

STC NEWS/NOUVELLES

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EDITOR'S COMMENT

Bill Racz

I am pleased to welcome Michelle Picard-Aitkin as a student member of the editorial Board. Michelle has provided an article on the values of networking. Joanne Wan kindly agreed to provide a student's view of the 2005 annual meeting and symposium. In addition the abstracts of the recipients of the student awards are reprinted to allow all members of STC share in the excellence of science conducted by our students. We continue to provide our usual articles and commentary. I would be pleased to receive contributions to the STCNews/Nouvelles. My last article on poisons peeked the interest of at least one person as I received a phone call to discuss some of the contents and its implication. There is at least one reader out there!

The next year should prove to a busy but exciting year for the members of STC, especially those who are responsible for the organization of ICTXI. This issue as several past issues have contains a report from the organizing committee. Judging from the report, planning is well under way for what promises to be an exceptional meeting. The host city, Montréal, is one of the premier locations in Canada to hold a meeting. The Palais des Congrès is a superb venue for any meeting. I remember the last international meeting I attended at the Palais des Congrès, the International Union of Pharmacology meeting in 1993. The science was excellent and what better way to end a day of science then an evening in old Montréal. I am looking forward to the summer of 2007, not only because I will shed some of my responsibilities at Queen's, but I will be able to attend the ICTXI. I urge all members of the society to make plans for Montréal in July 2007.

DO I DARE SAY WHAT I REALLY THINK?

Bill Racz

As we have reached the half-way point in the first decade of the 21st century, it appears that most of the Universities are charting courses for the future. For the first time in 36 years at Queen's I have been invited to attend the annual meeting of the University Council. The Council is a body comprised of the Board of Governors, University administration and elected alumni, whose purpose is to determine the direction for Queen's University. The topic for the day: A strategic plan for "Engaging The World." Do they really want to know what I think? Do I have the courage to tell them? The answer may well lie in how much rhetoric (ok BS) I am prepared to take.

The role of a University has undergone major changes since I was hired in 1970. I was hired to teach students pharmacology and toxicology. Yes, I was expected to conduct research but teaching undergraduate students was at least an equal partner, and I was expected to place a considerable effort in teaching. Gerry Marks, made all young faculty practice their lectures to other faculty before delivering them to students. Today we hire researchers and if they do some teaching, that is a bonus, but research carries the day. In Canada unlike the, United Kingdom, it is the undergraduate students who through tuition and government grants generate the income required to support the infrastructure for graduate studies and research. Yet most institutions have allowed undergraduate classes to become larger, there has been a reduction in the laboratory component of most science programs including toxicology and in some case there has been limited investment in the state of the art teaching facilities and equipment. How many chairs

are there in universities whose sole purpose is to enhance the educational experience of our students, other than in research? Fortunately there are some, but certainly not as many as research chairs. I know that most will argue that research “helps teaching”. Where is the evidence? Indeed a study conducted in Ontario some 10 to 15 years ago concluded that in the best possible case research does not harm teaching and often is detrimental.

Do I dare tell my university that we are neglecting our educational responsibilities to both graduate and undergraduate, but especially to undergraduate students? Do I dare tell them that in my view universities need to decide if they wish to be educational institutes or research institutes and if they wish to be the latter, it should be clearly enunciated and we should find the funds to support these activities from a source other than undergraduate students. The Ontario Government I believe has recognized this dichotomy at least in terms of funding medical students. The medical schools in Ontario as well as other provinces, were mandated to increase enrolment to help alleviate the shortage of physicians in Ontario and nationally. The medical schools receive additional funding for these students, but the province mandates that the bulk of the funds be spent educating future physicians. No diversion of funds for other activities. An interesting concept, accountability for the taxpayer’s dollar!

Do I dare tell them that to train excellent researchers, the training starts in year one of university and preferably much sooner in the educational system? Well educated undergraduates make good graduate students and they in turn are our researchers of the future. In short no one mission of a university should be sacrificed for another.

Maybe I will listen and have lunch; after all they did ask me to pay \$25.00 for lunch. It better be good.

Your views and response are welcome.

THE VIEW FROM MY CANOE



Don Ecobichon

My editor tells me that he is “thinking” of an issue of the newsletter and that I need to get my pen warmed up. It has been a quiet but interesting winter, with little snow to manage but lots of wildlife (various woodpeckers, cardinals, nuthatches, chickadees, bluejays, finches, and red, black and gray squirrels) at the feeders, and a small herd of seven whitetail deer who come looking for handouts of cracked corn or anything else, including sunflower seeds and peanuts from the feeders. We have even had a pack of coyotes – dad, mom and yearling pups – operating in the area and making lots of nightly noise!! Spring has arrived! Actually, it arrived twice since, in mid-February, six trumpeter swans came to the open water below the dam at Chaffey’s Lock and stayed in the area for about two weeks. On March 10th, large flocks of Canada geese began passing through on their way north. The male redwing blackbirds arrived on March 12th, becoming active competitors for birdseed at the feeders while staking out perfect territories in the frozen marshes in the hope of attracting that “right” female who will arrive sometime soon. The chipmunks have come out of hibernation twice now, once in the two-week warm spell in February and, more recently, in mid-March. It’s all about sex!

A recent bulletin from SOT listed the 25-year members for 2006, including Doug Arnold and George Becking who joined an illustrious group. Kudos!! A number of other friends and colleagues in the U.S. also achieved this distinction, some of whom I thought had been members longer than me.

In a recent issue of DISCOVER (March/06), there is an interesting legal ruling by U.S. District Judge John E. Jones on the “intelligent design” court case against the Dover, Pennsylvania School District. As stated “the fact that a scientific theory cannot yet render an explanation on every point should not be used as a pretext to thrust an untenable alternative hypothesis grounded in religion into the science classroom or to misrepresent well established scientific propositions. As the Dover case and final ruling make clear, real science involves more than merely claiming that an idea you dislike is wrong: You have to demonstrate your case with evidence, any alternative theory you float must be open to testing and challenge. The text of Judge Jones’ ruling can be found on the Discover.com website.

Chronic wasting disease (CWD), very similar if not identical to bovine spongiform encephalopathy (BSE), is found in deer and elk populations in western Canada (Alberta, Saskatchewan) and western U.S.A and has been detected in wild whitetail deer in New York State. The Ontario Ministry of Natural Resources is banning the importation of high-risk deer and elk parts (unprocessed antlers, heads, hides, hoofs, lymph nodes, eyes, spleens, mammary glands, entrails, internal organs and spinal columns). Some of this “stuff” should be left in the field where the animal has been dressed out. Hides and antlers must have all adhering tissue removed and can be imported only if they are in a sealed container and delivered to a licensed tanner or taxidermist within five days of entering Ontario. The province also has a testing program in place for deer shot during the hunting season in southern Ontario. Ontario joins Manitoba and 20 American states in banning such imports. No new elk have been imported since 2001 as part of the reintroduction of this species in Ontario but,

from what I have read, the herds are doing well, the pregnancy rate in females ranging from 18%-to-42% in individual herds. Betty will freak out when she sees one of these in her flower garden. Fortunately, we don’t have a herd near us, yet!

As a member of the Canadian Club of Kingston, I attended an interesting talk given by Dr. John Smol of Queen’s University on the topic of global warming as he sees it. His research takes him every July-August to the very northern tip of Ellesmere Island to study the diatoms, both living and fossilized, in mud cores from small freshwater ponds. Depending on the nutrient “flow” into these ponds and the acidity of the water, he has demonstrated a relatively constant spectrum of diatom types and populations from 4,000-8,000 years ago up until 200 years ago. At that point in time, populations have exploded along with new types being found, suggesting that global warming, even in this coldest of environments, began around the turn of the 19th century – the beginning of industrialization in Europe and North America. Interesting stuff! He had some great photographs of wildlife (hares, seals, ptarmigan) that, never having seen a human before, would sit and watch while they were approached to within a yard. No need for a telephoto lens. However, he did use one for a nice photo of a polar bear who was interested in their food cache.

I have promised myself that, this summer, Betty and I will spend more time in the canoe visiting interesting places around us and even doing some serious fishing. That is what retirement is supposed to be. However, today, a mess of leaves needs to be raked off the flower beds and lawn, possibly the earliest we have ever done it since moving to the country. The lakes are still frozen. Well, we are in the tail end of an ice age.

TIPS A MUST READ:

A colleague drew to my attention the March issue of Trends in Pharmacological Sciences Including Toxicological Sciences. This issue is a celebration of 75 years for the British Society of Pharmacology. There is a brief history of the Society followed by articles commenting on the current and future status of the Society and the Pharmacological science in Britain and beyond. Most of the articles chronicle the achievements of British scientists, but a good number of us delighted in and in some cases cursed this work as we studied for our PhD.

Comprehensive exams. The issue is a must read for anyone who has pharmacology and drug toxicity in their blood. Here is what Khem Jhamandas wrote.

“The first part of the issue has letters and opinion pieces on the need for in vivo and integrated pharmacology in the research training and teaching program, and includes a contribution by Mike Walker at UBC.

However, the most exciting aspect of the issue is a series of very interesting articles highlighting the achievements of British Pharmacology. Two of these are riveting: one, a history of quantitative analysis of drug-receptor interactions, deals with the work of icons of British Pharmacology, ranging from AJ Clark (founder of receptor theory) to Bernard Katz (endplate potential and quantal release of transmitter from nerves). It is also interesting to see some errors of thinking in this early work. For example, AJ Clark stated that atropine and acetylcholine were acting on different receptors, an error he later corrected! It also shows that although Clark was working at the same place as AV Hill, who derived the Langmuir equation on the basis of work on nicotine's action, he did not cite Hill's work that had a bearing on his pioneering work on

receptor pharmacology! The second one is by Geoff Burnstock, who proposed the purinergic hypothesis. Burnstock outlines the resistance to acceptance of this hypothesis and traces development of the work that ultimately resulted in cloning of the multiple ATP receptors that are now being implicated in the pathophysiology of disease.

For me personally, the most interesting aspect of these articles is the illustration that some research appears or is perceived as 'irrelevant' or 'esoteric' can come to have very profound significance years later!”





A STUDENT'S PERSPECTIVE

THE ART OF NETWORKING

By **Michelle Picard-Aitken**
M.Sc. Candidate, INRS-Institut Armand-Frappier

No scientist is an island, nor can a researcher survive without the support of funding, collaborators, and friends. While this no doubt seems obvious to veteran researchers, it is one of the first lessons a novice scientist, such as myself, must learn. Having recognized the need for this supporting scaffold, the next step is much harder: how to build and maintain the necessary contacts? In this, networking is key.

Why network?

Science is an extremely competitive field, yet teamwork is the rule rather than the exception. As the saying goes, there is strength in numbers, and much of that strength comes from sharing knowledge that is mutually beneficial. Whether it's the trick to getting a particular technique to work, getting access to that perfect control population, knowing in which direction the funding decisions will be leaning next year, or simply getting a job, success at every level depends on what you can learn from others. Sharing your own resources and expertise – and, just as important, showing others that you have expertise worth sharing – increases your own value, and increases the chances that others will seek you out.

Your graduate studies are an ideal platform on which to begin networking, as you begin carving out your place in the dynamic world of research. As your career progresses and you become an active member of a like-minded group of fellow scientists, you will be well positioned to influence the development and advancement of your field of research. Via your network, you can

wield your influence on various committees, receive invitations to give talks, organize meetings and symposia and coordinate activities that span academia, government and industry.

Speaking as a current graduate student, I look back and see that, for most of our lives, we have been encouraged to outperform and distinguish ourselves from our peers. While excelling at competition remains very much a part of a successful research career, we need to learn that some of our former rivals may now be our greatest allies. With a little practice and time, networking should become second nature, and an invaluable skill.

Who to network with and where?

Potential collaborators and contacts are everywhere, but the most useful are probably the ones you already know. It is always best to be introduced into an existing network rather than trying to build one from scratch, as strangers are more likely to trust and help someone who comes recommended, rather than the new kid on the block. Hence, look to your professors, friends and peers to build the foundation of your network, and let them help you branch out into their own circle of contacts. In time, you will be the one to facilitate ties between the different branches of your network.

Conferences, seminars, symposia, and other gatherings of fellow scientists are specifically designed to encourage mixing and discussions between people with similar research interests. Attend as many as you

can. Meet and greet activities, coffee breaks, and poster sessions are usually relatively informal, and provide many opportunities for expanding your network. Other opportunities are more random: a friend of mine was recently hired in the pharmaceutical industry, thanks to a tip from a person he met last year at a bicycle race!

Tips to effective networking

- **Talk to people!** This may seem obvious, but there is an art to approaching people, and it is harder still to engaging them in pleasant and constructive dialogue. If you have the chance, take the time to observe how the person interacts in a group setting before you approach them, or better yet, arrange for someone to introduce you. And while you may already have a request or goal in mind when initiating a meeting, start with a general question or a comment to show interest rather than launching directly into an aggressive sales pitch. In this way, you can ensure the other person is receptive to you, thus increasing the likelihood they'll want to help you.
- **Sell your science.** Prepare a short and snappy description of your work and your interests, ideally no more than a minute long. The person you're talking to can then ask you questions on what interests him or her specifically. Also, speak of your work with confidence and genuine enthusiasm, rather than with arrogance. Chances are

you'll make a good impression professionally as well as personally.

- **Remember who you've talked to, and what you talked about.** You may find it helpful to write yourself notes on business cards, or on those handy little notepads handed out at conferences. Record their area of expertise, when and where you met them, and other important notes, so you may search and find important people quickly. Keep all this information up-to-date and organized in a central location, such as an address book, or your computer. That way, six months from now when you realize you need an apoptosis expert, you'll know exactly who to call.
- **Maintain contact.** Not everyone keeps notes, so if you don't want to be forgotten, there are many ways to keep in touch. Follow-up promptly with an email, especially if you had promised to provide information, or if your contact had agreed to assist you in some way. Re-introduce yourself to people you've met previously, or if you happen to meet a mutual acquaintance, ask them to pass on your best wishes. As for people you've worked with or who will likely become a collaborator, let them know regularly what you've been up to; this is particularly relevant for past professors and supervisors whom you might need as references.

- **Keep your eyes and ears open.** Opportunities abound, often where you least expect them – all you need to do is recognize them as such. In many cases, you can learn as much from casual observation as from direct questions.

As a graduate student, maintaining a healthy network is vital to your career. Performance evaluations and formal references from past professors and employers may well get your academic career started, but it's who you know, how you sell your science and the strength of your reputation that will keep it rolling in new and exciting directions. And remember: if no scientist is an island, then it is never too late to start building bridges.



**REPORT FROM ICTXI
ORGANIZING COMMITTEE:
Malle Jurima-Romet, David Josephy and
Doug Arnold.**

Since the fall of 2005, planning activities for the 11th International Congress of Toxicology (ICT XI) have focused largely on the scientific program of the Congress. Both the National Scientific Program Committee and the International Scientific Program Committee (ISPC) have had active roles in the development of this program. The ISPC, composed of 29 members from 15 countries, and representing different sub disciplines of toxicology, participated in the initial ratings of proposals for scientific symposia, debates, round tables and continuing education courses. Together

with members of the National Program Committee, ISPC members also served on subcommittees responsible for selecting topics and speakers within each selected session. A draft program was prepared in December 2005 and presented in turn to the ICT XI Organizing Committee and the ISPC for review and comment. Further rounds of review and revision took place during the first two months of 2006 and a final program was presented by Daniel Cyr (Chair of the Scientific Program Committee) to the ISPC during the SOT meeting in San Diego.

Continuing education courses will be offered during the day on Sunday July 15th preceding the official opening of the Congress. Following the opening ceremonies on Sunday evening, the Deichmann lecture will be presented by Allan Okey, from the University of Toronto, who will be speaking on An Ah Receptor Odyssey to the Shores of Toxicology. The rest of the scientific program over the next three and a half days will include 4 plenary lectures, 35 scientific symposia, 2 roundtables, 1 debate session, and 3 full days of posters.

The first announcement for ICT XI was distributed electronically to over 90,000 email addresses in October 2005. Nearly 17,000 of the messages were viewed within the first four hours, demonstrating the power of electronic dissemination! The ICT XI website (www.ict2007.org) continues to be the main source of up-to-date information on the Congress and we are grateful to many other toxicology organizations that have set up links from their websites.

The Local Arrangements Committee has started planning the congress events and social program. In addition to the opening

and closing ceremonies, a student evening is being planned for Monday July 16th, and a social evening for all registrants and accompanying persons is planned for Tuesday evening, with a choice of several different water-related activities (cruise boat, water rafting or kayaking, etc.). The Congress banquet will be held on Wednesday evening.

The Financial Contributions Committee has prepared a brochure outlining the available sponsorship opportunities and benefits to the sponsoring

organization. Several contributions have been received; however, we are still far short of the \$250,000 CAD target that we need to achieve for a financially successful Congress. The ICT XI Organizing Committee is looking for help from all IUTOX members to identify potential corporate sponsors and provide contacts names where possible. ICT XI had a promotional booth at SOT San Diego and judging by the high level of interest amongst SOT attendees who visited the booth, we anticipate a successful congress in terms of attendance.

STC AWARD OF DISTICTION RECIPIENT: DR. ALLAN B. OKEY



David Riddick, Barbara Hales, Allen Okey and Sheldon Roth

Allan B. Okey of the University of Toronto, recipient of the STC Award of Distinction for 2005, is an internationally recognized expert and scholar in the area of dioxin toxicology, he serves as an outstanding ambassador for Canadian toxicology on the world stage, and he is a very deserving recipient of the STC Award of Distinction for his outstanding and sustained

contributions to the science of toxicology in Canada over the past 38 years.

Although Allan received all of his formal education and training in the United States, his entire professional career has taken place in Canada. He was recruited as a new Assistant Professor in the Department of Biology at the University of Windsor. It is interesting to note that he began this academic career in 1967 before officially completing his Ph.D. program requirements and without the need for any post-doctoral training (how times have changed!). After 13 years at the University of Windsor, Allan spent 9 years at the Research Institute of the Hospital for Sick Children in Toronto. In 1989, he began a 12-year reign as Chair of Pharmacology at the University of Toronto and he remains fully active as a Professor in this department at the present time.

Allan's outstanding and sustained contributions to toxicological research

during his professional career in Canada, which has spanned nearly four decades. Space does not permit us to go into great detail on these contributions, so we have chosen to highlight just a few of the truly seminal landmark discoveries made by Allan during various phases of his career. Our brief discussion is focused on the five selected papers that were included with the nomination.

[1] Allan's early work at the University of Windsor focused on the roles of environmental contaminants and estrogens in mammary carcinogenesis. The landmark paper by Okey & Bondy [Science 200: 312-4, 1978] established that psychoactive cannabinoids do not possess direct-acting estrogenic activity. Work in this area was clearly ahead of its time if we now consider the tremendous interest in toxicology on environmental estrogens and endocrine disruption.

[2] Allan's focus on estrogens changed forever when he embarked on a sabbatical leave in the late 1970's in the laboratory of Dr. Daniel Nebert, then at the NIH in Bethesda MD. Around this time, a high affinity receptor for polycyclic aromatic hydrocarbons (e.g. 3-methylcholanthrene, MC) and halogenated aromatic hydrocarbons (e.g. 2, 3, 7, 8-tetrachlorodibenzo-*p*-dioxin, TCDD or "dioxin") had just been discovered by Dr. Alan Poland's group. The collaboration with Dr. Nebert was extremely productive and began for Allan a fascination with dioxin toxicology that is still going strong. A landmark paper by Okey et al. [J Biol Chem 254: 11636-48, 1979] showed for the first time that ligands like TCDD trigger the translocation of the receptor from the cytoplasm to the nucleus where it binds DNA. At this time, they also coined the name for the receptor protein, the aryl

hydrocarbon receptor or AH receptor, and this has had a lasting effect on the toxicological world for the past 25 years.

[3] Much of the early work during these pioneering days of the AH receptor field relied on a powerful genetic model. Certain mouse strains like C57BL/6 were responsive in that they showed dramatic induction of cytochrome P450 1A1 (CYP1A1) following exposure to MC-type compounds. Other mouse strains like DBA/2 were relatively non-responsive. At The Hospital for Sick Children, the Okey group solved a major puzzle in this field when they demonstrated that DBA/2 mice have a modified AH receptor protein that binds prototypical ligands like TCDD with a 10-fold lower affinity than the receptor found in C57BL/6 mice [Okey et al. Mol Pharmacol 35: 823-30, 1989].

[4] Allan's laboratory is also recognized internationally as the first group to be able to detect and characterize the AH receptor in human samples. A landmark paper in this regard is the widely cited study of human placental AH receptor by Manchester et al. [Cancer Res 47: 4861-8, 1987]. The ability to study the biochemical and molecular properties of the human AH receptor has had major impacts on our understanding of human risk assessment.

[5] One of the most exciting aspects of this nomination is that Allan's research on the AH receptor and dioxin toxicology is currently in full stride and has recently entered the new realm of toxicogenomics and bioinformatics. Allan has been the recipient of long-term funding from the CIHR (formerly MRC) and the NCIC, and this funding is now allowing him to tackle a daunting question that has intrigued him for some time: dioxin toxicity is the result of the alteration of expression of which critical

genes? Allan is currently using a microarray approach to identify genes whose regulation differs in response to TCDD treatment in highly sensitive and highly resistant rat strains. This work has developed from a strong collaboration that Allan has with Dr. Raimo Pohjanvirta from Kuopio, Finland. The bioinformatic aspects of this work are beginning to yield fruit, as exemplified by the important recent paper by Boutros et al. [Biochem Biophys Res Commun 321: 707-15, 2004] which characterized a novel response element in DNA by which dioxins may exert certain of their effects.

Allan's research has been reported to date in 129 refereed papers, reviews and book chapters. Several of these contributions have been cited in the literature well over 100 times each. You will learn from his c.v. the numerous ways that he has contributed to the scientific community by serving on grant review committees, journal editorial boards, conference organization committees, etc. We just highlight two very high profile contributions to the toxicology community on the international stage. In the mid 1980's, Allan served as a consultant involved in the U.S. EPA's re-assessment of dioxin risk assessment methods. In 1995, he served as a member of an international delegation that visited Vietnam to study long-term health effects of spraying of Agent Orange during the Vietnam War. Our focus has been on Allan's considerable research contributions, but we also want to briefly highlight his substantial teaching contributions and his skill as an academic administrator. Allan was Chair of the Department of Pharmacology at the University of Toronto from 1989 to 2001. This was a very challenging era of fiscal constraint and Allan provided outstanding leadership during these difficult years. Budget reductions forced some significant down-sizing of the core faculty, but under Allan's leadership, the Department of

Pharmacology continued to offer an impressive array of excellent academic programs and the pressures to merge with other departments were resisted by Pharmacology. We have emerged from this era with strength, enthusiasm and confidence and the Department of Pharmacology is now actively growing and a novel inter-faculty structure, the Institute for Drug Research, is in its early stages. Allan played a critical role in laying the groundwork for these very positive developments. Allan is also an outstanding teacher and he makes significant contributions to the education of the next generation of toxicologists at the undergraduate and graduate levels. Through our large undergraduate Specialist Programs in Pharmacology and Toxicology and our large graduate program (which includes administration of the Collaborative Program in Biomedical Toxicology), it is hard to estimate the large numbers of students and trainees that Allan has reached with his entertaining, stimulating, provocative and accurate methods of instruction. In his own laboratory, Allan has successfully trained 22 graduate students and 9 post-doctoral fellows. Many of these trainees have gone on to productive careers in academia, industry, government and consulting. As one example, Dr. Michael Denison is now at the University of California Davis and is an internationally recognized leader in the field of dioxin toxicology.

Allan is a worthy recipient of the STC Award of Distinction primarily because of his outstanding and sustained contributions to the science of toxicology in Canada. In addition, Allan has been a very strong supporter of the STC in the most important way, at the grass-roots level. Allan is an active participant and frequent invited speaker at the STC Annual Symposium. For many years, he has encouraged membership

in the STC among colleagues and students and there is normally a very strong showing by Okey trainees at the STC poster sessions. Allan has recently been selected by the National Scientific Program Committee for ICTXI to deliver the prestigious Deichmann Lecture when Montréal hosts the world in 2007.

STC Special Service Award



Dr. Gordon Krip

This year we were privileged to be able to honour Gordon Krip, STC Executive Director with a Special Award for Outstanding Service to STC. I will not try to list the many functions of the Executive Director but suffice it to say that the society would not function as well as it does without the tireless efforts of Gordon. In presenting the award Barbara Hales, outlined his contributions to STC and recounted the anecdotes provided by the members of the society who had the privilege of working closely with Gordon.

NOMINATIONS FOR AWARDS

The Society of Toxicology of Canada has two awards, the STC Velyein Henderson award honours an individual who has made a significant contribution to the discipline of toxicology in Canada and the STC Award of Distinction honours those individuals who have made outstanding and sustained contribution to the science of toxicology in Canada and/or the Society of Toxicology of Canada.

The terms of these awards and the criteria to submit a nomination can be found on the SCT web site: www.stcweb.ca Nominations should be submitted to the Secretary STC CP/PO Box 517, Beaconsfield, Quebec H9W 5V1 prior to July 31, 2006.

Report on the STC 2005 Annual Meeting and Symposium:

Bill Racz

The topic for the 2005 STC symposium “The Impact of Toxicants on Child Health/Impact des substances toxiques sur la santé des enfants” was well received by those in attendance. The symposium was divided into four sessions each covering a different aspect of the topic. The four areas were: Current Mechanistic Approaches to Understanding Developmental Toxicity; Biomarkers of Children’s Health, Current Regulatory and Risk Analysis Approaches to Children’s Health and The Identification, Prioritization and Health Risk Assessment of Existing Chemicals in Canada: Addressing Children’s Health. While I enjoyed all the speakers, I was pleased to see the inclusion of student presentations in three of the four sessions. Another innovation for this symposium was the introduction of the GlobalTox Lecture in Contemporary Toxicology. The 2005 GlobalTox lecturer was Dr. Michael Holsapple, ILSI Health and Environmental Sciences, who spoke on current approaches to assess risk to the developing immune system.

As in previous years Cantox sponsored awards for the posters, presented by students, deemed by the judges to be the most meritorious:

The top poster by a student in a MSc program was “In Vivo Endocrine Regulation of Rat Hepatic Aryl Hydrocarbon Receptor Expression and Function” by Anne K. Mullen, supervisor David S. Riddick. Department of Pharmacology, University of Toronto.

The award for the best poster by a PhD. Candidate was “Phosphorylated H2AX Foci Induction in Rat Zygotic Pronuclei Following Chronic Paternal Cyclophosphamide Exposure” by Tara S. Barton, supervisors Bernard Robaire and Barbara F. Hales, Departments of Pharmacology and Therapeutics and Obstetrics and Gynecology, McGill University.

The two abstracts are reprinted on pages 14 and 15.



Student recipients of poster and travel awards.

This year our student travel award winners were:

Helen Badham, Queen's University
Pamela Brown, Queen's University
Jeannette Comeau, Queen's University
Fawzy Elbarbry, University of Saskatchewan
Katherine Guindon, Queen's University
Crystal Lee, University of Toronto
Isabelle Létourneau, Queen's University
Margaret Loniewska, University of Toronto
Anne Mullen, University of Toronto
Garth Oakes, University of Western Ontario
Mandy Lee Olsgard, University of Saskatchewan
Julia Perstin, University of Toronto
Annmarie Ramkissoo, University of Toronto
Lorig Sarkissian, University of Western Ontario
Rana Sawaya, University of Toronto
Emily Tung, Queen's University
Joanne Wan, Queen's University
Andrea Wong, University of Toronto

GRADUATE STUDENT EVENTS AT THE STC ANNUAL MEETING

Joanne Wan, Ph.D. Candidate, Queen's University

In addition to the informative and engaging scientific presentations, the Program Committee of the 2005 STC Annual Symposium incorporated two additional initiatives for students. New for this year was a special presentation by Keith Robinson, of Charles River laboratories on "Reproductive Toxicology and Nonclinical Pediatric Testing of Pharmaceuticals and Biotechnology Products". This useful session covered various aspects of study design regarding the six major reproductive life cycle stages and pediatric pre-clinical testing. Handouts containing interactive questions provided a handy resource that students could reference long after the meeting. Another feature for this year was oral presentations featuring Students and Post-Doctoral fellows. This gave students an opportunity to present research in an

event. These two initiatives were well received and it is hoped that they can continue at future symposia.

The Annual Meeting also meant the return of the popular "Career Session" night. Students and Post-Doctoral researchers had the opportunity to learn about career journeys taken by established academic, government and industry toxicologists. The crowded atmosphere at this event was a tribute to the quality of interaction among attendees – and perhaps to the delicious pizza and beer. Based on the number of students who approached the speakers, it is clear that this event was well appreciated. Thank you to the organizers and the Program Committee on a successful meeting and for incorporating more Student and Post-Doc oriented events at the annual symposia.

IN VIVO ENDOCRINE REGULATION OF RAT HEPATIC ARYL HYDROCARBON RECEPTOR EXPRESSION AND FUNCTION

Anne K. Mullen and David S. Riddick.

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The aryl hydrocarbon receptor (AHR) is a ligand-activated transcription factor that mediates the *effects* of aromatic hydrocarbons (AHs), such as 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin (TCDD) and 3-methylcholanthrene. The adaptive response to AHs has been extensively studied, particularly the induction of drug-metabolizing enzymes, such as cytochrome P450 1A1 (CYP 1A1) CYP 1A2, CYP 1B1, and various phase II detoxification enzymes. AHs also produce toxic responses *in vivo*, including hepatotoxicity, disruption of endocrine homeostasis and alterations in cell proliferation and differentiation. Given these diverse responses to AHs, factors that regulate the expression and function of the AHR itself are of interest because of the potential differences in sensitivity that may be caused by altered AHR levels. *In vitro* evidence suggests that changes in AHR expression can modulate AH responsiveness. For example, lowering AHR expression via a small-interfering RNA approach decreases CYP1A1 induction by AHs in cell culture. However, the *in vivo* regulation of hepatic AHR expression is poorly understood and the impact of changes in AHR expression on AH responsiveness is unclear. With respect to the hormonal regulation of the AHR, our laboratory showed that hypophysectomy (HYPX) decreases hepatic AHR protein and TCDD-binding in male rats. This observation suggested that the AHR is positively regulated by pituitary-dependent factors *in vivo*; however, these factors have yet to be identified. We initially focused on adrenal

glucocorticoids (GCs) as candidate pituitary dependent hormones in this response, since GCs have been shown to increase AHR dependent hormones in this response, since GCs have been shown to increase AHR expression in rat liver, sensitizing rats to the diverse *effects* of AHs. Male rats were either adrenalectomized (ADX) or underwent sham surgery, and then rats were treated with either dexamethasone (DEX) or vehicle. Hepatic AHR expression was analyzed by measuring AHR mRNA using reverse transcription-polymerase chain reaction, AHR protein by immunoblot analysis, and [³H]TCDD-binding levels by sucrose density gradient fractionation. Neither ADX nor DEX treatment had a significant effect on hepatic AHR expression, as assessed at the mRNA, protein and TCDD-binding levels. We conclude that GCs are *not* important regulators of rat hepatic AHR expression *in vivo* and are not likely to be the pituitary-dependent factors responsible for the difference in AHR expression observed between HYPX rats and their sham counterparts. Other potential pituitary-dependent regulators of AHR expression and function will be studied *in vivo* to better understand the hormonal regulation of the AHR and how different hormonal states can influence sensitivity to AHs. [Support: NSERC, CIHR]

PHOSPHORYLATED H2AX FOCI INDUCTION IN RAT ZYGOTIC PRONUCLEI FOLLOWING CHRONIC PATERNAL CYCLOPHOSPHAMIDE EXPOSURE

Tara S. Barton¹, Bernard Robaire² and Barbara F. Hales³.
Departments of Pharmacology and Therapeutics¹ and Obstetrics and Gynecology,

Paternal drug exposure prior to conception is a source of detrimental effects on the developmental competence of the embryo. Chronic preconceptional cyclophosphamide (CPA) exposure leads to aberrant zygotic regulation of the dynamic epigenetic processes of DNA methylation, histone H4 acetylation as well as dysregulated zygotic gene activation, demonstrating that paternal exposure to this alkylating agent induces epigenetic disturbances in chromatin structure and function early post-fertilization.

Histone H2AX is rapidly phosphorylated at sites of DNA double strand breaks and subsequently concentrates repair proteins in the vicinity of the DNA lesions. The goal of our study was to determine the effect of preconceptional paternal CPA-exposure on the induction of H2AX phosphorylation in the zygote. Sprague-Dawley rats were given CPA by gavage for 4-5 weeks. During the fifth week, males were mated overnight with two control females in proestrus; 1-cell embryos were collected. Histone H2AX phosphorylation was assessed using a monoclonal anti-phosphorylated H2AX at serine 139 (YH2AX). Optical sections were recorded using confocal laser scanning microscopy, z-stacks were reconstructed and 3-D images were quantitatively analyzed.

The number of yH2AX foci was significantly higher in paternal pronuclei of zygotes sired by CPA-exposed males at pronuclear stages 1 and 2 (PN1-2) (P=0.014)

and continued to increase dramatically at PN3 (P<0.001), PN4 (P<0.001) and PN5 (P=0.018), compared to corresponding controls. Interestingly, in maternal pronuclei the numbers of yH2AX foci were consistently low throughout zygotic development in embryos fertilized by CPA-exposed spermatozoa, similar to both parental genomes in control zygotes. The striking induction of yH2AX in response to paternal DNA damage was further evidenced by significantly greater focal volumes from PN1 through PN5 (P<0.03) in paternal pronuclei; the maternal genome was not different from controls.

For the first time, we have shown that preconceptional CPA treatment alters spermatozoal chromatin integrity in a manner that is immediately recognized by an amplified H2AX phosphorylation response in the paternal pronucleus. Zygotes sired by CPA-exposed males were hyperacetylated and hypomethylated in male pronuclei, compared to controls, indicative of an active chromatin state. The presence of persistent yH2AX foci in the damaged paternal genome suggests the accumulation of repair proteins that may further alleviate transcriptional repression during the repair process. Inefficient repair of the various DNA lesions and/or aberrant epigenetic programming of DNA damaged sites may lead to persistent modifications of the histone code, potentially leading to heritable genomic instabilities. Supported by CIHR.

REPORT FROM THE STC 2006 SYMPOSIUM PROGRAM COMMITTEE

The STC Program Committee is pleased to announce the preliminary program for the 39th Annual Symposium of the Society of Toxicology of Canada, to be held at the Delta Centre-Ville, 777 University St., Montréal, Quebec, on December 4th and 5th, 2006. The theme this year will be "Genomic and Epigenomic Determinants of Toxicant Response" and will include sessions on "Epigenetics and Gene-Environment Interactions", "Chemical Exposure and Epigenetic Changes", "Genomics and Epigenomics in Human Diseases", "Nutritional Toxicology" and "Epidemiology of Occupational Exposure to Toxicants". We are also planning a Special Student Workshop to be held on the Monday afternoon and, as last year, we will be providing the opportunity for students to give oral presentations during the program.

Gerard M. Cooke, Kannan Krishnan and
Lynne LeSauter.

NOMINATIONS FOR STC BOARD OF DIRECTORS

The schedule of STC events in 2007 has the AGM scheduled in July with ICTXI, and the 2007 call for nominations will occur earlier than normal to allow for elections at the AGM in July, 2007. Thus we have two sets of nominations to announce, for 2006 and 2007.

FOR 2006:

Call for nominations for STC Councillor (Industry):

Councillor: During a three-year term of office the Councillor participates in meetings of the Board of Directors, providing advice and counsel, acting as liaison with specific committees as directed by the President, updating the STC Policy Manual and is a member of the Awards committee. In addition, the Councillor may be assigned a specific task by the President to assist in the management of the Board. This year we are looking for nominations from the industrial sector.

**Please forward all nominations to Dr.
Barbara Hales (Barbara.hales@mcgill.ca)
by August 31, 2006.**

FOR 2007:

Call for nominations for STC Vice- President, STC Secretary and STC Councillor (Government).

Vice-President: This person automatically becomes President at the end of the two-year-term as VP and then Past President for an additional two-year term. Besides filling in for the President when necessary, the major duties of the VP are to oversee the development of the plans for the Annual Symposium and to function as the liaison of the Board of Directors with the Editor of News/Nouvelles and Executive Director to

ensure smooth and timely publication of the newsletter.

Secretary: The Secretary serves a three-year term. He or she is responsible for the agenda and minutes of meetings of the Board of Directors and the Annual General meeting, correspondence and interactions with other organizations on behalf of STC.

Councillor: During a three-year term of office the Councillor participates in meetings of the Board of Directors, providing advice and counsel, acting as liaison with specific committees as directed by the President, updating the STC Policy Manual and is a member of the Awards committee. In addition, the Councillor may be assigned a specific task by the President to assist in the management of the Board. For 2007 we are looking for nominations from the government sector.

Please forward all nominations to Dr. Barbara Hales (barbara.hales@mcgill.ca) by November 1, 2006.



CONFERENCES, MEETINGS AND WORKSHOPS

2006

June 14-16:

Third Northern Lights Conference
Saskatoon, Saskatchewan

July 2-7:

The 15th World Congress of
Pharmacology (IUPHAR 2006)
Beijing, China
<http://www.iuphar2006.org>

2006

Sept. 20-24:

Eurotox 2006/th CTDC Congress
Cavtat/Dubrovnik, Croatia
www.eurotox2006-6ctdc.org

Oct.22-26:

14th North American ISSX Meeting
Rio Grande, Puerto Rico, USA
<http://www.issx.org/>

Nov.5-9:

27th SETAC NA
Montréal, Quebec
<http://www.montreal.setac.org>

Dec. 4-5:

The 39th STC Annual Symposium
“Genomic and Epigenomic
Determinants of Toxicant Response”
Montréal, Quebec.

2007

March 25-29:

Society of Toxicology Annual
Meeting
Charlotte Convention Centre,
Charlotte, N.C.

July 15-19:

11th International Congress of
Toxicology, ICT-XI,
Montréal, Quebec
<http://www.ict2007.org/>

2008

July 27-The IXth World Conference

Aug. 1: on Clinical Pharmacology and
Therapeutics

Quebec City, Canada
<http://www.cpt2008.com/>

