
Incoming Members of CSBMCB Executive Board 2002-2003

Dr. John ORLOWSKI, Vice-President

John Orłowski was born in London, England in 1956, but shortly thereafter emigrated with his family to Montreal, Quebec, where he received his formative education. As a high school student, his academic strengths lay in the physical sciences - mathematics, physics and chemistry. However, he found himself more captivated by the complexities of biological systems, and what better place to pursue this interest than right next door at McGill University, well respected for its strengths in the biological/biomedical sciences. John undertook his undergraduate studies in the Department of Biology, majoring in the Molecular, Cellular, and Developmental Biology program. It was during this time that he became intrigued by exciting developments in the field of endocrinology, particularly following a series of biochemistry lectures by Samuel Solomon on the molecular diversity of steroid hormones and their mechanisms of action. These lectures were seminal in the sense that they seeded his aspiration to become a biomedical scientist, quelling any earlier thoughts of pursuing a career in family medicine.

Following completion of his baccalaureate, John pursued his interests in steroid hormone action at Queen's University in Kingston, Ontario, where he obtained his M.Sc. and Ph.D. degrees in Biochemistry under the supervision of Albert Clark. By coincidence, Albert Clark had completed his doctoral studies with Samuel Solomon about a decade earlier, and had formed a strong research group investigating mechanisms of androgen action, utilizing the prostate gland as a model system. Up to this point, most of the research in this area had been performed using whole animals or tissue explants, yet there were indications from developmental studies that molecular communication between the epithelial and stromal cells of the prostate was critical for

organ development. John's project was to investigate whether these two cell types metabolized androgens (as well as estrogens) differently and, if so, how this might influence prostate growth and differentiation. This was particularly challenging as few studies to that point had been successful in

separating and maintaining these distinct cell types in primary culture for sufficient periods of time to permit detailed characterization. Moreover, techniques to resolve and quantify the myriad of newly discovered steroid metabolites in an efficient manner were still in their infancy. Through considerable trial and error, John developed a number of innovative methodologies that accomplished just that and uncovered significant differences in each cell type's ability to form and clear biologically active androgens as well as to express androgen-dependent proteins, providing new insights into androgen-mediated differentiation of the prostate. Being persistent is perhaps one of his traits and he is forever grateful for the strong support, encouragement and patience of his mentor. In later years, he also had the opportunity to finally thank Samuel Solomon for those early motivational lectures; and Samuel now affectionately refers to John as his academic grandson!

John also found life at Queen's to be enriching in areas outside his academic pursuits. Initially acting as the Biochemistry representative on the Graduate Student Society Council, he subsequently went on to serve terms as Vice-President, President and Past President of the Society where he contributed significantly to the development



and implementation of a university-wide policy regarding working conditions for graduate teaching assistants. He also served in various other capacities, including President and Past-President, on the Board of Directors of Queen's Grad Club, a semi-autonomous organization that catered to the other, some might say more important, needs of graduate students - i.e., providing the best assortment of fine brews and weekend entertainment on Campus! In 1984, he was the recipient of the Queen's Tricolour Award, bestowed by the student body "For Outstanding Contribution to the University Community". While honoured by the recognition, John best describes the award as a reflection of the collective contributions of several individuals who tried to make a small improvement in graduate student life at Queen's.

After completing his Doctorate towards the end of 1985, John decided that to better understand the molecular mechanisms underlying hormonal control of tissue differentiation, it was essential to acquire skills in molecular biology, particularly in the field of gene transcription where considerable advances had been made. As good fortune would have it, an opportunity arose in the laboratory of Jerry Lingrel at the University of Cincinnati College of Medicine. Jerry's laboratory was already well known for its pioneering work on understanding transcriptional regulation of globin gene expression during development, and had just received international acclaim for cloning the genes for the catalytic alpha and beta subunits of the sheep Na⁺/K⁺-ATPase, one of the most extensively studied ion transporters in mammals because of its importance in forming the plasma membrane electrical potential. During the course of this work, they also discovered the existence of novel isoforms for the alpha subunit. These developments were tremendously exciting as they were amongst the first mammalian ion transporters to be cloned and represented a wonderful opportunity for study at the transcriptional level. Supported by an Medical Research Council of Canada Postdoctoral Fellowship, John performed some of the initial characterizations of the tissue-specific, develop-

mental and hormonal regulation of the various Na⁺/K⁺-ATPase subunit genes. It was during the course of these studies that John became fascinated by ion transporters and their diverse contributions to cell and organ function.

At the end of his postdoctoral fellowship, John accepted a faculty position in the Department of Physiology at McGill University, where he has remained since. He has continued his research on ion transporters, but shifted his focus to the study of mammalian Na⁺/H⁺ exchangers which contribute significantly to cellular acid-base and volume homeostasis. His most significant scientific contributions include the molecular cloning of novel members of the mammalian Na⁺/H⁺ exchanger gene family that are targeted not only to the plasma membrane but also to distinct organellar compartments, supporting broader physiological roles for these transporters than previously anticipated. This research has also been greatly enriched by a productive and enjoyable collaboration with Sergio Grinstein at the Hospital for Sick Children in Toronto, who has provided not only a strong intellectual stimulus, but also a cell biological component, to these studies. Since his appointment at McGill University, John has been the recipient of Scholarships from the "Fonds de la Recherche en Sante du Quebec" and is presently supported by an Investigator Award from the Canadian Institutes of Health Research. His research is currently funded by grants from the Canadian Institutes of Health Research and the Kidney Foundation of Canada. Over the last several years, John has been actively involved in the peer-review process, serving on Scientific Review Committees for the "Fonds de la Recherche en Sante du Quebec", the Heart and Stroke Foundation of Canada and the Canadian Institutes of Health Research. He is also currently a member of the Editorial Board for the Journal of Biological Chemistry.

John has been quite impressed by the high quality of the Winternational and Summer Symposium series sponsored by the CSBMCB, and welcomes the opportunity to contribute to its mission of promoting science in Canada.

Dr. Caren HELBING, Councillor

I was the kind of kid that needed to know how things worked. For my third birthday, I received a toolbox, complete with real hammer and saw (I think this is banned now for safety reasons)! I'd spend many hours examining insects in the backyard or building something or other. My undergraduate years studying Biological Sciences at the University of Windsor were spent learning many details about living organisms in a broad sweep from the molecular to the population. My father, a physicist, was amazed at the sheer volume of memorization that needed to be done compared to learning the fundamental physical equations and then working with those. My first introduction to research was a memorable one in the laboratory of Paul Hebert (now at U. of Guelph). Up until that point in my life, I had never imagined that *Daphnia* could be so diverse and fascinating! Paul's enthusiasm for science (embodied in his frequent leaps over lab furniture) had a lasting impression on me. I spent two summers working in his lab and witnessed pioneering work into characterizing crustacean populations living in different environmental conditions. This included trips up to Churchill, Manitoba and Igloolik, Nunavut, where hoards of mosquitoes were battled daily in the name of science! The following summer was spent studying genotoxicity in the lab of Michael Petras. Again a fascinating world opened up that was bringing me into the organism and studying the effects of chemical exposures on DNA damage. In those years, I was fortunate to have received two NSERC summer studentships. Seeing how scientific knowledge is generated first-hand and being involved in discovery is invaluable training. A subsequent honors thesis project with Alden Warner on cysteine protease inhibitors in dystrophic mice made it clear to me that research was what I wanted to do. I interviewed for graduate positions in several places. I made a point of visiting each place that I was interested in to get a feel for the people and the environments. I found this to be extremely informative, going beyond the glossy brochures!

Dr. Warner recommended that I go chat with Burr Atkinson in the Zoology Department at the

University of Western Ontario. My interest was piqued when he mentioned that Burr was interested in frog metamorphosis as a model developmental system. I learned the amazing fact that only a single hormone (thyroid hormone) was required to trigger the complete remodelling of the tadpole into a frog. I wanted to learn more, so I joined Burr's lab in 1988 armed with a NSERC 1967 scholarship. I spent many, long hours mastering molecular techniques and two-dimensional gels in my quest for understanding how the tadpole liver managed to produce the entire urea cycle during metamorphosis in anticipation of the need for these



enzymes to deal with nitrogenous waste on land as a frog. Not many gene sequences were known at that time and I cloned several of the urea cycle enzymes from the bullfrog. I also cloned the first bullfrog thyroid hormone receptor and demonstrated the sequential up-regulation of the receptor and urea cycle enzymes during natural and precociously-induced metamorphosis. Since Burr's lab was also actively involved in understanding the mechanisms controlling the stress response, particularly heat shock, I cloned a hsp30 gene and showed that it was thyroid hormone-responsive. In order to elucidate the mechanisms involved in thyroid hormone responsiveness in different tissues with different metamorphic fates, I showed that thyroid hormone-responsive gene transcripts are differentially affected by heat shock and that their responses are tissue context-dependent. As I was busy developing my scientific skills, my mother (a multi-talented lecturer in German with degrees in social work, languages and education), would always remind me that it was important to have balance and encouraged me to develop other skills. Heeding her advice, I was actively involved in grad student government,

organized a university-wide grad student research symposium and became involved with the “Let’s Talk Science” program that was just getting off the ground. I was responsible for training several undergraduate students in the lab keeping in mind how valuable the experience was for me when I was an undergrad. I completed my doctorate in 1993 and was given the Detweiler Award for the best Ph.D. in Zoology; an award that was shared that year with my husband, Dennis Churchill, who was working in Stan Caveney’s lab on gap junctions.

Dennis and I decided to go to Calgary for postdoctoral work. The move was a daring one for me in that I decided to do my postdoctoral work in cancer research focussing on the role of the *c-myc* oncogene in regulating cell proliferation and apoptosis. This oncogene is often found to be up-regulated in cancer cells and the degree of overexpression correlates with prognosis of the tumour. I was intrigued by the creative science that was being done at the University of Calgary in Randy Johnston’s lab and was convinced that this would greatly benefit my development as a scientist. As anyone who has worked on *c-myc* can attest to, it is particularly difficult to work on. Thousands of papers have been published, yet we still understand relatively little about how *Myc* really works in cells. I decided to follow the lead from another postdoc in Randy’s lab at the time, Cheryl Wellington, who was developing a tetracycline-regulated gene expression system for studying RNA stability. Gossen and Bujard had just published their novel eukaryotic gene expression system that seemed perfect to study the early cellular effects of *c-myc* overexpression in native cells. With a great deal of effort, the *tet-myc* cells were made and used to show surprising relationships between cyclin-dependent kinase activities and the induction of apoptosis and quiescence. At the same time, Igor Garkavtsev, a postdoc in Karl Riabowol’s lab next door had discovered the *ING* tumour suppressor. In collaboration with them, I showed that *ING* could regulate *c-myc*-induced apoptosis. Later studies from several labs supported *ING*’s role in apoptosis and some have linked *p53* with this regulation.

Discussions with fellow postdocs and the inability to answer the seemingly simple question of “How many postdocs are there at the University of Calgary and who are they?” gave birth to a joint venture with Cheryl Wellington in an ambitious survey of Canadian postdocs. Through the unwavering support of Randy, Hans van de Sande and Matt Spence, NSERC and SSHRC, we garnered the expertise of Marja Verhoef and ended up with the questionnaire responses of over 1300 postdocs covering all disciplines. The work helped raise awareness about postdoctoral issues and contributed to positive steps taken by research councils and universities to improve the postdoctoral experience. The birth of another venture also occurred with the arrival of my son in 1997.

A chance to lecture in part of Leon Browder’s Developmental Biology course helped consolidate my love for teaching and encouraged me to pursue an academic career. In 1999, I joined the Department of Biochemistry and Microbiology at the University of Victoria as a NSERC university faculty award recipient. Over my postdoctoral years, I was exposed to several examples where multiple cellular outcomes could be produced by the same stimulus. If one could understand how a cell decides when it will proliferate or apoptose, perhaps one could harness that information to design ways to induce cancer cells to selectively kill themselves. In designing my own research program, I decided to go back to the tadpole metamorphic system to address how a single extracellular signal is capable of eliciting multiple, sometimes paradoxical, cellular outcomes. Through the hard work of a talented team, my laboratory has made novel contributions in three areas. First, we have developed a unique frog cDNA array for the analysis of gene expression in multiple species. We have used this to analyse gene expression in the regressing tadpole tail during natural and precocious metamorphosis and have uncovered novel gene targets. In collaboration with Environment Canada and the US Environmental Protection Agency, we are using this technology to identify disruptors of thyroid hormone action. Second,

we have cloned frog ING genes and have shown that their expression is controlled by thyroid hormone. ING proteins appear to be involved in regulating cell fate. Third, we have shown that cyclin dependent kinases are essential for thyroid hormone-dependent apoptosis. We are currently developing the lab's proteomic capabilities to be able to assess the relationship between the transcriptome and proteome in thyroid hormone-dependent pathways.

It's been an exciting four years as an assistant professor: teaching new classes, setting up a new lab, and giving birth to my daughter in 2001. During my entire training in Canada, I am grateful for the wonderful interactions that I have had with the many talented scientists that make up our community. I am very excited about representing the CSBMCB community as an executive board member and hope to contribute to our success in the bright future ahead!

Dr. Linda PENN, Councillor

The journey of how and why I became a research scientist is credited to two influential groups of people that made an enormous impact during my early years. The first were my parents. As first generation Canadians of Ukrainian extraction they were in the small hotel business in northern Ontario town and worked hard and long hours to ensure their children had all the opportunities a life in Canada could offer. I think my earliest experiment was to perfect the Shirley Temple. My folks taught me the value of a strong work ethic and provided me the opportunity to appreciate the payback of trying your best at whatever you tackle.

The second major influence in the early years came from two extraordinary high school teachers. Now living just outside of Toronto, I was fortunate to have a female math teacher — Mrs. Howatson — who encouraged a handful of girls to pursue their love of math. Importantly she also taught us to simply 'go for it' and do what we like to do even though the rest of the world expected us to focus and excel in 'Home Ec', a course that prepared you to be the perfect homemaker. The other educator that deserves special mention is a

chemistry teacher, who came alive when working with those who participated in science fair projects. His enthusiasm for science was infectious. To my pleasant surprise, in Grade 11 he arranged for me to spend a full week with the electron microscope at the Ontario Science Centre. That week really changed everything. There was no turning back. I was hooked. Science was cool. I only hope my own children are similarly encouraged by such caring and extraordinary teachers in whichever field they thoroughly enjoy and wish to further pursue.



What about later in life and the more formal scientific training? My stint with the EM at the Science Centre taught me there was a microscopic world out there that was fascinating. This led me to a B.Sc. in Microbiology at the University of Guelph where I was inspired by virology as taught by Peter Dobos. I liked the logical and ordered gene regulation required for productive viral replication. That various viruses had adapted to their host with specialized genomes, coat proteins and mechanisms to release progeny was astounding. I then acquired a job in industry, bought my first car and married my husband Richard Penn. After a few months, the boredom of working as a quality control technician made us realize it was time for me to go back to school. With Richard's encouragement I then conducted my Ph.D. with Bryan Williams at The Hospital for Sick Children/University of Toronto studying the cellular genes involved in the antiviral effects of interferon. Bryan was a wonderful mentor who really let me carve my own path in research, learning from both my successes and failures. It was an exciting time in research as recombinant DNA technology (molecular biology) was just taking off. Journal club at Sick Kids was always

one of the highlights of the week and involved PI's such as Ron Worton, Roy Gravel and Manuel Buchwald as well as post-doctoral fellows who have since become top Canadian research scientists, such as Lap-Chee Tsui, Peter Ray, Irene Andrulis, Bob Korneluk and Martin Breitman. Journal club often included a debate over the implications of the latest discoveries that continued well past the hour. This enthusiasm for science and knowledge only fueled my own passion for research.

During my Ph.D., it became clear that interference could block cell division as well as viral replication but how this magic bullet worked as an antiproliferative agent remained unclear. Indeed, the molecular mechanism of tumorigenesis was largely a black box. To dive into this field and learn about cancer I conducted my post-doctoral studies in London, UK at the Imperial Cancer Research Fund. My direct supervisor was Hartmut (Hucky) Land who would insist we discuss the long-term implications of the latest results, not just tomorrow's gel. The focus was the product of the myc oncogene and the discovery of a negative feedback loop that enabled autoregulation at the level of gene transcription. The strength of working in a strong and focussed Research Institute enabled me to also enjoy the teachings and participate in the discoveries of other scientists at the ICRF, such as Gerard Evan. Understanding how Myc can drive the development of such a wide-range and large number of human cancers became my Holy Grail and the primary topic with which I would establish my own research lab.

Returning to Canada I held a complex position at The Hospital for Sick Children in Toronto. On the clinical side, I developed novel molecular assays to identify the presence of pathogenic viral genomes in patient samples and ran a molecular diagnostic lab. On the research side, we began to tackle the Myc question thanks to generous funding from the NCIC. Moreover, on the home front, we initiated our own studies of growth and development and were blessed with two children (Jessica and Adam). Needless to say this was a crazy and fragmented period of

time. In addition to research I learned about administration, turn-around-times, budgets, fighting for equipment, and how to metastasize space. Science is a funny business. We just become proficient at research and suddenly we are swamped with all the issues of running a small business. With my clinical duties taking precedent, conducting research became a treat and would not have been possible without the support of colleagues like Sean Egan and John Dick, mentors - such as Bob Phillips and Brenda Gallie, as well as the stellar folks in their labs, including Paul Hamel, Eldad Zackzenhaus, Lina Dagnino and Rod Bremner, who have each established their own independent research program here in Canada. After becoming Senior Scientist at Sick Kids I elected to focus exclusively on research. However, the Ontario Cancer Institute was moving to its new location in the heart of the research belt in Toronto and an opportunity to join the OCI team could not be ignored. Indeed, moving to the OCI enabled me to focus all efforts exclusively on research with a powerful force of Research Scientists all similarly tackling the cancer problem.

Briefly, the lab now focuses on two major areas of research. We continue to work on understanding the regulation and function of Myc oncoprotein with emphasis on identifying the molecular program triggered by Myc as a regulator of gene transcription, delineating the key interactors required for Myc-induced transformation and understanding how Myc potentiates apoptosis. In addition, we are developing novel anti-cancer agents that target the Myc pathway. Indeed, we also aim to exploit the unique apoptotic potential of cells of malignant transformation in an effort to uncover novel agents that target tumour cell destruction without causing collateral damage to neighbouring normal cells. To this end, we have agents in both early and late stage development. We have enjoyed continuous funding from both NCIC and CIHR and more recently from venture capital funds as well as American granting agencies. Of course, all of this was only possible with the dedicated trainees and staff that have participat-

ed and contributed to the research along the way. Moreover, it has been particularly rewarding to be able to collaborate with stellar Canadian scientists from coast to coast on these projects. In recent years these include Ivan Sadowski (UBC), Mark Minden (OCVPMH), Cheryl Arrowsmith (OCI/PMH), David Andrews and Brian Leber (McMaster), Jim Dimitroulakos (Ottawa) and Rick Langler (Mnt. Allison).

Why get involved in the CSBMCB? I have tried to highlight some of the many bright and dedicated Canadians who have held a major role in helping to shape my scientific career. Hearing the stories of many of my Canadian colleagues over the years, it is not unusual to find researchers like myself who did not grow up in an environment full of test tubes and museums. Yet through exposure at school, soon learned that our curiosity gene(s) could be satisfied through a career in research. We must ensure the next generation of Canadian Scientists has the same or better support that we enjoyed. Despite this conviction, I

found I was a member of several American societies and actively participated in their conferences and committees yet was not similarly involved in the Canadian equivalent. My goal as councilor is to increase membership and awareness of the CSBMCB. Beware, if your name was mentioned in this piece, I will be looking for your membership and participation in this important Canadian Society!

In addition to direct research, I am on the Board of Directors and Vice-President of the Canadian Cancer Society/Ontario Division, Graduate Admissions Coordinator for the Dept of Medical Biophysics/University of Toronto and sit on many grant panels both here and abroad. Thanks to Richard for encouraging me to pursue this unique career. Spouses of scientists deserve special mention for all the ups/downs of this business, the absenteeism particularly during grant season, acceptance that the work is never done, and that research is an addiction to which we have (happily) fallen victim.



CSBMCB Executive Board – Front row: Claude Lazure, Leon Browder, Linda Penn, John Orlowksi, Fred Palmer. Back row: David Litchfield, Joseph Casey, David Andrews, Caren Helbing, Eugene Tustanoff, Bruce Waygood.