NATIONAL CAPITAL AREA CHAPTER

SOCIETY OF TOXICOLOGY NEWSLETTER

Web Edition

July, 2004 **Issue 17**

Editor—Gary Burin
202-828-8980

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Message from the President

by David Jacobson-Kram

In my year as President Elect I have had the opportunity to meet and work with the officers and many members of the chapter. I have been mightily impressed with the time, energy and dedication that this group commits to chapter functions. The major responsibility of the President Elect is to plan the fall and spring symposia. I have been fortunate indeed to have had a number of individuals willing to help plan the program, contact potential speakers and help with the many logistical arrangements required for a successful symposium. Through their efforts we have had two well integrated, well attended and scientifically rewarding meetings. My thanks to all of you who pitched in. Dr. Harry Milman will have this responsibility in the coming year and I urge you all to give him suggestions for topics, help with planning and most of all attend the symposia.

This past year has really driven home to me the importance of the regional chapters. They represent an

important means of networking with our local colleagues and an important vehicle for influencing the national organization. I think that the members of this chapter are in an interesting place at an important time in the history of toxicology. We are witnessing a metamorphosis of our field from being descriptive and phenomenological to being molecular and mechanism based. These changes will impact many sub disciplines, not the least of which will be regulatory toxicology. This is a great time to be a member and to get involved.

NCAC-SOT Executive Board Members – 2004-2005

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Student Vice- Representative	Mashael Y Al- Namaeh (’05-’06) Howard University 703-566-5500; mashael@doctor.com

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National Capital Area SOT, Spring 2004 Symposium

Topic: Novel Methods for Detecting Hepatotoxic Agents
Location: National Library of Medicine, Bethesda, MD

Date: June 8, 2004

Speakers and presentation titles:

John R. Senior, M.D., FDA, Center for Drug Evaluation and Research -- **Detecting Liver Injury: Drug-Induced or Not?**

Correct attribution of causality as to whether a case of acute liver injury is drug-induced or not is among the more difficult problems in medicine. Drugs or other substances, or their metabolites produced by the liver, may cause liver injuries that mimic all known liver diseases. There is no pathognomonic test or finding, including biopsy, that proves the injury is drug-induced. The diagnosis therefore must be made by ruling out all other possible causes. This is often not done well or thoroughly, so that the data gathered too frequently allow concluding only that the liver injury was “possibly” or “probably” drug-induced. We chose to address one aspect of this problem: whether we could be reasonably certain of detecting and diagnosing serious liver disease that was NOT drug-induced. The work was done as an innovative research collaboration between the Food and Drug Administration and the Merck Research Laboratories, where the clinical representative served not as a regulator but as a cooperative research partner with the pharmaceutical industry statistician. We examined a large database of 3301 study participants randomized to placebo and observed repeatedly (20 times) over more than 5 years. We found that serum transaminase elevations were very poorly predictive of serious liver disease, were often transient and unexplained. Only when the transaminase elevations (3-fold) were persistent or progressive and either accompanied or followed by rises in serum bilirubin (2-fold) was the liver disease clinically significant or serious. The combination of a test for hepatocellular injury and a measure of overall liver function was as sensitive as the transaminase alone but far more specific in detecting 6 of 6 cases of serious liver disease incident among 3248 ambulatory participants on placebo for 5 years. Thus, we could be reasonably sure we could detect serious non-drug-induced liver injury or disease by this combined injury-function test as a biomarker, the same combination that the late Hyman Zimmerman reported for drug-induced liver injury. The methods for exclusion of non-drug causes, and correct and quantitative attribution of causality, will require further work.

Yvonne Dragan, Ph.D., FDA, National Center for Toxicological Research **-- Biomarkers of Liver Toxicity and Disease**

Hepatotoxicity is the number one reason for drug recall and hence it is of concern to the FDA and to the American public. Drug induced toxicities account for nearly half of the cases of acute liver failure in adults over age 50 in the US. There is a need for better predictive tests for agents that have the potential to cause liver toxicity in humans. In addition, early biomarkers of adverse liver effects from exposure to agents are needed and should be developed. Factors that trigger hepatic cell death, permit hepatocyte survival, and trigger hepatocyte proliferation are potential biomarkers. Techniques such as Seldi based proteomics and NMR-based metabonomics provide tools for the development of biomarkers of toxicity and disease. Specific, sensitive, and predictive biomarkers for the induction of liver toxicity and the potential for progression to fulminant liver failure need to be identified and are the long term goal of this proposal. Animal toxicity data can be used as a surrogate to predict potential human liver toxicity.

James H. Kelly, Ph.D., Amphioxus Cell Technologies -- **Predictive Hepatotoxicity: Correlations in a Structural Database**

We have employed a human liver cell line and a series of high throughput *in vitro* toxicology assays to examine the structural basis of hepatotoxicity in several families of compounds. The data show that such a system can provide fine discrimination among structural variants. We have examined thiazolidinediones, nonsteroidal anti-inflammatories, fluoroquinolones, and antihistamines with known hepatotoxic properties to show that there is a clear structural basis for the problems encountered with these compounds. With this idea in mind, we are screening a large number of compounds in an attempt to build a predictive toxicology database which, when coupled to the experimental system, can be used to eliminate hepatotoxic liabilities early in the drug development process. The data are gathered directly into software for experiment management, MDL Assay Explorer®. The results are then collated to the associated structure and functional information for each compound using ChemBioAE®. Using cyp1A induction as an example, we are able to show that compounds with similar mechanisms of action, such as ERK inhibition, are common inducers. Likewise, unrelated compounds with similar structural features, such as aristolochic acid and apomorphine, also induce.

Neal Jensen, Ph.D., In Vitro Technologies -- **In Vitro Assessment of Necrosis and Apoptosis Using Human Hepatocytes**

Hepatotoxicity is the most common side effect of new chemical entities (NCE). While hepatotoxicity is generally described as a necrotic event, apoptosis may also play an important role in chemically-induced hepatotoxicity. A number of different models have been used for evaluating the hepatotoxicity of NCEs, including *in vivo* animal studies and various cell-based assays. Isolated human hepatocytes have been used to study the metabolism and toxicity of drug candidates. Human hepatocytes offer several advantages as an *in vitro* model. They provide human-specific results, testing can be carried out with small amounts of compounds, and animal use is minimized. Human hepatocytes can be obtained in different formats for use in the evaluation of hepatotoxicity by necrotic or apoptotic pathways. Freshly isolated hepatocytes can be used in suspension or plated as monolayers for short- or long-term toxicity studies. In addition, hepatocytes can be cryopreserved, thawed as needed, and used in suspension for evaluation of drug toxicity. Recently, cryopreserved hepatocytes have become available which, when thawed, can form monolayers to be used in place of fresh hepatocyte monolayers for metabolism or toxicity studies. Different methods for measuring necrosis (MTT, ATP, LDH) and apoptosis (Caspase, DNA fragmentation) using hepatocytes in various formats will be discussed.

Steven Yee, Ph.D., NIH, National Heart, Lung and Blood Institute --**Susceptibility Factors in Idiosyncratic Drug-Induced Liver Injury**

Drug-induced liver disease (DILD) is a common cause of life-threatening, acute liver failure and is a major reason drugs are removed from clinical development and widespread use. Because of its idiosyncratic nature, accurate prediction of which new drugs will cause DILD and who will be at risk for the development of this disease is difficult. Likewise, the pathogenesis of DILD is complex and appears to involve the formation of reactive drug metabolites that affect critical biochemical functions or elicit an immune response. Recent studies, however, have demonstrated that an alteration in the balance of protoxicants and

protectants in the liver can also influence susceptibility to DILD. Environmental influences, such as the inflammagen bacterial lipopolysaccharide, and/or genetic polymorphisms may affect this balance. Indeed, concurrent inflammation can enhance susceptibility to a variety of hepatotoxicants, including drugs, and result in the generation of numerous injurious, protoxicant inflammatory mediators. Moreover, the deficiency of key protective factors in the liver – such as anti-inflammatory cytokines and others – can lead to increased tissue susceptibility, often through unchecked protoxicant activities. Hence, the balance between these susceptibility factors may play a critical role in the overall pathogenesis, with increased levels of protoxicants or decreased levels of protectants leading to this disease. Identification of such factors through the use of toxicogenomics, proteomics and metabonomics will be ideal in better understanding the mechanism and facilitating the prediction of DILD, thereby preventing the removal of otherwise beneficial drugs from the market.

Thomas Flynn, Ph.D., FDA, Center for Food Safety and Applied Nutrition -- **Multi-endpoint Profiling of Suspect Hepatotoxicants in Cultured Hepatocytes**

Hepatotoxicity is the leading cause of post-market withdrawal of drugs and of warning notices for dietary supplements. The present study evaluated the effects of model compounds, some with known hepatotoxicity, on human (HepG2/C3A, WRL-68) and rat (Clone-9) hepatocyte cell lines. Cells were exposed to multiple concentration levels of test agent (up to the limit of aqueous solubility but not more than 1 mg/mL) for up to 48 hr. Specific endpoint assays, which could all be conducted in a plate reading fluorometer or luminometer and which model known mechanisms of hepatotoxicity, included: generation of reactive oxygen species (dichlorofluorescin); depolarization of mitochondria (rhodamine 123); steatosis (nile red); induction or inhibition of cytochrome P450 activities (EROD, BOROD); cell viability (liver enzyme release, Alamar blue, total ATP); and apoptosis (caspase 3). All parameters were normalized for total double stranded DNA content (H33258) per well. Each model compound generated a unique response profile based on which endpoint showed a concentration-related increase, decrease, or no change. Only 3 of 12 compounds tested showed significant cytotoxicity. For some model compounds that are human drugs and have known hepatotoxicity (e.g., valproic acid), some endpoints responded at concentrations comparable to therapeutic blood levels and in ways consistent with the compound's known mechanism of toxicity. These findings suggest that this test system may serve as a screening assay for hepatotoxicity of food- or dietary supplement-related compounds.

William Mattes, Ph.D., Genelogic, Inc. -- **The Use of Microarray Technology to Predict Hepatotoxicity in Humans**

Because numerous industrial and pharmaceutical chemicals have been found to cause damage to the liver, testing for hepatotoxicity remains a key component in the safety assessment of a new chemical entity. While standard animal models generally predict human hepatotoxicity, there are a number of examples of compounds whose human liver injury was not forseen in rodent models. Gene Logic has taken the premise that gene expression data from livers of compound-treated rats may be contain signals predictive of human hepatotoxicity. To this end studies were conducted with a series of known human and rodent hepatotoxins, as well compounds known to be safe. A database of gene expression results for various treatment times and doses was constructed, and then used to build predictive models composed of hundreds of gene responses. The models are of three types: a model predicting general hepatoxicity, models predicting various pathologies or mechanisms, and models identifying similarity of an unknown compound to one in the reference database. Examples of the results of these models for two paradigm compounds, tacrine and

felbamate, will be presented.

Student Poster Abstracts:

Benchmark Dose Modeling of Mercury-Induced Acute Renal Failure in Sprague-Dawley Rats with Renal Insufficiency Compared to Healthy Controls.

Ronald P. Brown, ***Emily F. Madden***, Peter L. Goering
Center for Devices and Radiological Health, FDA, Silver Spring, Maryland 20903.

Experimentally induced renal insufficiency (RI) increases the sensitivity of rodents to the adverse effects of a subsequently administered nephrotoxic agent. Since patients with renal insufficiency are at increased risk of developing acute renal failure (ARF) following exposure to nephrotoxic compounds compared to healthy individuals, the use of animal models of renal insufficiency improves the clinical relevance of toxicity test results used for the safety assessment of drugs and chemicals released from medical device materials. Benchmark dose (BMD) modeling was used to quantify the magnitude of the increased sensitivity in male Sprague-Dawley rats with RI, compared to healthy controls, following an iv injection of mercuric chloride ($HgCl_2$). RI was induced by 3 daily sc injections of gentamicin (250 mg/kg). Healthy control animals received sc saline for 3 days. $HgCl_2$ (0.025 to 0.5 mg Hg/kg) was administered on Day 4 and blood was collected for analysis 24 hours after $HgCl_2$ injection. The dose-response relationship is based on the number of animals in ARF, defined as 2x the mean value of BUN in healthy, non-mercury exposed animals. $BMD50_{[control]}/BMDL50_{[RI]}$ ratios were calculated using six different BMD quantitative models. BMD ratios for mercury-induced ARF were in the range of 3-14, with only one dose ratio > 10. Assuming a similar increased sensitivity exists for patients with RI exposed to mercury or other nephrotoxic agents compared to healthy persons, these results suggest that the default uncertainty factor of 10 used in noncancer risk assessment to account for interindividual variability in a population response to a given dose of a compound is adequately protective in most cases.

Development and Validation of a Gentamicin-Induced Subclinical Renal Injury Model in Rats.

Emily F. Madden, Ronald P. Brown, Peter L. Goering,
Center for Devices and Radiological Health, FDA, Silver Spring, Maryland 20903.

Patients with pre-existing risk factors are prone to developing acute renal failure following exposure to certain drugs or nephrotoxicants. Recognition of this increased sensitivity has led to a proposal to use animal models of renal failure as an adjunct to standard safety assessment studies. Healthy animals are used predominately in safety testing, but drugs and medical devices are often prescribed to patients with underlying diseases, such as renal insufficiency. There are disadvantages associated with existing renal failure models, including use of survival surgery and protracted development time. Also, animals in overt renal failure may be insensitive to low doses of nephrotoxicants. The goal of this project was to develop a model of subclinical renal injury (SRI), validate it against other renal failure models, and assess its sensitivity to a challenge nephrotoxicant. To develop the SRI model, male Sprague-Dawley rats were dosed daily with 250 mg/kg gentamicin sc for 3 days. BUN, blood creatinine, and urinary protein/creatinine ratio

values in gentamicin-treated rats were similar to controls, but urinary NAG levels increased by 5-fold. SRI persisted for up to 7 days. The sensitivity of our SRI model was validated with a NOAEL dose of $HgCl_2$. Gentamicin-treated rats challenged with 0.25 mg Hg/kg iv exhibited a 2-fold increase in BUN, blood creatinine, urinary NAG and urinary protein/creatinine levels after 24 hours. However, two models of renal failure -5/6 nephrectomy and a 40 mg/kg/day x 10-day gentamicin dosing regimen- did not demonstrate increased sensitivity of the kidney to $HgCl_2$. In conclusion, our SRI model avoids disadvantages associated with existing renal failure models and demonstrates increased sensitivity to Hg compared to healthy animals. [Supported in part by FDA OSHC.]

Seasonal metal content measured in Baltimore **PM_{25} seas samples correlates with cytokine and chemokine release in an *in vitro* assay system**

***Robert J. Mitkus*[1]**, Jan L. Powell[1], J P. Pancras[2], John M. Ondov[2], and Katherine S. Squibb[1]

[1]University of Maryland Department of Epidemiology and Preventive Medicine

[2]University of Maryland Department of Chemistry and Biochemistry

The association between human cardiopulmonary disease and exposure to fine particulate matter (PM2.5) has been well established. Metals are hypothesized to be responsible for this relationship, as well as the inflammation that has been measured in vivo after exposure to PM2.5. To test this hypothesis, we exposed human alveolar type II cells (A549) and monocytic-like cells (RAW 264.7) to fine particulate matter (PM2.5) collected in 2002 at the Baltimore Supersite during summer and winter intensive sampling periods. Production of the chemokine, MCP-1, was measured from alveolar epithelial cells, while the release of the pro-inflammatory cytokine, TNF-a, was quantitated from monocytes in two similar in vitro assay systems. Mean levels of TNF-a for July 17-19 were 1800.8 (+/- 1092.1) pg/ml, while mean levels for November 19-25 were 1994.7 +/- 1455.0 pg/ml. MCP-1 release for July had a mean value of 101.1 +/- 223.4 pg/ml, whereas it was -836.2 +/- 246.5 pg/ml for November. A comparison of the concentrations of eleven metals measured by GFAAS revealed that Al, Fe, and Zn were the most abundant in both the July (Fe>Al>Zn) and the November (Fe>Zn>Al) samples. Statistical analyses demonstrated significant Pearson correlations ($P<0.05$) between ambient Fe and Cu concentrations and subsequent TNF-a and MCP-1 release for both sampling periods. Ambient Al concentrations from both July and November correlated with TNF-a release. In contrast, Zn correlated well with TNF-a ($r = 0.507$) released in response to the November samples and MCP-1 ($r = -0.576$) released in response to the July samples. Our results demonstrate that summer and winter samples differed in the associations between metal content and induced cytokine or chemokine release and that MCP-1 inhibition correlates well with Zn concentration in these samples. They also support the reports of other investigators that certain metals measured in PM2.5 affect the expression and release of specific intercellular signaling molecules in in vitro systems. *Supported by USEPA Supersite grant R82806301*

Chlorpyrifos Alters Functional Integrity and Structure of an In Vitro BBB Model: Co-cultures of Bovine Endothelial Cells and Neonatal Rat Astrocytes

Damani K. Parran

Dept. of Biomedical Sciences and Pathobiology and Laboratories for Neurotoxicity Studies, Virginia Tech, Blacksburg, VA

The blood-brain barrier (BBB) is a structural and functional interface between the circulatory system and the brain (Rubin *et al.,* 1991). Organophosphorous compounds such as chlorpyrifos (CPF) may cross the BBB and disrupt BBB integrity and function (Yang and Aschner, 2003). To determine events that may contribute to CPF toxicity, we used an in vitro BBB model in which bovine microvascular endothelial cells (BMEC) and neonatal rat astrocytes were co-cultured. We hypothesized that CPF is metabolized by the BBB to CPF-oxon leading to an inhibition of esterase activity and a disruption of the BBB. The co-culturing of BMECs and astrocytes resulted in tight junction formation as determined by electron microscopy, electrical resistance and western blot analysis of two tight junction-associated proteins (ZO-1 and e-Cadherin). We observed time dependent increases in ZO-1 and e-Cadherin expression and electrical resistance during BBB formation, which were maximal after 9 to 13 days of co-culturing. The CPF concentration and production of its metabolites were monitored by HPLC following 24 hr exposure to CPF. We found that the BBB metabolized CPF, with the metabolite 2, 3, 6-trichloro-2-pyridinol being the major product. CPF and its metabolites were detected on luminal and abluminal side of the BBB suggesting that CPF crossed this barrier. CPF was also detected intracellularly and on the membrane inserts. At tested concentrations (0.1 –10 mM), CPF inhibited both carboxylesterase (CaE) and cholinesterase (Calhau *et al.*, 2002) activities by 43% to 100%, while CPF-oxon totally inhibited CaE and ChE activity in concentrations as low as 0.1 mM. CPF also caused a concentration-dependent decrease in electrical resistance, with significant inhibition observed at 1 nM and complete loss at 1 mM. These data show that low concentrations of CPF and its metabolites are trapped within the BBB. These metabolites, especially CPF-oxon, contribute to the inhibition of CaE and ChE activity, as well as the alteration of BBB integrity and structure.

A chronic, escalating dose of methamphetamine (METH) diminishes monoaminergic neurotoxicity in adult rats

***D.L. Graham*[1,2],** P.-A.H. Noailles[1], K.G. Becker[4], W.H. Wood III[4], B. Ladenheim[1],T.H. Moran[3], and J.L. Cadet[1]

[1]Molecular Neuropsychiatry Branch, DHHS/NIH/NIDA/IRP, [2]Program in Toxicology, University of Maryland School of Medicine, [3]Department of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine, [4]Gene Expression and Genomics Unit, DHHS/NIH/NIA, Baltimore, MD

Methamphetamine (METH) is an illicit drug with neurotoxic properties, and its use in the United States is escalating to epidemic proportions. Repeated administration of the drug causes behavioral tolerance, which leads to increases in the amount of drug self-administered by humans in order for them to maintain the euphoric effects. The present study sought to investigate whether a chronic, escalating dose (ED) of METH might cause neurotoxicity. Adult male Sprague-Dawley rats were injected with METH or saline according to an ED schedule for two weeks, followed by a challenge with either saline or METH (10 mg/kg every 2 hrs X 3). Brain regions were extracted at 2 or 24 hrs following the last injection. In HPLC analyses, a METH challenge caused a significant decrease in both dopamine (DA) and serotonin (5-HT) in the striatum of saline pre-treated animals. However, this depletion was significantly attenuated in animals that received the ED regimen of METH prior to the challenge. These results suggest that the ED schedule causes induction of protective mechanisms or suppression of protoxic events that render the animals resistant to METH toxicity. Using microarray technology, the bases for the pathways involved are also being assessed.

Treasurer Report by Laurie Roszell

NCAC-SOT Treasurer Report
July, 2004

Spring Meeting: June 8, 2004

Meeting-related income:

		No.	Recieved
Registration:			
	Symposium		
	Members		
	Regular (35)	34	$ 1190
	Student (0)	9	$ 0
	Non-Members		
	Regular (45)	44	$1980
	Student (10)	1	$ 10
Membership			
	Regular (20)	8	$ 160
	Student (10)	0	$ 0
	Total income:		$3340

Meeting-related expenses:

Supplies :	$ 35.51
Printing (program)	$ 37.80
Award plaque	$ 83.18
Room rental	$ 0.00
Catering:	$ ~625.00
Audio visual	$ 0.00
Poster boards	$ 1449.25
Student awards	$400.00
Total meeting expenses:	$ 2630.74

Net meeting income: $709.26

Current Assets:

Checking account (5/28/2004): $ 6906.04
Annual net assets (July 2004): $ 9,524.55

Graduate Student and Post-doctoral Events

Our chapter has had another successful year of graduate student and post-doc events. On November 19, 2003, graduate students and post-docs from the University of Maryland, Virginia Tech, Howard University, Johns Hopkins University, and the USFDA met at Howard University to attend the second annual NCAC Career Enhancement Day. Organized entirely by Rob Mitkus (University of Maryland) and Melinda Pomeroy (Virginia Tech), with special support from outgoing NCAC President Sid Green, the day was entitled "Skills You Can Use for Your Future: *Interviewing*." Attendees were treated to a day of talks and Q&A on the skills necessary for interviewing successfully for post-graduate positions in the private and public sectors. Feedback on the day was once again extremely positive, and a third Student Day has been planned for November 3, 2004 in conjunction with the Fall Symposium (Nov. 2), at the National Library of Medicine.

The 43rd Annual national SOT meeting in Baltimore offered many opportunities for students and post-docs. The Student Advisory Committee (SAC), which is composed of the student representatives from each of the regional chapters in the US, organized and planned several student events, including the Student/Post-Doctoral Fellow Mixer, Lunch with an Expert program, and the symposium, "Life as a Toxicologist—A Graduate Student and Post-Doc Primer to Careers in Toxicology." In addition, the 2002 NCAC Student Day "Symposium on Effective Presentations" was offered as a lunchtime session at the 2004 meeting. Notably, our chapter's 2003 Career Enhancement Day program has been tentatively accepted as a sunset session for SOT 2005.

The NCAC-SOT Spring Symposium was held on June 8 at the National Library of Medicine. First place in the lunchtime student poster competition, an historical part of the Spring Symposium, was awarded to Emily Madden, PhD, a post-doc at the USFDA in White Oak. Winners of this year's Bern Schwetz Student Travel Award, as well as a host of other information for grad. students and post-docs can be found at our chapter website (http://www.toxicology.org/isot/rc/ncac/Default.htm).

Welcome to incoming Student Representative, Melinda Pomeroy, and Vice-representative, Mashael Al-Namaeh (Howard U.). Many thanks to our outgoing rep, Rob Mitkus.

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From the Student Representative

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by Melinda Pomeroy-Black

As many of you are aware, I am the incoming student representative to the Student Advisory Council (SAC) of SOT for our regional chapter. First off, I'd like to offer a hearty "thank you" to Rob Mitkus, the outgoing student rep, for his outstanding work last year. Before Rob left the position, we were working on a couple of projects.

We submitted our student day theme from November 2003, "Interviewing Skills for Graduate Students and Post-Docs " as a session for SOT 2005. The committee accepted our proposal as a Sunset Session, so be sure to look for it in New Orleans!

Another project, we began discussing were ways to improve the NCAC webpage for students and post-docs. Over the summer, the webpage will be updated to include a link for students and post-docs. On the dedicated student/post-doc section of the webpage, you will find several items that you may need a quick link to, including:

- index of past Student Days,
- contact information for the current student representatives,
- NCAC membership application,

- link to SAC,
- upcoming Student Day info,
- and links to the funding opportunities, placement services, and the specialty section websites of SOT.

Speaking of specialty sections, I'd like to remind all the students that along with your paid SOT membership, you can join a specialty section for FREE! That's right—nada, zip, zilch. I joined a specialty section myself this past year and found it to be very beneficial at SOT, where I made one-on-one contacts with people in my field at the specialty section meeting. Joining the specialty section definitely helps with the networking factor since it's such a smaller scale than the SOT meeting itself. I opted in to the listserv for my specialty section and periodically receive announcements of post-doc positions in my field, which is extremely helpful to me right now.

Finally, I want to introduce our incoming student vice-representative, Mashael Al-Namaeh of Howard University. Mashael and I will be working together to plan the Student Day 2004. The topic for the upcoming Student Day will be "Scientific Writing" and will include professionals speaking on how to write competitive grants (or thesis proposals), such as drawing the reader in, active or passive voice, writing abstracts, in-house revising and editing, and writing introductions and summaries. Writing is a skill that separates the lions from the lambs throughout your career and we hope many of you are able to attend. Until then, please feel free to contact us at mpomeroy@vt.edu or drmashael@aol.com.

Coming Soon, NCAC SOT's New and Improved Web Site

The NCAC-SOT's web site is currently undergoing major revision and updating. When completed, the chapter's web site will be your one source for up-to-date information on current chapter activities as well as a link to past activities. Features will include: alerts on upcoming chapter activities; abstracts and Powerpoint presentations (if authorized by the presenter) from NCAC-SOT symposia; a dedicated Student Member section; current and past chapter newsletters. The NCAC-SOT chapter web site can be accessed through the National SOT's website or directly at: http://www.toxicology.org/memberservices/regionalchapter/ncac/Default.htm
Please bookmark the chapter web site for easy access. Also, please forward suggestions for items you would like to see included on the web site to NCAC-SOT webmaster Tom Flynn (tflynn@cfsan.fda.gov).