National Capital Area Chapter
Society of Toxicology Newsletter
Electronic Edition

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M. Biggs, Editor

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CHAPTER MISSION STATEMENT

The National Capital Area Chapter of the Society of Toxicology (NCAC-SOT) was established to provide a regional focus for scientists of all disciplines interested in toxicology. The Chapter acts to:

- Sponsor and co-sponsor symposia on current issues in toxicology
- Provide annual awards to an outstanding student and postdoc in toxicology to assist in attending the annual meeting of the SOT
- Maintain communication with the National SOT regarding current toxicology and regulatory concerns
- Sponsor Regional Chapter events at the SOT Annual Meetings

MESSAGE FROM PRESIDENT

Dear Fellow Members:

It is clear that the NCAC-SOT is in good shape with a growing and dynamic membership and a solid fiscal situation. Going forward, I suggest that we build on the scientific and risk assessment strengths of our members across the local participating universities, Federal agencies, and NGOs to increase the size of our chapter and take advantage of our geographical location. During the next year, we will continue to hold high-quality Spring /Fall scientific meetings and sponsor/co-sponsor innovative, high- impact seminars and colloquia at local universities and Federal agencies, which will provide networking opportunities for students and postdoctoral fellows.

Another thought would be for us to highlight our members' publications, emphasizing graduate students and postdoctoral fellows, by posting publication citations in the NCAC-SOT newsletter and website for informational purposes. The main goal would be to bring visibility to the excellent research being conducted by our members and focusing on those early in their careers. I would like to get some feedback on the merit of this idea. Please feel free to contact me at drtox@earthlink.net with your comments, and I will share them with the other Council members for discussion. An overall purpose of the above efforts would be to create an atmosphere of scientific excitement and enthusiasm, which will hopefully stimulate other toxicologists from our geographic area to participate in the NCAC-SOT and allow us to continue to grow as an SOT chapter.

Best regards to all and I wish you a great Summer.

Bruce A. Fowler Ph.D.
NCAC-SOT President

MESSAGE FROM THE GRADUATE STUDENT REPRESENTATIVES

Greetings SOT-NCAC Students,

We recently held our Annual Spring Symposium, *Mechanism of Cell Injury and Cell Death-Applications for Mode of Action Risk Assessment,* at the Hall of States in Washington, D.C. Speakers addressed a variety of topics from the roles of cell death proteins to translation of basic cell death mechanisms. The symposium finished with a question and answer panel, business meeting, and a social happy hour at Kelly's Irish Times.

During the symposium, students and Post-docs participated in a poster competition. We would like to thank all of the participants for presenting their research and congratulate the winners of the competition. Haritha Potineni received third place, Spencer Todd received second place, and Abhishruti Parihar received first place.

We also have a new Vice Student Representative, Suzanne Martos. She joined SOT-NCAC in May. We highly encourage student participation. This gives you the opportunity to apply for

NCAC-SOT awards as well as network with professionals from government, academia and industry. Please get in contact with us if you have additional questions or want to get involved! You can also contact us online. Find us on ToxChange, and follow us on Facebook (SOT NCAC Group) and Twitter (SOTNCAC) to keep up with current events within the local chapter!

Your Student Representatives,

Abhishruti S. Parihar and Suzanne Martos
sot.ncac.officers@gmail.com

MESSAGE FROM THE POST-DOCTORAL REPRESENTATIVE

Dear NCAC-SOT Postdocs,

I would like to start out by thanking all of the postdocs who took time out of their busy schedules to attend the NCAC-SOT Annual Spring Symposium. Postdoctoral participation is crucial for the success of our regional meetings and provides a great opportunity to share your work with other NCAC-SOT members.

Anyone interested in exploring the wide variety of career paths available to toxicologists should consider registering for the Fall Career Webinar. The webinar is entitled 'Exploring Alternative Career Paths in Toxicology' and will be held on September 18. Be on the lookout for emails with attendance information from the Postdoctoral Assembly (PDA) in the coming weeks.

As a reminder, registration for the 2014 annual meeting in Phoenix is currently open and the deadline for abstract submission is October 7th. In addition, the PDA is currently accepting applications for the 'Best Postdoctoral Paper Award' through October 9th. If you have published a paper that has made a significant impact in the field of toxicology I highly encourage you to apply (http://www.toxicology.org/ai/spd/PD-PubAwardAnn.asp). There are also a number of additional postdoctoral award deadlines approaching which can be found on the SOT website (http://www.toxicology.org/ai/af/awards.aspx).

If you have any questions or suggestions don't hesitate to contact me (chad.brocker@nih.gov).

Have a great summer!

Sincerely,

Chad Brocker, Ph.D
NCAC-SOT Postdoc Representative

NCAC-SOT MEMBERSHIP DETAILS

Did you remember to renew both your SOT and NCAC memberships this year?? Annual membership fees for NCAC-SOT are only $25 for regular memberships and $10 for full-time students. These negligible fees are used to fund our symposium each year and to support a myriad of student activities, including student awards, travel supplements, and K-12 outreach.

If you have not yet renewed your regional chapter membership, please do so today! You can do so online at http://www.toxicology.org/script/loginredirect2.asp?page=dues, or just fill out and mail in the membership application found at the end of this newsletter. It's never too late to renew your NCAC-SOT membership for 2013!

NCAC-SOT EXECUTIVE BOARD MEMBERS

President:	Bruce Fowler (2013-2014) ICF International 703-934-3324 bfowler@icfi.com
Vice-President/ President-elect:	LCDR Mark Miller (2013-2014) US Environmental Protection Agency 202-566-0454 mfmillertime@gmail.com
Past President/ Councilor	Cal Baier-Anderson (2013-2014) US Environmental Protection Agency 202-564-1933 baier anderson.caroline@epamail.epa.gov
Secretary:	Erik Janus (2012-2015) Monsanto Company 202-383 2866 erik.janus@monsanto.com
Treasurer:	Christopher Sheth (2012-2015) US Food and Drug Administration 240-402-3163 Christopher.Sheth@fda.hhs.gov
Councilors:	Melanie Biggs, Newsletter editor (2012-2015) Consumer Product Safety Commission 301-987-2593 mbiggs@cpsc.gov
Councilors:	David Szabo Website coordinator (2013-2016) US Food and Drug Administration 240-402-4042 David.Szabo@fda.hhs.gov
	Susan A. Laessig Student Liason (2013-2016) US Environmental Protection Agency 202-564-5232 laessig.susan@epa.gov
Postdoctoral Representative:	Chad Brocker (2013-2015) National Institute of Health Chad.brocker@nih.gov
Graduate Student Representative:	Abhishruti Saitu Parihar University of Maryland School of Medicine 410-706-7307 Asparihar@umaryland.edu
Graduate Student Vice Representative:	Suzanne Martos Johns Hopkins Bloomberg School of Public Health 480-620-2769 smartos@jhsph.edu

2013 SPRING SYMPOSIUM AND ABSTRACTS

The Spring meeting of the NCAC-SOT Chapter was held on May 23, 2013 at the Hall of States in Washington, DC. The theme was "Mechanisms of Cell Injury/ Cell Death- Applications for Mode of Action Risk Assessment". The meeting was attended by approximately 80 participants from the local regional chapter area. Dr. Dean Jones from Emory University was the key note speaker followed by presentations from Drs. Gary Fiskum, (University of Maryland – Baltimore), J. Marie Hardwick (Johns Hopkins University), and Rita Schoeny (U.S.EPA). The lectures featured a progression of scientific information on current knowledge on mechanisms of cell injury/ cell death and how this basic scientific information may be used for risk assessment practice. The results of this meeting will hopefully stimulate interest and support for efforts at the U.S. EPA and other Federal agencies to incorporate modern scientific tools into risk assessment practice.

The meeting also included 12 judged poster presentations by postdoctoral fellows and graduate students during the luncheon break. The winners were 3rd place - Haritha Potineni, 2nd place - Spencer Todd, and 1st place - Abhishruti Parihar. Congratulations to all of the winners, and thank you to all who participated.

Overall, the meeting was highly successful in terms of scientific excellence, active student/postdoctoral participation, and attendance.

Speaker Abstracts

Keynote Address: Translational Toxicology: Integrative Mechanisms of Cell Death and Environmental Disease

Dean Jones, Ph.D., Emory University, Atlanta, GA

Abstract: Risk assessment and low-dose exposure biomonitoring are well-developed areas of translational toxicology. They both benefit from mechanistic understanding of hazards, but for toxicities clearly linked to specific exposures, neither critically depends upon such understanding mechanism. This talk focused on the challenging problem of addressing toxicity when the toxic agent does not independently cause disease but rather adversely impacts ongoing disease processes. Such toxicities may be common for developmental, cardiovascular, neurodegenerative, endocrine, digestive and other diseases, but are difficult to detect and virtually impossible to prove in the context of complex disease mechanisms and heterogeneities of the genome and exposome. New capabilities in chemical profiling by high-resolution metabolomics for personalized medicine portend a dramatic change in approach to study such toxicities. Quantitative information on >20,000 chemicals will be obtainable within an affordable cost structure for routine use in clinical medicine. With entry of such information into cumulative databases, one can perform metabolome-wide association studies (MWAS) of diseases, demographics and exposures. This supports a reverse translational toxicology in which chemical exposures are a component of the systems biology of disease. Application of high-resolution metabolomics in small cohorts provides examples of new chemical associations with disease. Importantly, integrative omics, in which metabolomics is combined with genomics, epigenomics, transcriptomics, and proteomics, already demonstrates

that complex mechanisms of disease can become tractable by reverse translation of chemical associations in human MWAS to animal and cell models of exposure.

Roles of the Mitochondrial Membrane Permeability Transition Pore in Mediating Cell Injury and Cell Death

Gary Fiskum, Ph.D., University of Maryland – Baltimore, Baltimore, MD

Over 3000 articles have been published focusing on the mitochondrial membrane permeability transition (MPT). The MPT refers to a non-selective increase in the permeability of the inner membrane to ions and solutes with molecular weights <1500 that is induced by a combination of accumulated mitochondrial matrix Ca^{2+}, oxidative stress, and the presence of free fatty acids. The MPT is inhibited by physiological levels of adenine nucleotides and Mg^{2+}, and by some cyclophilin drugs, e.g., cyclosporin A. While the MPT may play a physiological role in regulation of mitochondrial and cytosolic Ca^{2+} levels in cell microenvironments, its role in triggering cell death is better characterized. Opening of the permeability transition pore (PTP) results in matrix proton influx and Ca^{2+} efflux, resulting in inner membrane depolarization and uncoupling of electron transport from ATP formation. Left unchecked, the MPT therefore results in net ATP hydrolysis, cellular deenergization, collapse of transmembrane ionic gradients, and necrotic cell death. Recent evidence indicates that the molecular identity of the PTP is dimers of the mitochondrial F1F0 ATP synthase, whose formation occurs in response to structural modifications of the closely associated protein cyclophilin D caused by elevated Ca^{2+} and cysteine sulfhydryl oxidation. Examples of medical problems associated with cell death induced by PTP opening include cardiac, brain, and renal ischemia, heart failure, and toxicity induced by heavy metals, ethylmercury, acetaminophen, and even alcohol. Mitochondria within tumor cells are typically resistant to PTP opening, which may increase resistance of cancer cells to chemotherapy. Such resistance can be due to increased expression of anti-death proteins, e.g., Bcl2 and $Bclx_L$. While the MPT may contribute to the release of mitochondrial proteins, e.g., cytochrome c, that trigger apoptotic cell death, most evidence indicates that PTP opening is far more effective at inducing necrotic cell death. Drug development and clinical trials that are directed at either inhibiting or activating PTP opening are in progress, aimed at inhibiting the death of normal cells and promoting the death of cancer cells, respectively.

Roles of BCL-2 proteins in linking energetics to apoptosis

J. Marie Hardwick, Ph.D., Johns Hopkins University, Baltimore, MD

Abstract: Both anti- and pro-apoptotic Bcl-2 family proteins are important for embryonic development, for neuronal activity, and for mitochondrial dynamics. They are expressed in many adult tissues, and are deregulated in many tumors. However, the conserved biochemical function that explains how the 3-dimensional structure shared by pro- and anti-apoptotic Bcl-2 family proteins functions to regulate cell death remains a mystery. We have uncovered unexpected pro-survival functions of pro-apoptotic Bax, Bak and Bad in animals and in cultured cells, and we have found novel activities and pro-death functions of the anti-apoptotic Bcl-2 and Bcl-x_L proteins. In search of the biochemical mechanisms to explain their normal cellular functions in healthy cells, we have studied Bcl-2 family proteins in regulating metabolism and mitochondrial membrane structure using several model systems including mammalian knockout mouse neurons and their mitochondria, synthetic lipid vesicles and yeast

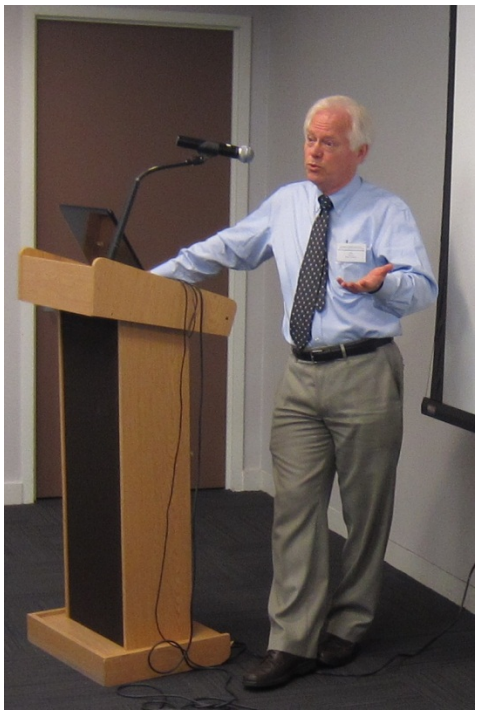
genetics. Exploration of knockout mice has uncovered a role of Bcl-x_L in regulating mitochondrial membrane potential via complex V, supported by studies in yeast (*Saccharomyces cerevisiae*) lacking the beta subunit of the F_1F_O ATP synthase. We further developed yeast as a model system for the study of gene-dependent cell death, leading to new insight into the global effects of mutations in any one gene (potentially triggered by environmental toxins) on genome evolution. These studies have uncovered an unexpected degree of genome evolution leading to the identification of new human disease genes.

Translation of Basic Scientific Information on Mechanisms of Cell Injury / Cell Death for Chemical Risk Assessment

Rita Schoeny, Ph. D., US EPA, Washington, DC

No abstract available.

Key note speaker Dr. Jones



Symposia attendees

2013 FALL SYMPOSIUM

NCAC-SOT is in the process of planning the annual fall symposium. We are still working on the details so please look for emails soon with more information.

2014 ANNUAL SOT MEETING INFORMATION

The SOT 53rd Annual Meeting is March 23–27, 2014, at the Phoenix Convention Center in Phoenix, Arizona. Online registration is now open and abstract submittal ends October 7, 2013. Housing is now open also. See http://www.toxicology.org/AI/MEET/AM2014/am.asp for more information.

NCAC-SOT Treasurer's Report – July 12, 2013

by

Chris Sheth, Treasurer

Account activity since last report

(Dated December 17, 2013 in January 2013 Newsletter)

November 30, 2012 (Closing balance)				**$8, 416.99**
Debits				
	Girl Scout Science Day	Science Supplies, etc.	$1,330.17	
	2013 Annual SOT Meeting – San Antonio	Reception	$1,912.23	
		Poster Awards	$1,650..00	
	NCAC-SOT Spring Meeting - May 23, 2013 "Mechanisms of Cell Injury and Cell Death-Applications for Mode of Action Risk Assessment"	Hall of States	$1,915.72	
		Name badges	$79.99	
		Poster boards	$414.00	
		Student Poster Awards	$600.00	
		Speaker Travel	$344.31	
		Lunch	$904.43	
	Total Debits		**$9,150.85**	(-$733.86)
Credits				
	Dues		$3,080.00	
	NCAC-SOT Spring Meeting - May 23, 2013 "Mechanisms of Cell Injury and Cell Death-Applications for Mode of Action Risk Assessment"	Pre-meeting registration	$1,200.00	
		Onsite registration	$540.00	
	Total Credits		**$4,820.00**	($4,086.14)
June 30, 2012* (Closing balance) *Most recent bank statement in our possession.				**$4,110.05**

National Capital Area

MEMBERSHIP APPLICATION

Name: _____

Affiliation: _____

Address _____

_____

City: _____

State: _____ Zip Code: _____

Area Code: _____ Phone: _____FAX:_____

E-mail: _____

Membership Type _____ Full Member ($25) _____ Student ($10)

Please check the most appropriate responses:

SOT Member	Highest Degree Attained		Type of Affiliation
_____ Yes	_____ A.S.	_____ M.P.H.	_____ Academia
_____ No	_____ B.A.	_____ M.S.	_____ Consulting
	_____ B.S.	_____ M.A.	_____ Contract Lab
	_____ D.V.M.	_____ Ph.D.	_____ Government
	_____ D.V.M./Ph.D.	_____ Sc.D.	_____ Industry- Chemical/Petroleum
	_____ M.D.	_____ V.M.D.	_____ Industry- Pharmaceutical
	_____ M.D./Ph.D.	_____ V.M.D./Ph.D.	_____ Industry- Other
			_____ Other- _____

Please complete the information above and send with a check, money order or credit card (payable to National Capital Area Chapter SOT, no POs) to the address below. The NCAC SOT will review your application, and you will be notified within 30 days. Those not accepted will receive a full refund. ***Current RC members: please do not use this form since your renewal dues are billed annually through SOT.***

Payment Type: Money Order_____ Check _____ Credit Card _____
Credit Card # _____ Exp date _____
Name on Card _____

Signature _____

Send to:
Christopher Sheth, Treasurer *11102 Lund Place*
NCAC-SOT *Kensington, MD 20895*
Sheth.Christopher@epa.gov