has a lower pH (1.8±0.3) than pH in fed samples (2.7±0.7). In addition, fasted human gastric fluid has a lower capacity to reduce Cr(VI) per L stomach fluid (approximately half) as compared to fed gastric fluid. The results of these experiments are used to support human health risk assessment by modeling the extent of Cr(VI) escaping reduction in the stomach during fed and fasted states.

PS 1297 Temporal Changes in Rat Liver Gene Expression after Cadmium and Chromium Exposure

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Our Nation's Guardians are at risk of exposure to a variety of environmental health hazards throughout their normal duty activities including deployments, training exercises, and homeland defense situations. Metals are widely used in large quantities in a number of industrial processes and are common environmental toxicants, which increases the possibility of our Soldiers being exposed at toxic levels. While metal toxicity has been widely studied, the exact mechanisms of toxicity remain unclear. In order to further elucidate these mechanisms and identify candidate biomarkers, rats were exposed via a single intraperitoneal injection to three concentrations of $CdCl_2$, $NiCl_2$ and $Na_2Cr_2O_7$, and livers were harvested 1, 3, or 7 days after exposure. Cd and Cr accumulated in the liver at 1 day post-exposure, while there was no accumulation of Ni. Cd levels remained elevated over the length of the experiment, while Cr levels declined. Differentially expressed genes were identified via microarray analysis. Both common and uniquely modulated transcripts and perturbed pathways were identified for the metal species. Enriched pathways and functions included hepatic injury, inflammation, cell cycle, tissue repair, and cancer. This work provides insight into the temporal effects and mechanistic pathways involved in acute metal intoxication, which may lead to the identification of candidate biomarkers.

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PS 1297a Toxicogenomic Study in Rat Thymus of F1 Generation Offspring following Maternal Exposure to Silver Ion

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Silver-containing compounds or their mixtures are widely applied as antimicrobial agents onto food packaging materials, often in direct contact with the food. The extensive use of silver in the food industry raises concerns about its safety, toxicity and health risk. Data currently available revealed that in utero exposure to silver could adversely affect the developing immune system. However, further studies are needed to confirm that the previously observed adverse effects are due to silver ion alone, and to define the no observed effect level (NOEL). In the present study we used a toxicogenomic approach to study the effect of silver ion on the developing thymus at the transcriptional level using whole genome microarrays. Global gene expression changes in rat thymus of F1 generation pups at post natal day 26 following maternal exposure to silver acetate at 0, 0.4, 4.0, or 40.0 mg/kg in drinking water are reported here. Five female and 5 male pups were included in each dosing group. Gene expression profiling analyses identified only about a dozen differentially expressed genes (DEGs) in each dose group using a loose criterion of fold change (FC) > 1.5 and unadjusted $p < 0.05$, regardless whether the analysis was conducted within each gender group or with both gender groups combined. No dose-dependent effect was observed on the number of DEGs. In addition, none of these genes had a false discovery rate (FDR) < 0.05 after correction for multiple testing. These results indicate silver acetate up to 40.0 mg/kg did not affect gene expression in the developing thymus. Combined with the observation that thymus-to-body-weight ratios were not affected, and no histopathological abnormalities in thymus were identified in the pups, the current study using a toxicogenomic approach suggests that in utero exposure to silver ion up to 26.0 mg/kg (equivalent to 40.0 mg/kg silver acetate) did not have an adverse effect on the developing thymus.

PS 1297b Assessing Toxicity of FeMn Dust Particles from a South African Ferromanganese Smelter Works: *In Vitro* Studies on Primary Rat Astrocytes and BEAS-2B Cells

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Occupational exposure to manganese (Mn) may result in development of diseases associated with the lungs and brain. Even though evidence of Mn associated diseases exists, some studies have found no association between manganese levels in blood or urine and indicators of neurotoxic effects.
This study investigated the effects of ferromanganese (FeMn) dust, from a ferro-manganese smelter works, on primary rat astrocytes and human bronchial epithelial (BEAS-2B) cells. Particle size distribution, surface area and trace elemental composition were analyzed. Particle uptake was studied using dark field microscopy and viability determined using the xCELLigence RTCA system based on cell adherence. Nuclear translocation of Nrf2 and Nf-κB was studied using western blots and genotoxicity determined by the alkaline Comet assay. Min-U-Sil 5 was used as benchmark particles.
The presence of nano sized FeMn and its cellular uptake in both cell lines was confirmed. Treatment resulted in a dose-dependent decrease in viability of both cell lines for both particle types, with crystalline silica producing higher toxicity compared to FeMn.
Short term exposure to FeMn and silica led to an increase and long term exposure to a decrease in translocation of both the Nrf2 and Nf-κB transcription factors, in both cell types tested. This indicates that after longer periods of exposure, the antioxidant defences were unable to overcome the oxidative stress induced by these particles.
Results indicate that access of FeMn ultrafine particles to the brain may be possible in smelter workers, resulting in direct disturbances of cellular toxicity, viability and markers of oxidative stress in astrocytes. Lung epithelial cells come into contact with these particles first, thus resulting in similar disturbances in BEAS-2B cells. These results and further toxicity studies could help to establish more reliable biomarkers of Mn effect and exposure.

PS 1297c Interference Study of Conventional Assays, Caused by Gold Nanoparticles (AuNPs) Exhibiting Surface Plasmon Resonance (SPR)

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Plasmonic engineered NPs are popular in consumer- and medical-based industries due to their unique surface characteristics. Identifying the toxicity of NPs is critical given the increased exposure. The toxicity of NPs is often determined using conventional colorimetric and optical high-throughput toxicity systems that rely on absorbance, luminescence or fluorescence signals. However these systems are prone to interference by the NPs, which lead to erroneous results.
This study assessed citrate-capped AuNPs interference with:
1) Three cell viability systems (toxicity)
2) Three fluorescent dyes often used in high-throughput systems (geno-/toxicity)
3) The isolation, quantification and analysis of RNA (genotoxicity)
The AuNPs exhibited optical interference with the detection system and direct adsorption of assay components with two of the assays. In addition, the distinct SPR and large surface area of AuNPs lead to a quenching in fluorescence of all three fluorescent dyes. Total RNA, isolated from untreated BEAS-2B bronchial human cells, was spiked with AuNP. The resultant sample was quantified and a concentration-dependant quenching of the absorbance spectrum was observed. The RNA purity absorbance ratios were also altered. Differences were not observed using electrophoretic analyses of RNA integrity. However, treatment of BEAS-2B cells, with NPs under non-cytotoxic test conditions, showed slight RNA absorption interference between 190-220 nm. In addition, interference varied depending on the point of NP application and the use of RNA stabilising solutions.
Toxicity results should be interpreted with caution when using conventional systems. The best alternative would be the use of a system independent of dyes or optical devices such as those that implement impedance technology. The isolation, quantification, purity and integrity are critical points of analyses for RNA-based techniques. Hence, the observed quenching effect would cause quantification errors and obscured integrity validation for gene expression studies.

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