third tetratricopeptide repeats (TPR 3) domain], while the other (Q228R) was present between the TPR 1 and TPR 2 domains. Prior evidence suggests that a single point mutation within AIP TPR region can negatively affect AIP-protein binding, which could potentially disrupt AIP-HSP90 binding and compromise AHR protein integrity and cellular localization. Although this study found limited evidence of *AIP* SNPs of functional consequence, the results suggest that one or two *AIP* SNPs could result in decreased sensitivity to DLC exposures. Further investigation of the impact of these *AIP* SNPs on AHR signaling is warranted.

PS 1367 ASSOCIATION OF GENETIC VARIATIONS IN ANTIOXIDANT ENZYME GENES WITH DIISOCYANATE-INDUCED ASTHMA IN EXPOSED WORKERS.

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Diisocyanates are the most common cause of occupational asthma induced by low-molecular-weight agents. It has been shown that diisocyanates induce oxidative stress when they react with specific proteins in human airway epithelial cells and this process contributes to the pathogenesis of diisocyanate-induced asthma (DA). In this respect, variability in the antioxidant defenses may play a role in DA susceptibility. A case-control study was conducted to investigate whether genetic variations within antioxidant enzyme genes, glutathione S-transferases (GSTM1-GSTT1, GSTM3, GSTP1), manganese superoxide dismutase (MnSOD) and microsomal epoxide hydrolase (EPHX1), play a role in susceptibility to DA. The study population consisted of 252 workers exposed to diisocyanates (hexamethylene diisocyanate, methylene diphenyl diisocyanate, and toluene diisocyanate) of which 102 were diagnosed with DA based on a positive specific inhalation challenge. Genotype analysis was performed on genomic DNA, using a 5' nuclease PCR assay. The EPHX1 SNP (rs2740171) and GSTT1 gene deletion were associated with altered risk of developing DA after adjusting for potential confounders. Since EPHX1 and GSTT1 genes are important components of lung defense against oxidative stress, variations in these genes which regulate their expression may represent important disease modifiers and contribute to DA susceptibility.
This work was supported in part by an NIEHS IAG (Y1-ES-0001), NIOSH/CDC R01 OH 008795, and CDC Seed Funding for Public Health Genomics Research Program.

PS 1368 SULT1A1 GENE COPY NUMBER VARIATION (CNV) REAL-TIME QUANTITATIVE PCR (qPCR) ASSAY: AN OPPORTUNITY FOR POPULATION GENETIC COPY NUMBER VARIATION MEASUREMENT FOR ENHANCEMENT OF HUMAN HEALTH RISK ASSESSMENT OF GENETICALLY SENSITIVE SUB-POPULATIONS.

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Gene copy number variation (CNV) represents a novel source of heritable structural genetic variation in the human genome, and a potentially rich source of inter-individual phenotypic variation in the human population. Sulfotransferase 1A1 (SULT1A1) is a phase II xenobiotic metabolizing and detoxifying enzyme involved in the sulfonation of many different chemical and biochemical substrates. SULT1A1 single nucleotide polymorphism (SNP) variation in enzyme functional activity has implications for human population variation in toxicogenetics and pharmacogenetics, and SULT1A1 copy number variation has potentially comparable implications. A real-time quantitative polymerase chain reaction (qPCR) germline gene CNV laboratory assay was developed to determine the inherited gene copy number in human genomic DNA in the SULT1A1 gene. The assay employs fluorescent dual-labeled oligonucleotide hydrolysis probe chemistry and is capable of high-throughput large-scale analyses in laboratory and population studies. SULT1A1 germline gene copy number in a panel of human Coriell Cell Repository DNA samples was determined using the $2^{-\Delta\Delta CT}$ quantitative method, and demonstrates the application of the CNV assay. SULT1A1 germline gene copy number variation may represent a significant risk factor in gene-disease population association studies. SULT1A1 germline gene copy number variation may also be an important factor in modulating internal dosage of toxicological agents and modulating efficacy of pharmacological agents which are SULT1A1 chemical substrates.
[The opinions expressed herein are those of the author and do not necessarily reflect those of the U.S. Environmental Protection Agency.]

PS 1369 CHARACTERIZATION OF WHOLE GENOME AMPLIFIED (WGA) DNA FOR USE IN GENOTYPING ASSAY DEVELOPMENT.

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Genome-wide genotyping assays often require substantial amounts of input DNA. To overcome the problem of limited clinical sample DNA, WGA methods have been developed. The multiple displacement amplification (MDA) method using phi29 polymerase has become the preferred choice because of its high processivity and low error rate. The uniformity of the amplification process across the genome has not been extensively characterized. In this study, we use array-based comparative genomic hybridization to evaluate DNA copy number variations (CNVs) produced in amplified DNA by two MDA kits: GenomiPhi (GE Healthcare) and Repli-G (Qiagen). The Agilent Human CGH array with 1 million features was used in this study together with DNA samples from a normal patient and two patients with cystic fibrosis. Each of the amplified DNA samples was compared to its native unamplified DNA with 4 independent replications. Hierarchical clustering analysis showed that there are significant differences between amplified and unamplified DNA samples with a median correlation of r=0.56. The correlations within unamplified (r=0.98) and amplified (r=0.96) groups, and the correlation between the amplification methods (r=0.94) were very high. Pair-wise testing was used to identify the probes that had CNVs changes. More than 20% of probes had fold changes greater than 2 after amplification compared to unamplified DNA samples. Application of a segmentation algorithm to reduce possibly spurious signals reduced to 15% the number of probes with more than 2-fold changes. Examination of the cystic fibrosis gene region showed no obvious CNV changes caused by the WGA process, suggesting that utility of the WGA DNA may depend on the particular use. These results indicate that challenges remain when WGA is applied for clinical use.

PS 1370 MUTAGENICITY OF RARE METAL AND METAL OXIDE NANOPARTICLES: COMPONENTS AND PARTICLE SIZES.

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Nanoparticle of rare metals are used various products, however it is not enough to evaluate their carcinogenicity. Mutagenecity of four rare metals, indium oxide (In2O3), dysprosium oxide (Dy2O3), tungsten oxide (WO3) and molybdenum (Mo), that were defined particle diameter was demonstrated by in vitro bacterial reverse mutation assay (Ames test) using Salmonella thphimurium TA98, TA100, TA1535, TA1537 and Escherichia coli WP-2 uvrA strains. Size distribution of nano-sized rare metals in suspension was measured by dynamic light scattering photometer (DLS). All nano-sized rare metals were denoted as < 100 nm particle diameter (BET) by manufacturer, but the DLS results showed mean particle diameters for nano-sized In2O3, Dy2O3, WO3 and Mo, in suspension at 391.0 nm, 565.2 nm, 545.5 nm and 213.2 nm, respectively. Solubility of these metal compounds against neutral aqueous solutions was very low. Nano-sized Dy2O3 revealed strong mutagenic potential dose-dependently in all five bacteria strains tested with and without metabolic activation in Ames test, although micro-sized particles showed weak mutagenesis in two bacterial strains. Nano-sized In2O3 showed positive mutagenic response in TA1537, and nano-sized WO3 showed positive response in TA98 dose-dependently. While the micro-sized particle of these metal oxides showed no mutagenesis in the test bacterial strains. Both nano-sized and micro-sized Mo particles did not show any mutagenic effect. Although the mechanism of uptake the nano-sized metal compounds into the bacterial cells is unclear, size distribution and component of metal particles might influence their mutagenic effect. These results suggested that mutagenic effects of rare metals depend on their components and particle size, greater in nano-size than micro-size.
Acknowledgements: This research was partially supported by the Ministry of Education, Science, Sports and Culture, Japan, Grant-in-Aid for Young Scientists (B), 20710027 to G.H.

The Toxicologist

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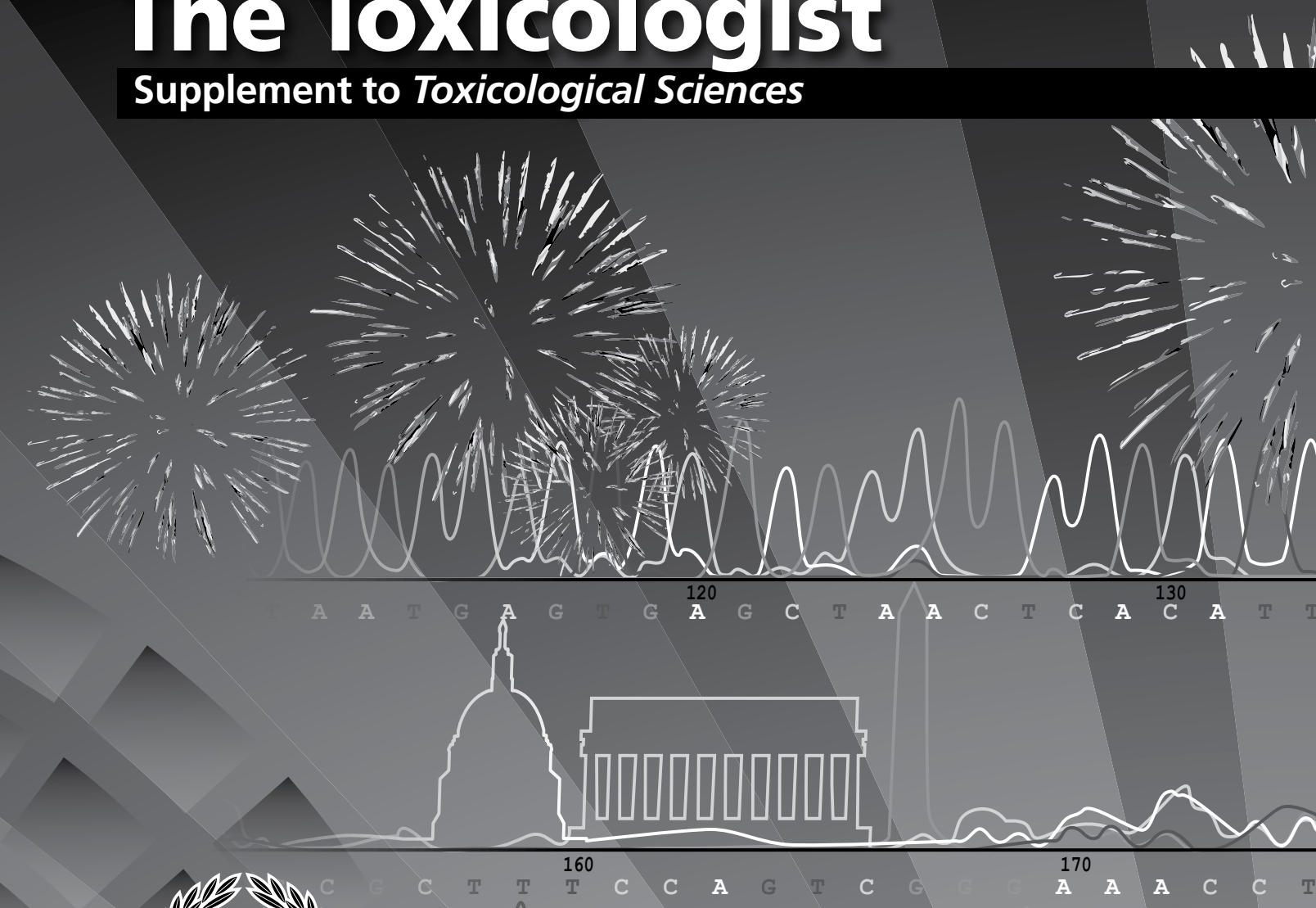

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An Official Journal of the Society of Toxicology

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 120, Supplement 2
March 2011

www.toxsci.oxfordjournals.org

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 50th Annual Meeting of the Society of Toxicology, held at the Walter E. Washington Convention Center, March 6–10, 2011.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 578.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 606.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence.

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