
2003 Society Award Designates

Dr. Victor Ling, BC Cancer Research Centre, Vancouver, B.C. has been chosen to receive the 2003 Roche Diagnostics Prize for Biomolecular and Cellular Research and the 2003 CSBMCB's Merck Frosst Award has been granted to Dr. Charles M. Boone, Banting and Best Department of Medical Research, University of Toronto. The 46th Annual General Meeting of the Canadian Society of Biochemistry, Molecular and Cellular Biology will be held July 20 -24, 2003 at the Toronto Convention Centre conjointly with the 19th Congress of International Union of Biochemistry and Molecular Biology. Both of our Society's Award Lecturers have been honoured by being designated as Plenary Speakers at the 2003 IUBMB Congress.

Dr. Victor Ling

Dr. Ling's primary research accomplishments stem from his discovery in 1972 of multi-drug resistance (MDR). This was truly a pioneering effort, since it was rare at that time to induce and study mutants in mammalian cells. Subsequent investigation by Dr. Ling showed that P-glycoprotein is associated with MDR. He then cloned the gene for P-glycoprotein and transfected it into mammalian cells to show that it is responsible for MDR. Cloning also facilitated the characterization of P-glycoprotein, its relationship to hemolysin B, its identification as a member of the ABC-transporter superfamily and characterization of related genes of medical relevance.

Cancer cells acquire the metastatic phenotype during disease progression. Dr. Ling showed in 1982 that metastatic variants are stochastically generated at a high rate in tumour cell lines and that this can account for the correlation between cancer progression and genome instability. He subsequently showed that poor clinical outcome in a number of cancers is the consequence of P-glycoprotein expression. This provided a potential approach to cancer therapy, which Dr. Ling applied successfully in 1995 when he demonstrated that cyclosporine A inhibition of P-glycoprotein greatly improves long-term response to chemotherapy of children with retinoblastoma.



Dr. Ling plays a major leadership role in the cancer community in Canada. He developed the Division of Structural Biology at the Ontario Cancer Institute and recruited a number of Canada's premier structural biologists into the Division. This greatly increased Canada's profile in structural biology and had a major impact on cancer research in this country. He currently serves as Vice President (Research) at the BC Cancer Agency and as Vice-Dean (Cancer Research) at the University of British Columbia. He also developed and leads a cancer genomics program in BC, funded by Genome Canada. Dr. Ling established the BC Genome Sequencing Centre as an integral component of the BC Cancer Agency. This was the first sequencing centre in Canada to be directly linked to a cancer treatment organization. He recruited Michael Smith to be the first Director of the Centre. This initiative ultimately led to the establishment of the Centre for Integrated Genomics and a new Cancer Research Centre. In addition to his efforts in British Columbia, Dr. Ling serves on the Board of the National Cancer Institute of Canada and the Governing Council of CIHR.

Vic Ling is a distinguished scientist and a true academic leader. He is a credit to the Canadian biochemistry community and a worthy recipient of the Roche Diagnostic Award.

Dr. Charles Boone

Dr. Boone is one of Canada's foremost young biochemists - his work in proteomics has been internationally recognized because it has provided important concepts concerning the way that multiple signalling pathways are connected in a single cell, to control state changes in response to extracellular signals.

Dr. Boone demonstrated outstanding research abilities as a graduate student in Biology with Dr. Howard Bussey at McGill University. He demonstrated that the unprocessed precursor of a secreted protein could have a unique biological function and he defined the series of genes which encode proteins in the pathway of α -glucan biosynthesis; some of these genes are essential for viability and represent antifungal drug targets. These findings formed the basis for a patent on glucan genes which provided intellectual property for the founding of an antifungal drug discovery company, Mycota Biosciences. In his postdoctoral studies, Charlie became interested in signal transduction. He determined that the third intracellular loop of the yeast a-factor receptor, Ste3, functions as a negative regulatory domain. In this work, he was the first to characterize a constitutive G protein-coupled receptor.

In independent studies, Dr. Boone became interested in cell polarity and the role of signalling to actin and myosin assemblies. In 1997, he was able to demonstrate that formins, which are involved in the establishment of cell polarity in *Drosophila* oocytes and embryos, link Rho-type GTPase signalling molecules to actin assembly proteins. He followed this work up in 2000, with a study showing that SH3 domains in myosin-1 bind the yeast homologues of human WASP and WIP. Since these proteins link actin assembly and signalling molecules, Dr. Boone was beginning to put together a very important signalling complex involved in cell polarity and motility. His studies provided the first evidence that myosin-1 motors participate in motility through a role in actin assembly. In his most recent work in this area, he showed that yeast formins assemble actin cables. This observation provided a very simple model for the control of polarized cell growth in yeast cells: signalling molecules activate formin proteins, which assemble actin cables at a growth site



to guide myosin motor-directed secretion.

In later studies, Dr. Boone's interest in signalling through protein-protein interactions led him to a collaboration with Rosetta Inpharmatics to use microarrays to look at changes in transcription that could be related to activation of parallel MAP kinase pathways in a single cell. His studies in this field provide the very best illustration of how DNA microarrays can be used to trace signalling networks. They also illustrate Dr. Boone's early interest in using the most elegant emerging technologies to advance his ideas.

Most recently Dr. Boone has been involved in large scale proteomics efforts. One of these is the investigation of protein-protein interactions on a genome scale in yeast. In one study, he collaborated with 10 other laboratories to map 191 protein-protein interactions that control cell polarity development in yeast. In a second study, initiated in his laboratory, but ultimately involving 4 laboratories, two different protein-protein interactions networks for yeast SH3 domain proteins were generated: one was derived from phage display ligand consensus sequences and another from two-hybrid interaction assays. This prototype study will be expanded as a rapid and general method that can be implemented readily for analysis of protein complexes formed through other peptide recognition modules. It will be equally useful for other organisms with a sequenced genome.