are provided along with the role of the Community. Lead isotopic analyses can provide significant benefits to regulatory agencies, interested parties, and the community where the signature is able to be characterised with a high degree of certainty.

PS 2125 SIMULATION OF HEAVY METAL CONTAMINATION OF FRESH-WATER BODIES: TOXIC EFFECTS IN THE CATFISH AND ITS AMELIORATION WITH COCONTAMINATION WITH GLYPHOSATE.

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The toxic implications of fresh water contamination with zinc in the catfish, Clarias albopunctatus (Lamonte and Nicole, 1927), and the effect of a co-contamination with a sub-lethal dose ofglyphosate (Roundup) was studied using the static bioassay model. Thirty six fish were divided into 3 equal groups. Fish in Group 1 were placed in normal tap water, and served as the control group, while fish in Groups 2 and 3 were placed in water contaminated with ZnSO4 and ZnSO4 + glyphosate, respectively. The study lasted for 96 hours (though sampling was done at the 48th hour). Biochemical markers of toxicity were measured and the fish liver and gill histology were studied using standard protocols. The results show that ZnSO4 was significantly toxic to the fish only after 96 hours. Co-contamination of the water with both toxicants was found to ameliorate the toxic effects of ZnSO4 significantly. The metal chelating property of glyphosate may be responsible for the observed attenuation of toxicity in the fish in Group 3

PS 2126 MANAGING HUMAN HEALTH RISK THROUGH A COMPREHENSIVE AIR-MONITORING PLAN AT A FORMER MGP SITE.

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Monitoring for potential emissions from a Manufactured Gas Plant (MGP) remediation site is implemented to reduce or prevent a potential inhalation pathway for VOCs such as benzene, toluene, ethylbenzene, and xylenes; and contaminated particulates acting as a conduit for PAHs and heavy metals. This risk management case study presents a USEPA-approved air monitoring program implemented to manage human health risks at a former MGP site located in the southeast U.S. Risk-based Acceptable Air Concentrations (AACs) were developed and a sampling regime established to monitor potential emissions to maintain contaminant concentrations below the AACs. The AAC for benzene was based on carcinogenic effects using the current IUR from the USEPA's IRIS database. The AACs for toluene, ethyl benzene, and xylenes were based on non-carcinogenic effects using the current RfC from the IRIS database. The AACs for the carcinogenic PAHs were based on carcinogenic effects using the current IUR from California EPA. The AAC for respirable particulate matter (PM10) was the National Ambient Air Quality Standard (NAAQS) for PM10 and was used as a surrogate for both the PAHs and heavy metals. Site-specific AACs were calculated using a target cancer risk (TR) value of 1X10-4 for carcinogens and a target hazard quotient (THQ) of 1 for non-carcinogens. The exposure duration used was based on a twelve-month project duration and an exposure time of 24-hours per day; equations, toxicity values and sources were based on USEPA's Regional Screening Levels website (2009). A total 535 twenty-four hour time weighted samples (269 VOC samples and 266 PAH samples) were collected over the project duration. Only minor levels of VOCs and PAHs were detected and no results were above the AACs. These time-weighted averages demonstrate that the real-time air monitoring and control measures implemented at the Site effectively maintained concentrations below the AACs and were protective of human health.

PS 2127 INDUCTION OF NAD(P)H:QUINONE OXIDOREDUCTASE: INTERPLAY BETWEEN AH RECEPTOR AND NRF2.

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NAD(P)H:quinone oxidoreductase (NQO1) catalyzes the obligatory two electron reduction of quinones and quinoide compounds bypassing redox cycling and production of reactive oxygen radicals and protecting cells from toxicity. Induction of NQO1 is considered as a model for analyzing transcriptional regulation of many cytoprotective enzymes and proteins. The aryl hydrocarbon receptor (AhR) mediates the induction of NQO1 by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and benzo[a]pyrene (Bap); whereas, the antioxidant-activated receptor/transcription factor Nrf2 is critical for induction by antioxidants such as tert-butylhydroquinone (tBHQ). Induction of the genes by AhR agonists or antioxidants requires "dioxin response element" (DRE) or "antioxidant response element" (ARE), respectively. We previously reported a cross-interaction between AhR and Nrf2 signal transduction is required for induction of NQO1 by TCDD (Ma et al, Biochem J 377, 205-213, 2004). In this study, we analyzed the interaction between AhR and Nrf2 at the promoter of NQO1. Chromatin immunoprecipitation analyses revealed that treatment with TCDD recruits both AhR and Nrf2 to the promoter region where a DRE and an ARE locate; the finding is in agreement with the result from genetic studies in which induction by TCDD or Bap was shown to require both AhR and Nrf2. TCDD-induced binding of AhR and Nrf2 to DNA is time-dependent. Consistent with the activation of Nrf2, TCDD treatment inhibits Keap1-dependent ubiquitination and proteasomal degradation of Nrf2 resulting in the stabilization and nuclear accumulation of Nrf2. Co-immunoprecipitation experiments revealed that AhR directly interacts with Nrf2 in the presence of TCDD. Our findings demonstrate that AhR interacts with Nrf2 to control induction of NQO1 by AhR ligands.

PS 2128 ESTROGEN RECEPTOR ALPHA AND ARYL HYDROCARBON RECEPTOR DIFFERENTIALLY MODULATE THE TRANSCRIPTIONAL ACTIVITY OF NUCLEAR FACTOR ERYTHROID-2-RELATED FACTOR 2 (NRF2).

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Nuclear Factor-Erythroid 2 Related Factor 2 (NRF2) regulates the expression of a battery of Phase II detoxifying enzymes and provides cellular protection against electrophiles and oxidative stress. Sulforaphane (SFN) is a naturally occurring NRF2 activator in cruciferous vegetables and has been undergoing clinical trials for the prevention of breast cancer due to its pro-apoptotic and anti-mitotic effects in MCF7 breast cancer cells. Modulation of the NRF2 signalling pathway by estrogen receptor alpha (ERα) and the aryl hydrocarbon receptor (AHR) was investigated in this study. SFN induced NADPH-dependent oxidoreductase 1 (NQO1) and heme oxygenase I (HMOX1) mRNA expression, which was significantly diminished when MCF-7 ER+ cells were co-treated with various estrogenic compounds with the exception of diindodylmethane (DIM). DIM+SFN induced NQO1 and HMOX1 mRNA to levels greater than SFN alone. RNAi-mediated knockdown of AHR abrogated the supra-induction effect of DIM+SFN on NQO1 and HMOX1 expression, whereas knockdown of ERα abrogated the inhibitory effect of resveratrol (RES). In cells treated with SFN+17beta-estradiol (E2), ChIP assays revealed significant decrease in p300 recruitment which coincided with 1) decreased local Histone H3 Lysine 9 acetylation and 2) time-dependent increase in ERα recruitment at the NQO1 and HMOX1 enhancer regions. Taken together, our findings suggest that both ERα and AHR modulate the activity of NRF2. E2-mediated repression of HMOX1 and NQO1 might involve the recruitment of ERα, resulting in a decrease in p300 recruitment and an associated decrease in local H3K9Ac:H3. This study is funded by the Canadian Breast Cancer Foundation (CBCF) Doctoral Fellowship, the CBCF Grant Program and Canadian Institutes of Health Research Operating Grant.

PS 2129 NUCLEAR FACTOR E2-RELATED FACTOR-2 (NRF2) REGULATES P-GLYCOPROTEIN EXPRESSION AT THE BLOOD-BRAIN BARRIER (BBB) BY ACTING THROUGH P38 MAP KINASE.

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At the BBB, the ATP-driven efflux pump, P-glycoprotein (Pgp) is a major impediment to CNS pharmacotherapy. Signals that modulate Pgp transport function are complex and not fully mapped. Recent studies show that Pgp is upregulated by xenobiotics acting through nuclear receptors. Here we show that ligands for Nrf2 increase Pgp-mediated transport and transporter protein expression in rat brain capillaries. Nrf2 senses oxidative stress and induces multiple cytoprotective proteins, including antioxidant and glutathione generating enzymes, but its ability to modulate transport proteins is largely unexplored. We used freshly isolated rat brain capillaries, a fluorescent Pgp substrate and confocal microscopy to monitor chages in Pgp transport activity. Exposing capillaries to the Nrf2 ligand, sulforaphane (SFN, 0.1-10 μM), a naturally occurring compound present in cruciferous vegeta-

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