

## P68

**Correlation between CYP1A1 RNA Transcript, Protein Level, Enzyme Activity, and DNA Adducts in Primary Normal Human Mammary Epithelial Cells Exposed to Benzo[a]pyrene.** Divi RL<sup>1</sup>, Lindeman TE<sup>1</sup>, Shockley ME<sup>1</sup>, Keshava C<sup>2</sup>, Weston A<sup>3</sup>, Poirier MC<sup>1</sup>. <sup>1</sup>National Cancer Institute, Bethesda, MD, United States, <sup>2</sup>National Center for Environmental Assessment, EPA, Research Triangle Park, NC, United States, <sup>3</sup>Division of Respiratory Disease Studies, NIOSH, CDC, Morgantown, WV, United States.

Benzo(a)pyrene (BP) undergoes metabolic activation and forms DNA adducts. The goal of this study is to identify the key players that contribute to BP-DNA adduct formation in mammary epithelial cells. We quantified RNA copies/ng cDNA (RNA cpn) of *Cytochrome P450 1A1 (CYP1A1)* and *CYP1B1*, genes which code for metabolic enzymes that form r7, t8, t9-trihydroxy-c-10-(N<sup>2</sup>-deoxyguanosyl)-7,8,9,10-tetrahydrobenzo[a]pyrene (BPdG), the major BP-DNA adduct, and *NAD(P)H:Quinone Oxidoreductase 1 (NQO1)*, which codes for NQO1 that converts BP quinones to less toxic hydroquinones. Primary normal human mammary epithelial cell (NHMEC) strains from 16 healthy women and MCF-7 breast cancer cells were used for comparison. We found 56-836 and 251-13234 *CYP1A1*, 336-5587 and 4133-57077 *CYP1B1*, and 5943-40112 and 4456-55887 NQO1 RNA cpn in unexposed and BP exposed (4  $\mu$ M, 12h) NHMECs, respectively. NHMECs had 7.47 (median; range: 0.85-15.8) BPdG adducts/10<sup>8</sup> nucleotides while MCF-7 cells had 790 adducts. In the NHMECs, a linear association ( $p=0.0015$ ) was observed between BPdG adducts and BP-induced *CYP1A1*, and no correlation with other genes examined. Western blots of 4 NHMEC strains, chosen for different levels of BPdG adducts, showed a linear correlation ( $p=0.013$ ) between BPdG and *CYP1A1*, but none between BPdG and *CYP1B1* or NQO1. Ethoxyresorufin-O-deethylase (EROD) activity, which measures *CYP1A1/1B1* together, correlated ( $p=0.038$ ) with BPdG in NHMECs, and was highly induced by BP in MCF-7 cells. Overall, the data suggest that *CYP1A1* is critical for BPdG adduct formation in NHMECs. The 10-fold higher adduct level found in BP-exposed MCF-7 cells, compared to NHMECs, appears likely due to high EROD activity.

## P69

**Use of Directed Evolution to Study Substrate Discrimination by ALKBH2.** Lepore AL, Troll C, Alexander DL, Camps M. University of California, Santa Cruz, Santa Cruz, CA, United States.

The human DNA repair enzyme ALKBH2 is a direct repair enzyme that acts to remove cytotoxic methyl damage and mutagenic etheno adducts from DNA. While previous research has uncovered many important structural features of ALKBH2, it is still unknown how the enzyme discriminates between these two types of DNA damage given that once they are flipped into the active site of the enzyme, these two lesions occupy nearly identical positions in the active site. In order to identify key residues involved in the discrimination of methyl and etheno lesions, we are screening a collection of ALKBH2 mutants previously selected for increased protection to exposure to the methylating agent MNNG for differential methyl versus etheno repair. As a screening method, we use lysogenic infection of a phage treated with the SN2 methylating agent methyl methane sulfonate (methylation repair) or chloroacetaldehyde (etheno repair). We identified mutants in this library that selectively reduce methyl repair while leaving etheno repair, and plan to confirm these results genetically by looking at differences in mutation expression and biochemically by mass spectrometry. The identification of mechanisms of substrate discrimination for ALKBH2 should facilitate the production of adjuvant ALKBH2 inhibitors specific for methyl repair. These inhibitors would enhance the therapeutic effect of methylating agents while minimizing the potential carcinogenic effects of etheno-induced mutagenesis.

## P70

**Low-Dose H<sub>2</sub>O<sub>2</sub> Induced Clustered DNA Lesions and Mutagenesis: Contribution of Error-Prone NHEJ Repair Pathway.** Sharma V, Collins LB, Svenberg JA, Nakamura J. University of North Carolina, Chapel Hill, NC, United States.

Although the induction of oxidatively induced clustered DNA lesions (OCDLs) has been believed as a finger print of radiation-induced DNA damage, few studies have also associated elevated levels of OCDLs with chronic inflammation and human malignancies. There is a knowledge gap regarding formation of OCDLs/DSBs as a result of low levels of endogenous/exogenous oxidative stress (OS) and their role in mutagenesis. Therefore, in the present study, we sought to understand the generation of OCDLs and OS induced mutagenesis caused by low levels of H<sub>2</sub>O<sub>2</sub> and identify DNA repair pathways that may affect OS induced susceptibility to mutagenesis. Low concentrations of H<sub>2</sub>O<sub>2</sub> actually found in cells during inflammatory processes were taken. Interestingly, DNA Damage Response analyses in DT40 cells, using reverse genetic approach, revealed hypersensitivity of Rad54, Rad51c, XRCC2, Ku70 and Lig IV deficient cells to H<sub>2</sub>O<sub>2</sub>, indicating the potential role of DSBs in H<sub>2</sub>O<sub>2</sub> toxicity. High levels of 8-oxo-dG lesions and OCDLs measured with a modified PFGE version were also found in H<sub>2</sub>O<sub>2</sub> exposed cells. The induction of OCDLs and DSBs directed us to investigate the role of error-prone NHEJ in mutagenesis. Ku70, DNA PKcs and Lig IV (NHEJ proteins) deficient cells revealed a drastic decrease in mutation frequency despite the presence of equivalent levels of 8-oxo-dG as in the wild-type DT40 cells. Our results indicate that OS, even at low levels, can cause clustered DNA damage that leads to DSBs with complex DNA ends and repairing such complex DSBs with NHEJ increases the likelihood that mutations will result.

## P71

**BPA Modulates Repair of Oxidative DNA Damage by Base Excision Repair Pathway.** Gassman NR, Stefanick DF, Horton JK, Wilson SH. Laboratory of Structural Biology, National Institute of Environmental Health Sciences, National Institute of Health, Research Triangle Park, NC, United States.

Bisphenol A (BPA) has become a target of intense public scrutiny since concerns about its association with human diseases such as obesity, diabetes, reproductive disorders, and cancer have emerged. Several recent studies have linked genotoxicity of BPA with the generation of oxidative DNA damage. Reactive oxygen species (ROS) that damage DNA are generated by metabolism of BPA and can generate DNA strand breaks and damaged DNA bases. Base excision repair (BER) is responsible for removing oxidative base lesions, such as 8-oxo-2'-deoxyguanosine (8-oxoG), and repairing single strand breaks (SSBs), yet the relationship between BPA and BER has yet to be examined. Further, the ubiquitous nature of BPA causes continual exposure of the human genome concurrent with the normal endogenous and exogenous insults to the genome, and this co-exposure may impact DNA damage response and repair. To determine the effect of BPA exposure on repair of oxidative DNA damage, DNA repair proficient and deficient cell lines were co-exposed with BPA and the oxidizing agent, potassium bromate. Repair-deficient cell lines were found to be more sensitive to the generation of oxidative damage; however, in the presence of BPA an enhanced cell survival was observed coupled with increases in the 8-oxoG content of the DNA. This protective effect and increased DNA lesion load resembles a DNA glycosylase-deficient cell phenotype, suggesting that initiation of BER is suppressed by BPA. The role of BPA in suppression of DNA repair and reduction of cell death will be discussed.

An International Journal Specializing in  
Environmental Mutagenesis

Volume 55  
Number S1  
September 2014

# EMGS Abstracts

Supplement to *Environmental and Molecular Mutagenesis*



Integrating Environmental, Genomic,  
and Health Research

45<sup>th</sup> Annual Meeting  
September 13–17, 2014



Environmental  
Mutagenesis and  
Genomics Society

Orlando, Florida

## In this issue:

Abstracts from the Environmental Mutagenesis and Genomics Society  
45th Annual Meeting, September 13–17, 2014, Orlando, Florida  
Program Chair: Suzanne M. Morris | New Investigator Co-Chair: Michelle C. DeSimone

# Environmental and Molecular Mutagenesis

JOURNAL OF THE ENVIRONMENTAL MUTAGENESIS AND GENOMICS SOCIETY

(FORMERLY ENVIRONMENTAL MUTAGEN SOCIETY)  
OFFICERS, ENVIRONMENTAL MUTAGENESIS AND GENOMICS SOCIETY

President O. Olivero	Vice President S. Morris	Vice President- Elect B. Engelward	Past President M. Ljungman	Secretary B. Parsons	Treasurer B. Shane	Journal Editor F. Marchetti	Executive Director T. Masson
<b>COUNCILORS</b>							
R. Benz C. Gibbons W. Kaufmann	M. Manjanatha J. Nicolette	S. Smith-Roe R. Snyder	R. Sobol G. Spivak	K. Sweder H. van Gijssel	S. Wallace D. Wilson III	K. Witt R. Young	

## ASSOCIATE EDITOR

David M. Wilson III  
National Institute on Aging  
Baltimore, Maryland

## EDITOR-IN-CHIEF

Francesco Marchetti  
Health Canada  
Ottawa, Ontario

## ASSOCIATE EDITOR

Carole Yauk  
Health Canada  
Ottawa, Ontario

## EDITORIAL BOARD

Volker Arlt  
King's College London  
London, United Kingdom

Robert Heflich  
FDA/NCTR  
Jefferson, Arkansas

Malcolm Lippert  
Saint Michael's College  
Colchester, Vermont

Ronald D. Snyder  
RDS Consulting Services  
Maineville, Ohio

Janet E. Baulch  
UC Irvine  
Irvine, California

George R. Hoffmann  
Holy Cross College  
Worcester, Massachusetts

R. Stephen Lloyd  
Oregon Health & Science University  
Portland, Oregon

Christopher M. Somers  
University of Regina  
Regina, Saskatchewan

Sonja I. Berndt  
National Cancer Institute  
Bethesda, Maryland

Nina Holland  
UC Berkeley  
Berkeley, California

Carlos Menck  
Universidade de São Paulo  
São Paulo, Brazil

Peter J. Stambrook  
University of Cincinnati College of Medicine  
Cincinnati, Ohio

Stefano Bonassi  
IRCCS San Raffaele Pisana  
Rome, Italy

Masamitsu Honma  
National Institute of Health Sciences  
Tokyo, Japan

Joel Meyer  
Duke University  
Durham, North Carolina

Gisela Umbuzeiro  
State University of Campinas – UNICAMP  
São Paulo, Brazil

Kerry L. Dearfield  
U.S. Department of Agriculture  
Washington, DC

George Johnson  
Swansea University  
Swansea, United Kingdom

William F. Morgan  
Pacific Northwest National Laboratory  
Richland, Washington

Jan Van Benthem  
National Institute for Public Health and the  
Environment (RIVM)  
Bilthoven, The Netherlands

David DeMarini  
U.S. EPA  
Research Triangle Park,  
North Carolina

William Kaufmann  
University of North Carolina  
Chapel Hill, NC

Hannu Norppa  
Finnish Institute of Occupational Health  
Helsinki, Finland

Karen Vasquez  
University of Texas MD Anderson Cancer  
Center  
Smithville, Texas

Dana Dolinoy  
University of Michigan  
Ann Arbor, MI

Catherine Klein  
New York University School of Medicine  
Tuxedo, New York

Barbara Parsons  
FDA/NCTR  
Jefferson, Arkansas

Ulla Vogel  
Technical University of Denmark  
Søborg, Denmark

Azeddine Elhajouji  
Novartis Pharma AG  
Basel, Switzerland

Andrew Kligerman  
U.S. EPA  
Research Triangle Park, North Carolina

R. Julian Preston  
U.S. EPA  
Research Triangle Park,  
North Carolina

Paul White  
Health Canada  
Ottawa, Ontario

James C. Fuscoe  
FDA/NCTR  
Jefferson, Arkansas

Iain Lambert  
Carleton University  
Ottawa, Ontario

Orlando D. Schärer  
Stony Brook University  
Stony Brook, New York

Errol Zeiger  
Errol Zeiger Consulting  
Chapel Hill, North Carolina

Sheila Galloway  
Merck Research Laboratories  
West Point, Pennsylvania

Qing Lan  
NCI  
Bethesda, Maryland

Peter Schmezer  
German Cancer Research Centre  
Heidelberg, Germany

Luoping Zhang  
University of California Berkeley  
Berkeley, California

© 2014 Wiley Periodicals, Inc., a Wiley Company. All rights reserved. No part of this publication may be reproduced, stored or transmitted in any form or by any means without the prior permission in writing from the copyright holder. Authorization to photocopy items for internal and personal use is granted by the copyright holder for libraries and other users registered with their local Reproduction Rights Organisation (RRO), e.g. Copyright Clearance Center (CCC), 222 Rosewood Drive, Danvers, MA 01923, USA ([www.copyright.com](http://www.copyright.com)), provided the appropriate fee is paid directly to the RRO. This consent does not extend to other kinds of copying such as copying for general distribution, for advertising or promotional purposes, for creating new collective works or for resale. Special requests should be addressed to: [permissionsuk@wiley.com](mailto:permissionsuk@wiley.com).

**ENVIRONMENTAL AND MOLECULAR MUTAGENESIS** (ISSN: 0893-6692 [print]; ISSN: 1098-2280 [online]) is published monthly in January, March, April, May, June, July, August, October, December by Wiley Periodicals, Inc., through Wiley Subscription Services, Inc., a Wiley Company, 111 River Street, Hoboken, NJ 07030. **Postmaster:** Send address changes to ENVIRONMENTAL AND MOLECULAR MUTAGENESIS, Journal Customer Services, John Wiley & Sons Inc., C/O The Sheridan Press, PO Box 465, Hanover, PA 17331. **Send subscription inquiries** c/o John Wiley & Sons, Inc., Attn: Journals Admin Dept UK, 111 River Street, Hoboken, NJ 07030, (201) 748-6645.

**Production Editor:** Christine Haller (Email: [jmlprodem@cadmus.com](mailto:jmlprodem@cadmus.com)) **Advertising:** Karl Franz (Email: [KFranz@wiley.com](mailto:KFranz@wiley.com)) **Commercial Reprints:** Lydia Supple-Pollard (Email: [lsupple@wiley.com](mailto:lsupple@wiley.com))

**Author Reprints (50–500 copies):** Order online: <http://www.sheridanreprints.com/orderForm.html> Email: [chris.jones@sheridan.com](mailto:chris.jones@sheridan.com) **Information for subscribers:** *Environmental and Molecular Mutagenesis* is published in 9 issues per year. Institutional subscription prices for 2014 are: Print & Online: US\$1,663 (US), US\$1,789 (Canada/Mexico), US\$1,852 (Rest of World), €1,218 (Europe), £964 (UK). Prices are exclusive of tax. Asia-Pacific GST, Canadian GST and European VAT will be applied at the appropriate rates. For more information on current tax rates, please go to [www.wileyonlinelibrary.com/tax-vat](http://www.wileyonlinelibrary.com/tax-vat). The price includes online access to the current and all online back files to January 1st 2009, where available. For other pricing options, including access information and terms and conditions, please visit [www.wileyonlinelibrary.com/access](http://www.wileyonlinelibrary.com/access). **Delivery Terms and Legal Title:** Where the subscription price includes print issues and delivery is to the recipient's address, delivery terms are Delivered at Place (DAP); the recipient is responsible for paying any import duty or taxes. Title to all issues transfers FOB our shipping point, freight prepaid. We will endeavour to fulfil claims for missing or damaged copies within six months of publication, within our reasonable discretion and subject to availability. **Publisher:** *Environmental and Molecular Mutagenesis* is published by Wiley Periodicals Inc., 350 Main St., Malden, MA 02148-5020. **Journal Customer Services:** For ordering information, claims and any enquiry concerning your journal subscription please go to [www.wileycustomerhelp.com/ask](http://www.wileycustomerhelp.com/ask) or contact your nearest office. **Americas:** Email: [cs-journals@wiley.com](mailto:cs-journals@wiley.com); Tel: +1 781 388 8598 or 1 800 835 6770 (Toll free in the USA & Canada); **Europe, Middle East and Africa:** Email: [cs-journals@wiley.com](mailto:cs-journals@wiley.com); Tel: +44 (0) 1865 778315; **Asia Pacific:** Email: [cs-journals@wiley.com](mailto:cs-journals@wiley.com); Tel: +65 6511 8000. **Japan:** For Japanese-speaking support, Email: [cs-japan@wiley.com](mailto:cs-japan@wiley.com); Tel: +65 6511 8010 or Tel (toll-free): 005 316 50 480. **Visit our Online Customer Get-Help** available in 6 languages at [www.wileycustomerhelp.com](http://www.wileycustomerhelp.com). **All Subscribers:** Claims cannot be honored beyond four months after mailing date. Duplicate copies cannot be sent to replace issues not delivered because of failure to notify publisher of change of address. **Cancellations:** Subscription cancellations will not be accepted after the first issue has been mailed. *Environmental and Molecular Mutagenesis* accepts articles for Open Access publication. Please visit <http://olabout.wiley.com/WileyCDA/Section/id-406241.html> for further information about OnlineOpen. **Back issues:** Single issues from current and prior year volumes are available at the current single issue price from [cs-journals@wiley.com](mailto:cs-journals@wiley.com). Earlier issues may be obtained from Periodicals Service Company, 11 Main Street, Germantown, NY 12526, USA. Tel: +1 518 537 4700. Fax: +1 518 537 5899, Email: [psc@periodicals.com](mailto:psc@periodicals.com). **Wiley's Corporate Citizenship** initiative seeks to address the environmental, social, economic, and ethical challenges faced in our business and which are important to our diverse stakeholder groups. Since launching the initiative, we have focused on sharing our content with those in need, enhancing community philanthropy, reducing our carbon impact, creating global guidelines and best practices for paper use, establishing a vendor code of ethics, and engaging our colleagues and other stakeholders in our efforts. Follow our progress at [www.wiley.com/go/citizenship](http://www.wiley.com/go/citizenship). **Abstracting and Indexing Services:** The Journal is indexed by Science Citation Index, MEDLINE, and SCOPUS. For a complete list of A&I services please visit the journal homepage at [www.wileyonlinelibrary.com/journal/em](http://www.wileyonlinelibrary.com/journal/em). For submission instructions, subscription and all other information visit: [wileyonlinelibrary.com/em](http://wileyonlinelibrary.com/em). **Disclaimer:** The Publisher and Editors cannot be held responsible for errors or any consequences arising from the use of information contained in this journal; the views and opinions expressed do not necessarily reflect those of the Publisher and Editors, neither does the publication of advertisements constitute any endorsement by the Publisher and Editors of the products advertised. Printed in the United States of America by Cadmus Communications, a Cenveo company. Access to this journal is available free online within institutions in the developing world through the HINARI initiative with the WHO. For information, visit [www.healthinternetwork.org](http://www.healthinternetwork.org).

ISSN 0893-6692 (Print)

ISSN 1098-2280 (Online)

View this journal online at [www.wileyonlinelibrary.com/journal/em](http://www.wileyonlinelibrary.com/journal/em)

This journal is printed on acid-free paper.

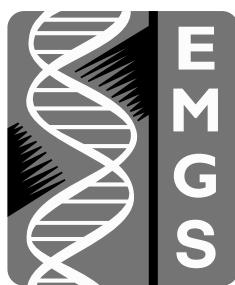
# EMGS Abstracts

**Supplement of *Environmental and Molecular Mutagenesis***  
Journal of the Environmental Mutagenesis and Genomics Society

Volume 55, Number S1 ..... 2014

Annual Meeting Agenda .....	S2
Keynote Speaker Abstracts .....	S18
Lecture Abstracts .....	S18
Debate Lecture Abstracts .....	S18
Forum Abstracts .....	S19
Symposia Abstracts .....	S20
Platform Abstracts .....	S33
Poster Abstracts .....	S40
Author Index .....	S64

Volume 55, Number S1, was posted the week of August 17, 2014.



# **Environmental Mutagenesis and Genomics Society**

## **45<sup>th</sup> Annual Meeting**

**Integrating Environmental, Genomic,  
and Health Research**

**September 13–17, 2014**

**Hilton Orlando Lake Buena Vista  
Orlando, Florida**

**Program Chair: Suzanne M. Morris, PhD**

**New Investigator Co-Chair: Michelle C. DeSimone, PhD**

**EMGS Headquarters**  
1821 Michael Faraday Drive, Suite 300  
Reston, Virginia 20190  
Telephone: 703.438.8220 Fax: 703.438.3113  
Email: [emgshq@emgs-us.org](mailto:emgshq@emgs-us.org)  
Website: [www.emgs-us.org](http://www.emgs-us.org)