Bulletin

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

2005

www.csbmcb.ca

Happy 100th birthday to the ASBMB!

The Canadian Society of Biochemistry, Molecular and Cellular Biology and its members wish to extend their best wishes to our close cousins, the American Society for Biochemistry and Molecular Biology, on the occasion of their centennial.

Of course, many of the members of CSBMCB are also members of the ASBMB, so it is with genuine enthusiasm that we share in the delight of reflecting on 100 years of ASBMB and the Journal of Biological Chemistry. To this end the CSBMCB has contributed a gift of sponsorship for the 2006 Annual General Meeting and Centennial Celebrations in San Francisco, April 1-5, 2006. **Happy 100th, ASBMB!**

ASBMB

CSBMCB SCBBMC

FRONT COVER IMAGE: Supplied by Dr. J. N. Mark Glover, University of Alberta
BACK COVER IMAGE: Supplied by Dr. Eric D. Brown, McMaster University

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CSBMCB President's Report

Dr. David Y. Thomas

Introduction

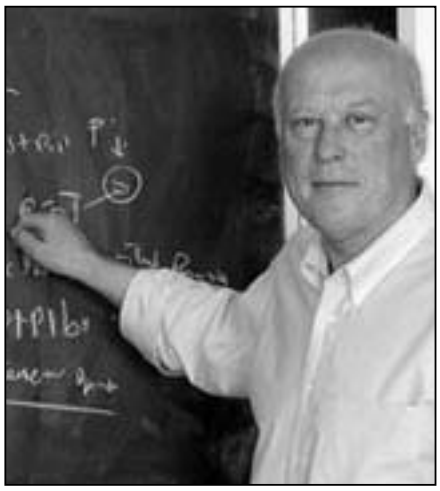
This has been an interesting year for biomedical science and for me, as the President of the CSBMCB, an exciting and busy one. Although most of my attention has been on what can be broadly termed "advocacy", there are a number of other issues that will continue to develop.

Our major concern is, of course, funding for research. The case for biomedical research in general, and basic biomedical research in particular, has always to be made. To be fair, the relevance of projects on the cell cycle studies in yeast and frog's eggs, or oligonucleotide chemistry, or random retrovirus insertions in mice, to, for example, cancer, can be difficult to explain to the public, bureaucrats and our elected representatives, but, as we know, they were essential contributions to our understanding of the cancer process. Perhaps we need better education of our fellow citizens and politicians. Certainly we need to learn how to more effectively communicate the value of fundamental research.

Thanks

The CSBMCB owes its smooth running and dynamism to a small number of dedicated individuals. The administrative functions of CSBMCB are contracted out to the office of the CFBS, where they are ably handled by Wafaa Antonious, the CFBS manager and her assistant Laila Riad. The CFBS, under contract from the CSBMCB, administers our membership list, deals with subscriptions, and distributes communications to our members and for our annual meetings. They also work with Stephen Lau, who manages our website.

I am proud to be working with the dedicated group of volunteers that comprise the CSBMCB board. Vince Duronio (UBC), our Treasurer and Albert Clark (Queen's), our Secretary, have, and are doing, a wonderful job. Dev Mangroo (Guelph), Frances Sharom (Guelph), Linda Penn (U of T), George Chaconas (Calgary), Guy Poirier (Laval), and John Orlowski (McGill) serve the CSBMCB in myriad ways. I would also like to thank Joe Casey (U of A) whose (metaphorically) large shoes I had to fill, and who steered me through a number of sensitive issues. The next President of the CSBMCB is Eric Brown (McMaster) and although my feet are smaller, I look forward to working with him.



Advocacy

Advocacy is one of the most important services that the CSBMCB offers to the community, and the past year has been very eventful. As all of you probably know, there was a letter to Science signed by 40 of our colleagues protesting the method of review employed by Genome Canada. They had employed a due diligence on co-funding and management of the projects by KPMG. Projects had to pass this process before being scientifically peer-reviewed. Although many of us were not in favour of protesting Canadian science funding in this way, many of our colleagues wanted to show their support for the fundamental principle of scientific peer review to find the best science. Thus we hosted the Canadian Science Petition (http://www.csbmcb.ca/e_index.html) and currently we have 1,363 signatures.

Some of the original signatories and myself arranged a meeting with David Emerson, who was then the Liberal cabinet Minister of Industry Canada. Unfortunately, he was not at the meeting, but we did find out that the Federal Government was conducting a review of all genomics funding. We solicited your opinions to

submit a brief to the review. We expressed our support for genomics funding; it impacts most of what we all do these days. However, we questioned the mechanism by which it is currently distributed. For example, you questioned the effectiveness of large scale projects that have to accomplish their goals in 3 or 4 years; and there were many advocates for smaller scale projects that use the considerable genomics information that is already freely available to all of us. Dr. Janet King, Director of the Life Sciences Branch of Industry Canada, recently gave a presentation of how this review is being conducted and the data analyzed. Surprisingly, although many government departments and Genome Canada receive specific funding for genomics, NSERC and CIHR (which both fund genomics projects) do not receive any of this funding. The Federal Genomics Review should be available to us all soon.

For the CIHR external review, Joe Casey solicited your opinions and submitted a brief on behalf of the CSBMCB. A major concern of many of us was the change from the 80:20 funding system that captured the best grants, to a 100:0 system. The reasons for this change are not very clear. It certainly supposes that all grants panels see the same quality of applications, and that all areas of health research are equally well-developed in Canada. I think we all know of outstanding biomedical grant applications scoring over 4 that have not been funded. Other issues of concern were the large number of CIHR institutes of uneven effectiveness; the increasing emphasis on Team grants; the declining proportion of the total CIHR budget that goes to biomedical research; and the low number of biomedical researchers on the Governing Council of the CIHR.

The CFBS, of which the CSBMCB is an associate member, has carried out advocacy and information sessions for parliamentarians in Ottawa over the years. Bruce Sells, who as Executive Director, carried out these functions superbly, has decided to retire. He has been replaced by Art Olson, a biochemist trained at the University of Alberta who has been a deputy minister in several departments in Ottawa, and has a wealth of knowledge and experience of the Federal government. We look forward to working with him (http://www.cfbs.org/newsletter.html).

It is clear to me that Canada needs a formal Science Policy. We no longer have a Science Minister, and research is a "dispersed function" that is distributed among many federal departments. We do have a Federal Science Advisor, Dr Arthur Carty, but he has a staff of 7 to attempt to coordinate all science policy for Canada. One example of this lack of coordination is between the foundations, such as the Canada Research Chairs, the Canada Foundation for Innovation, and the granting councils. I think we all know, or know of, investigators who receive funding for salary and equipment and then do not succeed in obtaining an operating grant. Broader questions on how much Canada should invest in research, what are our strengths, what areas should we develop, are all important to ensure that the taxpayer's money is well spent. The branding of Canada as a great place to do research and a technological powerhouse is essential in a global economy where many countries are newly investing in research.

It is also clear that we need to have advocacy to Federal and Provincial governments and to the granting agencies on issues that directly affect CSBMCB members. There are two new initiatives here. The first is that Joe Casey is now Vice-President of Advocacy and Promotion for the CSBMCB for a period of 3 years. Please contact him with your ideas and concerns. Another development is from an idea of Reinhart Reithmeier's for the creation of the Council of Biomedical Chairs. As we found that the acronym CBC was apparently already taken, this new organization will be called the CCBC (the Canadian Council of Biomedical Chairs). It will become, we hope, an effective channel for communication with the granting councils, politicians, and bureaucrats.

Finally, the most effective advocates for research are us, the researchers. Contact your local and federal politicians about your successes and concerns. Invite them to your lab, enthuse them!

International

One area in which the CSBMCB can play a more active role is in international linkages. The CSBMCB is a member of the International Union of Biochemistry and Molecular Biology, and the International Federation for Cell Biology. Joel Weiner has done stalwart service on the IUBMB over the years, and was instrumental in bringing the IUBMB meeting to Canada in 2004. You will remember that because of the SARS outbreak, the meeting was moved from Toronto to Montreal and fused with the HUPO meeting. The outcome was a very successful well-attended meeting in Montreal. Canada needs more Joels! The CSBMCB and its members should work to not only promote Canadian scientists at international meetings, but also to promote Canadian venues for more scientific meetings. We have many superb locations that are readily accessible to all the world's scientists.

CSBMCB Awards

The recognition of the achievements of our colleagues is always a pleasure. In 2005, Mark Glover, University of Alberta, and Eric Brown, McMaster University, were the worthy recipients of the Merck Frosst prize. This is an annual award to biochemists, molecular biologists or cell biologists with less than ten years of independent research experience, who have made major achievements. Many of our leading researchers have received this award. The Roche Diagnostics prize for 2005 was awarded to our distinguished colleague Dr. Chris Bleakley from the University of Alberta.

Recognizing the successes of our colleagues is always one of the great pleasures of scientific life. Nominations are always welcome, and nominees are considered for three years. Please contact Albert Clark (Queen's) clarkaf@post.queensu.ca.

Meetings

I am pleased to report that the CSBMCB is in a robust state of health. The formula of a single high-quality "Gordon Research" type conference per year has paid off. The 2005 48th Annual Meeting of the CSBMCB at the Banff Centre for the Arts, on "Cellular Dynamics" organized by the two "Ricks", Rick Wozniak and Rick Rachubinski, was a masterpiece of this genre - outstanding presentations, superb attendees, both harmony and controversy in an idyllic setting with great skiing. What scientist could wish for more?

The 49th Annual Meeting 2006 of the CSBMCB is on Membrane Proteins in Health and Disease and is being organized by a committee chaired by Reinhart Reithmeier. The meeting will be held at the White Oaks Conference Resort and Spa in Niagara-on-the-Lake, Ontario. Reinhart and the Local Organizing Committee have put together a fantastic programme of stellar scientists and I hope to meet many/most of you there.

The 50th Annual Meeting of the CSBMCB will be in Montreal July 4-8, 2007 on the topic of "Systems and Chemical Biology". Eric Brown and myself are chairing the organizing committee (presently Mike Hallett, McGill; Guy Poirier, Laval; Dan Figeys, U of Ottawa; and the meeting coordinator, Nancy Dufour). We are developing a dynamic scientific programme. The meeting will be held at a venue that will provide affordable accommodations and is just a short stroll away from the Montreal Jazz Festival. For this 50th meeting we would like to contact as many of the original members of the Canadian Biochemical Society as possible and have your recollections of the founding and early days of our Society. Please contact me at david.thomas@mcgill.ca if you would like to contribute.

Membership

Our membership can always be increased and we rely upon our members to broadcast the advantages of the CSBMCB. We had an influx of new members from the PENCE network his year. This was organized by Steve Withers (UBC) who wished to set up a mechanism so that PENCE network members could continue to meet regularly. Many PENCE participants were already CSBMCB members and we welcome the new members.

Finally, it has been a pleasure to serve as President of the CSBMCB. I look forward to continuing to play an active role and I encourage you, too, to play an active role in your society.

Incoming Member of the CSBMCB Executive Board 2005-2006

Dr. Eric Brown, Vice-President

I grew up in rural southern Ontario and attended high school in Dundas, a little town West of Hamilton that lays claim to an international 'cactus festival.' Guelph became my second home after high school – I spent 10 years there completing my undergraduate and graduate degrees. The latter began with a Masters in the Food Science department with Dr. Rickey Yada where I discovered my passion for protein biochemistry studying the stability of fungal aspartic proteases on the pretext that they were key ingredients in cheese-making. It was, nevertheless, as a Ph.D. candidate in Biochemistry at Guelph that my future was cemented in molecular approaches to understanding the puzzles of bacterial physiology in the laboratory of Dr. Janet Wood. There I studied the PutA protein, a fascinating flavoprotein that binds to and represses its own operon in addition to interacting with the cell membrane where it catalyzes the oxidation of proline.

After receiving my Ph.D. in 1992, I accepted a postdoctoral fellowship to train with Dr. Christopher Walsh in the department of Biochemistry and Molecular Pharmacology at Harvard Medical School where I worked to describe the mechanisms of enzymes in bacterial cell wall biosynthesis. There I learned a great deal about pre-steady state kinetics, characterizing enzyme intermediates and enzyme inhibitor complexes. During the same period I embarked on studies of the dispensability of cell wall biosynthesis genes in E. coli, a collaboration that placed me in the laboratory of Dr. Roberto Kolter in the Department of Microbiology and Molecular Genetics at Harvard Medical School. After postdoctoral studies, I decided to stay in the Boston area and work in the biotechnology sector where I spent more than three years, principally at Astra Research Center Boston, using enzymology and molecular genetic approaches to develop drugs against the gastric pathogen Helicobacter pylori. While in Boston I became a huge admirer of the city and was an enthusiastic sampler of New England attractions, especially its pro sports venues, golfing and Irish pubs.

After six years in Boston, I elected to return to Canada to develop an independent research program and took up a position in Department of Biochemistry at McMaster in July of 1998, first as a CIHR Scholar and now as a Canada Research Chair. Perhaps indelibly marked by my time in pharma, my group has adopted the motto 'the only good bacterium is a dead bacterium.' We have concentrated to date on addressing the inadequacies of conventional antibiotics with research into new approaches to the discovery of antibacterial drugs. Those directions have included careful analyses of the phenotype associated with loss of novel and essential functions to help us understand their importance to bacterial physiology. We have likewise occupied ourselves with rigorous biochemical studies of key proteins in an effort to learn more about their roles in physiology and to facilitate their exploitation in antibacterial drug discovery. Most recently, we have been developing chemical genomic approaches where, with the benefit of state of the art small molecule screening, we are working toward building a chemical-genetic interaction network for the essential physiology in bacteria. Since returning to the Hamilton area, it's been great to spend time again with family and old friends. I attribute any perspective I have to my wife Zuhal and seven year old Jacob, not to mention my very average skills in golf and ice hockey.

Minutes of the 48th Canadian Society of Biochemistry, Molecular and Cellular Biology Annual General Meeting

Banff Conference Centre, Banff, Alberta
Friday, March 18, 2005, 15:00-17:00 h

Chair: Dr. Joseph R. Casey, President, CSBMCB

Board Members in Attendance: Joseph Casey, David Thomas, John Orlowski, Linda Penn, Dev Mangroo

762. Approval of Agenda

The agenda was approved as circulated on a motion from Dr. Andrews which was seconded by Dr. Thomas.

763. Approval of Minutes of the 47th AGM

No changes were requested. The minutes were approved as circulated on a motion from Dr. Andrews which was seconded by Dr. Thomas.

764. Business Arising from the Minutes

1. The CSBMCB Website needs revision. Drs. Mangroo and Brown have volunteered to monitor the Web pages for errors and areas that need updating, and then communicate this information to Dr. Duronio who is responsible for maintaining the Website.

2. The email survey of our membership regarding advocacy issues was completed by Dr. Casey. A report was written and circulated, and will be included in the upcoming issue of the Bulletin.

3. The next Board meeting will be held in Montreal in October/November 2005.

4. The potential commercial deal with 'Brain Hunter' was cancelled as it was thought to be too restrictive and difficult to implement.

5. Drs. Orlowski and Penn have volunteered to serve as co-Editors of the LINK.

765. President's Report

1. Upcoming CSBMCB Meetings

2006- Planning for the 49th Annual meeting is well under way. A committee headed by Reinhart Reithmeier (University of Toronto) is organizing the meeting "Membrane Proteins in Health and Disease" at Niagara-on-the-Lake (Ontario) from May 31- June 4, 2006.

2007- The 50th Anniversary meeting for CSBMCB will be something special! David Thomas (McGill) and Eric Brown (McMaster) head the organizing committee for this meeting on "Systems Biology," which will be held in summer 2007 in Montréal, Québec.

2. CSBMCB Awards

One of the most important roles of CSBMCB is to recognize excellence in Canada's biochemists, molecular biologists and cell biologists. In 2005 we awarded the Merck-Frosst Award for meritorious research by a scientist in the first 10 years as an independent scientist jointly to Mark Glover of the Department of Biochemistry, University of Alberta, and Eric Brown of the Department of Biochemistry, McMaster University. Winner of the Roche Diagnostics Award for 2005 was Dr. Chris Bleackley, of the Department of Biochemistry, University of Alberta.

3. Advocacy Survey

Results of our advocacy survey show that many of CSBMCB members are passionate about science

policy and support the CSBMCB in an invigorated approach to advocacy for our member's research interests. The message to us was clear: continue to push the interests of CSBMCB with members of the federal government, but also have a greater dialogue with the granting councils.

4. Science Policy and Advocacy

One of the key roles of CSBMCB is to keep government officials aware of the needs of biochemists, molecular biologists and cell biologists. Our ongoing efforts in this direction include our support of the Canadian Federation of Biological Societies (CFBS). Part of your CSBMCB membership supports the advocacy efforts of CFBS. Bruce Sells, executive director of the Canadian Federation of Biological Societies, has developed excellent contacts with Parliamentarians. Through working with Bruce we have affected CFBS policy and gained access to Parliamentarians for discussions. Clearly the major issue confronting CSBMCB members is sustained, or increased operating budgets and we continue to press this point in all of our meetings with the government. The good news is that advocacy efforts work. Parliamentarians and senior government officials know about the importance of our research, but still need continued polite pressure.

Over the last year we have taken on two new initiatives in our advocacy efforts. First, we helped to sponsor the "Leader's Forum for Health Research in Canada" (see report at http://www.cfbs.org/newsletterLeadersFrm.html). The goal of the event was to bring together a wide range of Canadians working in health research, to try to drive a common view and thereby increase research support. We are hopeful that from the Leader's Forum will come more effective advocacy for our research activities. Second, we have begun to develop interactions with the Council for Health Research in Canada (CHRC). CHRC has emerged as an effective group advocating on behalf of health researchers. Since their interests are very much aligned with ours we have begun to work with them, with the hope of affecting their policy to the benefit of CSBMCB members. Working with CHRC we hope to amplify our advocacy efforts.

5. CSBMCB and PENCE

The funding of Protein Engineering Network of Centres of Excellence (PENCE) ended in 2005. The Canadian Proteomics Initiative (CPI), which had its annual conferences sponsored by PENCE, is now considering in what form to continue. Discussions are underway to decide how CSBMCB and CPI/PENCE can interact in the future to benefit both organizations.

6. Membership

CSBMCB needs a strong membership base in order to thrive. Annual membership fees provide the operating budget for the society. Of equal importance is to have a large numerical base of support. When we lobby politicians on policy they want to know how many scientists we represent. How valid is our voice? With a strong membership base we can advocate strongly for Canadian biochemists, molecular biologists and cell biologists. CSBMCB councilor Linda Penn (Toronto) has done a terrific job to build our membership through several initiatives. Among these, Linda has found CSBMCB representatives at departments at Universities across the country. My thanks to those who agreed to take on this task!

7. Communications

We thank CSBMCB Councilor, Frances Sharom (Guelph), for putting the Bulletin together. We also thank CSBMCB Departmental representatives for supplying the departmental news reports! The CSBMCB Link is now one year old. The link is published three times per year and serves as a more regular way to communicate with the CSBMCB. The link contains articles about the science successes of CSBMCB members and reports on science advocacy efforts of the CSBMCB. We thank founding Editor, Caren Helbing (Victoria), for her great work on The Link. John Orlowski (McGill) and Linda Penn (Ontario Cancer Institute) will take over as co-Editors.

8. Thank you(s)

CSBMCB is an active organization with a surprising amount going on behind the scenes. Keeping CSBMCB running requires the efforts of many people, some of whom I would like to thank here. CSBMCB has contracted CFBS to take care of

some of our administrative needs. Wafaa Antonious, CFBS Manager, Administration and Planning, has been tireless in her efforts to keep us on track; from dealing with our electronic communications, to our website and financial affairs. Laila Riad, CFBS Administrative Assistant, has also worked with Wafaa on our behalf. Kim Bournat of the Department of Physiology, University of Alberta, has been very helpful with secretarial assistance, in particular with the advocacy policy survey.

The annual meetings of CSBMCB occur because of the hard work of many people. The 2004 CSBMCB meeting was organized by Terry Hébert (Université de Montréal). Terry put together an outstanding program on "Cell Signaling" From the Membrane to the Nucleus", which was held at Mt. Tremblant Québec.

In most organizations, and CSBMCB is no exception, it is actually the Secretary and Treasurer who do most of the work. This has been particularly true over the last year for our Secretary Albert Clark (Queen's U.) and Treasurer, Vince Duronio (UBC). Vince and Albert have done a terrific job, working with dedication as we all have scrambled to figure out how to function after our long-time Treasurer (Fred Palmer) and Secretary (Gene Tustanoff) retired a year ago.

Each of the members of the CSBMCB board is an active researcher, who has given up their time to attend our board meetings and ensure that the Society runs efficiently and effectively. This year Eric Brown (McMaster), Frances Sharom (Guelph) and Dev Mangroo (Guelph) have infused the board with enthusiasm as new CSBMCB Councilors. David Thomas, Chair of Biochemistry at McGill, has stepped up to act as CSBMCB Vice-President and will be President next year. Caren Helbing (Victoria) has completed her term as Society Councilor, with many thanks for her significant contributions to the editing and production of the last two issues of The LINK! John Orlowski will soon be completing his three years as Vice-President, President and Past-President of CSBMCB. John put tremendous energy and creativity into his time on the CSBMCB executive and set a great example for those of us following him.

9. Future Outlook

The future looks bright. The current CSBMCB board is energized and full of ideas. The challenge is to convince the government to continue to increase research funding. However, lobbying efforts are paying off. From discussions with the government it is clear they have heard our message. Increasing CSBMCB membership gives us more clout when we lobby. The recent advocacy survey was a shot in the arm; many CSBMCB members feel strongly about policy issues, and thankfully, for the most part our views seem to represent the survey responses. CSBMCB annual meetings continue to be a source of pride. These meetings have attracted considerable positive feedback for their combination of cutting-edge science in enjoyable places. We are certain that the upcoming scheduled meetings will continue to be outstanding. It has been a pleasure to be involved in honouring Canada's amazing scientists with CSBMCB awards.

It was moved by Dr. Thomas and seconded by Dr. Andrews that the President's Report be received.

CARRIED.

766. Past-President's Report

Dr. Orlowski reported that he has been re-organizing the electronic files of the former Secretary, Dr. Gene Tustanoff. Most of these have already been transferred to the new Secretary, Dr. Albert Clark, with the remaining to be transferred shortly. Furthermore, he intends to gradually digitize the older documents of the Society for archival purposes.

Dr. Orlowski also reported that he wrote a brief article to be published in the upcoming edition of the Bulletin summarizing some of the highlights and his impressions of the 2004 AGM held at Mont Tremblant. He also organized and catalogued all the pictures taken at the 2004 AGM for inclusion in the Bulletin.

767. Vice-President's Report

Dr. Thomas began his report by thanking Dr. Casey for his term as President of CSBMCB.

Dr. Thomas next reported on his activities related to advocacy for the CSBMCB community.

1. Advocacy

I attended the CFBS Sixth Annual Strategic Planning Meeting on Saturday, November 20, 2004. This was an interesting meeting with representation from a wide variety of life sciences research organizations both in the academic and government sectors and the granting agencies. A report of the meeting can be found at http://www.cfbs.org/current.html. The CFBS certainly represents a large number of Canadian Life Scientists with diverse interests. Whether it can represent all those interests effectively is another question. The value of membership in the CFBS for the CSBMCB may also be somewhat diminished when Bruce Sells retires. I suggest that we revisit the membership of CSBMCB in the CFBS at our next board meeting. Other lobbying and advocacy routes for us could be the 'Partnership Group for Science and Engineering' (PAGSE see http://www.pagse.org/en/main.htm) and the 'Council for Health Research in Canada' (CHRC see http://www.chrc-crsc.ca/). In addition, Reinhart Reithmeier Chair of the Department of Biochemistry at University of Toronto, has suggested the founding of the Canadian Biochemistry Chairs (provisionally the CBC) as a coordination and advocacy group. The CBC could have advocacy roles with the government and with the granting agencies. I will be helping him set this up.

2. Meetings

The 50th Annual General Meeting of CSBMCB in 2007 will be held in Montreal at the time of the Montreal International Jazz Festival (end of June, beginning of July).

Receipt of Dr. Thomas's report was moved by Dr. Casey and seconded by Dr. Penn.

CARRIED.

768. Treasurer's Report

Dr. Duronio was unable to attend the AGM, but sent along his report (below) which circulated to those in attendance. The report was read by Dr. Casey.

1. Preamble

I'm sorry that I was not able to join you in Banff for this tremendous meeting. I have summarized some of the relevant issues that I've been dealing with. I look forward to hearing from any of you that may have questions.

2. Financial statements

I have attached the financial statements that were submitted for inclusion in the bulletin. They include the audit for 2003 and an unofficial statement for 2004. This was provided by Wafaa, as she enters all financial information and thus can generate reports relatively easily. The only change that should be noted is the additional $5000 recently promised from the Institute for Cancer Research that will be credited to the income for the 2004 meeting. Thus, our loss for last year will be just under $6500. However, this is more than made up for by the gain in value of the special fund, which increased year over year by over $35,000. I am pleased to let you know that the fund value was just over $401,000 as of March 4th and thus we are benefiting from a favourable market at the moment. The attention provided by Mark Wilson of BMO Nesbitt Burns has been excellent. He speaks to me about every decision in great detail, giving sound rationale for any changes in the investments.

3. CFBS Contract

I have also attached the most recent version of the contract with CFBS, with a breakdown of activities (of Wafaa and Laila) billed to CSBMCB. The amount we paid for 2004 is greater than originally anticipated, but perhaps it might have been expected given that there were a lot of changes occurring last year due to changes in treasurer, secretary, move to completely electronic communication with members, and with a relatively complicated audit. We should wait to see what the 2005 expense will be, and perhaps do a review of the contract to determine whether we are getting good

value. Note that we are paying several dollars for each student or postdoctoral fellow that signs up. While I suppose this is not a big problem, one issue that has been a bit problematic is any paper forms filled out by students. These end up being hard to read in many cases, and the data has to be entered manually. We should not allow such applications, making a policy that student and postdoctoral fellow applications will only be accepted using the online form.

4. Membership

For 2005, I tried to be a bit more pro-active by getting out membership invoices before the end of 2004, and there has been a second notice sent out a couple of weeks ago. As an aside, I realized I should have sent the notices in both English and French – did this with the second one, but not the first. The numbers so far look encouraging. We have somewhere around 220 paid up members. I noted from looking at a recent list that there were at least 22 members who were new, which might be a reflection of the membership drive working. A third invoice will be going out to delinquent members in the next couple of weeks. I suggest I make use of our university reps to make personal contact about a month or so after that. I think this should be no more than 5 or 6 persons per university, so it should not be a big burden. There are also those who may not have paid the last year or two, but are still on our list, and just ignore messages. I have been instructing Laila to remove members from the list when they have not paid for two years, and have not responded to email requests. We are also following up by mail with anyone for whom we do not have an email, or the email doesn't work. Let me know if anyone sees any problem with my approach to this.

5. Website

At our executive meeting, I discussed an online members database, and perhaps other changes to the website. I have not yet had a chance to contact Stephen Lau to get more concrete estimates of cost and what this would look like. I will try to follow up on this soon. Please let me know if anyone has specific ideas for changes – I think we discussed trying to get a completely new design for the site.

Receipt of Dr. Duronio's report was moved by Dr. Thomas and seconded by Dr. Penn.

CARRIED.

769. Secretary's Report

Dr. Clark was unable to attend the AGM. Instead, Dr. Orlowski acted as Secretary. No report was submitted.

770. Councillor's Report

a. CSBMCB University/Research Institute Representatives: Dr. Penn reported that after considerable effort, approximately 40 individuals from institutions across the country have agreed to serve as local representatives/liaisons for the Society. Dr. Penn was thanked and commended for her extraordinary efforts in organizing this initiative.

b. Bulletin: Dr. Sharom was unable to attend the AGM, but communicated to the Board that the 2004 issue of the Bulletin was in press and will be shipped shortly.

771. New Business

a. CSBMCB contract with CFBS: see Treasure's report.

b. Canadian Proteomics Initiative (CPI): Dr. Steve Withers made a brief presentation on behalf of the Canadian Proteomics Initiative (CPI) to establish an alliance with CSBMCB to help support their annual meetings now that their former sponsor, PENCE, will cease to exist as an organization in 2005.

After considerable discussion, a motion was proposed that:

"The Society approve the establishment of a relationship between CPI and CSBMCB, with the goal of maintaining the existence of the CPI. The nature of this relation must be approved by the Board of CSBMCB, and subsequently ratified by both the Boards of CSBMCB and CPI/PENCE by the end of October 2005."

MOTION CARRIED.

c. Presentation on 2006 Annual General Meeting: Dr. Reinhart Reithmeier provided a detailed scientific and financial plan (appended) for the upcoming 49th AGM entitled 'Membrane Proteins in

Health and Disease' to be held at the White Oaks Conference Resort in Niagara-on-the-Lake, Ontario from May 31-June 4, 2006.

Dr. Reithmeier was commended for his fine efforts on what promises to be a very exciting and stimulating meeting.

d. CSBMCB policy on meeting sponsorship: Dr. Casey reported that a draft document describing the Society's policy on sponsoring conferences other than our own AGM should be completed shortly for presentation and final approval by the Board.

e. Other business: Dr. Thomas was sent an email from the Editor of Biochemistry and Cell Biology requesting funding to sponsor a meeting on chromatin structure and epigenetics. The consensus was that a formal proposal should be made before a decision could be reached.

Dr. Reithmeier suggested that the Society should change its name to something simpler. After some discussion, it was generally felt that the current name should be maintained.

772. Adjournment

The meeting was adjourned at 17:05 PM on a motion from Dr. Casey which was seconded by Dr. Thomas.

APPENDICES

[I]

Treasurer's Report – CSBMCB

Treasurer's note: With the change of the treasurer's office from Dr. Fred Palmer to Dr. Vincent Duronio, a complete audit was undertaken for the 2003 fiscal year (Jan. 1-Dec. 31, 2003) by Ms. Tammy Bastarache (Ottawa, ON) which had not been done for several years. The application of strict accounting rules resulted in some adjustments being made to previous financial statements, but these were primarily due to deferred expenses and revenues. A decision was made by the executive to retain Ms. Bastarache as the society's accountant, and do a yearly audit. In this year's bulletin, I include numbers from the official audit for 2003, as well as an unofficial financial statement for 2004.

[II]

49th Annual Meeting and Conference of the Canadian Society of Biochemistry, Molecular and Cellular Biology (CSBMCB/SCBBMC)

Membrane Proteins in Health and Disease

Organizing Committee

Reinhart Reithmeier (Chair), University of Toronto (r.reithmeier@utoronto.ca)
David Andrews, McMaster University (andrewsd@mcmaster.ca)
Frances Sharom, University of Guelph (fsharom@uoguelph.ca)
Joseph Casey, University of Alberta (joe.casey@ualberta.ca)
Jean-Yves Lapointe, Université de Montréal (jean-yves.lapointe@umontreal.ca)
Rob Reedijk (Administrative Assistant), University of Toronto (rob.reedijk@utoronto.ca)

DATE
Wednesday, May 31, 2006-Sunday, June 4, 2006

LOCATION
White Oaks Conference Resort
253 Taylor Road
Niagara-on-the-Lake
Ontario, Canada L0S 1J0
www.whiteoaksresort.com
Tel: 1-905-688-2550 or 1-800-263-5766

The five star White Oaks Conference Resort and Spa is located in Niagara-on-the-Lake just off Queen Elizabeth Way, about 1 h drive from Toronto or Buffalo. The Resort is completely non-smoking and features a superb fitness/sports club and spa. It is central to Niagara's best wineries, golf courses, hiking trails and is very close to Niagara Falls with all its attractions. Sessions are held in the morning and evening, with afternoons free to partake in other activities.

HOTEL CONTACT
Randi Etherington
Tel: 1-905-704-5685 or 1-800-263-5766, ext. 5685
Reinhart Reithmeier will be the contact person

REGISTRATION

Meeting	Hotel/CSBMCB
Accommodation	Hotel

REGISTRATION FEES

Faculty (non-member)	$400
Faculty (member)	$325
Students and Fellows (non-members)	$350
Students and Fellows (members)	$275

Off-site registration supplement (coffee breaks, breakfast, lunch and dinner) $150 per day ($600 total)

ACCOMMODATION

- 200 rooms reserved (both single and double)
- 4 nights includes breakfast, lunch and dinner plus continuous coffee breaks

$704 ($176 per person per night double occupancy) + gratuity and taxes (~$910 total)

$1012 ($253 per person per night single occupancy) + gratuity and taxes (~$1,300 total)

PARTICIPANTS

Goal is 250 people (includes 30 Speakers and members of Organizing Committee)

FACILITIES

Grand Event Room A/B
Lecture seating for up to 300

Grand Event Room C
Poster and exhibit display

Lobby
Registration desk and coffee breaks

Sunhill Dining Room
Breakfast, lunch and dinner for 250

Studio 8
Board meeting (15 people)

Ballroom
Saturday banquet with wine

MEALS

Breakfast
Morning coffee break
Lunch
Afternoon coffee break at posters
Dinner
Banquet on Saturday with wine

Cash bar (Thursday and Friday, 4:00-6:00 pm) with poster sessions

Cash bar (Thursday and Friday, 10:00-12:00 pm) with poster sessions

AUDIOVISUAL

- Large white screen in Grand Event Room
- LCD projector(s) with backup projector
- Podium with microphone (wireless)
- Pointer
- Table for laptops

POSTER BOARDS

- 25 double-sided poster boards (4' high x 6-8' wide) to be rented and delivered
- Exhibitor space (10 exhibitors @ 10 ft x 10 ft each) in coffee area)

ABSTRACTS AND POSTERS

Frances Sharom

- Abstract submission, template, poster competition, travel awards, oral presentation
- Poster judging
- Travel awards

CSBMCB LIAISON

Joe Casey

- Web site
- Awards lectures, travel awards, banquet, poster awards, plaques,
- Merck Frosst Representatives

BIOCHEMISTRY AND CELL BIOLOGY SPECIAL ISSUE

Editors: Carol Cass and Joel Weiner
Meeting Report: Frances Sharom
Papers and abstracts

FUND RAISING AND EXHIBITOR BOOTHS

David Andrews and Jean-Yves Lapointe

FRENCH TRANSLATION

Jean-Yves Lapointe

CIHR TRAINING PROGRAM SYMPOSIUM

Wednesday, May 31, 2005 2:00-5:00 p.m with coffee and cookies
Charles Deber

BUDGET

EXPENSES

Speakers Costs	
30 speakers @ $1,000 travel	$30,000
Accommodation 30 @$1,300	$40,000
Transportation for speakers from and to airport	$ 3,000
Web-site set-up for registration	$ 1,500
Advertising (web-site, posters)	$ 2,000
Opening mixer (1 free drink, snacks)	$ 3,000*
Poster Board Rentals (25 Boards)	$ 3,000
Wine for Banquet (100 bottles @ $30)	$ 3,000*
Icewine gift for Speakers (30 @ $35)	$ 1,000*
Miscellaneous office costs/room rentals	$ 2,000
Administrative Assistant	$ 2,000
Coffee Breaks	Included
Lecture and Dining Room Rentals	Included
Audiovisuals	Included
Accommodation for registrants	Directly with hotel
Total	**$90,500**

*sponsored events

REVENUES

Registration (200 total)	
50 Faculty (Members) @$325	$16,250
50 Faculty (Non-members) @ $400	$20,000
50 Graduate Students and Fellows (Members)@ $275	$13,750
50 Graduate Students and Fellows (Non-members)@$350	$17,500
CSBMCB (refundable)	$ 5,000
CIHR Training Grants	$10,000
Department of Biochemistry (Toronto)	$ 2,000
Other Departments	$10,000
Exhibitors (10 @ $2,000)	$20,000
Sponsors (corporations)	$10,000
Total	**$112,500**

TRAVEL AWARDS

Expenses
Revenues

POSTER PRIZES

Expenses
Revenues
Exhibitors booths (10 @ $2,000 each, free registration for 2)

SPONSORS

CSBMCB	$5,000
Department of Biochemistry, University of Toronto	$2,000
CIHR	
CIHR Training Program in Structural Biology of Membrane Proteins Linked to Disease	$5,000
CIHR training Program in Membrane Proteins and Cardiovascular Disease	$5,000

CSBMCB/SCBBMC Audit

Statement of Financial Position

December 31	2004	2003
Assets		
Current assets		
Bank	$7,058	$11,130
GST receivable	3,201	305
Accounts receivable & accrued membership fees	5,107	1,282
Prepaid expenses	-	6,000
	15,366	18,717
Investments – at market value (Note 3)	385,719	354,503
	$401,085	$373,220
Liabilities and surplus		
Current liabilities		
Accounts payable & accrued liabilities	$14,253	$5,036
Deferred revenue	4,299	10,019
	18,552	15,055
Net assets	382,533	
358,165	$401,085	$373,220
Statement of Changes in Net Assets		
Net assets, beginning of year	$358,165	$344,232
Excess of revenues over expenses for the year	24,368	13,933
Net assets, end of year	$382,533	$358,165
Statement of Revenue and Expenses		
Revenue from operations		
Memberships	$15,743	$15,998
Corporate contributions	66,812	33,000
NRC loan forgiveness-	--	25,000
Annual meeting & other	7,028	1,554
	89,583	75,552
Investment revenue		
Interest, dividends & other investment income	14,655	13,689
Realized & unrealized capital gains	21,561	45,122
	36,216	58,811
Expenses		
Gifts	1,700	-
Funding & other sponsorship	4,500	-
Annual meeting	65,385	82,580
Bank & credit card fees	1,073	655
Board meetings	8,139	10,125
Bulletin	6,079	7,761
Management fees	8,160	4,473
Dues & subscriptions	1,317	464
Computer support	-	5,708
Lobby expenses	-	78
Newsletter	1,765	2,880
Publicity	-	1,955
Office	275	1,218
Postage & courier	163	333
Audit	2,875	2,200
	101,431	120,430
Excess of revenues over expenses for the year	$24,368	$13,933

Statement of Cash Flows		
Cash flows from operating activities		
Cash received from members and events	$80,038	$84,289
Cash paid to suppliers	(89,110)	(121,354)
Cash flows from operating activities	(9,072)	(37,065)
Cash flows from investing activities		
Investment income	14,655	13,689
Proceeds from sale of investments	76,976	49,300
Purchase of investments	(62,291)	(15,628)
	29,340	47,361
Net change in cash and cash equivalents	20,268	10,296
Cash and cash equivalents, beginning of year	23,850	13,554
Cash and cash equivalents, end of year	$44,118	$23,850
Cash and equivalents is made up of:		
Bank account	$7,058	$11,130
Cash held with investment broker	37,060	12,720
	$44,118	$23,850

Investments – at market value		
Nesbitt Burns Canadian $ account	**2004**	**2003**
Cash & short term investments$	37,060	$11,462
Fixed income	70,714	87,383
Common equity	224,790	203,841
Investment trusts	49,333	50,559
	381,897	353,245
Nesbitt Burns U.S. $ account (in Canadian $)		
Cash & short term investments	-	1,258
Common equity	3,822	-
	3,822	1,258
	$385,719	$354,503

Income Statement (Cash basis) 1/1/2005 to 12/31/2005

REVENUE	
Membership Revenue	
CSBMCB Membership Fees	16,413.44
CFBS Membership Fees	12,560.00
Membership Total	28,973.44
Annual Meeting	
Meeting Sponsors	26,500.00
Annual Meeting Registration	0.00
Exhibits Revenue	0.00
Meeting Revenue Total	26,500.00
Other Revenue	
Member List Sale	600.50
Website	700.00
Miscellaneous Revenue	0.00
Total Other Revenue	1,300.50
TOTAL REVENUE	56,773.94
EXPENSE	
Bulletin Expenses	
Bulletin Printing	5,321.65
Bulletin Mail out	771.24
Total Bulletin	6,092.89
Annual Meeting Expenses	
Exhibit & Facility Expenses	0.00
Receptions & Banquets	0.00
Speakers Travel & Expenses	2,010.09
J Manery Fisher Award	1,000.00
MerckFrosst Award	11,250.00
Roche Award	2,500.00
Awards Total	14,750.00
Meeting Supplies	73.98
Other Meeting Expenses	250.00
Meeting Total Expenses	17,084.07
Other Expenses	
CFBS Fees	13,573.08
The Link Expenses	0.00
Admin Printing	2,575.00
Lobby Meetings & Travel Expenses	0.00
Science Policy Funding	0.00
Other Meetings Sponsorship	1,750.00
Other Org. Mmb. Fees (IFCB & PABMB)	3,782.77
Board Meetings & Travel Expenses	6,557.33
CFBS Admin Contract	16,425.01
Other Expenses Total	44,663.19
General & Administrative Expenses	
Accounting & Legal	0.00
Advertising & Promotions	384.83
Courier & Postage	0.00
Credit Card Sales Discount fees	818.92
Credit Card Interest & fees	12.00
Interest & Bank Charges	83.14
Website Expenses	4,550.00
Total General & Admin. Expenses	5,848.89
TOTAL EXPENSE	73,689.04
NET INCOME	(16,915.10)

Special Fund

Market Value, 12/31/2004	385,721.48
Withdrawals in 2005	17,000.00
Market Value, 12/31/2005	400,560.85

Treasurer's note:
The above auditor's report is for the 2004 financial year and gives the official figures for that year. In the unofficial income statement for 2005 there is a net loss reported for the year. This will not be the case when the accounts are settled from our successful annual meeting held in Banff in March 2005. We will be receiving those funds early in 2006, but they will be credited to the 2005 fiscal year.

The Advocacy and Lobbying Report
Update

The CSBMCB has been very active on your behalf this year. The Canadian Science Funding petition is hosted on the CSBMCB website (http://www.csbmcb.ca/e_index.html). The petition arose from a well-publicized protest of some of our colleagues about the review of co-funding and project management by accountants for the last Genome Canada competition. Applications had to pass this step before the quality of their science was reviewed. There was a fundamental principle in research funding at stake, and we agreed to host the petition so that our colleagues can show their support for this principle. Currently there at 1,863 signatures. Following up on this we scheduled a meeting with David Emerson who was at that time the Liberal Minister of Industry Canada. Although he could not attend the meeting we had a productive meeting with some Industry Canada staff and then with the Federal Science Advisor, Dr. Arthur Carty and Dr. Peter Nicholson from the Prime Minister's office (Dr. Nicholson is now the head of the new Canadian Academies of Science).

We solicited your opinions for two focused advocacy efforts. The first was for the Federal Genomics Review that is reviewing all funding for genomics and proteomics research. The report will be ready in May 2006. The second was organized by Joe Casey for our input into the external review of the CIHR. For both, the response from CSBMCB members was excellent and eloquent.

Another initiative suggested by Reinhart Reithmeier is the Canadian Council of Biomedical Chairs. This would be a more focused lobby group representing the biomedical basic sciences to governments and granting agencies.

The CFBS has now a new Executive Director, a biochemist trained at the University of Alberta, Dr. Art Olson. Art has a lot of experience in working in government departments and we look forward to working with him

The most effective voices for research are us, the researchers. Let your community and MP know about your successes and concerns. Maybe we can all adopt an MP and have them working in our labs for a day?

48th Annual Meeting of the CSBMCMB: A Glowing Report of our 2005 Meeting

Joe Casey, Past-President CSBMCB

The 48th annual meeting of CSBMCB was held from March 16-20 2005 at the Banff Centre, Banff Alberta, with the Topic, "Cellular Dynamics." The meeting was a spectacular success, which came as no surprise, because all the ingredients were there: a stellar line-up of speakers, the magic of a Rocky mountain setting, and good weather for skiing (and science).

The meeting began strongly with a keynote presentation by Nobel Laureate, Dr. Günter Blobel (Rockefeller University). In the unenviable position of following up a talk by a Nobel Prize winner were this year's co-recipients of the CSBMCB award for researchers in the first ten years of independent career (the Merck-Frosst Prize), Dr. Mark Glover (University of Alberta) and Eric Brown (McMaster University). Rounding out the first evening was Dr. Chris Bleackley (University of Alberta), winner of the Roche Diagnostic Award for a senior researcher.

Meeting organizers Dr. Rick Wozniak and Rick Rachubinski of the University of Alberta, along with their organizing committee, deserve our thanks for assembling a diverse set of sessions that provided an overview of the state of the art in cell biology today. Session topics were "Organelles of the Secretory Pathway", "Emerging Technologies", "Imaging Technologies", "Organelle Inheritance", "Protein Folding", "Nuclear Dynamics", "RNA Localization" and "Systems Approaches to Cell Biology." Together, these sessions highlighted the strength of CSBMCB meetings: providing cutting edge science on a focused topic and in an excellent setting. The opportunity to experience high quality science in a relatively small meeting makes for an unforgettable time, indeed. Many aspects of the meeting were memorable, but without doubt the quality of modern imaging techniques was evident throughout the talks, and is clearly now central to cell biology. Students commented on the fact that virtually all the talks were glowing with fluorescent proteins!

Based on numbers, the meeting was a great success, attracting 157 attendees, 68 posters and 50 speakers drawn from Canada, the United States, the Netherlands and Switzerland. Eleven students from across Canada won travel awards from Merck Frosst to support their attendance at the meeting. Eight prizes for outstanding poster presentations (three supported by Roche Diagnostics, and five provided by the CSBMCB) were awarded to graduate students and postdoctoral fellows.

The Banff meeting extended the series of recent memorable CSBMCB meetings, which have combined outstanding science in a small meeting with a relaxed setting. We look forward to the 2006 CSBMCB Meeting in Niagara-on-the-Lake!

Travel and Poster Award Recipients for the 2005 CSBMCB Annual Scientific Meeting

Banff, Albert

POSTER PRIZES

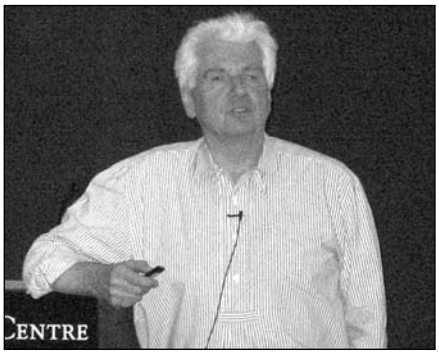
AWARDEE	UNIVERSITY	SUPERVISOR
Roche Diagnostics Poster Prizes		
Monica Fagrasanu	University of Alberta	Dr. Richard Rachubinksi Dr. John Aitchison Dr. Gary Eitzen
Lisa Hawnylak-Gara	University of Alberta	Dr. Richard Wozniak
Yinyan Zhang	University of Toronto	Dr. David Williams
Jake Duerckson Poster Prize in Cell Biology		
Andrei Fagrasanu	University of Alberta	Dr. Richard Rachubinksi
CSBMCB Poster Prizes		
Deborah Pinchev	McMaster University	Dr. Ray Truant
Veronica Provencher	University of Alberta	Dr. Luis Schang
Nicole Quenneville	University of British Columbia	Dr. Elizabeth Conibear
Rob Scott	University of Alberta	Dr. Richard Wozniak

TRAVEL PRIZES

AWARDEE	UNIVERSITY	SUPERVISOR
Merck Frosst 11 x $750 awards		
Denice Bay	University of Manitoba	Dr. Deborah Court
Morgan Fullerton	University of Guelph	Dr. Marika Bakovic
Michelle Kean	University of Guelph	Dr. Marc Coppolino
Kent Klemmer	University of Manitoba	Dr. Hughes Goldie
Lin Li	University of Manitoba	Dr. Jim Davie
Mary Ellen Olsten	University of Western Ontario	Dr. David Litchfield
Deborah Pinchev	McMaster University	Dr. Ray Truant
Dmitri Satsoura	McMaster University	Dr. David Andrews
Jeffrey Sharom	University of Toronto	Dr. Mike Tyers
Ben Strub	University of Guelph	Dr. Dev Mangroo
Johnny Tkach	University of Toronto	Dr. John Glover

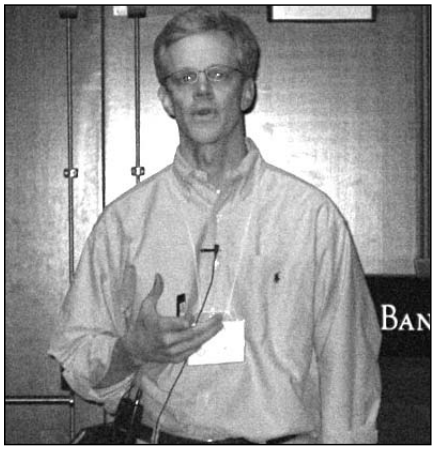
Scenes from the 2005 CSBMCB Annual Meeting

Richard Wozniak, Chair of the CSBMCB Scientific Organizing Committee for the 2005 Banff Conference



Keynote Address by Nobel Laureate Dr. Günter Blobel, Rockefeller University

The 2005 co-winner of the Merck Frosst Prize, Mark Glover of the University of Alberta, gives his award lecture



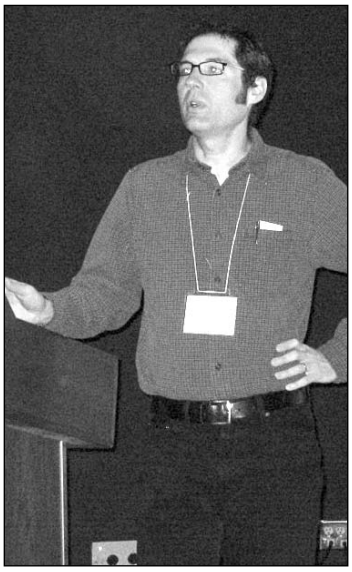
The 2005 co-winner of the Merck Frosst Prize, Eric Brown of McMaster University, gives his award lecture

Mark Glover (left) and Eric Brown (right) receive their award plaques for the 2005 Merck Frosst Prize from Dr. Brian Kennedy (centre), Senior Scientist, Merck Frosst Canada

The 2005 winner of the Roche Diagnostics Prize, Chris Bleackley of the University of Alberta, gives his award lecture

Chris Bleackley receives his award plaque for the Roche Diagnostics Prize from a representative of Roche Diagnostics

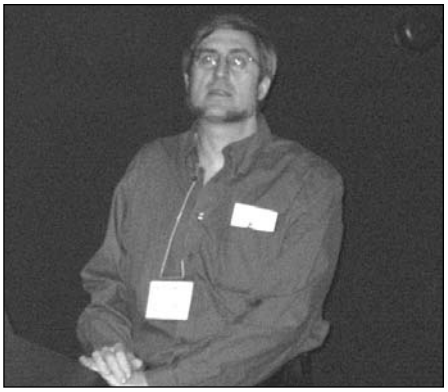
CSBMCB members David Thomas, Reinhart Reithmeier, and Joe Casey discussing the finer aspects of the local brew at the Opening Reception sponsored by Merck Frosst Canada



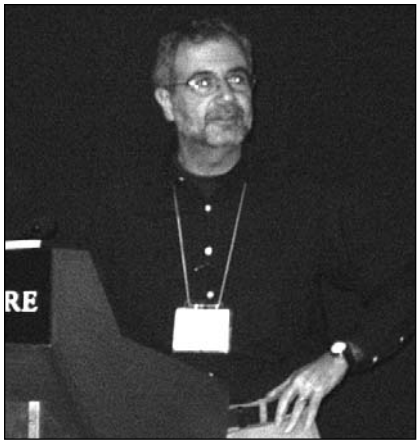
Joe Casey, President of CSBMCB, addressing the audience

Seminar presentation by Scott Emr, University of California, San Diego

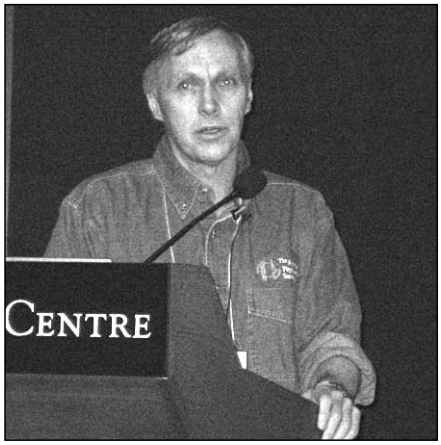
Seminar presentation by Charles Barlowe, Dartmouth College



Seminar presentation by David Andrews, McMaster University



Seminar presentation by Juan Bonifacino, National Institutes of Health, Bethesda

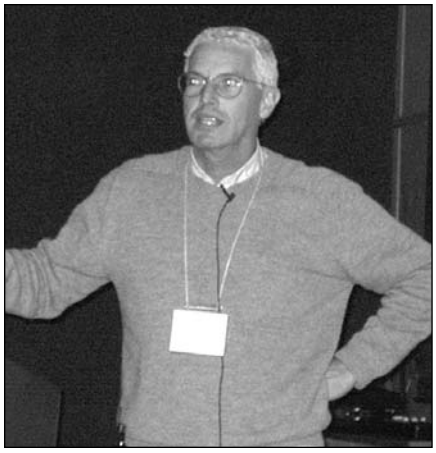


Seminar presentation by Sergio Grinstein, Hospital for Sick Children

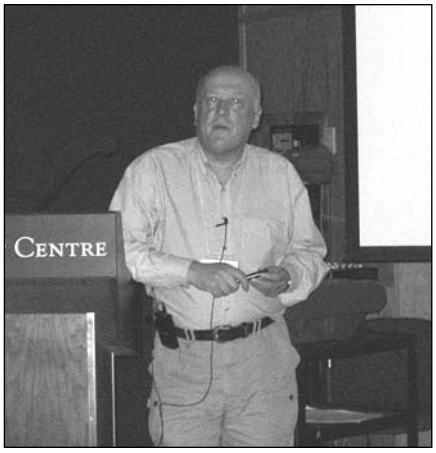
Seminar presentation by Jennifer Lippincott-Schwartz, National Institutes of Health, Bethesda

View from the Banff Conference Centre

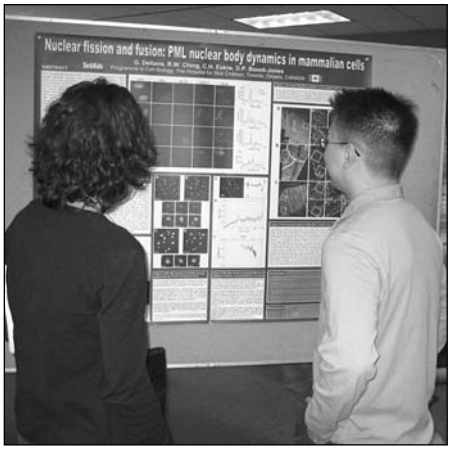
Enjoying the local ski scene



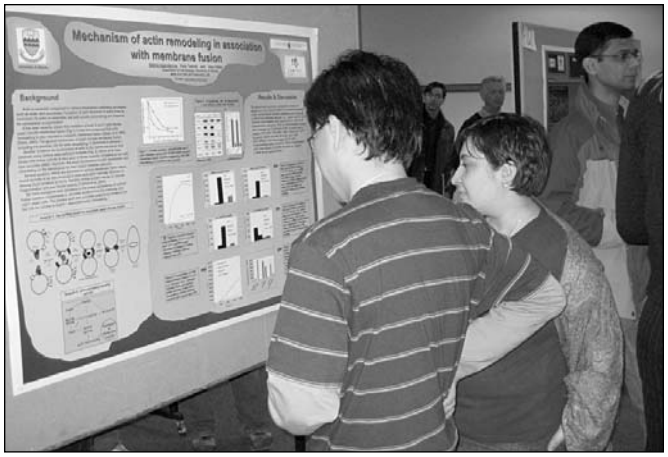
Seminar presentation by Tom Kirchhausen, Harvard University



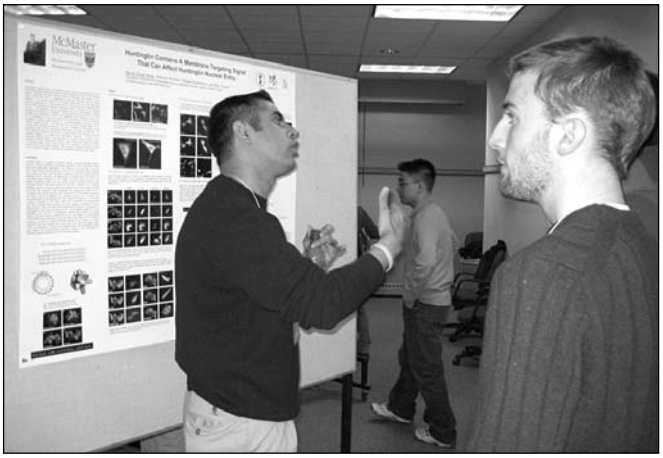
Seminar presentation by David Thomas, McGill University



Poster Session



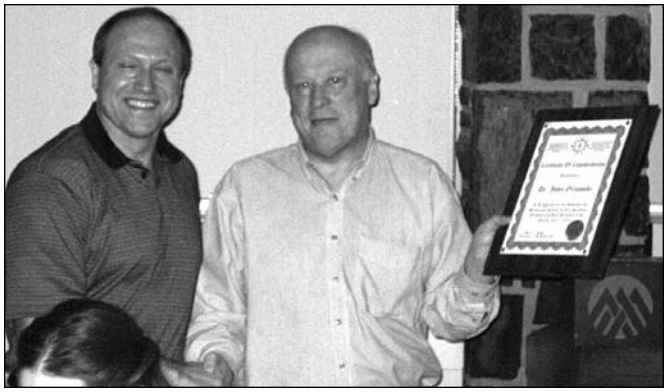
Poster Session



Poster Session

Poster Session

The 'Stanley Cup' of science



Presentation by David Thomas, Vice-President of the CSBMCB, of the "Certificate of Commendation" to Dr. John Orlowski in recognition of his meritorious service as Vice-President, President and Past-President of the Society (2002-2005)

Presentation by Joe Casey, President of the CSBMCB, of the "Certificate of Commendation" to Dr. Richard Wozniak in recognition of his meritorious service as Chair of the Organizing Committee for the 48th Annual Meeting of the Society

Recipients of the Roche Diagnostics Awards and the CSBMCB Awards for the best poster presentations

Recipients of the Merck Frosst Student Travel Awards (not present: Denice Bay and Kent Klemmer)

Socializing at the local pub

Membrane Proteins in Health and Disease

49th Annual Meeting and Conference of the
Canadian Society of Biochemistry, Molecular and Cellular Biology
(CSBMCB/SCBBMC)
May 31 – June 4, 2006
White Oaks Conference Resort and Spa
Niagara-on-the-Lake, Ontario, Canada

Scientific Program

Wednesday, May 31, 2006

6:00 pm	Dinner	

Session I **Plenary Lectures** (Chair: Joel Weiner)

Sponsored by the Institute of Genetics, Canadian Institutes of Health Research

7:30 pm	Ron Kaback (UCLA)	Gambling with lac permease
8:15	Peter Agre (Duke)	Aquaporin water channels: from atomic structure to clinical medicine
9:00 pm	Mixer	

Thursday, June 1, 2006

7:00 am	Breakfast	

Session II **Structural Biology of Membrane Proteins** (Chair: Reinhart Reithmeier)

Sponsored by the CIHR Strategic Training Program in the Structural Biology of Membrane Proteins Linked to Disease

8:30 am	Charles Deber (Toronto)	Hydrogen bonds matter: misfolding of membrane proteins in human disease
9:10	Natalie Strynadka (UBC)	Structure-based analysis of antibiotic targets on the bacterial membrane
9:50	Invited talk from abstracts	
10:10	Coffee	
10:40	Francesca Marassi (Burnham)	NMR studies of the regulatory subunits of the Na/K-ATPase
11:20	Robert Stroud (UCSF)	A two billion year old tale of membrane protein transport- still with us today!
12:00 noon	Lunch	
4:00 pm	Poster Session I (Coffee and Cash Bar)	
6:00 pm	Dinner	

Session III **Regulating Membrane Permeability** (Chair: Janet Wood)

7:30 pm	David Andrews (McMaster)	Regulation of membrane permeability by apoptosis proteins Bax and Bcl-XL
8:10	Art Johnson (Texas)	Maintaining the ER permeability barrier during protein trafficking
8:50	Invited talk from abstracts	
9:10	John Collier (Harvard)	Insertion of toxins into membranes
10:00-12:00	Poster Pub (Cash Bar)	

Friday, June 2, 2006

7:00 am	Breakfast	

Session IV **Dynamics of Membrane Proteins** (Chair: Christine Bear)

8:30 am	Frances Sharom (Guelph)	Fluorescence studies of P-glycoprotein
9:10	Francisco Bezanilla (UCLA)	Molecular basis of voltage-gated channels
9:50	Invited talk from abstracts	
10:10	Coffee Break	
10:40	Eduardo Perozo (Chicago)	Pore dynamics and the gating mechanism of KcsA
11:20	Peter Tieleman (Calgary)	Computational studies of ABC transporters

Friday, June 2, 2006 (Contíd)

12:00 noon	Lunch and CSBMCB Board Meeting	
4:00 pm	Poster Session II (Coffee and Cash Bar)	
6:00 pm	Dinner	

Session V **Transporters and Disease** (Chair: Larry Fliegel)
Sponsored by the CIHR Strategic Training Program in Membrane Proteins and Cardiovascular Disease

7:30 pm	Joseph Casey (Alberta)	A membrane transport metabolon implicated in cardiac hypertrophy
8:10	Jean-Yves Lapointe (MontrÈal)	Properties of the tumor suppressor SLC5A8 Na^+/monocarboxylate cotransporter
8:50	Invited talk from abstracts	
9:10	David MacLennan (Toronto)	Calcium pumps, pump regulatory proteins and cardiomyopathy
10:00-12:00	Poster Pub (Cash Bar)	

Saturday, June 3, 2006

7:00 am	Breakfast	

Session VI **Trafficking Defects in Membrane Proteins** (Chair: John Orlowski)

8:30	Reinhart Reithmeier (Toronto)	Trafficking defects of the chloride/bicarbonate anion exchanger 1
9:10	Michel Bouvier (MontrÈal)	Rescue of misfolded G-protein coupled receptors
9:50	Invited talk from abstracts	
10:10	Coffee Break	
10:40	Gergely Lukacs (Toronto)	Cellular basis of misfolded CFTR removal from the cell surface
11:20	Michael Caplan (Yale)	Membrane protein trafficking in polarized cells: partners and pathology
12:00 noon	Lunch	

Session VII **Workshop on Membrane Protein Crystallization (**Chair: Gil PrivÈ)

1:30 pm	Presentations	
5:00 pm	CSBMCB Annual General Meeting	

Session VIII **CSBMCB Awards Lectures** (Chair: David Thomas, President CSBMCB)

6:00 pm	Merck Frosst Prize Lecture	
6:40	Jeanne Manery Fisher Memorial Lecture	
7:30 pm	Banquet and Awards Presentation	

Sunday, June 4, 2006

7:00 am	Breakfast	

Session IX **Assembly and Disassembly of Membrane Proteins** (Chair: John Baenziger)

8:30 am	Igor Stagljar (Toronto)	Interactive proteomics of membrane protein assemblies
9:10	Tom Rapoport (Harvard)	Getting proteins across membranes
9:50	Invited talk from abstracts	
10:10	Coffee Break	
10:40	David Williams (Toronto)	Calnexin and calreticulin: glycoprotein folding machines of the ER
11:20	Jeff Brodsky (Pittsburgh)	ER associated degradation of CFTR: lessons from yeast
12:00 noon	Lunch and Departure	

Schedule Announced

The ASCB 46th Annual Meeting

December 9-13, San Diego, CA

Mary Beckerle, President ■ Anthony Bretscher, Program Chair ■ Arshad Desai, Local Arrangements Chair

KEYNOTE SYMPOSIUM

Saturday, December 9

Frontiers in Cell Biology—6:00 pm

Thomas R. Cech, Howard Hughes Medical Institute

SYMPOSIA

Sunday, December 10

Coordination of Adhesion and Migration—8:00 am

Denise Montell, Johns Hopkins Medical School
Clare Waterman-Storer, The Scripps Research Institute
Kenneth Yamada, National Institute of Dental & Craniofacial Research/NIH

Deciphering Evolution—10:30 am

Sean Carroll, University of Wisconsin–Madison/HHMI
Eric Jarvis, Duke University Medical Center
David Kingsley, Stanford University School of Medicine/HHMI

Monday, December 11

Mechanisms in Mitosis—8:00 am

Rebecca Heald, University of California, Berkeley
Lucille Shapiro, Stanford University School of Medicine
Ronald D. Vale, University of California, San Francisco/HHMI

Developmental Decisions—10:30 am

Hans Clevers, Netherlands Institute for Developmental Biology
Elliot Meyerowitz, California Institute of Technology
Susan Strome, Indiana University

Tuesday, December 12

Membrane Assembly and Dynamics—8:00 am

Gillian Griffiths, University of Oxford
Janet Shaw, University of Utah
Marino Zerial, Max Planck Institute of Molecular Cell Biology & Genetics

From Cellular Mechanisms to Therapeutic Intervention—10:30 am

Susan Lindquist, Whitehead Institute for Biomedical Research
Christine Seidman, Harvard Medical School/HHMI
Xiaodong Wang, University of Texas Southwestern Medical Center/HHMI

Wednesday, December 13

Functional Networks—8:00 am

Susan Mango, University of Utah
Kevan Shokat, University of California, San Francisco
Tian Xu, Yale University School of Medicine/HHMI

Stem Cell Biology—10:30 am

George Q. Daley, Children's Hospital Boston
Elaine Fuchs, Rockefeller University/HHMI
Margaret Fuller, Stanford University School of Medicine

MINISYMPOSIA

Apoptosis
Eileen White, Rutgers University
Junying Yuan, Harvard Medical School

Applications of Biosensors
Atsushi Miyawaki, RIKEN Brain Science Institute
Alice Ting, Massachusetts Institute of Technology

Cancer Mechanisms
Lisa Maria Coussens, University of California, San Francisco
Mary J.C. Hendrix, Children's Memorial Research Center/Northwestern University Feinberg School of Medicine

Cell Cycle
Mary Dasso, National Institute of Child Health & Human Development/NIH
Jonathon Pines, The Wellcome Trust/Cancer Research UK

Cell Migration
Diane L. Barber, University of California, San Francisco
Gregg G. Gundersen, Columbia University College of Physicians & Surgeons

Computational Applications in Cell Biology
Douglas A. Lauffenberger, Massachusetts Institute of Technology
Alex Mogilner, University of California, Davis

Cytoskeleton, Adhesion and Disease
Kathleen J. Green, Northwestern University Feinberg School of Medicine
Alpha S.K. Yap, University of Queensland

ECM and Cell Signaling
Jean E. Schwarzbauer, Princeton University
Christopher Turner, SUNY Upstate Medical University

Endo- and Exocytosis
Todd Graham, Vanderbilt University
Margaret Scott Robinson, CIMB/The Wellcome Trust

Epigenetics and Chromatin Remodeling
Peggy Farnham, University of California, Davis
Andrew Feinberg, Johns Hopkins University School of Medicine

Epithelial Organization and Morphogenesis
Andrea I. McClatchey, Massachusetts General Hospital
Ulrich Tepass, University of Toronto

GTPases in Cellular Traffic
Francis Barr, Max Planck Institute of Biochemistry
Shou-ou Shan, California Institute of Technology

Host Pathogen Interactions
Jorge Galan, Yale University School of Medicine
Francoise Gisou Van Der Goot, University of Geneva Medical School

Imaging
J. Richard McIntosh, University of Colorado
Eva Nogales, University of California, Berkeley/HHMI

Immune Cell Adhesion and Recognition
Andrey Shaw, Washington University School of Medicine
Colin Watts, University of Dundee

Intermediate Filaments and Disease
Don W. Cleveland, University of California, San Diego
Colin Stewart, NCI-Frederick

Kinetochores and Centrosomes
Michel L.F. Bornens, Institute Curie, Paris
Peter Todd Stukenberg, University of Virginia School of Medicine

Life at the Microtubule Plus End
Anna Akhmanova, Erasmus University
Kevin Vaughan, University of Notre Dame

Mechanisms of Actin Dynamics
Bruce Lane Goode, Brandeis University
Dorit Hanein, The Burnham Institute

Mechanisms of Cell Polarity
Patrick Brennwald, University of North Carolina at Chapel Hill
Chris Q. Doe, University of Oregon/HHMI

Membrane Traffic in Disease
Esteban Carlos Dell-Angelica, University of California, Los Angeles School of Medicine
Daniel Klionsky, University of Michigan

Microtubule Motors
Erika L.F. Holzbaur, University of Pennsylvania
Claire E. Walczak, Indiana University

Motile and Sensory Cilia
Kathryn Anderson, Memorial Sloan-Kettering Cancer Center
Elizabeth F. Smith, Dartmouth College

Myosin-based Movement
Folma Buss, Cambridge University
Arturo DeLozanne, University of Texas

Neural Degeneration and Regeneration
Zhigang He, Harvard University
Stephen Strittmatter, Yale University School of Medicine

Nuclear Pore and Traffic
Michael P. Rout, Rockefeller University
Katherine S. Ullman, University of Utah

Organelle Inheritance and Maintenance
Liza A. Pon, Columbia University College of Physicians & Surgeons
Michael Schrader, University of Marburg

Regulation of the Cytoskeleton
Keith W.T. Burridge, University of North Carolina at Chapel Hill
Anne J. Ridley, Ludwig Institute for Cancer Research

RNA and Development
Oliver Hobert, Columbia University College of Physicians & Surgeons/HHMI
Roy Parker, University of Arizona/HHMI

Signaling in Development
Marcos Gonzalez-Gaitan, Max Planck Institute of Molecular Cell Biology & Genetics
Alexandra Joyner, New York University School of Medicine/HHMI

Stem Cells
M. Kathryn Barton, Carnegie Institution of Washington
Linheng Li, Stowers Institute of Medical Research

Synapse Assembly and Plasticity
Ann Marie Craig, University of British Columbia
Nancy Y. Ip, Hong Kong University of Science & Technology

For more information, contact the ASCB at (301) 347-9300, ascbinfo@ascb.org or www.ascb.org.

Conserved P-loop GTPases of Unknown Function in Bacteria: An Emerging and Vital Ensemble in Bacterial Physiology

Eric D. Brown

Antimicrobial Research Centre and Department of Biochemistry and Biomedical Sciences, McMaster University, Hamilton

Abstract

Establishing the roles of conserved gene products in bacteria is of fundamental importance to our understanding of the core protein complement to sustain cellular life. P-loop GTPases and related ATPases represent an abundant and remarkable group of proteins in bacteria that in many cases have evaded characterization. Here, efforts aimed at understanding the cellular function of a group of eight conserved, poorly characterized genes encoding P-loop GTPases, *era, obg, trmE, yjeQ, engA, yihA, hflX, ychF*, and a related ATPase, *yjeE*, are reviewed in considerable detail. While concrete cellular roles remain elusive for all of these genes, and considerable pleiotropy has plagued their study, experiments to date have frequently implicated the ribosome. In the cases of *era, obg, yjeQ* and *engA*, the evidence is most consistent with roles in ribosome biogenesis, though the prediction is necessarily putative. While the protein encoded in *trmE* clearly has a catalytic function in tRNA modification, the participation of its GTPase domain remains obscure as do the functions of the remaining proteins. A full understanding of the cellular functions of all of these important proteins remains the goal of on-going studies of cellular phenotype and protein biochemistry.

Introduction

While genomics has provided staggering amounts of sequence information, it has simultaneously expanded the sphere of the uncharted. Since the completion of the first genome sequence for a free-living organism (*Haemophilus influenzae*) in 1995 bacteriologists have been faced with the dilemma that about one third of the genes in any microbe typically encode uncharacterized proteins (Tatusov et al. 2000). Estimates for the human genome have been similar in magnitude (Lander et al. 2001; Venter et al. 2001) and there is now an emerging consensus that a key hurdle facing life scientists is the assignment of function of uncharacterized genes. While we might have expected the uncharacterized fraction of genomes to encode auxiliary functions, it has become clear from microbial genomics that many uncharacterized proteins are highly conserved and carry out critical roles. In particular, the P-loop GTPases and related ATPases form a relatively large group of conserved and often indispensable proteins in bacteria where there is a paucity of functional characterization. Indeed, this group of proteins has become the subject of intensive study by several groups and has been the subject of several reviews (Caldon and March 2003; Caldon et al. 2001; Leipe et al. 2002; Mittenhuber 2001; Morimoto et al. 2002). The often essential nature and broad conservation of these uncharacterized proteins suggests that they play central roles in bacterial physiology. This review, while reasonably comprehensive across the most relevant work, focuses on the careful genetic and biochemical studies that are steadily improving our understanding of the functions of conserved, uncharacterized GTPases in bacteria.

P-loop GTPases and related ATPases in bacteria

GTPases function as crucial molecular switches in a broad variety of biochemical processes. The majority of GTPases are part of a vast class of

homologous proteins known as P-loop NTPases that share a mononucleotide-binding fold and catalyze hydrolysis of the β–γ phosphate ester bond of the nucleotide. Of all the nucleotide binding folds, the P-loop fold is by far the most abundant; it has been estimated that 10-18% of predicted gene products are P-loop NTPases (Koonin et al. 2000). Structurally, P-loop NTPases are α/β proteins that are characterized by an *N*-terminal Walker A motif consisting of a flexible loop spanning a b-strand and helix with the signature GxxxxGK[ST], where the function of this loop is to position the triphosphate moiety of the nucleotide (Walker et al. 1982). A Walker B motif is distal and contains a conserved carboxylate-containing residue, aspartate or glutamate. The conserved acidic residue is located at the end of a typically hydrophobic b-strand and has the role of coordinating a Mg^{2+} cation that also has interactions with the β and γ phosphates (Walker et al. 1982).

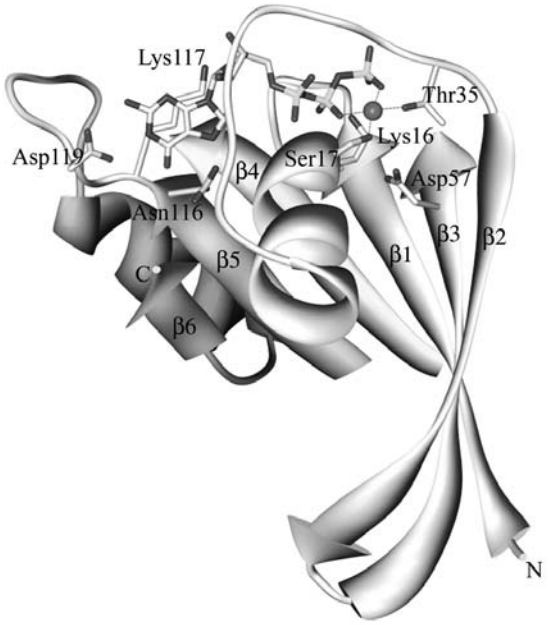


Figure 1. Structural core of β-strands and associated loops in the GTPase domain of p21 Ras (PDB identifier 1CTQ). The strand topology and Walker motifs characteristic of P-loop GTPases (β1 through β6) of the TRAFAC class are emphasized through the removal of extraneous loops and helices in the structure. Of note is the antiparallel nature of the strand β2 adjacent to the Walker B strand β3. Highlighted are the bound non-hydrolyzable GTP analogue 5'-guanylylimidodiphosphate (GMP-PNP), Walker A (GxxxxGK[ST]) residues K16 and S17, Walker B (hhhDxxG) residue D57, GTPase specificity ([NT]KxD) residues N116 and D119, and the TRAFAC class-specific residue T35. Also shown is a bound Mg^{2+} molecule (magenta sphere).

The P-loop GTPases share a common structural core having an arrangement of strands and loops in the GTPase domain characterized by the prototype Ras protein (Figure 1). Koonin and colleagues developed a phylogenetic classification of P-loop GTPases and related ATPases by dividing some 60 distinct, ancient groups into two large classes (Leipe et al. 2002). The first is the TRAFAC (translation factor-related) class that includes classic GTPases, such as translation factors and the extended Ras family, as well as some ATPases such as kinesin and myosin. The second class was called SIMBI after its three largest subgroups, the signal recognition GTPases, the MinD superfamily and the BioD superfamily. The TRAFAC class encompasses the proteins discussed in this review and is characterized by a conserved β-strand topology where strand 3, adjacent to the Walker B strand, is uniquely anti-parallel and there is a conserved threonine or serine with a key role in Mg^{2+} coordination in the loop preceding β-strand 3 (Bourne et al. 1991; Leipe et al. 2002). Other features of P-loop GTPases include a specific form of the Walker B (hhhDxxG), where h is a hydrophobic amino acid, and the glycine amide interacts with the γ-phosphate, and a distal [NT]KxD, not found in other P-loop NTPases, that imparts specificity for guanine over other nucleotide bases.

Table 1 highlights a group of eight conserved bacterial P-loop GTPases and a related ATPase. These encompass TRAFAC class P-loop NTPases, present in the model bacterium *E. coli*, that are most broadly conserved and remain poorly characterized for physiological function in bacteria. Indeed, apart from well-characterized translations factors such as IF2, EF-tu and EF-G, the vast majority of bacterial P-loop NTPases in this class remain functionally obscure (Leipe et al. 2002). The table details the conservation of orthologues for this group of eight in 43 microbes spanning 30 major phylogenetic lineages as determined by Koonin and colleagues in the clusters of orthologous groups (COG) database (http://www.ncbi.nlm.nih.gov/COG/old/). The patterns of conservation reveal that, while broadly conserved among eubacteria, these genes are absent in archaea, apart from *hflX*, *yihA* and *ychF*. The latter, *ychF*, is present in all 30 phyloge-

Table 1.
Conserved, bacterial, P-loop GTPases (and a related ATPase) of unknown function.

Gene[1]	Conservation[2]	Phenotype	Biochemistry	Proposed role[3]
era *bex*	-------QVDRLB CEFGHSNUJX-TW	essential in E. coli; cell division defect; chromosome segregation defect; altered ribosome profile; genetic interactions with ksgA, dnaG and rbfA; slow growth and sporulation defect in B. subtilis	slow GTPase; binds 16S rRNA, cell membrane and MazG; KH domain-mediated RNA binding; GTPase stimulated by RNA; x-ray structure; cryo-em co-structure with 30S	ribosome biogenesis
obg *yhbZ* *obgE* *cgtA*	------YQVDRLB CEFGHSNUJXITW	essential; chromosome segregation defect; genetic interactions with, rrmJ, recA and recB; chemical- genetic interactions with replication inhibitors	slow GTPase; binds 50S and 30S ribosome; co-fractionation with ribosomal proteins and RNA; x-ray structure; novel N-terminal Obg-fold	ribosome biogenesis
trmE *mnmE* *thdF*	------YQVD-LB CEFGHSNUJXITW	deficiency in 5-methy-laminomethyl-2-uridine (U34) of tRNAs; synthetic lethality with unknown mutation(s)	fast GTPase; t-RNA modification; x-ray structure; N-terminal formyl-tetrahydrofolate binding, C-terminal G-domain	t-RNA modification
yjeQ *rsgA* *yloQ*	-------QV-RLB CEFGHSN-J--TW	slow growth; filamentous; chemical-genetic interactions with translation inhibitors; altered ribosome profile	slow GTPase; binds 30S ribosome; GTPase stimulated by 30S; x-ray structure; central circularly permuted G-domain; N-terminal OB-fold; C-terminal Zn finger	ribosome biogenesis
engA *der* *yfgK* *yphC*	-------QVDRLB CEFGHSNUJXITW	essential; filamentous; chromosome segregation defect; genetic interaction with *rrmJ*	slow GTPase; x-ray structure; two adjacent G-domains; C-terminal KH-like domain	ribosome biogenesis
yihA *ysxC*	AOM-K-YQV--LB -EFGHSNUJX--W	essential; filamentous; septation defect	binds GTP and GDP	____
hflX *ynbA*	-OM-KZ-QVDRLB CEFGHSN-J-I--	high frequency of lysogenization (hfl) locus	____	____
ychF *yyaF*	AOMPKZYQVDRLB CEFGHSNUJXITW	____	binds GTP and nucleic acid; x-ray structure	____
yjeE *ydiB*	-------QVDRLB CEFGHSNUJXIT-	essential	slow ATPase; binds ADP and YjeF; x-ray structure	____

[1] The *E. coli* gene name is listed along with synonyms, including that for the orthologue from *B. subtilis*.
[2] Conservation has been reported for 43 genomes as documented in the COG database (http://www.ncbi.nlm.nih.gov/COG/old/) according to the following legend: A, *Archaeoglobus fulgidus;* O, *Halobacterium sp. NRC-1;* M, *Methanococcus jannaschii, Methanobacterium thermoautotrophicum;* P, *Thermoplasma acidophilum, Thermoplasma volcanium;* K, *Pyrococcus horikoshii, Pyrococcus abyssi;* Z, *Aeropyrum pernix;* Y, *Saccharomyces cerevisiae;* Q, *Aquifex aeolicus;* V, *Thermotoga maritime;* D, *Deinococcus radiodurans;* R, *Mycobacterium tuberculosis, Mycobacterium leprae;* L, *Lactococcus lactis, Streptococcus pyogenes;* B, *Bacillus subtilis, Bacillus halodurans;* C, *Synechocystis;* E, *Escherichia coli K12, Escherichia coli O157, Buchnera sp. APS;* F, *Pseudomonas aeruginosa;* G, *Vibrio cholerae;* H, *Haemophilus influenzae, Pasteurella multocida;* S, *Xylella fastidiosa;* N, *Neisseria meningitidis MC58; Neisseria meningitidis Z2491;* U, *Helicobacter pylori, Helicobacter pylori J99, Campylobacter jejuni;* J, *Mesorhizobium loti, Caulobacter crescentus;* X, *Rickettsia prowazekii;* I, *Chlamydia trachomatis, Chlamydia pneumoniae;* T, *Treponema pallidum, Borrelia burgdorferi;* W, *Ureaplasma urealyticum, Mycoplasma pneumoniae, Mycoplasma genitalium.*
[3] Proposed roles, where applicable, are based on the balance of experimental evidence to date.

netic lineages. Interestingly only four of these widely conserved genes, *ychF*, *obg*, *trmE* and *yihA*, are also found in the eukaryote, *S. cerevisiae*. This finding is consistent with the outlook to date that, while eukaryotic G-proteins are celebrated for their roles in transmembrane receptor-mediated cell signaling, prokaryotic GTPases appear not be involved in analogous processes in bacteria. Table 1 also summarizes information pertaining to the phenotype of the null mutant or, in the case of essential genes, the phenotype associated with depletion of the gene product in a conditional mutant. Indicated in addition, are salient findings from biochemical studies, often with recombinant proteins *in vitro*. Where reasonable, I have proposed a physiological function for each of these proteins that, in my view, best sums the data published to date. Below, I present that analysis supported by phenotypic and biochemical characterization of these loci with an emphasis on recent publications.

Studies of phenotype and biochemistry of conserved bacterial P-loop NTPases

Era, the first discovered bacterial GTPase, was named for its Ras-like GTPase domain (Ahnn et al. 1986) and has been extensively studied. Only recently has a resolution regarding its physiological function begun to develop. Era was shown to be essential in *E. coli* more than a decade ago (Gollop and March 1991; Lerner and Inouye 1991) and subsequent studies have shown cross-species complementation by orthologues from several bacteria (Pillutla et al. 1995; Zuber et al. 1997). The *B. subtilis* orthologue Bex was shown to be dispensable in that organism but led to a slow growth phenotype and was vital to sporulation (Minkovsky et al. 2002). *E. coli* Era has been proposed to regulate cell division (Britton et al. 1998; Johnstone et al. 1999; Lu and Inouye 1998). Depletion of Era led to filamentous cells having normal DNA replication and nucleoid segregation but apparently blocked for cell division. In *B. subtilis*, on the other hand, depletion of Bex led to diffuse, unsegregated chromosome in elongated cells, suggesting a role, prior to division, in nucleoid segregation (Minkovsky et al. 2002). Interestingly, a mutant in *E. coli era* was isolated as a suppressor of a temperature sensitive *dnaG* mutant encoding DNA primase (Britton et al. 1997). Microarray and other studies have linked era function with energy metabolism (Inoue et al. 2002; Pillutla et al. 1996; Powell et al. 1995). Much phenotypic work on *era* has suggested a role in ribosome function. Depletion of Era leads to an increase in dissociated 30S and 50S subunits (Sayed et al. 1999) and to an accumulation of 17S rRNA, an unprocessed precursor of 16S rRNA (Inoue et al. 2003). Relevant genetic interactions noted for *era* include the gene *ksgA* (Lu and Inouye 1998), coding for a 16S rRNA dimethyltransferase and *rbfA* (Inoue et al. 2003), encoding a cold shock protein that specifically associates with 30S ribosomal subunits.

Biochemical studies of Era have focused on its GTPase activity, protein structure and interactions. Purified recombinant Era has a slow GTPase activity (k_{cat} ~ 1 h^{-1}) that is stimulated many fold by interaction with RNA(Meier et al. 2000; Sullivan et al. 2000). X-ray crystallographic analysis revealed a two lobe structure for Era with an *N*-terminal GTPase region and a C-terminus that contains a signature KH RNA binding domain (Chen et al. 1999). Indeed, this C-terminal domain has been repeatedly implicated in the 16S RNA binding activity of Era (Hang and Zhao; Hang et al. 2001; Inoue et al. 2003; Johnstone et al. 1999; Meier et al. 1999; Meier et al. 2000) and in its interaction with the 30S ribosomal subunit (Sayed et al. 1999). Most recently a co-structure of Era in complex with the 30S ribosomal subunit validated much of the biochemical and phenotypic data that pointed to a *bona fide* interaction with the ribosome (Sharma et al. 2005). The co-structure shows Era in complex with the 3' region of 16S rRNA in a cleft between the head and platform of the 30S subunit, locking it in a conformation that is unfavorable for association with the 50S subunit. Interestingly, Era is in the S1 protein binding site. The co-structure of Era with the 30S subunit is compelling in itself and ties together many of the biochemical and phenotypic studies of this bacterial GTPase. Thus Era appears to have a role in the assembly of the 30S subunit, perhaps by chaperoning the 16S rRNA. Presumably the

assembly process would be complete with Era dissociation and S1 incorporation.

The next best studied bacterial P-loop GTPase is Obg. The *obg* gene was first discovered in *B. subtilis* (Trach and Hoch 1998). It has been studied in a wide variety of organisms including *E. coli, B. subtilis, Streptomyces coelicolor* and *Caulobacter crecentus*, and shown to be essential for cell growth (Arigoni et al. 1998; Kok et al. 1994; Maddock et al. 1997; Morimoto et al. 2002), sporulation (Vidwans et al. 1995) and morphological differentiation (Okamoto and Ochi 1998). Pleiotropy has characterized the consquences of Obg depletion in cells just as it has for Era. Cell filamentation, defective chromosome partitioning and altered DNA replication have been reported (Foti et al. 2005; Kobayashi et al. 2001; Slominska et al. 2002). Depletion of the Obg orthologue in *C. crescentus* resulted in slow growth and reduced levels of 50S ribosomal subunit (Datta et al. 2004). Genetic interactions discovered so far for *obg* have pointed to ribosome function and to DNA replication. The *obg* gene was selected from a random genomic multicopy library for supressors of an *E. coli* mutant in *rrmJ*, encoding a 23S rRNA methyltransferase (Tan et al. 2002). Most recently, a transposon insertion mutant in the 3' end of *obg* was isolated in a search for mutants sensitive to DNA replication inhibitors (Foti et al. 2005). In the same work, similar chemical-genetic interactions were noted in a dominant negative mutant directed at the GTPase function of Obg and synergism was evident between *obg* mutants and null mutants in DNA repair genes *recA* and *recB*.

The Obg protein has a very slow intrinsic GTPase activity with turnover recorded for pure recombinant proteins from *B. subtilis* and *C. crescentus* on the order of 1 h^{-1} (Buglino et al. 2002; Lin et al. 1999; Welsh et al. 1994). High resolution structural details for Obg to date have included both apo and nucleotide-bound forms of the proteins from *B. subtilis* and *Thermus thermophilus* (Buglino et al. 2002; Kukimoto-Niino et al. 2004). Co-structural information came from studies of the *B. subtilis* protein where ppGpp nucleotide, an effector molecule of the stringent response, was discovered at the active site of the crystallized protein (Buglino et al. 2002), however, the physiological relevance of the ligand remains obscure. Obg is a two domain protein with a unique *N*-terminal glycine rich region, nicknamed the Obg domain, and a C-terminal GTP-binding domain. These domains share a significant interaction interface that is mediated in part by the conserved GTPase switch elements. Indeed, some significant conformational changes were noted in the nucleotide bound and apo forms suggesting the likelihood of nucleotide dependent signaling between the two folds. A number of biochemical studies have suggested that Obg has an affinity for ribosomes, in particular the 50S subunit (Lin et al. 1999; Sato et al. 2005; Wout et al. 2004; Zhang and Haldenwang 2004). Interestingly, "pull-down assays" with the *E. coli* protein have revealed association of Obg with 16S and 23S ribosomal RNAs as well as with several ribosomal proteins, including RNA helicase CsdA and chaperone ClpA. Particularly interesting, in light of the unanticipated co-structure Obg with ppGpp, was finding of Wout and coworkers that recombinant *E. coli* Obg copurified with SpoT, the ribosome-associated (p)ppGpp hydrolase/synthetase enzyme with a role in the stress response . The simplest interepretation of the phenotypic and biochemical evidence available to date is that Obg has a role in ribosome biogenesis.

Gene *trmE* was identified more than twenty years ago in the isolation of mutants that were deficient for the synthesis of 5-methylaminomethyl-2-thiouridine based on a phenotype of reduced read through of UAG codons (Elseviers et al. 1984). Many years later it was found to be allelic with *thdF*, a gene previously shown to be involved in thiophene and furan oxidation (Alam and Clark 1991), and was shown to be a GTPase that was essential for viability in some genetic backgrounds, presumably due to synthetic lethal interaction(s) (Cabedo et al. 1999; Yim et al. 2003). TrmE is thought to be a key enzyme in the mult-step modification of the wobble position uridine (U34) in tRNAs. The altered base is capable of base pairing with G and A but not with C or U, a feature that is important for mixed codon families and influences frameshifting during translation (Brierley et al. 1997; Urbonavicius et al. 2003). Compared to

most bacterial GTPases, TrmE has a high intrinsic GTPase activity, with a turnover of more than 500 h^{-1} (Yamanaka et al. 2000). A recent x-ray crystallographic study of the protein revealed an *N*-terminal formyl-tetrahydrofolate binding domain, a central helical domain with a conserved cysteine-containing motif, and a C-terminal Ras-like fold (Scrima et al. 2005). These investigators proposed that TrmE catalyzes the first step of 5-methylaminomethyl-2-thiouridine synthesis with formylation of position 5 of the uridine, a step that is probably activated by a covalent adduct with the conserved cysteine (Yim et al. 2003). While the chemical role of TrmE in t-RNA modification is becoming apparent, the importance of the GTP binding and hydrolysis functions of TrmE remain unclear. It seems likely, nevertheless, that the GTPase function of TrmE has a role in the t-RNA modification steps. It was noted by Scrima and coworkers that significant conformational rearrangements would be necessary to accomplish the proposed chemical steps (Scrima et al. 2005). The G-domain of TrmE may therefore have a role in transducing the energies of binding and hydrolysis of GTP into conformational changes which make the chemistry possible.

While the first accounts of investigations on *era*, *obg* and *trmE* are now decades old, studies of the balance of genes in Table 1, including *yjeQ*, have been post-genomic. Despite initial reports of indispensability (Arigoni et al. 1998; Kobayashi et al. 2003) gene *yjeQ* has been shown to be expendable in *E. coli* and *B. subtilis* (Campbell et al. 2005; Freiberg et al. 2001; Himeno et al. 2004). The early conclusions of an essential phenotype are probably derivative of a slow growth defect that has been recently demonstrated for the *B. subtilis* and *E. coli* mutants (Campbell et al. 2005; Himeno et al. 2004). Depletion of the *yjeQ* orthologue in *B. subtilis* resulted in the accumulation of 30S and 50S ribosomal subunits and sensitivity to antibiotics that bind at the peptide channel or peptidyltransferase centre of the ribosome (Campbell et al. 2005). That work also demonstrated a profound filamentous phenotype in the *B. subtilis* mutant. Pure, recombinant *E. coli* YjeQ protein showed a low intrinsic GTPase (~ 10 h^{-1}), characterized by burst kinetics where GTP hydrolysis was shown to exceed catalytic turnover by some 45,000-fold (Daigle et al. 2002). That work documented an extraordinary disconnection between fast chemical steps of GTP hydrolysis and slow release of products GDP and/or phosphate. Such a disconnection is, of course, paradigmatic of the capacity of GTPases to store and transduce the energy of GTP binding and hydrolysis into a signal imparted to a partner protein. In the case of YjeQ and its orthologues, it's now clear that the partner is the ribosome (Campbell et al. 2005; Daigle and Brown 2004; Himeno et al. 2004). Cell fractionation studies revealed that YjeQ was in low copy in *E. coli* and bound entirely to ribosomes (1:200, YjeQ:ribosomes) (Daigle and Brown 2004). Recombinant YjeQ bound stoichiometrically and tightly to the 30S subunit of the ribosome in the presence of a non-hydrolyzable GTP analogue and the GTPase activity of YjeQ was shown to be stimulated many fold by the 30S subunit of the ribosome(Daigle and Brown 2004; Himeno et al. 2004). Two x-ray studies have revealed the structural details of YjeQ and its orthologues (Levdiko et al.; Shin et al. 2004). The protein is characterized by an unusual connectivity where the G-protein motifs are circularly permuted. This central permuted GTPase domain is flanked by an *N*-terminal oligonucleotide binding (OB) fold and a C-terminal Zinc-binding domain. The OB-fold was found to be critical to both 30S binding and ribosome stimulated GTPase activity (Daigle and Brown 2004). At present it appears very likely that YjeQ has a role in ribosome function where its stoichiometry with ribosomes would be most consistent with a catalytic role in ribosome biogenesis.

The gene *engA* has been shown to be essential in *Neisseria gonorrhoeae* (Mehr et al. 2000), *E. coli*, (Hwange and Inouye 2001) and *B. subitlis* (Morimoto et al. 2002). The depletion of EngA was shown to result in filamentous cells with defective chromosomal segregation in *E. coli* (Hwange and Inouye 2001) and in curved elongated cells with condensed nucleoids in *B. subtilis* (Morimoto et al. 2002). Like *obg, engA* at high copy was shown to rescue the growth defects of a null mutation in the gene coding for the heat-

induced rRNA methyltransferase, *rrmJ* (Tan et al. 2002). X-ray crystallographic studies have highlighted a unique structural feature of the EngA protein, namely, tandem GTPase domains (Robinson et al. 2002). These adjacent *N*-terminal GTPase domains are followed by a C-terminal domain that is analogous to KH domains, but lacks structural features that are indicative of the RNA-binding capacity of such protein folds. While there's clearly a paucity of data to propose a role for EngA, ribosome biogenesis seems a likely function given the phenotype and structure of this conserved GTPase.

Several studies of the dispensability of gene *yihA* point to an essential role for the encoded protein in both *E. coli* and *B. subtilis* (Arigoni et al. 1998; Wang and Kuramitsu 2003). Depletion of YihA in *E. coli* led to filamentation and a block in cell division steps beyond nucleoid segregation (Dassain et al. 1999). Recombinant *E. coli* YihA protein was purified and shown to bind GDP with micromolar affinity (Lehoux et al. 2003). Because of its potential as a therapeutic target for new antibacterial drugs, YihA was recently the subject of an assay development effort where affinity capillary electrophoresis was employed to look for small molecules interacting with the protein (Lewis et al. 2004). The latter work highlights a remarkable bit of irony in the field. The conserved bacterial GTPases are regarded as exciting targets for new antibacterial drugs, and yet these proteins lack the functional characterization necessary for conventional target-based drug discovery efforts.

The *E. coli hflX* gene is present in a locus that governs the lysis-lysogeny decision and has been implicated in controlling the proteolysis of the λ phage cII repressor (Noble et al. 1993). Thus far, the dispensability of *hflX* appears unaddressed. HflX protein is the founding member of a family within the Obg-HflX superfamily of conserved GTPases and, to date, is completely uncharacterized (Leipe et al. 2003).

YchF is in a subfamily of Obg-like proteins about which much is unknown, including its dispensability. The crystal structure of YchF revealed an *N*-terminal P-loop GTPase domain, a central coiled coil domain and a C-terminal half β-barrel (Teplyakov et al. 2003). In addition to the structural work, these researchers used fluorescence microscopy to demonstrate that the pure recombinant protein could bind both GTP and nucleic acid. The latter experiments were motivated by the observation of a deep and positively charged cleft among the three domains. This line of investigation highlights the capacity of structural studies to provide testable hypotheses for biochemical studies aimed at understanding the function of uncharacterized proteins.

The last of the conserved P-loop proteins considered here is YjeE, an essential (Allali-Hassani et al. 2004; Freiberg et al. 2001) ATPase that has been somewhat enigmatic to structural classification. The structure of the orthologue from *Haemophilus influenzae* was solved as part of a structural genomics initiative and while its fold is reminiscent of that of the TRAFAC class of P-loop NTPases, it also has some significant structural similarity to P-loop kinases (Teplyakov et al. 2003). The protein has thus been proposed to fill a "topological niche." Allali-Hassani and coworkers (Allali-Hassani et al. 2004) showed that depletion of YjeE led to slow growth and that proposed Walker mutants, K41A, T42A and D80Q, were impaired for complementation of the growth defect. Indeed, while the former two variants were clearly in the Walker A motif, D80 appears to have been wrongly assigned to the Walker B motif. This is due to the presence in YjeE of an additional parallel β-strand (strand 4) between strands 1 and 3 of the typical TRAFAC fold depicted in Figure 1 (Leipe D.D, personal communication, 2005). This would make E108 the actual conserved Walker B carboxylate-containing residue with D80 playing an important but nevertheless mysterious role. A very low ATPase activity (1 h^{-1}) was characterized for the recombinant protein, as well as a micromolar affinity for ADP using fluorescence resonance energy transfer from a conserved active site tryptophan to fluorescently labeled ADP (Allali-Hassani et al. 2004). YjeE has been proposed to function in cell wall biosynthesis based on phylogenetic pattern, its presence in bacterial genomes is coincident with known cell wall

enzymes, and on genome context, it is often found near the cell wall amidase *amiB*. In any case, phenotypic or biochemical experiments that support this proposal have yet to be reported.

Conclusions

It is clear that the celebrated role of eukaryotic GTPases in receptor-mediated cell signaling is a paradigm that is not applicable to bacteria. Even so, bacterial GTPases have on balance proven comparatively refractory to functional understanding. Despite decades of study, for example of *era, obg,* and *trmE*, there remains much to learn still regarding the cellular function of these conserved bacterial GTPases. Pleiotropic effects associated with lesions in these particular loci has been especially confounding, though recent investigations have come to focus on what is likely their true cellular role, ribosome function. Examinations of *yjeQ, engA, yihA, hflX, ychF* and *yjeE*, on the other hand, have been relatively recent and post-genomic. Here too, the evidence gathered to date appears to point to the ribosome, at least for *yjeQ* and *engA*. In sum, the progress of research into this important group of proteins indicates that, in contrast to the high throughput genomic studies that generated their sequences, functional understanding will be advanced one gene/protein at a time through concerted investigations of cellular phenotype and *in vitro* biochemistry.

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Structural Basis for Phosphorylation-dependent Signaling in the DNA Damage Response

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Abstract

The response of eukaryotic cells to DNA damage requires a multitude of protein-protein interactions that mediate the ordered repair of the damage and arrest of the cell cycle until repair is complete. Two conserved protein modules, BRCT and FHA domains, play key roles in the DNA damage response as recognition elements for nuclear Ser/Thr phosphorylation induced by DNA damage-responsive kinases. BRCT domains, first identified at the C-terminus of BRCA1, often occur as multiple tandem repeats of individual BRCT modules. Our recent structural and functional work has revealed how BRCT repeats recognize phospho-serine protein targets, and have revealed a secondary binding pocket at the interface between tandem repeats that recognizes the amino acid 3 residues C-terminal to the phospho-serine. We have also studied the molecular function of the FHA domain of the DNA repair enzyme, PNK. This domain interacts with threonine-phosphorylated XRCC1 and XRCC4, which is responsible for the recruitment of PNK to the sites of DNA strand break repair. Our studies have revealed a flexible mode of recognition that allows PNK to interact with numerous negatively charged substrates.

Introduction

Cells have evolved to deal with a bewildering complexity of DNA damage, from relatively small base lesions to single and double strand breaks in the DNA backbone. The repair of DNA damage in general involves multiple steps and several enzymatic activities. The DNA intermediates generated en route to repair are believed to often be more mutagenic than the original damage, and it appears that scaffold proteins are utilized to efficiently shuttle these DNA intermediates between the various repair enzymes that are required at successive steps in the repair process. In addition, specific cell cycle checkpoints can effectively delay progression through the cell cycle in response to DNA damage, to allow the cell time to repair damage before replication.

Very recent work has uncovered unique protein signaling modules that are specific to the DNA damage response. Here I review recent structural and functional work from our laboratory that reveals fundamental principles of phospho-protein recognition utilized by BRCT and FHA proteins – modules that are key to the regulated cellular response to DNA damage. Our studies reveal the structural basis for why specific mutations in BRCA1 BRCT repeats are associated with breast and ovarian cancer, and could be used to develop new cancer therapies that modulate these interactions.

BRCT repeats

BRCT repeats were first discovered at the extreme C-terminus of the breast cancer-associated protein, BRCA1, but were later shown to exist in a large family of proteins that are linked to the cellular response to DNA damage (1-4) (see http://www.sanger.ac.uk/cgi-bin/Pfam/getacc?PF00533 for the Pfam listing of the BRCT family). The BRCT repeats in BRCA1 are essential for the tumor suppressor function of the protein as protein truncation and missense variants within the BRCT have been shown to be associated with human breast and ovarian cancers (reviewed in (5)).

We determined the X-ray crystal structure of the two BRCT repeats of BRCA1 ((6), Figure 1). The structure revealed that the two repeats adopt similar folds, and pack together in a head-to-tail manner. This interaction is stabilized by the packing of a single helix from the N-terminal repeat against a pair of helices from the C-terminal repeat and the inter-repeat linker. While this structure alone did not reveal the molecular function of the protein, we nevertheless could use it as a basis to predict the effects of specific mutations, with the underlying hypothesis that the function would be disrupted by mutations that disrupt the structure of the domain. We also developed a simple proteolytic assay to directly test the conformational stability of BRCA1 BRCT variants (5).

While most of the cancer-causing missense variants cause a dramatic destabilization of the BRCT fold, some of the mutations led to a more modest increase in proteolytic susceptibility. One of these mutations, M1775R, was particularly interesting as this was one of the first characterized BRCT mutations to be linked to cancer(7, 8). We were able to crystallize and determine the structure of this variant, which revealed a subtle rearrangement of side chains around the site of the mutation, and a perturbation of the surface features of the protein (Figure 1) (9). However, a key question remained:

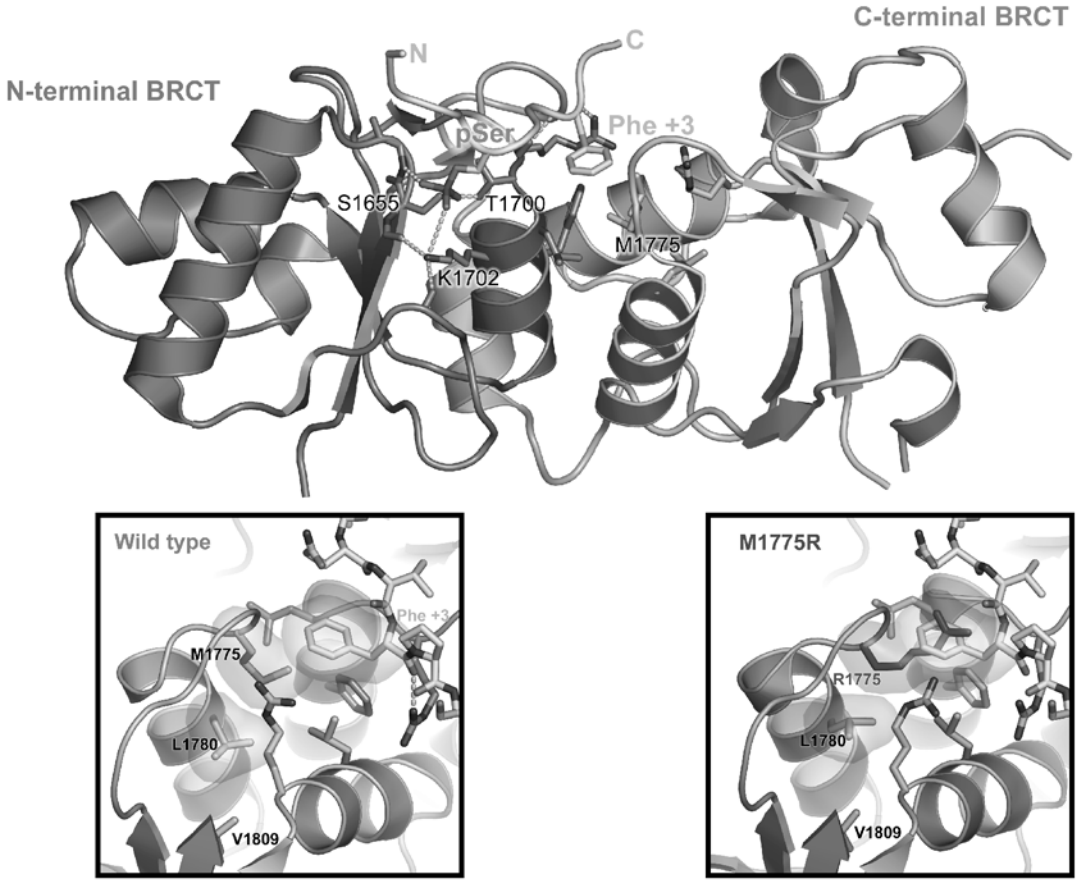

Figure 1. Structures of the BRCA1 BRCT domain and interactions with phosphopeptides
Top panel. Structure of the BRCA1 BRCT domain bound to a pSer-x-x-Phe peptide target. The N- and C-terminal BRCT repeats, the inter-repeat linker and the bound peptide are distinguished by different shadings. Residues important for peptide recognition are shown as sticks.
Bottom panels. Details of the Phe +3 binding pocket in the wild type structure (left), the M1775R variant (right). Note that the M1775R and V1809F structures were determined in the absence of a bound peptide. The peptide shown in the M1775R panel is overlaid from the wild type structure.

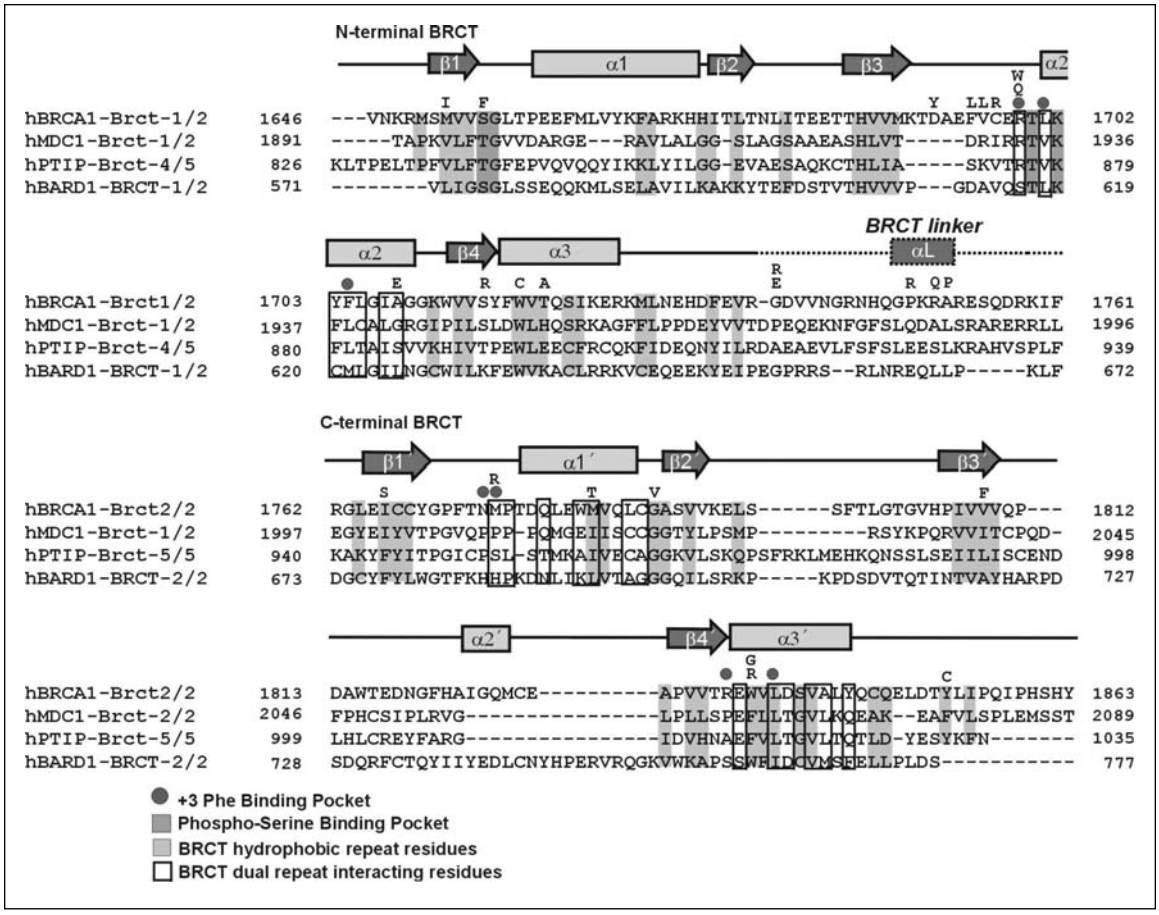

Figure 2. Sequence alignment of BRCT repeat proteins

The amino acid sequence alignment of the tandem BRCT repeats from BRCA1, MDC1 PTIP and BARD1 is shown, with the secondary structure from the BRCA1 BRCT crystal structure. The residues that contact the pSer are shaded, and the residues that form the Phe binding pocket are marked by circles. Missense mutations which have been assayed for interactions with the peptide are displayed above the sequence. Residues involved in inter-repeat BRCT interactions are boxed. Adapted from (14).

is the defect associated with this mutation due to the somewhat reduced stability of this variant, or does the alteration of the protein surface perturb an important interaction surface?

Late in 2003, a major breakthrough in our understanding of BRCT function came when work from the laboratories of Junjie Chen and Mike Yaffe revealed that the tandem BRCT repeats of BRCA1 functions as a phospho-peptide binding module (10, 11). The BRCA1 BRCT is highly selective for the sequence pSer-X-X-Phe. These interactions were shown to mediate the association of BRCA1 with the DNA helicase BACH1, which is essential for the correct functioning of the G2/M cell cycle checkpoint(10, 12), and with the transcriptional co-repressor, CtIP (13). These authors also showed that BRCT repeats from other proteins also functioned as phospho-peptide binding modules, implying that phospho-peptide binding might be a conserved function for BRCT repeats in the DNA damage response.

To understand how the BRCA1 BRCT recognizes its specific phospho-peptide target, we determined the structure of the BRCA1 BRCT bound to a high affinity peptide derived from an in vitro peptide selection experiment containing the pSer-X-X-Phe motif (14) (Figures 1 and 2). Similar structures have also been determined by other groups (15, 16). The structure revealed a phospho-serine binding pocket in the N-terminal BRCT repeat,

and a phenylalanine binding pocket in a groove formed at the interface between the two repeats. Key residues that constitute the phospho-serine pocket include Ser 1655, Gly 1656, and Lys 1702, which all directly recognize the phosphate moiety. Thr 1700 also plays an important role in phosphate recognition, as it hydrogen bonds with Ser 1655, keeping the serine hydroxyl in a rigid orientation appropriate for phosphate recognition. This [Ser-Gly…Thr-X-Lys] motif is conserved in a variety of other BRCT repeats, suggesting that many of these proteins will also bind phospho-serine containing peptides (4, 14) (Figure 2). Indeed, a number of other BRCT-containing proteins, including PTIP, 53BP1, and BARD1, have now been shown to have phospho-peptide binding activity(10, 11, 17).

To directly test the phospho-serine binding capacity of our set of 25 BRCT missense variants, we assayed the ability of a pSer-X-X-Phe peptide to specifically pull down *in vitro* transcribed/translated BRCT variants, compared to a non-phosphorylated control. Our results demonstrated that the structural integrity of the BRCT domain was required for phospho-peptide recognition, as none of the missense variants that highly destabilized the protein fold specifically bound the pSer peptide. The results confirmed the importance of the residues of the phosphate recognition pocket as mutation of any of these residues to alanine completely destroyed the ability of the protein to bind phospho-peptide (14).

The Phe at the +3 position relative to the pSer is bound in a deep groove at the interface between the two repeats (Figure 1). This interaction explains the fact that both BRCT repeats are needed for peptide binding, and loss of part of the C-terminal repeat is associated with hereditary breast cancer. BRCT domains are most commonly found as tandem repeats in other proteins involved in the DNA damage response, and sequence analysis suggests that the head-to-tail packing of the BRCT repeats in BRCA1 is conserved in other repeats (4, 6). Thus it is likely that this secondary recognition groove at the repeat interface is conserved in other BRCT repeat proteins. However, lack of sequence conservation of residues that line the groove suggest that the peptide binding specificity of other BRCT repeat binding proteins may be different.

The importance of several of the residues that line the phenylalanine binding pocket was also tested using the pull down assay (14). Mutations of many of these residues were found to disrupt specific phospho-peptide interactions. For example, mutation of Arg 1699, which interacts with the backbone of the phenylalanine, to either Trp or Gln, completely abrogated binding. The cancer-associated mutation, M1775R, also resulted in a complete loss of peptide binding. Interestingly, M1775 lies at the bottom of the inter-repeat groove and makes close van der Waals contact with the phenylalanine. Superposition of the M1775R mutant structure on the structure of the BRCT-peptide complex reveals that the substituted arginine side chain occupies the phenylalanine binding pocket, suggesting that this mutant is impaired in binding pSer –X-X-Phe targets (14) (Figure 1).

Significant advances have been made in the understanding of the molecular function of the BRCA1 BRCT repeats, and these studies have allowed us to understand the molecular defects associated with a number of previously uncharacterized sequence variants in this region of the protein. However, it remains to be shown what the function of phospho-serine binding is in the context of the intact protein. Do these interactions facilitate rearrangements in the overall structure and organization of the BRCA1 complex? Do these interactions affect that ubiquitin ligase activity of BRCA1? Answers to these questions will not only help to detail molecular mechanisms that underlie hereditary breast cancer, but will help to define mechanisms that regulate the cellular response to DNA damage.

FHA domains

FHA (Forkhead-associated) domains are ~80-100 amino acid domains that play key signaling roles in multiple cellular processes such as signal transduction, transcription, vesicular transport, and protein degradation, in addition to the DNA damage response (18). The structures of a number of FHA domains are now known, both free and in complex with phospho-peptide targets, and studies of the

FHA domains from the DNA-damage response proteins Rad53 and Chk2 have been particularly informative in revealing the peptide binding specificities of these proteins. In general, FHA proteins differ from BRCT domains in that they are highly specific for phospho-threonine, as opposed to phospho-serine-containing targets.

However, like BRCT domains, the Rad53 and Chk2 FHA domains exhibit marked selectivity for specific sidechains 3 residues C-terminal to the phosphorylated residue. In the case of the N-terminal FHA domain from Rad53, the specificity is for negatively charged residues at this position, which is recognized by an arginine residue (Arg 83, Figure 3) (19). In contrast, the Chk2 FHA shows selectivity for hydrophobic residues at the pThr+3 position, which is bound in a largely hydrophobic pocket (20).

FHA function in Polynucleotide kinase (PNK)

PNK is a bifunctional 5'-kinase/3'-phosphatase that is responsible for the processing of damaged DNA ends at both double and single stranded breaks, as well as in base excision repair pathways(21-24). PNK activity is often essential to restore the 5'-phosphate/3'-hydroxyl termini that are required for DNA polymerase and ligase activities to complete the repair of these lesions.

PNK contains, in addition to its catalytic kinase and phosphatase domains, an N-terminal FHA domain, which targets the enzyme to sites of repair and exhibits a different substrate selectivity than previously studied FHA domains. The FHA

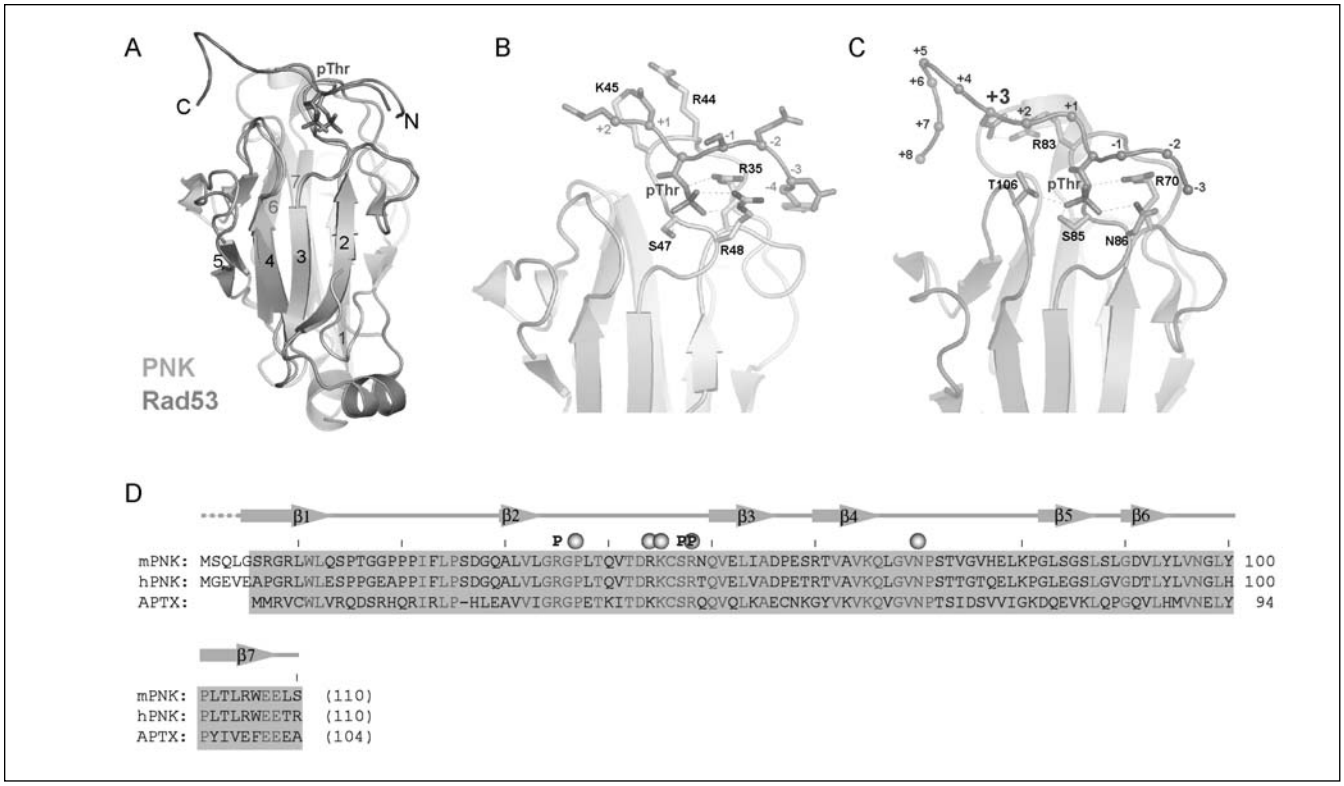

Figure 3. Phospho-threonine peptide recognition by the FHA domain of PNK

A. Structural alignment of the FHA domain – peptide complexes from Rad53 (dark grey) and PNK (light grey). Strands are numbered according to the order in the PNK FHA.

B and C. Details of PNK-phospho-peptide (B) and Rad53-phospho-peptide (C) recognition . FHA sidechains that make critical interactions with the peptide are shown as sticks and the FHA domains are in the same orientation for comparison. Note that the critical interaction involving Arg 83 which specifies an aspartate at the pThr+3 position in Rad53 is missing in PNK. D. Sequence alignment of FHA domains from PHK and APTX. P indicates residues that recognize the target pThr, while the green balls indicate other residues that contact the peptide.

domain of PNK specifically recognizes CK2 phosphorylated forms of the single strand break repair scaffold protein, XRCC1, and the double strand break repair protein XRCC4, interactions which are required to direct PNK to sites of damage(21, 23). Peptide array binding experiments have demonstrated that the PNK FHA, unlike other FHAs, exhibits its highest degree of selectivity for sequences N-terminal to the phospho-threonine, rather than C-terminal (23).

To understand the structural basis for the recognition of phosphorylated XRCC4 and XRCC1 by the PNK FHA, we determined the structure of this domain bound to an XRCC4-derived phosphopeptide (Ac-YDES(pT)DEESEKK-CONH2, Figure 3)(25). The structure reveals that the phosphothreonine residue is recognized in the same way as in other FHA domains, utilizing the invariant Arg 35 and Ser 47, as well as the highly conserved Arg 48, which each ligate the phosphate group.

Comparison of the sequences surrounding the phospho-threonine in the XRCC1 and XRCC4 target sequences reveal a predominance of acidic residues both N- and C-terminal to the phosphothreonine. In XRCC1, there is the additional possibility of multiple phosphorylations by the acidophilic kinase CK2 in the vicinity of the primary site of phosphorylation (21). This, together with peptide binding array studies, has indicated that the FHA preferentially binds acidic target peptides. The structure of the PNK FHA explains this preference (Figure 3B). The peptide binding surface is highly positively charged; key basic residues within this surface are Arg 44, Lys 45 and Arg 48, which are presented on two loops which together comprise a peptide-binding cradle. Arg 48, in addition to its role in phosphate recognition, is also poised to select for the acidic Asp at the peptide pThr-3 position. Arg 44 adopts different orientations in each of the 3 distinct FHA-peptide complexes in the crystallographic asymmetric unit, indicating a significant degree of flexibility in this residue that could allow it to interact with either the pThr-2 or pThr+1 positions. In the XRCC4 target, both the -2 and +1 residues are negatively charged. Arg 44 and Arg 48 are essential for peptide recognition as mutation of these residues (to alanine for Arg 44, or asparagine for Arg 48) completely destroys the ability of the PNK FHA to bind the XRCC4 phospho-peptide. Lys 45 could provide additional electrostatic recognition for negatively charged residues at pThr+1 and pThr+2, however, mutation of this residue to alanine has a negligible affect on the peptide binding affinity, suggesting that this residue plays only a minor role, if any, in phospho-peptide selection. There is no interpretable electron density for the peptide chain C-terminal to the pThr+2 position, indicating that this region of the target is highly mobile and, in contrast to other the peptide targets of other FHAs, is not bound by the FHA domain.

The PNK FHA is quite distinct at the amino acid sequence level from most other FHA domains, and this is reflected in its unusual mode of peptide recognition. The PNK FHA is however, highly similar to the FHA of aprataxin (APTX), a protein associated with the neurological disorder ataxia-oculomotor apraxia and likely also involved in DNA repair (26, 27) (Figure 3D). Interestingly, APTX also associates with both XRCC1 and XRCC4 and it has been proposed that competition between APTX and PNK for XRCC1 or XRCC4 may provide a mechanism for the regulation of PNK activity (28, 29).

The peptide-contacting residues, including Arg 44, Lys 45, and Arg 48, are all conserved in APTX, suggesting that the mode of peptide recognition in this protein could be similar to that seen in PNK. However, the pThr+3 position appears to be important in the APTX:XRCC1 interaction, since mutation of Glu to Ala at this site in XRCC1 abolished the binding to APTX (29). APTX has a single positively charged residue, Lys 75 (corresponding to Pro 81 in PNK), which could approach the pThr+3 residue to provide sequence selectivity at this position.

Interestingly, while the PNK FHA recognizes its negatively charged targets using a complementary, positively charged binding surface, all of the electrostatic interactions that we have identified between the FHA domain and the acidic residues N- or C-terminal to the pThr are relatively long (> 3.5 Å) and are expected to be relatively weak

(Figure 3B). This may allow the PNK FHA to recognize several similar but non-identical acidic target peptides in both XRCC1 and XRCC4. It may also be that we have not yet identified the highest affinity target for the PNK FHA. Peptide selection studies have not revealed dramatic binding preferences such as the preference of the BRCA1 BRCT for phenylalanine/tyrosine at the pSer+3 position. The fact that CK2, the kinase responsible for phosphorylation of both XRCC1 and XRCC4, phosphorylates clusters of residues in these targets in an autocatalytic manner, presents the possibility that the PNK FHA may bind most tightly to multiply phosphorylated targets.

Implications for cancer therapy

Inhibitors of proteins involved in DNA repair and DNA damage-associated cell cycle checkpoints offer potential leads for new anti-cancer therapeutics. For example, inhibitors of BRCA1 could provide an avenue of attack for breast and ovarian tumours which are BRCA1+, but have been disabled in an alternative checkpoint system. PNK inhibitors might provide a means to increase the efficacy of traditional, DNA-targeting drugs by reducing the ability of the tumours to repair the damage induced by the therapy. Signaling processes involving BRCT and FHA domains have been shown to be essential in these systems and the detailed analysis of the principles that underlie phospho-peptide recognition in these systems could provide a basis for the rational design of inhibitors.

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A Molecular View of Cytotoxic T Lymphocyte Induced Killing

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Cytotoxic T lymphocytes (CT) and natural killer (NK) cells serve to protect us against viruses and tumours, and are key players in rejection of transplants and autoimmune disorders. They seek out and bind to targets, then deliver signals that result in the ultimate demise of the recognized cell. In this article I will summarize a number of the contributions that my laboratory has made to understanding how these effectors bring about target cell destruction. Other researchers have made numerous and significant contributions and we have recently published more comprehensive reviews (1,2,3).

Granzyme B – A natural born killer

The major efforts of research in my laboratory have been directed at understanding the nature of these death signals at the molecular level. Most of the early work in this area focused on electron-dense granules that exist in the cytoplasm of cytolytic effecter cells. It was believed that they contained the lytic molecules that mediated cell death. When the CTL bind to a target the granules polarize to the contact surface with the target and thus the cytolytic effector(s) is delivered in a directed fashion.

One of the first proteins to be isolated from the granules was perforin. Biochemically purified perforin can readily bring about lysis of red blood cells and it was envisaged that this membraneolytic activity was solely responsible for target cell death. However, it was soon realized that although perforin could mediate membrane damage, it was unable to initiate DNA fragmentation. The latter being a hallmark of death when a target cell is treated with intact CTL (4).

At this time my laboratory had isolated a gene that encoded a serine protease that is now known as granzyme B (5). Expression of the protease correlates with the killing activity of CTL and the protein is found in granules (6,7). In collaboration with Michael James we predicted that this proteolytic enzyme would cleave substrates at aspartate residues (8). This is considered to be a very unusual specificity for a serine protease and was a critically important idea in our understanding of how granzyme B might bring about death. However, another important result came from Arnold Greenberg (Manitoba), who demonstrated that perforin supplemented with granzyme B (called fragmentin by Arnie) could recapitulate both membrane damage and DNA fragmentation. The model of CTL-mediated lysis was then modified to include granzyme B as a major player. The granules now delivered both perforin and granzyme, and then perforin created the channel through which the protease fused to gain access to the target cell cytoplasm. Through the cleavage of substrates, granzyme B initiated a program of cell death that includes membrane disruption and DNA fragmentation that we now refer to as apoptosis (9).

Obviously a critical question was the identity of these substrates. Bob Horwitz (MIT) had identified a key protein necessary for apoptosis in nematodes which he named ced3. This is a cysteine protease that requires activation through proteolytic cleavage at an aspartate residue. This was exactly the specificity we had predicted for grB (8,10). With considerable help from Don Nicholson (Merck Frosst) we were able to prove that the mammalian homologue of ced3, caspase3, was indeed a critical substrate for grB (11). To prove this in vivo we generated CTL from wild type and grB knock out mice and used these to kill targets. With the wild type CTL we saw very nice activation of caspase 3 but with the knock outs this was completely suppressed (12).

The story seemed complete with grB acting on caspase 3 to initiate apoptosis as depicted in the left side of Figure 1. As usual experimental results seemed to get in the way of this nice model. When we used an inhibitor of caspase 3, DEDV-CHO, DNA fragmentation was nicely suppressed but other features of death, notably membrane damage, were not. The model was then modified to account for these findings (12,13). The activation of caspase resulted in DNA fragmentation but other grB-substrates needed to be cleaved in order to bring about membrane damage. The model at this time is given in Figure 1 where we have grB cleavage of caspase 3 leading to apoptosis but now with another arm to the pathway. Again we were left with the critical question regarding the identity of these proteins.

Mitochondrial involvement in death

A very important clue came from experiments that we were conducting on Bcl-transfected cells in order to study Fas-mediated killing. To our surprise numerous independent clones of transfected cells were not only resistant to Fas killing but also to both membrane lysis and DNA fragmentation mediated by grB. A major site of action of the anti-apoptotic Bcl2 is mitochondria. We therefore tested whether mitochondrial disruption was occurring in the granzyme pathway. Cells were labeled with a fluorescent dye that accumulates in healthy mitochondria but is lost when the organelle is compromised. When these cells were used as targets for either grB or CTL there was rapid loss of the dye. Interestingly this occurred in the presence of caspase inhibitors, thus arguing for the involvement of a direct effect of grB in the pathway to mitochondrial disruption (14).

The mechanism for Fas mediated killing involves caspase 8 which cleaves a proapoptotic member of the Bcl2 family, Bid. This cleavage occurs at aspartate-59, but close by is another sequence that looked like a good grB substrate. Using a variety of *in vitro* and cellular assays we were able to prove that Bid is indeed a good substrate for grB and that its activation is critical in mitochondrial effects in association with Bax (15,16).

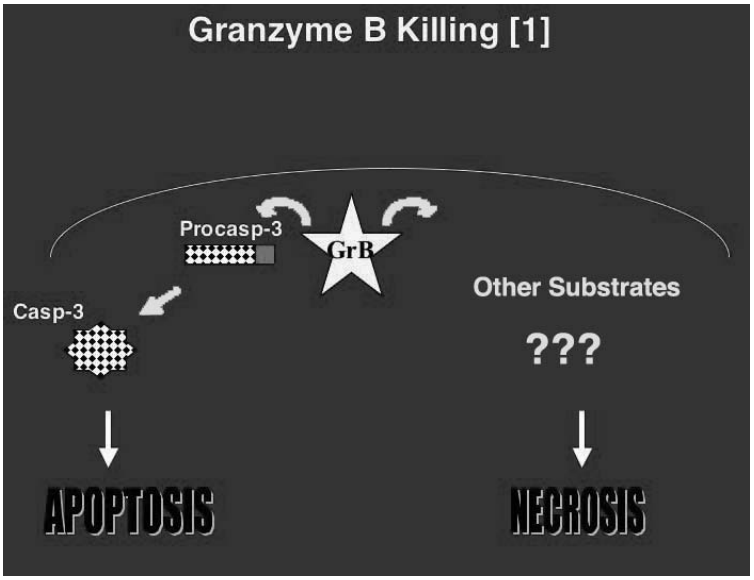

Figure 1 Granzyme B Killing [1]. The simplest view of killing suggested passage of grB through a perforin channel and then cleavage of caspase 3 to bring about apoptosis. Further experiment suggested that some aspects of cell death were caspase independent and therefore cleavage of alternate substrates was proposed.

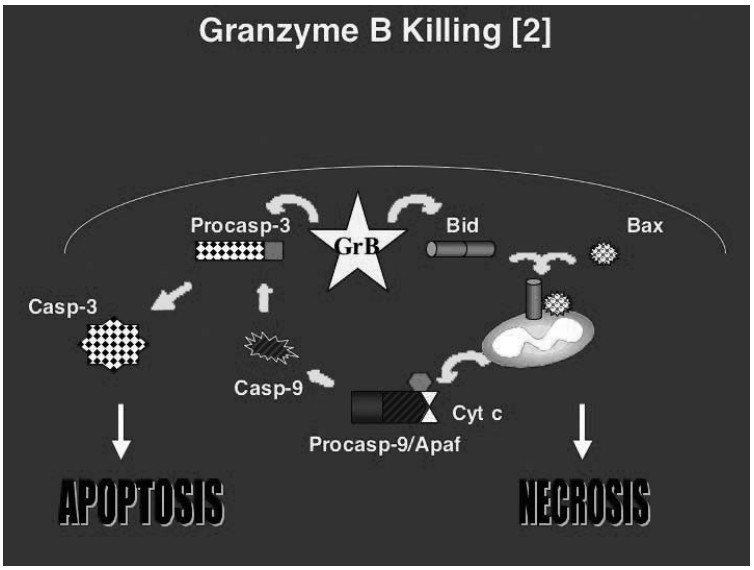

Figure 2 Granzyme B Killing [2]. Internalized grB cleaves and activates caspase 3 to bring about apoptosis. Further cleavage of Bid causes translocation with Bax to the mitochondria. This can lead to release of cytochrome c into the cytoplasm which stimulates formation of the apoptosome. As a result caspase 9 is activated which can amplify the cleavage of caspase 3. In addition disruption of mitochondrial functions can lead to necrotic death.

Granzyme B can thus initiate cell death through at least two pathways. The first involves activation of caspase 3 and secondly via mitochondrial disruption after cleavage of Bid (17,18). This latter route would lead to loss of mitochondrial functions and ultimately necrotic death. However, cleaved

bid also brings about translocation of cytochrome c into the cytosol which is critical in formation of the apoptosome and activation of caspase 9. Our model (Figure 2) evolved to suggest that the mitochondrial pathway could result in activation of caspase 9 (and caspase 3) and necrosis through disruption of mitochondria function. We tested whether caspase 9 was essential for grB-mediated killing by transfection of cells with a dominant negative version of the enzyme. While the inhibitory version of caspase 9 could efficiently abrogate Fas-mediated death (known to go through caspase 9), it only minimally suppressed grB-mediated DNA fragmentation. Thus the mitochondrial involvement in the granzyme pathway did not appear to require caspase 9 (19).

The Safety Brake Model

In reviewing our Bcl2 inhibition results we noted that caspase 3 cleavage was blocked at p20 when the transfected cells were treated with granzyme B. This was identical to the Western blot profile we observed when cells were killed in the presence of a caspase 3 inhibitor. In order to understand this result it needs to be appreciated that caspase 3 activation is a two stem process. The first involves the direct action of grB on the precursor p32 molecule to produce p20 and p10 fragments. Then the low level of activity of the enzyme is enough to promote self catalytic proteolysis of p20 to p19. The resulting p19/p10 heterodimer is the fully active form of caspase 3. Thus Bcl2 is acting to inhibit, indirectly, the self catalytic step.

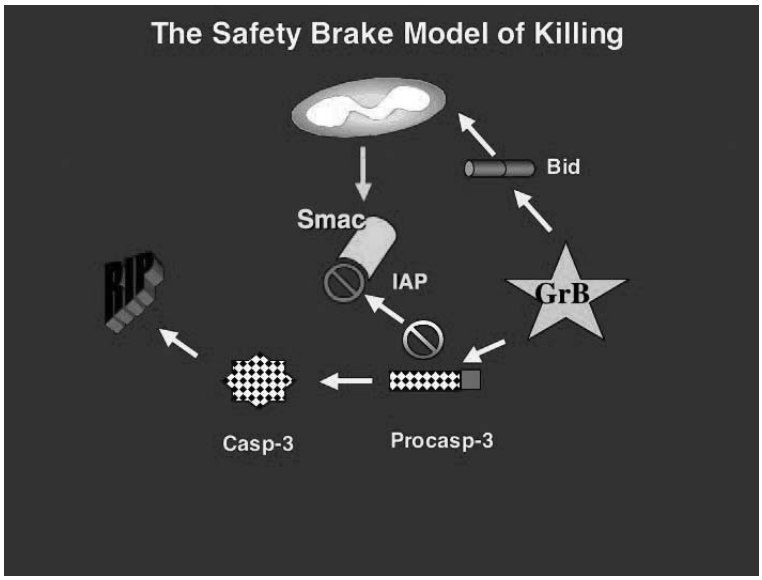

Figure 3 The Safety Brake Model of Killing. Granzyme B cleaves caspase 3 but activation of caspase 3 is blocked by IAPs. In order to overcome this inhibition Bid cleavage results in Smac release from the mitochondria and binding of SMAC to IAP. Only then is full caspase 3 activity revealed.

The activity of caspases can be suppressed in the presence of inhibitors of apoptosis proteins (IAPs) with Bob Korneluk and Peter Liston (CHEO). We therefore asked whether the IAP family member XIAP could block grB-mediated caspase 3 activation *in vitro*. Indeed when we added XIAP to grB and caspase 3 we saw a build up of p20. In addition when a cell line was infected with an adenovirus encoding XIAP we observed almost complete blockade of the DNA fragmentation normally seen with grB (19).

Many cells express IAPs but caspases can still be activated. This is achieved by the action of proteins (e.g. SMAC/Diablo/Omi) that efficiently bind to IAPs and thus overcome the IAP-mediation inhibition of caspase activity. In our *in vitro* assay with grB, caspase 3 and XIAP, a SMAC peptide was indeed able to overcome the p20 blockage and appearance of p19 was seen.

Taking this together we have proposed a "Safety Brake Model of Killing" (Figure 3) in which grB cleavage of caspase 3 is analogous to pressing the gas pedal. However, the hand brake (IAP) is on so apoptosis does not proceed. Only after bid cleavage and SMAC release from the mitochondria can the death pathway proceed (2,19).

Our model works well for the reductionist view of killing with purified grB but does not explain the situation with intact CTL. While Bcl2 can efficiently block grB-mediated death it is not particularly effective when targets are treated with intact effector cells. This result is mirrored in the activation of caspase 3, where in the purified system activation is inhibited by Bcl but with cells it is not. We believed that the simplest explanation was that CTL killing involves whole granules and these likely contained other lytic effectors. However, when intact granules were used in killing or caspase 3 activation assays, Bcl2 transfected targets were refractory. Our current hypothesis is that

cell-cell contact between effector and target is important. Perhaps a signal is transduced into the target that inactivated the Bcl2 inhibitory activity. The molecular basis of this mechanism is currently under investigation.

The hole story is not the whole story

Returning to one of the early models of killing, it was believed that perforin acted to create a channel, in the target cell membrane, through which granzyme could pass. There is very little evidence, however, for this model and in fact perforin has never been shown to allow passage of a 30 kDa protein (the approximate mass of grB). Indeed we observed that grB, with a fluorescent tag, could be taken up into cells independently of perforin (20). On the basis of these observations it was proposed that a receptor existed for the proteinase, and we provided evidence that the mannose-6-phosphate receptor could act to internalize grB (21).

In early studies we demonstrated that uptake was dependent on the presence of the receptor and this could be inhibited by mannose-6-phosphate. However, it became apparent that some cell types did not appear to require the receptor as M6P inhibition was minimal when purified grB was used. The strange result was that these same cells were sensitive to M6P inhibition when intact granules were used as the killing signal. It turns out that grB exists in a very high molecular weight form in granules or in freshly isolated degranulate material. This complex contains minimally granzymes, perforin and proteoglycan and is capable of killing targets. As depicted in Figure 4 we can envisage at least three possibilities. Perforin could polymerize to create a channel for granzyme to pass which is shown on the left side. On the right hand side the whole complex binds to the receptor and is internalized with perforin mediating release from endosomes. The alternative (shown in the middle) has grB binding nonspecifically to the membrane with perforin stimulating same kind of repair mediated entry. Experimentally killing with the degranulate material can be inhibited through expression of a dominant negative dynamin protein with the target cell. In contrast death induced by purified grB is not sensitive to the inhibitor (22). We interpret this to mean that killing with the complex depends on receptor-mediated endocytosis, a process known to depend on dynamin. Obviously the extent of the inhibition will depend on the amount of free versus complexed grB that is present within the immunologic synapse (Figure 4).

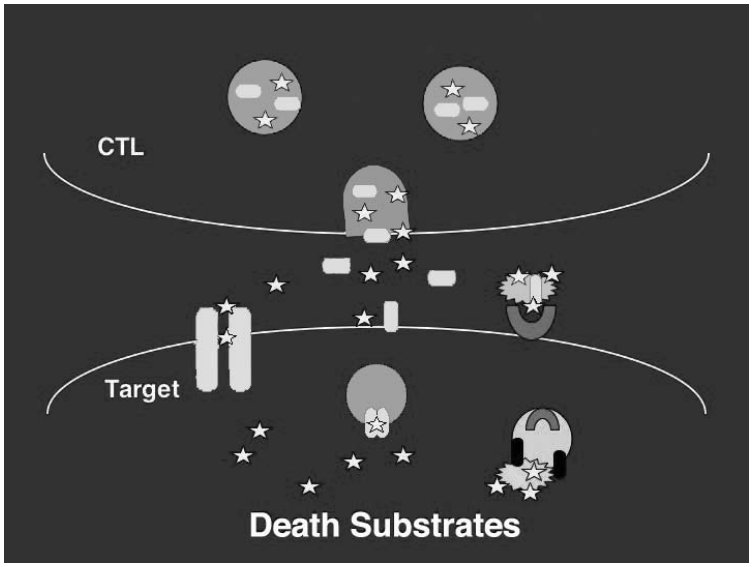

Figure 4 Models of Granzyme Entry. Granzyme B is present in the CTL-granule as a complex with perforin and proteoglycan. This complex is stable after degranulation and thus may bind intact to the receptor (right hand side). After internalization perforin will mediate release of grB into the cytosol. Alternately if the complex dissociates grB could either pass through a perforin channel (left hand side) or be taken up by a perforin-induced repair mediated pathway (middle).

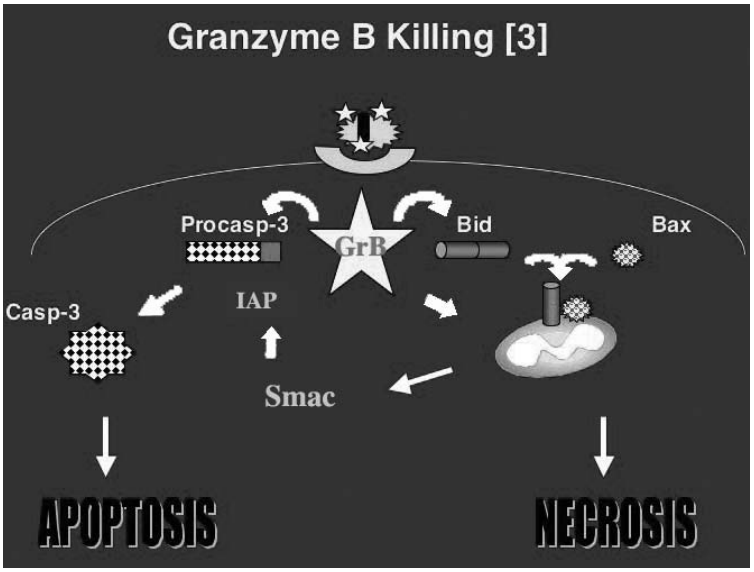

Figure 5 Granzyme B Killing [3]. In this current model grB is taken up as a complex. Once released in the cytosol it brings about the cleavage of caspase 3, disruption of mitochondrial functions and release of regulators of apoptosis.

Interestingly when targets that express the DN were treated with intact CTL a significant inhibition of death was observed (22).

We believe this pathway could be quite important as the M6PR, under its other guise as the insulin like growth factor 2 receptor, has been characterized as a tumour suppressor in a wide variety of human tumours. Thus lack of expression of the receptor on the cell surface could be a strategy to avoid the lethal consequences of recognition by a CTL or NK cell.

A Work in Progress

Over the years our model of killing has evolved to take into account new and often unexpected results. Our almost current view of granzyme B-mediated death is shown in Figure 5. Once grB is internalized, via interaction with a receptor, it can bring about the demise of the cell via numerous pathways including cleavage of caspases, disruption of mitochondrial function, and release of key apoptosis regulatory proteins. However it is also known that the proteinase cleaves other substrates that may also contribute to the death of the unfortunate target. This may appear to be overkill but may be not, when you consider that the function of these cytolytic effectors is to combat viruses that have a variety of tricks to preserve themselves. In addition most of our experimental data is generated with *in vitro* systems and it is clear that the situation with intact CTL and *in vivo* responses will likely be more complex. As we strive to move to more physiologically relevant experiments it is likely that additional pathways will be revealed. We believe that understanding these pathways to death and strategies for survival will provide vital information for the development of immunotherapeutics.

Acknowledgements

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Canadian Biochemistry, Molecular Biology and Cell Biology on the Flat Earth

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It is not news to us in basic biomedical research in Canada that funding of fundamental research has reached a cross-roads and the path for Canadian science is heading downwards. The results from recent CIHR competitions tell the story all too well. The cutoff for funding is well above 4.0. Any grant rated 4.0 or higher is considered by peer reviewers to be excellent. Thus, CIHR is not funding excellent science. Those of us who have served on peer review committees know that these grants are first rate, world-class science. The cutoff for funding only a few years ago was in the high 3s (e.g. ~3.8). These grants are rated as very good. At that time we knew that CIHR was not funding grants that certainly deserved to be funded. Grants with a rating of 3.5 or lower had some major problems and the committee members rarely felt that the grant should be funded. Thus, the number of highly qualified grants submitted to CIHR that are not being funded has increased significantly. In hard numbers, in March 1998, the MRC had 945 applications and funded 403 with a success rate of 42%. In March 2005, the CIHR had 1678 applications and funded 478 for a success rate of 28.5 %. In the September, 2005, competition, 1833 grants were submitted and 454 were funded at a success rate of 25%. Thus, only a few more grants are being funded in 2005 than in 1998. It is true that the average amount per grant has increased from $74,400 in 98-99 to $111,483 in the September, 2005, competition (1.5-fold increase). However, in 1998-99 the MRC budget was $245 million and this increased to $657 million in 2005-6 (2.68-fold increase). However, these numbers ignore inflation. When inflation is taken into account, we can see that the budget of CIHR has approximately doubled whereas the value of a CIHR grant has remained static. Clearly, basic researchers have not made the case for the importance of basic science to the CIHR President, the Council or the Canadian government for improved funding.

One policy that has endured in the transition from MRC to CIHR is the budget reduction policy. When the peer review committees rank grants, they also examine budgets and make recommendations to the Council. The committees on which I participated are tough on budgets and rarely approve budgets as submitted. Thus, the peer reviewers are not generous since they know that money taken from one budget will be available to fund another. Thus, the committees recommend a minimum dollar amount that is perceived to be necessary to accomplish the proposed research. Nevertheless, in every grant competition that I can remember, the governing Council reduced the peer reviewed budget from somewhere between 10 and 20 percent. In the September, 2005, competition the budget reduction was an average of 18%. Thus, a bare-bones budget is skewered by the governing Council. These are tough decisions. Every time the Council has been faced with either funding fewer grants with recommended budgets or slicing the budget and funding more grants, the latter option has been chosen.

If you are wondering where the 2.7-fold increased government funding is going, investigate the CIHR web site (e.g., www.cihr-irsc.gc.ca/e/25845 .html) and you will see the results for 2006. Note that a request for applications (RFA) for a topic entitled "Scoping Reviews and Research Synthesis: Priority Health Services and System Issues" generated 22 applications, 11 of which were funded (50% success rate).

The point from the discussion so far is that we as basic medical researchers have not successfully made the case for improved funding of operating grants. The result is that our resources are stretched, that excellent grants are not funded and the Canadian biomedical research effort is spiraling downward. We are therefore compromised in our ability to compete internationally that will no doubt have a negative impact on the economy of Canada and the development of improved health care in our country.

The rather dismal course of events has occurred during the last ten years at a time where there was a change of attitude of the Canadian Government that has had a very positive impact on universities and biomedical research. As noted above, the funding for MRC/CIHR has nearly tripled. Particularly, impressive has been the development of the Canadian Foundation for Innovation, which has made large investments in infrastructure to support research, and the Canada Research Chairs program, which eventually will provide salary support for 2000 university faculty members. Thus, we have the space, the equipment and faculty salaries to support biomedical research, but operating budgets are limiting our abilities to produce world-class science and to compete internationally. What is the point of having the infrastructure to do research if the funding for conduct of the research is inadequate?

International science on the flat earth

Over the Christmas vacation I had the time to read a book by Thomas Friedman entitled "The World is Flat". Mr. Friedman is a highly respected columnist for the New York Times. The thesis of his book is that third world countries can, and now are, competing internationally due to the remarkable developments in the digital revolution, the internet and the governments of these countries. No longer do people from India need to come to Canada to participate in new technologies, since these developments have empowered them to be able to do this work in their own country. This is a book that we as scientists would benefit from reading and digesting.

Ten years ago India and China were not major players on the world scientific scene. Now they are connected and competing in the global market place since much that used to be done in Toronto can now be done at a much reduced cost in Bangalore, India, or Dalian, China, and many other places. The governments of these countries see the economic benefits and are developing policies to assist entrepreneurs.

Mr. Friedman also notes that this is true in science. In India, for example, they have a strong tradition in excellent teaching. But graduates were handicapped because the employment opportunities after earning a Ph.D. were limited. With the improved economies of India, China and other countries, these governments are better able to direct dollars into research, including biomedical research. Because their costs are much lower, they are able to compete in science with fewer dollars. It is not unusual now to see papers in Science or Nature from China, and not just from Chinese trainees working in North America, Europe and other established centres of the world. The international recognition of China in science is exemplified by the recent inclusion in 2006 of the Chinese journal "Cell Research" in the Nature family of journals. North Americans are publishing in Cell Research and the trend will no doubt continue.

Thus, Canadian biomedical researchers are no longer just competing with countries such as the United States and Japan, but also with newer players on the flattened earth. How long will it be before the chronic under-funding of investigator-initiated operating grants in Canada and the downward trend in funding basic research put Canadian biomedical research in a league with Portugal that has never had a serious profile in health-oriented research. Will Canada follow in the footsteps of Argentina that in previous times had a significant research commitment? Since the devaluation of the Argentine currency a few years ago, the scientists are struggling heroically to have a world presence. One aspect of the tragedy is that the scientists in Argentina are very well trained, as those of us who have had Argentine postdoctoral fellows in our labs can testify. Thus, while China

and India are seeing improvements in their research environments and capacity, Argentina is heading in the other direction.

Biological research is booming in Singapore

Singapore is a small island-country of 683 sq km in diameter (3.5 times the size of Washington, D.C.) with a population of 4.4 million. Unlike the situation in Canada, the government of Singapore has made a huge commitment to basic research. In addition to the traditional areas of research at the National University of Singapore and the academic hospitals of this small nation, the government is investing heavily in biological research. In 2002, Biopolis was established with three objectives. First, Biopolis is to be a focal point for scientific talent to do world-class research and to serve as fertile training ground for undergraduate and graduate students. This magnet of talent is the single most crucial element required for expansion of the biomedical industry. The second stated objective is to integrate and synergize the capabilities and resources of research institutes and to encourage cross-disciplinary research. Third, Biopolis is to bridge research in the private and public sector by creating an environment that fosters exchange of ideas and close collaboration. The expectation is not only that biomedical research will be greatly enhanced, but that there will be very significant economic dividends. Such developments and the inspired support of government attracted Novartis to establish a public-private partnership called the Novartis Institute for Tropical Diseases in Singapore. So it is not only the government that is spending money in Singapore on fundamental biological research.

We don't have to come to Singapore to learn about the economic benefits of support of basic medical research since a stunning example is found in Alberta. The Alberta Heritage Foundation for Medical Research was started in 1980 by the visionary government of Peter Lougheed. In the 25 years of it existence, AHFMR with its nearly $1 billion endowment has certainly changed the picture of health research as well as health care in Alberta. The bonus has been the substantial economic benefit derived from this investment. AHFMR has been such a success story that the current government of Ralph Klein has pledged to boost the endowment by $500 million over a 3 year period.

Future generations and biomedical research

When I speak to colleagues in the United States, there is a definite concern about the lack of interest of college graduates in a career in biomedical research. One only needs to read the literature to see that many more papers originating in the United States have foreign graduate students and postdoctoral fellows as lead authors compared to the last century. I see the same trend in Canada but perhaps to a lesser extent. In one sense this may not be a problem since this trend supports the thesis that biomedical research is an international affair and may the best people in the world work in the best labs. On the other hand, it seems unfortunate that our best students are not pursuing a career in research. I am not concerned about those excellent students who choose to study Medicine. After all, one day I might be their patient and I want a smart, dedicated doctor to take care of me. Moreover, occasionally physicians choose a research career subsequently and these rare individuals are badly needed.

To attract the best students into science, I think there are two major problems that need to be addressed. First, in a recent commentary in the journal Cell by Bruce Alberts (2005), he suggests we should change the way we teach science in high schools and in the first years of university and thereby attract more students into science careers. He discusses his own career and how he was almost turned off science by the early courses at Harvard. He likens many of these lab courses to being more like cooking lessons. I always tell prospective graduate students that doing research is almost nothing like the lab courses they have taken. Dr. Alberts says, "Our goal as teachers and educators should be to expose our students to the discovery process and to excite them about challenges at the frontiers of knowledge". Amen. Toward this end, one program that we have in Alberta is a very strong summer research program for undergraduates largely funded by AHFMR. If they end up in a first-rate lab, the

student obtains first hand experience of research and the excitement that comes with it. AHFMR even has a small program for high school students to work in vibrant labs. I hope that Canadian scientists and teachers re-examine the way science is taught with Bruce Alberts' goal firmly in mind.

The second problem is the view by the next generation that a career in science is almost a lottery. They see 75% of scientists fail in their attempt to obtain a grant from CIHR. Why should they put all of this sweat and effort into becoming a scientist, produce an excellent grant and then not be funded? I guess they have a point. It would not be fun to be a scientist and yet have minimal or no funds to conduct research. Thus, the need to persuade the Canadian Government and most Provincial Governments to invest more in research is an issue for current scientists but also impacts on the quality of students we attract into science.

What should we do?

We need to get proactive in informing the Government and the public about the many benefits of basic biomedical research. We have all heard this many times over our careers yet little is ever done. I am as guilty of inaction as most other Canadian scientists. I am busy doing my science, getting cutting-edge research accomplished so that I can publish in the best journals and survive in the next grant competition I enter. I am also a teacher of the next generation. And I have other commitments such as reviewing grants and research papers.

I don't really know how to gain access to governments, or speak to the public who pay the research bills. But if someone said that they had organized a meeting with 3 MPs from Edmonton, and would ask me to come and talk to these public servants, I would be there. I would like to tell them that my basic, curiosity-driven research on phospholipids is having an impact today on the possible treatment of persons with heart disease, stroke or persons with non-alcoholic steatohepatitis. The data are there. Basic research is fundamental to the next generation of treatments of human disease.

Thus, I suggest that CSBMCB takes the money from their endowment and dues and hire someone full time whose job is to work with the universities to set up appointments with government ministers, MPs, MLAs and anyone else who will listen. That person should give us ideas of how to talk to these people. We would then be in a better position to make the case for biomedical research and its many benefits.

A person such as this could work with the universities to get us to present public lectures to high schools and civic organizations so they can understand science and its multitude of benefits. In Singapore, the university has such an outreach program. They have asked us to give such a public lecture to the three top high schools in this country. But no-one ever asked us to do this in Edmonton, or when we lived in Vancouver. It was a lot of work for us to prepare this lay lecture in the first place. But now it is done and is just waiting for someone to ask us to give this type of lecture in Edmonton or in Ottawa next time we are there.

We also need to be organized by this new person to talk to members of the CIHR governing council and President Alan Bernstein. These are the people who have made these decisions to support other initiatives at the expense of investigator-initiated research. They decided to limit investigator-initiated research grants and budgets and expand other programs with the large influx in resources from the Canadian Government. We need to persuade them that support of basic biomedical research is heading towards a crisis that is already having a multitude of serious consequences.

Finally our universities, our faculties of education and our public schools need to take a very hard look at the way science is taught. They need to pay attention to the call to action by Bruce Alberts.

Footnote:

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Promoting Innovation: 1950s - 2005

Dr. Bruce Sells

CFBS Executive Director

The last 50 years have witnessed considerable evolution in the attention paid by the Federal Government to research. During this period, however, the financial support has not always been consistent and this lack of a consistent commitment has resulted in lost opportunities for Canada to compete effectively in the world of ideas, and thus advance this country both socially and economically.

What I would like to do in this "brief" is to review the changes that I, and a number of colleagues of my generation, have observed during our period in scientific research and to communicate some of the advances and frustrations that we have noted in attempting to compete in a global environment. These experiences are meant to form a backdrop for the creation of an organization that is designed to communicate the benefits of research to "decision-makers" for the advancement of Canada's productivity.

EARLY DAYS

During the 1950's when many of us were in graduate school, only a small number of organizations, such as the Banting Foundation, provided fellowships for graduate training. Government departments, including the Defence Research Board, granted funds for particular projects but the involvement of the Federal Government in underwriting university research was small. Often, Canadian researchers depended upon the generosity of the N.I.H. in the U.S. to fund their investigations adequately. Obtaining support for post-doctoral studies in Canada was also extremely difficult if one depended on a Canadian source. The major agency at that time was the Canada Council that accepted applications from individuals in both Arts and Science disciplines. The success rate was low, and again those of us in the life sciences applied to American organizations such as the Damon Runyon Fund and the Jane Coffin Childs Foundation. Success with Damon Runyon allowed me, for example, to study for three years in Europe.

Returning to Canada in 1960, however, was disappointing. Few exciting opportunities were available for individuals with advanced training, especially in molecular biology, which was just emerging as a new discipline. Many of us consequently gravitated to the U.S., where recruitment of trained investigators was active and support for research could be obtained from the NIH or NSF and a number of non-governmental agencies.

CHANGING ATTITUDES

With the migration of many investigators from Canada to find "greener pastures" where research funding was available, concern started to emerge in our Federal Government. This was evidenced by the appearance of governmental representatives sent to the U.S. to interview expatriate Canadian scientists. While at St. Jude Children's Research Hospital, I spoke with one delegate and was asked the reasons for my departure from Canada. I suspect that my responses concerning the lack of research support in Canada were similar to others who received such visits.

The year 1960 was characterized by the formation of the Medical Research Council (MRC), with a modest budget of $ 2.3 million. In 1978 the Natural Sciences and Engineering Research Council (NSERC) was created with an initial budget of $112 million. Prior to 1978, NSERC-type awards were provided by the National Research Council (NRC). Growth of the MRC budget during the 1960s, and the rise in political awareness that research should be better supported, encouraged many expatriates to return to Canada. My own research group at that time of four post-docs, a graduate student and technician migrated from St. Jude Hospital in Memphis, Tennessee to the Medical School being established at Memorial

University, Newfoundland, to set up a lab in Molecular Biology, with assurance that our initial financial needs would be met by funds provided by the Federal Government. A decade earlier it is unlikely that this could have occurred. Since then, research scientists have observed a rollercoaster ride of peaks and valleys in the level of funding provided by Parliament. The increasing investment in the research enterprise consequently attracted the attention of politicians, and the requirement that the scientific community liaise with "decision-makers" if researchers were to expect sustained and increased support.

THE ROLE OF THE CANADIAN FEDERATION OF BIOLOGICAL SOCIETIES (CFBS)

With its inception in 1957, CFBS initially played an important role in bringing together the various disciplines in the Biological Sciences. Its major focus was the annual scientific meeting, which was designed to act as a vehicle for better interaction amongst researchers. The model for this organization was the Federation of American Societies of Experimental Biology (FASEB).

With the emerging emphasis on research in this country, expansion of Canadian universities, and growth in the number of life science investigators, the demand for funding increased dramatically. Consequently, individual CFBS members started to act as advocates for greater Federal funding. In addition, members of the research community began letter-writing campaigns to MPs to communicate the benefits of research. The need for a central office to interact with the government in Ottawa became a necessity. Subsequently, in 1985 CFBS moved its office from Saskatchewan to Ottawa, and the CFBS Executive appointed an Executive Director with the role of interacting with "decision-makers" (parliamentarians, senior government officials and granting agencies).

In the Life Science community, questions are often heard concerning the need for CFBS to be involved in advocacy. The underlying reason relates to the background of most "decision-makers". In Parliament the vast majority of MPs are NOT scientists. They have expertise in other areas. Many other groups with different requests are vying for the attention of "decision-makers" for financial support. CFBS, therefore, has an important role to play in informing parliamentarians and other "decision-makers" about how investing in life science research can help Canada in moving forward both socially and economically. Since 1985 this is what CFBS has tried to accomplish. The recent election, with the large number of new MPs, provides CFBS with a challenging opportunity to ensure that its message is conveyed. Our recently developed seminar program with the Parliamentary Library will allow CFBS to inform MPs about life science issues that may appear in legislation.

CFBS REDEFINES ITSELF

1. Advocacy and Innovation

In the 1990s two major complaints were heard regarding CFBS. One related to the Annual Meeting, which will be discussed below, and the second related to advocacy. There was a perception that CFBS interests were "too biomedical" and thus excluded important members of the life sciences community. Consequently, efforts were made to be more effective in our communication to the membership. To overcome this misconception, CFBS developed an updated website where advocacy activities and "briefs" are posted, and also issued communications to our members called "CFBS Alerts".

As a prelude to meeting "decision-makers", issues are defined and a "brief" prepared in response to requests from the societies and discussions with colleagues in Ottawa. Efforts are made to ensure that the issues represent the spectrum of concerns voiced by our membership. For example over the past several years the following were items of interest to the broad life sciences community: 1. The need for highly qualified personnel. 2. Support for "indirect costs of research". 3. Promotion of partnerships between Federal/Provincial Governments for a strategy regarding funding for post-secondary education. 4. Sustained financial support for the Granting Councils. CFBS supported the establish-

ment of: i) CIHR, ii) Canadian Academics of Science and iii) the position of Science Advisor to the Prime Minister.

To ensure that topics of concern to individual groups/societies are discussed with "decision-makers", special visits are organized. Most of our discussions with parliamentarians and senior personnel in government fall under the broad topics outlined in the CFBS "brief" and/or in the "brief" prepared by individual societies. Over the past 7 years the number of visits to parliamentarians and senior government officials has grown. 1. Each May, CFBS organizes visits for both members of the CFBS Societies and for the Canadian Council of University Biology Chairs (CCUBC) with members of parliament, officials of granting agencies and particular government departments. This represents between 15 and 20 visits. 2. By request, CFBS also organizes similar visits for particular Societies of CFBS. The Canadian Society of Zoologists (CSZ) has taken advantage of this opportunity, and CFBS sets up meetings with individuals of special interest to them. 3. As a member of the Canadian Consortium for Research (CCR), CFBS serves on its steering committee and participates in a series of visits throughout the year promoting the concerns of life scientists. 4. Each autumn, CFBS and members of the Chemistry and Physics Community spend two days with decision-makers to encourage government to increase its investment in innovation, and to make suggestions to assist the process. 5. To enhance its ability to get its message to "decision-makers", CFBS continues to be a member of the Partnership Group in Science and Engineering (PAGSE). Each year, PAGSE presents a "brief" to the Finance Committee containing issues it believes will enhance Canada's position as an innovative society. Many of these issues are those supported by our membership. 6. The CFBS Executive Director is in conversation with the Executive of Research Canada (an alliance for health discovery) to ensure that our membership with that organization will be mutually beneficial. CFBS, we believe, has played an important role in voicing the concerns of the life sciences constituency, with many of the issues that we have promoted being addressed.

2. CFBS Annual Meeting

A chronic complaint, in the past, from the society membership had been the character of the Annual Scientific Meeting. While the annual assembly was useful in bringing researchers together in a social sense, it failed, over time, to meet the scientific needs of the members attending. The quality of the presentations was not in question. However, given the move of research to become more focused, and the large number of scientific conferences devoted to more focused topics, CFBS turned to a thematic format starting with the 2000 meeting. This approach, and the increase in the funds that CFBS allocated to attracting high quality speakers, have resulted in conferences that provide greater depth in subject matter than previous annual meetings. The success of this approach has been variable.

Another approach is to model the CFBS scientific conference after the Keystone Meetings in the US, where a series of Canadian conferences would be held each year involving various life science societies. Since 2004, CFBS had been encouraging member and non member societies to be involved in such a meeting format. Societies meeting under that format will benefit from CFBS' office experience and capabilities in meeting organization, while the society would be responsible for the program organization. This format would allow Canadian life science research to be highlighted and interdisciplinary information exchanged. A form of this has been implemented by CSBMCB, and is also being done this year by CFBS in Saskatoon with the Canadian Light Source Users. Efforts designed to introduce this approach on a larger scale have not yet been accepted.

3. Services to Societies

After a period of time, organizations need to re-examine their role. Over the past seven years CFBS has attempted to assess how it can better serve the life science community. This was done in part by initiating an annual strategic planning session to identify problems and determine solutions. Since 1985, many changes have occurred in our community that affect the life of researchers and

the ability of CFBS to function effectively. The following are some of the important ones: 1. Reduced university operating budgets. 2. A smaller number of university life science faculty members. 3. Less time available to members of the life science community to spend in Society activities. 4. Decreasing membership in the life science Societies. 5. Increased number of life science conferences devoted to special topics.

Decreasing university operating budgets have resulted in a significant drop in university support staff. In the past CFBS, could rely on faculty members with access to secretarial help if they were involved in life science society activities. Elimination of such positions has meant that fewer faculty members have the backup support to devote to "extracurricular" activities. Coupled with fewer faculty members in many institutions and their increased workload, this has resulted in less time for volunteer organizations. CFBS had, therefore, to consider how it could "fill the gap". Consequently, CFBS has developed contracts with several societies to act as a secretariat for a variety of functions previously handled by society executive. These contracts provide the opportunity for societies to obtain assistance in bookkeeping, website monitoring, maintaining a database of members, as well as help with individual society annual meetings.

CONCLUDING COMMENTS AND OBSERVATIONS

A major difficulty faced by many non-profit scientific organizations has been the drop in enrolment of new members. It would appear that new young investigators are not "joiners". This may be characteristic not only of the scientific community, but also of a broader trend including involvement in the political process. Given the drop in interest by young people in the recent election, we will have to be inventive to ensure that our societies remain vibrant organizations.

What CFBS has attempted, therefore, over the past seven years, to provide services to the Life Science Community and to respond to issues of major importance to our membership. Given the increased pressures on our members, CFBS, in addition to playing a role as the corporate memory, has attempted to serve as a secretariat for Societies that desire this service. Consequently, CSBMCB, CPS and CCUBC have signed service contracts with CFBS. These contracts improve links between the Societies and CFBS, and at the same time provide savings to the contract holders as well as producing additional income for CFBS. The CFBS website has also provided a link to job postings, again creating another service and producing income for the Federation. Introducing these services has helped the CFBS budget, without increasing membership fees which have not changed over the past decade.

The most important function that CFBS can provide remains its ability to act as a voice for life science research. While individual societies can meet with "decision-makers", the message being delivered can often have greater impact when it comes from 9,000 researchers compared to a few hundred. CFBS is always on the look for new organizations with similar interest to form partnerships. CFBS has partnered with other organizations larger than itself, CCR and PAGSE, to ensure that its particular issues can be advanced in an even larger forum. The major role of CFBS, as representative of the life sciences, is to ensure that the life sciences community has a strong voice by seeing that a growing partnership evolves amongst Canadian researchers.

Over the past seven years, it has been satisfying to observe the changing response to our proposals. In our early visits to "decision-makers" we had to convince them that what we were promoting was in Canada's best interests (and not "feathering our own nest"). In later years, the discussions became more of a partnership in which we attempted to articulate solutions to problems to help Parliament make Canada a more innovative society.

It is imperative to mention that CSBMCB is one of the initial societies that worked to create CFBS. What needs to be remembered is that CFBS is a creature created by the societies and it can only be effective when it is serving the needs of the societies. It is important, therefore, that societies

clearly articulate their needs and that CFBS responds effectively.

An issue that CFBS has had to deal with concerns how to develop its interaction with individual Societies. Each Society has a particular character and wishes to preserve its independence. Some societies were under the false perception that membership with CFBS would lead to the loss of their independence. CFBS has been sensitive to this concern and has tried to ensure that this does not happen. One example relates to the CFBS Annual Meeting and individual Society meetings. If a Society decides to participate in the CFBS program theme, then CFBS picks up the costs of the venue and invited speaker. If on the other hand a society that is a member of CFBS wishes to organize its own scientific meeting, CFBS will contribute to help defray the cost of a speaker. Improvements in the CFBS financial base would permit greater generosity.

An ongoing concern that many of us have had relates to the length of the tenure of Society Presidents. One year, we perceive, is too short. Only at the end of her/his term in office has the incumbent become aware of the major problems and can start to consider solutions. We are also aware that it is difficult to have individuals serve for more than one year. When Al Matheson was President of CSBMCB (then CBS), more than 20 years ago, attempts were made to change the President's term in office to two years. Unfortunately, this proposal was defeated. It may be time to reconsider this option.

Since this will be my last year as Executive Director of CFBS, the above is a summary of the last seven years. It has been challenging, often frustrating, but always interesting.

(I would like to acknowledge my colleague Ms. Wafaa Antonious, who helped in the editing of this article).

WHO DO WE SERVE?

Charles R. Scriver

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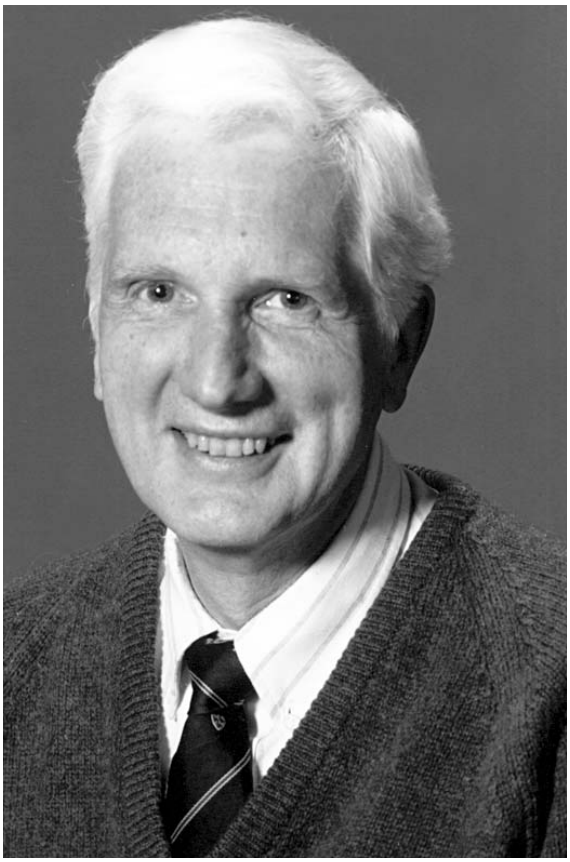
My career has been an unanticipated odyssey. One might ask: How did you get to here from there? The answer could be: If I had wanted to go to here, perhaps I wouldn't have started from there. How much of the journey has been by choice and how much by chance, you, the reader, will decide.

When I was at University, I majored in Geography and Comparative Literature. I intended to become a graduate student in the Department of Geography at McGill University, at that time the most outstanding department in the world. But I did a strange thing - by choice; I made one application to study medicine. The Admissions Committee of the Medical Faculty at McGill University invited me in, and I accepted. Most of the remaining moves on the journey were a result of chance before choice. With the help of some superb teachers, I discovered that medicine can be both a degree in human biology and an enquiry into its dysfunctions. The opportunity also presented itself to learn about "healing", an important part of medicine.

After graduation (in 1955), I followed the usual path through the internship and residency programs, at which time, I began to appreciate the importance of a particular medical question: Why does this person have this disease now? Later, I found its biological counterpart: each person is unique in biological inheritance and identity, which would translate into a biological view of medicine, and the axiom, "treat not just the disease; treat the patient".

Careers may reflect the role of mentors and I was fortunate in mine. John Beck, Ronald Christie and Alan Ross influenced the route my subsequent journey would take. Alan Ross arranged for my clinical studies to continue at Harvard where I was allowed to indulge in seeking answers to the questions I mentioned above, and I was involved there in the discoveries of two new diseases in two patients. Both diseases happened to be Mendelian disorders of metabolism, although at the time I did not recognize how well I would be imprinted by those two young patients. John Beck and Ronald Christie helped me to apply for a McLaughlin Traveling Fellowship, to pursue clinical and laboratory experience with Professor Charles Dent at University College Hospital Medical School in London, England. It was there that I discovered what I really wanted to do: although I was 29 years old, with two degrees and 4 years committed to the study of clinical medicine, I wanted to be a clinician-scientist. Harry Harris (Kings College,



London), Charles Dent and Alex Bearn (on sabbatical in London) were now my mentors, in human biochemical genetics; they convinced me to pursue my interests.

Accordingly, I used the chromatographic techniques of the day to investigate one of the patients I had cared for at Harvard. I discovered hyperprolinemia, a heretofore unknown inborn error of metabolism. I also observed that the patient's urine contained three amino acids in excess (proline, hydroxyproline and glycine), whereas the excess in blood was restricted to proline. I experienced one of those sudden insights (I can recall place and time of day) and I surmised that an excess of proline could saturate a shared transporter in the renal tubule and at the same time displace its other substrates, if all three used a shared mediated transport system. (This was quite novel thinking in human biology for the time - the late 1950s). I tested the hypothesis by infusing myself with proline (I was not hyperprolinemic) and the triad of hyperaminoaciduria appeared in my own urine. Two other hardy post-docs in the lab thought this was fun and we repeated the experiment two further times. I was able to present these findings a year later on the plenary session of the American Society for Clinical Investigation and to publish them both in *Nature* and the *New England Journal of Medicine*.

While in London, I met the original patients with "Hartnup disease". My mentors considered the Hartnup phenotype to be an inborn error of amino acid *metabolism*. I noticed that the findings in the patients were compatible with an inborn error of membrane transport involving a subset of neutral amino acids (again, a novel insight for the times). I was already attuned to think about membrane-located carriers that could recognize group-specific sets of substrates. I thought the Hartnup transporter would be expressed in epithelial cells in both kidney and intestine, probably in the brush-border membrane. I was challenged to produce evidence to support my hypothesis, and I did so. The *New England Journal of Medicine* later published the evidence.

In 1960, I was committed to be Chief Resident in Pediatrics at the Montreal Children's Hospital. The prospect was not delightful. There were better clinicians than myself, and I wanted to continue in research. Alan Ross, my Chairman of Pediatrics, recognized this and supported my wish to develop a lab. Furthermore, he nominated me for a Markle Scholarship and for 5 subsequent years, I was "protected". Thus, I became Canada's first human biochemical geneticist on Faculty. The appointment at McGill allowed me to work with extraordinary colleagues, to create newborn screening programs (for early diagnosis and treatment of genetic diseases) and with those colleagues to create the Quebec Network of Genetic Medicine (Scriver CR et al. *Science* 200 : 946-952, 1978 [PMID 644337]).

By the early 1970s, my colleagues and I were immersed in human biochemical genetics and in the investigation of several new inborn errors of amino acid metabolism. For example, we discovered that there was a subset of vitamin (cofactor)-responsive hereditary disorders of amino acid metabolism, a finding of great significance for the treatment of these particular problems, which we now believe (or know) to involve mutations affecting binding kinetics of the coenzyme or a chaperone-like effect in response to pharmacological doses of the agent. We were also involved in the development of new methods to screen, counsel and treat a variety of Mendelian disorders such as phenylketonuria, Tay-Sachs disease and thalassemia in individuals, families and communities. With hindsight, it was the beginning of "community genetics" (while moving biochemical genetics along), and of an era when something could truly be done to ameliorate "genetic disease". It is not surprising that our involvement in such "translational knowledge" would focus on the treatment of genetic disease, and for over 25 years we have been engaged in a meta-analysis of the modes, progress and efficiency of treatments. Enough to say that biochemists and cell biologists will find challenges enough for many careers here …!

In other sectors, we continued to investigate mediated membrane transport of amino acids and of phosphate anion. The interest in phosphate trans-

port arose through an investigation of infantile rickets which in Quebec, at the time, appeared as an annual quasi-epidemic related to vitamin D Inborn errors of metabolism are Mendelian (single-gene) disorders and one tends to think of them rather simplistically; that there is more to consider became a broader theme of our work. For example, homeostasis or the central tendency of metrical trait values (e.g. measured genotypes of amino acid values in plasma) is a classic complex trait. We generated data on the frequency distribution of amino acid values in normal subjects and found both inter- and intra-individual variation; data implying that each person had his or her own measured genotype (i.e. a form of biological individuality). It was my personal introduction to ways of thinking about inherited susceptibility to and risk for common but complex disease. Further discernment came when we measured plasma amino acid values in patients with the Hartnup phenotype. It had become apparent that very few persons with the Hartnup transport phenotype (the aminoaciduria), as detected by newborn screening, ever developed the Hartnup disease phenotype. We found that the individuals who developed the disease phenotype were low outliers for the measured genotype (i.e. the aggregate values for the plasma amino acids involved in the Hartnup transport disorder). While the Hartnup transport disorder is Mendelian, the Hartnup disease phenotype is a complex trait involving the background genotype and putative modifier loci controlling amino acid homeostasis. Furthermore, we found that one could predict a person at risk for the Hartnup disease phenotype and could counsel and respond accordingly.

Our work then became focused on phenylketonuria (PKU), the inborn error of phenylalanine catabolism involving deficient activity of phenylalanine hydroxylase (L-phenylalanine monooxygenase EC 1.14.16.1). Interest in this genetic disease grew significantly when an effective treatment (by low phenylalanine diet) was discovered in the 1950s. PKU became the condition that changed the outlook on medical opportunities for the management of human genetic disease. Our review (1980) for the New England Journal of Medicine focused the mind upon unsolved problems in PKU and when others cloned the PAH gene, a new era of research could begin; we were involved in it as follows:

1. Newborn screening in worldwide populations provided opportunities to sample PAH mutations identified through patients with hyperphenylalaninemia. Evidence of allelic stratification in human populations emerged with the paradigm that "the history of the population is the history of the allele". We studied this paradigm in detail and became population-geneticists - of a sort.

2. We formed an international consortium and created an online locus-specific mutation database (www.pahdb.mcgill.ca), which became a prototype for LSDBs; it is linked to the newly created Human Variome Project. PAHdb has also taken us into another world and we became involved in bioinformatics and databases.

3. Whereas treatment of PKU was a highly significant development in the field of human medical and biochemical genetics, treatment was neither easy nor pleasant for the patient. We helped to improve the organoleptic properties of the low phenylalanine diet. We also learned that delivery of diet products to patients could be a real problem. In response, we created the National Food Distribution Center as a purchasing and distribution resource for Canada, approved by the Federal and provincial governments. We became food merchants of sorts.

4. Our LSDB showed that 63% of PAH alleles are missense alleles. By means of in vitro expression analysis, we were among the first to show that missense alleles cause misfolding of nascent protein with subsequent aggregation and loss to the proteasome. The paradigm of misfolding proteins due to allelic variation has become a general one in genetics. We had penetrated a little way into the proteomic world.

5. It was known that the phenylalanine hydroxylase reaction required the catalytic cofactor tetrahydrobiopterin (BH4). The scene was set for the discovery of patients reflecting locus heterogeneity rather than allelic heterogeneity. The

locus heterogeneity reflects genes and enzymes involved in synthesis and recycling of BH4. If one could monitor the newborn for evidence of disorders in synthesis or recycling of cofactor, one could identify the affected patient early. This is important because the correct treatment requires replacement of cofactor by pharmacological means; the low phenylalanine diet is not sufficient. Our screening program in Quebec was the first in the world to address this issue systematically.

6. Whereas a few rare patients will have inborn errors of BH4 metabolism, others far more numerous will respond to pharmacological doses of the 6R-BH4 isomer, even though they do not have a primary disorder of cofactor homeostasis. In a collaborative study with colleagues at the Scripps Institute, benefit from cofactor was shown to reflect a chaperone-like effect in some patients; the response is allele-specific. Here was an early demonstration of patient – and allele-specific therapy in a genetic disease. This work creates a new demand for BH4 being met by a corporate response (BioMarin, CA) and a clinical trial. Thus we became involved with the corporate world and the FDA.

7. Lately, we have been investigating enzyme substitution therapy in PKU, using recombinant phenylalanine ammonia lyase (PAL) from yeast. We obtained proof-of-principle (pharmacological and physiological) with PAL substitution in an orthologous mouse model of PKU. This again led to collaboration with the corporate world (BioMarin, CA) – and also introduced us to the animal world of orthologous phenotypes and genes as counterparts of human disease.

The Howard Hughes Medical Institute put me on their SAB for a decade and I was able to play a role in getting the Human Genome Project underway (which may yet evolve into a "Human Phenome Project" (see J Inherit Metab Dis 27:305-317, 2004. After the genome - the phenome? [PMID 15190190]). How the field of human biochemical genetics has evolved and what it now offers was the subject of another recent essay (see J Inherit Metab Dis 24:93-116, 2001 [PMID 11405353]).

Much time has been spent writing (in long hand) grant applications, progress reports, and articles. It is what we do, is it not! Sometimes the peer review system seems to be the worst possible one; yet it remains the best we have, as I have experienced it.

Education and teaching (academic and public) have always been on the agenda, and quite heavily so. But if the reader has reached this point, you will have noticed recurrent use of the plural pronoun. "We" is the appropriate word because it refers to the extraordinary patients, colleagues, graduate students, and post-doctoral fellows who have populated the place of business these many years; the ones whose names are visible in the papers and remembered in my mind. And then there is the family (the 6 of us plus extensions), at a place I call home, without whom none of this narrative would have happened.

Too much information in this essay! Is there any wisdom? If I could send a message, it would be to highlight the influence and importance of mentors; the joy emanating from creative compatible colleagues; the need to be protected with time to think; the need for good space and stable funding. I thank the McGill institutions, and all the persons and agencies who made those attributes available.

The title at the beginning of this essay is: Who do we serve? To end it, I would add: How do we serve? Why do we serve? The answers fill the days...

The CSBMCB enters its 50th year; the beginnings

David B. Smith

(once Editor, CBS Bulletin)

I have been asked to remember some memories about the start of our society in the mid-50's. I find that there are only wisps left and practically none of my associates of those days are still around to help fill out. It was a pleasure to phone the ones I found, but their memories are no more robust than mine.

Compared to the facilities I left at the University of Toronto in 1950, the Applied Biology Division of the National Research Council was very up-to-date. Bill Cook had equipped his lab with a Spinco ultracentrifuge (very low serial number), Tiselius electrophoresis, fraction collectors that worked, practically everything you needed for your project could be obtained. And there was a group of young gung-ho biochemists getting set to do great things. They began to get impatient with the venerable Canadian Physiological Society and the old fogies in Toronto and Montreal who ran it. After all, if you had a paper on the chemistry of hemoglobin, it was likely to be put in a section on Heart and Lung. So they agitated for a new Society. There must have been others elsewhere but they are not in my memories. Things came to a head at a meeting at the University of Ottawa in 1957 – a meeting chaired with great decisiveness by Gordon Butler.

Gordon's article, Recollections on the Foundation of the Canadian Biochemical Society, appeared in Vol. XIX No.1 June 1982 of the Bulletin of the Canadian Biochemical Society. There are references to Gordon Young's book and Art Mako's article, but these add little more. Art's article does quote from meeting minutes: "A meeting of biochemists was held at 8:00 pm on October 9, 1957 in the Auditorium of the Medical Building of the University of Ottawa. The meeting was under the chairmanship of Dr. G.C. Butler and Dr. D.H. Laughland acted as secretary. Seventy persons were in attendance and their names and address were recorded." I have suggested to the Editor that Gordon's paper be reprinted.

Recollections on the Foundation of the Canadian Biochemical Society

Gordon C. Butler

Division of Biological Sciences, National Research Council, Ottawa

It has been said that a person's memoirs should begin at Chapter Two. If I were to write a story of my life it would have ten chapters and what I describe here would be around Chapter Five. I have never felt the urge to put on paper any on my memories, first of all because I doubt if anyone would find them interesting (what might be read with most interest, I mustn't write) and secondly because I am not trying to vindicate any part of it.

However, Dave Smith, the Editor of this bulletin, asked me to provide some copy and I couldn't refuse him because he was the first student to obtain a Ph.D. under my supervision in the Biochemistry Department at the University of Toronto, 1947-1957. Moreover, in 1982 the Biochemical Society has been in existence for 25 years, so Dave and I agreed that I might tell something about its beginnings, not so much the minutes of what happened – which are recorded in the E.G. Young's book, "The Development of Biochemistry in Canada", and reproduced by A.M. Marko's article in this Bulletin of June 1979, written on the occasion of my superannuation – but some impressions of the atmosphere in which it came about.

I am indebted to E.G. Young for the facts collected in his book. At the time I wondered if his laborious compilations merited the efforts involved but I now acknowledge that all biochemists in Canada will be forever in his debt.

In 1936 when I became a graduate student in Biochemistry at Toronto, scientific societies, as we know them today, were almost non-existent. There were the Toronto Biochemical Society (of which I was a member 1935 – 38 and 1947 – 57), the Toronto Physiological Society, the Montreal Physiological Society (of which I was a member 1940-42); these held local gatherings to present the results of research in progress. Each was very much like a club and seemed to fit the definition in Samuel Johnson's 1755 dictionary, "club" – an assembly of good fellows meeting under certain conditions". In fact the Biochemical Society of the U.K., of which I was a member 1938-40, was originally called the Biochemical Club. The Canadian Physiological Society in its early days also had this character. The meetings were small with an attendance rarely exceeding 50 and most of those present knew each other quite well. In those days travel funds were rare with the result that the meetings were largely attended by local members. Travel to meetings was by automobile and usually at the member's own expense. I well remember attending a meeting of the Toronto Biochemical Society at the Ontario Agricultural College (OAC) in Guelph (an affiliate of the University of Toronto. In those days graduate degrees earned at OAC could be bestowed only by the U. of T.). G.F. (Guy) Marrian, my Ph.D. supervisor, took four of us graduate students in his car leaving in the afternoon and returning at the end of the meeting, driving through the winter night in an unheated car which was, however, full of brave talk and cigarette smoke. In those days people didn't worry about themselves or others smoking.

If one had a specially good paper to present he looked for a larger forum. The two most obvious possibilities were the federation of American Societies of Experimental Biology and the Royal Society of Canada. In 1936 and 1937 I had isolated an unknown steroid from the urine of women with adreno-genital syndrome and proved the steroid to be pregnane-3(a),17,20-triol (in the nomenclature of the time). Guy Marrian thought this work should be presented in a prominent place so he encouraged me to give a paper at the Spring, 1937 meeting of the American Society of

Biological Chemists in Memphis, Tennessee. R.D.H. (Don) Heard and I drove down there and back in my father's car. This was the greatest adventure of my life to that date. Naturally we paid our own expenses (about $100 each). The meeting was held in a hotel with two simultaneous sessions, about 50 attending my presentation. E.A. Doisy was the only one who commented on the paper.

Later that summer Marrian thought we should treat Canadians to a presentation of the same work and introduced me to a meeting of the Royal Society in Toronto. I still remember the presentation in the north lecture room of the old Medical Building on a hot May day with the auditorium filled to capacity.

In those days when national scientific societies were lacking or embryonic the Royal Society filled an important role by providing at its annual meeting an occasion for scientists to present their work to a large audience from all parts of Canada. These wider audiences were due to the practice of the Royal Society to provide financial assistance to its fellows to bring them to annual meetings. With the growth of many subject-oriented scientific and professional societies this function of the Royal Society is no longer necessary and it has been largely abandoned.

Following the Second World War the Canadian Physiological Society that I had joined in 1940 for a membership fee of $1.00 grew in membership and importance. Its annual meetings became more important occasions for the presentation of research results and those of us who participated found it a most congenial club.

I remember at a meeting at Queen's University listening to a fine paper delivered by G.H. (Harold) Ettinger; the audience was so small (not more than six) that I felt as though I were having a private lesson in physiology, an impression no doubt enhanced by Ettinger's friendly, avuncular manner.

I also remember a meeting held at the Seigniory Club in Montebello in the autumn of 1941. There were almost no other guests around and the four-dozen of us attending had the hotel to ourselves. There were memorable conversations in the cozy bar and great fun afterwards playing hide and seek around the pillars of dimly lit lobby.

By 1953 the membership of the CPS had grown to 320, seventy of whom were biochemists. There were also appreciable numbers of anatomists, pharmacologists, nutritionists, chemical pathologists and practitioners of other sorts of medical research. Many Canadian biochemists did not belong to the CPS, accusing that organization and its members of representing only medical biochemistry; there was an element of truth in this.

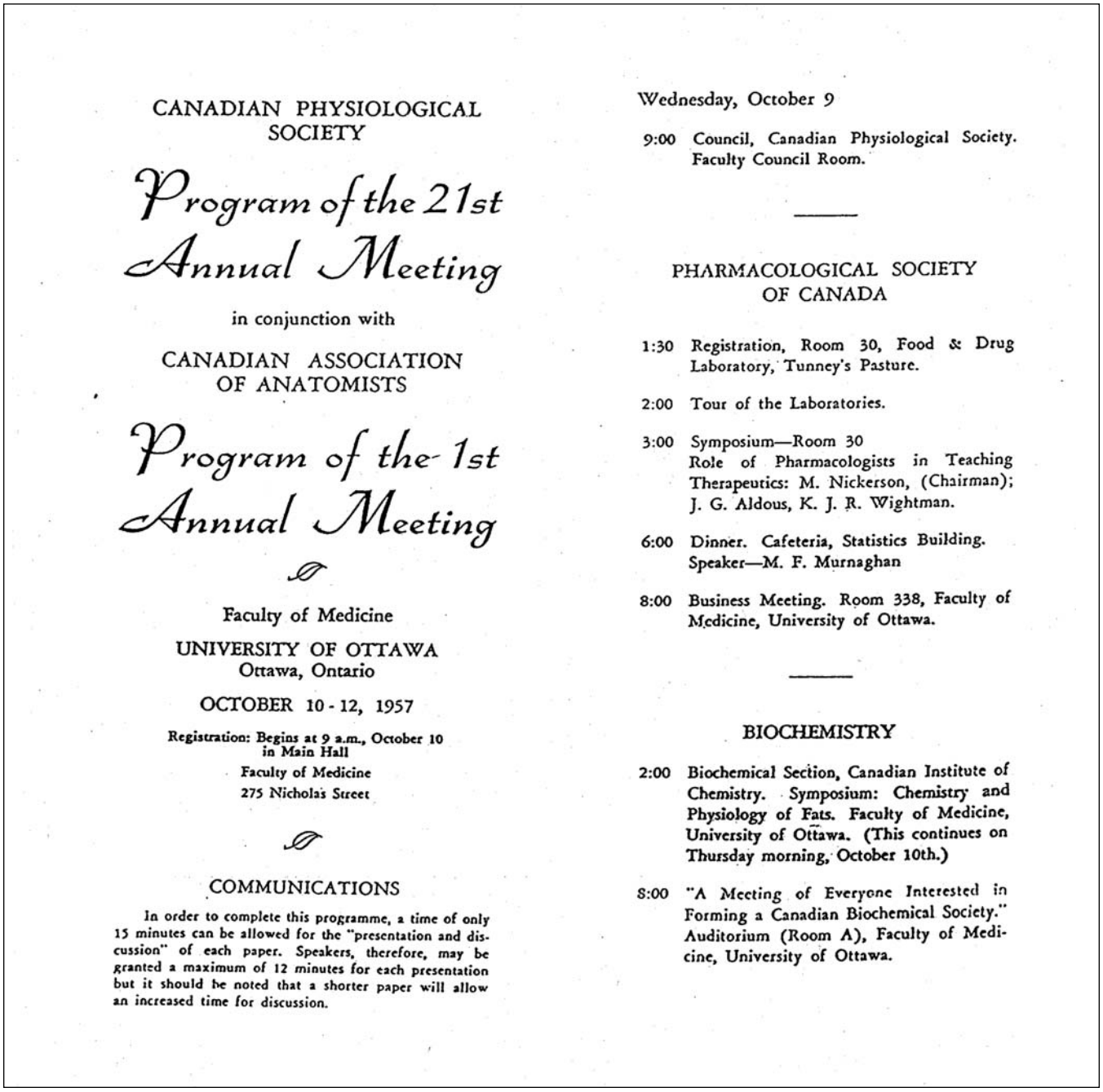
The first biochemistry departments in Canada were in medical faculties and there they have found their most congenial homes. They seemed to do better than those in science faculties or as sub-departments of chemistry.

Another large group of biochemists was to be found in the biochemistry division of the Canadian Institute of Chemistry (CIC). These biochemists tended to be more oriented towards biochemistry of plants and industrial biochemistry. One group of these belonged to the Ottawa Biological and Biochemical Society (OBBS); they, led by Ross Colvin, Ralph Hochster, Dave Smith and Don Whitaker, began to talk about the need for a Canadian Biochemical Society.

Within the CPS, I and many other biochemists were quite happy with our "club", but some of them, notably C.C. (Colin) Lucas, E.W. McHenry and E.G. (Gordon) Young, talked to me at a meeting of the CPS from 1955 on, about forming a Canadian Biochemical Society and urging me to take a lead in "getting one going". Some of us wondered if there would be enough support for a separate society. Finally, at the CPS meeting in Montreal in 1956 the matter came to a head when we heard that the anatomists and pharmacologists were going to separate from the CPS and form new societies. We all agreed that if we formed separate societies we should immediately reunite as a Federation modeled on the one in the U.S.A.

It is interesting to recall some of those discussions in a Canadian context. We were repeatedly asked by officers of the CPS, "Why would you want to

separate?" and "What is it that biochemists really want?" I had two answers to these questions: "They want an organization in which all biochemists can feel at home with their own kind and which can command their loyalty," and "As soon as they form their own society they will reunite with other biological scientists in a federation".



CANADIAN PHYSIOLOGICAL SOCIETY

Program of the 21st Annual Meeting

in conjunction with

CANADIAN ASSOCIATION OF ANATOMISTS

Program of the 1st Annual Meeting

Faculty of Medicine

UNIVERSITY OF OTTAWA
Ottawa, Ontario

OCTOBER 10 - 12, 1957

Registration: Begins at 9 a.m., October 10 in Main Hall
Faculty of Medicine
275 Nicholas Street

COMMUNICATIONS

In order to complete this programme, a time of only 15 minutes can be allowed for the "presentation and discussion" of each paper. Speakers, therefore, may be granted a maximum of 12 minutes for each presentation but it should be noted that a shorter paper will allow an increased time for discussion.

Wednesday, October 9

9:00 Council, Canadian Physiological Society. Faculty Council Room.

PHARMACOLOGICAL SOCIETY OF CANADA

1:30 Registration, Room 30, Food & Drug Laboratory, Tunney's Pasture.

2:00 Tour of the Laboratories.

3:00 Symposium—Room 30
Role of Pharmacologists in Teaching Therapeutics: M. Nickerson, (Chairman); J. G. Aldous, K. J. R. Wightman.

6:00 Dinner. Cafeteria, Statistics Building. Speaker—M. F. Murnaghan

8:00 Business Meeting. Room 338, Faculty of Medicine, University of Ottawa.

BIOCHEMISTRY

2:00 Biochemical Section, Canadian Institute of Chemistry. Symposium: Chemistry and Physiology of Fats. Faculty of Medicine, University of Ottawa. (This continues on Thursday morning, October 10th.)

8:00 "A Meeting of Everyone Interested in Forming a Canadian Biochemical Society." Auditorium (Room A), Faculty of Medicine, University of Ottawa.

2006 Society Award Designates

Dr. Joe Casey, from the Department of Biochemistry, University of Alberta, has been chosen to receive the Merck Frosst Prize for meritorious research by a young Canadian scientist with ten years or less of independent research in the areas of biochemistry.

Dr. Frances Sharom, from the Department of Molecular and Cellular Biology at the University of Guelph, has been selected to receive the Jeanne Manery Fisher Memorial Lectureship award for outstanding contributions by a Canadian woman scientist to research, teaching or society in the fields of biochemistry, molecular or cellular biology.

These awardees will be presenting Plenary Lectures at the 49th Annual General Meeting of the Canadian Society of Biochemistry, Molecular and Cellular Biology to be held May 31 – June 4 2006 at White Oaks Inn Conference Resort in Niagara-on-the-Lake, Ontario.

The 2006 CSBMCB Merck Frosst Prize
Dr. Joe Casey

Dr. Joe Casey was born Lansing, Michigan, where his father completed his Ph.D. in Psychology at Michigan State University, and immigrated to Canada with his family in the summer of 1967. Joe spent his primary school days in Kingston, Ontario and went to high school in downtown Toronto. From 1983-1987, he studied biochemistry at Queen's University, Kingston. During those years he worked for two summers in the plant physiology laboratory of Dr. Ken Budd, Department of Biology, where he learned about biochemistry as a lifestyle by coming into the lab at all hours to take readings of cyanobacterial growth. Joe's last summer as an undergraduate was spent with Dr. John Elce, Department of Biochemistry, where he further honed his protein purification skills on calpain and learned a lot about immunochemistry. His first exposure to molecular biology was in the laboratory of Peter Davies, where he completed his B.Sc. honours thesis on antifreeze gene chromatin

In 1987, with a fresh B.Sc., Joe moved to the Department of Biochemistry, University of Toronto, to work with Dr. Reinhart Reithmeier, where he spent five years trying his hand at just about every protein chemical and biophysical technique that could be thrown at the erythrocyte membrane anion exchanger, Band 3. For postdoctoral work, Joe decided that he would like to combine molecular biological approaches with protein chemical techniques, he went to work with Dr. Ron Kopito at Stanford University.

In 1996, Joe moved to the University of Alberta, to join the Membrane Transport Group in the Department of Physiology, initially as an Assistant Professor, and as a Full Professor since 2006. Since 2002, he has been cross-appointed to the Department of Biochemistry. Joe has received salary support awards from MRC and the Alberta Heritage Foundation for Medical Research (AHFMR) and is currently a Senior Scholar of AHFMR.

With funding from CIHR and the Heart and Stroke Foundation, Joe's lab has focused on the study of structure, function and regulation of plasma membrane bicarbonate transport proteins. Since 1997, he has been a member of the Membrane Protein Group, headed by Dr. Marek Michalak.

The 2006 Jeanne Manery Fisher Memorial Lectureship Frances Sharom

Dr. Frances Sharom was born in Newcastle-upon-Tyne, U.K. and emigrated to Canada with her family after completion of her A-levels.

During her high school years in England she developed a keen interest in chemistry, especially the biological aspects. Frances registered in the Honours Chemistry program at the University of Guelph and graduated with a degree with distinction. For three summers she worked in the laboratory of the Department Chair, Dr. Allan Colter, carrying out kinetic experiments on redox reactions of nicotimamide derivatives with quinones. This work stimulated her interest in research and led her to pursue graduate studies at the University of Western Ontario. There, her supervisor was Dr. Chris Grant in the Department of Biochemistry; she was his first graduate student. Her research focussed the use of spin-labelling to study the behaviour of neutral glycolipids, gangliosides and integral glycoproteins in reconstituted membrane bilayers. The ESR spectroscopy was carried out in the laboratory of Dr. Jim Bolton in the Department of Chemistry. These spin-label studies were the first of their kind and advanced the knowledge on the behavior of individual membrane components.

After completing her Ph.D., Frances moved to Malaysia with her husband, but the difficult political situation there at the time forced them to return to Guelph over a year later, where she worked with Dr. Alan Mellors as a postdoctoral fellow. Her research in his laboratory focussed on the effects of various hydrophobic toxicants on membrane-bound 5¢-nucleotidase. Following her postdoctoral work, she received an NSERC University Fellowship and began her faculty career as an Assistant Professor in the Department of Chemistry and Biochemistry. In 1994, she was promoted to Professor. Frances served a term as Director of the Guelph-Waterloo Centre for Graduate Work in Chemistry and Biochemistry from 1991-1994, and in 2003, she became Director of the Biophysics Interdepartmental Group, an interdisciplinary graduate program at the University of Guelph. In May 2004, she and the other biochemistry faculty moved from Chemistry and Biochemistry to the new Department of Molecular and Cellular Biology.

Frances' research laboratory group works in three areas – the P-glycoprotein multidrug transporter, lipid rafts and GPI-anchored proteins, and the NPC1 protein that is defective in Niemann-Pick Type C disease. Her research group been instrumental in the development of fluorescence spectroscopic tools for studying the structure and function of these membrane proteins. Her research has been supported by NSERC, the National Cancer Institute of Canada, and the Ara Parseghian Medical Research Foundation. Frances currently holds a Canada Research Chair in Membrane Protein Biology in the Department of Molecular and Cellular Biology at the University of Guelph.

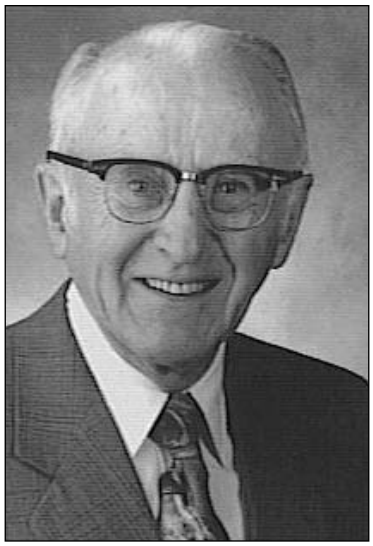
Obituary

Dr. Allan G. Gornall, B.A., Ph.D., D.Sc., F.R.S.C
1914-2006

Dr. Eugene Reno Tustanoff, Professor Emeritus of Biochemistry'
University of Western Ontario

Dr. Allan Gornall peacefully passed away at the age of 91 in Toronto on March 15. As Treasurer of the Canadian Physiological Society, and one of a small group of biochemists who were restless to see the formation of a Canadian Biochemical Society (CBS), he helped foster the establishment of our Society in 1957. He also served as the Honorary Treasurer of the Canadian Federation of Biological Societies during its formative years from 1957-1962. He was responsible for the formation of a joint committee of the CBS and the Canadian Society of Clinical Chemists (CSCC), which he chaired from 1970-75, whose purpose was to direct the attention to Clinical Chemistry as a challenging career opportunity for biochemists.

Dr. Gornall was born in River Hebert, Nova Scotia, in 1914. As his father, a Methodist Minister, moved a number of times to various Maritime parishes, Dr. Gornall's early academic life was influenced by these venue changes. He entered Mount Allison University and graduated with a B.A. degree (cum laude) in chemistry in 1936, and then went on to receive his Ph.D. in Pathological Chemistry from the University of Toronto in 1941. Working under the supervision of Professor Andrew Hunter, Dr. Gornall investigated the relationship that ammonia played between citrulline and ornithine in the urea cycle for his Ph.D. dissertation. Enlisting in the Royal Canadian Navy in 1942, he served as a clinical chemist at the Royal Canadian Naval Hospital in Halifax during World War II, retiring in 1946 with the rank of Lieutenant Commander. His subsequent career in effect spans the history of clinical biochemistry in Canada, and his contributions to its development are legion. After the war, Dr. Gornall returned to Toronto as an Assistant Professor in Dr. Hunter's Department, and rose through the ranks to become Chairman of the Department of Pathological Chemistry in 1966. He held the Chair of the Department, which in 1972 was renamed the Department of Clinical Chemistry, for the next ten years. He retired from U of T in 1980 as an Emeritus Professor.



As evidenced by a long series of publications, his research interests were broad and productive, particularly in the field of plasma proteins and endocrinology. His seminal paper "Determination of serum proteins by means of the biuret reaction", published in 1946, in the Journal of Biological Chemistry, became a "classic", the 9th most frequently cited scientific publication over the next thirty years. In 1949, as a Nuffield Scholar, he studied steroid endocrinology in Edinburgh with G.F. Marrian, and then used this experience to further his work in delving into the biochemistry of aldosterone over the following two decades, which resulted in more than a hundred publications.

He became a keen champion of academic clinical chemistry and was responsible for the high standards which were achieved in his Department. He instituted the post-doctoral diploma course at the university for Ph.D. clinical chemists, and also initiated the refresher courses held biennially in Toronto in early summer. Dr. Gornall was a founding member of the Canadian Society of Clinical

Chemists (CSCC), and was a prime mover and founding Fellow in the formation of the Canadian Academy of Clinical Biochemistry in 1986. This last project occurred during his so-called retirement, which featured a schedule many younger people would describe as exhausting. He has edited both the First and Second Editions of "Applied Disorders of Clinical Biochemistry", and contributed several chapters to this popular textbook as well. Travelling widely in North America and abroad, he presented invited lectures on the education of clinical biochemists to AACC sections across the U.S. (1974-75) and in Australia, New Zealand, and Japan (1977). In 1978 Mount Allison University conferred on him the honorary degree of Doctor of Science, and in 1989 the CSCC bestowed on him its first “Award for Outstanding Contribution to Education”.

When Dr. Gornall's final edition of Applied Biochemistry of Clinical Disorders was published, he turned his talents of critical investigation from clinical biochemistry to the less material composition of the nature of man and the philosophical capabilities of the human mind. As a member of Leaside United Church, many of his articles were published in a book under the title "Understanding God and the Ultimate Reality of Love", published by Lancelot Press. More recently, his thinking enlarged to the existence of spiritual energy which would enrich lives, and further moral values and justice in the human community. In this vein, he expressed his thoughts in the form of prayers which called for the growth of wisdom, compassion and love in our lives. Included in some of the texts was a profound belief in the eternal nature of each human spirit. Allan Gornall sought to leave a lasting mark on this world, both professionally and spiritually and his written words in books and scientific papers provide his research findings and his personal views for the benefit of those who follow.

NEWS FROM MEMBER DEPARTMENTS

Dalhousie University

Department of Biochemistry and Molecular Biology

Correspondent: Mike Gray

Because Dalhousie has not reported for the past two years, this is a good opportunity to briefly highlight some key events from that period, before touching on the current activities of the Department of Biochemistry and Molecular Biology.

In June 2004, **Ted Palmer** stepped down as Acting Head. Ted had retired in June 2003 but had graciously agreed to stay on as Acting Head while the search continued for his successor. In June 2004, another long-time member of the Department, **Cathy Lazier**, retired. Ted and Cathy were among the cadre of recruits that followed appointment of **Chris Helleiner** as Head in 1963, as the Department expanded into new quarters in the Tupper Building (1967-68). Chris retired in 1995 but continued to provide a valuable teaching contribution for the ensuing nine years. In June 2005 Chris was feted at the Department's annual retreat, having been named the first Professor Emeritus in the Department, a most fitting recognition of his contributions over many years. Regretfully, Chris has relinquished his post-retirement teaching appointment, but Ted and Cathy have stepped into the breach, and we are greatly pleased to have them continue on a part-time basis.

David Winter, another (very) long-time member of the Department, who provided invaluable technical service for more than 40 years, also retired in June 2004. David had an extraordinary capacity to fix and do just about anything, and we sorely miss his skills and camaraderie. However, David remains "on call" for us and is ever willing to step in when needed.

Your correspondent began a 3-year term as Head in July 2004, and our first task was to find a new departmental Administrator. **Julie Walker**, who had served as Administrator for both Biochemistry & Molecular Biology and Physiology & Biophysics for over 10 years, accepted the same position and new challenges in the Department of Biology. We were fortunate to recruit **Dawn Schmidt**, who joined the Department in September 2004. Sadly, we will begin the search all over again in January, when the Schmidt family moves to Ottawa.

The past two years have seen a flurry of renovations to accommodate the burgeoning research programs of various faculty members. Within that period, the groups of **Roger McLeod, Cathy Too, Paola Marignani** and **John Archibald** have moved into newly enlarged and refurbished quarters. Office space has also been provided for **Barry Lesser**, who has a major teaching responsibility for Biochemistry courses in the Schools of Pharmacy and Nursing. The Department is making a concerted effort to replace obsolete equipment (recently including two autoclaves) and Department members have been successful in acquiring new instrumentation through targeted equipment grant applications. A recent NSERC award to **Stephen Bearne** and **David Byers**, for example, has financed the purchase of an isothermal titration calorimeter to support work in protein studies.

With my appointment as Head, we have initiated a successful recruitment drive. We are delighted to welcome our newest Assistant Professor, **Barbara Karten**, who arrived on November 1, 2005. Barbara's interests are in cholesterol homeostasis in the brain, Niemann-Pick type C disease, and cholesterol import into mitochondria. Barbara comes to us from a very productive post-doctoral stint with Jean Vance in Edmonton. We are certainly happy to accept Alberta's largesse! Recruitment for a second probationary tenure-track position is well advanced, with a short list of candidates compiled and interviews slated to take place in January and February 2006. In order to add strength to the area of *Structure, Function and Metabolism of Biomolecules* (one of the Department's three broad research themes), we are seeking an individual

with interests in the structure and function of biomolecules, particularly the biochemistry of nucleic acids and/or enzymology.

David Waisman, currently at the University of Calgary, is scheduled to arrive in April 2006 to take up an appointment as Professor and Canada Research Chair in Cancer Biology. David, recruited through the auspices of the Dalhousie Cancer Research Program (DCRP), adds a third Tier I CRC to the Department's current complement. **Chris McMaster** (primary appointment in Pediatrics), Tier II CRC in Biosignalling, has recently brought his talents to the administrative sphere by taking on the role of Assistant Dean Research (part-time) in the Faculty of Medicine, with special responsibility for Graduate Student and Postdoctoral Affairs.

Department members garnered a number of internal and external awards over the past year. At the fifth annual Faculty of Medicine Community of Scholars Dinner, hosted by the Dalhousie Medical Research Foundation, departmental secretary **Barbara Bigelow** received one of two *Staff Awards for Professional Excellence*, while Associate Professor **Andrew Roger** received the *Award of Excellence for Basic Medical Research*. **Roisin McDevitt**, senior clerk who oversees the Department's graduate program, was awarded the 2005 Distinguished Service Award from the Faculty of Graduate Studies in recognition of her long-standing and extraordinary service to graduate-level education at Dalhousie. Nationally, **David Byers** (primary appointment in Pediatrics) shared the 2005 Sanofi Pasteur Research Award of the Canadian Pediatric Society with IWK colleague **Bob Bortolussi**.

The Department continues to draw substantial operating grant support from various funding agencies, with successful applications in 2005 at CIHR (**Stephen Bearne** and **Paul Liu**) and NSERC (**Paul Liu, Christian Blouin, Vanya Ewart, Andrew Roger and Rick Singer**). Our postdoctoral and graduate students also continue to compete successfully in various competitions, with awards coming from the Killam Trust, CIHR, Spanish Ministry of Science and Education, Cancer Care Nova Scotia and the DCRP Cancer Research Training Program.

For a fuller account of departmental activities and successes, I invite you to visit our revamped departmental website (http://www.biochem.dal.ca/; click on "Good News Stories"). Website guru and curator **Paul Briggs** deserves much of the credit for the new look, as well as for creating on-line databases, such as the "Good News" archive, that have made updating information on publications, personnel, etc., easy and straightforward. Kudos to Paul.

The Dal group wishes colleagues across the country a happy, productive and prosperous (particularly in regards to research grants!) year for 2006.

McMaster University

Department of Biochemistry and Biomedical Sciences

Correspondent: Eric Brown

It has been a great year with a new name, the Department of Biochemistry and Biomedical Sciences (BBS), which was adopted in 2004 to reflect the research interests of a growing department, and emerging strengths in the health sciences. On the research front we have had a bumper year. Our faculty fared well in CIHR competitions with successful renewals and high scores in their panels. There were also some especially noteworthy publications from of the department this year including work by **John Hassell** and **Natasha Kurpios** on control of gene expression in spermatogonial stem cells that was published in the August 18th 2005 issue of *Nature*. Justin Nodwell's work made the cover of the *Proc. Natl. Acad. Sci. USA* (Vol. 101, issue 31). **Joaquin Ortega's** first paper as an independent investigator made the cover of the *J. Mol. Biol.* (Vol. 346, issue 5). In his first "made at McMaster" paper, Joachin reported the 3-dimensional reconstruction of the PA200-20S proteasome complex. Also, **Eric Brown** was named the co-winner of the CSBMCB's Merck Frosst Prize, which recognizes outstanding research achievements among early career scientists in Canada.

Undergraduate program:

We welcomed a new faculty member to the department, **Paulina Dlugosz** (B.Sc. and M.Sc., Biochemistry, McMaster) who is working with the Undergraduate Curriculum Committee to develop a new and invigorated laboratory experience. This endeavor is a continuation of an Imperial Oil Learning and Innovation Grant that was awarded to the Department two years ago. Chief among this effort is a move to implement a laboratory program that will stress inquiry-based approaches to biochemistry, and will make our program among the most innovative in the country. In September, the department hosted its second annual Welcome Barbecue. We welcomed back all of our undergraduate students including 100 new students to level II of our program. In October, the Department hosted a "Twist and Turns" event for the fourth year, as part of the Engineering and Science Olympics. Over 900 high school students converged on campus to participate in a variety of events to compete for McMaster University entrance awards.

Graduate program:

The department was very successful in graduate recruitment this year, with 18 new students accepted into the program. Several students received scholarships, and the graduate population at BBS is now one quarter supported by scholarships, which is a testament to the exceptional quality of students in the program.

Graduate student **Mark Pereira**, from Eric Brown's lab, was awarded the Karl Freeman Prize for top student seminar in the department. Graduate students **Amit Bhavsar** and **Jeff Schertzer** had back-to-back papers on wall teichoic acid polymerization in a fall issue of *J. Biol. Chem.* PhD student **Natasza Kurpios** presented a seminar at the Gordon Research Conference in Barga, Italy, on May 10, 2004. **Casey Fowler** and **Razvan Nutiu** each won a poster award at the 2005 Ribo-Club Opening Session in Sherbrooke, Quebec. **Razvan Nutiu** won a Runner-up award in the NSERC Innovation Challenge competition, and won the top prize in the poster competition at the Biocontact 2005 conference in Quebec. M.Sc. student **Gladys DeLeon** attended the CBDN Conference in Banff where she received an award for her poster presentation.

Several Ph.D. candidates successfully defended their theses: **Matthew Annis** (Andrews lab), **Mike Hudson** (Nodwell lab), **Tariq Mukhtar** (Wright lab), **Tamara O'Connor** (Nodwell lab), **David Piluso** (Capone lab). There were also several M.Sc. theses defended: **Ayesha Ahmed** (Trigatti lab), **Girija Dhekney** (Berti lab), **Paulina Dlugosz** (Andrews lab), **Rachael Summerfield** (Junop lab).

Faculty highlights:

V. Ananthanarayanan, Christy Thompson and **Helen Atkinson** filed a Provisional patent application on 'Inhibitors of collagen biosynthesis,' based on the results published in *J. Med. Chem.* Also, Ananth and PhD student **Aaron Kermin** had a paper published in *Biochim. Biophys. Acta.* **Eric Brown** presented keynote lectures at the Annual General Meeting of the National Research Council's Genomics in Health Initiative and at the inaugural symposium of the Groupe de Recherche Universitaire sur le Médicament of the Université de Montréal. **Evert Nieboer** officially retired on June 30, 2005 but will continue his research program. He has just been awarded a $1 million grant to study population health in the Cree Nation in Quebec. **John Capone** has taken on the challenge of running the Faculty of Science as its new Dean, starting July 1, 2005 after finishing a very successful 5 year term as Associate Dean of Research in the Faculty of Health Sciences. **Richard Epand** delivered the plenary lecture at the international conference in Belgium on "Motifs for peptide interactions with membranes and their functions". He also gave a talk at the Biophysical Society Meeting in Long Beach, CA where he and collaborators also presented six posters. Richard was an invited speaker at the Workshop on Biological Membranes: Structure and Function, Ohio Center for Technology and Science, Columbus, Ohio and an invited symposium speaker at the meeting "Membrane Biophysics of Antimicrobial Peptides", Ann Arbor, MI. Richard has been appointed Executive Editor of the Biomembranes section of

Biochim. Biophys. Acta. **Jack Gauldie** has been appointed as Director of the Institute of Molecular Biology and Biotechnology (MOBIX). **Alba Guarné** received a New Investigator award from CIHR, and a 5-year maintenance grant for the X-ray equipment, also from CIHR. **John Hassell** gave seminars entitled "Molecular and functional characterization of mammary epithelial stem cells and breast cancer stem cells" at the Ontario Cancer Institute in Toronto on Mar 11; the Ottawa Health Research Institute/University of Ottawa on June 29; the Cold Spring Harbor lab in New York on Aug 26; and McGill University on Sept 8. He presented a seminar at the McLaughlin Centre for Molecular Medicine at the University of Toronto on Nov 16, "Molecular and functional characterization of tumor initiating cells propagated in vitro". **Paul Higgs** has co-authored a textbook along with Teresa Attwood (Manchester, UK) on Bioinformatics and Molecular Evolution, which was published in January 2005 by Blackwell. **Yingfu Li** attended several international meetings during the summer months including the 2005 IUPAC Congress in Beijing (invited speaker) and the 4th International Symposium on Nucleic Acids Chemistry in Fukuoka (Keynote speaker). **Joaquin Ortega** was awarded the New Opportunities Fund grant from CFI/OIT which he is going to use to upgrade the existing Field Emission Gun electron microscope in the Materials Science and Engineering Department for the capability of cryoelectron microscopy with biological samples. It will be the first such microscope in Eastern Canada able to image biological samples at liquid nitrogen temperatures. **Sujata Persad** received a 3 year CIHR operating grant ($89,613/yr) and she was also successful in the CFI/OIT New Opportunities funding program. **Ray Truant's** laboratory has published several manuscripts this year involving imaging collaborations. In January, Ray and John Capone published a study on the PPARa nuclear hormone receptor binding protein in *J. Cell. Sci*. The same issue of the journal had an independent study on ataxin-1 protein of spinocerebellar ataxia type 1 from the Truant lab. In August, the labs of Truant and Brown published a collaborative work involving bacterial imaging and GFP fusion proteins in *Bacillus* species (*J. Biol. Chem.*) Ray also recently published a collaborative manuscript with the lab of Dr. Steven Ferguson at the Robarts Institute at the University of Western Ontario in J. Biol. Chem. on the role of a huntingtin binding protein in triggering one type of glaucoma. **Jeffrey Weitz** contributed to the 80th Anniversary issue of *J. Clin. Invest*. His paper on clot-bound thrombin and heparin inhibition, from 1990, remains one of the most highly cited papers from the journal's 80-year history. **Gerry Wright** attended the CBDN Conference in Banff, and delivered the Van Cleave lecture on Nov 3 at the University of Regina, Sask. He was co-editor of a special issue of Chemical Reviews on Antibiotic Resistance (Feb 2005) and contributed two papers to the issue, one with his Ph.D. student, **Tariq Mukhtar**, and the other with **Eric Brown**.

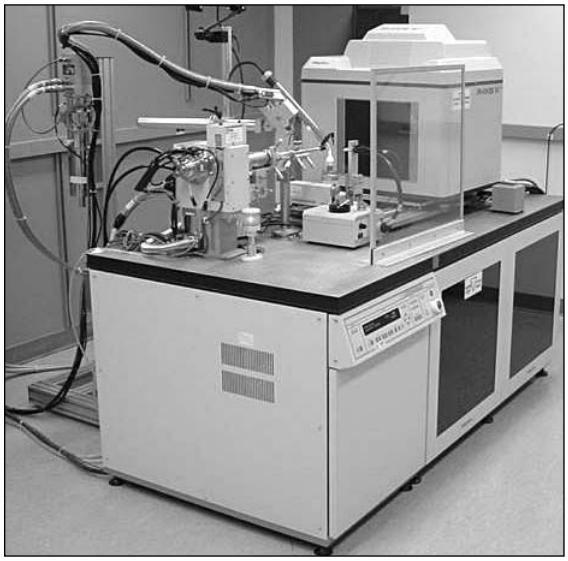
McMaster High Throughput Screening Laboratory:

The McMaster HTS Lab screened more than a million micro-wells this year in 8 large-scale and about two dozen pilot-scale campaigns for researchers at McMaster and across Canada. This year the McMaster HTS Lab was at the centre of a countrywide initiative in chemical biology, the Canadian Chemical Biology Network, aimed at establishing a national chemical compound collection and a network of screening centers. Also among this year's highlights was a special October issue of *J. Biomolecular Screening* that featured several papers presenting results from the McMaster HTS Lab's international competition in computational screening.

Simon Fraser University

Department of Molecular Biology and Biochemistry
Correspondent: Christopher Beh

This first report from the Department of Molecular Biology and Biochemistry at Simon Fraser University celebrates both our 5th anniversary as a Department, and the 40th anniversary of the founding of SFU. In 5 short years, our Department has grown to 23 faculty, 73 graduate students, 12 postdoctoral fellows and research associates, and has made major contributions toward research excellence in British Columbia. This includes awards to the faculty of NSERC University Faculty Awards, 3 CIHR New Investigator/Scholar Awards, 4 MSFHR Scholar and 1 Senior Scholar Award, and an ASI Provincial Research Fellowship. In addition, two Canada Research Tier 1 Chair positions are held by department faculty. **Dr. David Ballie** holds a CRC in genomics for his work in Caenorhabditis elegans genomics and bioinformatics, while **Dr. Jamie Scott** holds a CRC in recognition of her research in immunology, particularly with regard to phage display and HIV vaccine development. Our students and postdoctoral fellows have also been very successful in fellowship competitions. Even though our Department has a short history, it already has an established record of achievement.



Newly installed equipment for macromolecular X-ray crystallography in the SFU Molecular X-ray Crystallography and Biophysics Facility

Department highlights:

In the past year we said good-bye to **Dr. Michael Smith**, our first Chair. Upon his retirement from SFU, Dr. Smith moved to the Department of Biology at Weill Cornell Medical College in Qatar. **Dr. Bruce Brandhorst**, who took up the reins as our new MBB Department Chair, has already met several challenges. In addition to the formidable challenge of extracting the necessary infrastructure to meet the needs of a growing department, Dr. Brandhorst led the Department through its first external review. He and the faculty are also grappling with an explosion of undergraduates keen on the academic offerings of the Department. In the short span of 5 years, the MBB Department now provides the largest undergraduate majors program in the SFU Faculty of Science, and hosts many students in its research labs. The Department also offers undergraduate majors programs with Business and Computing Science. Although daunting, the demands are positive signs of growth and indicate the Department's importance to research and academics at SFU.

New faculty:

The diverse research interests of our faculty can be broadly described as focused on cell & developmental genetics, structural biology, and bioinformatics/genomics. In the past year, we added to our ranks in these research areas with the hiring of **Drs. Edgar Young** (gated ion channels), **Lisa Craig** (bacterial pili and pathogenesis), and **Dr. Jack Chen** (bioinformatics/neuroscience), who will join us next year. Before starting at SFU, Dr. Young completed his postdoctoral research at Columbia University in New York, Dr. Craig finished her postdoctoral research at the Scripps Institute in La Jolla, CA, and Dr. Chen will be joining us from Cold Spring Harbor Laboratories in New York. **Dr. Lynne Quarmby** (cilia and microtubule dynamics) also joined us this year when she transferred from the SFU Department of Biological Sciences. In the coming year, the Department is seeking to hire a virologist and an immunologist (as a joint initiative with the new

SFU Faculty of Health Sciences), with a focus on vaccine development as part of an initiative to create a new interdisciplinary graduate program in infectious diseases. Our Department also hopes to fill a Chair in Pharmaceutical Genomics and Bioinformatics to be endowed by the BC government and private donors.

Research highlights:

Since the Department's inauguration, several prominent areas of research have emerged. In different but complementary scientific approaches, **Drs. Michel Leroux, Willie Davidson, Lynne Quarmby**, and **David Baillie** have made important and unanticipated links between cilia and diseases such as Bardet-Biedl syndrome and polycystic kidney disease. SFU has emerged as a major centre for *C. elegans* developmental genetics, cell biology, and genomics. **Drs. Nancy Hawkins, Michel Leroux**, and **David Baillie, Jack Chen** (in 2006) from MBB and **Dr. Harold Hutter** from Biosciences, lead a variety of complementary studies that exploit the experimental advantages of *C. elegans* as a model system. **Drs. Esther Verheyen, Nick Harden, Barry Honda, Brandhorst** and **Chris Beh** contribute to the Department's expertise in cell and developmental genetics/genomics, with their research in signal transduction in Drosophila, echinoids, and yeast. **Drs. Peter Unrau** and **Dipankar Sen** have brought research prominence to the Department through their studies of the evolution, mechanisms, and engineering of nucleic acid enzymes. **Drs. Mark Paetzel, Fredric Pio, Michel Leroux, Lisa Craig**, and **Edgar Young** bring expertise in protein structure analysis and make use of the new X-ray crystallography facility funded by CFI. **Drs. Rosie Cornell** and **Jenifer Thewalt** round out our Department's multifaceted structure group with their studies on membrane lipid organization and phospholipid enzymology. This functional and structural research is complemented by the bioinformatics program led by **Drs. Fiona Brinkman, Fredric Pio, and David Baillie**, with systems support from **Dr. Duncan Napier**. Along with UBC and the BC Cancer Agency, the Department is part of a CIHR graduate training program in Health Bioinformatics. Several members of the Department are engaged in a very active interdepartmental biophysics initiative that hopes to initiate a new undergraduate program as well as promoting research interactions.

Sponsored scientific meetings:

Last year the Department hosted national and provincial meetings to encourage dialogue between Drosophila researchers from across Canada, and to foster contact between cell biologists from the major campuses in British Columbia. **Drs. Verheyen** and **Harden** organized the annual Drosophila meeting, which was held at SFU on a beautiful weekend in May. **Drs. Hawkins** and **Beh** organized the second annual BC Cell Biology Retreat, which was held on a particularly rainy weekend in April at the Loon Lake Conference Centre in Maple Ridge, BC. By all accounts, both meetings were successful - weather notwithstanding.

Université de Sherbrooke

Department of Biochemistry

Correspondent: Marcel Bastin

Under the leadership of **Dr. Jean-Pierre Perreault**, our new Chair as of July 2004, the Department is pursuing its interest in the study of protein and nucleic acid structure and function. Three new staff members have recently joined us as Assistant Professors.

Martin Bisaillon who arrived in June 2002 got his Ph.D. in Microbiology and Immunology from the University of Montreal and did a postdoctoral fellowship at the Sloan-Kettering Institute. He is interested in the molecular mechanism of proteins involved in the synthesis and maturation of messenger RNAs, particularly those of pathogenic organisms. Martin's work is supported by the CIHR and the NSERC. He is a

CIHR new investigator scholar.

Eric Massé joined the Department in January 2004. He got his Ph.D. in Microbiology and Immunology from the University of Montreal and got postdoctoral training at the NIH National Cancer Institute in Bethesda. Eric's research interest is the molecular mechanism of small regulatory RNAs with the general purpose of developing new strategies to fight infection. His work is supported by the CIHR. He is a CIHR new investigator scholar.

Xavier Roucou joined the Department in June 2004. He got his Ph.D. from the University of Bordeaux in 1996 and did postdoctoral fellowships in Melbourne, Geneva and at The Lady Davies Institute in Montreal. His research deals with the identification of neurotoxic molecules in prion-associated diseases. His work is supported by the CIHR. He is the recipient of a Junior 2 schloarship from the FRSQ.

Additional information can be obtained from the Department web site :
http://www.usherbrooke.ca/biochimie/

L'Université Laval

Correspondant : Guy Poirier

Le **Dr Michel G. Bergeron**, professeur titulaire au Département de biologie médicale, a reçu le prix Wilder-Penfield (sciences biomédicales) lors de la cérémonie de remise des Prix du Québec 2005 qui s'est déroulée à l'Assemblée nationale le 8 novembre. Ces prestigieux prix étaient remis par M. Claude Béchard, ministre du Développement économique, de l'Innovation et de l'Exportation, et Mme Line Beauchamp, ministre de la Culture et des Communications, qui n'ont pas manqué de souligner que les Prix du Québec étaient « l'instrument privilégié par lequel le gouvernement exprime sa reconnaissance à des hommes et à des femmes pour leur parcours professionnel à l'origine d'avancées marquantes dans des disciplines touchant la culture et les sciences ». Clinicien-chercheur renommé, rappelons que le Dr Bergeron est le fondateur du Centre de recherche en infectiologie de l'Université Laval.

Le Dr Michel G. Bergeron a été nommé membre de l'Académie canadienne des sciences de la santé. Cette importante nomination couronne la reconnaissance du Dr Bergeron comme chercheur émérite dans le domaine médical et biomédical.

Membre du Centre de recherche en infectiologie, le professeur **Dr. Guy Boivin** dirigera la Chaire de recherche du Canada (Niveau 1) sur les virus en émergence et la résistance aux antiviraux. Les travaux de la chaire visent à concevoir de nouvelles méthodes diagnostiques et à développer des approches préventives et thérapeutiques innovatrices pour lutter contre les virus émergents. L'équipe du professeur Boivin a mis au point un outil de détection rapide de séquences génétiques spécifiques à la plupart des familles de virus connus ou en émergence. Cet outil permettra de mieux cibler le bon médicament à prescrire à chaque patient et ainsi freiner la progression de la résistance aux antiviraux.

La construction du Centre Génomique est commencée au CHUL ; il abritera les plateformes de génomique, bioinformatique et protéomique de même que le Centre de recherche en Infectiologie de l'Université Laval.

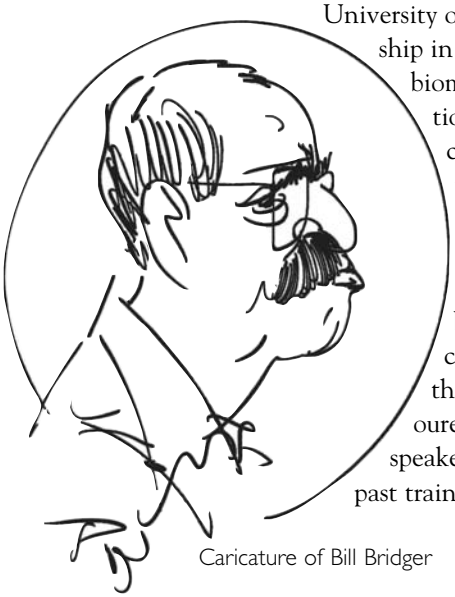
À l'Hôtel-Dieu de Québec, la construction du Centre de recherche translationel est presque terminée ; les chercheurs du CHUQ en biologie cellulaire et moléculaire pourront ainsi transférer leur recherche fondamentale à la clinique.

University of Alberta

Department of Biochemistry

Correspondent: Bernard Lemire

This year, we established the **William A. Bridger Lectureship in Biochemistry** to commemorate his service to the Biochemistry Department at the University of Alberta, and his leadership in promoting and expanding biomedical research and education. The Department has created an endowment fund, the earnings of which are to be used to bring annually to this campus a distinguished scientist in biochemistry, molecular or cellular biology. This year, the Department was honoured by visits from three speakers who were Bill Bridger's past trainees: Susan Lees-Miller (Department of Biochemistry and Molecular Biology, University of Calgary), Maureen O'Connor-McCourt (Senior Research Officer and Group Leader of the Receptor, Signaling and Proteomics laboratory at the Biotechnology Research Institute, Montreal), and Hans Vogel (Department of Biological Sciences, University of Calgary).



Caricature of Bill Bridger

Bill Bridger, a native of Winnipeg, obtained a B.Sc. in Honours Chemistry and a Ph.D. in Biochemistry at the University of Manitoba under the supervision of Dr. L.H. Cohen. He moved to UCLA for postdoctoral studies with the recent Nobel Laureate, Paul D. Boyer. In Boyer's lab, Bill was beguiled by the enzyme succinyl-CoA synthetase and it remained the focus of his research. In 1967, Bill joined the Department of Biochemistry at the University of Alberta. He moved through the ranks to full professor (1977), spent 1984-1985 as a visiting professor at the Rockefeller Institute in New York, and in 1987 became Chair of the Department of Biochemistry. Six years later, Bill assumed the role of Associate Vice-President (Research) and served in that position until January 1993, when he officially retired from the U of A to become Vice-President (Research) at the University of Western Ontario. His career at the University of Alberta has demonstrated the highest levels of achievement in research, teaching, and administration. In 2001, Bill became Founding President and CEO of the newly established Alberta Ingenuity Fund. In this capacity, he played a key role in the development of long-term strategies for knowledge discovery and top-quality training of scientific personnel in the Province of Alberta until his retirement in 2004. He served as the Canadian Biochemical Society (CBS) Secretary, Vice-President, and then President. In 1980, Bill was the recipient of the Ayerst Award of the CBS, given for outstanding biochemical research, and in 1989, he was named a Fellow of the Royal Society of Canada. In 2005, Bill was the recipient of the ASTECH award for Outstanding Contribution to the Alberta Science and Technology Community.

Bill Bridger with the three speakers at the first William A. Bridger Lectureship in Biochemistry. Left to right: Susan Lees-Miller, Maureen O'Connor-McCourt, Bill Bridger, Hans Vogel.

• The following individuals were recognized for their years of dedicated service at a ceremony held on November 23, 2005: **Carole Dodd** (25 years), **Nancy Ehrman** (25 years), **Dawn Lockwood** (25 years), **Chris Bleackley** (30 years), **Brian Sykes** (30 years), **William Wolodko** (30 years) and **Ronald McElhaney** (35 years). Congratulations!!!

• **Michael James** was the recipient of the Faculty of Medicine and Dentistry Mentorship Award, which recognizes outstanding performance in the mentoring of graduate students and postdoctoral fellows. The Award consists of a $1,000 cash award and a commemorative certificate.

• **Dr. Joel Weiner** was named a 2005-2006 Killam Annual Professor to recognize his record of outstanding scholarship and teaching, and his substantial contributions to the community beyond the University. Each Killam Annual Professor is presented with a $3,500 prize and a plaque.

• **Dr. Mark Glover** received Canada's highest honour in biochemistry, the Merck Frosst Prize for 2005, awarded by the Canadian Society of Biochemistry, Molecular and Cell Biology. The award recognizes researchers with less than 10 years of independent experience who have made ground-breaking discoveries. Mark is honoured for his work on BRCA1, a gene associated with human hereditary breast cancer.

• **Dr. Chris Bleackley** was awarded the 2005 Roche Diagnostics Award for Outstanding Research Achievements by the Canadian Society of Biochemistry and Molecular and Cellular Biology, for his work on the mechanisms cytotoxic T cells use to induce death in virus-infected and tumor targets.

• **Dr. Michael Schultz** was awarded the 2005-2006 McCalla Research Professorship, which provides release time from teaching duties to enable McCalla Professors to focus on research/creative projects.

• **Professor Eckard Wimmer**, of the Department of Molecular Genetics and Microbiology at Stony Brook University School of Medicine, gave an outstanding presentation entitled "Studies on the Life Cycle of a Chemical called Poliovirus" for the 18th John S. Colter Lecture in Biochemistry.

• The 8th Annual Department of Biochemistry Doug Scraba Memorial Golf Tournament attracted over 120 golfers. As usual, **Perry D'Obrenan** and **Roger Bradley** arranged for the beautiful golf weather and organized a great BBQ.

• A bumper crop of 22 enthusiastic new graduate students was welcomed in September.

• **Drs. Ruthven Lewis** and **Michael James** received the Alberta Centennial Medal, which celebrates Alberta's first 100 years by paying tribute to Albertans whose achievements have benefited their fellow citizens, their community and their province.

Lining up for the 8th annual Doug Scraba Golf Tournament. Start your engines!!

University of British Columbia

Correspondents: Chris Proud and Vince Duronio

The buzz at UBC over the past year has been about the opening of the new Life Sciences Centre. The building was one of the largest of its kind to be built in Canada and was supported by the BC government as part of the expansion of the medical school, which will eventually be doubling in size. A new feature of the expanded medical school is the addition of satellite campuses in Victoria and Prince George. Thus, the lecture theatres are all video linked to the remote sites using state of the art equipment. The researchers in the building are part of the 'Life Sciences Institute', as highlighted in the Biochemistry department report, and have moved from dozens of locations across campus.

Off-campus, there are also major changes happening at the VGH site, where new academic and clinical space is being combined into a new building, which will lead to the demolition of most of the old parts of the hospital. There are plans to reveal the original Victorian style core of the hospital, which was hidden by decades of unsightly additions. This will become a new conference centre, surrounded by green space. This area is right across from the brand new BC Cancer Research

Centre, which also opened last year, moving out of very sub-standard facilities that they had been occupying.

A welcome announcement in terms of funding came when the Michael Smith Foundation for Health Research was given a renewed mandate, and commitment for a further 5 years of funding. Health-related research in BC has benefited tremendously from the salary support for personnel, ranging from studentships to senior scientist support. In addition, research groups have been able to obtain support for infrastructure programs, which provides badly needed funds that are difficult to obtain from traditional grant programs.

Department of Biochemistry and Molecular Biology Highlights

New Head: Dr. Christopher Proud, formerly Head of the Division of Molecular Physiology in The School of Life Sciences at the University of Dundee, U.K., succeeded Dr. Roger Brownsey (Acting Head) as Head of the Department of Biochemistry and Molecular Biology in March 2005. Dr. Proud's research concerns the signaling pathways that control the protein synthetic machinery of mammalian cells, and the ways in which defects in these pathways cause diseases such as cancer, hypertrophy and inflammatory disease.

New Faculty: Dr. Leonard Foster joined the Department as an Assistant Professor in January 2005, having spent more than three years as a post-doctoral fellow in the group of Professor Matthias Mann at the University of Southern Denmark. Leonard is applying Fourier transform mass spectrometry and quantitative proteomics to study the dynamic changes in the composition of organelles as they mature or develop. Currently he is studying the maturation of phagosomes and Salmonella-containing vacuoles, as well as changes undergone by lipid rafts in response to receptor activation.

New Laboratories: during Summer 2005, almost all the research labs of the Department moved into the brand new Life Sciences Institute at UBC's Point Grey campus (www.lsi.ubc.ca). The research activities within the LSI are organized thematically into Research Groups and individual members of the Department belong to the following research groups: Bacterial Adaptation & Response Networks; Centre for Blood Research; Chemical Biology & Disease; Diabetes; and Genes, Development & Health.

Awards: a number of members of the Department won awards in 2005. These include **Dr. Brett Finlay** (Jacob Biely Faculty Research Prize); **Dr. Richard Barton** (Killam Teaching Prize); **Dr. Pieter Cullis** (Barre Award of the University of Montréal and the UBC Alumnus Award for Research in Science & Medicine); and **Dr. Lawrence McIntosh** (UBC Faculty of Medicine Distinguished Medical Research Lecturer Award). **Dr. Philip Hieter**, an Associate member of the department, was elected a Fellow of the Royal Society of Canada.

University of Calgary

Department of Biochemistry and Molecular Biology

Correspondent: Leon W. Browder

The Department of Biochemistry and Molecular Biology in the Faculty of Medicine, the University of Calgary, is a diverse department with a highly productive research program. We also administer the genomics, proteomics and bioinformatics infrastructure that facilitates the research activities of biochemists and molecular biologists in Calgary and beyond. The department consists of 51 faculty members plus 20 adjunct appointees.

The department offers graduate training leading to Ph.D. and M.Sc. degrees in Biochemistry and Molecular Biology. . Members of the department supervise more than 170 graduate students.

Transitions:

David Wilson, former Research Assistant Professor has accepted a position as Assistant Professor at the University of Adelaide, South Australia.

Dr. Hans van de Sande completed service as Vice-Dean of the Faculty of Medicine in 2004 and took a well-deserved sabbatical during 2005.

Dr. Karl Riabowol has also returned from a productive sabbatical at Humboldt University in Berlin.

Dr. Randy Johnston was named Interim President of Genome Alberta after serving for several years as President of Genome Prairie.

Dr. Floyd Snyder, who has a joint appointment in this department, completed service as Head, Department of Medical Genetics.

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

Dr. Marvin Fritzler, who holds the holds The Arthritis Research Chair in the Faculty of Medicine, has been awarded a Centennial Medal by the Province of Alberta in recognition of his outstanding scientific career and his meritorious service to the Province of Alberta

Dr. Hans van de Sande was named to the Order of the University of Calgary during Spring Convocation in recognition of his long history of devotion to academic research and leadership within the scientific and medical communities.

Dr. Jay Cross was named Research Scientist of the Year by the Association of Professors in Obstetrics and Gynaecology (APOG) of Canada.

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

Dr. Minh Dang Nguyen (Assistant Professor). Minh Dang's primary appointment is in the Department of Clinical Neuroscience. He studies the role of the cytoskeleton in neural development and neorodegeneration.

Dr. Kenneth Ng (Adjunct Assistant Professor). Ken's research is on X-ray crystallographic and biochemical studies of RNA-dependent RNA polymerases and carbohydrate-binding proteins.

Dr. Jane Shearer (Research Assistant Professor). Jane studies the mechanisms regulating glucose and fatty acid metabolism.

Training Opportunities

Members of the Department of Biochemistry & Molecular Biology conduct exciting, leading edge research, are well funded by international, national and provincial agencies, and publish extensively in the very best journals. We invite potential graduate students and post-doctoral fellows to give Calgary careful consideration. Not only do we offer excellent training opportunities for young scientists, but the natural beauty surrounding Calgary is breathtaking, providing year-round recreational opportunities.

We invite you to visit our website at www.ucalgary.ca/bmb

Extraordinary Science in an Extraordinary Location!

Department of Biological Sciences, Faculty of Science

Correspondent: Raymond J. Turner

The Biochemistry program at the University of Calgary is taught to undergraduates by biochemists in the Faculty of Science. Our group consists of two senior instructors **Elke Lohmeier-Vogel** and **Robert Edwards**, five AHFMR scholars/scientists **(Marie Fraser, Kenneth Ng, Elmar Prenner, Peter Tieleman and Hans Vogel)** and four regular faculty members **(Gene Huber, Greg Moorhead, Raymond Turner and Vanina Zaremberg)**. One 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 molecular rather than cellular biochemistry. We have a very good relationship with faculty members in the Faculty of Medicine who also contribute teaching in some of our courses.

Although we all have productive research programs, a major emphasis here is on teaching undergraduates. Our program encourages a research project in the senior year, and this year we had over 40 students working in our labs, as well as a

few doing their projects in labs within the Faculty of Medicine. Once again, the final presentations from our undergraduates at the spring and summer undergraduate research symposiums were outstanding, humbling some of us by what they can do with Powerpoint. The quality of research performed by our undergraduates was exemplary this year, with several of their final papers contributing to peer-reviewed journal submissions. We take considerable pride in our undergraduate program, and during the past year we reworked the organization of several courses. A key change was to convert our fourth-year one-semester biochemistry laboratory techniques course, to split it over two semesters and move it to the third year of program. The goal of this change is to provide more experimental background for our students, and to better prepare them for their senior year research projects. This fall was the change-over year and although chaotic, huge efforts from **Rob Edwards, Elke Lohmeier-Vogel**, and **Vanina Zaremberg**, as well as technical support from Mike Gaunt, helped make it happen. The new course arrangement will also help solve the problem of the disparity of workload the students experience between the fall and winter semesters of their senior year. Although all programs are in some flux, over the past 3 years we have made significant changes to the content of our courses, and in the organization of the delivery of the biochemistry program. We already have a very high exit poll satisfaction rate, and we are continuing to strive to strike a balance between the goals of the students and our program, and the budget and university directions.

Elke Lohmeier-Vogel returned for a month to the Department of Applied Microbiology, at the University of Lund in Sweden, to finish off some research from her sabbatical leave the year before. During this time she also took the opportunity to become more familiar with advanced recombinant DNA methods, and she then applied this information to the changes in our biochemistry laboratory course described above. She very much enjoyed her interactions with **Isabelle Barrette-Ng**, who was brought in as a sessional lecturer to help out with introductory courses that Elke covers.

This fall also saw a change in our department as a whole that included a new department head, **Jeff Goldberg**, a zoologist from the University of Alberta. He has championed the restructuring of our department from a division structure (Biochemistry, Zoology, Plant Biology, Ecology, Cell Molecular and Microbiology, as well as biological sciences general degree) to three large research groups. Thus the majority of us now find ourselves within the biomolecules, cells and microbes research group. With all these changes you can imagine it has been an interesting and challenging year for our Biochemistry Division chair R**ob Edwards**.

Here we would like to take this opportunity to introduce the newest member of our group, **Vanina Zaremberg**. Vanina came to us from a post-doctoral position at Dalhousie University. Her work focuses on the regulation of phospholipid and triacylglycerol (TAG) synthesis, which plays a critical role in disorders such as obesity, diabetes and atherosclerosis. The synthesis of glycerophospholipids and TAG begins with the acylation of glycerol-3-phosphate by glycerol-3-phosphate acyltransferase (GPAT) to form lysophosphatidic acid (lysoPA) that is immediately converted to phosphatidic acid (PA). GPATs are thought to be key points of regulation of general lipid metabolism. The pathways of glycerolipid biosynthesis were elucidated in the 1950's, and despite considerable advances in the field, the mechanisms governing the regulation of PA biosynthesis, the specific molecular mechanisms controlling the rate-limiting GPAT step, and the precise determinants mediating lipid metabolic pathway partitioning, are not known. Understanding this gap in knowledge is a central issue in cell biology. Vanina uses a yeast model system to characterize the biological, biochemical and molecular mechanisms of yeast GPATs, and is also working towards isolation of the elusive human microsomal GPAT.

Presently there are 31 graduate students, 15 post-doctoral fellows, and 9 research associates/technicians spread throughout our labs. This year, 27 undergraduates in Biochemistry and 8 MSc, 2 MSc/MD and 5 PhD students graduated from our programs. 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. Success of our graduate students has been outstanding during the past year. **Joe Harrison** won a North American competition for the Merck-Frosst research symposium highlighting graduate student excellence, and also won the university's J.B. Hyne Award for research excellence. **Justin MacCallum** and **Walter Ash** obtained NSERC Canada PhD Graduate Studentships. **Stephanie Kernaghan** was awarded the Jim & Josie Gray Award and the Jake Duerkson Memorial Scholarship. **Gopi Sutendra**, now a PhD student at the University of Alberta, won the departmental Sharon Wilkins Graduate Teaching Assistantship Award of Excellence (interestingly the biochemistry graduate students tend to win this award more often than others in our department).

Our biochemistry undergraduates also did well at graduation, taking home several prizes this year, with the stars being **Jessica Gifford** (Society of Chemical Industry Award, and George Drumond Biochemistry award), **Richard Cormack** (Sonia Scurfield Scholarship), **Dylan Silver** (Gerald Roberts Mortimer & Victor Emanuel Mortimer Bursary), and **Andrew Wong** (Dr. James Zimmerman Memorial Bursary), and another 7 students winning the undergraduate Merit Award. It is nice to see that the majority of these students have now entered graduate studies rather than going into medicine.

Our research programs are well funded by NSERC, CIHR, AHFMR, AIF, CFI, Heart and Stroke, as well as some industrial relationships. Some key highlights of funding have led to our Biophysical Characterization Labs being completed as part of the CFI-funded Alberta-wide Cybercell project, led at Calgary by **Hans Vogel**. This gives us a laboratory containing calorimeters, fluorescence, absorption, infrared and circular dichroism spectrometers, as well as light scattering. A second lab provides for protein purification infrastructure, with FPLCs, centrifuges and work space. Additionally, a 500 MHz NMR spectrometer with cryoprobe was installed. Furthermore, **Peter Tieleman's** biocomputing group has started using a new 640 processor Beowulf supercomputer. Finally, through another initiative of **Hans Vogel**, we are now set up to do metabolomics by NMR.

Raymond Turner's sabbatical leave was approved and he spent the fall at the University of Bologna, Italy, examining the bioenergetics of photosynthetic bacteria and their processing of metal oxyanions. There he educated the group in bacterial biofilm growth methods, with the aim of developing applications for photosynthetic bacterial processing of heavy metals and other environmental contaminants. He also had the pleasure of participating as a Professor in Residence, lecturing in a molecular microbiology course. Going from one of the youngest universities in Canada to the oldest established university in the world provided an interesting contrast. Raymond also did a small seminar tour of southern Europe, presenting his diverse research interests from microbiology to membrane protein folding to photochemistry.

Other personal highlights from members of our group include the following. **Marie Fraser** and **Rob Edwards** received tenure. **Peter Tieleman**, our high profile biocomputing expert, was promoted to full Professor, renewed by AHFMR as a Senior AHFMR Scholar, and received a CIHR New Investigator award. Both **Peter Tieleman** and **Hans Vogel** continue to be in demand for speaking at national and international conferences, and their dance cards are quite full with visits to institutions worldwide. **Peter Tieleman, Hans Vogel** and **Marie Fraser** also find themselves on grant review panels. Both **Greg Moorhead** and **Hans Vogel** received Killam Faculty Fellowship awards for their program excellence, which relieves them from teaching duties to focus more on their research. Over the past year, the majority of our biochemists have been recognized for their research prowess.

For more information about the biochemistry group in the Department of Biological Sciences visit:
http://www.bio.ucalgary.ca/divisions/biochem/index.html.

University of Guelph

Department of Molecular and Cellular Biology

Correspondent: Frances Sharom

New Science Complex building update

The pace of the building schedule for the new Science Complex has been proceeding rapidly over the past year. The Phase 1 research and teaching section was completed in July-October 2004. Its research wing now accommodates the research labs and offices of the former Microbiology Department and the Biochemistry group, who make up about 2/3 of the faculty in the new Department of Molecular and Cellular Biology. The first part of Phase 2 is scheduled to open in July 2006, and will accommodate the two Science deans, new administrative offices for the Molecular and Cellular Biology and Chemistry departments, various seminar rooms, as well as new teaching labs for the biology undergraduate programs. The final part of Phase 2, scheduled to open in mid-2007, will accommodate the research lab and offices of the remaining members of our department, primarily the molecular biologists and cell biologists, as well as all the members of the new Department of Integrative Biology. When all the moves are over, the approximately 45 members of the department will all be housed together in the new complex, together with the Advanced Analysis Centre (AAC), which will include 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.

Matt Kimber

Steffen Graether

New faculty additions

Two new faculty members joined the Department as Assistant Professors in the past year, strengthening the department's structural biology component.

Matt Kimber received his graduate training at the University of Toronto, in the Department of Molecular and Medical Genetics, under the supervision of Dr. Emil Pai. He worked on the X-ray crystal structure of the chloroplast b-carbonic anhydrase from Pisum sativum. Matt then spent 5 years as a Senior Scientist in the structural biology division of Affinium Pharmaceuticals in Toronto. His responsibilities included solving, analysing and documenting novel protein structures, and their complexes with proprietary compounds, using X-ray crystallography, as well as data mining and development and implementation of novel crystal screening and refinement strategies. He is currently hard at work setting up his new research space, which he shares with Steffen Graether. Matt was recently awarded an NSERC operating grant, so his research program is off to a good start.

Steffen Graether comes to us from Brian Sykes lab at the University of Alberta, where he was a Research Associate for several years. He obtained his PhD degree from Queen's University, working with Zhongchao Jia on antifreeze proteins using both X-ray crystallography and NMR spectroscopy. Steffen was the first person to determine the structure of an insect antifreeze protein (from spruce budworm), and discovered that it had a new b-helical fold. He continued his work on antifreeze proteins in the Sykes lab, using NMR spectroscopy to characterize the dynamics and structure of the proteins at different temperatures. Steffen has also recently obtained an NSERC operating grant, and is planning to both continue his work on antifreeze proteins and extend it to other water-binding proteins, such as the dehydrins.

Congratulations

Congratulations to Marc Boileau, a staff member in the department, for his publication of the Towers of Time, which pays homage to the construction of monumental federal buildings after Confederation in 1867. The new skyscrapers of the time, complete with towers and clocks, would compete with spires, cisterns and silos in the rural

skylines of Canada. Marc is a member of Canada's National History Society, and has studied and travelled widely. He has employed his exceptional contacts with local and architectural historians in Ontario to construct these sketches.

Goodbyes

John Phillips, former Chair of the Department of Molecular Biology and Genetics, officially retired from the university in 2005. A well-attended retirement party took place in October, at which John received a chair (from the Dean's Office), a U of G watch (from the department) and a travel gift certificate (from friends and colleagues). John is not actually leaving us, since he intends to continue running his very active research lab for several more years. His research interests lie in genetic and molecular studies of the role of oxygen radical metabolism in disease and aging. John's group has identified and characterized genes specifying oxygen radical defence functions, and has generated some very interesting mutant and transgenic models of disease and aging in mice and Drosophila.

Derek Bewley, of the former department of Botany, was named University Professor Emeritus at the Winter 2006 Convocation Ceremony at the University of Guelph. Derek retired in 2005, but is actively maintaining his research program and research, which is focused mainly on the involvement of cell wall degrading enzymes, the hemicellulases, in germination and fruit development and ripening.

William (Bill) Wong has been a member of University of Guelph community since the autumn of 1978, when he started as a research associate in the laboratory of **Benjamin Lu**, now a Professor Emeritus in our department. He continued as a Research Associate in the laboratories of **Ross Nazar** and **Alan Wildeman**, while assuming an instrumental role in the teaching of undergraduate and graduate students, and in facilitating the day-to-day operations of what was then the Department of Molecular Biology and Genetics. Bill continually went beyond the requirements of his job in his teaching efforts, departmental duties, and continual assistance with research labs. He was responsible for the maintenance and daily functioning of a wide variety of departmental equipment, and without his tireless effort and dedication to maintaining it, many research and teaching programs would have been compromised. Further to his regular duties, Bill served for 18 years on the departmental Health and Safety committee, and was responsible for assisting with the co-ordination of a highly intensive summer course to teach high school teachers molecular techniques that they could take back to their classrooms.

Bill was responsible for teaching and mentoring a countless number of undergraduate and graduate students in molecular biological and cloning techniques. Bill was a laboratory demonstrator and coordinator for a large number of courses, including Laboratory Methods in Molecular Biology I, which was named "Best Undergraduate Course" in Fall 1997. Thereafter, Bill became the instructor and demonstrator for Laboratory Methods in Molecular Biology II, at which time he re-modelled the course and brought real-life research problems to his students. For both courses, Bill was able to take realistic research scenarios and mould them into well-designed, straightforward experiments for third year students. Bill ensured that all students in his courses were challenged, and that they learned advanced techniques used daily in molecular biology and biochemistry research laboratories

In June 2005, Bill retired from the University of Guelph, which was a tremendous loss to faculty, staff and students in our department. Bill has been described by his colleagues as loyal, hard-working, patient, and humble. Students have described him as a wonderful mentor and one of the best laboratory instructors they had in their undergraduate program, and that because of him they "could not be better prepared for graduate school and real-life research scenarios". Bill's hard-work, loyalty, and long-standing commitment to the University of Guelph will be remembered for many years to come.

University of Manitoba

Department of Biochemistry and Medical Genetics

Correspondents: Klaus Wrogemann and Jim Davie

The great news is that we have a new head! Starting April 1, 2006 **Louise Simard** will take over the reins of our department, which resulted from a merger of Biochemistry & Molecular Biology and Human Genetics in 1999 and now has 19 primary and some 25 cross-appointees. **Jane Evans** was the first head and her term ended in June 2005. She is enjoying a well-deserved Research/Study Leave to boost her research in malformation syndromes and limb development. **Klaus Wrogeman** is currently Acting Head. **Louise Simard** comes to us from the Centre de Recherche de l'Hôpital Sainte-Justine Montreal, Quebec, where she is currently an Associate Professor in the Faculty of Medicine, University of Montreal; Director, Neurological and Mental Health Disorders Research Team, and Consultant for the Molecular Diagnostic Laboratory, Medical Genetics Service, Hôpital Sainte-Justine. Dr. Simard received her undergraduate degree from Concordia University, her B.Sc. degree from McGill in 1981 and her Ph.D. from the University of Toronto in 1987. Dr. Simard's expertise in genetics, molecular biology, molecular diagnostics, and her strong reputation in the field of motor neuron diseases, especially spinal muscular atrophy, make her ideally suited for the diverse interests in our department and we are very excited about her arrival in Winnipeg.

Leigh Murphy was honored with a YMCA-YWCA Women of Distinction Award for extraordinary achievements in the field of science. Dr. Murphy is a Senior Scientist with the Manitoba Institute of Cell Biology, Professor in the Department of Biochemistry and Medical Genetics, and Chair of the Breast Cancer Research Group at the University of Manitoba.

Jim Davie's work was placed in the top 1% of cited authors for journals in Life Sciences. Jim, who is Director of the Manitoba Institute of Cell Biology, is the recipient of a Tier I Canada Research Chair in Chromatin Dynamics. He has been re-appointed as Editor of the journal *Biochemistry and Cell Biology* for another 5-year term. The journal is doing quite well, receiving an impact factor of 3.193 in 2004. Jim was co-organizer of the FASEB summer conference "Nuclear Structure and Cancer" held in June 2004.

Marek Los was attracted from the University of Münster, Germany with a Tier II Canada Research Chair on new cancer therapy development. Marek is an MD/PhD with training from the Universities of Krakow, Poland and Heidelberg, Germany, and has a strong reputation in the field of apoptosis research.

Louise Simard

Leigh Murphy

Jim Davie

Geoff Hicks, a Senior Investigator at the Manitoba Institute of Cell Biology has risen to international prominence for his groundbreaking work on his global approach to isolating a complete set of gene knockouts in mice. 2005 was a banner year for Geoff. His CRC Tier II chair in functional genomics was renewed and together, with other Winnipeg scientists, he will receive up to $9 million worth of government and private funding, the largest portion of it coming from Genome Canada. The expertise in transgenic mice received an extra boost by attracting **Hao Ding** and **Xiali Wu** from the Samuel Lunenfeld Research Institute. Hao holds a CRC Tier II chair in "genetic modeling". Hao has medical degrees from Shanghai University, a PhD from Louvain, Belgium, and received extensive postdoctoral training at Mount Sinai under Andras Nagy. Hao and Xiali have already developed numerous models useful in the study of embryonic development.

Marek Lo

Geoff Hicks

Many colleagues, students and postdocs were again actively involved in the ***Canadian Student Health Research Forum***, which includes a national CIHR-sponsored student poster competition. This annual event has risen to nation prominence. As always, it was organized by Ed Kroeger, of the Dean's Office, and drew 600 participants from across the country. The 2005 Symposium topic was "Infection, Immunity and Health", and was organized by Kent Hayglass, Immunology: http://www.umanitoba.ca/faculties/medicine/research_days/index/index.html.

The 2006 Symposium will be held on June 8 2006, on the topic of "Aging". Students interested in participating and visiting Winnipeg should contact the website for more information.

University of Saskatchewan

Department of Biochemistry

Correspondent: Rob Warrington

Oleg Dmitriev has been appointed recently as an Associate Professor in the Department of Biochemistry at the University of Saskatchewan. Oleg earned his Ph.D. at the Moscow State University in Russia, studying bioenergetics of ATP synthesis in marine bacteria under Vladimir Skulachev. As a post-doc, Oleg received an Alexander von Humboldt fellowship to pursue his research on the mechanism of ATP synthesis in bacteria at the University of Osnabrueck in Germany. For several years, Oleg worked as a staff scientist at the University of Wisconsin in Madison. He used high-resolution NMR and molecular modeling to study the structure of the proton channel of the E. coli ATP synthase with Bob Fillingame. Recently, Oleg joined forces with

Svetlana Lutsenko (Oregon Health and Science University) to work on the structure of the soluble domains of the Wilson disease ATPase. As a new member of the Biomolecular Structure Cluster at the University of Saskatchewan, Oleg will continue his research in the field of structure and molecular mechanism of the membrane transport proteins by NMR.

Dr. Jeremy Lee's University of Saskatchewan spinoff company, Adnavance Technologies Inc., has attracted a $3.85 million investment from four venture capital organizations to develop biosensors for diagnosing disease, novel DNA-based vaccines, and a new method for producing hydrogen for fuel cells.

The biosensor and vaccine projects are based on M-DNA, a metal-bearing form of DNA discovered by Jeremy Lee in the Biochemistry Department. The metal gives M-DNA some interesting properties. In vaccines, for example, M-DNA appears to improve immune response, possibly because it resists the enzymes that quickly break down regular DNA. DNA-based vaccines are much easier to make than conventional vaccines so they can be deployed more quickly and cheaply – attractive traits when combating emerging diseases. Lee and his research team will collaborate with researchers at the Vaccine and Infectious Disease Organization at the University of Saskatchewan for this project. The M-DNA biosensor project will be based at Paracelsus Technologies Inc., a wholly-owned Adnavance subsidiary in Vancouver. The aim is to create a diagnostic tool that will quickly yield information on genetic disease and bacterial infection, allowing doctors to prescribe appropriate treatment.

The third project involves a new approach for hydrogen production using sunlight. The method is similar to photosynthesis in plants, in that it splits hydrogen from water and stores it in a chemical form. This project is supported by the National Research Council's Industrial Research Assistance Program.

University of Toronto

Department of Biochemistry

Correspondent: David Williams

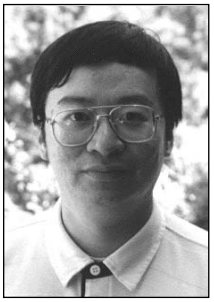
The year 2005 has been a busy one for the Department, with the addition of three new faculty members and a search ongoing for a fourth, an increase in Canada Research Chairs to 14, the growth of our graduate program to 110 students, and the opening of the new Centre for Cellular and Biomolecular Research. We maintain an up-to-date, very image-rich "News and Events" page on our Departmental website at: http://biochemistry.utoronto.ca/news. We invite you to visit periodically and see what your friends and colleagues in Toronto are up to.


Lynne Howell


Bill Trimble


Allen Volchuk


Shoshana Wodak


Hue-Sun Chan

FACULTY NEWS

A number of our faculty and staff members had noteworthy accomplishments during the past year. We were pleased to learn that **Lynne Howell, Bill Trimble, Allen Volchuk** and **Shoshana Wodak** received Canada Research Chairs and that **Hue-Sun Chan's** Chair was successfully renewed.


Byron Lane

Emil Pai was elected President of the Canadian Institute for Synchrotron Radiation. **Cliff Lingwood** has been very active on the speaking circuit with invited talks at the XVIIIth International Symposium on Glycoconjugates in Florence, at a Satellite Symposium on Glycobiology in Tuscany, and as a Session Convenor at the American Society of Microbiology in Orlando. **Reinhart Reithmeier** has been busy as Chair of the Organizing Committee for the 49th Annual Meeting and Conference of the CSBMCB to be held May 31 - June 4, 2006 in Niagara-on-the-Lake. The theme is "Membrane Proteins in Health and Disease" and registration has

already begun at: http://www.csbmcb.ca/2006 conference.

Professor Emeritus, **Byron Lane**, has just completed a privately published tribute to the University of Toronto Schools (UTS), an institution which, for nearly a century, has been the secondary-school adjunct of the University of Toronto. As a UTS alumnus (class of '52), Byron has tried to break new ground by exploring, in some depth, the reasons why UTS acquired its reputation as the premier secondary school in Ontario. This reputation took root during the slightly more than half century after UTS opened its doors in 1910, in a period when the exit gates from secondary-school education and the entry gates to higher education in Ontario were regulated by a set of province-wide standardized matriculation examinations (1891-1967). The book is titled *University of Toronto Schools. An Academic History of the Era of Province-Wide Standardized Matriculation Examinations in Ontario*.

Russell Bishop expressed his fondest best wishes to all members of the Department when he announced his intention to accept a position as an Associate Professor in the Department of Biochemistry and Biomedical Sciences at McMaster University in the spring. Russell has struggled with the 2 h commute from his home in Paris, Ontario and was overheard commenting on the move to McMaster "it's only an hour away by GO train... !" Russell has been a very active and collegial member of our Department - we will sorely miss our tallest professor as well as his good humour and enthusiasm for science.

Business Officer **Suzanne D'alvise** was presented with a Twenty-Five Year Service Award in recognition of significant service to the University of Toronto. Thanks to Suzanne for all of her hard efforts on our behalf over the years!

EVENTS

A substantial event this year was the opening of the Terrence Donnelly Centre for Cellular and Biomolecular Research (CCBR). The essence of the CCBR as stated on their website (http://tdccbr.med.utoronto.ca) "lies in three programmes that span the leading areas of biomedical research: Bioengineering and Functional Imaging, Integrative Biology, and Models of Disease. The Donnelly CCBR premise is that each programme - and the entire Centre - will thrive best if it includes biological, physical, computer and engineering scientists working together in a communal setting". Dr. Brenda Andrews is the Donnelly CCBR Director. Three Biochemistry faculty members, Drs. Grant Brown, Liliana Attisano, and Igor Stagljar, will move their laboratories to the CCBR.

Our Annual Research Day, held at the Old Mill Inn on May 17th 2005, was another great success with more than 200 participants. Oral presentations by faculty and students, numerous poster presentations, great food, and good spirits all combined to create a terrific experience for faculty and students alike. This is also the venue for our annual Theo Hofmann lecture which was presented by **Lila Gierasch**, Professor and Head of the Department of Biochemistry & Molecular Biology, University of Massachusetts-Amherst. Lila's lecture was entitled "Navigating a challenging folding landscape: folding and aggregation of a beta-clam protein in vitro and in vivo."


So many biochemists!

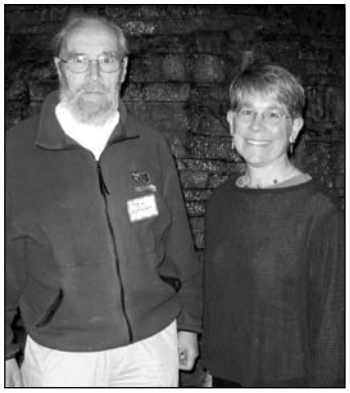
APPOINTMENTS

We were delighted to welcome three new Faculty members in 2005.


Angus McQuibban


Igor Stagljar

Matthew Moyle (left) with the Schachter family



Theo Hofmann Lecturer Lila Gierasch with Theo Hofmann

Angus McQuibban joined us this summer as an Assistant Professor. Angus just completed post-doctoral studies with Matthew Freeman at the MRC Laboratory of Molecular Biology in Cambridge, U.K. His research focuses on molecular mechanisms of mitochondrial membrane dynamics and their relation to cell function.

Igor Stagljar also arrived this summer to take up a position as an Associate Professor. Igor was previously an Assistant Professor at the University of Zurich. He is interested in membrane protein interactions and in the maintenance of genome stability. Igor is well known internationally for his development of the membrane yeast two-hybrid system using a split-ubiquitin approach. Upon Russell Bishop's departure he will also assume the title of the Department's tallest professor!

John Rubenstein

Finally, **John Rubinstein**, a Scientist at the Hospital for Sick Children, was appointed as an Assistant Professor. During his Ph.D., John honed his skills in electron cryomicroscopy of ATP synthase with Sir John Walker in Cambridge, U.K. He continues to study the structure of macromolecular assemblies, with particular emphasis on the proteasome, and is also keenly involved in the development of methodology in electron cryomicroscopy.

We are also actively recruiting one additional Assistant Professor and a Lecturer at this time. Our congratulations go to **Walid Houry** and **Igor Stagljar**, who were awarded tenure this year.

GRADUATE STUDIES

A new graduate event took place this year, the **Benjamin Schachter Memorial Lecture**. From 1934-1939 Benjamin Schachter worked in the Department of Biochemistry conducting research on female sex hormones, isolating and identifying conjugated oestrone sulphate (Premarin). He worked from 1939-1949 at Canada Packers, starting the Research and Development Department, researching hormones and vitamins, and set up and headed a plant for the synthetic production of vitamin D3, essential to the war effort. To honour Benjamin Schachter's memory, a donation was made to the Department by his family. The funds are being used to support an annual lectureship in his memory. The graduate students select and host the speaker who is a graduate from our Department.

This year's speaker was **Dr. Matthew Moyle**, who was a graduate student with Dr. James Ingles and graduated in 1989. Dr. Moyle is now Vice-President of Research at Tanox Inc., Houston, Texas. Dr. Moyle's lecture was entitled: "From Asthma to Osteoporosis: The Discovery and Development of New Monoclonal Antibody Therapeutics"

The Department holds its graduate student poster competition as part of its Annual Research Day. Our guest poster judge was this year's Theo Hofmann Lecturer, Lila Gierasch, Professor and Head of the Department of Biochemistry & Molecular Biology, University of Massachusetts-Amherst.

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

Winners in the Ph.D. category were: **Lellean Jebailey** (Klip lab): "Insulin induced actin remodeling in L6 muscle is regulated by the small GTPase Rac"; **Ben Pinder** (Smibert lab): "Posttranscriptional regulation of nanos mRNA"; and **Yinan Zhang** (Williams lab): "Functions of ERp57 in the folding and assembly of MHC class I molecules".

Winners in the M.Sc. category were: **Lia Cardarelli** (Davidson lab): "Mapping the protein surfaces and interactions important in the assembly of Bacteriophage lambda"; **Sagar Dugani** (Klip lab): "Morphological characterization of insulin-responsive GLUT4 compartments in L6 muscle cells"; and **Rishi Rakhit** (Chakrabartty lab): "Monomeric/misfolded SOD1 detected in mouse models of ALS using a designed antibody".

The winner in the postdoc category was: **Anna Gribun** (Houry lab): "The ClpP double-ring tetradecameric protease exhibits plastic ring-ring interactions and the N-termini of its subunits form flexible loops that are essential for ClpXP and ClpAP complex formation.".

Additional graduate awards:

David Williams with graduate students

The winners of the **Beckman Paper of the Year Award** for 2004 were:

Meryl Nelson for her paper "Drosophila Cup is an eIF4E-binding protein that functions in Smaug-mediated translational repression". Nelson, Leidal, and Smibert (2004) EMBO J. 23:150

Beckman Paper of the Year winners Meryl Nelson (left) with Grad. Coordinator David Williams and Jennifer Marles with Chair Reinhart Reithmeier

Jennifer Marles for her paper "Protein-protein interaction affinity plays a crucial role in controlling the Sho1p-mediated signal transduction pathway in yeast". Marles, Dahesh, Haynes, Andrews and Davidson (2004) Mol. Cell 14:813

Chris Tsang (left) and Johnny Tkach receive the Scott Prize from Graduate Coordinator David Williams

The annual David Scott prize for outstanding all-round graduate student was a tie this year, jointly awarded to Chris Tsang (Trimble lab) and Johnny Tkach (Glover lab). Johnny and Chris were selected on the basis of research excellence and outstanding contributions to the Department and fellow students.

Congratulations to all winners for their achievements.

University of Victoria

Department of Biochemistry and Microbiology

Correspondent: Claire Cupples

Dedicated Faculty Member Receives Teaching Award

Ed Ishiguro has been a faculty member in the Department of Biochemistry and Microbiology at UVic for the last 29 years. During this time he has taught courses at every possible level, while researching bacterial stress response mechanisms. From 1995-2003, he was the Chair of the Department, a position which gave him the opportunity to shape it profoundly, to the benefit of those who choose a science education at this institution.

The research carried out by Ishiguro has a practical direction, leading to possible clinical applications. Focusing on the starvation response in bacteria, he has paid particular attention to proteins which interact with bacterial ribosomes. Some of these interactions lead to tolerance to antibiotics such as penicillin. If you can prevent the activity of these proteins, blocking the stress response, the bacteria will then be susceptible to the drug. This makes the proteins themselves potential targets for antibacterial drugs.

As enthusiastic as Ishiguro is about his research, he is even more passionate about his teaching. During his time at UVic, the student population has grown from 6,000 to 16,000. The Department to which he has gladly devoted so much time has grown in parallel. When he first arrived it was typical for 4th year courses to have only 5 or 6 students; now 40 is fairly typical. However, class sizes have little impact on his approach to teaching.

Ishiguro's teaching philosophy is to make the course content crystal clear and make it relevant. His methods have been influenced by many teachers in his life, beginning with his parents who taught him the value of hard work. Others have included his mentor Ralph Wolfe, well known for his own work in microbial biochemistry, who taught him for 5 years. These influences, combined with Ishiguro's own passion and experience, have come together to create a powerful teaching style.

In keeping with his dedication to the students, Ishiguro has had a hand in expanding the opportunities open to them while they are here. He has been a champion of a strong undergraduate laboratory program in microbiology, an effort which has been blessed by outstanding microbiology laboratory instructors such as Barb Currie and Judy Wise. Likewise, he feels that Dr. Rozanne Poulson and her predecessor Dr. Jackie Somers have developed one of the best coop programs in Canada. His influence can also be felt beyond the Department. A course on biochemistry in human health that he developed cuts through some of the mystery surrounding modern biomedical approaches to medicine, to the benefit of non-science students.

Recently Ishiguro's dedication to teaching has led to the much deserved receipt of an award from the Faculty of Science for Excellence in Teaching for the 2004/2005 year. This comes on something of a sad note, as he faces retirement at the end of the academic year. UVic and its Biochemistry/Microbiology Department have been a wonderful place for him, and he just doesn't feel ready to leave. He is of the belief that teaching is in itself an art form to be learned, and that is a journey he is far from ready to give up.

Head Laboratory Instructor Celebrates Milestone

Glen Pryhitka celebrates 30 years in the Department this year. He came to the University of Victoria in August of 1975 having just graduated from UBC with a Bachelors of Science in Biochemistry. He has been here ever since. During that time he has availed himself of many opportunities to further his own knowledge, and has worked hard to impart that knowledge to the students.

In Pryhitka's early years here, summers were spent learning new techniques in biochemistry and microbiology so that they could be incorporated into the labs. Working with faculty members, such as Tom Buckley, he mastered processes such as manual DNA sequencing and use of HPLC. With

the administrative load that comes with heading up the biochemistry laboratory program, he doesn't have the chance to do this kind of work anymore, but is still dedicated to improving the quality and value of the courses offered.

Pryhitka gratefully acknowledges the Department's commitment to the undergraduate laboratory program. Even now, work is underway to prepare a new 3rd year laboratory class. A full year course, it would offer students the chance to approach the materials offered in intermediate biochemistry and microbiology in an integrated format. The idea is to streamline and modernize the labs so that 4th year students can be given a serious, research-oriented project.

Some of Pryhitka's most memorable impressions and fondest memories from the last 30 years have come from the growth of the Department. When he first arrived at UVic, there were only 4 faculty members in the Department, and no graduate students. Now there are 16 faculty and 36 graduate students. Similarly, 4th year lab classes have gone from an enrolment of 3 to around 60.

Pryhitka recalls that in 1975 the lab facilities were located in the army-surplus huts near the campus tennis courts. As of December, it is 20 years since a move to the Petch Building, which he feels was a major step in the development of the laboratory program. As growth has continued, the current facilities are once again stretched to their limits. However, with the support of the Chair and other members of the Department, opportunities for expanding the lab facilities are being explored.

Pryhitka believes strongly that students "learn by doing" and attempts to emphasize this within the laboratory program. He also understands that it is impossible to impart the enormous amount of information that has been acquired over the last decade alone, and this also influences his teaching philosophy. It is imperative that students learn how to process information by developing critical thinking skills. As such, it is his intention that students learn from their undergraduate laboratory experience, while enjoying it and developing the skills needed to meet the challenges of the next decade in biochemistry.

The Graduate Student Poster Symposium

Each fall, students in the Department of Biochemistry and Microbiology participate in the Graduate Poster Symposium. The intent of the symposium is to allow students to present data from their research and practice their skills in presenting that work. Students aren't marked, and participation is not mandatory, though most choose to avail themselves of the opportunity. At the end of the Symposium several prizes were awarded to students whose research contributes to areas on the cutting edge of their field.

Teresa Francescutti took home the ViagenX prize for her work in molecular pharming of an anti-trypanosomal cationic peptide in potato. This work was done in the lab of **Dr. Santosh Misra**, with the help of UVic's Dr. Terry Pearson and Dr. Hancock from UBC. The peptide is targeted against the protozoan parasite Trypanosoma brucei, the organism responsible for African sleeping sickness. This disease causes considerable loss of life in both humans and cattle in sub-Saharan Africa, and is difficult to treat. By producing these anti-trypanosomal peptides in potatoes, it should be possible to use the plant directly as an edible treatment, or to process it into a concentrated therapeutic agent.

Working in **Dr. William Kay's** lab, **Deanna Gibson** won the senior grad student prize for her work on the discovery of three novel extracellular polysaccharides associated with the extracellular matrix of Salmonella enterica Enteritidis. These molecules are only expressed when the bacteria are found as communities, biofilms. They were previously undiscovered because most often scientists look at individual cells. These factors may be necessary for the organism's long term survival and persistence in the environment. Studying biofilms therefore offers a more realistic view of bacterial life, and can therefore offer significant information on how to treat infections.

Eric Tran won the poster award for junior grad student, with Spencer Alford and Dominik Domanski as runners up; 23 posters were entered in the Fall Symposium, and each one of them represents only a subtle echo of the dedication that the Biochemistry and Microbiology Graduate students put into their work.

University of Waterloo

Department of Biology

Correspondent: Bernard Duncker

It was another year of transition in the University of Waterloo Biology Department. In February we were all shocked and saddened to learn that **Marilyn Griffith** had suddenly passed away after suffering a stroke. Marilyn was one of our most honoured colleagues, having recently added the Killam Prize to a long list of awards for her innovative work on molecular mechanisms of plant stress responses. Marilyn's expertise, enthusiasm and friendship are all greatly missed, as is the familiar sound of her laughter in our hallways.

There were several changes in key positions over the course of 2005 involving Biology faculty. **Brian Dixon** is our new Associate Department Chair, **Owen Ward** became the new director of the Science and Business program, while **Bill Taylor** was appointed Associate Dean of Science for Research. **George Dixon** was reappointed for a second three-year term as Dean of Science.

Several faculty members were the recipients of major awards over the past year, including **Mungo Marsden** and **Christian Jacobson**, who received CFI New Opportunities funding for an 'Integrated Facility for Gene Discovery and Molecular Imaging', as well as **Kirsten Mueller** and **Bernie Duncker** who were both recipients of Ontario Early Researcher Awards. Two major NSERC equipment grants were also awarded to groups of researchers within the department, for new DNA sequencing and flow cytometry facilities.

The influx of new faculty members continued in 2005 with the addition of **Bruce Reed** (*Drosophila* development) who joins us from the University of Toronto, and **David Spafford** (*Lymnaea* neurobiology) who recently completed his postdoctoral studies at the University of Calgary.

Brian Dixon

Marilyn Griffith

Kirsten Mueller

University of Western Ontario

Department of Biochemistry
Correspondent: Eric Ball

In fall 2005, the Department opened a new wing which represents the near-completion of the Medical Sciences Building renovation project. The department main office has now moved into its new space, as have many of the faculty. We can look forward to only a few more months of occasional floods, power failures and falling debris, before the last of the faculty move into their new digs in 2006.

Dr. Ted Lo has completed two highly successful five year terms as Departmental Chair. Under Ted's leadership the Department saw unprecedented growth in both teaching and research programs. Ted is spending the year on a well-deserved leave and will return in the summer of 2006. Ted's place will be temporarily filled by **Dr. Chris Brandl** as acting Chair while the search for a successor goes on.

Another faculty member currently on leave is **Dr. David Litchfield**, who is on sabbatical in North Carolina working in the labs of Tim Haystead and Lee Graves. Dave is learning the ins and outs of using mass spectrometry and protein sequencing to study protein phosphorylation events. Dave was a triple award winner this year, receiving a 2005 Faculty Scholars award, a Dean's award of excellence in research, and an alumni award for professional achievement. As well, he has been appointed Director of the new Functional Proteomics Facility.

Several faculty received CFI awards: **Dr. Mellissa Mann**, for analysis of various ART procedures to identify periods of susceptibility that may lead to abnormalities like intrauterine growth retardation, premature birth and low birth rate; **Drs. Megan Davey** and **David Edgell** for regulation of DNA processing events; and **Dr. James Choy** for the study of how naturally disordered proteins are involved in human disease.

Among other faculty achievements, **Dr. Megan Davey** also received the Harold E. Johns Award for biomedical research, given by the National Cancer Institute of Canada, and a CCS Research Scientist Award. **Dr. Fred Possmayer** won a Dean's Award of Excellence in Research, and **Drs. Fred Dick** and **Richard Rozmahel** received Ontario Early Researcher Awards. **Dr. Victor Han** has been appointed Associate Dean of Research for the Faculty of Medicine and Dentistry.

York University

Department of Biology
Correspondent: Imogen Coe

Research and teaching in biochemistry, molecular and cellular biology continue to thrive at York University, primarily in the Department of Biology, but also in the Departments of Chemistry and Kinesiology & Health Science, and increasingly, in an interdisciplinary manner across the Faculty of Science and Engineering and the university as a whole. We continue to see increases in the numbers of undergraduates and graduate students coming to York to study life sciences - a trend that appears to be common across the country. Recruitment of new personnel is a priority and we are currently in the process of hiring faculty in the areas of organic chemistry, biochemistry, molecular and cellular biology, physiology and molecular neuroscience. Continuing our tradition of outstanding young investigators, **Dr. Scott Kelly** (Biology) received an Early Researcher award (formerly known as PREA) while **Drs. Michael Scheid** (Biology) and Gary Sweeney (Biology) were successful in obtaining CIHR salary awards for New Investigators. **Dr. Chun Peng** (Biology) was awarded the prestigious Ontario Women's Health Council/CIHR IGH mid-career award and **Dr. Denise Henriques** (K&HS) was awarded the Polanyi award for medicine and physiology. **Dr. Andrew White** (Biology) was awarded a prestigious Steacie Fellowship for his contributions to our fundamental understanding of RNA viruses.

In addition to a Steacie Fellow, York is also home to Canada's leading young scientist (under 40) for this year, as determined by the Steacie Award, which went to **Dr. Doug Crawford**, a neuroscientist in the Department of Psychology.

Dr. Michael Siu (Chemistry) continues to lead an internationally recognized group in proteomics, and is a founder of the Ontario Cancer Biomarkers Network (OCBN) funded through OCRN. Dr. Siu was also awarded the F.P. Lossing Award for his significant contributions in mass spectrometry and became the Associate Vice-President of Research (Science and Technology) at York University. **Dr. Ron Pearlman** (Biology) continues to work tirelessly on behalf of York University, and hosted the inaugural Gairdner/OGI high school science program where Drs. Andrew Fire and Tak Mak spoke to a group of enthralled high school students. Dr. Pearlman also now sits on the Medical Advisory Board of the Gairdner Foundation and, in his spare time, has taken on the challenge of being Interim Dean of Graduate Studies at York. Continuing the theme of engaging the next generation, **Dr. Logan Donaldson** (Biology) led a team of talented Grade 10 high school students (from University Toronto Schools) to success in the Sanofi Pasteur Biotech Challenge, where they won the GTA Regional final. Dr. Donaldson now has four Grade 12 students who have just started their project for this year's contest. **Dr. Tara Haas** (K&HS) has been appointed to the CIHR Institute of Circulatory and Respiratory Health.

Handling the increasing number of undergraduates in life sciences continues to be a challenge with shrinking budgets and ageing infrastructure. A new Biomedical Sciences undergraduate program has been established in the Department of Biology, which will likely attract yet more students. In addition, York University recently approved the establishment of a new faculty, the Faculty of Health. This new faculty will house the departments of Psychology and Kinesiology & Health Sciences, as well as a number of small programs. This new faculty will bring together a very broad range of teaching and research activities in the areas of health, from Petri dishes to populations, and establish new paradigms for our understanding of human health.

Overall, faculty in the biochemistry, cell and molecular biology area have been very successful in obtaining operating funding from CIHR, NSERC, NCIC, HSF, etc. as well as major infrastructure funding.

Dr. Coe (correspondent), who took over as Chair of the Department of Biology in January 2005, is delighted to report that both she and the department have survived her first year in office. We look forward to continued success in the areas of biochemistry, molecular and cell biology at York University.