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IS SCIENCE FADIST?

by **Bill Racz**

How often have we heard an investigator complain “I got funded but the reviewers want me to be more molecular”? This statement and another by one of the speakers at a recent STC symposium: “There are two hundred thousand molecular biologists in the United States who can put a gene into any host but only 10 who can comprehend the biological significance of that action.” Obviously both of these statements were quoted to make a point. Has science become too one dimensional? Must all scientists do the same type of work without due regard for the technique and approach that is best suited to test the hypothesis? As I have reflected on my career over the past 40 years, I have observed some of the changes in science. These are my jaded impressions.

As young graduate students 40 years ago, we were taught that cyclic AMP was the mediator of all drug action including toxicity and would explain most drug responses at least those that were beneficial. (Sutherland and Rall had just published their landmark paper). We now recognize that Cyclic AMP does not explain all drug action, that there are far more cyclic nucleotides involved in drug action and that there are many processes of drug action and reaction that do not involve cyclic nucleotides.

The cyclic AMP era was followed by calcium. Xenobiotics modulated free cytosolic calcium as a mechanism of drug action. This concept waned in the 1980s and was revitalized as the fluorescent dyes allowed for the estimation of intracellular calcium concentrations and calcium was purported to be the final common pathway of cell death. It is for some agents but certainly not all. Calcium plays a number

of key roles in cell death but there is a complex array of mediators involved in these processes.

The cyclic AMP era was followed by the prostaglandins. The prostaglandins probably had the shortest fad of most “hot topics” in the past 40 years. Prostaglandins as cyclic AMP were the centre of the universe, and all biological responses had to have a product of arachidonic acid metabolism as part of the mechanism.

Prostaglandins were followed by nitric oxide. The observations that nitro glycerin was bioactivated to nitric oxide which in turn dilated vessels and that nitric oxide was produced endogenously stimulated a flurry of activity. To my horror in the 1990s it was proposed that nitric oxide produced by Kupffer cells in the liver may have a role in hepatocyte injury. Now all I need to hear is that carbon monoxide, in minute amounts is required for CYP 450 function.

PCBs, the poison of the 80s, occupied the time of toxicologists for at least a decade and still do for some.

Throughout the late 1970s and the 80s, immunology was going to cure cancer and a significant portion of research effort was expended in this area. This activity probably contributed more to the science of immunology than to our understanding of the carcinogenic process and cancer in general.

What about reactive oxygen species? Once the sole domain of toxicologists. In the last decade many other areas of science have been studying ROS as a potential mechanism for biological response to agents and potential causes of disease.

Apoptosis once considered as a type of cell death observed by pathologists and a few others, has permeated every discipline in the biological sciences.

We are now in the era of genomics, and proteomics. At the 2005 SOT annual meeting there was an emphasis on genomics and the role of genomics in toxicological evaluation. To prove the adage wrong, that you can't teach an old dog new tricks, I attended a number of symposia on this topic. I attended symposia on a variety of genomic topics, I will give a few examples: "The Future of Molecular Genetic Therapeutics", High Throughput Screening Approaches in Genetic Toxicology" and "Beyond Liver Toxicogenomics: Gene Expression Based Biomarkers in Non-Hepatic Tissues". While I enjoyed these sessions, there is something about a slide that depicts the sequence for a gene or a gene array at 8:00

AM, especially after dinner in the French Quarter of New Orleans the evening before, that may have been lost on me.

But it appears to me that science has a tendency to adopt a flavor of the month approach and for whatever reason we tend to develop science as a large meandering stream, and we all must have our canoes in that stream. This approach has some negative consequences as the scientists that are trained during an era have similar expertise. This may well reduce the diversity of scientists needed now and in the future.

On a final note, at the SOT meeting I also attended a symposium on bioterrorism. As I reflect on the hours of symposia I attended, I have come to the conclusion that I have more expertise in bioterrorism than I do in toxicogenomics.

THE PERSPECTIVE OF THE PRESIDENT: STC IN APRIL 2005 - Barbara Hales

2004 was a very successful year for STC. Our symposium in December was great! Thanks to Dino Manca and the Program Committee members for all your work, and to all of you who participated. Congratulations, again, to Gail Bellward, the recipient of our Award of Distinction, and to Daniel Cyr, our Henderson award recipient. STC's new "face" on the world (see <http://www.stcweb.ca>) has improved access to information; gradually, we propose to replace our paper communications with you more and more with electronic channels. As you will have noticed on the dues statements you should have received recently, credit card payments are in to stay, too, thanks to Daniel Cyr, our very capable Treasurer, and to Gordon Krip, our hard working

Executive Director. The Board has not changed too much this year. We are grateful to Jeff Kawamoto for staying and agreeing to be re-elected as Secretary: Jeff keeps us all on track. We acutely miss Genevieve Bondy's contributions to the Board, but we are already realizing that our new Councilor, Timothy Schrader, will fill her shoes! Welcome, Tim! Genevieve, we will not forget you!

The Board has met twice since the December 2004 Symposium, first by teleconference at the end of January and second last weekend at the Delta in Montreal. The upcoming 2005 Symposium (Monday and Tuesday, December 5-6), at the Delta Hotel in Montreal, was a major item on the agenda

at both meetings. Louise Winn and her Scientific Program Committee are assembling a great symposium on “The Impact of Toxicants on Child Health”, a topic very close to some of us! Topics will range from considerations of the underlying mechanisms of the effects of toxicants on child health, to the elucidation of biomarkers, to current regulatory and risk analysis approaches. The focus will be on the identification and prioritization of existing chemicals in Canada that present a risk to children’s health. As always, outstanding guest speakers, in concert with cutting-edge poster presentations, will create a scientifically exciting meeting! To this we bring back our highly successful Sunday night session geared specifically for trainees, on “Careers in Toxicology – from an academic, industrial or government perspective”. New this year, and fitting with the focus on child health, we propose to offer a workshop for trainees who are interested in learning more about study designs in the assessment of reproductive and developmental toxicity. The President’s reception and banquet on Monday night will round out the social aspects of the meeting!

The very first International Congress of Toxicology (ICT I) was held in Toronto in 1977. Thirty years later, at the Montreal Palais de Congres, in July 2007, STC, together with NRC, will host ICT XI. 2005 promises to be a very busy year for Malle Jurima-Romet and other members of the ICT XI Executive Committee as they enter the implementation stage of their activities in planning for this Congress. If you are not yet involved, and would like to be, please contact Malle (Malle.Jurima-Romet@mdsps.com) to see how you can help. One decision that the STC Board made this weekend was to cancel the STC Annual Symposium for December 2007, so that all of us, and all of you, can concentrate on putting together the best International Congress of Toxicology ever. The STC Annual General Meeting will be scheduled during ICTXI in Montreal. Make a note of it in your agenda today!

Barbara Hales (barbara.hales@mcgill.ca)

THE 2004 AWARD OF DISTINCTION: GAIL DIANNE BELLWARD, B.SP., M.Sc. Ph.D.



Gail Bellward and Sheldon Roth

The award of distinction honours those individuals who have made an outstanding and sustained contribution to the science of toxicology in Canada and/or the Society of Toxicology of Canada. It is my pleasure to summarize Gail Bellward’s contributions and why she was such a deserving candidate for this award. I will not list all of Gail’s accomplishments as they are too numerous.

Gail Bellward was educated in British Columbia obtaining all three of her degrees, including a doctorate in medical pharmacology from that university. She was appointed initially as a lecturer in 1966 and as an Assistant Professor in 1967 in the faculty of pharmaceutical sciences at her alma mater. She has served this faculty with distinction continuously since her first appointment with the exception of three one year stints, one a postdoctoral-fellowship in clinical pharmacology at Emory University (1968-1969) and two sabbaticals. After her academic appointment in 1967, Gail quickly rose through the ranks, reaching the rank of professor in 1979. Her last academic appointment was as Associate Dean, Research and Graduate Studies in the faculty of Pharmaceutical sciences.

Gail's research career has centered on the study of the cytochrome P-450 (CYP) enzymes, as an important family of enzymes responsible for the metabolism of drugs and chemicals. She has been particularly interested in the mechanisms that control the synthesis and activity of the CYPs and the pharmacological and toxicological effects that result from changes in the CYP isoenzyme pattern. Some of her important contributions and findings include:

- In her studies on sexually dimorphic metabolism, her laboratory was one of the first to demonstrate that dieldrin-contaminated food caused decreased reproductive capacity and viability in offspring in mice in conjunction with the ability to induce CYPs.
- Demonstration that CYP 2E1 was specifically induced in the diabetic state due to elevated levels of plasma ketone levels.

- In her studies on the differential sensitivity to inhibitors, she concluded that CYP metabolism was not the sum of the individual isoenzyme activity, but rather the activity of the predominant highest affinity enzyme.
- Enhancing our understanding of the mechanism of inhibition of CYPs by cimetidine by determining that in the rat cimetidine is biotransformed to an active inhibitor that is selective for CYP 2C11 and 2C6.
- She was principal investigator of a large multi-disciplinary group that studied the effects of dioxin from pulp and paper effluent on the environment. This work demonstrated that the extent of exposure of great blue herons and cormorants to dioxin correlated with the degree of toxicity observed in these species. An observation later confirmed in the laboratory.

In 1997 Gail was awarded the Janssen-Ortho Award in recognition of her contributions to research.

Gail Bellward's contribution to the scientific community in Canada and STC are numerous. As I can't describe them all I will give a few highlights.

- Pharmacological Society of Canada (PSC) secretary from 1977 to 1980.
- PSC Consecutively Vice President, President and then Past-President from 1985 to 1991.
- CNC-IUPHAR junior delegate 1994 and senior delegate 1998.
- STC Vice-President, 1993-1995; President, 1995-1997; Past-President 1997-1999. Gail was the first woman president of PSC and STC.

- Gail has served on several scientific committees, provincial, national and international. In particular she was a member of the Science Management Committee, Toxic Substances Initiatives, Health Canada and Environment Canada.

Until recently Gail maintained a very active teaching load, contributing to the education of undergraduate and graduate students. The students under her tutelage have won a number of prestigious awards. She has trained 18 masters and doctoral students and a large number of undergraduate students had the privilege of working with her. As stated above, Gail has been particularly involved in administration in the faculty, where she served as Assistant and then Associate Dean, Research and Graduate studies for

Over 9 years. She has served on virtually every committee within her home university.

The award was presented by Sheldon Roth Past-President STC at the 2004 annual meeting. In accepting the award Gail commented that it was an honour to join the group of previous awardees and that some of these senior members (read old) of STC were in attendance. She could not believe that that she was a contemporary of some of the previous recipients. Well Gail speaking as one of the POOGs, YOU are now one of us.

CONGRATULATIONS.

Prepared by Bill Racz with the help of Sheldon Roth

STC VEYLIEN HENDERSON AWARD

DR. DANIEL CYR



Dan Cyr (left) and Michel Charbonneau

The STC Veylien Henderson Award honours an individual who has made a significant contribution to the discipline of toxicology in Canada. In the submission for Dr. Cyr, Michel Fournier stated “He is one of the very limited numbers of researchers combining laboratory and field approaches, having a unique expertise

with rodents as well as with wildlife species exposed to xenobiotics under field conditions. In both approaches he has developed state-of-the-art molecular biology tools designed to assess impacts of chemicals on male reproductive systems as well as giving input of cellular and molecular mechanisms of toxicity. These combined approaches developed by Dr. Cyr make him a key researcher in the development of several research networks such as the Canadian Network of Toxicology Centre, the Réseau de recherché en santé environnementale (human health driven network supported by Foods de Recherche en Santé du Québec), and the Réseau de recherché en écotoxicologie du Saint-Laurent (ecosystem health network supported by Valorisation Recherche Québec). Dr. Cyr set up toxicogenomics

facilities in support of the research of these networks.

Dr. Cyr has been very active in our Society, acting as the treasurer since 2002. He has been particularly committed to training programs and to the teaching of toxicology in Canada. I am therefore very pleased to present Daniel G. Cyr for the STC's Veylien Henderson Award."

The following is a summary of Dr. Dan Cyr's contribution to Toxicology.

One area of research of the Cyr Laboratory is endocrine disrupting chemicals and their effects on both wildlife and mammalian species (Brown et al., 2004, *Environ Toxicol Chem* 23, 1680; Haddad et al., 2004. (in press)). This work has yielded significant scientific contributions, which have also received considerable media coverage, pertaining to the presence of estrogenic compounds in the St. Lawrence River and their effects on resident fish species and the potential risks to humans who consume fish from the St. Lawrence (Aravindakshan et al., 2004, *Toxicol Sci* 78. 156). These studies were the first to demonstrate an extensive contamination of the St. Lawrence. River which originates approximately 20 kms upstream from the island of Montreal and in the Ottawa River, and extends more than 30 kms downstream of Montreal. Male fish (spottail shiners) exposed to these estrogenic compounds have reduced sperm production and delayed spermatogenesis. Furthermore, more than one third of the fish, at the most contaminated sites, exhibit intersex, a condition in *which* ovarian follicles grow within the testis. Given the volume and water flow of the St. Lawrence, these observations highlight a severe degree of chemical contamination in proximity to the City of Montreal. Previous studies had reported that many

Montrealers ate fish from the St. Lawrence. In some cases it was reported that people eat as much as 30kg/year. Studies by Cyr's group demonstrated that feeding fish from estrogen contaminated sites to rats during the period of lactation can result in permanent effects on the male reproductive tract of the developing males. When these rats reached adulthood, they produced fewer sperm and sperm of lesser quality (Aravindakshan et al. 2004 *Toxicol Sci* 81. 179). This appeared to result from alterations in spermatogenesis and may be related to a decrease in cellular communication in the testis. Current studies have shown that nonylphenol, a contaminant present at the sites where the estrogenic effects were observed, can decrease intracellular communication in cultured Sertoli cells by decreasing the expression and altering the phosphorylation status of connexin43. This effect appears to occur via a MAP kinase pathway, and independently of a protein kinase C pathway (Aravindakshan and Cyr in prep). Together these observations have provided novel information on the contamination of the St. Lawrence and perhaps more importantly have demonstrated that humans may be at risk of the effects from endocrine disrupting chemicals present in fish. Given the large number of reports that have shown the presence of endocrine disrupting chemicals in the aquatic ecosystem, the fact that these chemicals may be passed up the food chain to impact the endocrine and reproductive functions of fish-eating animals and humans, represents a significant contribution to assessing the risk of endocrine disrupting compounds.

Another area in which Dr. Cyr and his group have made significant contributions has been in understanding the role of cellular interactions in the male

reproductive tract and the effects of contaminants on these critical interactions. (Cyr et al., 2003. "The third International Conference on The Epididymis", The Van Doren Company Charlottesville, VA, pp 50-59). As a postdoctoral fellow at McGill University, Dr Cyr was the first person to report the presence of cadherins in the mammalian testis and the epididymis. His studies' not only identified the presence of these cell adhesion molecules in the male reproductive, tract but also demonstrated that these were regulated by androgens, thereby demonstrating that hormones could regulate cell-cell interactions (Cyr et al., 1992, *Endocrinology* 131; 139, 130:353). They have, since shown that cadherins and catenins, a family of cytoplasmic proteins which link the cadherins to the cytoskeleton and are involved *in* intracellular signaling, associate with zonula occludens proteins to initiate the formation of epididymal tight junctions (Debellefeuille et al., *Endocrinol.* 144:5040). These tight junctions are responsible for formation of the blood-epithelial barrier which is necessary for sperm maturation. Few studies have focused on the proteins that comprise the epididymal tight junctions, Gregory et al., (2001 *Endocrinology* 142; 854) have shown that Claudin-1 (Cldn-1) mRNA transcripts and proteins are present prior to birth in the rat and that Cldn-1 was localized to epididymal tight junctions. Studies on the regulation of epididymal Cldn-1 indicate that both androgens and other testicular factors are key regulators of Cldn-1. Interestingly, in the other regions of epididymis there does not appear to be any regulation of testicular factors. Thyroid hormones are also important regulators of Cldn-1. In propylthiouracil-induced neonatal hypothyroidism, Cldn-1 was absent throughout the initial segment, caput and corpus epididymis in PTU treated rats (St. Pierre et al., 2003 *Biol Reprod* 68:1232).

While the understanding of junctions is an essential component of male reproduction, tight junctions are also altered by environmental contaminants (Cyr et al., 2004. *Écotoxicologie Moléculaire: Principes fondamentaux et perspectives de développement*). A study by Barthelemy et al. (in prep) has shown that *in utero* exposure to tributyltin (TBT) results in alterations in epididymal tight junctions when the pups reached adulthood. To understand the mechanism of action of TBT, Cyr's group has recently developed a rat epididymal cell line, the first of its kind. The cells of this unique cell line express the same junctional proteins as those present in the intact epididymis (Dufresne et al., submitted). Dr. Cyr and his lab have also cloned the rat Cldn-1 promoter and are in the process of demonstrating the regulation of the Cldn-1 gene using luciferase constructs that have been transfected into epididymal cells.

Finally, a third area of research in which Dr. Cyr has made a significant contribution has been the role of intercellular communication in modulating hexachlorobenzene (HCB)-mediated hepatic tumour formation (a collaborative study with Dr. Charbonneau's lab at INRS-Insitut Armand-Frappier). HCB is an epigenetic carcinogen, and a clear sexual dimorphism exists for tumour formation in the rat. These studies demonstrated, using dye-transfer assays, that HCB decreases or inhibits intracellular communication (Plante et al., 2003 *Carcinogenesis* 23, 1243). Detailed studies indicated that this effect was associated with a loss of expression of both connexin 32 and 26 in the rat liver. This effect was gender-specific and was not mediated by estrogens. Since intercellular communication is considered as anti-tumorigenic, it is believed that the loss of intercellular communication

predisposes the cells of the liver to tumour formation. More recent studies suggest that this effect is, in part, mediated by a general formation. More recent studies suggest that this effect is, in part, mediated by a general phenomenon in which the expression of almost 30% of the genome is silenced in female rates exposed to HCB (Alt et al., in prep). Whether or not this effect is mediated by DNA methylation or acetylation is one aspect of ongoing research in Dr. Cyr's lab.

Thus far Dr. Cyr has already made several noteworthy contributions to the fields of environmental toxicology and reproductive biology. His studies in ecotoxicology and mammalian toxicology are unique in Canada in terms of linking environmental effects to human health. There is no doubt that Cyr's innovative research efforts will continue to be highly productive and advance the field of reproductive cell and molecular toxicology.



THE VIEW FROM MY CANOE **Don Ecobichon**

With the good weather in the last two weeks of March, spring came with a bang, and the arrival of the migratory birds, particularly large flocks of Canada geese. We have had seven tundra swans on the open water below the dam in Chaffey's Lock, black and white bufflehead ducks, merganser ducks, assorted geese, redwing blackbirds and our resident pair of hawks, as well as our robins. The snow has almost disappeared, leaving only the ice in the lakes and streams. Supplies of bird seed for the winter feeders are low and no more will be purchased. The major task is

to convince our deer to leave us alone when the garden starts to come. Betty is already designing her battle plan!

The current "fad" or "chemical of the year" in toxicology appears to be the polybrominated diphenyl ethers (PBDEs), a class of about 25 chemicals used as flame retardants in foams, textiles, plastics, electronic products, carpets, etc. They are relatives of the polychlorinated and polybrominated biphenyls and share most of their properties such as environmental persistence, indestructibility, bioaccumulation in food chains and some interesting toxicological properties, including hepatic enzyme induction, alteration of thyroid hormone levels, neurotoxicity (impaired memory, learning disabilities), body burdens in adipose tissue acquired from foods and transferred to breast milk. The levels are still low – 10 ppt (milk), 23 ppt (cheese), 384 ppt (butter), 242 ppt (sausage), 1,942 ppt (farmed salmon) and 3,638 ppt (farmed rainbow trout) – but they will climb as they are "out there" in the environment already and have not as yet reached their peak. Think of all of the old computers and television sets that are sent to Southeast Asia by the shipload where they are scavenged for copper wire, etc., the remainder being burned in open fires with the release of the volatile PBDEs and dispersal around the world to end up in the Arctic and Antarctic wildlife. Remember DDT in penguins? I predict a 30-year span before we see levels decline – like PCBs in Great Lakes wildlife, etc.

Speaking of which, the *Saturday Globe and Mail* (March 26th) had a long article, based on a talk with Gail Bellward and Len Ritter among others, on chemicals in our environment (food, furniture, paints, cosmetics, soaps, etc.). All were preaching avoidance and prudence to avoid phthalates, volatile organic

chemicals (low and zero VOC paint), pesticides, bisphenol-A (plastic bottles), formaldehyde (particle board), PCBs, etc. Nice picture of Gail though!

Arising from a retreat held by the Queen's University Faculty of Medicine in October, 2004, some interesting information was published recently on the shortage of family physicians in Ontario, and the challenges faced in attracting students to this discipline. Reasons that students choose Family Medicine as a career included: lifestyle control, rural practice, varied scope of practice, shorter postgraduate training, provision of continuity of care, wide variety of interest areas, better management of family responsibilities during practice, and preferred generalist approach. Reasons for not choosing Family Medicine as a career included: underpaid versus specialties, lack of prestige, family doctors seem to burn out, derogatory comments against family medicine (by whom?), increased workload, unclear of future primary care reform, and aversion to running a business. Surprising! Given that Ontario is attempting to organize doctors to be associated with clinics and that Betty and I are lucky to be associated with a local clinic (and well served at that), I might also add that such physicians are well paid, have regulated hours, have no overhead expenses and have excellent support staff (management, nursing) available every day at no cost to themselves. Family Medicine is the frontline of patient care!

Pressure is being brought to bear on those large medical journal publishers who have religiously denied open-access to the latest medical discoveries except at a cost. Patients' rights groups are raising hell about it being ethically wrong to charge for such access. The U.S. NIH has announced that, as of May of 2005, all

research work that it has helped to finance is to be made available on-line to all comers, and free, within a year of that research having been published in a journal. The NIH will spend \$3-\$4 million a year to support electronic archiving of these papers, this being managed by America's National Library of Medicine. According to NIH statistics, the \$30 billion each year on research leads to a publication of around 60,000 papers annually, some 11% of the total published in the medical field. They say that the actual impact is 30-50% of the most important papers having had NIH sponsorship. Publishers are going to have to adapt. How? The NIH is saying that the biomedical publishers have 12 months to make a profit, something that will not please them. If publishers balk, there is the possibility that those journals may lose a large proportion of the best research papers. Also in support of open-access is the Wellcome Trust, a large Britain-based charitable research foundation. It appears that things are tightening up!

Those who know me are aware of my aversion to the electronic world of computers and, yes, this column is written in longhand and edited before being typed and sent by e-mail to the Editor, Bill Racz. That is why I attach the following story obtained from a friend who loves the internet.

A Minneapolis couple decided to go to Florida to thaw out during a particularly icy winter. They planned to stay at the same hotel where they spent their honeymoon 20 years earlier. Because of hectic schedules, it was difficult to coordinate their travel schedules. So, the husband left Minnesota and flew to Florida on Thursday, with his wife flying down the following day.

The husband checked into the hotel. There was a computer in his room, so he decided to send an e-mail to his wife. However, he accidentally left out one letter in her e-mail address, and without realizing his error, he sent the email.

Meanwhile, somewhere in Houston, a widow had just returned home from her husband's funeral. He was a minister who was called home to glory following a heart attack. The widow decided to check her e-mail, expecting messages from relatives and friends. After reading the first message, she screamed and fainted. The widow's son rushed into the room, found his mother on the floor and saw the computer screen which read:

To: My Loving Wife

Subject: I've Arrived

Date: October 16, 2004.

I know you're surprised to hear from me. They have computers here now, and you are allowed to send e-mails to your loved ones. I've just arrived and have been checked in. I see that everything has been prepared for your arrival tomorrow. Looking forward to seeing you then! Hope your journey is as uneventful as mine was.

P.S. Sure is hot down here!



BOOK REVIEW – Don Ecobichon

“The Okinawa Diet Plan” B.J. Willcox, D.C. Willcox and M. Suzuki. Clarkson Potter/Publishers (Random House), New York, 2004, pp. 1-419. \$35.95 CDN.

I watched a book review interview with Bradley Willcox on TVO one night late

last autumn and was impressed with the amount of science brought into the discussion of why Okinawa (in the Ryuku Islands spread out below Japan towards the Philippines) had the largest number of octa-, nona- and centagenarians of any place in the world. Many of these people, both male and female, lead active lives, some still working.

In 1994, the Willcox brothers, one a medical doctor, the other a nutritional biochemist, were studying the impact of body fat on hormone-associated cancers when they interviewed Mr. Toku Oyakama, an immigrant to Canada from Okinawa, who was 105 years old but looked like 70 years of age. He and his 92-year-old wife maintained a traditional Okinawan diet all of their lives. His description of Okinawa citizens, their diet, etc. was the impetus for the Willcox brothers to go there, supported originally by an MRC grant.

This is a fascinating and thoughtful book, bringing into discussion the concept of caloric density (the number of calories in a specific amount of any given food – 1-gram unit) – the more calories in 1 gram of a specific food, the less of it you can eat without gaining weight. Also discussed are the concepts of glycemic index (rate of conversion from carbohydrate to blood sugar – some of this the work of David Jenkins at U of T) and insulin scores for various food groups. You guessed it – the Okinawan diet has low carbohydrate content of the type(s) that is only slowly converted to blood sugar. The Okinawans eat frequently but only small portions. For example, having miso soup at the beginning of a meal reduces the amount of the main course you would consume to feel full. We tried that. It works!

The chapters are well referenced, leading me to look at some of the data. In the

references, I found one that led me to a 1935 paper on diet restriction and its effects on life span, health and body size in rats – a hot item even today that no one wants to touch given the myriad of studies conducted using ad libitum feeding. There is a good index at the back, helpful for finding points of interest you ticked off on the way through. This is a book worth reading!

Perhaps the best chapter, certainly the longest (156 pages), is the Okinawan diet recipes – to get you started on a semi-Okinawa diet, all with readily available ingredients for the most part. We have tried a few of these, and they are excellent. Perhaps this is why I can't find the book as it lives with Betty's cookbooks.

BOOK REVIEWS



Bill Racz

Hot Spot Pollutants: Pharmaceuticals in the Environment. Volume Editors, Daniel R. Dietrich, Simon F. Webb and Thomas Petry. Published by Elsevier Academic Press, 2005. This book deals with the occurrence and fate of pharmaceuticals in the environment. The 18 chapters represent updated papers that were presented at three symposia in Europe, Statuskolloquium in Environmental Toxicology, in Konstanz, Germany (2001), Special Session at the Society of Environmental Toxicology and Chemistry, in Vienna Austria (2002), and the 11th European Congress on Biotechnology in Basel, Switzerland (August 2003). Part II of the book deals with the occurrence, fate and removal of pharmaceuticals from the aquatic environment. Sulfonamides and

sunscreens are used as examples of potential pollutants.

Part III examines the effect of pharmaceuticals on a number of aquatic species and a description of a number of tests that are used to study the effect. Part IV describes the principal considerations in risk assessment of pharmaceuticals in the environment and attempts to answer question such as, can mammalian toxicological data be translated to aquatic species? Finally part V describes risk assessment procedures. The book contains a large amount of research data and references. The general sections of this book will provide background for this field, while the focused sections will serve as a useful reference.

Essentials of Medical Geology—Impacts of the Natural Environment on Public Health, Editor in Chief, Olle Selinus. Published by Elsevier, 2005. This multi-authored publication is intended to be used as a textbook in a course in Medical Geology. It will also serve as a useful reference. The book is organized into sections. Section 1 covers environmental biology, section 2 covers exposures and pathways and the interrelationships among the natural environment, geology, and health. Section 3 on environmental toxicology, pathology, and medical geology discusses the medical aspects of the interaction of mammalian species with their environment. Section 4 describes the tools and techniques employed in studying medical geology. This textbook covers a wide range of topics, radon in air and water, arsenic in groundwater, fluoride in natural waters, environmental epidemiology and medicine, and speciation of elements to list a few.

REPORT ON THE ANNUAL SYMPOSIUM – 2004 “RELATIONSHIPS BETWEEN HEALTH AND THE ENVIRONMENT: THE ROLE OF TOXICOLOGY”

The Program Committee, chaired by Dino Manca with Louise Winn and Gerard Cooke as members, organized an exciting and educational symposium.

The first session “Identifying the problem – Air, Soil, Water, Food.”

presented evidence that living in urban centres with elevated levels of outdoor pollution do not live as long as those Canadians who are fortunate to live in a pristine environment. The question that was left unanswered, will there be improvements in public health as urban pollution levels decrease?

Dr. B. Birmingham reported on the process utilized by the Ministry of the Environment, Ontario in conducting human health risk assessments of communities impacted by contamination from air, water and soil. The Ministry of the Environment conducted surveys measuring metal contamination in soils. Nickel and lead were the two metals of greatest concern. Based on the observed levels and the estimated exposure, intervention levels were recommended depending on the use of the area, e.g. playground.

Dr. G. Van Der Kraak discussed the changing nature of determining the toxic effect of industrial effluents on fish and other aquatic species. As government regulations and industrial standards have reduced effluent contamination he proposed that there is a need to adopt non-lethal methods of assessing toxicity. Research must now focus on the more subtle and chronic effects. Studies must assess reproduction and development, immune function, growth, and stress as some of the new endpoints.

Dr. J. Rodericks addressed the issue of food as a source of chemical exposure. Food is the most complex chemical mixture to which humans are exposed. Assessing the toxicity of food is complicated as most constituents in food will increase health risks if exposure is excessive but many of these constituents will confer health benefits at appropriate doses. Consideration must be given to a range of substances, from natural constituents to contaminants to dietary supplements. The latter being a major problem.

Dr. E Silbergeld told the audience that mercury compounds have been previously assessed and regulated on the basis of developmental neurotoxicity. She suggested that recent studies indicate that additional toxic effects of Hg must be considered. Both adults and children are sensitive to the neuropsychological effects of the metal. In addition Hg exposure is associated with overproduction of specific antibodies and a lupus-like syndrome. *(Dr. Silbergeld's presentation was sponsored by GlobalTox.)*

The next speaker Dr. R. Vincent described the effect of chronic air pollution on health. The epidemiology studies indicate that individuals are at risk at concentration that had previously considered to be a trivial internal dose of the pollutants. Exposure to urban pollution is associated with elevated levels of endothelin-1, which has major effects on the cardiovascular and respiratory systems. For example a 25 % increase in endothelin-1 is associated with an unfavorable prognosis in congestive heart failure. Pollutants enhance the denovo synthesis of the endothelins.

Dr. M. Fournier gave a number of case studies that examined the effect of xenobiotics on the immune system of aquatic species. Pronephric macrophages from mummichogs exposed to pulp mill effluent, sampled near the discharge sourced demonstrated less phagocytic activity that animals sampled at more distant locations. In another example bivalves were found to be a good sentinel for toxicological monitoring of an ecosystem.

Dr. W. Foster reviewed the controversial area of the effects of environmental toxicants on female reproductive capacity, a topic of concern to the public. Of particular note was the effect of smoking on female reproduction. Smokers vs. nonsmoker exhibit longer times to conceive, premature ovarian failure, and reduced invitro fertilization success. Side stream smoke appears to have the same effect as main stream smoke.

Dr. S. Perreault-Darney discussed the effect of chemicals in drinking water that may affect male fertility. The haloacetic acids are of particular interest as they form during disinfection of drinking water. These compounds cause decreased sperm motility and a decrease in some sperm proteins required for fusion with the ovum. Both of these changes are indicators of infertility.

The third session of the symposium, emerging Issues and Priorities for Research, presented a review of models used to determine the health risks of chemical mixtures. The utility of physiological based pharmacokinetic models in assessing the risk of mixtures was highlighted.

The second priority area requiring attention discussed was the presence of pharmaceuticals and personal care

products in the environment. In his talk Dr. Sanderson referred to the vast number of pharmaceutical and fragrances that are potential pollutants. There are ecotoxicological data on only 1 % of the 5000 of these products in use. A significant number of these products are predicted to be extremely toxic or very toxic to aquatic species but as the exposure is low, the risk is also low. Any risk assessment must consider that exposure is to a mixture and not a single entity. Dr. A. Okey using dioxin sensitivity between species as an example, discussed the role of genetics in understanding the mechanism of and response to toxicants. By combining aryl hydrocarbon receptor polymorphisms that cause distinct dioxin-response phenotypes with gene expression studies it may be possible to identify the genes responsible for dioxin toxicity.

The last speaker of the session, Dr. M. Alae, introduced the hot topic of the emergence of polybrominated flame retardants as a potential environmental pollutant. The use of these compounds has increased and is a component of many polymers, which are found in numerous household and consumer products. Recent data suggests that the concentrations of the polybrominated flame retardants are increasing in the environment.

A highlight of the annual symposium and meeting are the poster sessions. This year we were treated to 48 excellent posters, a majority of these were presented by research trainees.

The Society of Toxicology of Canada encourages students to attend the annual symposium by providing travel awards for students. For 2004, \$3,300.00 was made available for student travel. The recipients of the student travel awards were: Laura Romero and Kathleen Nichols both from the University of Guelph, Pamela Brown,

Erica Defoort, Katherine Guindon, Joanne Wan and Helen Badham all from Queen's University, Katie Chan, Ivy Moffat, Rana Sawaya and Nandita Shangari from The University of Toronto.

Through the generosity of Cantox, Inc. there are two prizes for student posters, one for the best poster by a student in a doctoral program and one for the best poster presented by a student in a Master's

program. The poster deemed by the judges to be the "best" poster by a doctoral student was presented by Ivy Moffat, University of Toronto and by a Master's student by Tania Onica, University of Guelph. The abstracts of these two posters are reprinted below for all members of the society to see the high quality of work conducted by our students.

REPORT FROM THE STC 2005 SYMPOSIUM ORGANIZING COMMITTEE

Louise Winn

The STC Program Committee is excited to announce the preliminary program for the 38th Annual Symposium of the Society of Toxicology of Canada, to be held at the Delta Centre-Ville (777 University Street, Montreal, Quebec) on December 5-6, 2005. The theme this year will be "The Impact of Toxicants on Child Health" and will include sessions on "Current Mechanistic Approaches to Understanding Developmental Toxicity", "Biomarkers of Children's Health" "Current Regulatory and Risk Analysis Approaches to Children's Health." The program will conclude with a special session from the Existing Substance Division,

Environmental Contaminants Bureau of Health Canada on "The Identification, Prioritization and Children's Health Risk Assessment of Existing Chemicals in Canada." Additionally, this year the Program Committee is pleased to announce that a special student workshop will be held on Monday afternoon entitled "Reproductive Toxicology and Non-clinical Pediatric Testing of Pharmaceuticals and Biotechnology Products". Furthermore, the Committee is also introducing the opportunity for students to give oral presentations during the program this year.

See the back cover for the program announcement.

**CANTOX AWARD FOR BEST PhD STUDENT POSTER /
BOURSE CANTOX POUR LA MEILLEURE AFFICHE
(ÉTUDIANT(E) DE TROISIÈME CYCLE)**

**ALTERNATIVE SPLICING IN RAT ARYL HYDROCARBON RECEPTOR
(AHR) ALTERS CONSTITUTIVE AND DIOXIN EXPOSED GENE
EXPRESSION PATTERNS**

Ivy D. Moffat¹, Paul C. Boutros*¹, Jouko Tuomisto, Raimo Pohianvirta*²³⁴, Allan B. Okey¹

¹ Department of Pharmacology, University of Toronto, M5S 1A8, Canada;

²Department of Food & Environmental Hygiene, University of Helsinki; ³National Veterinary & Food Research Institute, Kuopio; ⁴National Public Health Institute, Kuopio, FIN-70701, Finland

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD, “dioxin”) is a potent environmental toxicant whose effects are initiated via binding to the AHR, a ligand—dependent transcription factor. Pathways leading to dioxin toxicity remain elusive. To identify these pathways we examined global gene expression profiles in a genetic model of dioxin resistance. Our objective is to identify key AHRregulated genes responsible for dioxin lethality and associated toxicities. We possess a powerful genetic model of dioxin resistance. The Han/Wistar (*Kuoplo*) (H/W) rat [LD50>9600Hg/kg] is >1000-fold resistant to acute TCDD lethality compared with the Long-Evans Turku AB (LE) rat strain [LD50≈10 mg/kg]. H/W rats have a point mutation in the AHR transactivation domain that creates 3 potential splice variants resulting in 2 potential protein products that appear to protect from the lethal effects of TCDD. The deletion variant has a deletion of 43 amino acids and the insertion variant has an insertion of 7 amino acids and a deletion of 45 amino acids. Multiple crosses between H/W and LE (combined with TCDD challenge) generated 2 additional lines: one has the H/W AHR variants (AHR-H/W) and the other the LE wild-type AHR (AHR-WT). Using realtime QPCR we determined that resistant rats express greater amounts of the insertion splice variant than deletion splice variant and little or no AHR-WT. Further, TCDD did not alter the expression pattern of the splice variants. We next characterized constitutive and dioxin-responsive (100 mg/kg for 3 hr, 19 hr or 4 days) hepatic gene-expression profiles in resistant versus sensitive rats using Affymetrix Genechips®. Classical dioxin-responsive genes (such as *CYP1A1*, *CYP1A2*, *ALDH3A1*) continued to be induced normally in rats with both receptor types. However, a few genes differ in their constitutive (basal) expression and/or response to dioxin between resistant versus sensitive animals, e.g. *CYP7A1* and metallothionein. RT-PCR confirms these differences in gene expression ($r=0.96$, $P=0.00001$, $n=66$). Further pharmacological screens coupled with AHR-null mice are revealing genes in the pathway leading to AHR-mediated dioxin lethality as well as genes with a unique signature in dioxin responsiveness.

CANTOX AWARD FOR BEST MSc STUDENT POSTER
BOURSE CANTOX POUR LA MEILLEURE AFFICHE
(ÉTUDIANT(E) DE DEUXIÈME CYCLE)

TRANSCRIPTIONAL REGULATION OF HUMAN CYTOCHROME P450 2A6

Tania Onica* and Gordon M. Kirby. Department of Biomedical Sciences, University of Guelph, ON, N1G 2W1.

CYP2A6 is a member of the human CYP2A gene subfamily expressed in the liver, and catalyzes the metabolism of nicotine as well as several tobacco-related procarcinogens. Despite its toxicological importance, the mechanism of CYP2A6 regulation is poorly understood. Previous work has shown that CYP2A6 is inducible in primary human hepatocytes by xenobiotics including dexamethasone, rifampicin and phenobarbital, suggesting the involvement of the glucocorticoid receptor (GR), the pregnane X receptor (PXR) as well as the constitutive androstane receptor (CAR). The aim of this work was to investigate the molecular mechanism(s) controlling CYP2A6 induction. Analysis of progressive deletions of the 5'-flanking region (-2469 to +12) of CYP2A6 suggests that a glucocorticoid response element (GRE) may reside within the proximal promoter as all deletion constructs including one with a region between —239 to +12 are inducible by dexamethasone. Accordingly, treatment of transfectants with the GR antagonist RU486, inhibits the dexamethasone-mediated transactivation of this region. The GRE is currently being mapped by deletional analysis and site-directed mutagenesis. Additionally, the CYP2A6 luciferase constructs were not responsive to overexpression of hPXR and mCAR followed by treatment with the prototypical PXR and CAR activators rifampicin, phenobarbital or 1,4-Bis(2-(3,5-dichloropyridyloxy)]benzene (TCPOBOP). These data indicate that PXR and CAR are not involved in CYP2A6 regulation within the —2469 to +12 region, although these receptors may regulate CYP2A6 through further upstream distal response elements. Supported by the Natural Sciences and Engineering Research Council of Canada.

REPORT FROM THE ICT XI ORGANIZING COMMITTEE

The Organizing Committee is now in the 'implementation phase'. The official ICT XI website (www.ict2007.org) is active. The website serves as our main communication tool to the external community for up-to-date information on the Congress.

At the recent SOT meeting in New Orleans, we hosted another ICT XI promotional booth and benefited from face-to-face interactions with the IUTOX EC, representatives from member societies and individual scientists. During SOT, the International Scientific Program Committee (ISPC) for ICT XI met for the first time. More than 20 members were present. It was gratifying to see such an enthusiastic response.

The ICT XI scientific program is beginning to take form, even as more proposals continue to be received -- after the mid-February deadline. The number of proposals received is now over 120 and the National Scientific Program Committee has been hard at work screening and 'binning' these to present themes and subject areas to the ISPC for an initial evaluation. The next step will involve identifying appropriate speakers and presentation topics for integration into the framework of the program. This will be a reiterative process, with input from the ISPC, who will be meeting again at EUROTOX 2005 in Krakow, Poland. An International Advisory Committee (IAC) to the ICT XI Organizing Committee has also been established. Its membership

reflects the geographical and professional composition of IUTOX member societies. The role of the IAC will be to advise the Organizing Committee on the overall ICT XI program and to facilitate communications with the member societies. The Local Arrangements sub-committee is beginning to plan out the schedule of 'official' events associated with the Congress, and select venues for off-site 'social' activities. In summary, an excellent team is in place, and with the strong support we have from IUTOX and the international community, we are well positioned to host the most successful ICT ever.

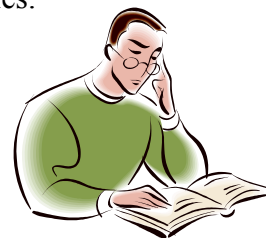
Prepared by David Josephy, Secretary, and Malle Jurima-Romet, President, ICT XI Organizing Committee

EDUCATION CORNER

Bill Racz

In the fall issue of STC News/Nouvelles, I posed a question to the members of the society. "If you were to design a laboratory program in toxicology for undergraduate students, what key elements/topics would you include?" I promised to publish a summary of the responses, which will be easy as the members appear to be silent on the topic.

I wish to raise another issue. It has been at least 10 years since the society discussed the contents of a training program in toxicology. Is it time to revisit those deliberations? Perhaps the program committee might wish to report in a future News/Nouvelles.



STC PRIX DU MÉRITE

But:

Le but de Prix du mérite est d'honorer les personnes qui ont apporté une contribution remarquable et soutenue au domaine de la toxicologie au Canada ou à la bonne marche de la Société de toxicologie du Canada.

Comité de sélection:

Les récipiendaires seront choisis par un comité de sélection formé de quatre membres de la Société, le président sortant de la Société qui présidera la comité, un des conseillers, ainsi que deux membres réguliers choisis par le bureau de direction, mais qui ne font pas partie.

Candidatures:

Les candidatures doivent être soumises par deux membres réguliers de la Société. Un membre ne peut soumettre plus d'une candidature chaque année. Les candidatures doivent être déposées auprès du président du comité de sélection avant le 1^{er} Juillet de l'année de la remise du Prix. Les documents suivants doivent être soumis à l'appui des candidatures:

1. un résumé d'au plus deux pages décrivant la contribution du candidat ou de la candidate au domaine de la toxicologie ou au fonctionnement de la STC;
2. des copies d'au plus cinq manuscrits ou documents pertinents produit par le candidat ou la candidate.
3. un curriculum vitae du candidat ou de la candidate, ainsi qu'une notice biographique à l'intention du monde de la presse

À moins que les parrains des candidats ou des candidates ne souhaitent qu'il ne soit autrement, les candidatures non retenues

STC AWARD OF DISTINCTION

Purpose:

The purpose of the STC Award of Distinction is to honour those individuals who have made outstanding and sustained contributions to the science of toxicology in Canada and/or the Society of Toxicology of Canada

Selection Committee:

Recipients shall be chosen by a committee of four members drawn from the Society: the Past President who shall act as chairperson, one of the councilors, and two members appointed by the Board from the general membership and who are not members of the Board.

Nominations:

Nominations must be made by two regular members of STC, in good standing, but no member may nominate more than one candidate during any one year. Nominations for the Award shall be made to the Chairperson of the Selection Committee before July 1 of the year of the award. Nominations must be accompanied by:

1. A summary, not to exceed two pages, describing the nominee's contribution to the science of toxicology and/or to the STC.
2. Copies of no more than five manuscripts and other documents considered by the sponsor to be pertinent to the award.
3. The nominee's curriculum vitae and a brief biographical sketch suitable for press release.

Nominees who are not granted the award in the year of nomination will be automatically included among the nominees in the two subsequent years unless the sponsors express otherwise.

l'année de leur dépôt seront réactivées automatiquement lors des deux années suivantes. Les parrains verront alors à mettre à jour les dossiers déjà soumis.

Le Prix et sa remise:

Le Prix consistera en une plaque ou en toute autre marque tangible de reconnaissance. La remise du Prix se fera lors de la réception du Président, à l'occasion du Colloque annuel de la Société.

Critères:

La comité de sélection se basera sur les critères suivants:

1. le ou la récipiendaire devra avoir apporté une contribution remarquable et soutenue au domaine de la toxicologie au Canada ou avoir apporté une contribution sous la forme d'états de service remarquable et soutenus au sein de la Société de toxicologie du Canada.
2. c'est au comité de sélection qu'il incombera de porter un jugement éclairé sur le mérite de la candidature.
3. la décision du comité de sélection sera finale. Un seul prix sera remis à chaque année, mais si de l'avis du comité de sélection aucune candidature n'est méritante, le Prix ne sera pas remis.

On peut obtenir des informations sur les activités et les prix de la STC ainsi que sur la façon de joindre les rangs de la Société en écrivant à l'adresse suivante :

Secrétaire de la STC
C.P./P.O. Box 517
Beaconsfield, Quebec H9W 5V1

Sponsors will be invited to update previously submitted information.

Award and Presentations:

The award will be in the form of a plaque or other suitable memento. Presentation of the award will be made at the President's reception during the Annual Meeting.

Criteria:

The following criteria will guide the Selection Committee:

1. The recipient should have demonstrated outstanding and sustained contributions to the science of toxicology in Canada and/or the recipient should have provided outstanding and sustained service to the Society of Toxicology of Canada.
2. The Selection Committee will exercise discretion regarding the relative contribution of the recipient to the science of toxicology in Canada and service to the Society of Toxicology of Canada.
3. The decision of the Selection Committee shall be final. Only one award may be made annually, and there is no obligation or duty to make the award when, in the opinion of the Selection Committee, there is no qualified candidate.

Information about STC's activities, awards, and/or membership application forms may be obtained by contacting:

Secretary STC
C.P./ P.O. Box 517
Beaconsfield, Quebec H9W 5V1

STC PRIX VEYLIEN HENDERSON

Par ce Prix, la STC cherche à reconnaître l'importante contribution à la toxicologie d'une personne œuvrant au Canada. Les conditions d'éligibilité sont les suivantes:

1. être citoyen(ne) canadien(ne) ;
2. être âgé(e) de moins de 45 ans en date du 1^{er} Juillet de l'année de l'obtention du Prix ;
3. être mis(e) en nomination par un membre régulier en règle de la Société. Ce membre devra faire parvenir au Secrétaire de la Société:
 - a) une lettre d'appui à sa recommandation;
 - b) un résumé de deux pages soulignant la contribution remarquable du candidat ou de la candidate;
 - c) un curriculum vitae complet et une liste des publications du candidat ou de la candidate;
 - d) des tirés à part d'au plus cinq (5) publications reflétant bien les activités de recherche du candidat ou de la candidate.

Le tout doit être transmis au secrétaire, à l'adresse habituelle de la société, avant le 1^{er} Juillet de l'année de la remise du Prix.

Secrétaire de la STC
C.P. / P.O. Box 517
Beaconsfield, Québec
H9W 5V1

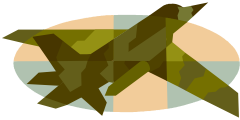
STC VEYLIEN HENDERSON AWARD

This STC award honours an individual who has made a significant contribution to the discipline of toxicology in Canada. The conditions of the award are as follows:

1. the candidate must be a Canadian citizen;
2. the candidate must be under 45 years of age as of July 1 of the year in which the award is given;
3. the candidate must be nominated by one regular member of the society (in good standing) who will supply the Secretary with:
 - a) a supporting letter of recommendation;
 - b) a two page resume describing the significant contribution made;
 - c) a complete curriculum vitae and publication list; and
 - d) reprints of not more than 5 papers best reflecting the candidate's research.

All of the above should be sent to the Secretary, at the STC address by July 1 of the year of application for this award.

Secretary STC
C.P. / P.O. Box 517
Beaconsfield, Quebec
H9W 5V1



Conferences, Meetings and Workshops:

2005

- June 19-21 Society of Toxicologic Pathology Annual Meeting
Washington, DC
- June 21-24 The Canadian Federation of Biological Societies Annual Meeting
“Second Northern Lights Summer Conference”
University of Guelph, Guelph, Ont.
- August 29-
September 2 First International Conference on Pharmaceutical Drugs, Development,
Prescription and Consumption: Interdisciplinary Perspectives for a
Common Future
Montreal, Quebec
- October 16-20 The Society of Environmental Toxicology and Chemistry (SETAC)
Latin America 7th Annual Meeting
Santiago, Chile
- December 5-6 STC Annual Symposium
“The Impacts of Toxicants on Child Health”
Montreal, Quebec.

2006

- March 5-9 Society of Toxicology Annual Meeting
San Diego, CA.

2007

- July 14-21 11th International Congress of Toxicology, ICT-XI
Montreal, Quebec





38th Annual Symposium

The Impact of Toxicants on Child Health

*Monday and Tuesday, December 5-6th 2005
Montreal, Quebec, Canada*

**Delta Centre-Ville
777 University Street
Montréal, Québec
H3C 3Z7**

Presentations by International Experts

- **Current Mechanistic Approaches to Understanding Developmental Toxicity**
- **Biomarkers of Child Health**
- **Current Regulatory and Risk Analysis Approaches to Child Health**
- **Identification and Prioritization of Existing Chemicals in Canada**

Detailed information and registration forms available at:

http://www.stcweb.ca/annualsymposium_e.htm



38^e Symposium Annuel

Impact des substances toxiques sur la santé des enfants

*Les lundi et mardi, 5 et 6 décembre 2005
Montréal, Québec, Canada*

**Delta Centre-Ville
777, rue University
Montréal, Québec, Canada
H3C 3Z7**

Présentations par des Experts Internationaux

- **Approches mécanistes actuelles pour la compréhension de la toxicité du développement**
- **Biomarqueurs de la santé des enfants**
- **Approches actuelles de réglementation et d'analyse de risque relatives à la santé des enfants**
- **Identification et classement par ordre de priorité des substances chimiques existantes au Canada**

Pour renseignements et formulaires d'inscription voir:

http://www.stcweb.ca/annualsymposium_f.htm