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# 49th Annual Meeting of the CSBMCB:

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The 49th Annual Meeting and Conference of the Canadian Society of Biochemistry and Molecular & Cellular Biology (CSBMCB) on "Membrane Proteins in Health and Disease" was held from May 31 to June 4, 2006 at the White Oaks Conference Resort and Spa in Niagara-on-the-Lake in Ontario. The Organizing Committee, consisting of Reinhart Reithmeier (Toronto), David Andrews (McMaster), Frances Sharom (Guelph), Joseph Casey (Alberta) and Jean-Yves Lapointe (Montréal) put together an excellent program featuring presentations by over 25 scientists from Canada and the United States. The talks were of uniformly high quality and they generated considerable discussion during the question period. The meeting was very popular, attracting close to 200 delegates, over half of whom were graduate students or post-doctoral fellows, from North America and as far away as Hong Kong.

The meeting began on Wednesday evening with a "Plenary Session" chaired by Joel Weiner. The first two speakers, Ron Kaback (UCLA) and Nobel Laureate, Peter Agre (Duke), set a high standard, as they engaged the audience in work they carried out that led to a detailed understanding of the molecular basis of membrane transport of sugars and water. The evening finished with a lively Mixer sponsored by Merck-Frosst Canada, which included a birthday celebration for Ron Kaback, who is now of an indeterminate age.

The second session on Thursday morning on the "Structural Biology of Membrane Proteins" was chaired by Reinhart Reithmeier. The four speakers covered various approaches that are used to determine membrane protein structures. Charles Deber (Sick Children's Hospital, Toronto) spoke on his work using model peptides to mimic transmembrane helix-helix interactions. Natalie Strynadka (University of British Columbia) described her work using crystallography to determine the structures of the key proteins involved in bacterial

pathogenesis. Michael Maguire (Case-Western Reserve) described a fascinating new membrane protein structure, that of the bacterial magnesium channel, CorA. Francesca Marassi (Burnham) described the use of solid state NMR to determine the structure of transmembrane proteins and their interaction with other membrane proteins. The final speaker, Robert Stroud (UC San Francisco), gave a fascinating talk on the structures of families of membrane proteins involved in ammonium/ammonia, glycerol and water transport.

The Thursday evening session chaired by Janet Wood (Guelph) on "Regulating Membrane Permeability" started with Michael Caplan (Yale) who spoke on membrane protein trafficking in polarized cells with a focus on polycystin 1 and interacting proteins. This was followed by a presentation by David Andrews (McMaster) on the regulation of membrane permeability by interaction and conformational dynamics of apoptosis proteins Bcl-2 and Bax. James Coulton (McGill) presented his studies on the structure of the TonB/FhuA complex, which appeared in *Science* the next day. John Collier (Harvard) spoke on his studies of anthrax toxin translocation across membranes.

The Friday morning session IV on "Dynamics of Membrane Proteins" was chaired by Christine Bear (Sick Children's Hospital, Toronto) and began with Frances Sharom (Guelph), this year's winner of the Jeanne Manery Fisher Award. Dr. Sharom was recognized for her innovative studies of the P-glycoprotein drug efflux pump, particularly for the use of fluorescence spectroscopy. Francisco Bezanilla (Chicago) spoke on the molecular basis of voltage-gated channels. Jennifer Baker, a Ph.D. student at the University of Toronto, gave an excellent presentation of her NMR studies of the intrinsically disordered R domain of CFTR. Eduardo Perozo (Chicago) continued with the channel theme and described the pore dynamics

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and gating mechanisms of KcsA, a bacterial potassium ion channel.

Joseph Casey, this year's winner of the Merck-Frosst Prize, described his ground-breaking work on the role of anion exchangers in cardiac hypertrophy in Session V on "Membrane Proteins and Disease", chaired by Howard Young (Alberta). Dr. Casey presented compelling data on the linkage of carbonic anhydrase with bicarbonate transporters, and the role this interaction plays in regulating bicarbonate transport. Jean-Yves Lapointe (Université de Montréal) discussed the transport properties of a novel sodium-dependent monocarboxylate transporter. Shawn Li (Western) gave a short talk on a SH2 containing module, SAP, that regulates receptor signaling. The final talk was by John Orłowski (McGill), who spoke about sodium proton exchangers, interacting proteins and their role in cardiac physiology.

"Membrane Protein Trafficking" was the topic of Session VI, chaired by Carol Cass (Alberta). Mutations in the genes encoding membrane proteins often cause disease. These mutations may affect the functionality of the proteins directly, but often cause misfolding or trafficking defects. Art Johnson (Texas) provided a beautiful overview of how fluorescently-tagged nascent polypeptides can be used to characterize the machinery involved in translocating proteins across the ER membrane and into the lumen. Michel Bouvier (Université de Montréal) presented important findings from his group that mis-folded G-protein coupled receptors (GPCRs) can be rescued from ER retention and transported to the cell surface by the application of membrane-permeant antagonists. Ray Truant (McMaster) identified a membrane association signal in the protein huntingtin that can modulate vesicle targeting and nuclear entry. Reinhart Reithmeier (Toronto) spoke about his group's studies of trafficking defects of the chloride/bicarbonate anion exchanger that are linked to diseases affecting the red cell and the kidney. The session finished with a presentation by Gergely Lukacs (Sick Children's Hospital, Toronto) who pointed out that the instability of mutant membrane proteins at the cell surface can cause rapid internalization, thereby reducing function.

Session VII was a "Workshop on Membrane Protein Crystallization", organized and chaired by Gilbert Privé (University Health Network, Toronto). This session was attended by many people who have, until now, only dreamed about determining the structure of their favourite membrane protein. The speakers engaged the audience as they talked about the challenges and successes they faced in this task. It was gratifying to know that persistence pays off, and the increase in the number of membrane protein structures paralleled the increase in the structures of soluble proteins, only off-set by about 50 years! Critical issues, such as the use of various expression systems (expression of mammalian membrane proteins remains a challenge), the precise design of the construct (removing the tag), the choice of detergent (dodecyl maltoside remains the clear winner), high throughput surveys (crystallize what you can express), etc. were highlighted by the panel of speakers: Gilbert Privé (UHN, Toronto), Joanne Lemieux (Alberta), Mark Dumont (Rochester), and Chris Koth (Vertex).

The workshop was followed by a panel discussion on "Biomedical Research Funding in Canada". The panel members included Joel Weiner (Alberta), David Thomas (McGill), Phil Branton (CIHR, McGill) and Jim Woodgett (SLRI, Toronto). This lively interchange highlighted the positive impact of the transition of MRC to CIHR with respect to the number and size of grants. There was however a consensus that the interests of basic biomedical sciences were not well represented at CIHR, particularly within the Governing Council. Also, too few resources were being devoted to open grant competitions, with the ever increasing numbers of RFAs. It was felt that our community must do more to reach out to key decision makers to inform them of the benefits of the basic biomedical research we do. We must also do a better job in engaging the public. The CSBMCB has made major strides in these directions lately. The various levels of government need to develop an integrated strategy with respect to research initiatives. "Research Canada", a new consortium of interested parties, may be useful in this regard. The CRC and CFI programs have provided salaries and equipment, but the granting agencies have not

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been able to keep up with the growth in research. The Annual Meeting of the CSBMCB followed, with a record turnout of members. The meeting highlighted the success the Society had achieved in organizing high quality conferences every year, and in being a powerful advocate for biomedical research in Ottawa.

Saturday evening was devoted to a gourmet banquet and the awards presentations. The Merck-Frosst and Jean Manery Fisher Awards were presented to Joseph Casey and Frances Sharom, respectively by David Thomas (McGill), President of CSBMCB. Because of the generosity of the Society and the sponsors of the meeting, a large number of travel and poster awards were presented to trainees.

The meeting wrapped up with a session on Sunday morning on "Assembly and Disassembly of Membrane Proteins". Tom Rapoport (Harvard) revealed his ideas concerning novel pathways for the degradation of ER proteins. Membrane proteins do not fold in isolation, but are assisted by chaperones that act to prevent aggregation. David Williams presented compelling evidence for a direct chaperone effect for calnexin and calreticulin beyond their well-defined carbohydrate-binding properties, and described the regulatory roles for ATP and calcium ions. Graduate student Pekka Maattanen (McGill) presented the structure of ERp57, a protein disulfide isomerase that acts in concert with calnexin to recruit substrate proteins. Jeff Brodsky (Pittsburgh) discussed the use of yeast as a model system to study the ER associated

degradation (ERAD) of mammalian membrane proteins like CFTR, as well as plasma membrane-associated quality control systems. In the final presentation, Igor Stagljar (Toronto) told the audience about novel technology his laboratory has developed to detect membrane protein interactions in high throughput mode, providing a preview of the theme of the 50th Annual CSBMCB Meeting to be held in 2007 in Montréal.

A highlight of the meeting was the two poster sessions that featured the work of graduate students, post-doctoral fellows and senior investigators. The evening "Poster Pubs" provided plenty of opportunity for lively discussions of the over 100 posters presented, and they went well into the evening.

Many people took advantage of the Hillebrand Winery and Niagara-on-the-Lake tour on Thursday afternoon, and the Niagara Falls tour on Friday afternoon. Others found time to participate in tennis and swimming at the Resort, or golf at nearby courses. People were very impressed with the friendliness of the staff at White Oaks and their attention to detail. The "continuous" coffee breaks and snack tables were greatly appreciated.

The feedback on the meeting and the quality of the presentations has been overwhelmingly positive. It is very gratifying that a great deal of excitement was generated among the younger people at the meeting about research in the area of membrane proteins, suggesting that this important field will continue to prosper well into the future.