the Department thanked Richard for all his contributions down the years, and wished him and Peggy every happiness for the future. Dr. Ross MacGillivray provided a really enjoyable retrospective of Richard's time in the Department (although even Ross doesn't go quite as far back as Richard!).

This year also brought another great crop of awards. Dr. Brett Finlay received the Order of BC, and was honoured as a distinguished alumnus of the University of Alberta. Dr. Lawrence McIntosh was very deservedly awarded a UBC Faculty of Medicine Killam Teaching Prize. In October 2007, Dr. Natalie Strynadka was the recipient of the Leaders in Medical Discovery Series (Distinguished Medical Research Lecturers award), and her lecture was entitled "Structure-based Antibiotic Discovery on the Bacterial membrane".

Every year, the Michael Smith lecture (hosted jointly with UBC's Michael Smith Laboratories; Nobel Prize for Chemistry, 1993) commemorates the life and outstanding contributions made by Dr. Smith to this University and to science. In November 2006, a huge - and enthralled - audience was treated to a superb talk by Dr. Peter Agre (Vice Chancellor – Science and Technology, Professor of Cell Biology, Duke University; 2003 Nobel Prize in Chemistry) entitled "Aquaporin Water Channels: From Atomic Structure to Clinical Medicine".

The Department's Zbarsky Prize (for the best research seminar by a Graduate Student) was won by Chris Jang for his presentation "Lost in Translation: The mechanics of viral internal ribosome entry sites". Barbara Lelj Garolla di Bard received the Marianne Huyer Memorial Award for the best biochemistry thesis of 06/07. The Department continues to enjoy excellent levels of success in funding from CIHR and other agencies, including Fellowships for four of our post-doctoral researchers, Drs. Igor D'Angelo, Danielle Krebs, Lianne McHardy and Raz Zarivach, and a New Investigator Award for LeAnn Howe, an Assistant Professor who studies chromatin remodeling in yeast.

University of Calgary

Department of Biochemistry and Molecular Biology

Correspondent: Leon W. Browder

Transitions

Dr. Jay Cross has been appointed Associate Dean (Research and Graduate Education) in the new Faculty of Veterinary Medicine. Jay retains joint appointment in our department in the Faculty of Medicine.

Dr. Jens Coorssen has been appointed Foundation Chair of Molecular Physiology, School of Medicine, University of Western Sydney (Campbelltown, NSW, Australia).

Dr. Julie Deans has returned from sabbatical to serve as our department's Graduate Program Coordinator.

Dr. Peter Forsyth has been named Director of the Southern Alberta Cancer Research Institute.

Dr. Ian Parney has accepted a position at the Mayo Clinic in Rochester, Minnesota.

Dr. Derrick Rancourt has returned from a very successful sabbatical at the MaRS technology convergence centre at the University of Toronto.

Dr. Jane Shearer has joined the Faculty of Kinesiology as an Assistant Professor. Jane retains a joint appointment in our department.

Dr. Mike Walsh has returned from a productive sabbatical at the University of Dundalk in Ireland.

We are pleased to acknowledge these recent accomplishments of members of our department

Dr. Christian Jacob supervised a team of students that placed in the gold category at the international Genetically Engineered Machine (iGEM) competition at MIT for their bacterial-plotter submission. The group of undergraduates also won first place in the poster competition at this prestigious event.

Dr. Sung-Woo Kim has been appointed as a Tier II Canada Research Chair in Cancer Research.

Dr. Jeb Gaudet has been appointed as a Tier II Canada Research Chair in Developmental Genetics.

Dr. Jonathan Lytton has been appointed as a Tier I Canada Research Chair in Molecular Cardiovascular Biology.

Dr. Al Yergey was awarded the 2007 Clinical/Adjunct Research Award for the Faculty of Medicine.

We are pleased to welcome the following new members to our department

Dr. Mark Bieda joined the department as a bioinformatician in January 2008. Mark obtained his undergraduate training in biochemistry at Harvard before obtaining his Ph.D. in Neuroscience at Stanford. He remained at Stanford for a short time on a postdoctoral fellowship before pursuing further postdoctoral training at the Santa Fe Institute and, most recently, at the University of California at Davis in Peggy Farnham's laboratory. Mark's background is in bioinformatics, genomics, neuroscience and translational research. His current research is in epigenomics and tiling array data analysis.

Dr. Savraj Grewal joined the department April 1, 2007. Savraj obtained his Ph.D. in 2001 from the Oregon Health Sciences University and conducted post-doctoral research in the laboratory of Dr. Bruce Edgar at the Fred Hutchinson Cancer Research Center in Seattle. His research involves examining growth control using Drosophila as a model system. His focus has been on the role of ribosome biogenesis in growth control.

We are pleased to welcome the following new adjunct members to our department

Dr. Zenobia Ali has been appointed Adjunct Assistant Professor. Dr. Ali is Education Coordinator for the Biotechnology Training Centre and Laboratory Coordinator in the Masters in Biomedical Technology Program.

Dr. John Chik has been appointed Adjunct Assistant Professor. John will conduct research in the Smooth Muscle Research Group of the Libin Cardiovascular Institute of Alberta and will teach physical bioscience in the Bachelor of Health Sciences Program.

Dr. Jesusa (Susie) Rosales has been appointed Research Assistant Professor. Susie studies the neutrophil-mediated immune response to infection and collaborates with Dr. Ki-Young Lee on cyclin-dependent kinases.

Dr. Navneet Sharma has been appointed Adjunct Lecturer. Navneet teaches in the Masters in Biomedical Technology curriculum. His research involves identifying substrates for proteases using innovative high throughput technology.

University of Calgary

Department of Biological Sciences
Faculty of Science

Correspondent: Raymond J. Turner

The past year has seen the first full year of the reorganization of our department into 3 clusters: the Biomolecule/Cells/Microbes cluster (BCM), Organismal Biology, and Ecology-Evolutionary Biology. Our group, the BCM, actually makes up about half of the department with the largest graduate program and a significant part of the undergraduates. As chair of the BCM cluster I am happy to give you this review of this year's fun and frivolities. As part of this year's pleasure of figuring out this new organization system, our department went through its unit review. We tried not to make it totally a navel-gazing exercise by trying to examine the good, the bad, and the ugly. Anyone who has gone through this exercise knows all the fun. With our department approaching 70 faculty, and processing the largest number of undergrads through our department than any other unit, of course there was lots of amusement generating the document. Anyway, it seemed that the external review was useful, as they noted our challenges and gave us some good suggestions.

Members in the Faculty of Science at the University of Calgary teach biochemistry to the undergraduates. The biochemistry group within the BCM consists of senior instructors Elke Lohmeier-Vogel, and Robert Edwards; AHFMR scholars/scientists Marie Fraser, Kenneth Ng, Elmar Prenner, Peter Tieleman and Hans Vogel; NSERC UFA Vanina Zaremberg; and regular faculty members Greg Moorhead and Raymond Turner. Similarly, the cellular and molecular biologists here contribute to the CMMB program (Cellular, Molecular and Microbial Biology). This group includes the AHFMR faculty of Steve Zimmerly and Dave Hansen, and regular faculty members Andre Buret, Lashitew Gedamu, Manfred Lohka, Carrie Shemanko, Howard Ceri, Hamid Habibi and Wic Wildering. Doug Muench also contributes the plant cell biology perspective to our programs. We have an increasingly strong group in plant biochemistry focused on plant metabolism and bioproducts that includes Peter Facchini (CRC Plant Biotechnology) and Dae-Kyun Ro (CRC in Plant Bioproducts). We also have an instructor, Isabelle-Barrette-Ng, who contributes to both programs. Additionally we now have the Institute of Biocomplexity and Informatics with the biological BCM members Sergei Noskov, Stuart Kauffman, Gordon Chua and Sui Huang.

An aspect that distinguishes us from those Biochemists in the Department of Biochemistry and Molecular Biology in the Faculty of Medicine is that most of us lean towards structural biochemistry with a focus on the molecular end rather than the cellular end of biochemistry. We have had a very good relationship with members in the Faculty of Medicine who have been very good at contributing teaching in some of our courses. Unfortunately, for a variety of reasons these contributions are rapidly coming to an end, leaving us with a loss of some good courses. This trend is now extending to the cellular side of things, leaving us with interesting challenges, yet we will continue to have strong programs.

This year our group graduated 25 undergraduates in Biochemistry, 37 in Cell and Molecular Biology, and 6 MSc, and 9 PhD students. Our graduate students have again been very successful in obtaining scholarship support at both the provincial and national levels with NSERC, CIHR, AHFMR, and AIF. The success of our graduate students has been outstanding during the past year. Highlights from our trainees' work include Justin MacCallum (supervisor Tieleman), with a noteworthy perspective/cover story in J. Gen. Physiol. on thermodynamics of protein side chain partitioning in membranes and a notable paper in PNAS on protein folding, which was the result of simulations on all of Canada's academic super computers (Canadian Internetworked Scientific Supercomputer 3 project). Joe Harrison's work (supervisor Turner) on yeast biofilms was noted in Nature research highlights and his paper on persister cells in Environ. Microbiol. quickly rose to the top 25 most cited papers in that journal. Additionally, Svetlana Boukina (supervisor Tieleman) had a nice paper in

Biophys. J., with a cover figure on large-scale transformations of lung surfactant.

So what have we been up to the past year? Two of us have been on sabbatical. Rob Edwards spent some time in Africa on his new interests in the chemical and bioactive properties of biochar. Lash Gedamu was also off to Ethiopia on his World Health Initiatives regarding *Leishmania*. Peter Tieleman is spending his sabbatical at the University of British Columbia where he is enjoying working on some of his own projects of improving lipid bilayer computational models. He also now finds himself on the editorial board of another journal, Channels. He is now also involved with the National Initiatives Committee of Compute Canada. He continues to be in high demand as an invited speaker as one of Canada's top computational structural biologists.

Some of our members have received some interesting recognitions. Audre Buret received the research excellence award from the Canadian Association of Gastroenterology as well as an NSERC synergy Award. Greg Moorhead was one of the 2 keynote speakers at the University of Alberta Signaling Retreat. And for one of our newest members, Sergei Noskov, two of his papers have received some rapid recognition. His 2007 paper in J. General Physiology is nominated for the Paul Grainfield Award by the Society for General Physiology, and a second published in J. Biophysical Chemistry, is listed in the Top-25 downloaded papers. He has also given invited talks at the Biophysical society meeting and the American Chemical Society meeting.

Peter Facchini has received considerable media coverage largely focused on an industrial contract and NSERC Strategic Grant aimed at the development of opium poppy varieties with novel pharmaceutical alkaloid phenotypes in an ultra-secure copper mine in Flin Flon, Manitoba. Raymond Turner gave a talk at the annual general meeting of the UK microbiology society on the controversial structure of the membrane protein EmrE in March. From there he was off to the University of Paris (Sud) to give talks on EmrE and transient protein interactions in protein maturation pathways. He then went on to Italy where he received a Senior Visiting Fellowship at the Instituto di Studi Avanzati, University of Bologna. The fellowship was for a month, where he gave lectures to undergrads as well as public lectures on topics of microbial-metal interactions, bioremediation, and excited-state reactions.

We had a fairly large event this fall with Gerrit Vourdoow and the installment of his NSERC Industrial Chair in Petroleum Microbiology. This was quite an accomplishment, as he was able to bring together 8+ companies to contribute to the Chair. This is great for Gerrit, but also puts Calgary in the position to become very strong in the area of environmental microbiology, as the Chair comes with two additional junior positions to be recruited in 2008 and a second in 2009. Gerrit continues his interest in physiology and bioenergetics of sulfate-reducing bacteria.

Gene Huber, our excellent colleague and mentor who had the ability to excite even the lowliest pre-med student about enzymology, spent his first year retired and slowly decreasing the size of his lab. Luckily, Gene is not leaving us and his downsizing is allowing him into a lab closer to the X-ray suite so as to continue to examine the molecular mechanism of glycosidases. Manju Kapoor, a keen molecular biologist also followed as similar pathway, relinquishing her lab to a new recruit, and consolidating her research to share a lab with Ken Sanderson. It is this generous downsizing and sharing of labs by our retired professors that has allowed space to be freed up for new recruits.

Our research cluster saw the addition of several new faculty. One aspect of our recruitments over the past two years is to have more multidisciplinary individuals who can contribute to more than one program/area. The challenge in recruitment of course arises from Calgary's inflation rate and expensive housing market. Regardless, we have excellent new recruits. The increase in faculty numbers comes from two avenues. One is an increase in a funding envelope for increasing our undergraduate numbers, and the second is through the creation of the interdisciplinary Institute of Biocomplexity and

Informatics (IBI) where a number of members reside in our department and now contribute to our programs.

Recruits to our group via the IBI include Sui Huang, who comes to us via Harvard with his focus in systems biology. He was successful in obtaining CFI funds and his lab is presently under construction. His research is investigating how gene regulatory networks and gene expression noise control cell fate determination, using novel functional genomics tools and theoretical concepts from complex systems sciences. The research thus applies to stem cell biology as well as tumorigenesis, which are caused by flaws in differentiation dynamics. There is currently neither a defined molecular mechanism nor a coherent formal theory for explaining how multipotent cells make fate decisions, and how stochasticity and deterministic instruction jointly influence this process. He aims to use single-cell level analysis to learn (i) how transcriptome-wide gene expression noise generates a functional heterogeneity in clonally identical multipotent stem or progenitor cells, such that individual cells are randomly pre-poised to adopt different cell fates; and (ii) what is the molecular and dynamical basis of this non-genetic heterogeneity. A second recruit in the IBI is Gordon Chua who is also interested in deciphering biological networks of transcriptional regulation and genetic interactions as part of his contribution to the areas of systems biology research. He is currently adapting the yeast *Schizosaccharomyces* pombe for several functional genomic approaches, including microarray expression profiling, synthetic genetic array mapping, chemical genetic profiling and systematic overexpression analysis to study and map these networks. He wishes to take a multidisciplinary collaborative approach by working closely with molecular, computational and theoretical scientists focused on understanding the topology and general rules governing transcriptional-regulatory and genetic-interaction networks. The IBI group is beginning to develop new courses and expects to offer both undergraduate and graduate courses in systems biology and functional genomics.

Other faculty additions include Peter Dunfield who came to us in the late fall via New Zealand. His interest is in the biochemistry, physiology and environmental microbiology of extreme halophiles, and he hopes to investigate the saline and alkaline lakes in southeastern Alberta. John Cobb also joined us, transferring from the Faculty of Medicine; his research uses limb development in the laboratory mouse as a model system to study how transcription factors control the development of specific structures. Specifically the focus is on the short-stature homeobox-containing gene 2 (Shox2), which he has shown is absolutely required for the development of the proximal bones of the limbs, the humerus and femur. He is seeking to identify the genes downstream of Shox2 that are responsible for its function and the evolutionarily conserved enhancers that control Shox2 expression.

Well folks, that's all for a 2007 retrospective. If anyone is interested in coming to Calgary to give a talk and have a visit, let me know and we can explore possibilities. For more information about our biochemistry group in the Department of Biological Sciences visit: www.bio.ucalgary.ca/research/BCM.html.

University of Guelph

Department of Molecular and Cellular Biology

Correspondent: Frances Sharom

New Science Complex building completed

Construction of the new Science Complex was finished as of mid-2007. By the end of July 2007, Phase II was completed and personnel from the former departments of Molecular Biology & Genetics and Botany had settled in to the new building. The over 45 members of the Department are now finally together under one roof in the new $144 million, 390,000 square feet complex. The 19,000 square feet Advanced Analysis Centre (AAC) on the first floor of the Science Complex includes state-of-the-art NMR spectroscopy, X-ray crystallography, electron microscopy, confocal

microscopy, and mass spectrometry instrumentation, as well as other analytical services such as DNA sequencing. Overall, the building accommodates approximately 2,600 faculty, students and staff from the College of Biological Science and from part of the College of Physical and Engineering Science. Undergraduate teaching laboratories and research labs for each of the departments are located in close proximity to encourage exchange between the two.

New faculty addition

Emma Allen-Vercoe joined the Department as an Assistant Professor in the past year, strengthening the department's cellular microbiology group. Emma began her research career with undergraduate and graduate studies at the Central Veterinary Laboratories and the Centre for Applied and Microbiological Research (CAMR), UK, under the direction of Prof. Martin Woodward, where she studied the enteric pathogen *Salmonella enterica* serovar *Enteritidis*. She spent a brief postdoctoral period at CAMR, learning to work with technically challenging pathogens such as *Mycobacterium tuberculosis* and *Campylobacter jejuni*, before relocating to Canada in 2001 to take up a postdoctoral position at the University of Calgary, under the joint direction of Drs. Rebekah DeVinney and Mike Surette. Here she worked on enteropathogenic and enterohemorrhagic *E. coli* (EPEC and EHEC), using cell and molecular biology techniques to probe the interactions of their type III secretion systems with host cells. In 2004, Emma won a Fellow-to-Faculty Transition award through the Canadian Association of Gastroenterology. This award allowed her to develop an independent research program aimed at the study of the normal human microflora and its influence on human health and disease, a program that she brought to Guelph in December 2007. Emma is currently hard at work setting up her new research laboratory, where she is focussing on the study of the normal human gut microflora, both in disease and in health, and is supported by an operating grant from the Crohn's and Colitis Foundation of Canada, CCFC.

In memoriam

The department was deeply saddened by the untimely loss of long-time faculty colleague Terry Beveridge, who died on September 10 2007 at the age of 62 after a valiant battle with liver cancer. Terry was a pre-eminent microbiologist of his generation, and still at the

peak of his career. On Saturday, September 29, more than 180 people from across Canada and the U.S. attended the Symposium on Biofilm, Geomicrobiology and Bacterial Cell Surfaces in honour and recognition of Terry for the impact of his research and scientific achievements in the field of Microbiology. Following the formal part of the program, attendees were invited to a wine and cheese reception in the Science Complex Atrium. Later that evening, over 160 people, including Terry's wife Jan, son Braden with wife Becky, and daughter Bree with her fiancé Aaron, sat down to dinner at the Italian Canadian Club. The day was filled with science, reminiscing and of sharing fond memories of Terry. A memorial scholarship fund has been created in Terry's honour, and two scholarships will be awarded annually to assist graduate students with travel costs to attend scientific meetings.

Retirement

Cecil Forsberg officially retired on August 1 2007, after three decades of service to the University of Guelph. He has been a major contributor to all activities of the former Department of Microbiology and, more recently, MCB. We still see Cecil in the hallways as he continues to pursue his research program as a Professor Emeritus. During the past year, Cecil was elected to Fellowship in the American Academy of Microbiology. This award justly recognizes his extensive contributions and his dedication to the discipline over the course of an outstanding career.

Congratulations!

Nina Jones was awarded an Early Researcher Award (ERA) by the Ontario government. These awards are directed to full-time Ontario researchers within the first five years of the start of their independent academic research career. Nina also received operating grant funding from the Kidney Foundation of Canada.

John Dawson was named a recipient of the 2007 Provost's Award for Innovation in Teaching and Learning at the University of Guelph. The award recognizes John's development of innovative teaching approaches in the Biochemistry program and his commitment to student learning. He was recognized for developing Fold, a mock scientific e-journal that allows students to gain experience in writing and peer-reviewing scientific papers. Fold was launched in 2004 in a fourth-year course called "Structure and Function of Macromolecules." In addition to completing a project in protein folding, about 40 students pair up to write a research article for review by their classmates and possible publication in the journal, which resembles a professionally produced electronic publication.

Our Chair, Chris Whitfield, won a University of Guelph Faculty Association Distinguished Professorial Teaching Award in 2007. He was also elected a Fellow of the Royal Society of Canada (Life Sciences), a premier honour for any academic, reflecting outstanding research contributions.

Derek Bewley, University Professor Emeritus, was elected a Corresponding Member of the American Society of Plant Biologists 'in recognition of distinguished accomplishments in the science of plant biology'. This is a lifetime membership award for researchers from outside of the United States and is decided by a ballot of the society's membership. This prestigious award was initiated in 1932 and Derek is the first Canadian to receive it.

Rob Mullen received the 2007 C.D. Nelson Award in Plant Physiology from the Canadian Society of Plant Physiologists. The award is made annually to an individual who has made "outstanding research contributions to plant physiology" within the first 10 years of holding an independent position.

University of Lethbridge

Departments of Biological Sciences, Chemistry and Biochemistry, and Physics

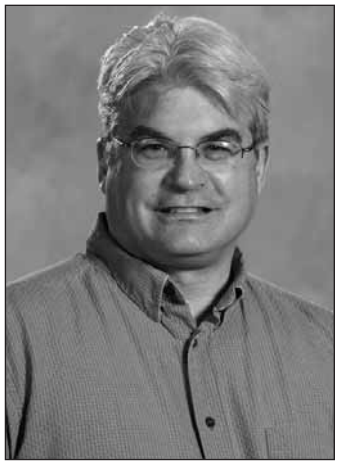
Correspondent: James E. Thomas

Biochemistry at the University of Lethbridge is a multidisciplinary major delivered by several Departments. Focus within the group is varied with expertise in agriculture, cancer research,

microbial biochemistry, nucleic acid biochemistry (in particular in RNA), and nutrition, as well as areas of health and theory.

Dr. Ute Kothe is Assistant Professor in Biochemistry at the Department of Chemistry and Biochemistry since October 2006. Her work has significantly increased our understanding of accurate decoding of mRNA by the ribosome. Based on her experience in studying the prokaryotic ribosome, Ute's research now focuses on the complex process of ribosome biogenesis. In particularly, she is investigating the early stages of ribosome formation when the ribosomal RNA becomes modified by small ribonucleoproteins. This work can lead to the development of new nanomachines based on biomolecules such as RNA and proteins, as well as to the identification of new drug targets.

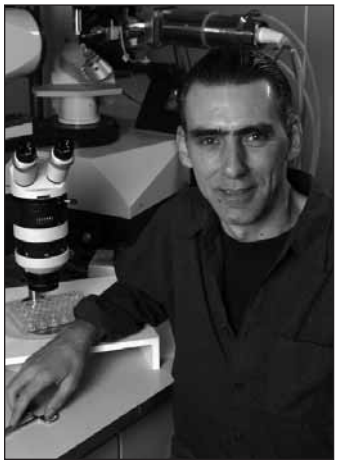
Dr. Hans-Joachim Wieden joined the Department of Chemistry and Biochemistry in January 2005 and was awarded a Canada Research Chair in Physical Biochemistry as well as an Alberta Ingenuity New Faculty award in 2007. With the steady emergence and spread of antibiotic resistant pathogens, the development of new antibiotics is increasingly important. This research program focuses on the study of antibiotic function in order to develop novel antibiotics. In particular, antibiotics are under study that target the cellular machinery of the pathogen responsible for translating genetic information into functional proteins. Other research is looking at the molecular dynamics of elongation factors, which is supported through the AIF New Faculty award. HJ's work focuses around a unique combination of state-of-the-art biophysical techniques involving fluorescence spectroscopy, fast kinetics (quench flow/stopped flow), biochemistry, molecular biology, and molecular dynamics.



Dr. Brent Selinger is an Associate Professor in the Department of Biological Sciences and Coordinator of Agricultural Biotechnology at the University of Lethbridge. Brent is interested in the genetics and biochemistry of microbial hydrolytic enzymes, microbial ecology of animal digestive tracts and surface waters and biological control of cattle ectoparasites. His research group in currently characterizing a unique family of phytate degrading enzymes related to protein tyrosine phosphatases (PTP). A large collection of PTP-like phytase genes is currently being used to address questions about the molecular and biochemical characteristics of this family as well as mechanisms of action, structure/function relationship and biological function. A variety of techniques are used in Brent's research, including aerobic and anaerobic microbiology and molecular biology (e.g., gene cloning and overexpression, protein purification and characterization, and mutagenesis).

Dr. Roman Przybylski is an AVAC Chair in the Department of Chemistry and Biochemistry. Roman is working on the development of antioxidants for edible oils and food systems; the effects of endogenous edible oil components on stability, performance and nutritional value; and the assessment of food

products and raw materials for compounds with nutritional and nutraceutical properties. Recent projects include development of analytical techniques to assess antioxidant potency of different plant origin components, assessment of chemical activity of minor oil components during frying; formation of trans fatty acids during processing and food preparation; and designing oils for specific food application by manipulating their composition.



Dr. Steve Mosimann is an Associate Professor with the Department of Chemistry and Biochemistry at the U of L. Steve's research involves development of an understanding of the mechanism of mRNA turnover and the formation of long-lived mRNA species. Other research involves ribosome biogenesis in Archaea. Much of Steve's research involves X-ray crystallography, which creates a three-dimensional map of the electron density associated with the macromolecule(s) of interest and ultimately a three-dimensional structural model. As the structure and function of macromolecules are intimately connected, these models provide functional insights and lay the groundwork for an understanding of biological function at the molecular level.

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

Dr. James Thomas is an Associate Professor in the Department of Biological Sciences, and Coordinator of Biochemistry at the University of Lethbridge. Part of his research focus is in the area of microbiology, looking at cause and effect associations in the occurrence of waterborne pathogens, in particular in relation to agriculture, ecology and urban/industrial activities. In collaboration with the Canadian Water Network, and Dr. Victor Gannon and Dr. Eduardo Taboada from the Public Health Agency of Canada, Jim is using metabolic fingerprinting of environmental isolates of Enterococcus and Salmonella as a means of bacterial source tracking, and genomic characterization of environmental isolates of E. coli O157:H7 and Campylobacter to develop clinical assays for use in environmental testing. Jim also is working with Dr. Surya Acharya, Adjunct Professor with the University of Lethbridge and a Research Scientist with Agriculture and Agri-Food Canada, Dr. Manjula Bandara and Dr. Darcey Drieger, Adjunct Professors with the University of Lethbridge and Research Scientists with Alberta Agriculture Food and Rural Development in Brooks, Alberta to develop new forages for the livestock and dairy industries and, new value added functional food and nutraceutical crops to help diversify our agricultural industry.

Dr. Igor Kovalchuk is an Associate Professor and Board of Governor Research Chair with the

Department of Biological Sciences at the University of Lethbridge. Igor is working on plant genome stability. Specifically, he is looking at the influence of various abiotic (UV, draught, heavy metals, high temperatures) and biotic (pathogens, specifically viruses) factors on plant genome integrity. He is also examining the mechanisms of protection that are developed by plants against the pathogens, the various types of signals that plants use to warn non-targeted tissues, and the genes involved in various steps of DNA repair, specifically, double strand breaks.

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

Dr. Olga Kovalchuk is an Associate Professor and Board of Governor Research Chair with the Department of Biological Sciences at the University of Lethbridge and the Associate Member (Fundamental Stream) of the Southern Alberta Cancer Research Institute. Olga is an active member of several professional societies and Editorial Board member of the Mutation Research. The Kovalchuk laboratory works in the rapidly evolving, challenging area of cancer research. Their program is devoted to uncovering the molecular mechanisms of cancer development and new approaches to cancer prevention, diagnostics and treatment. They have a particular interest in the effects of radiation, and they are working to minimize the harmful effects of radiation, while maximizing its therapeutic potential.

Dr. Roy Golsteyn is an associate professor in the Department of Biological Sciences at the University of Lethbridge. Roy is studying how cancer cells respond to clinical treatments, with the goal to identify new biochemical pathways that might be used in future treatments. When cancer cells have damaged DNA, they engage a biochemical pathway named the DNA damage checkpoint. This pathway permits the cell to repair the damage, or if this is not possible, it causes them to die. Recently, it has been shown that cancer cells can escape a DNA damage checkpoint and enter a stage called "mitotic catastrophe." Mitotic catastrophe is poorly understood at the molecular level although it appears to be a major mechanism in the cellular response to DNA damage, including damage induced by cancer therapies. Roy's laboratory is working on characterization of mitotic catastrophe in cancer cells, identification of potential biomarkers in cancer drug therapy, and characterization of early-stage anti-cancer compounds to understand their mechanism of action.

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

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

Dr. Stacey Wetmore is appointed in the Department of Chemistry and Biochemistry as an Associate Professor and Canada Research Chair in Computational Chemistry. Stacey's research uses calculations on computers to understand DNA damage and repair mechanisms, as well as the properties of modified DNA components that have a variety of biochemical and medicinal applications. Current areas of research in the Wetmore lab include understanding DNA damage due to phenoxyl radicals and the mechanism of action of enzymes involved in the base excision repair process, where particular emphasis is being placed on understanding the glycosidic bond cleavage in damaged nucleotides catalyzed by DNA glycosylases. Although calculations on biological systems require significant computer resources, these calculations are possible at the University of Lethbridge due to the recent establishment of a high-performance computer cluster that is composed of 170 quad-core processors (680 cores in total).

Dr. François Billaut joined the Department of Kinesiology and Physical Education at the University of Lethbridge in September 2006 as an Assistant Professor in Exercise Physiology. François has a strong background in biochemical (biopsy technique) and electrophysiological (electromyography analysis, M-wave) investigations of the exercising human body. His most recent work has shown the impact of biological sex on exercise performance and skeletal muscle fatigue during sprint activity, and the effects of acute exercise fatigue on electromyographic parameters, especially an impairment in inter-muscle coordination. His work has significantly increased our understanding of the neuromuscular fatigue during exercise in

human to optimise training methods, and develop wellness conditioning programs. In the future, François will continue to address the differences between men and women in muscle and arterial oxygenation trends (assessed via near-infrared spectroscopy and blood samples) during exercise.

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

Dr. André Laroche is an Adjunct Professor in the Department of Chemistry and Biochemistry at the University of Lethbridge, and a Research Scientist in Plant Molecular Genetics with Agriculture and AgriFood Canada at the Lethbridge Research Centre. André is currently investigating stress biology in plants due to abiotic (e.g., low temperature) or biotic (e.g. pathogenic fungi) factors, and more recently is involved in the development of transgenic triticale as a bioindustrial crop for materials and energy production. He is using functional genomic tools such as large scale sequencing; transcriptome profiling with DNA chips for screening large arrays of genes; real-time PCR to focus on specific genes, and transient and stable expression of candidate genes to assess their role and contribution in a plant cell; and proteomic analyses using 2D-gel electrophoresis and protein sequencing.

Dr. Oliver Lung is an Adjunct Professor with the Department of Biological Sciences. Oliver is a Research Scientist at the Canadian Food Inspection Agency in Lethbridge. His research is focused on developing methods for rapid and simultaneous identification and typing of agriculturally important animal viruses such as avian influenza virus, food-and-mouth disease virus and their differentials; and improving and expanding baculovirus-based agri-biotechnological applications. His group uses biochemistry, molecular biology, cell biology and virology techniques as well as tools such as electronic microarrays, microsphere arrays and slide microarrays for genetic typing of animal viruses.

Dr. Alicja Ziemienowicz joined the team of Dr. Igor Kovalchuk in October 2007, as a Research Associate, and later became a Research Professor in the Department of Biological Sciences at the University of Lethbridge. Alicja's research interests include: (1)

genetic transformation of eukaryotic cells, (2) nucleo-cytoplasmic transport of proteins and nucleic acids, (3) DNA replication, repair and recombination in plant cells, and (4) plants as renewable energy sources. One of the main topics of her study is Agrobacterium-mediated plant transformation. In particular, Alicja is investigating the mechanism of integration of Agrobacterium T-DNA in the plant genome, by identifying plant factors involved in this process.

Dr. Ken Vos is an Associate Professor in the Department of Physics at the University of Lethbridge. Ken is a theoretical physicist and one of his research interests is pharmacokinetics. Pharmacokinetics describes the motion of a drug in the human body and its interaction with the human body. The human body is highly heterogeneous and hence the transport and chemical reaction processes occurring within the human body are highly anomalous. The primary focus of the research is to develop physiologically accurate theoretical models of the drug transport and interaction with the human body.

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

University of Manitoba

Department of Biochemistry and Medical Genetics

Correspondent: Klaus Wrogemann

Some tidbits from our department with the clear understanding that other noteworthy items will have been missed:

Dr. Francis Amara, Associate Professor, received the prestigious University of Manitoba Presidential Outreach Award on November 21st, 2007. Francis has promoted life sciences education in schools in the North End, Winnipeg School Division. He founded the Head Start Aboriginal Biomedical Youth Program including being a mentor to Aboriginal students. He co-founded the Sierra Leone Refugee Inc, thereby providing leadership, aiding newcomers to Canada and guiding new immigrants in all aspects of daily living in the Sierra Leone Community in Manitoba. In addition, he has also organized the Summer Institute for High School Science Teachers in the Winnipeg School Division. Francis has established the summer school programs in the Faculty of Medicine for elementary school children, and has been instrumental in seeking partnerships for the Faculty of Medicine with the Winnipeg Foundation and the Winnipeg Boys and Girls Club. Francis is particularly dedicated to ensuring relationships between the Faculty of Medicine and the school system, and the successful integration of refugee children into the Manitoba school system.

Geoff Hicks, Associate Professor, CRC II chair, and Director of the Centre for Mammalian Functional Genomics at our University, is one of

the co-leads on the NorCOMM project, the Canadian component of an international co-operative effort to knock out every gene in the mouse. The other co-lead is Janet Rossant, Chief of Research at Sick Kids at the University of Toronto. The aim is to create a resource for Canadian and international researchers investigating the cause and treatment of human diseases. In fact, the NorCOMM project invites Canadian researchers to nominate their genes of interest for consideration for targeting. The Centre is located in the Manitoba Institute of Cell Biology at the University of Manitoba in Winnipeg. NorCOMM is supported by major funding from Genome Canada and is managed by Genome Prairie, uniting expertise in cellular and functional genetics at academic centres across Canada. NorCOMM is a founding member of the International Knockout Mouse Consortium (IKMC). Together with partner projects EuCOMM, KOMP, and TIGM, the aim is to achieve complete coverage of the mouse genome.

K. Dakshinamurti (Dakshi), Professor Emeritus in his tenth year, and internationally renowned expert on vitamins, continues to travel and to work on book chapters concerning vitamins as cofactors and potential treatment agents. He is currently part of the organizing committee of the Second International Interdisciplinary Conference on Vitamins, Coenzymes, and Biofactors under the aegis of the International Union of Biochemistry. The conference will be held in Athens, Georgia in October 2008.

Dr. Louise Simard, Professor and Head, was one of the authors, together with Thomas Klonisch (Human Anatomy and Cell Science), Janice Dodd (Physiology) and Judy Anderson (now Head of the new Department of Biological Sciences) of the winning proposal for a recruitment initiative in the Faculty of Medicine. It is to develop a new program in Regenerative Medicine with a focus on stem cells relevant to human disease. The initiative entails six new positions and is expected to provide a most welcome boost to the basic sciences departments in the Faculty of Medicine.

University of Toronto

Department of Biochemistry

Correspondent: David Williams

Biochemistry in Toronto celebrates its 100th Birthday!

Founded in 1907-08 by Professor Archibald Byron Macallum, the Department of Biochemistry at the University of Toronto was the first department dedicated to this discipline in Canada, and amongst the very first in the world. During the ensuing century, the Department has flourished in its missions in research and education, graduating over 350 Ph.D. and 370 Master's degree students and teaching thousands of undergraduate life science and medical students. The present day Department has 56 faculty members and about 200 graduate student and postdoctoral trainees. A research powerhouse, the Department has published over 1000 papers in the last five years alone. The many achievements of the Department are highlighted by Professor Emeritus Marian Packham in "100 Years of Biochemistry at the University of Toronto: An Illustrated History".

To celebrate these achievements, we will be holding a 100th Anniversary Symposium from May 28-30, 2008, encompassing the major scientific themes of the Department: Proteins, Molecular Information Transfer, and Molecular Cell Biology. Our speakers are drawn from our alumni, our present faculty, and international researchers who have a connection to the Department. Interspersed with the scientific content, there will be several short vignettes dealing with different aspects of Departmental history. The research accomplishments of our current trainees will also be prominently showcased. Social events, such as the opening reception and the gala banquet, will provide opportunities for trainees to mingle with speakers and other guests, and for alumni to exchange stories (scientific or otherwise) amongst themselves and with current members of the Department. Please join us for what promises to be a scientifically rich and socially rewarding event. For more information, see our Anniversary website at:
http://www.biochemistry.utoronto.ca/news/100.html

Faculty News and Research Highlights

Chair Reinhart Reithmeier has been chosen as one the Faculty of Medicine 2007 W.T. Aikins Award winners for his sustained excellence in undergraduate teaching. Along with former Aikins Award winners Charles Deber and Roy Baker, Reinhart teaches to over 1,200 students in our Introductory Biochemistry course. As past Vice President and now President of the CSBMCB, Reinhart keeps busy with advocacy, writing Opinion Pieces and Letters to the Editor in the Toronto Star on research funding. He also launched a campaign for a "National Health Research Week" to better inform the public and politicians as to the benefits of health research. Reinhart is the CIHR Delegate for the University of Toronto and serves on CIHR New Investigators Panel. He has also been busy with editorial work having just completed a 10 year term on the Editorial Board of the Journal of Biological Chemistry, edited a special issue of Biochemistry


Reinhart Reithmeier

and Cell Biology on "Membrane Proteins in Health and Disease" and a special issue in the journal Methods on "Structural Biology of Membrane Proteins". Following a highly successful 5 year review, Reinhart has been re-appointed as Chair of the Department of Biochemistry for a second term.

Walid Houry, along with Joaquin Ortega at McMaster, are organizing the 8th International AAA meeting to be held at the Kingbridge Centre in Toronto on July 12-16, 2009. The meeting will feature world renowned and international speakers working to decipher the structure and mechanism of function of the AAA+ (ATPases Associated with diverse cellular Activities) superfamily of ATPases. Members of this superfamily use the power of nucleotide binding and hydrolysis to direct molecular remodeling events such as protein degradation, vesicular fusion, peroxisome biogenesis, and the assembly of membrane complexes. Also co-organizing a meeting is Hue-Sun Chan who will be running the Conference on Knots and other Entanglements in Biopolymers: Topological and Geometrical Aspects of DNA, RNA and Protein Structures. The conference will be held in September 2008 at the Abdus Salem International Centre for Theoretical Physics (ICTP) in Trieste, Italy (website: http://cdsagenda5.ictp.trieste.it/full_display.php?smr=0&ida=a07172). Even well after retirement, Harry Schachter remains a highly sought after speaker, with invitations to the Institut für Chemie, Universitaet für Bodenkultur, Vienna, Austria; to the "Symposium in honor of Bert Dorland", Divisie Biomedische Genetica, Universitair Medisch Centrum, Utrecht, The Netherlands; and to the workshop on "Theoretical Glycobiology: The Third Language of Life", Santa Fe Institute, Santa Fe, NM.

This was a year for some outstanding research achievements by our faculty members. Daniela Rotin and postdoc Aleixo Muise at Sick Kids discovered that mutations in the gene encoding protein tyrosine phosphatase sigma is associated with ulcerative colitis and that mice lacking this gene spontaneously develop colitis (Curr. Biol. 2007 17:1212). Bill Trimble and grad students Emily Joo and Mark Surka published an influential paper in Developmental Cell demonstrating that mammalian septin SEPT2 is required for scaffolding non-muscle myosin II and its kinases. This appears to be an important event ensuring full activation of myosin II that is necessary for the final stages of cytokinesis (Dev. Cell 2007 13:677). Where is phosphatidylserine located? As described in a recent paper in Science, Sergio Grinstein and grad student Tony Yeung developed a genetically-encoded fluorescent probe to detect phosphatidylserine in the cytosolic leaflets of cellular membranes in intact cells. They found PS enriched in the plasma membrane and along the endocytic pathway, and found that it confers negative surface charge that targets proteins there (Science 2008 319:210).

Events

A beautiful sunny day greeted 230 participants in our Annual Research Day held on May 29th. The day highlighted work by our students and post-docs in the form of posters and several oral presentations. Selected talks from some junior faculty also added to the eclectic mix. This has become the traditional venue for our annual Theo Hofmann lecture which was presented this year by Jennifer Lippincott-Schwartz, NICHD, NIH, who presented an extremely engaging seminar entitled: "Emerging Fluorescence Technologies for the Analysis of Protein and Organelle Localization, Turnover and Topology in Living Cells". Terrific science, a wonderful BBQ lunch in the sun and great spirits all combined to create a wonderful research day experience for all. For some photos of the event, go to: http://biochemistry.utoronto.ca/news/news_archive/news_2007/research_day_07.html

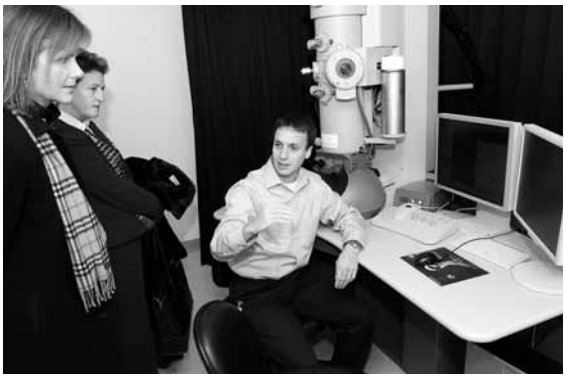
On November 29th, 2007, The Hospital for Sick Children and the Faculty of Medicine at the University of Toronto held an open house for their

A record turnout of biochemists made the 2007 Research Day memorable

new Electron Cryomicroscopy (cryo-EM) Facility, based at the Hospital for Sick Children. The Facility was made possible by awards totalling more than $1.6M to Dr. John Rubinstein, a member of the Molecular Structure and Function Program in the Hospital's Research Institute and the University's Biochemistry Department. The cryo-EM facility contains one of only a few 200 kV Field Emission electron microscopes in Canada optimized for imaging of protein complexes in a frozen hydrated state. The cryo-EM method has become one of the main tools for the structural analysis of macromolecules and macromolecular assemblies. Special guests at the event included MPP Hon John Wilkinson (Minister of Research and Innovation), Ms. Suzanne Corbeil (CFI), Dr. Kevin O'Brien Fehr (CFI Director and Director, R&D Alliances, GlaxoSmithKline Inc.), Dr. Alastair Glass, (Deputy Minister, MRI), and Ms. Jane Kirkwood, (Manager, Innovation Branch, MRI).

A symposium entitled "Machines, Macromolecules and Medicine" was presented with lectures by Drs. Lynne Howell, Lewis Kay and John Rubinstein and introductions and comments from Drs. Janet Rossant (Chief of Research, SickKids Research Institute) and Peter Lewis (Vice Dean, Research and International Relations, Faculty of Medicine). Invited guests and members of the Toronto research community were also given an opportunity to tour the cryo-EM facility.

The Department of Biochemistry hosted Bruce Alberts when he was in Toronto to receive an honorary degree on Nov. 16, 2007. Bruce Alberts



John Rubinstein describes the cryo-EM to visitors Suzanne Corbeil (CFI) and Jane Kirkwood (Manager, Innovation Branch, Ontario Ministry of Research and Innovation

is a former Gairdner Award winner for his work on DNA replication and he served as President of the National Academy of Sciences (USA) from 1992 to 2005. He is currently a Professor at the University of California, San Francisco, and Editor-in-Chief of Science. Undergraduates know him as the lead author of "Molecular Biology of the Cell" and "Essential Cell Biology." The citation was delivered by Larry Moran, a former graduate student of Alberts. Following the ceremony, Professor Alberts met with students and faculty at a reception held in the Biochemistry Department. Many of the undergraduates and

graduate students brought copies of their textbooks and Bruce was happy to sign them and to reveal some of the stories behind producing a best-selling book. There were even some faculty members in the lineup for autographs.

Very enjoyable social events included our Annual Ski Day and Annual Golf Day, both of which are organized by graduate students. Photos can be found at: http://biochemistry.utoronto.ca/news/news_archive/news_2007/news_2007.html

Front row: Bruce Alberts (left) with Chancellor David Peterson back row from left: Chair Reinhart Reithmeier, Vice Dean Research Peter Lewis, Dean of Medicine Catharine Whiteside, President David Naylor, Governing Council Chair Jack Petch, Prof. Larry Moran, Dean of Graduate Studies Suzanne Pfeiffer, and Prof. Jacqueline Segal

Appointments

Stephane Angers

We were delighted to welcome Stephane Angers to the Department in 2007 as an Assistant Professor. Stephane has his primary appointment in the Faculty of Pharmacy. He obtained his Ph.D. in Biochemistry from the Université de Montréal with Michel Bouvier followed by postdoctoral work with Randall Moon at the University of Washington. His research focuses on functional proteomics of Wnt and Hedgehog signalling and on the mechanisms of ubiquitination by Cullin-4 E3 ligases. Stephane also holds the Canada Research Chair in Functional Architecture of Signal Transduction.

Dr. Roula Andreopoulos was promoted to the rank of Senior Lecturer in the Department. Roula's primary duty is to coordinate BCH210 Introductory Biochemistry. With over 1,000 undergraduate students registered from a wide variety of programs, the organization of this course is quite a challenge - a challenge that Roula has taken on with energy and drive. Recently, Roula has honed her lecturing skills in BCH210 during the summer session to a diverse class of over 200 students. Roula also acts as an Instructor in our BCH370 Laboratory Course in Biochemical Techniques.

Roula Andreopoulos

The Department is also actively recruiting two additional Assistant Professors at this time. More information is available on the University of Toronto website under “Current Academic Positions”:

http://link.library.utoronto.ca/academicjobs/display_job_detail_public.cfm?job_id=2572

Graduate Studies

Our third annual Benjamin Schachter Memorial Lecture took place on June 21st this year. Named in honour of former graduate student Benjamin Schachter, who conducted research in the Department from 1934-1939, this lectureship is organized by our graduate students who select a prominent graduate from our Department. This year's speaker was John Challice, Vice President and Publisher Higher Education for the U.S. division of Oxford University Press. John, who was a graduate student with Jacqueline Segall, gave a very engaging and informative lecture about how

one embarks on a career in scientific writing, aptly titled "Leaving the Bench: From Scientist to Scientific Journalist and Publisher!"

John Challice (second from right) with BGSU president Eden Fussner (right), his graduate supervisor Jacqueline Segall, and grandchildren of Benjamin Schachter, Cobi Druxerman (left) and Jonathan Schachter

An integral part of the Department's Annual Research Day is its graduate student poster competition. Our guest poster judge was this year's Theo Hofmann Lecturer, Jennifer Lippincott-Schwartz, NICHD, NIH. Coming from NIH, Jennifer does not have daily exposure to students and she was bowled over by the calibre of our graduate research. Jennifer will be returning next year to shop for post-docs!

Lecturer Jennifer Lippincott-Schwartz

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

Winners in the Ph.D. category were: Ben Pinder (Smibert lab): "Post-transcriptional regulation of nanos mRNA"; Usheer Kanjee (Houry lab): "X-ray Crystal Structure of the E. coli Inducible Lysine Decarboxylase (LdcI), Novel Regulation by (p)ppGpp"; and Shrivani Sriskanthadevan (Siu lab): "The C-terminal Domain of DdCAD-1 is Involved in the Nonclassical Transport Pathway via Contractile Vacuoles".

Winners in the M.Sc. category were: Jean-Philippe Julien(Pai lab): "Structural insights into the mechanism of neutralization of the nmAb 2F5 against HIV-1: conformations of the CDR H3 extended loop and residues located at the C-terminus of the DKW core"; Wioletta Glowacka (Rotin lab): "Investigation of trafficking and function of lysosomal transmembrane protein LAPTM5"; and Derek Ng (Deber lab): "Peptide approaches to the mechanism of myelin proteolipid protein (PLP) oligomerization"; and Jenny Hsu (Yip lab): "Molecular Dynamics Simulations of Indolicidin Association with Model Lipid Bilayers".

The winner in the postdoc category was: Allison Ferguson (Chan lab): "Desolvation Effects in Folding: Rates and Topology"

Additional graduate awards:

The winner of the *Beckman Coulter Paper of the Year Award* for 2006 was: Tania Roberts (Brown lab) for her paper "Slx4 regulates DNA damage checkpoint-dependent phosphorylation of the BRCT domain protein Rtt107/Esc4" Roberts, TM, Kobor, MS, Bastin-Shanower, SA, Ii, M, Horte, SA, Gin, JW, Emili, A, Rine, J, Brill, SJ, and Brown GW. (2006) Mol. Biol. Cell. 17:539-548

Tania Roberts receives the Beckman Paper of the Year award from Grad. Coordinator, Jim Rini

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

Jim Rini, presents the David A. Scott Award for best all-round graduate student to Costin Antonescu. Costin, who was on his honeymoon at the time, demonstrated his exceptional commitment to the Department by showing up at Research Day, along with his new bride, Allison Guy, to receive the award

Outstanding Teaching Assistant awards went to Sian Patterson and Dana Patterson (no relation) for their exceptional performance as teaching assistants in our BCH371 and BCH 210 courses, respectively.

Undergraduate Coordinator, Roy Baker, presents TA awards to Sian Patterson, left, and Dana Patterson

Congratulations to all winners on their achievements.

University of Victoria

Dept of Biochemistry and Microbiology

Correspondent: Robert Burke

Since our last contribution to the CSBMCB Bulletin we have passed a busy year. There have been many important developments, but awards and our persistent growth seem to be the ones most noteworthy.

Several faculty and staff were recognized with awards in the last year. Alisdair Boraston's research program earned him the Faculty of Science Award for Research Excellence. Al's research program is the study of protein-carbohydrate recognition in metabolic and non-metabolic processes and he uses structural biological approaches complemented with physical-chemical methods. Bob Olafson, a recent retiree from the department was awarded the Craigdarroch Gold Medal for Career Achievement in Research. Bob was responsible for the establishment of the University of Victoria-Genome BC Proteomics Centre, which continues to be a very successful component of our department. Barb Currie was the first laboratory instructor to receive the Faculty of Science Award for Excellence in Teaching. Barb has a long history of inspirational teaching in our introductory microbiology course. As well, Marty Boulanger and Al Boraston were awarded Michael Smith Foundation for Health Research Scholar Awards. Marty also was awarded a CIHR New Investigator award. All of these are well deserved and the department took great pride in their achievements.

We continue to have exceptional interest from students in all of our academic programs. For instance, we lead the Faculty of Science in growth of undergraduate enrolment. Since 2001 enrolment in our undergraduate program has increased by two-thirds, and graduate enrolment has doubled. There seems to be unabating interest from prospective students in molecular science. We have outgrown our undergraduate teaching labs and are trying to find ways to maintain the hands-on learning in small groups that has become

Barb Currie (left), a laboratory instructor in the department receives the Faculty of Science Award for Excellence in Teaching from the Dean of Science Tom Peterson, noting Barb's inspirational contribution to introductory microbiology. Al Boraston (right) is receiving congratulations from Robert Burke, Chair of Biochemistry and Microbiology for being awarded the Faculty of Science Award for Excellence in Research, Dean Peterson looks on.

a central theme to programs in biochemistry and microbiology. Our graduate program saw the introduction of a new core course in the first year and we are continuing to work to develop our graduate program into a well-structured curriculum that will, in turn, enhance our research and undergraduate teaching programs. We believe that our graduate program will become a model for advanced education that has the potential to lead the biomedical disciplines at the University of Victoria.

One place where growth has been exceptional is in our co-op program. During the past 10 years this program has grown from the smallest of the University of Victoria optional co-op programs to the largest. From 2001 to 2007, annual placements grew from 114 to 170, representing an increase of 64% over six years. By comparison, at the same time there was about a 1% growth in other science co-op programs. Making this happen is no small accomplishment and we owe the success of this program to Rozanne Poulson, our co-op coordinator. Rozanne is our talent spotter for exceptional students and invariably she finds gems who she tirelessly recruits to the co-op program. Rozanne has lots of students to choose from as the success of students in the program provides a great deal of word of mouth advertising. A persistent concern for co-op coordinators is the prospect of running out of suitable jobs. Rozanne seems never at a loss to find jobs for our students. She invariably places her students and is often able to find jobs for students in other departments.

The department is thriving and each year seems to bring more opportunities. Like many departments in the molecular life sciences we find our subject relevant to students' interests and society's concerns. The demands can be taxing, but we are fortunate to live in such interesting times.

University of Western Ontario

Department of Biochemistry

Correspondent: Eric Ball

After a search process that spanned a couple of years Dr. David Litchfield was prevailed upon to take up the Department Chair position and began his term in September 2007. Both Dave's lab and the Functional Proteomics Facility that he directs moved to renovated space in the Medical Sciences Building. Dave continues his vigorous research program in mechanisms of signal transduction; notably concentrating on the protein kinase CK2.

The Department was fortunate to attract several new faculty members. Dr. Bonnie DeRoo became

an assistant professor with her lab located in the London Regional Cancer Centre. Bonnie comes to us from the National Institute of Environmental Health Sciences labs at Research Triangle Park, North Carolina. She is continuing to investigate estrogen receptors and human disease, notably using receptor knockout mice. Dr. Peter Rogan has been hired as Professor from the University of Missouri, Kansas City MO. Peter has a longstanding interest in human genetics and the applications of bioinformatics. His research involves genomic and bioinformatic approaches to predict and study the effects of mutations that alter splicing. Dr. Joe Torchia of the Department of Oncology was cross-appointed in the Biochemistry Department. Joe area of interest is gene regulation and nuclear signalling pathways.

We were sad to say goodbye to Dr. Chris Grant, long-time professor and NMR specialist, who retired and has moved to the west coast for family reasons (and probably to avoid the winters). Chris was awarded a Lifetime Achievement Award for teaching by the Schulich Faculty of Medicine and Dentistry.

University of Waterloo

Dr. Josh Neufeld

Dr. Zoya Leonenko

Department of Biology

Correspondent: Bernie Duncker

2007 marked the 50th anniversary of the University of Waterloo, and for the Biology Department it represented another year of growth.

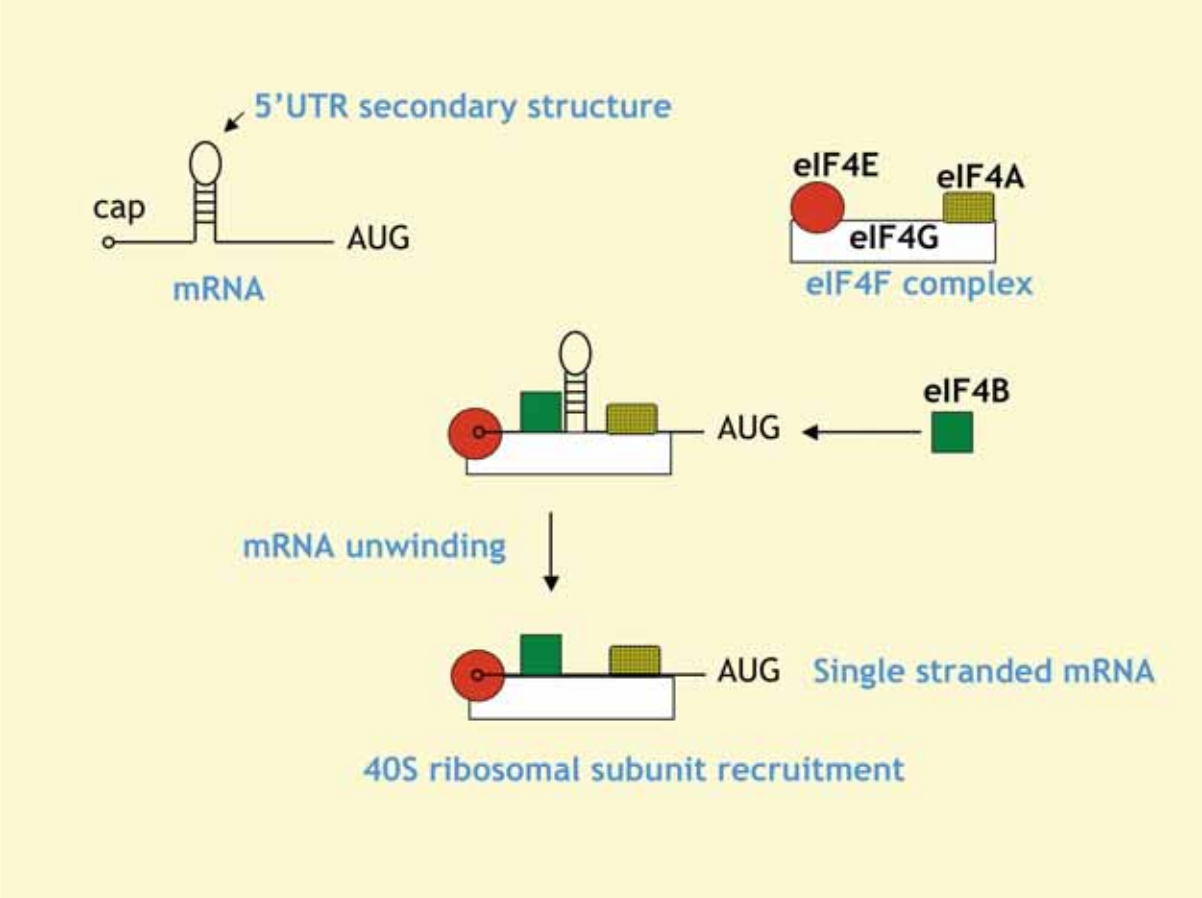
Dr. Josh Neufeld, an environmental microbiologist studying microbial diversity joined us following postdoctoral studies at the University of Warwick, and we also welcomed the arrival of Dr. Zoya Leonenko, a biophysicist studying lipid-protein interactions (jointly appointed to the Department of Physics and Astronomy) who was previously at the University of Calgary.

Two of our colleagues, plant geneticist Dr. Susan Lolle and plant biochemist Dr. Simon Chuong were recipients of NSERC accelerator awards in the first year of this new program. Microbiologist Dr. Bernie Glick came to the end of his second and final term, after six years as Department Chair. While we search for a new Chair of Biology, his predecessor, Dr. Bill Taylor is serving as Acting Chair.

Dr. Susan Lolle

Dr. Simon Chuong

Dr. Bernie Glick



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