TOM Hughes

GEMS

Genetics and Environmental Mutagenesis Society

25th Annual Fall Meeting

"Current and Future Issues in Environmental Toxicology"

Monday October 29, 2007

Radisson Hotel
150 Park Drive
Research Triangle Park, NC

2007 Board of Directors

Officers

President
Greg Stuart*
NIEHS
MD E3-01
PO Box 12233
RTP, NC 27709
(919) 541-5424
stuart@niehs.nih.gov

President-Elect
Rose Anne McGee*
NIEHS
MD EC-30
PO Box 12233
RTP, NC 27709
(919) 541-0752
mcgee1_@niehs.nih.gov

Secretary
Gloria Jahnke
Private Consultant
8405 Union Grove
Church Road
Chapel Hill, NC 27516
(919) 967-5558
gjahnke@bellsouth.net

Interim Treasurer
Gloria Jahnke**
Private Consultant
8405 Union Grove
Church Road
Chapel Hill, NC 27516
(919) 967-5558
gjahnke@bellsouth.net

2005-2007 Councilors

Errol Zeiger
Errol Zeiger Consulting
800 Indian Springs Road
Chapel Hill, NC 27514
(919) 932-3778
zeiger@nc.rr.com

Jayne Boyer
UNC-CH CB# 7525
Dept. of Pathology
4105 Neuroscience
Research Bldg.
Chapel Hill, NC 27599
(919) 966-6921
jayne bover@med.unc.edu

Janice Allen*
NIEHS MD EC-30
PO Box 12233
RTP, NC 27709
(919) 541-7556
allen9@niehs.nih.gov

Webmaster
Frank Stack
Alpha-Gamma Technologies
4700 Falls of the Neuse Rd.
Suite 350
Raleigh, NC 27609
(919) 882-3913
fstack@alpha-gamma.com

2006-2008 Councilors

Jeffrey Ross
US EPA
NHEERL MDB143-06
RTP, NC 27711
(919) 541-2974
ross.jeffrey@epa.gov

Mac Law
NCSU
College of Veterinary Medicine
Raleigh, NC 27606
(919) 515-7411
mac_law@ncsu.edu

Cindy Innes*
NIEHS
PO Box 12233
RTP, NC 27709
(919) 541-4721
innes@niehs.nih.gov

Corporate Sponsor Coordinator
Julie Ginsler
PerkinElmer
Life & Analytical Sciences
(919) 553-4698
Julie.ginsler@perkinelmer.com

Membership Coordinator
Carolyn Harris
4107 Kildrummy Ct
Durham, NC 27705
(919)401-9787
carolynharris@privatedata.com

2007-2009 Councilors

Stephen B. Little
US EPA
NCCT MD D343-03
RTP, NC 27711
(919) 541-0963
little.stephen@epa.gov

Dan Shaughnessy*
NIEHS MD EC-21
PO Box 12233
RTP, NC 27709
(919) 541-2506
shaughn1@niehs.nih.gov

Kristine L. Witt*
NIEHS MD EC-32
PO Box 12233
RTP, NC 27709
(919) 541-2761
witt@niehs.nih.gov

Student Member
Dana Dolinoy
Duke University Medical Center
Box 3433
Durham, NC 27710
(919) 684-6203
dcd@duke.edu

Post-Doctoral Member
Dario C. Ramirez*
NIEHS MD FO-02
PO Box 12233
RTP, NC 27709
(919)541-3866

* Individual serves in his/her personal capacity
** Replacing Susan Ross

GEMS

Genetics and Environmental Mutagenesis Society

P.O. Box 13475, Research Triangle Park, North Carolina 27709

Dear GEMS Members:

It is a special honor for me to welcome you to our 25th Annual Fall Meeting! I'd like to congratulate President-Elect RoseAnne McGee for putting together an outstanding program focused around the topic "Current and Future Issues in Environmental Toxicology." Being the 25th Anniversary Meeting, the duties associated with planning and organizing this meeting were especially challenging, and RoseAnne dedicated herself to making this a memorable event. Continuing this success, I can't think of a better individual to take over as President for the coming year.

I would like to extend a very special thank you to our Corporate Sponsors, many of whom are long-term benefactors and supporters of our Society. A special time slot has been reserved for the Corporate Sponsors, who will exhibit their most current products and laboratory equipment. In return for their support, we encourage each of you to show your appreciation by discussing with them your laboratory needs. Regardless of whether or not you are directly involved "at the bench," please take some literature and contact information, for your laboratory, or a colleague.

GEMS operates on a volunteer basis, with the continuance of the Society dependent on the tireless contributions of our Members, particularly our Board of Directors. At this time I would especially like to thank the Board Members for 2006-2007, including President-Elect RoseAnne McGee, Treasurer Susan Ross, Secretary Gloria Jahnke, and Councilors Janice Allen, Jayne Boyer, Cindy Innes, Mac Law, Stephen Little, Jeff Ross, Dan Shaughnessy, Kristine Witt, and Errol Zeiger, Student Member Dana Dolinoy, and Post-Doctoral Member Dario Ramirez. I would also like to acknowledge our Membership Coordinator, Carolyn Harris.

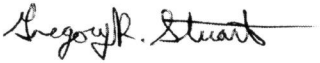
There are a number of other people who deserve special recognition for their efforts on behalf of GEMS, including Kristine Witt, who arranges for the various awards (plaques, etc.) for the Spring and Fall meetings, and Julie Ginsler, our Corporate Sponsor Representative. I'd also like to single out the tireless efforts over many years of three individuals:

Treasurer Susan Ross for exceptional dedication to service; Webmaster Frank Stack, who most recently designed our new web site (http://gems-nc.org/); and Secretary Gloria Jahnke, who has tirelessly assisted with the Program Guides, Meeting Registrations, and for the last several months, has also doubled as Treasurer, following Susan Ross' return to school as a full-time student. I would also like to acknowledge the contributions past-President Diane Spencer, who is always available to help with the assembly of the Program Guides and the Registration Table, and Councilor Cindy Innes, who has also helped out at the Registration Table for the past several meetings. Last but not least, I'd like to thank several Board and General Members have served as "anonymous" judges at the Fall Meetings. To these, and all other unnamed individuals, I extend our collective expressions of appreciation.

GEMS provides an important contribution to the local scientific community through our Annual Spring and Fall Meetings. In addition to providing a forum for local and invited Speakers focused around themes of current interest, these meetings provide an opportunity for all interested individuals to participate, interact, and get to know each other's scientific interests. One of the most important activities of GEMS is to encourage the growth and development of our young scientists. The GEMS meetings offer students and young scientists the opportunity to learn something new about in area in which they might not be very familiar, and permit their interaction with colleagues and other mentors. I encourage our junior colleagues to take full advantage of this opportunity, and our more senior Members to "greet and meet" these individuals.

I have truly enjoyed my multi-year tenure on the GEMS Board as Councilor, President-Elect and President, and my interactions with an exceptional group of people. It has been an honor and privilege to serve as your President. A main focus of my Presidency has been to try to increase the interest and participation of the local scientific community, including students, with regard to GEMS. Given the many demands on all of us, particularly in a locale such as RTP with its myriad conferences and seminars, this has been especially challenging. I am therefore heartened by the continuing and strong expression of interest by those willing to serve on the Board of Directors. I am fully confident that GEMS will continue to succeed and lead the local scientific community, for the next 25 years and beyond!

Sincerely,



Greg Stuart,
GEMS President

DAVID PRICE
4TH DISTRICT
NORTH CAROLINA

COMMITTEE ON APPROPRIATIONS
CHAIR, HOMELAND SECURITY
COMMERCE, JUSTICE AND SCIENCE
TRANSPORTATION, HOUSING AND
URBAN DEVELOPMENT

CONGRESS OF THE UNITED STATES
HOUSE OF REPRESENTATIVES
WASHINGTON, DC 20515

2162 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515
(202) 225-1784

5460 TRINITY ROAD, SUITE 205
RALEIGH, NC 27607-3815
(919) 859-5999

88 VILCOM CENTER, SUITE 140
CHAPEL HILL, NC 27514-1689
(919) 967-7924

N.C. MUTUAL PLAZA
411 WEST CHAPEL HILL STREET
DURHAM, NC 27701-3842
(919) 688-1504

www.price.house.gov

August 10, 2007

Genetics and Environmental
Mutagenesis Society Fall Meeting
Radisson Hotel
Research Triangle Park, North Carolina

Dear Participants:

Thank you for providing a respected forum at your fall meeting to share GEMS's expertise and interest in genetic factors and environmental agents that may pose genetic risks to humans. Your discussions of *Current and Future Issues in Environmental Toxicology* will enhance the safety of all our citizens, and I hope that your time together will add to your knowledge base and inspire your commitment to this important work. I regret that I am unable to join you on October 29 because of prior commitments and votes in Washington.

I am delighted that GEMS offers substantive awards to young people pursuing careers in environmental sciences and know that interest from adult role models will encourage the junior scientists' advancement. Thank you for incorporating that support into your mission.

Congress has an obligation to continue its investment in biomedical and environmental research, and I will continue to be your advocate. Please let me know when I can be of assistance in the future.

Sincerely,

David Price
Member of Congress

DP:ra

Special Thanks to NIEHS, The Hamner Institutes for Health Sciences, Dr. David Doolittle and RJ Reynolds Tobacco Company for their financial support.

AGENDA
25th Fall Meeting

Genetics and Environmental Mutagenesis Society

October 29, 2007

Radisson Hotel
150 Park Drive
Research Triangle Park, NC

"Current and Future Issues In Environmental Toxicology"

8:00 - 8:30 Registration and Beverages

8:30 - 8:45 Welcome: Dr. Greg Stuart, GEMS President,
Speaker Introduction: RoseAnne McGee, GEMS President-Elect

8:45 - 9:00 Opening Remarks: Dr. Sam Wilson, Acting Director, NIEHS

9:00 - 9:45 Dr. Randy Jirtle, Radiation Oncology, Duke University, *"Epigenetics: The New Genetics of Toxicology"*

9: 45 - 10:30 Dr. Andrew Maynard, Woodrow Wilson International Center for Scholars, Smithsonian Institution, *"Nanotechnology: The next big thing, or much ado about nothing?"*

10:30 Sponsor Exhibits (Beverages served)

11:00 Poster Presentations

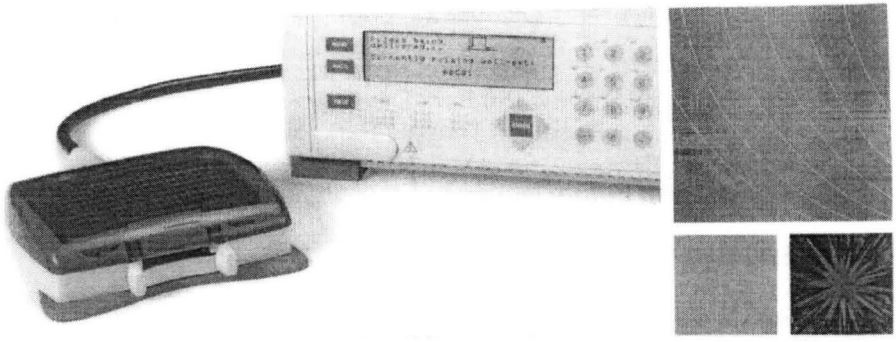
11:45 - 1:00 Lunch
Business meeting during lunch - 25 years of GEMS, Sponsor Recognition

1:00 – 2:30 Presented Papers (6)

2: 30 - 3:15 Dr. Ann Richard, National Center for Computational Toxicology, United States, Environmental Protection Agency, *"Toxico-Cheminformatics: A New Frontier for Predictive Toxicology"*

3:15 Announcement of Award Winners – Poster Presentations, Presented Papers, Presidents Travel Award to the Environmental Mutagen Society (EMS) Meeting

3:30 – 5:00 Reception



Optimize for
Better Results

Gene Pulser MXcell™ Electroporation System

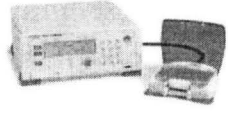
Optimize Your Research Time
- Use a preset optimization protocol or a gradient protocol to decrease programming time
- Process an entire multiwell plate in 2 minutes or less

Optimize Your Resources
- Use fewer cells and less sample — siRNA or DNA — by defining electroporation parameters

Optimize Your Reading Time
- Take advantage of Bio-Rad's extensive library of electroprotocols

Optimize Your Experimental Conditions
- Program up to 24 electroporation protocols, with replicates, on a single plate

Optimize Your Bench Space
- Perform high-throughput screening and standard laboratory-scale experiments



For more information, contact senior account manager Fran Moses at 1-800-878-3425 x1813 or e-mail fran_moses@bio-rad.com

BIO-RAD

Invited Speakers

Dr. Randy Jirtle is Professor of Radiation Oncology at Duke University. He is a member of the Duke University Program of Genetics, the Duke University Cell and Molecular Biology Training Program, and the Duke Lemur Center's Internal Advisory Committee. He received MS and PhD degrees from the University of Wisconsin-Madison. Dr. Jirtle was also a Postdoctoral Fellow in Physiology at the University of Wisconsin-Madison. He is an author on over 150 publications and 18 book chapters. Published articles from Dr. Jirtle's laboratory have been featured on the covers of several journals, including *Genome Research*, *Bioessays*, and *Molecular and Cellular Biology*. Invited talks include the Szulman Lecture and the Fetterman Endowed Lecture at the University of Pittsburgh, the National Cancer Institutue Distinguished Seminar Lecture on "Evolution of Imprinted Cancer Susceptibility Genes", and the Nobel Symposium on Epigentic Reprogramming in Development and Disease. Dr. Jirtle is an editorial board member for the journals, *Hepatology*, *Toxicological Sciences*, *Comparative Hepatology*, and *Epigentics*. His research interests focus on epigenetics, genomic imprinting and disease susceptibility. Dr. Jirtle's laboratory has identified the imprinted *mannose 6-phosphate/insulin-like growth factor 2 receptor (M6P/IGF2R)* as a tumor suppressor gene that is mutated in breast, esophageal, head and neck, liver, lung and prostate cancers.

ABSTRACT
Epigenetics: The New Genetics of Toxicology
Randy L. Jirtle, PhD, Department of Radiation Oncology,
Duke University Medical Center, Durham, NC

Traditional research on the combined effects of the environment and genetics on individual variation in disease risk examines the relationship between disease susceptibility, environmental exposures and germline mutations in the coding and promoter regions of genes. Such research efforts have highlighted the importance of genotype in human diseases. It is now clear, however, that a full understanding of environmental interactions with the genome will also require epigenetic mechanisms to be taken into account.

Human epidemiologic studies provide strong evidence that prenatal and early postnatal environmental factors influence the adult risk of developing a variety of chronic diseases, such as cancer, cardiovascular disease, diabetes, obesity and even behavioral disorders like autism and schizophrenia. Moreover, the link between what we are exposed to *in utero* and disease formation in adulthood appears to involve epigenetic modifications, like DNA methylation at metastable epiallele and imprinted gene loci [1].

Genomic imprinting is an epigenetic form of gene regulation that results in monoallelic, parent-of-origin dependent gene expression [2]. The functional haploid state of imprinted genes makes them susceptibility loci for diseases since a single genetic or epigenetic mutation can alter their function. We have recently developed a computer-learning algorithm that identified 600 imprinted-candidate genes in the mouse [3]. Interestingly, humans are predicted to not only contain fewer imprinted genes, but the repertoire is strongly species dependent [4]. By mapping the human imprinted-gene candidates onto the landscape of disease risk defined by linkage analysis, we are now poised to determine the importance of imprinting in the etiology of complex human diseases and neurological disorders.

Genes with metastable epialleles have highly variable expression because of stochastic allelic changes in the epigenome rather than mutations in the genome. The viable yellow agouti (A^{vy}) mouse harbors a metastable *Agouti* gene because of an insertion of a transposable element. We have used the A^{vy} mouse to investigate the importance of nutrition in determining the susceptibility of offspring to adult diseases [5,6]. We have shown that maternal dietary supplementation during pregnancy, with either methyl donors (i.e. folic acid, vitamin B_{12}, choline and betaine) [5] or genistein [6], decreases adult disease incidence in the offspring by increasing DNA methylation at the A^{vy} locus. Moreover, these nutritional supplements can counteract the CpG hypomethylation caused by the endocrine disruptor, bisphenol A [7]. (Supported by NIH grants ES13053, ES08823, ES015165 and T32-ES07031, and DOE grant DE-FG02-05ER64101).

References

1. Jirtle, R.L., and Skinner, M.K. Environmental epigenomics and disease susceptibility. *Nat. Rev. Genet.* 8: 253-562, 2007
2. Jirtle, R.L., and Weidman, J.R. Imprinted and more equal. *Am. Sci.* 95: 143-149, 2007.
3. Luedi, P.P., Hartemink, A.J., and Jirtle, R.L. Genome-wide prediction of imprinted murine genes. *Genome Res.* 15: 875-884, 2005.
4. Luedi, P.P., Dietrich, F.S., Weidman, J.R., Bosko, J.M., Jirtle RL, and Hartemink, A.J. Computational and experimental identification of novel human imprinted genes. *Genome Res.* 17: (in press) November, 2007.
5. Waterland, R.A., and Jirtle, R.L. Transposable elements: targets for early nutritional effects on epigenetic gene regulation. *Cell. Mol. Biol.* 23: 5293-5300, 2003.
6. Dolinoy, D.C., Weidman, J.R., Waterland, R.A., and Jirtle, R.L. Maternal genistein alters coat color and protects A^{vy} mouse offspring from obesity by modifying the fetal epigenome. *Environ. Health Perspect.* 14: 567-572, 2006.
7. Dolinoy, D.C., Huang, D., and Jirtle, R.L. Maternal nutrient supplementation counteracts bisphenol A-induced DNA hypomethylation

in early development. *Proc. Natl. Acad. Sci. USA* 104: 13056-13061, 2007.

Dr. Andrew Maynard serves as the Chief Science Advisor to the Project on Emerging Technologies at the Woodrow Wilson International Center for Scholars. He received a PhD from the Cavendish Laboratory at Cambridge University, studying ultrafine aerosol particle collection and analysis. From 2000-2005, Dr. Maynard was a Senior Science Fellow at the National Institute for Occupational Safety and Health (NIOSH), establishing research programs in both ultrafine aerosol analysis and in nanotechnology. The focus of the NIOSH nanotechnology research program was to better understand the occupational health risks of nanomaterials and to develop guidelines for workplace exposures to these materials. Dr. Maynard has served as a member of the Nanomaterial Science, Engineering and Technology subcommittee of the National Science and Technology Council (NSET) and co-chaired the NSET working group on Nanotechnology Health and Environment Implications (NEHI). Dr. Maynard is a member of the Executive Committee of the International Council on Nanotechnology and chaired the International Standards Organization Working Group on size selective sampling in the workplace. He holds an Associate Professorship at the University of Cincinnati and is an Honorary Senior Lecturer at the University of Aberdeen, United Kingdom. He serves on the editorial boards of *Nanotoday*, the *Journal of Nanoparticle Research*, the *Annals of Occupational Hygiene and Nanotoxicology* and is an author on over 80 scientific publications.

ABSTRACT

Nanotechnology: The next big thing, or much ado about nothing?

Andrew D. Maynard, Chief Science Advisor, Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, Washington DC

Nanotechnology—engineering products at near-atomic and molecular scales—has variously been described as a transformative technology, an enabling technology and the next technological revolution. Even accounting for a certain level of hype, a heady combination of high-level investment, rapid scientific progress and exponentially increasing commercialization, point towards nanotechnology having a fundamental impact on society over the coming decades. The unprecedented control that nanotechnology is giving us to place groups of atoms exactly where we want them, is opening up the doors to truly innovative developments, including stronger, lighter materials; new ways of producing, storing and using energy; faster, more powerful computers; and highly specific medical treatments. Yet the same properties that make the products of nanotechnology so exciting also have the potential to be harmful in

unique ways (Oberdörster, Stone et al. 2007). Understanding how these new nano-materials might cause harm is an essential first step towards developing successful and sustainable nano-industries (Maynard, Aitken et al. 2006). Undoubtedly, emerging nanotechnologies do have the potential to become the "next big thing"; but only if we get things right at the start and ensure that we know enough about the risks to fully realize the benefits (Maynard 2007).

References

1. Maynard, A., D. (2007). "Nanotechnology: The next big thing, or much ado about nothing?" Ann. Occup. Hyg. 51: 1-12.
2. Maynard, A. D., R. J. Aitken, et al. (2006). "Safe handling of nanotechnology." Nature 444(16): 267-269.
3. Oberdörster, G., V. Stone, et al. (2007). "Toxicology of nanoparticles: A historical perspective." Nanotoxicology 1(1): 2 - 25.

Dr. Ann Richard is a Principal Investigator in the National Center for Computational Toxicology at the United States Environmental Protection Agency in the Research Triangle Park in North Carolina. She received a PhD in Physical Chemistry from the University of North Carolina at Chapel Hill and received BA/BS degrees in Mathematics and Chemistry at the State University of New York at Oswego. Dr. Richard did her postdoctoral work at the US EPA in the Carcinogenesis Metabolism Branch. She is the recipient of numerous awards in the EPA National Health & Environmental Effects Laboratory, including awards for her work in the Computational Toxicology Program on the Distributed Structure-Searchable Toxicity (DSSTox) Public Database Network. She has been an invited speaker for numerous symposia and scientific meetings including the American Chemical Society, the Society of Toxicology, and the Environmental Mutagens Society. She is an on editorial boards member for *Mutation Research* and *Chemical Research in Toxicology*, serves on several advisory boards including the ILSI Working Group on Prediction of Developmental Toxicity, the LeadScope LIST Workgroup for Implementation of ToxML standard ontologies, and the Advisory Committee for Predictive Toxicity Challenge I, and has authored or co-authored over 50 publications.

ABSTRACT

Toxico-Cheminformatics: A New Frontier For Predictive Toxicology, **Ann Richard**, National Center for Computational Toxicology, Mail Drop D343-03, US EPA, RTP, NC

Efforts to improve public access to chemical toxicity information resources, coupled with new high-throughput screening (HTS) data and efforts to systematize legacy toxicity studies, have the potential to significantly improve predictive capabilities in toxicology. Important developments include: 1) large and growing public resources that link

chemical structures to biological activity and toxicity data in searchable format, and that offer more nuanced and varied representations of activity; 2) standardized relational data models that capture relevant details of chemical treatment and effects of published in vivo experiments; and 3) the generation of large amounts of new data from public efforts that are employing HTS technologies to probe a wide range of bioactivity and cellular processes across large swaths of chemical space. Chemical structure effectively links data across diverse study domains (e.g., 'omics', HTS, traditional toxicity studies), toxicity domains (carcinogenicity, developmental toxicity, neurotoxicity, immunotoxicity, etc) and database sources (EPA, FDA, NCI, PubChem, GEO, ArrayExpress, etc.). The DSSTox database network is evolving to more effectively support these capabilities. In addition, public initiatives (such as ToxML) are developing systematized data models of toxicity study areas, including mutagenesis, and introducing standardized templates, controlled vocabularies, hierarchical organization, and powerful relational searching capability across newly captured data. Cheminformatics and data models, in turn, are providing the underpinning for the large public HTS efforts of the NIH Molecular Libraries Initiative, as well as new toxicity-targeted HTS programs within the EPA and the NIEHS National Toxicology Program. These initiatives are turning the structure-activity paradigm on its head, using chemicals to probe biological space and generating "biological profiles" of chemicals that, along with chemical structure considerations, offer the promise of providing richer, and more relevant and predictive associations to in vivo responses. *This work was reviewed by EPA and approved for publication, but does not necessarily reflect EPA policy.*

Dr. Samuel H. Wilson joined the NIEHS in his present capacity in 1996. He has fostered basic medical research and disease prevention research during his tenure. He was instrumental in helping develop NIEHS' programs in genetic susceptibility, functional genomics, children's health research, minority institutions' research, and community outreach. Wilson also has strengthened partnerships between the NIEHS and other federal agencies concerned with environmental health. He received his training in medicine and biochemistry at Harvard Medical School, and began his research career at the NIH in 1970. In 1991, he moved to the extramural community to found a center focused in the areas of genetic toxicology and structural biology. An active researcher, Wilson is the principle investigator of the DNA Repair and Nucleic Acid Enzymology Group in the Laboratory of Structural Biology at the NIEHS. He has authored more than 300 research articles.

NOTES

GEMS 2007 Corporate Sponsors

Alpha-Gamma Technologies, Inc. offers a diverse line of life science and environmental services, including toxicologically relevant health-based risk assessments and regulatory development. We have expertise in bioinformatics, statistical modeling, and epidemiological analyses. We provide custom software, database products, network communications, Internet/network security, and quality assurance.

BARTLETT-WILLIAMS SCIENTIFIC RESOURCES
239 Flemington Road, Chapel Hill, NC 27517
Manufacturers' representative that supplies laboratory disposable and capital equipment, along with "niche" products for the biotechnology community.
Ann Williams, (919) 967-8111 justcallann@bartlett-williams.com
and **R. Gaye Rose**

Bio-Rad provides choices for methodologies, protocols, and products for protein purification and protein analysis to gene expression analysis. Bio-Rad offers an array of products relating to amplification, chromatography, electrophoresis, gene transfer, imaging, expression proteomics, multiplex suspension arrays, RNAi Solutions, and protein interaction analysis.
Fran Moses, Senior Account Manager, 1-800-876-3425, Ext. 1813, fran_moses@bio-rad.com

BioTrove's OpenArray is a nanoscale high throughput PCR platform supporting real-time qPCR, SNP genotyping, and endpoint detection. It is ideal for studies where panels of genes have been identified and large sample numbers need to be run.
Peter Bent, Account Manager, 919-688-4853, pbent@Biotrove.com

BMG LABTECH

BMG LABTECH offers the most complete line of microplate readers available. These have been designed to provide you with comprehensive solutions for life science, drug discovery, development and academic research. BMG LABTECH's broad line of multifunctional plate readers offers an immense range of measurement possibilities.
Scott Klayner, Product Specialist, 1-919-806-1735
scott.klayner@bmglabtech.com

GE Healthcare Life Sciences, a leading provider of biotechnology systems, products and services, was formed from GE Technologies and Amersham Biosciences and specializes in Chromatography, Imaging, Cellular Analysis and Molecular Biology Technologies.
Monica Nichols, Account Manager, 1-800- 526-3593 x5375,
MonicaNichols@ge.com
Beth Nye, Account Manager, 1-800-526-3593 x5664,
beth.nye@ge.com

Guava Technologies is a biotechnology company that develops, manufactures and markets unique integrated cellular analysis systems for the life science researcher's benchtop. The company is revolutionizing the way that cell culture monitoring and cell screening assays are performed, by providing compact micro-volume scale systems that make common assays in cell-based analysis accessible at the benchtop. Guava's products have broad applications to life sciences research, drug discovery and biopharmaceutical production today, but also offer potential for use in clinical testing and blood processing, as well as other areas where single cell analysis is important.
Todd Lewis, Regional Sales Manager, 919-412-9768
tlewis@guavatechnologies.com

ILS is a leading contract research organization that provides a comprehensive portfolio of research and testing services to our federal and commercial clients. Our GLP-compliant services include general toxicology, genetic toxicology, pharmacokinetics, molecular biology, histopathology and clinical research support. Our scientists have broad experience with animal models and *in vitro* systems.

ISC BioExpress is a full line distributor of the name brand supplies & equipment that life science labs have come to trust. Recent growth in the past 5 years now enables us to rival larger distributors like Fisher & VWR. Call on ISC BioExpress when shopping for reagents & biochemicals, consumables & disposables and capital equipment like centrifuges, thermal cyclers, freezers, refrigerators and all benchtop apparatus including pipetters, microscopes, homogenizers, pH meters, low volume spectrophotometers and much more.
Rob Blackman, Sales Rep, (919) 740-2313
rblackman@bioexpress.com

Microbiology International offers the highest quality laboratory automation systems available worldwide. We will feature the WASP spiral plater (eliminates most serial dilutions) and the ProtoCOL bacterial colony counter (ideal for Ames assay and mouse lymphoma studies.) Visit our website www: 800ezmicro.com for other laboratory automation systems.
Joyce Hahnel, Account Representative, 1 (800) 396-4276
joyce.hahnel@800ezmicro.com

A leading provider of innovative products and services. Cell culture filtration, Antibody based products, Protein purification and detection, Stem cell products, Cell signaling products, Respiratory/enterovirus detection products, Screening products, Kinase/GPCR/Ion channel, Biomarker and protein detection services, Lab Water Purification , Analytical sample prep devices
Pete Harrell, Senior Applications Specialist, 1 (800) 221-1975 x6612
pete_harrell@millipore.com

NALGENE® nunc™

Thermo SCIENTIFIC

MβP Molecular BioProducts

In addition to laboratory equipment, **Thermo Fisher Scientific** manufactures laboratory consumables such as **Nalgene, Nunc**, and **MBP** products as well as **Finn Pipettes** and tips. Look for our **Nunc** tissue culture plates, dishes, flasks, and assay plates, **Nalgene** and **Nunc** cryo storage systems, **Nalgene** filters, carboys, bottles, containers and general labware, **MBP Molecular BioProducts ART** aerosol resistant pipet tips, pipet tips for robotic systems, and **Finn Pipettes** (manual and electronic) in both single channel and multi channel.

Bob Sale: bob.sale@thermofisher.com
(919) 606-2041 (UNC Chapel Hill and East including RTP)
Doug Schweizer: Douglas.schweizer@thermofisher.com
(919) 395-0083 (Duke and West, and Southern VA)

You never know where your research will lead you, but we can help you get there. We offer a wide variety of labeling and detection technologies including radiochemical, chemiluminescent and fluorescent labeling and detection technology. Our offering includes the Victor and Envision Multi Detection Plate Readers, Scintillation Counters, Geliance Gel Doc Systems, Microarray Scanners, Automated Liquid Handling and several platforms for GPCR analysis and cellular based assays.

Julie Ginsler, Account Manager, (919) 522-6741
Julie.ginsler@perkinelmer.com
Jeremy Sanders, Instrument Specialist, (919) 491-8267
Jeremy.sanders@perkinelmer.com

RJReynolds

R.J. Reynolds , an indirect subsidiary of Reynolds American Inc. (NYSE: RAI), is the second-largest tobacco company in the U.S. They have supported the GEMS Society for several years.

Roche Applied Science

The Art of Biochemistry

The Art of Biochemistry - *Inspiring the imagination and intellect for life science research and industry.* With more than a century of experience in its field, Roche Applied Science is one of the world's leading producers of reagents and systems for life science research.

Susan Barbee, Account Manager, 800.845.7355 ext. 28063, susan.barbee@roche.com

USA SCIENTIFIC

USA Scientific offers precise solutions for research. We offer a wide range of laboratory consumable products, such as: pipet tips, centrifuge tubes, PCR tubes and plates, gloves and tissue culture flasks, bottles and plates as well as fetal bovine serum. In addition to consumables we also offer pipettors, freezer boxes and racks, centrifuges, electrophoresis equipment and laboratory organization solutions.

Eric Thelen, Account Executive, 919-805-1611, Thelen@nc.rr.com

VISEN MEDICAL

VisEn's FMT System and Optical Probe Portfolio harness the well-known power of fluorescent technology in vivo by providing quantifiable molecular reporting in a range of diseases from deep within the body. VisEn's imaging probes are designed to provide a robust range of biologically specific imaging readouts in vivo. VisEn now offers over 20 different molecular probes for imaging key biologic processes and pathways in vivo, with more expected to be launched this year.

Elizabeth Bowman, Account Manager,ebowman@visenmedical.com

ACKNOWLEDGMENTS

The GEMS membership thanks each and every corporate member. Corporate members not only supply the society with necessary financial support, but also supply the members with essential technical information and equipment.

The GEMS membership and Board of Directors acknowledge and appreciate your support, and the society looks forward to your participation in 2008.
Thank you!

Happy Holidays and best wishes for the New Year.

Poster Presentations

*P1 Fuctionality and Viability of Rat Hepatocytes Cultured on SAMs Modified ITO Substrates

Rajendra K. Aithal [1], **Christa Watson** [2], Deepak P. Kumaraswamy [1], David K. Mills [1],3, Debasish Kuila [2]
Department of Chemistry, [2] North Carolina A&T State University, Greensboro, NC 27406
[1] Institute for Micromanufacturing,
[3] School of Biological Sciences,
[1] Louisiana Tech University, Ruston, LA 71272

Development of cell culture platforms (CCPs) for drug toxicity screening requires a suitable choice of substrate facilitating efficient attachment and proliferation of cells. Biocompatibility, maintenance of cell phenotype and long-term functionality of cell culture are parameters that govern the choice of substrate. Self assembled monolayers (SAMs), ordered molecular assemblies formed by the adsorption of a surfactant onto a solid surface, provide a means to regulate surface chemistry more precisely and enhance surface properties facilitating enhancement of cell adhesion. Hepatocytes, liver cells, were seeded on indium tin oxide (ITO) substrates modified with SAMs of: 3-(aminopropyl) triethoxysilane [APTES, -NH2 end group], 1-octadecanethiol [1-ODT, -CH3 end group] and 3-(mercaptopropyl)triethoxysilane [MPS, -SH end group]. Liver specific functions such as total protein synthesis and lactate dehydrogenase (LDH) leakage along with cell viability and quantitative proliferation were determined. These studies provide valuable resources for studying cell-substrate interactions and arrive at a suitable choice of substrate for the development of stable SAM based cell culture platforms (SCCPs). Our goal is to develop bioreactors for drug toxicity screening and novel biosensors for detection of pathogens and toxicants.

* Ms. Watson is a doctoral candidate in the Energy and Environmental Sciences Program, North Carolina Agricultural and Technical State University, Greensboro, NC

P2 The DNA polymerase γ Y955C disease variant associated with PEO and parkinsonism mediates the incorporation and translesion synthesis opposite 7,8-dihydro-8-oxo-2'-deoxyguanosine

Rachelle J. Bienstock(2),Maria A. Graziewicz(1),
William C. Copeland(1,2)

(1)Laboratory of Molecular Genetics and (2)Scientific Computing Laboratory, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC 27709 (2) Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC 27599

DNA polymerase γ, encoded by the POLG gene, is responsible for the repair and replication of mitochondrial DNA . The Y955C mutation in POLG leads to autosomal dominant progressive external ophthalmoplegia (PEO) with other severe phenotypes. PEO patients with this mutation can further develop parkinsonism or premature ovarian failure. Mouse and yeast Y955C models show an increased amount of oxidative lesions and increased mtDNA damage. In DNA pol γ, Tyr955 plays a critical role in catalysis and high fidelity DNA synthesis. 7,8-dihydro-8-oxo-2'-deoxyguanosine (8-oxo-dG) is one of the most common oxidative lesions in DNA and can promote transversion mutations. Mitochondria are thought to be a major source of endogenous reactive oxygen species that can react with dG to form 8-oxo-dG as one of the more common products. DNA polymerases can mitigate mutagenesis by 8-oxo-dG through allosteric interactions from amino acid side chains, which limit the anti-conformation of the 8-oxo-dG template base during translesion DNA synthesis. Here, we show that the Y955C pol γ displays relaxed discrimination when either incorporating 8-oxo-dGTP or translesion synthesis opposite 8-oxo-dG. Molecular modeling and biochemical analysis suggests that this residue, Y955, in conjunction with Phe961 helps attenuate the anti-conformation in human pol γ for error free bypass of 8-oxo-dG and substitution to Cys allows the mutagenic syn conformation. Collectively, these results offer a biochemical link between the observed oxidative stress in model systems and parkinsonism in patients, suggesting that patients harboring the Y955C POLG mutation may undergo enhanced oxidative stress and DNA mutagenesis.

*** P3 The Effect of Age on Xenobiotic Metabolizing Enzyme Activity in Rat Liver Microsomes**

Camilla Mills * and Michael DeVito
North Carolina Central University (NCCU) and US Environmental Protection Agency (USEPA)

In the U.S., the number of aging adults is rapidly growing. By 2030, the number of elderly persons aged 65 and older is projected to double to 70 million. Many biochemical and physiological changes occur during the aging process which may affect the correlation between exposure, dose, and response to environmental chemicals. Normal aging of organs and

systems in the body results in decreased function in numerous areas. Because the liver is a key site of metabolism, it is probable that the hepatic clearance of environmental chemicals is altered in the aging adults. Additional research is needed to determine whether older adults are at risk for having an altered sensitivity to such chemicals. The objective of this research is to illustrate that age-dependent changes in xenobiotic metabolizing enzymes may result in older adults being more susceptible to environmental chemicals or pollutants. Young and old Brown – Norway (4, 12 and 24 months) and Fisher (6, 11, 18 and 24 months) rats were sacrificed, livers were removed and hepatic microsomes were prepared. Using these hepatic microsomes, ethoxyresorufin O-deethylase (CYP1A1), methoxyresorufin O-deethylase (CYP1A2), pentoxyresorufin O-deethylase (CYP2B2), caffeine biotransformation (CYP1A2), and deltamethrin clearance (CYP2C) activity were determined. Minimal changes in enzyme activity were observed in the Brown – Norway rats at the various ages. In the Fisher rats, CYP1A1 activity increased with age, with the 24 month old animals having the highest activities. CYP2B activity decreased in the 18 and 24 month old groups. CYP1A1/CYP1A2 activity (detected by the MROD assay) and CYP1A2 (detected by the caffeine biotransformation assay) showed minimal changes in enzyme activity at the different ages. Further research into the effects of aging on the metabolism of environmental chemicals may provide insight into potential altered sensitivity of the elderly to environmental pollutants. (This abstract does not represent USEPA policy).

*Ms. Mills is a NCCU Graduate Student, who has conducted her Masters research in Dr. DeVito's Laboratory at the US EPA within the EPA/NCCU Cooperative Research Training Agreement.

***P4 Genotoxicity Evaluation of Aresnic Compounds in the Mouse Lymphoma Assay. Mutational Spectrum Analysis**

Carolina Soriano, Amadeu Creus and Ricard Marcos
Group of Mutagenesis, Department of Genetics and Microbiology, Universitat Autònoma de Barcelona, 08193 Bellaterra, Cerdanyola del Vallès, Spain: CIBER Epidemiología y Salud Pública, ISCIII, Spain. (carolina.soriano@uab.es)

In this work we evaluated the mutagenicity of several arsenic compounds at the thymidine kinase (*Tk*) gene by using the mouse lymphoma assay (MLA). Moreover, we studied the mutational spectrum of arsenic trioxide using the induced mutant colonies. **Methods:** L5178Y was the cell line used at MLA. Cells were cultured and treated with different concentrations of the selected compounds, which have been two inorganic (sodium arsenite and arsenic trioxide) and four organic (monomethylarsonic acid, dimethylarsinic acid, tetraphenylarsenium and

arsenobetaine) compounds. In addition, we studied the mutational spectrum of arsenic trioxide using molecular techniques such as PCR and sequencing, analyzing the induced large/small mutant colonies of MLA. **Results:** The MLA results show that sodium arsenite, arsenic trioxide, monomethylarsonic acid and dimethylarsinic acid are genotoxic showing a clear dose-response pattern, but arsenobetaine and tetraphenylarsenium have shown negative results. Inorganic compounds are the most potent genotoxic agents tested. The small/large colony ratio increased over concentration which could indicate a clastogenic effect of the arsenic compounds. On the other hand, the results of the mutational spectrum with the large/small colony mutants of arsenic trioxide demonstrate that this trivalent arsenic compound induces mainly chromosomal mutations. **Discussion**: Our results reveal that inorganic arsenicals are more genotoxic than pentavalent methylated forms (MMA and DMA). Otherwise, the organic forms, arsenobetaine and tetraphenylarsenium are non-genotoxics. Furthermore, our data from mutant colonies induced by arsenic trioxide reinforce the idea that arsenic is effective in inducing chromosome mutations, in accordance with previously published results.

*Ms. Soriano is graduate student from the Universitat Autonoma de Barcelona (Spain), and staying for three months at UNC as a visiting scholar.

*** P5 UVA and Visible Light Induced Cytotoxicity of Fullerol in Human Lens Epithelial Cells**

Albert R. Wielgus [1], Joan E. Roberts [2], William K. Boyes [3], Usha Andley [4], and Colin F. Chignell [1],
[1] LPC, NIEHS, RTP, NC 27709, [2] Fordham University, New York City, NY 10023, [3] Neurotoxicology Division, NHEERL, EPA, RTP, NC 27711, [4] Washington University School of Medicine, St. Louis, MO 63110

The water-soluble, hydroxylated fullerene [fullerol, nano-$C_{60}(OH)_{22-26}$] has several clinical applications including use as a drug carrier to bypass the blood ocular barriers. We have assessed fullerol's potential ocular toxicity by measuring its cytotoxicity and phototoxicity induced by UVA and visible light *in vitro* with human lens epithelial cells (HLE B-3). Accumulation of nano-$C_{60}(OH)_{22-26}$ in the cells was confirmed spectrophotometrically and by light microscopy. Metabolic activity of the cells and cytoplasmic membrane permeability were estimated using MTS and LDH assays, respectively. Apoptosis and necrosis of HLE B-3 cells was quantified using flow cytometry. Interaction of fullerol with α-crystallin, a major lens protein was monitored by dynamic light scattering. Fullerol showed cytotoxicity to HLE B-3 cells maintained in the dark at

concentrations higher than 20 μM. Exposure to either UVA or visible light in the presence of >5 μM fullerol induced phototoxic damage. When cells were pretreated with lutein, N-acetyl cysteine, or L-ascorbic acid derivatives prior to irradiation, only the carotenoid significantly protected against fullerol photodamage. Apoptosis was observed in lens cells treated with fullerol whether or not the cells were irradiated, in the order UVA > visible light > dark. Dynamic light scattering showed that in the presence of the endogenous lens protein α-crystallin, large aggregates of fullerol were reduced. In conclusion, fullerol is both cytotoxic and phototoxic to human lens epithelial cells. Although the acute toxicity of water soluble nano-$C_{60}(OH)_{22\text{-}26}$ is low, these compounds are retained in the body for long periods, raising concern for their chronic toxic effect. Before fullerols are used to deliver drugs to the eye, they should be tested for photo- and cytotoxicity *in vivo*.

* Dr. Wielgus is post-doctoral fellow in the Photochemistry and Photobiology Workgroup, Laboratory of Pharmacology and Chemistry at NIEHS.

* An asterisk by the abstract number indicates that a presenter is competing for the Best Presented Paper or Poster Award. The Best Presented Paper will receive up to $1500 to be used to defray costs associated with attendance at a national meeting of his or her choice, pending Board approval. A winner in each of the three categories of Poster Award competition (post-doctoral fellow, technician and student) will receive a monetary award of $250. Candidates for the Presidents Travel Award are listed. The one time President's Travel Award will be used to the defray costs to the Environmental Mutagen Society meeting in 2008. If there are an insufficient number of entrants in any category, the Board of Directors will make alternate decisions regarding awards.

Additional Poster Presentation

*P6 $p19^{Arf}$ Expression in Transient Vasculature Systems of the Developing Mouse

Amy McCalla-Martin,[1,2], J. Derek Thornton [1], Michelle N. Mary [1], Stephen X. Skapek [1,3]
[1] St. Jude Children's Research Hospital, Memphis, TN, [2] North Carolina State University, College of Veterinary Medicine, Raleigh, NC,[3] University of Chicago Department of Pediatrics, Chicago, IL,

Recently it has been shown that the tumor suppressor gene Arf functions in regulation of perivascular cells of the developing mouse eye. These cells were specifically identified as the subtype of perivascular cells known as pericytes. Absence of the Arf gene results in retrolental accumulation of pericytes, and failed regression of the hyaloid vasculature system, a system which normally regresses in the early postnatal period in mice. The primary lesions culminate in retinal and lens degeneration and are reminiscent of the disease Persistent Hyperplastic Primary Vitreous in humans. Due to these findings, we sought to explore Arf's potential role in regulating pericytes of other vascular systems. We developed an Arf-LacZ reporter mouse in which Arf-expressing pericytes could be identified by xgal staining of whole mount preps of latex perfused and nonperfused vascular systems. $Arf^{LacZ/+}$ mice showed expected promoter activity in known Arf-expressing tissue (pericytes of the hyaloid artery and the seminiferous tubules). In addition, promoter activity was detected in pericytes of the umbilical arteries and the umbilical vein. In the $Arf^{LacZ/LacZ}$ knockout mice, abnormal accumulations of Arf–promoter-active pericytes could be seen in the vitreous as well as associated with the umbilical vessels. This data indicates that Arf is instrumental in regulating pericytes in multiple transient developmental vascular systems. Further understanding of this regulation may help in understanding vasculogenic abnormalities as well as provide therapeutic value in regulating tumor vasculature.

* Ms. McCalla-Martin is a doctoral candidate in the NCSU College of Veterinary Medicine, Raleigh, NC

NOTES

***T1 5-Methylchrysene Effects on Mutagenicity in Binary Mixtures with a Potent Metabolite or BaP: Antagonism in Cells Expressing hCYP1B1, But Additivity in Cells Expressing hCYP1A1.**

Sarfaraz Ahmad [1], Sandra Leone-Kabler [1], Johannes Doehmer [2], Charles S. Morrow [1], and Alan J. Townsend [1]
[1] Department of Biochemistry, Wake Forest University School of Medicine, Winston-Salem, NC, USA and [2] GenPharm Tox., Munich, Germany.

Polycyclic aromatic hydrocarbons (PAHs) are believed to induce cancer via metabolic activation by cytochrome P-450 (CYP) enzymes (primarily hCYP1B1 and hCYP1A1). Most carcinogenicity studies examine single chemicals; however, environmental pollutants occur in complex mixtures. We investigated potential antagonism or synergy of a mixture of the parent compound 5-methylchrysene (5-MC) and its 1,2-dihydro-1,2-dihydroxy-5-methylchrysene intermediate (5-MC-1,2-diol), using V79 cell lines stably transfected with either hCYP1B1 or hCYP1A1. We examined the inhibition of hCYP1B1 or hCYP1A1 in live cells at various concentrations of 5-MC. Activity of hCYP1B1 (IC_{50} ~ 70 nM), but not hCYP1A1 was inhibited by 5-MC in the fluorogenic Vivid assay. Addition of increasing 5-MC concentrations led to a dose-dependent decrease in cytotoxicity of the metabolite 5-MC-1,2-diol in hCYP1B1-expressing cells (IC_{50} values of 5-MC-1,2-diol alone = 0.054 μM; increased to 0.42 μM with 0.5 μM 5-MC added). 5-MC-1,2-diol alone (up to 1 μM) or in combination with 5-MC (up to 1 μM) were not cytotoxic in V79MZ control cells (no CYP expression). The mutation frequency at the *hprt* locus was also studied in hCYP1B1 cells exposed to 5-MC-1,2-diol (0.1 μM) in the presence or absence of 5-MC (1.0 μM). Significantly fewer mutant colonies were induced by combined exposure of 5-MC-1,2-diol (0.1 μM) and 5-MC (1.0 μM) (595 ± 54 colonies/10^6 cells) as compared to 5-MC-1,2-diol alone (753 ± 69 colonies/10^6 cells). The decrease in mutagenicity is likely due to significant inhibition of hCYP1B1 activity by 5-MC. In contrast, mutagenicity of after combined exposure to 5-MC-1,2-diol and 5-MC was significantly increased in hCYP1A1 transfected cells as compared to either PAH alone, consistent with the weak inhibition and strong mutagenicity of 5-MC in these cells. Mutagenicity of benzo[a]pyrene (BaP) was also significantly inhibited by 5-MC (1.0 μM) in hCYP1B1 cells but not in hCYP1A1 transfected cells. Similar to 5-MC-1,2-diol, an additive effect on mutation frequency of BaP in hCYP1A1 was noted in the presence of 5-MC. These results indicate that the presence of 5-MC results in a net antagonism of the mutagenicity of 5-

MC-1,2-diol or BaP in cells expressing hCYP1B1, due to the predominance of strong inhibition of hCYP1B1 by 5-MC in comparison to its activation to mutagenic metabolites. In contrast, weak inhibition of hCYP1A1 by 5-MC, together with relatively strong activation by hCYP1A1 results in net additivity of mutagenesis of 5-MC in combination with of 5-MC-1,2-diol or BaP.

* Dr. Ahmad is a Postdoctoral Fellow in the Biochemistry Department Wake Forest University, School of Medicine, Winston-Salem, NC

***T2 The Effects of Ethanol on Amniotic Fluid-Derived Stem Cells**

J.A. Hipp, J.D. Hipp, S. Soker, A. Atala, Wake Forest Institute for Regenerative Medicine, WFUSM, Winston-Salem, NC 27157

Ethanol is teratogenic and exerts pleiotrophic effects in the developing embryo. However, the effects of ethanol on stem cells remain unclear. Since stem cells have the ability to self-renewal and differentiate into multiple cell types, they can be used as a tool to elucidate mechanisms of ethanol's effect on organogenesis. Amniotic fluid-derived stem cells (AFSC) are multi-potent stem cells that express embryonic stem cell markers, differentiate in vivo into all 3 germ layers when injected into blastocysts, and have the capacity to differentiate in vitro into bone, muscle, fat, endothelium, liver, and neurons. Because this cell type has the capacity to differentiate into numerous types of cells, it provides an intriguing new model system with which to analyze potential mechanisms underlying the genesis of fetal alcohol spectrum disorders (FASD). We therefore exposed AFSC to varying ethanol concentrations to examine the impact of ethanol on stem cell properties. Our results demonstrate that ethanol exposure in vitro for 48 hours inhibits cell proliferation of AFSC by inducing a G1/S phase arrest without causing cell death. Microarray analysis identified a down-regulation of genes involved in cell growth, proliferation, and DNA replications and identified an up-regulation of genes involved in differentiation. The decrease in cell proliferation and increase in differentiation may suggest ethanol's role in inducing early maturation of AFSC.

* Ms. Jennifer Hipp is a graduate student in the Wake Forest Institute for Regenerative Medicine, Wake Forest University, School of Medicine, Winston-Salem, NC

***T3 Obesity and Perinatal TCDD Exposure Increases Mammary Tumors in FVB Mice**

Michele A. La Merrill[1,2,3], Linda S. Birnbaum[4], Robert D. Cardiff[5], David W. Threadgill[1,2,3].
Curriculum in Toxicology[1], Department of Genetics[2], Center for Environmental and Health Susceptibility[3], UNC, Chapel Hill, NC 27599. NHEERL[4], US EPA, 109 TW Alexander Drive, Durham, NC 27709. Center for Comparative Medicine[5], Department of Pathology and Laboratory Medicine, UCD, Davis, CA 95616.

Risk of breast cancer has been consistently shown to correlate to total lifetime exposure to estrogens. Because both TCDD exposure and the state of obesity interact with the estrogen pathway, we wanted to investigate how TCDD and obesity interact with mammary cancer susceptibility in a mouse model. Several rat models suggest that prenatal TCDD exposure promotes chemical models of mammary cancer. Therefore, at 12.5 days post conception, we exposed nulliparous FVB females to 1 μg/kg of TCDD. To model diet-induced obesity, the litters were put on high or low fat diet at parturition. Female offspring were exposed to DMBA at post-natal days (PND) 35, 49, 53, and monitored thereafter for tumor development. Lean DMBA-treated FVB without TCDD exposure had the longest tumor latency. Obese DMBA-treated FVB had substantially more mammary tumors than lean FVB. Tumors grew faster among obese litters compared to lean. While no mammary tumors arose in lean litters perinatally exposed to TCDD and a third of unexposed obese litters had mammary tumors, every obese litter perinatally exposed to TCDD had at least one mammary tumor. Among obese mice, exposure to TCDD was associated with a doubled mammary tumors incidence. TCDD was associated with adenomyoepitheliomas, lesions that are rare in DMBA-treated mice. In summary, obesity increases the sensitivity of FVB to DMBA-induced mammary carcinogenesis. Perinatal TCDD exposure appears to further increase the sensitivity of obese FVB. (This abstract does not reflect agency policy.) Supported by NCI grants (U01CA105417 and U01CA134240) to D.W.T.; Department of Defense Fellowship (BC050873) to M.A.L.; NIEHS Training Grant (T32ES007126); and NIH Center Grants (P30ES010126, P30DK056350 and P30CA016086).

* Ms. LaMerrill is a doctoral candidate in Toxicology at the University of North Carolina at Chapel Hill, Chapel Hill, NC

***T4 Two-Dimensional Gel Electrophoresis for the Analysis of Replication Stalling Effects of DNA Adducts in Human Cell Lines**

Amy L. Sloat, Dana C. Upton, Eric Routh, James P. Vaughn, Fred W. Perrino, Steven A. Akman,
Cancer Biology Department, Wake Forest University Health Sciences, Medical Center Boulevard, Winston-Salem, NC 27157

Ethanol is a carcinogen linked to a variety of cancer types, including esophageal, breast, liver, and endometrial. The formation of guanine adducts at the N2 position occurs upon the dehydrogenation of ethanol to acetaldehyde. Although the mechanisms for ethanol carcinogenesis are not fully understood, it is possible that point mutations and recombinations resulting from N2-ethyl-deoxyguanosine may play a role. N2-ethyl-deoxyguanosine is known to cause decreased progeny yield and increased the mutant fraction in both bacteria and human cell lines. These results are consistent with the hypothesis that N2-ethyl-deoxyguanosine may have replication fork stalling effects. Our studies focus on the effects N2-ethyl-deoxyguanosine adducts have on replication and the recombination that may result. Brewer-Fangman 2-dimensional gel electrophoresis methods are being developed to analyze the first round of replication of a modified pLSX plasmid in the absence and presence of N2-ethyl-deoxyguanosine adducts. Two-dimensional gels separate forks, bubbles, and double forks on the basis of their differences in mass in one dimension and structure and mass in the second dimension. Transfection of the pLSX plasmid into HeLa cells shows effective cell synchronization with mimosine. The release time from mimosine has been optimized to maximize the first round of replication, and the replication intermediates have been enriched with the use of BND cellulose columns. Post-replication digestion of the circular plasmid, opposite the SV40 origin, followed by 2-dimensional gel electrophoresis verifies bubble and fork arc replication patterns for the control pLSX plasmid. Transfection with the N2-ethyl-deoxyguanosine containing pLSX plasmid is expected to show accumulation patterns in the bubble arc as well as the generation of double fork patterns consistent with recombination at the stalled site.

* Ms. Sloat PhD is a post-doctoral trainee of Dr Steve Akman, Professor of Internal Medicine and Cancer Biology, Wake Forest University Health Sciences, Winston-Salem, NC

*T5 The N^2-Ethylguanine Adduct Primarily Exerts its Biological Activity via Replication Blockade

Dana C. Upton [1], Xueying Wang [1], Patrick Blans [2], Fred W. Perrino [1], James C. Fishbein [2], and Steven A. Akman [1]
[1] Wake Forest University Health Sciences, Winston-Salem, NC and [2] University of Maryland – Baltimore County, Baltimore, MD

Alcohol exposure is known to cause cancer, but the exact mechanism(s) of carcinogenesis are unknown. Ethanol and its metabolite acetaldehyde are known to cause DNA damage. Exposure to either ethanol or acetaldehyde can result in DNA adduct formation. Under physiological conditions, the primary DNA adduct formed after reaction of acetaldehyde and DNA can be reduced to N^2-ethylguanine (N^2-ethylGua). N^2-ethylGua has been detected in the blood and urine of human subjects. While N^2-ethylGua has been shown to block replicative DNA polymerases *in vitro*, little work has been done indicating the biological effects of the adduct. Considering the possibility that N^2-ethylGua might mediate some of the pro-carcinogenic effect of ethanol consumption, we sought to determine if N^2-ethylGua perturbs DNA replication *in vivo.* To do so, we inserted chemically synthesized N^2-ethylGua adducts site-specifically in a mutation reporting shuttle vector and observed the consequences of adduct-containing vector replication in various human cell lines. Our data show that the N^2-ethylGua adduct blocks translesion DNA synthesis in wild type HEK293 cells *in vivo.* Consistent with its replication blocking activity, N^2-ethylGua caused a decrease in the yield of progeny plasmids and a high prevalence of frameshift deletions. Previous *in vitro* work had shown that while replicative polymerases were blocked by N^2-ethylGua, the bypass polymerase η was not blocked. Using the same methodology, our experiments were repeated in cells lacking polymerase η. Our data indicate that polymerase η may play a role in the bypass of N^2-ethylGua *in vivo.* We therefore conclude that the mutagenic N^2-ethylGua adduct primarily exerts its biological activity via replication blockade.

* Ms. Upton is a graduate student at Wake Forest University Health Sciences, Wake Forest University, Winston-Salem, NC

***T6 The Type III Pantothenate Kinase in *Bacillus anthracis* is a likely candidate for therapeutic intervention against anthrax infection**

Carleitta Paige [1], Sean D. Reid [2], Philip Hanna [3] and Al Claiborne [1]

[1] Department of Biochemistry, Center for Structural Biology, [2] Department of Microbiology and Immunology, Wake Forest University School of Medicine, Winston-Salem, NC and [2] Department of Micrbiology and Immunology, [3] University of Michigan Medical School, Ann Arbor, MI

The first committed step in coenzyme A (CoASH) biosynthesis is catalyzed by pantothenate kinase (PanK). Of the three characterized bacterial PanK isoforms, *Bacillus anthracis* utilizes the type III PanK as its sole functional enzyme in 4´-phosphopantothenate synthesis. The type III PanK (*Ba*PanK) is the first structural gene in a tricistronic operon (*coaX-hslO-cysK-1*), which also encodes the redox-regulated Hsp33 heat shock protein and cysteine synthase A. Repeated attempts to generate a stable *coaX* deletion mutant in *B. anthracis* led only to clones retaining the wild-type locus, suggesting that *Ba*PanK is essential for growth. Therefore, we have generated the conditional *coaX* mutant that carries a copy of the wild-type *coaX-hslO-cysK-1* locus under the control of the IPTG-inducible P_{SPAC} promoter. As anticipated, the mutant displays essentially wild-type growth in BHI plus 50 μM IPTG; we did not, however, anticipate the growth observed ~7 hours post-inoculation in the *absence* of IPTG. This unexpected result is due to the development of a stable suppressor mutation; a point mutation (G→A) has been identified in the P_{SPAC} promoter, which may be responsible for the transcription observed for *coaX* (and *hslO-cysK-1*) genes in the absence of IPTG. Due to polar effects in the conditional mutant, we implemented gene disruption strategies to evaluate whether *hslO* and/or *cysK-1* were essential. We have shown that both *cysK-1* and *hslO* are not essential and therefore, do not contribute the conditional mutant growth phenotype. Thus, evidence to date supports *Ba*PanK as a potential target for therapeutic intervention against anthrax infection.

* Ms. Paige is a doctoral candidate in the Department of Biochemisty, Wake Forest University, Winston-Salem, NC

25th Anniversary Presidents' Travel Award

In honor of the 25th Fall Meeting Anniversary, the Past Presidents of GEMS desired to encourage young scientists, by conferring a one time Travel Award to the Environmental Mutagen Society 2008 meeting in Puerto Rico. The generosity of these individuals is one reason GEMS is so unique. The Society thanks you so much for your continued contribution to GEMS.

25th Anniversary Presidents' Travel Award Candidates

1. **Sophia C.E. Bolick, PhD** - NIEHS Postdoctoral Research Fellow, Genetic and Molecular Epidemiology Group, Laboratory of Molecular Carcinogenesis, NIEHS, Research Triangle Park, NC

2. **Patrick D. Brandt, PhD -** NIEHS Post-doctoral Research Fellow, Molecular and Genetic Epidemiology Group, Laboratory of Molecular Carcinogenesis, NIEHS, Research Triangle Park, NC

(1) **3. Dana C. Dolinoy, PhD** - Post-doctoral Fellow, Department of Radiation Oncology, Duke University Medical Center, Durham, NC

4. **Michelle C. DeSimone -** Howard Hughes Med-into-Grad Scholar Curriculum in Toxicology, Threadgill Laboratory, University of North Carolina at Chapel Hill, Chapel Hill, NC

5. Nancy M. Hanley - National Health & Environmental Effects Research Laboratory, Environmental Carcinogenesis Division, Molecular Toxicology Branch, US Environmental Protection Agency, Research Triangle Park, NC

(2) **6. Michele A. LaMerrill** - Curriculum in Toxicology, Department of Genetics, Center for Environmental and Health Susceptibility, UNC, Chapel Hill, NC

7. Amy Lynn Sloat, PhD - NIH Postdoctoral Research Fellow, Cancer Biology Department, Wake Forest University Health Sciences, Winston Salem, NC

8. Christa Watson – Doctoral Candidate in the Energy and Environmental Sciences Program, North Carolina Agricultural and Technical State University, Greensboro, NC

Dr. Larry Claxton, the first president of GEMS (1983-1985), has a BS in chemistry from Middle Tennessee State University, a MS in mammalian physiology from Memphis State University, and a PhD in genetics and public health administration from North Carolina State University. He has 35 years of experience as a genetic toxicologist with the United States government - first at the National Institute of Environmental Health Sciences and now at the US Environmental Protection Agency. Before returning to active research, Dr. Claxton was Director of the Environmental Carcinogenesis Division of the National Health and Ecological Effects Research Laboratory. His research has concentrated upon developing bioassay methods for evaluating complex environmental mixtures, identifying environmental mutagens and carcinogens, and developing new research approaches for hazard and risk assessment. He has served on committees for several international organizations (including WHO and ICPEMC) and EPA's Risk Assessment Forum, been an officer in several national societies, co-authored one book, co-edited five books, and been an author on over 150 peer reviewed scientific articles. In addition to three EPA Bronze Medals, Dr. Claxton has received seven EPA Scientific and Technical Achievement Awards (including a Level I Award) for his scientific publications. This last year he won the Alexander Hollaender Award from the Environmental Mutagen Society.

Dr. Andrew Kligerman (GEMS President1985-1986) received a BS in Zoology at Duke University, and obtained his MS and PhD in Cytogenetics at Cornell University studying chromosome damage in fishes. Upon publishing his first paper on the effects of radiation on fish chromosomes, unbeknown to him, he immediately became a world expert in this field, (The classic example of being a big fish in a small pond!). He received a postdoctoral fellowship at Cornell for one year and then moved on to the laboratory of Dr. George Michalopoulos in the Pathology Department at Duke University for a second postdoctoral fellowship. There he investigated chromosome damage in fibroblasts overlaid with hepatocytes as a co-culture for activation of promutagens. This was his start in mammalian genotoxicity (where he immediately became a small rodent in a big field!). A year an a half later he joined CIIT where he became the staff cytogeneticists investigating the clastogenic effects of industry priority compounds in rodents. However, after publishing several papers on the relative inactivity of many industrial commodity chemicals, he discovered that benzene was clastogenic at exposures below current OSHA standards. He found gainful employment at EHRT, Inc. as a Program Leader at the US EPA. There he worked with Dr. James Allen developing the rodent and human

parallelogram approach to risk assessment using rodent and human lymphocytes. A year later he became a Research Biologist with the US EPA focusing on the genotoxic effects of air and water pollutants using rodent and human lymphocytes. His current interests center on investigating the modes of action of arsenic and the effects of reactive oxygen species on chromosomes. He is currently the acting Branch Chief for the Cancer Biology Branch in the Environmental Carcinogenesis Division at the US EPA. He is currently on the editorial board *of Environmental and Molecular Mutagenesis* and *Mutation Research.*

Dr. Martha M. Moore (GEMS President 1987-1988) is the Director of the Division of Genetic and Reproductive Toxicology, National Center for Toxicological Research (NCTR), Food and Drug Administration, Jefferson, Arkansas. Previously, she was the Chief of the Genetic and Cellular Toxicology Branch, Environmental Carcinogenesis Division, National Health and Environmental Effects Research Laboratory, US Environmental Protection Agency, Research Triangle Park, North Carolina. Dr. Moore received a BA degree in Biology from Western Maryland College, Westminster, Maryland and a PhD in Genetics from the University of North Carolina at Chapel Hill. She has served on numerous EPA, FDA and other Government Agency advisory groups and committees. She is a member (and past Councilor) of the Environmental Mutagen Society, member (and past-president) of the Genotoxicity and Environmental Mutagen Society, member of the Genetic Toxicology Association, member of the United Kingdom Environmental Mutagen Society and member of the Society for Risk Analysis. She is a member of the Society for Toxicology and within SOT, Dr. Moore is a member of the Risk Assessment, the Regulatory and Safety Evaluation, the Occupational and Public Health and the Carcinogenesis Specialty Sections. She has served as a councilor for both the Epidemiology and Carcinogenesis SOT Specialty Sections and as the Secretary/Treasurer of the Occupational and Public Health Specialty Section. Her research interests include: (1) the development and utilization of mechanistically based in vitro and in vivo gene mutation assays (2) the interpretation and use of genetic toxicology data in cancer risk assessment and other regulatory decision-making and (3) the utilization and integration of genetic biomarkers in rodents and humans for public health protection.

David M. DeMarini (GEMS President 1988-1989) was born in Peoria, Illinois, USA. He received the BS (1972), MS (1974), and PhD (1980) in Biological Sciences (genetics) at Illinois State University, Normal, IL, studying under Dr. Herman E. Brockman. From 1980-1982, he did postdoctoral research at the Biology Division, Oak Ridge National Laboratory, Oak Ridge, TN. He then was a Research Geneticist at the

National Toxicology Program, National Institute of Environmental Health Sciences (NIEHS), Research Triangle Park, NC from 1983-1984. He began his current position as a Research Genetic Toxicologist at the US Environmental Protection Agency (US EPA), Research Triangle Park, NC in 1985. He is also an Adjunct Full Professor, School of Public Health, University of North Carolina, Chapel Hill, NC (1991-present). He is a member of the Environmental Mutagen Society (EMS), the Genetics Society of America (GSA), and the Genotoxicity and Environmental Mutagen Society (GEMS), of which he is a Past-President and Board Member. His editorial positions include Editor of *Mutation Research--Reviews* (1998-present), Co-Editor of *EMS Newsletter* (1988-1991), and Book Review Editor of *Environmental and Molecular Mutagenesis* (1989-1993). His Editorial Board memberships include *Mutation Research* (1985-1997), *Environmental and Molecular Mutagenesis* (1984-1989, 1993-present), *Mutagenesis* (1992-1995, 2005-present), *Environmental Health Perspectives* (1988-1993), *Teratogenesis Carcinogenesis and Mutagenesis* (1990-1992), *EMS Newsletter* (1986-1988), *Pan-African EMS Newsletter* (1994-present), and *Genes and Environment* (2006-present). He has organized conferences, symposia, and Alexander Hollaender Genetic Toxicology Training Courses internationally, and has given invited lectures at more than 85 conferences worldwide. He has chaired a variety of committees of the EMS, served on Council, and a Past-President of EMS (2000-2001). He was Program Chair for the 9th International Conference on Environmental Mutagens (9th ICEM) in 2005. He is the President of the International Association of Environmental Mutagen Societies (IAEMS) for 2005-2009. He has served on both (1986 and 2004) Tobacco Smoking and Cancer Monographs of IARC/WHO in Lyon, France, as well as the Drinking Water/Arsenic IARC Monograph (2004). He served on the US National Academy of Science's Steering Committee on Proteomics in 2002. He and his colleagues received the highest scientific achievement award given by the US EPA in 2004 for their work on the genotoxicity of arsenic. He has published 145 articles in mutagenesis (125 journal articles and 20 book chapters). His research interests are molecular mechanisms of mutagenesis, mutation spectra, complex mixtures, and biomarkers of mutation in humans.

Mr. Thomas J. Hughes, GEMS president for two terms (1989-1990, 1999-2000) is the Quality Assurance and Records Manager for the Experimental Toxicology Division (ETD) in the National Health and Environmental Effects Research Laboratory (NHEERL) at the U.S. EPA in Research Triangle Park (RTP), North Carolina. ETD conducts air and water research in pulmonary, cardiovascular, immunologic and pharmacokinetic systems in rodents. Tom was involved in World Trade Center (WTC) research, where a 20 member Team exposed mice to dusts from the WTC immediately after the 9/11/01 disaster. Tom has

been the ETD QA and Records Manager since September 1999. Before that, he was a laboratory scientist at the US EPA for five years, and a Principal Investigator in two contract laboratories for twenty years, were he conducted GLP testing for industrial clients, and toxicology testing for industry, NCI, EPA and NIEHS. Tom was the US EPA QA Manager of the Year in 2002. Tom was the President of GEMS for two terms. He and Tom Barfknecht formulated the idea for GEMS in the fall of 1982, and formalized the Society in 1983 and with the help of many RTP scientists. The fact that GEMS is celebrating 25 years of service to area scientists and students is due to dedicated members on the Boards of Directors and to the financial support of the corporate members of GEMS. Congratulations to GEMS on 25 years of scientific excellence!

David J. Doolittle, GEMS President from 1990 to 1991, is certified in Toxicology by the American Board of Toxicology and an elected member of the Academy of Toxicological Sciences. He earned a Bachelors of Science degree in Biology with a minor in Chemistry from the University of Wisconsin at Stevens Point, and a Ph.D. in Pharmacology and Toxicology from Michigan State University. Dr. Doolittle completed a postdoctoral fellowship in toxicology at the Chemical Industry Institute of Toxicology at Research Triangle Park, NC. In 1983, he joined the Rohm and Haas Company in Philadelphia as a Toxicologist. In 1985, Dr. Doolittle joined R.J. Reynolds Tobacco Company as a Senior Toxicologist, where he is currently Vice President of Product Evaluation. Dr. Doolittle has authored or co-authored more than 100 scientific manuscripts in the peer reviewed literature, and he has more than 100 published abstracts of scientific presentations. He co-authored the chapter on Genetic Toxicology in the newest edition of the Principles and Methods in Toxicology textbook, which will appear in 2007. He is an Adjunct Professor in the Toxicology Program at Duke University Medical Center and Adjunct Professor of Physiology and Pharmacology at Wake Forest University School of Medicine. David is married (Janet) and has two daughters; Lisa (21) currently enrolled at UNC in Chapel Hill, and Christie (20) currently enrolled at UNC in Wilmington. In his spare time he enjoys looking for his misdirected golf balls in the forests and swamps of North Carolina.

Dr. Bruce C. Casto, (GEMS President1991-1992) Sr. Research Scientist I, Division of Environmental Health Sciences College of Public Health, The Ohio State University received a BS (cum laude) in Biology from Morris Harvey College, assisted in the instruction of undergraduate nurses in Anatomy and Physiology and in Bacteriology. MS in Bacteriology from The Ohio State University, Graduate Assistant instructing medical, dental, veterinary, and nursing students in Bacteriology and Virology. MS thesis "Studies of Conditions Affecting the Production of Virus Plaques in Agar Cell Suspensions". ScD, Graduate School of Public Health, The

University of Pittsburgh., Accomplishments include the following: Characterization of virus receptors on human tumor cells for animal enteroviruses, herpesviruses, and adenoviruses; Conditions for inactivation of DNA viruses by $Mg^{++;}$ Discovery and naming of "adeno-associated viruses (AAV)"; Interactions between viruses and chemicals in induction of cell transformation; Development of focus assay for chemical transformation of mammalian cells; Improvement of media for UDS of hamster and human cells; Enhancement of DNA breakage assays using alkaline sucrose. Reviews appeared in the following: *Prog. in Exptl. Tumor Res. v18); Prog. in Medical Virology, vl6; Cell Biol. Molec. Biol., and Tumor Virol. l977; Adv. in Contemp. Environ. Toxicol. v1; In Vitro Toxicity Testing; and Appl. of Short-Term Bioassays in the Fract. and Anal. of Complex. Environ. Mixtures.* He has published over 170 scientific articles and book chapters, co-edited two books on human cell transformation, He served on four national committees, was a member of the Columbus Science Advisory Committee, a member of nine professional societies, and is a reviewer for five scientific journals.

Dr. Frederick J. de Serres served as president from 1992-1993. Since his diagnosis of alpha-1 antitrypsin deficiency in 1997, he started a new research program to investigate the genetic toxicology of this human genetic disease to determine its prevalence in other countries worldwide. This research has involved determining the prevalence of the two major AAT Deficiency alleles PIS and PIZ in the populations of 69 countries where there were genetic epidemiological studies performed by others in the peer-reviewed medical literature. He summarized the research published on individual countries or groups of countries in a paper recently accepted for publication in the Monaldi Archives for Chest Research (an Italian journal where he has before published). The data on these 69 countries have been grouped in to 12 major geographic regions to make it possible to compare prevalences in countries in close proximity. This research has demonstrated that AAT Deficiency is not just a disease of Caucasians but one that affects nearly all racial subgroups worldwide with widely varying prevalences. Notably absent from the database are data on countries in Central and South America, the Caribbean and many Eastern African countries. Constantly looking for new frontiers to explore, he started editing and publishing books on children's fairy tales. He will have a series of five books entitled Dmitri: the "Kind Storyteller" written by a young Russian (Oleg Karandeev) and another entitled "Misha's Dream". Also he is working with a young Texan named Christopher Forte and they are finalizing two books "The Cookie Monster" and "Toenalia" that will appear in print by the end of this year. All of these books will be available as e-books on the Internet. "There is life after what we were formally trained to do and what we have learned at the bench and from our scientific colleagues in our original profession has many applications in the 'real world'! You just have to find them!

Dr. R. Julian Preston, PhD served as president of GEMS from 1993-1994 and served as Director of the Environmental Carcinogenesis Division at the US Environmental Protection Agency from 1999 until August 2005. He is currently serving as Acting Associate Director for Health for the National Health and Environmental Effects Research Laboratory. Prior to his appointment with the US EPA, he served as the Senior Science Advisor at the Chemical Industry Institute of Toxicology in Research Triangle Park, North Carolina from 1991-1999. He was employed at the Biology Division of the Oak Ridge National Laboratory in Oak Ridge, Tennessee from 1970-1991. He also served as Associate Director for the Oak Ridge – University of Tennessee Graduate School for Biomedical Sciences. He currently also holds Adjunct Professor appointments at Duke University (Integrated Toxicology Programs) and North Carolina State University (Department of Toxicology). Dr. Preston received his BA and MA from Peterhouse, Cambridge University, England in genetics and his PhD from Reading University, England in radiation genetics. In addition to his employment, Dr. Preston is Chair of Committee 1 of the International Commission on Radiological Protection, a member of the US Delegation to the United Nations Scientific Committee on the Effects of Atomic Radiation and a member of several ILSI and IPCS committees. Dr Preston is also an Editorial Board Member of Mutation Research, Environmental and Molecular Mutagenesis and Health Physics. Dr. Preston's research and current activities have focused on the mechanisms of radiation and chemical carcinogenesis and the approaches for incorporating these types of data into cancer risk assessments. In order to be ready for these several activities, Dr Preston remains an avid runner.

Dr. Michael D. Waters (GEMS President 1994-1995) is a biochemist, genetic toxicologist and information scientist, with recent specialized experience in toxicogenomics database development. His research interests include evaluating and characterizing the role of gene mutation and gene expression in the induction of cancer, and applying this information to establish a biological basis for human risk assessment. He has over 20 years of laboratory experience with studies with cellular, molecular approaches including design and conduct of genotoxicity assays and chemoprevention studies in *in vitro* models; utilization of mechanistic approaches to understand the disease process; genomics, clinical and toxicologic pathology, and risk-based expertise. He serves as Adjunct Professor at the UNC and at Duke University and as Editor of *Mutation Research--Reviews*. Prior to joining ILS as Chief Scientific Officer, he directed the effort to develop the Chemical Effects in Biological Systems (CEBS) toxicogenomics knowledgebase at NIEHS (http://cebs.niehs.nih.gov). At NIEHS he served on the NIH Bioinformatics and Computational Biology Roadmap Working Group, the

FDA Advisory Committee for Pharmaceutical Science, Pharmacology and Toxicology Subcommittee, the Toxicogenomics and Risk Assessment Committee of the International Programme on Chemical Safety (IPCS), the Advisory Board of the Microarray Gene Expression Data (MGED) Society and the Scientific Advisory Board of the Rat Genome Database (RGD). Earlier at EPA he directed research in cellular pathology, biochemistry, and genetic toxicology in various posts including Genetic Toxicology Division Director. He also served as Assistant Laboratory Director at the EPA for several years with programmatic responsibility for the various environmental media and international research programs.

Dr. Michael D. Shelby served as president of GEMS from 1995-1996. He is Director of the NIEHS/NTP Center for the Evaluation of Risks to Human Reproduction. He has been at NIEHS since 1977, serving in the office of the Associate Director for Genetics, as head of the Mammalian Mutagenesis Section, as head of the Reproductive Toxicology Group and as Chief, Laboratory of Toxicology. Prior to joining NIEHS, he was a research associate at the Biology Division, Oak Ridge National Laboratory. He received his BS in biology (1966) from Central State College, Edmond, Oklahoma and his PhD in genetics (1973) from the University of Tennessee. His graduate training was in radiation mutagenesis and DNA repair. He has served as President of the Environmental Mutagen Society, the Genotoxicity and Environmental Mutagen Society, and the NIEHS Assembly of Scientists. He has been an editor of Mutation Research since 1980.

Dr. Byron E. Butterworth (GEMS President 1996-1997) received his PhD in Biochemistry in 1972 from the University of Wisconsin in Madison. He worked at the Du Pont Co. first in the Central Research Department where he conducted research on the molecular mechanism of action of antiviral agents, then as Chief of the Molecular Biology Section at the Haskell Laboratory for Toxicology and Industrial Medicine where he directed the program for developing and utilizing short-term tests for detecting potential mutagens/carcinogens. In 1977 he joined The Chemical Industry Institute of Toxicology (CIIT) as Head of the Department of Genetic Toxicology with responsibilities for guiding the research program in the areas of, mutagenesis, cell transformation, cytogenetics and DNA repair. He also served as Senior Scientist and Manager of the Cancer Program where he directed research on DNA repair, nongenotoxic mechanisms in carcinogenesis, chemically-induced cell proliferation, oncogene expression, and the use of transgenic animal models. Dr. Butterworth's laboratory is credited with developing key tissue-specific DNA repair assays including *in vivo* assays in rat hepatocytes, tracheal epithelial cells, and spermatocytes and *in vitro* assays in human hepatocytes, human bronchial epithelial cells, and

human mammary epithelial cells. Dr. Butterworth has mentored 13 postdoctoral fellows. He has made major contributions in understanding genotoxic and nongenotoxic modes of action of chemical carcinogens. The paper from his laboratory explaining the role of regenerative cell proliferation in chloroform-induced cancer received the Society of Toxicology's Board of Publication's Award for the Best Paper in the journal *Fundamental and Applied Toxicology* in 1995. Dr. Butterworth is a recognized advocate of using better science in public cancer policy. He is a Fellow and was a Member of the Board of The Academy of Toxicological Sciences and a member of the Roundtable of Toxicology Consultants and the Drug Information Association. He is a member of the American Association for Cancer Research, the Environmental Mutagen Society, the Society of Toxicology and the corresponding local chapters of those societies. He served as President of the Genotoxicity and Environmental Mutagen Society and as President of the Carcinogenesis Specialty Section of the Society of Toxicology. He holds adjunct appointments in the Department of Pathology of the University of North Carolina at Chapel Hill, and the Department of Microbiology, Pathology, and Parasitology of the College of Veterinary Medicine of North Carolina State University. He serves on the Editorial Board of *Mutation Research*. Dr. Butterworth is the author or coauthor of 120 scientific publications and 114 abstracts. In 2001 Dr. Butterworth became President of Butterworth Consulting, providing advice to the pharmaceutical and chemical industries, environmental groups, and regulatory agencies. Expertise includes a world class reputation and first hand experience in genetic toxicology, chemical carcinogenesis, and toxicology. Services include problem analysis and formulation of research strategies, regulatory compliance, the design and monitoring of studies, development of risk assessments, presentations to regulatory agencies, and acting as an expert witness.

Dr. Susan Elizabeth George served as GEMS president from 1997-1998. She is a founding member of the Department of Homeland Security (DHS), and a Science Advisor for the Chemical and Biological Countermeasures Division of the DHS Science and Technology Directorate. The Division focuses on threat awareness, surveillance and detection, bioforensics, response and restoration, and agriculture defense. Previously, she was Director of the Chemical and Biological National Security Program at the Department of Energy, where she set the strategy and research agenda for the post-9/11 chemical and biological civilian countermeasures development. Dr. George's major accomplishments include significant advances in the development of a national monitoring architecture for biological threat agents and response and restoration capabilities following a biological attack. Dr. George led the development of the "National Biomonitoring Architecture." She was a major contributor to the development and deployment of the BioWatch

Program, the Nation's first civilian environmental biothreat agent monitoring program. She initiated a DHS-Department of Defense pilot program, BioNet, to bring together disparate military and civilian detection and incident characterization in a local venue with application for national deployment. She also developed and transitioned the Program for Response Options and Technology Enhancements for Chemical and Biological Terrorism (PROTECT), the Nation's first civilian chemical detection and response capability, to the Washington Metropolitan Transit Authority. PROTECT is now being used by several cities. Dr. George co-chairs with the Environmental Protection Agency the Interagency Biological Working Group of the Subcommittee for Decontamination Standards and Technology. Under her leadership, guidance has been developed that has direct application to the public and private sectors. Dr. George has been the driving force for the development and transition of restoration plans, which reduce the restoration timeline, for potential incidents at airport, subway, and train venues. Dr. George is recipient of a 2007 NCSU Outstanding Alumna Award and the recipient of a 2007 Distinguished Presidential Rank Award.

Dr. Jack B. Bishop (GEMS President 1998-1999) is a staff scientist in the Toxicology Operations Branch of the Environmental Toxicology Program at the National Institute of Environmental Health Sciences (NIEHS). Bishop came to the NIEHS in 1985 from the US Food and Drug Administration's National Center for Toxicological Research in Jefferson, Arkansas where he spent ten years investigating chemically induced mutagenesis in rodent germ cells. Prior to that, Bishop was a Research Geneticist at the US Department of Agriculture's Honeybee Breeding and Stock Center Research Laboratory in Baton Rouge, Louisiana. Bishop is the Project Officer for the multi-generation reproductive toxicology contract used to evaluate reproductive and developmental toxicity of chemicals of interest to the National Toxicology Program (NTP). In addition to his duties as a Project Officer, he also conducts independent research studies of reproductive, developmental and genetic toxicity in rodent animal models as well as in human subjects. He has led the effort to develop biomarker assays for the NTP for the detection of genetic damage in rodent sperm, using fluorescence in situ hybridization (sperm-FISH) to identify and characterize mammalian germ cell mutagens. Bishop has over 30 years expertise in germ cell mutagenesis and environmental toxicology, with emphasis in reproductive, developmental and genetic toxicology, and has published over 60 scholarly publications in these areas. He has also given numerous invited presentations at national and international meetings. He is currently Treasurer and Executive Board Member of the Environmental Mutagen Society (EMS), and Past President of GEMS. He received a BA in biology/chemistry from McMurry College, Abilene,

Texas, in 1967, an MS in zoology from Louisiana State University, Baton Rouge, Louisiana in 1970 and a PhD in genetics from Louisiana State University in1974.

Dr. Michael Cunningham (GEMS president 2000-2001) received a BA in Biochemistry and Molecular Biology and a BA in Pharmacology from the University of California at Santa Barbara, and a PhD in Pharmacology and Toxicology from the University of Arizona in Tucson. Dr. Cunningham then served as a postdoctoral fellow at Sandoz Research Institute and Argonne National Laboratory before coming to the National Institutes of Health (NIH) at the National Institute of Environmental Health Sciences (NIEHS) in Research Triangle Park in 1987. He is presently a Chemist/Toxicologist in the Laboratory of Pharmacology and Chemistry of the National Toxicology Program (NTP) and a member of the Toxicology/Pathology Working Group in the newly established National Center for Toxicogenomics (NCT) at NIEHS. His research interests concern the mechanisms of toxicity and carcinogenicity of NTP chemicals.

Dr. Amal Abu-Shakra (GEMS president in 2001-2002) is the Chair of the Department of Biology at North Carolina Central University (NCCU), Durham, NC and the Program Director of the NCCU Minority Biomedical Research Support (MBRS) grant. Dr. Abu-Shakra received the BS degree in Agricultural and Food Sciences from the American University of Beirut (1979), the MS degree in Food and Management Science from the University of London, Untied Kingdom (UK) (1982), and the PhD in Biochemistry from the University of Surrey, UK (1986). She was a recipient of two consecutive postdoctoral fellowships (1987-1993): the National Institutes of Health (NIH) Fogarty Fellowship (cellular and genetic toxicology) at the National Institute of Environmental Health Sciences, RTP, NC (1987-1990), and a National Research Council (NRC) fellowship (mutagenesis and carcinogenesis) at the US Environmental Protection Agency, RTP, NC (1990-1993). She joined the faculty at NCCU as an Assistant Professor in Biology in 1994. She secured NIH (NIGMS/MBRS) funding through two consecutive research grants 1996-2001, conducted research within the multi-project NCCU NASA grant 2003-2005), and collaborated with researchers at New York University (Nelson Institute of Environmental Medicine; 1997-present); the US Food and Drug Administration (1995); NIEHS (participant in the Summers of Discovery Program (2002); and Duke University (2003-present). She has served on the Advisory Boards for NCCU's BBRI and BRITE Institutes, the FASEB/MARC program, the NCCU-Duke STEM program, among others. She has served as director of the USEPA/NCCU Cooperative Research Training Agreement 1999-2006 (grant is on no-cost extension until August 2007). She has advised the research of a large numbers of graduate students who completed their

MS degrees at NCCU, many of whom joined GEMS. In addition to service in GEMS, Dr. Abu-Shakra has been active in committee work with the Environmental Mutagen Society since 1998. Dr. Abu-Shakra is a recipeint of the ALCOA Excellence in Research Award, and of three Excellence in Teaching Awards: NCCU (2001); BC Powders (2002); and the UNC Board of Governors (2003). She is also the recipient of the J.L.Chambers Faculty Award for Excellence in Service (1998), NCCU College of Arts and Sciences Achievement Award (2002), and Office of Sponsored Research Awards for grant writing and management (2005, 2006).

Ms. Diane L. Spencer served as president from 2002-2003. She earned her BA in Biology at Rollins College and MS in Biology at the University of Miami. After coming to North Carolina, she worked under EPA Contract at Northrop Services, Inc. and EHRT, Inc. using bacterial mutagenesis assays to evaluate structure activity relationships. Since 1984, Diane has been employed as a Biologist at NIEHS. Her initial research program at NIEHS utilized the *in vitro* L5178 Mouse Lymphoma (MOLY) Assay to evaluate chemical mutagenesis and subsequently led to the development of a more accurate *in situ* assay using the MOLY cells. Other studies included investigations on the mechanisms of mutagenesis with specific emphasis on measuring mutation rates. Diane subsequently conducted research projects involved in assessing human risk associated with dioxin (TCDD) exposure. Using primary cell culture and molecular biology techniques, she developed an assay using human peripheral blood lymphocytes (PBLs) to measure constitutive and TCDD-induced expression of CYP1B1. This assay utilized a quantitative RT-PCR with product detection by gel electrophoresis. Other research projects using these techniques investigated correlations between TCDD exposure and CYP1B1 expression levels in PBLs of human subjects exposed accidentally or occupationally to TCDD. For the past four years, Diane has worked as a Biologist in the National Toxicology Program's Center for the Evaluation of Risks to Reproduction. Diane has been an active member of GEMS since it's inception in December 1982. She served on the GEMS Board of Directors as GEMS Secretary from 1985-1987, as Treasurer from 1993-1995 and as President-Elect/President.

Dr. Mark Miller served as president of GEMS from 2003-2004. He received his PhD in Pharmacology at Columbia University in 1983 and completed additional postdoctoral training at Massachusetts institute of Technology (MIT) and the National Cancer Institute (NCI). He held a faculty position at the University of Tennessee before joining the Wake Forest University School of Medicine in 1996, where he is a Professor of Cancer Biology. Mark has served on the Alcohol and Toxicology study section, is an *ad hoc* reviewer for several journals and NIH and EPA study sections, and has served as an officer in the SOT and GEMS.

Mark's laboratory have shown that different mutant Ki-*ras* alleles were associated with the histological stage of the lung lesions, leading to the development of a mouse model that conditionally expresses the mutant human Ki-*ras*^{G12C} allele in a lung-specific fashion utilizing a tetracycline-inducible promoter. These mice develop benign tumor lesions that remain extremely small and do not progress beyond the early adenoma stage. Thus, these mice represent the early stages of tumor development that would be seen in smokers and ex-smokers. To mimic the promotional phase of tumorigenesis, current studies are focusing on co-treating the mice with pro-inflammatory agents to drive tumor progression. Current studies are examining the gene pathways that drive tumorigenesis, the efficacy of potential chemopreventive agents and their mechanisms of action, and the efficacy of novel, mechanism-based anti-neoplastic agents that will specifically target the genetic lesions that are found to be altered in the tumors.

Dr. Barbara Shane served as president of the Genetics and Environmental Mutagenesis Society from 2004-2005. She received her PhD in Biochemistry at the University of the Witwatersrand in Johannesburg, South Africa. She worked as a post-doctoral research associate at Cornell University where she studied the interaction of dieldrin and hormones on reproduction in dogs. In 1983 she joined the Institute for Environmental Studies at Louisiana State University as an Assistant Professor in Toxicology where she rose up the ranks to Professor. In 1990 she became a Diplomat of the American Board of Toxicology. She spent eighteen months on sabbatical leave in 1994-1995 at the National Institutes for Environmental Health Sciences (NIEHS). Dr. Shane has more than 25 years of experience in toxicology with an emphasis in genetic toxicology involving the use of *in vitro* and *in vivo* mutation assays. From 2001-2003, Dr. Shane was the lead toxicologist on an NIEHS funded contract on the evaluation of *in vitro* assays to screen and identify compounds that potentially cause endocrine disruption in humans and wildlife. Currently, Dr. Shane is an Executive Secretary in the National Toxicology Program (NTP) at NIEHS where she coordinates the review of scientific reports on studies directed by scientists in the NTP. Dr. Shane co-edited one book entitled "Basic Environmental Toxicology" which has been used as a text in number of toxicology courses throughout the world. In 2000, she was elected a fellow of the American Association for the Advancement in Science. She has served as a grant reviewer for NIH and DOE and was on the editorial board of Environmental and Molecular Mutagenesis. She served on the Council for the Environmental Mutagen Society for three years, the Society of Toxicology (SOT) Committee on Public Communications for three years, organized two public symposia at SOT and coordinated two continuing education courses at SOT meetings. She served as the

Secretary/Treasurer for two years for the Carcinogenesis Specialty Section of SOT and is presently Vice-president of this Specialty Section.

Dr. Leslie Recio served as president of GEMS from 2005-2006. Les is a Diplomat of the American Board of Toxicology. He began his career in Genetic Toxicology at the University of Kentucky in 1980. His masters' thesis work was on the use of urine mutagenicity testing in the Ames assay to biomonitor exposure to mutagens. He then moved to Oak Ridge National Laboratory and completed his PhD work in the laboratory of Abraham Hsie working with the CHO/HGPRT assay. In 1986, he joined Tom Skopek's research group at CIIT and was introduced to the world of molecular biology and conducted mutational spectra studies in human cells. After completion of a postdoctoral fellowship in 1989, Les became a Senior Research Fellow in the Cellular and Molecular Toxicology Department of the Chemical Industry Institute of Toxicology (CIIT). During his tenure at CIIT, his research program used a number of *in vivo* transgenic mouse models, mutational spectra and gene expression profiling to assess mode of action for genotoxic chemicals. In 2002, Les joined Merck Research Laboratories as Head of the Microbial Mutagenesis Group where he was primarily responsible for the supervision and conduct of bacterial mutagenicity assays. In 2004, Les the joined Integrated Laboratory Systems, Inc. as Program Manager for Genetic Toxicology and is the Principal Investigator for the National Toxicology Programs' genetic toxicology testing and research program. Dr. Recio is on the Editorial Board of *Toxicological Sciences* (2006-present).

Dr. Gregory R. Stuart, president of GEMS from 2006-2007, received his PhD in Biology (2000) at the University of Victoria, BC, Canada, under the supervision of Dr. Barry Glickman, where he investigated the mutational specificity associated with ageing and dietary mutagens/carcinogens, using lacI transgenic rodents. Prior to joining Barry at University of Victoria, he completed his MSc in the Occupational Hygiene Programme (now the School of Environment and Health) at the University of British Columbia in Vancouver, BC, where he investigated the effects of an agricultural fungicide on lymphocytes. Following completion of his PhD, Greg moved to Dr. William Copeland's Mitochondrial DNA Replication Group at NIEHS, where he works (2001 - present) as a Special Volunteer under the supervision of Drs. Copeland and Micheline Strand (U.S. Army Research Office). His funding has been provided by North Carolina State University (2001-2002), Duke University Medical Center (2002-2005), and a National Academies National Research Council Research Associateship Award (2005 - present). Greg's research involves the study of genes that contribute to mitochondrial function and genome stability, using the yeast *S. cerevisiae*. This work has included the characterization of a

mitochondrial mutator (POS5 - encoding the mitochondrial NADP kinase), mitochondrial DNA polymerase gene mutations associated with human neuromuscular diseases, and a microarray study of oxidative stress and mitochondrial function. With regard to service to the broader scientific community, Greg occasionally peer-reviews scientific grant applications and manuscripts. He was a member of the Environmental Mutagen Society from 1994-2007, and with regard to GEMS, has served as a Councilor (2002-2005), President-Elect and President.

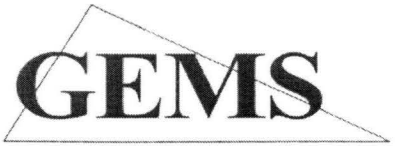
Special thanks to Steve McCaw, photographer with
Image Associates, and Eddy Ball, writer/editor,
NIEHS, Office of Communications and Public Liaison

INDEX

Andley U	P5
Ahmad S	***T1**
Aithal R	P1
Akman S	T4, T5
Atala A	T2
Beinstock R	P2
Blans P	T5
Boyer W	P5
Birnbaum L	T3
Cardiff R	T3
Chignell C	P5
Claibourne A	T6
Copeland W	P2
Creus A	P4
DeVito M	P3
Doehmer J	T1
Fishbein J	T5
Graziewicz M	P2
Hanna P	T6
Hipp JA	***T2**
Hipp J D	T2
Kuila D	P1
Kumaraswamy D	P1
LaMerrill M	***T3**
Leone-Kabler S	T1
Marcos R	P4
Mills C	***P3**
Mills D	P1
Morrow C	T1
Paige C	***T6**
Perrino F	T4, T5
Reid S	T6
Roberts J	P5
Routh E	T4
Sloat A	***T4**
Soker S	T2
Soriano C	***P4**
Threadgill	T3
Townsend A	T1
Upton D	***T5**, T4
Vaughn J	T4
Watson C	***P1**
Wang X	T5
Wielgus A	***P5**

*Competing for award
Bold number is primary author

NOTES



Genetics and Environmental Mutagenesis Society

P.O. Box 13475, Research Triangle Park, North Carolina 27709

http://www.gems-nc.org/

Membership Application or Renewal

Name: _____

Affiliation: _____

Address: _____

_____

City: _____ State: _____ Zip: _____

Telephone: _____ E-mail: _____

Dues: $10 per year (students $5 per year) Enter amount: _____

➔Please make checks payable to GEMS

➔Send to:

Gloria Jahnke, Interim Treasurer
GEMS
P.O. Box 13475
RTP, NC 27709

➔For a receipt, please check here ____

[redacted]t was prepared with the significant help of
[redacted]y Ahlmark and Mr. Kris Erwin.
Thank you!