

min). In summary, the radicals of BP and P exhibited a strong prooxidant activity, while the TBBPA had mild prooxidant activity. However, it was evident that TBBPA radicals can undergo redox reactions in the biological milieu altering the prooxidant/antioxidant balance and cause increased oxidative stress status. These findings are significant given the recent reports that zebrafish embryos and fish *Channa punctatus* have higher levels of lipid peroxidation products. Funds from the NanoHU Startup Award to Dr. Sainath Babu was used in this research. NanoHU was funded by the National Science Foundation HBCU-UP ACE Implementation, Award HRD-1238838 * Corresponding author: Sainath.babu@hamptonu.edu.

PS 2011 Production of Reactive Oxygen Species by BP-1,6-Q and Its Effects on the Endothelial Dysfunction: Involvement of the Mitochondria

Z. Jia¹, H. Shah¹, G. Gaje¹, A. Koucheki¹, H. Lee¹, H. A. Bibi¹, A. Martinez¹, M. A. Trush², H. Zhu³, and R. Li³. ¹University of North Carolina at Greensboro, Greensboro, NC; ²Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; and ³Campbell University School of Osteopathic Medicine, Buies Creek, NC.

Strong epidemiological evidence supports the association between increased environmental air particulate matter pollution and risk of developing cardiovascular diseases (CVDs), however, the mechanism remains unclear. As an environmental air pollutant and Benzo-a-pyrene (BP) metabolite, BP-1,6-quinone (BP-1,6-Q) is found in particulate phase of air pollution. This study was undertaken to examine the redox activity of BP-1,6-Q and mechanisms associated with it using EA.hy926, endothelial cells. Incubation of EA.hy926 cells with BP-1,6-Q at 0.01-1 μ M resulted in a significant stimulation of reactive oxygen species (ROS) production in a concentration-dependent manner. In isolated mitochondria, BP-1,6-Q also stimulated the production of ROS at sub-micromolar concentration implying the role of mitochondria in redox cycling of BP-1,6-Q. Furthermore, BP-1,6-Q-induced ROS was inhibited by Rotenone (Rot) and Antimycin A (AA), denoting the involvement of mitochondrial electron transport chain (METC) in redox cycling of BP-derived quinones in ROS overproduction. The effect of BP-1,6-Q-mediated ROS production on cellular adhesion molecules and inflammatory markers was further examined. It was found that BP-1,6-Q triggered endothelial-monocyte interaction and stimulated expression of Vascular adhesion molecule-1 (VCAM-1). These results suggest that the inflammatory effect of BP-1,6-Q on endothelial inflammation may be partially mediated by ROS generation and it subsequently stimulates chemokines and adhesion molecules.

PS 2012 Mucin Muc5ac Deficiency Enhanced Airway Susceptibility to Environmental Toxicants

H. Cho, L. Miller-DeGraff, R. Langenbach, and S. Kleeberger. NIEHS, Research Triangle Park, NC.

Gel-forming mucins protect respiratory tracts. MUC5AC is the major secreted airway mucin and has been associated with various diseases including asthma, chronic obstructive pulmonary disease, and fibrosis. To determine the role of Muc5ac in airway disorders in which abnormally heightened mucus is featured, *Muc5ac*-deficient mice (*Muc5ac*^{-/-}) and wild type mice (*Muc5ac*^{+/+}) were infected with respiratory syncytial virus (RSV, intranasal infection) or exposed to ozone (0.3 parts per million). Pulmonary and nasal airway injuries were assessed by bronchoalveolar lavage and histopathologic analyses. RSV was detected more intensely in nasal (septal epithelium and sub-epithelium, blood vessels) and pulmonary (bronchial epithelium, pleura) airways of *Muc5ac*^{-/-} mice, compared to *Muc5ac*^{+/+} mice (1 day post-RSV). Virus persisted in airways more highly until 5 days post-RSV in *Muc5ac*^{-/-} than in *Muc5ac*^{+/+}. Significantly higher lung RSV gene expression and epithelial cell death (by 1-3 days) as well as more severe perivascular-peribronchiolar edema, smooth muscle thickening and syncytia formation (by 3-5 days) was found in *Muc5ac*^{-/-} mice than *Muc5ac*^{+/+} mice after infection. RSV-increased septal epithelial damage and congestion in nasal airways were also more evident in *Muc5ac*^{-/-} relative to *Muc5ac*^{+/+}. Electron micrograph determined reduced storage of goblet cell secretory granules and increased contents of subepithelial mucoseroous glands in *Muc5ac*^{-/-} relative to *Muc5ac*^{+/+}. After 2-3 days of ozone exposure, nasal airways of *Muc5ac*^{-/-} mice developed more severe epithelial sloughing and hypertrophy in septum, expansion of subepithelial mucous glands, and lateral wall congestion, compared to those in *Muc5ac*^{+/+} nasal airways. Ozone significantly increased mid-septal intraepithelial mucus in *Muc5ac*^{+/+} but not in *Muc5ac*^{-/-}. In contrast, ozone significantly increased PAS-positive secretion and subepithelial mucosal gland enrichment in nasal airways only in *Muc5ac*^{-/-} mice. Results indicate that lack of *Muc5ac* impaired the nasal and pulmonary

airway defense against virus and ozone. Subepithelial mucoseroous glands in nasal airways may contribute to compensatory protective mechanism of *Muc5ac*^{-/-} mice.

PS 2013 Effect of Diet and Occupational Exposure in Different Rat Strains on Serum Biomarkers and Peripheral Blood Mononuclear Cell Telomere Length: Development of an Animal Model to Examine the Exposome

J. Antonini, V. Kodali, G. Boyce, K. Roach, T. Meighan, R. Salmen, M. Kashon, T. Boots, J. Roberts, P. Zeidler-Erdely, A. Erdely, and M. Shoeb. NIOSH, Morgantown, WV.

The exposome is a measure of all exposures of an individual and how those exposures relate to health. Important components of the exposome include lifestyle (diet), environmental and occupational exposures, and individual genetic predisposition. Mapping of the exposome could improve the understanding of disease and aid in prevention strategies and possible cures of many diseases. The goal was to develop an experimental model of the exposome by collecting biological samples during critical life stages of an exposed animal that are applicable to worker populations. Genetic contributions were assessed using three strains of male rats with different genetic backgrounds [Fischer-344 (F344), Sprague-Dawley (SD), Brown-Norway (BN)] maintained on a standard or high fat (HF) diet for 24 wk. At wk 7 during diet maintenance, groups of rats from each strain were exposed by inhalation of stainless steel welding fume (WF; 20 mg/m³ x 3 hr/d x 4 d/wk x 5 wk) or filtered air until wk 12 at which time some animals from each strain were euthanized. A separate set of rats from each strain were allowed to recover from WF exposure until the end of the 24 wk period. Bronchoalveolar lavage fluid and whole blood were collected at 7 wk (baseline before WF exposure), 12, and 24 wk to assess lung toxicity and to recover serum and peripheral blood mononuclear cells for general health and epigenetic analysis (telomere length), respectively. As expected, WF exposure had the greatest effect on lung responses, whereas the HF diet induced the most pronounced changes in serum analytes (e.g., triglyceride, AST, ALT) in most cases. Interestingly, PBMC telomere length was significantly shorter in the group of animals maintained on the HF diet that also were exposed to WF compared to the other groups. Generally, the exposome components of diet and WF exposure had the greater influence on the parameters measured compared to the changes associated with rat strain except for the body weight changes observed with the HF diet that were more pronounced in the inbred F344 and BN strains. An animal model can be useful in the study of the exposome as external lifetime exposures can be easily controlled and adverse health outcomes measured.

PS 2014 Nitroreduction Bioremediation of 3-Nitrobenzanthrone via Bacterial Metabolism

M. Friedman, and J. Field. University of Pennsylvania, Philadelphia, PA. Sponsor: J. Field, American Association for Cancer Research

3-Nitrobenzanthrone, the most potent mutagen currently known, is currently being produced in significant quantities, mostly from the emissions of diesel-fueled engines and industry. Not only is the amount produced a hazard in cities currently, but its prevalence is also on the rise due to the widespread use of diesel engines in Europe (around 42% of cars sold in the EU are diesel-powered) and smaller engines getting saddled with increasing loads, which raises the 3-NBA production dramatically. While this compound was previously thought to be too non-volatile to be degraded, certain types of bacteria can bioremediate this carcinogen via nitro-reduction. In order to remediate this compound, dozens of bacteria samples were tested for their bioremediation ability. Proof of remediation of this compound and identification of its metabolite was determined via UV-Vis spectrophotometry and comparing samples with wavelength absorbance of standard samples. Out of all the of the bacteria tested, two (*B. cereus* and *B. subtilis*) were able to metabolize 3-NBA, while two others (*B. megaterium* and an unidentified, soil sample-based bacteria) would grow significantly faster in the presence of 3-NBA. Nitro-reductases secreted from the bacteria metabolized 3-NBA, and a current investigation of a NCBI gene database for these bacteria will attempt to locate which genes allow the bacteria to produce these nitro-reductases. There are strong matches with genes such as CBO3577 and CBO0878. 3-NBA was injected into a solution of nutrient broth with bacteria and left to grow for two hours. After the bacteria were allowed to grow in this solution, the solution would turn pink (from yellow), and its wavelength absorbance would show peaks resembling those of 3-Aminobenzanthrone. 3-ABA is significantly less harmful to humans compared to 3-NBA. The reduction process from 3-NBA to 3-ABA is extraordinarily harmful and leads to DNA adducts. Allowing the bacteria to metabolize 3-NBA, rather than allowing the human body to do



58TH ANNUAL MEETING
& ToxExpo • MARCH 10-14, 2019

The Toxicologist

Supplement to *Toxicological Sciences*



OXFORD
UNIVERSITY PRESS

ISSN 1096-6080
Volume 168, Issue 1
March 2019

www.academic.oup.com/toxsci

The Official Journal of
the Society of Toxicology

SOT | Society of
Toxicology

Creating a Safer and Healthier World by Advancing
the Science and Increasing the Impact of Toxicology

www.toxicology.org