2014
SUPERFUND
RESEARCH PROGRAM
Annual Meeting

MAIN MEETING
SPEAKER BIOS & ABSTRACTS

UC BERKELEY SUPERFUND RESEARCH PROGRAM
SCIENCE FOR A SAFER WORLD

NIH National Institute of Environmental Health Sciences
Superfund Research Program

INDEX

SORTED A-Z BY SPEAKER NAME

LINNEA ANDERSON
Graduate Student, Brown University, linnea_anderson@brown.edu
Health Sciences

Linnea Anderson1, Ed Dere2, Susan Huse1, and Kim Boekelheide1
1Department of Pathology and Laboratory Medicine, Brown University, Providence, RI; and 2Division of Urology, Rhode Island Hospital, Providence, RI

SPEAKER BIOGRAPHY
I received my Bachelor of Science at Brown University, then attended the University of Edinburgh in Scotland for my Master of Science by Research. I returned to Brown University to enter the Pathobiology Doctoral Program, where I am a doctoral candidate in the lab of Kim Boekelheide.

TECHNICAL ABSTRACT

Molecular alterations in sperm are sensitive indicators of testicular dysfunction

Traditional endpoints used to measure male reproductive toxicity in humans, including semen and hormone analysis, are insensitive and unreliable; those used to monitor toxicity in animal studies, while sensitive, are not easily translatable to humans. It is therefore necessary to develop sensitive and reliable molecular biomarkers of testicular injury that can be used to both monitor human reproductive function and compare animal studies with human exposures. We approached this problem by exposing male rats to model testicular toxicants to identify sperm molecular alterations, as these can be compared to highly sensitive histopathological assessments of testicular function. Adult male rats were exposed to cyclophosphamide (CPP) for 12 weeks (1.4, 3.4, or 5.1 mg/kg/day p.o.) or 12 weeks plus a recovery period of 12 weeks (5.1 mg/kg/day p.o.) as a model of germ cell toxicity. Standard reproductive endpoints were examined; in particular, germ cell apoptosis and spermatid head retention were quantified as sensitive markers of damage. mRNA from cauda epididymidal sperm was analyzed for toxicant-induced alterations using a genome-wide microarray, then significant and robust alterations were further examined using qRT-PCR arrays and standard qPCR. We observed that CPP produced dose-dependent testicular injury that resolved after a 12-week recovery period. The levels of injury correlated with specific changes in transcript abundance, indicating a utility for these mRNAs as translatable biomarkers for male reproductive dysfunction. These transcripts will be examined in additional exposure settings, as well as both fertile and subfertile men to continue to validate the relevance of these alterations.

LAY ABSTRACT

Sperm biomarkers of male reproductive function

There are many chemicals and pharmaceutical drugs that cause damage to the male reproductive system when given at high levels or for long periods of time. In such a situation, whether by accidental environmental exposure or as prescribed by a doctor, it is important to monitor reproductive function of affected men. Unfortunately, the ways in which doctors can do this are limited and unreliable. It is also difficult to compare human exposures to tightly controlled scientific experiments because there are major differences in reproductive monitoring between men and laboratory animals. Researchers and doctors would benefit greatly from a reliable biological measurement (a â€œbiomarkerâ€□) of male reproductive function and fertility that applies to both men and laboratory animals. We proposed sperm as the source of these biomarkers; to test this, we exposed animals to a common chemotherapy drug and collected sperm after three or six months. We found that levels of certain mRNAs, which are sensitive readouts of DNA, were different in sperm from exposed versus unexposed animals. We think that these mRNAs are promising biomarkers, and with further research using both additional chemicals and human sperm, we can determine whether they are useful for a wider range of toxic exposures in both animals and humans.

JORDAN BAILEY
Postdoc, Duke University, jordan.bailey@duke.edu
Health Sciences

Bailey, JM and Levin, ED
Duke University

SPEAKER BIOGRAPHY

I received my PhD in cognitive and behavioral science, from Auburn University where I conducted research in behavioral toxicology. My dissertation work focused on methylmercury (MeHg)-induced changes in intracellular calcium regulation, and the functional evaluation of calcium channel antagonism in MeHg exposed rodents. At Duke I have focused on the development and adaption of behavioral assays for zebrafish that can be sensitive measures of toxicity. Most of my research has involved the characterization of early life pesticide and flame retardant exposure on later life behavioral endpoints in zebrafish.

TECHNICAL ABSTRACT

Using zebrafish to study neurobehavioral impairment caused a flame retardant mixture

Zebrafish have emerged as a complementary model for characterizing neurobehavioral toxicity and as such it is important to tap behavioral domains relevant to human toxicity. A behavioral test battery (BTB) characterizing zebrafish behavioral along several domains is used by our group. Here, the BTB is described and its utility in characterizing the behavioral effects of exposure to a flame retardant (FR) mixture is highlighted. FiremasterÂ® 550 (FM550) is the second most commonly used FR product in consumer goods and has been detected in household dust samples. However, neurobehavioral effects associated with exposure have not been characterized. We describe the effect of developmental exposure in zebrafish larvae, the persisting effects of this exposure on adolescent behavior, and the acute effects of exposure during adolescence. Developmental exposure to 0, 0.01, 0.1 or 1.0 mg/L via immersion spanned 0-5 days post fertilization, with larval testing on day 6 and adolescent on day 40. Acute exposure to 0, 1.0 or 3.0 mg/L spanned 24hrs, with testing 2hr or 1wk later. Persisting effects of developmental exposure manifested on one domain-specific task, i.e. a significant ($p < 0.01$) reduction in social behavior among all exposure groups. Acute adolescent effects were similar at the 2hr testing point but were attenuated thereafter. These data indicate that FR mixtures may cause persisting neurobehavioral alterations to social behavior in the absence of perturbations along other behavioral domains. This use of our BTB as well as this domain-specific effect of FM550 is discussed within the context of human exposures.

LAY ABSTRACT

Using an animal model to study the behavioral effects of exposure to a flame retardant mixture

The small freshwater zebrafish is useful as an animal model of human function; both simple and complex behavior can be measured in this species via a number of specialized tests. Tests are available that measure different aspects of behavior (e.g. learning, fear, social activity) and a behavioral test battery that includes a wide range of these tests is used by our group. Here, we characterize the behavioral effects of exposure to FiremasterÂ® 550 (FM550), which is the second most commonly used flame retardant mixture in consumer goods and has been detected in household dust. Despite its widespread use, the behavioral effects of contacting these chemicals are not well established. Therefore, we exposed zebrafish to several concentrations of FM550 either during their very early life (days 0-5 after fertilization) or briefly (24hrs) as adolescents and then measured changes in behavior. Fish exposed only very early in life were reared to adolescence in the absence of FM550, so that long term effects of exposure could be measured. When tested months after exposure, these fish did not engage in typical zebrafish social behavior despite normal performance on a variety of other tests. The fish just exposed briefly as adolescents also failed to engage in typical social behavior, however this deficit disappeared a week later. These data suggest that early life exposure to a flame retardant mixture might have specific behavioral effects that persist for months and are relevant to human function.

CANDACE BEVER
Postdoctoral Scholar, University of California, Davis, crspier@ucdavis.edu
Environmental Sciences and Engineering

Bruce Hammock and Shirley Gee
University of California, Davis

SPEAKER BIOGRAPHY

Candace Bever is currently a Postdoctoral Scholar in Dr. Hammock's laboratory at the University of California, Davis (UCD) and the Research Translation Coordinator for UCD's Superfund Research Program. Candace completed her PhD in Marine Science at the Virginia Institute of Marine Science (VIMS) at the College of William & Mary. She received a BS from Carnegie Mellon University and then completed a year of service as an AmeriCorps National Civilian Community Corps team member before enrolling in graduate school. Candace's research interest is in the fate of environmental contaminants. Her research focuses on the development and application of new immunologically-based methods for the rapid, on-site detection of environmental contaminants. She aims to develop new technologies intended for use in both human and environmental health monitoring applications.

TECHNICAL ABSTRACT

Immunoassays for small molecules that use novel single domain antibodies derived from camelids (VHH) in place of classical IgG antibodies

LAY ABSTRACT

From mice to alpacas: Detecting harmful chemicals using antibody technology

Antibody-based (immunoassay) technology has been effectively used as a screening tool for the detection of small chemical molecules. Traditionally, classical immunoglobulin G (IgG) antibodies typically from mice or rabbits are employed in these formats. More recently, we have been developing immunoassays for small molecules that use novel single domain antibodies derived from camelids (VHH) in place of classical IgG antibodies. VHH are 1/10th the size of, but bind as well as, classical antibodies. VHH also exhibit higher thermal stability, excellent solubility and chemical stability, likely due to their high refolding capacity. Their smaller size makes them ideal for genetic manipulation, which can be exploited for detection purposes. Because VHH DNA is easily cloned into plasmids, they are expressed in E. coli readily in high yield. The small molecule assays that we have developed for flame retardant chemicals, BDE-47 and tetrabromobisphenol A, as well as the pesticide pyrethroid metabolite, 3-phenoxybenzoic acid are among the most sensitive small molecule VHH assays reported, the first assays for environmental chemicals, and the first to use alpaca for VHH libraries. Furthermore, these VHHs have been employed in biosensor formats (e.g. electrode-based biosensor), further demonstrating their ease of incorporation into formats already developed for classical IgG antibodies.

AUDREY BONE
Graduate Student, Duke University, audreybone@gmail.com
Environmental Sciences and Engineering

Audrey Bone, Robert Tanguay and Richard Di Giulio
Duke University

SPEAKER BIOGRAPHY
Audrey Bone is a doctoral candidate in the laboratory of Dr. Richard Di Giulio at Duke University. She holds a B.S. in chemistry from Clemson University. Her current research focuses on incorporating environmental realism into the toxicity of nanoparticles in early life stage fish toxicity.

TECHNICAL ABSTRACT

The effect of photocatalysis of benzo(a)pyrene using titanium dioxide nanoparticles results on toxicity to larval zebrafish (Danio rerio)

Titanium dioxide nanoparticles (TiO2 NPs) are commonly used as a photocatalyst and as a UV-attenuator and are being investigated for use as a remediation aid at sites contaminated with organic compounds such as polycyclic aromatic hydrocarbons (PAHs). TiO2 NPs have the ability to produce reactive oxygen species when exposed to UV light in aqueous solution which oxidize organic compounds in a process known as photocatalytic degradation. Little is known about the potential toxicity of the resultant degradation products to vertebrates. In order to further explore the toxicity of these degradation products, solutions of 500 Âµg/L BaP, 0.5-10 mg/L TiO2 NP, and BaP + TiO2 NP were exposed to simulated sunlight (UV) or low UV lighting (no UV) for varying exposure times. The goal of this project was to complete a six week long K.C. Donnelly externship at Oregon State University in the laboratory of Dr. Robert Tanguay studying the toxicity of these degraded solutions by A) characterizing visible phenotypes associated with degradation products using the zebrafish developmental toxicity bioassay and B) exploring the toxicity mechanism by measuring the temporal and spatial cytochrome P4501A (CYP1A) expression and determine the role of the aryl hydrocarbon receptor paralogs in the toxicity. The study was unable to be completed as planned due to issues with the stability of degradation products being shipped from Duke University to Oregon State University. Although the degraded samples caused mortality and induction of CYP1A activity when used immediately, once frozen and shipped, degraded samples no longer exhibited any measureable toxicity. Multiple methods of sample preparation and shipping were attempted, but none were successful.

LAY ABSTRACT

Does breaking down the environmental pollutant benzo(a)pyrene using engineered nanoparticles reduce its toxicity to fish?

Certain types of nanoparticles are being considered for use in cleaning up polluted sites such as oil spills. However, the degraded chemicals that are produced by these nanoparticles could be more toxic than the original pollution. Therefore, we degraded benzo(a)pyrene, a common contaminant, using titanium dioxide nanoparticles and UV light. The goal of this project was to spend six weeks at the laboratory of Dr. Robert Tanguay at Oregon State University testing the degraded chemicals we produced to determine if they caused deformities in developing zebrafish eggs, and to see if they affected the production of a protein that responds to contaminant exposure known as CYP1A. However, once these degraded chemicals were shipped and frozen they were no longer toxic. Despite trying multiple methods of sample preparation and shipping, none were successful. However, I still gained valuable knowledge from my experience at a different lab and learned several useful techniques with which I had not previously been familiar.

CELIA Y. CHEN
Research Professor, Dartmouth College, celia.chen@dartmouth.edu
RTC/CEC

Celia Chen, Laurie Rardin, Nancy Serrell
Dartmouth College

SPEAKER BIOGRAPHY
Dr. Celia Chen is a Research Professor in the Department of Biological Sciences at Dartmouth College. She has been a lead scientist for 19 years in the Dartmouth Toxic Metals Superfund Research Program and has studied the fate and effects of metal contaminants in freshwater and estuarine ecosystems including the bioaccumulation and trophic transfer of mercury in lakes throughout the Northeast United States and coastal marshes from Maine to Maryland. Dr. Chen received her undergraduate degree in Biology and Environmental Studies at Dartmouth College, a masters degree in Biological Oceanography at the Graduate School of Oceanography of the University of Rhode Island and a Ph.D. in Ecology from Dartmouth College. She worked as a Staff Officer at the Marine Board of the National Research Council and has chaired regional and international workshops on mercury in marine ecosystems. She served on the U.S. EPA Science Advisory Board Mercury Review Panel and currently serves on the Science Advisory Board Ecological Processes and Effects Committee.

TECHNICAL ABSTRACT

LAY ABSTRACT

Connections Between Mercury Science and Policy from Sources to Seafood

How can we increase the role of science in informing policy? At the Dartmouth SRP, our RTC has developed a science-to-policy synthesis workshop model based on the successful completion of C-MERC, the Coastal and Marine Mercury Ecosystem Research Collaborative. Armed with the knowledge that In the U.S. and many regions of the world, more than 90 percent of human exposure to mercury (Hg) comes from the consumption of estuarine and marine fish, C-MERC brought together more than 70 scientists and policy experts to analyze and synthesize the science on mercury pollution in the marine environment from mercury sources to mercury in seafood. C-MERC authors published a series of 11 papers in peer reviewed journals and produced a synthesis report, â€œSources to Seafood: Mercury Pollution in the Marine Environmentâ€□, to inform policies and management actions under consideration at the local, national and international level to limit mercury exposure and safeguard human health. The timing of our C-MERC work was highly intentional: the C-MERC findings were communicated in presentations and discussions with government agencies in Washington, DC, and with delegations at the United Nations International Negotiating Conference in Geneva Switzerland during the development of the Minimata Treaty, a global instrument designed to control the predominant sources of Hg to the environment. C-MERC provides a model for a collaborative approach to bringing existing science to inform local, regional, and global environmental policy.

LEAH CHIBWE
Graduate Research Assistant, Oregon State University, chibwel@onid.orst.edu
Environmental Sciences and Engineering

Leah Chibwe1, Michael D. Aitken2, Jun Nakamura2, Staci L. Massey Simonich1,3
1Department of Chemistry, Oregon State University, Corvallis, Oregon 97330; 2Department of Environmental Sciences and Engineering, The University of North Carolina, Chapel Hill, NC 27599; 3Department of Environmental and Molecular Toxicology, Oregon State University, Corvallis, Oregon 97331

SPEAKER BIOGRAPHY

Leah Chibwe is a graduate student, originally from Zambia, at Oregon State University whose research focuses on developing an analytical method to identify and measure toxic compounds in soils that have undergone bioremediation. At Oregon State, she works with the Superfund Research Program under the guidance of Staci Simonich. At Chapel Hill, she worked in the laboratory of Michael D. Aitken and Jun Nakamura to learn and use the novel DT40 bioassay to identify soil compounds that are potentially toxic to genes.

TECHNICAL ABSTRACT

Identification and toxicity of polycyclic aromatic hydrocarbon (PAH) transformation products in bioremediated soils

The bioremediation of soils contaminated with polycyclic aromatic hydrocarbons (PAHs) is a concern due to the potential formation of more toxic oxygenated byproducts. PAHs are persistent in the environment, resistant to biodegradation, and some are known to have carcinogenic and mutagenic properties. Their oxygenated derivatives are more likely to be mobile in the environment, and could pose greater health risks. This study utilizes an effects-directed approach, combining toxicity analysis using the novel DT40 chicken bioassay, and gas chromatography mass spectrometry (GC/MS) for chemical analysis. The purpose of the study is to isolate and identify compounds in soil, which could potentially be the cause for increased toxicity in soil post bioremediation.
We developed an extraction method using pressurized liquid extraction (PLE), and fractionated the contaminants in the soil using silica solid phase extraction (SPE), by varying solvent elution polarity. The DT40 bioassay was then used to assess the toxicity of the different fractions. We observed an increase in the overall toxicity of the soil, and an increase in genotoxicity and mutagenicity in certain fractions post bioremediation.

LAY ABSTRACT

Investigating the toxicity and fate of PAHs in soil after bioremediation

Polycyclic aromatic hydrocarbons (PAHs) are a type of contaminant released through the incomplete combustion of organic matter. Bioremediation is used to remove the toxicity associated with PAHs in contaminated soil, but it's possible that the process might alter the PAHs in the soil causing an increase in toxicity.
We developed and applied a method that allowed us to investigate soil toxicity and the potential formation of toxic byproducts before and after bioremediation of contaminated soil .To help identify these toxic compounds, soil was separated into different portions based on polarity before analysis. We discovered an increase in toxicity in the overall soil, and in certain portions of the soil after bioremediation.

HILDA FADAEI
PhD student, University of Maryland Baltimore County, fhilda1@umbc.edu
Environmental Sciences and Engineering

Hilda Fadaei, Aaron Watson, Allen Place and Upal Ghosh
Department of Chemical, Biochemical, and Environmental Engineering, University of Maryland Baltimore County
Institute of Marine and Environmental Technology, UMCES

SPEAKER BIOGRAPHY

I am an Environmental Engineering PhD student at the University of Maryland, Baltimore County, working under the supervision of Dr. Upal Ghosh. My research focuses on fate and transport of PCBs in the environment. I'm currently studying the effect of bioavailability on PCB accumulation in aquatic organisms. My work involves the fundamentals of contaminant transfer between environmental compartments, sampling devices, and incorporating passive sampling measures in PCB bioaccumulation models. I received my M.S. in Environmental Engineering from University of Missouri and my B.S. in Chemical Engineering from University of Tehran.

TECHNICAL ABSTRACT

Measuring and modeling the effect of PCB bioavailability on accumulation in fish

While much work has been done demonstrating the effect of strong sorption of PCBs in sediments on bioaccumulation in benthic invertebrates, exposure to fish is less well understood. Black carbon in sediments present natively, or added as an amendment can greatly reduce porewater concentrations of PCBs, resulting in reduced flux from the sediment to overlying water and reduced bioaccumulation in benthic organisms. In the present study we performed laboratory aquaria experiments and modeling to explore how PCB sorption in sediments impacted exposure pathways and bioaccumulation in fish. Impacted sediments from a contaminated river treated with activated carbon to reduce bioavailability was used in the experiments along with untreated and control sediments. Results showed that porewater PCB concentration in impacted sediment was reduced by two orders of magnitude upon amendment with 4.5% powdered activated carbon. Sediment treatment reduced the PCB uptake in fish by a factor of 8 after 90 days. Freely dissolved concentrations in porewater and overlying water was measured by passive sampling and incorporated in equilibrium and kinetic bioaccumulation models for predicting uptake by fish. The fish exposed to untreated sediment did not reach equilibrium after 90 days of exposure. Uptake prediction with the kinetic model was generally within a factor of 2 compared to observed values for dominant PCB congeners. Our results indicate that by tracking changes in freely dissolved porewater and overlying water PCB concentrations, it may be possible to predict effectiveness of sediment remediation in reducing PCB uptake in the food chain, including fish.

LAY ABSTRACT

Measuring and modeling pollutant accumulation in fish

Cancer causing chemicals like polychlorinated biphenyls present in contaminated sediments can accumulate in fish and impact human health and the ecosystem. In this research we performed laboratory aquaria studies and modeling to understand how exposure to these chemicals is influenced by the association of the chemicals with different components in sediments. We show that when the chemicals are strongly bound to the sediments, the exposure to the fish is low and can be explained by the levels of dissolved concentrations of the chemicals in the water phase. By combining an emerging approach for the accurate measurement of the very low dissolved concentrations of chemicals with mathematical modeling of how fish is exposed to these chemicals, we were able to predict the accumulation of the chemicals in fish. Compared to the traditional approach of prediction based on total concentration of pollutants in sediments, our approach involving dissolved concentrations can lead to improved site-specific prediction of pollutant accumulation in fish.

SHOHREH F FARZAN
Postdoctoral Fellow, Geisel School of Medicine at Dartmouth, shohreh.farzan@dartmouth.edu
Health Sciences

Shohreh F. Farzan
Section of Biostatistics and Epidemiology, Department of Community and Family Medicine, Geisel School of Medicine at Dartmouth, Lebanon, NH

SPEAKER BIOGRAPHY
Dr. Shohreh Farzan is a postdoctoral fellow affiliated with the Dartmouth Toxic Metals Superfund Research group. Dr. Farzan is interested in chronic disease and long-term health outcomes in relation to toxicant exposure and potential genetic modifiers. Her current research focuses on arsenic exposure in relation to cardiovascular disease and pre-clinical markers of cardiovascular dysfunction and inflammation. Dr. Farzan is working to explore these health effects across a range of environmental exposure levels through complementary research projects within the New Hampshire Birth Cohort, the New Hampshire Health Study and the Columbia Superfund Health Effects of Arsenic Longitudinal Study (HEALS), with the goal preventing later-life disease by advancing our understanding of arsenic's contribution to cardiovascular disease initiation and progression.

TECHNICAL ABSTRACT

Cardiovascular effects of arsenic exposure

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide and high levels of arsenic exposure have been associated with increases in CVD risk. Arsenic exposure is a global issue and millions of individuals are chronically exposed to arsenic via contaminated water and foods. My KC Donnelly externship project focused on the relation between arsenic exposure and the risk of cardiovascular effects in two arsenic-endemic areas; Bangladesh, with data from the Health Effects of Arsenic Longitudinal Study (HEALS) and New Hampshire, USA, with data from the NH Health Study and NH Birth Cohort. In the NH Health Study, we examined CVD mortality in relation toenail arsenic concentrations and found that arsenic exposure was associated with increased ischemic heart disease mortality, particularly among smokers. In a preliminary analysis of the NH Birth Cohort Study, we found that environmentally present levels of arsenic exposure were associated with significant increases in systolic blood pressure and pulse pressure in women over the course of pregnancy. In a subset of HEALS participants, we analyzed the effect of arsenic exposure on blood pressure over time and in relation to genetic variants related to arsenic metabolism, vascular/endothelial function and inflammation that may alter an individual's susceptibility to arsenic's cardiovascular effects. Preliminary findings suggest a variant related to endothelial function and oxidative stress may interact with arsenic to increase pulse pressure over time. Together, these analyses have helped to inform the relation between arsenic and cardiovascular effects over a range of exposures, as well as establish ongoing collaborations between Dartmouth and Columbia Superfund researchers.

LAY ABSTRACT

Cardiovascular effects of arsenic exposure

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide and high levels of arsenic exposure have been associated with increases in CVD risk. Arsenic exposure is a global issue and millions of individuals are chronically exposed to arsenic via contaminated water and foods. My KC Donnelly externship project focused on the relation between arsenic exposure and the risk of cardiovascular effects in two arsenic-endemic areas; Bangladesh, with data from the Health Effects of Arsenic Longitudinal Study (HEALS) and New Hampshire, USA, with data from the NH Health Study and NH Birth Cohort. In the NH Health Study, we examined CVD mortality in relation toenail arsenic concentrations and found that arsenic exposure was associated with increased ischemic heart disease mortality, particularly among smokers. In a preliminary analysis of the NH Birth Cohort Study, we found that environmentally present levels of arsenic exposure were associated with significant increases in systolic blood pressure and pulse pressure in women over the course of pregnancy. In a subset of HEALS participants, we analyzed the effect of arsenic exposure on blood pressure over time and in relation to genetic variants related to arsenic metabolism, vascular/endothelial function and inflammation that may alter an individual's susceptibility to arsenic's cardiovascular effects. Preliminary findings suggest a variant related to endothelial function and oxidative stress may interact with arsenic to increase pulse pressure over time. Together, these analyses have helped to inform the relation between arsenic and cardiovascular effects over a range of exposures, as well as establish ongoing collaborations between Dartmouth and Columbia Superfund researchers.

REBECCA FRY
Associate Professor, UNC-Chapel Hill, rfry@unc.edu
Health Sciences

Rebecca C. Fry
Gillings School of Global Public Health, UNC-Chapel Hill, Chapel Hill, North Carolina

SPEAKER BIOGRAPHY

Dr. Fry is an Associate Professor in the Department of Environmental Sciences and Engineering at the Gillings School of Global Public Health at UNC-Chapel Hill. She also holds appointments in the Curriculum in Toxicology and the Lineberger Cancer Center. Dr. Fry received her Ph.D. in Biology from Tulane University and completed her post-doctoral training in toxico-genomics/environmental health at MIT. She is the Deputy Director of UNC's Superfund Research Program and leads one of three of the biomedical research projects where she is investigating the effects of prenatal cadmium exposure on infant health in populations in North Carolina. She is also funded by the NIEHS to understand the health effects associated with prenatal arsenic exposure in a cohort in Mexico. Building off her expertise is in the areas of DNA repair, toxico-genomics and systems biology, her research at UNC focuses on mechanisms of disease associated with toxic metal exposure early in life. A primary goal of Dr. Fry's research is to increase awareness of the deleterious impacts of exposures during the prenatal period and to improve public health initiatives to address this issue.

TECHNICAL ABSTRACT

Prenatal metal exposure and the epigenome

There is increasing evidence that toxic metals such as inorganic arsenic and cadmium can impact the epigenome including the modification of cytosines in the context of CpG methylation as well as altered small RNA signaling. Both these epigenetic modifiers can impact the expression of genes that play critical roles in biological pathways that regulate fetal growth and development. In our research we are examining the direct relationships between prenatal arsenic exposure, epigenetic modifications (i.e. CpG methylation) and functional changes in gene expression and birth outcomes in the BEAR pregnancy cohort in Mexico. The results of the research suggest that changes in DNA methylation that occur within specific regions of the genome such as within the transcription start site can be highly predictive of functional changes related to fetal growth. We have identified that arsenic is associated with the differential methylation of an imprinted gene KCNQ1, a key growth regulating gene. Additionally, our data highlight that miRNAs may influence gene expression to a greater extent than CpG methylation and impact immune-response pathways. Taken together, this information increases the mechanistic understanding of the links between toxic environmental metals, the epigenome, and health effects.

LAY ABSTRACT

Prenatal metal exposure and the epigenome

Prenatal arsenic exposure is associated with health effects at birth as well as health effects later in life. This research examines a potential mechanism that could underlie this, which is modification to the epigenome (i.e. â€œabove the genomeâ€□). These changes do not modify base sequences in DNA yet still influence the biology of the cell. Here we examine the relationship between prenatal arsenic exposure in a cohort in Mexico and changes to the epigenome, including both the addition of methyl tags on cytosines as well as changing the levels of small RNA molecules. Both of these changes impact gene expression or whether genes are â€œturned onâ€□ or â€œturned off.â€□ The identified changes provide insights into ways by which arsenic exerts its toxic effects during pregnancy.

DANIEL GUSENLEITNER
PhD Candidate, Boston University, gusef@bu.edu
Health Sciences

Daniel Gusenleitner1, Scott Auerbach2, David Sherr3, Stefano Monti1
1Section of Computational Biomedicine, Boston University
2National Institute of Environmental Health Sciences
3Environmental Health, Boston University

SPEAKER BIOGRAPHY
Daniel Gusenleitner is a research assistant in the Department of Bioinformatics at Boston University and working with Dr. Stefano Monti. He is interested in developing toxicogenomic models of environmental and chemical compounds in rodents and humans. These models not only offer a data-driven understanding of the mechanisms of action that eventually lead to carcinogenesis, but will also be utilized to develop a low-cost diagnostic screen to test new or undefined compounds for their carcinogenic potential. In October 2013, Daniel won first place in the Biomedical Student Poster Competition at the NIEHS Superfund Annual Meeting in Baton Rouge, LA. To view his abstract, click here.

TECHNICAL ABSTRACT

Genomic models of short-term exposure accurately predict long-term carcinogenicity and identify putative mechanisms of action

Despite an overall decrease in incidence of and mortality from cancer, about 40% of Americans will be diagnosed with the disease in their lifetime, and around 20% will die of it. Current approaches to test carcinogenic chemicals adopt the 2-year rodent bioassay, which is costly and time-consuming. As a result, fewer than 2% of the chemicals on the market have actually been tested. However, evidence accumulated to date suggests that gene expression profiles from model organisms exposed to compounds reflect underlying mechanisms of action, and that these toxicogenomic models could be used in the prediction of carcinogenicity.
In this study, we used a rat-based microarray dataset from the NTP DrugMatrix Database to test the ability of toxicogenomics to model carcinogenicity. We analyzed 1,221 gene-expression profiles obtained from rats treated with 127 well-characterized compounds and built a classifier that predicts a chemical's carcinogenic potential, and validated it on an independent dataset consisting of 2,065 profiles from 72 compounds. We confirmed and expanded upon previous studies implicating DNA damage, the peroxisome proliferator-activated receptor, the AhR receptor, and regenerative pathology in the response to carcinogen exposure.
Our results validate the toxicogenomic approach to predict carcinogenicity, show that the prediction of carcinogenicity is tissue-dependent, and provide evidence that, with a larger set of compounds, we would be able to substantially improve the prediction performance. For that we are currently translating our findings to human in-vitro systems, where we just analyzed 160 compounds using gene expression profiling, but also cytological profiling data a potential complementary assay.

LAY ABSTRACT

Genomic models are able to identify cancer causing chemicals and underlying biological mechanisms

Despite an overall decrease in cancer, about two in five of Americans will be diagnosed with the disease in their lifetime, and every fifth will die of it. Currently, 2-year long rat tests are used to determine whether or not a chemical causes cancer, which is expensive and takes a long time. As a result, less than one in fifty of the chemicals on the market have actually been tested. However, current research suggests that we can capture the biological changes that happen when rats or cell lines are exposed to a carcinogen by looking at gene expression and use them to test whether a compound potentially causes cancer.
In this study, we used a large-scale rat dataset from the National Toxicology program, the DrugMatrix Database, which includes gene-expression data from 1,221 rats treated with 127 well-known compounds. We built a model that is able to predict whether a chemical is a carcinogen, and validated it on an independent dataset that contains profiles from another 2,065 rats that were treated with 72 different chemicals. We confirmed and expanded upon previous studies, which includes the importance of damage to DNA and the activation of the aryl hydrocarbon receptor, a key player in environmentally caused cancer.
Our results show that gene expression data can be used to find carcinogens, show that different chemicals cause cancers in different tissues and provide evidence that, with a larger set of chemicals we would do an even better job at finding carcinogens accurately.

JAY JAMES
CEO, Picoyune, jayjames@picoyune.com
RTC/CEC

Jay James Ph.D., Jeffrey Crosby Ph.D.
Picoyune

SPEAKER BIOGRAPHY

Jay James Ph.D. is CEO of Picoyune, a company focused on instrumentation for chemical analysis. Their first instrument is a plasmonic sensor for mercury. Jay began his research on this topic at UC Berkeley under funding from the Superfund Research Program. Since starting in 2013, Picoyune has been awarded an SBIR grant from NIEHS, and won awards at several business plan competitions including first place in UC Berkeley's Launch Energy and Cleantech competition. Jay earned a B.S. in mechanical engineering from Cal Poly San Luis Obispo, and a Ph.D. in mechanical engineering at UC Berkeley.

TECHNICAL ABSTRACT

LAY ABSTRACT

Commercialization of a university technology using SRP and other institutional resources

During our SRP funded research at UC Berkeley on the interaction of mercury and gold nanoparticles, our inquiry moved from fundamental to practical. A supplement SRP tech-transfer grant allowed preliminary testing of the practical viability of our mercury sensor at the university. We filed for a patent and formed a company in an effort to commercialize the resulting technology. Our unique understanding of the technology was an asset, but institutional resources (courses, competitions, and grants) have been key to the development of the company. The courses offered by the UC Entrepreneurship Academy and the National Science Foundation's (NSF) I-Corps provided guidance specifically designed to help technologists grow a business. The customer discovery process advocated by the NSF I-Corps impacted our business model and provided understanding of our target market. We learned valuable lessons about the true pains and needs of the potential market and were able to change our direction before sinking more time and money into our initial business model. In the business plan competitions we tested our findings on a large number of business experts, further distilled our model, and raised some non-diluting funds. The Small Business Innovative Research (SBIR) grants offer another source of non-diluting funds to develop technologies. We have been awarded one SBIR from NIEHS and can provide insight into the application and award process.

MICHELE LA MERRILL
Assistant Professor, University of California at Davis, mlamerrill@ucdavis.edu
Health Sciences

Michele A. La Merrill and Christoph Buettner
University of California at Davis and Mount Sinai School of Medicine

SPEAKER BIOGRAPHY

Michele La Merrill has a PhD in Toxicology from University of North Carolina at Chapel Hill and a MPH from Mount Sinai School of Medicine, and is currently an Assistant Professor in the Department of Environmental Toxicology at University of California at Davis. She conducts epidemiological and experimental research on environmental chemicals that contribute to risk of obesity and diabetes.

TECHNICAL ABSTRACT

Superfund chemicals as risk factors for obesity and type 2 diabetes

Numerous chemicals remain on the Substance Priority List of the Superfund Amendments and Reauthorization Act. A subset of these chemicals, such as PCBs, DDT, DDE and PAHs, have been recently implicated in contributing to obesity. We provide evidence of these associations here, with a more in depth evaluation of DDT and DDE. Perinatal DDT exposure produced an early-life increase in body fat in female offspring. It also decreased energy expenditure and core body temperature, a key component of energy expenditure. When metabolically challenged by high fat feeding for 12 weeks in adulthood, female mice perinatally exposed to DDT developed glucose intolerance and hyperinsulinemia, major risk factors for type 2 diabetes. Perinatal DDT exposure combined with high fat feeding in adulthood further impaired thermogenesis as evidenced by reductions in core temperature and in the expression of numerous RNA that promote thermogenesis and substrate utilization in the brown adipose tissue of adult female mice. These observations suggest that perinatal DDT exposure impairs thermogenesis and metabolism which may increase susceptibility to obesity and type 2 diabetes in adult female offspring.

LAY ABSTRACT

Superfund chemicals as risk factors for obesity and type 2 diabetes

Numerous chemicals remain on the Substance Priority List of the Superfund Amendments and Reauthorization Act. A subset of these chemicals, such as PCBs, DDT, DDE and PAHs, have been recently implicated in contributing to obesity. We provide evidence of these associations here, with a more in depth evaluation of DDT and DDE. We have found that developmental DDT exposure produced an increase in body fat in female offspring during early adulthood. Obesity results from an imbalance in calories eaten and calories burned. We further found that developmental DDT exposure did not influence calories eaten or physical activity but decreased calories burned through metabolism as these mice were unable to maintain their target body temperature, a key calorie burning process. When metabolically challenged by high fat feeding for 12 weeks in adulthood, female mice perinatally exposed to DDT developed glucose and insulin problems consistent with elevated risk of type 2 diabetes. These observations suggest that perinatal DDT exposure impairs energy balance which may increase susceptibility to obesity and type 2 diabetes in adult female offspring.

ERIN MADEEN
Graduate Student, Oregon State University, madeene@onid.oregonstate.edu
Health Sciences

Madeen, E. P., Corley, R Turteltaub,K, Ognibene, T., Malfatti, M., Garrard, M., Sudakin, D., Mcquistan,T., Williams, D. E.
Oregon State University, Corvallis , OR, United States, Lawrence Livermore National Lab, Livermore, CA, United States, Pacific Northwest National Lab, Richland, WA, United States, Linus Pauling Institute, Corvallis, OR, United States.

SPEAKER BIOGRAPHY
Currently is a Ph.D. candidate in Environmental and Molecular Toxicology at Oregon State University, studying PAH metabolism and carcinogenesis in Prof. David Williams' Laboratory. Her focus is translational research of high dose animal model studies to human relevant exposures and potential risks. Utilizing human volunteers and controlled clinical studies with ultra sensitive accelerator mass spectrometry detection, her projects capture human metabolism of potential toxicants and environmentally relevant doses with no appreciable health risk. In addition to research, Erin is particularly interested in science communication and outreach. she mentors undergraduate students, leads high school outreach events, and is pursuing a teaching certificate.

TECHNICAL ABSTRACT

Environmentally Relevant In vivo Human Pharmacodynamic Analysis of the Polycyclic Aromatic Hydrocarbon, Dibenzo (def,p) chrysene: New Techniques For Relevant Exposures

Polycyclic aromatic hydrocarbons (PAHs) are formed from the combustion of materials containing carbon, such as in forest fires, or industrial applications. Oral exposure occurs from atmospheric deposition of PAHs to food crops, from flavoring or preserving food by smoking or by charcoal grilling. Several high molecular weight PAHs, including dibenzo[def,p]chrysene (DBC), are carcinogenic in laboratory animal models and are known or probable human carcinogens (IARC classes 1 and 2A). Previously, human in vivo metabolism studies of potentially toxic PAHs were not possible due to health risks from the dosage concentrations necessary for detection by traditional analytical methods. Accelerator mass spectrometry (AMS), provides the sensitivity necessary to detect environmentally relevant doses of PAHs, with de minimus health risk to human volunteers. Utilizing an HPLC interface, AMS is capable of uniquely identifying and quantitating parent PAH and enzymatically activated metabolites. We hypothesized that DBC pharmacodynamics and pharmacokinetics can be empirically determined from plasma utilizing ultra-sensitive liquid sample AMS following an environmentally relevant 29 ng oral dose, labeled with 5 nCi of 14C, administered to human volunteers. This environmentally relevant dose, identified by 14C in plasma, is found to be 15.9% activated to DBC diol, 14.9% DBC tetrol (unconfirmed), and 69.2% DBC parent. Both the parent and metabolites reach an early Tmax between 0.75 and 1.5 hours followed by a rapid elimination. This is the first pharmacodynamic data from human volunteers from controlled exposures. This data will be used to determine the accuracy of PB/PK modeling simulations for human health risk assessment.

LAY ABSTRACT

Human Metabolism of An Environmentally Relevant Dose of Toxicant Dibenzo[def,p]chrysene, New Technology For Translational Studies

The human toxicant, DBC (dibenzo[def,p]chrysene), can be detected and quantitated in human volunteers at environmentally relevant doses for health risk assessment. Some combustion products of the class polycyclic aromatic hydrocarbons, PAHs, including DBC are associated with cancer risk. Human exposure occurs from eating contaminated food crops or eating foods preserved or flavored by smoking or charcoal grilling. The health effects of these compounds are often studied in high dose animal models, which may not represent human low dose exposures. Data is needed to translate these results to human relevance. Utilizing an ultra sensitive detector classically used for carbon dating, accelerator mass spectrometry (AMS), we are able to quantify human metabolism from an environmentally relevant exposure to DBC, with no appreciable risk to human volunteers. The dose administered of 29ng DBC is less than is contained in a charbroiled burger. It is specifically isotopically labeled with 14-C, which is ultimately detected via AMS, allowing for unique identification and sensitivity. Results from human plasma indicatate that 69.2% of the circulating DBC was unmetabolized parent compound. 14.9% was DBC tetrol and 15.9% was DBC diol. The time of the highest concentration in plasma was between 0.75 and 1.0 hours post dose for both parent and metabolites, followed by rapid elimination. Only metabolized DBC is bio-reactive and capable of forming DNA adducts, a precursor to potential mutagenesis and cancer. Understanding the extent to which PAHs, such as DBC, are metabolized will help form realistic potential risk estimates following exposure.

RANCE NAULT
Graduate Assistant, Michigan State University, naultran@msu.edu
Health Sciences

R. Nault1,2, K.A. Fader1,2, D.A. Ammendolia2, S.Y. Lunt3, L. Newhouse3, T.R. Zacharewski1,2
1Center for Integrative Toxicology, Departments of 2Biochemistry & Molecular Biology, and 3Physiology, Michigan State University, East Lansing, MI, United States

SPEAKER BIOGRAPHY
Rance Nault is a PhD candidate in Biochemistry & Molecular Biology at Michigan State University with an extensive background in toxicology having completed a Masters in Chemical and Environmental Toxicology at the University of Ottawa, Canada. As part of the Superfund Research Program, his current studies explore the role of environmental contaminants on hepatic metabolic disorders using an â€˜omics' approach. Rance continuously seeks to incorporate cutting edge resources and technologies to further elucidate mechanisms of toxicity and disease through computational modeling and data integration. His ongoing projects involve the development of computational tools to aid in the assessment of toxic risk, which leverage recent advances in high performance and cloud computing solutions.

TECHNICAL ABSTRACT

Integrating Differential Gene Expression with Hepatic, Serum, and Urinary Metabolomes Identifies TCDD-elicited Interactions Between Disrupted Metabolic Pathways

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) elicits hepatic lipid accumulation that can progress to steatohepatitis with fibrosis in mice. To further investigate the hepatic effects of TCDD, female C57BL/6 mice were orally gavaged every 4 days for 28 days with sesame oil vehicle, 0.01, 0.03, 0.1, 0.3, 1, 3, 10, or 30 Âµg/kg TCDD. RNA-Sequencing identified 1,294 unique differentially expressed hepatic genes (|fold-change| â‰¥ 2.0, P1(t) â‰¥ 0.8) associated with oxidative stress, energy metabolism, immune response, and fibrosis. Targeted LC-MS/MS analysis detected 126, 72 and 130 metabolites in hepatic extract, serum and day 26 urinary metabolomes, respectively (vehicle, 3, 10 and 30 ug/kg only). Cytoscape was used to map differential expression and metabolite data onto 15 disrupted KEGG pathways that converged to carbohydrates, NADPH and acyl-CoAs. For example, decreased acyl-CoA levels and the concomitant down-regulation of acetyl-CoA acyl transferase (thiolase) and acyl-CoA synthetase (acetyl-CoA carboxylase) gene expression are indicative of Î²-oxidation inhibition and consistent with hepatic lipid accumulation. Furthermore, limiting acetyl-CoA production from Î²-oxidation compromises the TCA cycle resulting in an increase in oxaloacetate levels and impaired cholesterol biosynthesis. Collectively, integration of transcriptomic and metabolomic data suggests TCDD elicits systemic metabolic dysregulation associated with the dose-dependent progression of steatosis to steatohepatitis with fibrosis. Funded by SRP P42ES04911.

LAY ABSTRACT

Integrated analysis of metabolic disruption by TCDD

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) causes fat accumulation in the liver which can progress to inflammation and fibrosis, effects widely known as non-alcoholic fatty liver disease (NAFLD). We investigated this metabolic disruption by simultaneously measuring expression changes in thousands of genes or metabolites after TCDD treatment in mice. Gene and metabolite changes caused by TCDD were mapped to known 15 pathways involved in glucose and fat metabolism, two key players in NAFLD development. For example, a number of involved in fat metabolism (Î²-oxidation pathway)were expressed at lower levels consistent with decreases in fat breakdown products and the accumulation of fat in the liver. Î²-oxidation is also an important source of acetyl-CoA which can be used by the citric acid cycle (TCA cycle) and cholesterol synthesis pathways, both of which also show evidence of disruption by TCDD exposure. Considering these pathways together implicates acyl-CoAs as a central component to metabolic disruption by TCDD. The integration of results from these large scale studies has not only provided more information regarding the toxicity of TCDD and related compounds, but also identified a target that can be used to develop drugs for the treatment of NAFLD as well as more complex diseases such as liver cancer, cardiovascular disease and diabetes. Funded by SRP P42ES04911.

MICHAEL C. PETRIELLO
Doctoral Candidate, University of Kentucky, michaelcpetriello@gmail.com
Health Sciences

Petriello, Michael C 1, 2; Morris, Andrew2; Hennig, Bernhard2
1. Graduate center for toxicology, University of Kentucky, Lexington, KY
2. Superfund Research Center, University of Kentucky, Lexington, KY

SPEAKER BIOGRAPHY

I obtained my undergraduate degree from Muhlenberg College in Allentown, Pennsylvania with a double major in biology and environmental science. I then joined Dr. Bernhard Hennig's laboratory at the University of Kentucky Superfund Research Center in 2010. During my doctoral work I have been interested in identifying novel mechanisms of toxicity of environmental pollutants, specifically polychlorinated biphenyls, and developing ways to modulate this toxicity through nutritional intervention. I obtained an American Heart Association predoctoral fellowship to examine how bioactive nutrient metabolites called nitro-fatty acids can decrease inflammation, and how to better analyze and quantify their levels in humans.

TECHNICAL ABSTRACT

Bioactive nutrient metabolites protect against PCB-induced vascular inflammation

Data implicate correlations between persistent organic pollutants (POPs), like polychlorinated biphenyls (PCBs), and chronic inflammatory disorders such as cardiovascular disease. We have shown that coplanar PCBs can initiate the earliest stages of atherosclerosis including endothelial cell dysfunction and inflammation. Complete remediation of POPs remains the ultimate goal to reduce associated disease risks, but these processes are time consuming and expensive. Therefore, it is critical to identify and implement sensible means of biologically modulating or buffering against the toxicity of Superfund chemicals. Emerging data show that nutritional modulation, via the intake of diets high in anti-inflammatory nutrients, may help to prevent such associated disease risks. Currently, it is not known if protection is due to actions of parent nutrients or a set of bioactive metabolites created within the body. Therefore, the aim of this research was to determine if an endogenously formed bioactive metabolite (nitro-fatty acid) could modulate the toxicity of POPs. Vascular endothelial cells were pretreated with linoleic acid or nitro-linoleic acid and subsequently exposed to physiologically relevant concentrations of PCB 126. Interestingly, treatment with parent linoleic acid was pro-inflammatory as evidenced by increased mRNA levels (RT-PCR) of vascular cellular adhesion molecule-1 (VCAM-1), monocyte chemoattractant protein-1 (MCP-1) and caveolin-1 (Cav-1). These levels were exacerbated in linoleic acid/PCB treated cells. Importantly, the addition of a nitro group to linoleic acid prevented this exacerbated PCB effect. Understanding diet-pollutant interactions is a critical step towards more effective risk assessment and prevention of pollutant-induced disease for populations residing near Superfund sites. (NIH/NIEHS P42ES007380)

LAY ABSTRACT

Healthful nutrition can protect against environmental pollutant-induced inflammation

Multiple studies show links between environmental pollutants and chronic inflammatory disorders such as cardiovascular disease. Removing these pollutants from the environment is the ultimate goal to reduce associated disease risks, but these processes are time consuming and expensive. Therefore, it is critical to identify sensible means of buffering against the toxicity of hazardous chemicals. Emerging data now show that nutritional modulation, via the intake of diets high in anti-inflammatory nutrients, may help to prevent such associated disease risks. Currently, it is not known if this protection is due to parent nutrients or a set of bioactive metabolites formed within the body. Therefore, the aim of this research was to determine if a protective metabolite (nitro-fatty acid) could decrease the toxicity of environmental pollutants. Vascular cells were pretreated with the fatty acid linoleic acid, which is found in many inexpensive cooking oils, or nitro-linoleic acid (nitro-fatty acid metabolite) and subsequently exposed to the environmental pollutant polychlorinated biphenyl 126. Interestingly, treatment with the parent linoleic acid was pro-inflammatory by itself as evidenced by higher levels of multiple markers of biological stress. These levels were made even worse in linoleic acid plus PCB treated cells. Importantly, in the nitro-fatty acid groups, cells were protected from these toxic effects. Understanding diet-pollutant interactions is a critical step towards more effective risk assessment and prevention of pollutant-induced diseases for populations who reside near Superfund sites. (NIH/NIEHS P42ES007380)

JAMES W RICE
Postdoctoral Research Associate and State Agencies Liaison, Brown University, james_rice@brown.edu
Environmental Sciences and Engineering

James W Rice (1), Travis Bals (1), Eric M Suuberg (1), Robert M Burgess (2), Kim Boekelheide (1)
(1) Brown University, Providence, RI, USA
(2) US Environmental Protection Agency, ORD/NHEERL, Narragansett, RI, USA

SPEAKER BIOGRAPHY

James Rice is a post-doctoral research associate and the Engineering State Agencies Liaison for the Superfund Research Program (SRP) at Brown University's School of Engineering. James received a BS (2006) from Northeastern University and an ScM (2008) and PhD (2011) from Brown University, all in chemical engineering. James is interested in the fate and transport, chemistry, and thermodynamics of environmental contaminants, and on translation of scientific research to relevant stakeholders, such as regulators, environmental consultants, and community members. He advises and teaches students in both the laboratory and the classroom. He recently received the 2013 NIEHS KC Donnelly Externship Award, the Spring 2012 AIChE Best Paper Presentation Award, and a 2011 Sigma Xi Outstanding Graduate Student Award.

TECHNICAL ABSTRACT

Use of LDPE Passive Samplers for Monitoring PAHs in the Water Column of a Suburban, Freshwater Oil-Spill Site

Polycyclic aromatic hydrocarbons (PAHs) are common components of petroleum products that are sometimes released to surface and ground water via leaks and spills, often threatening water quality and ecosystem health. Contaminants that dissolve into water are most readily available for biological uptake and exposure, and can be monitored using passive sampling techniques. This study used low-density polyethylene (LDPE) polymer sampling strips deployed for a period of four weeks in the riverine environment of a Grafton, MA canal that is heavily contaminated by Bunker-C heating oil. The PAHs that were sorbed by the LDPE from the aqueous phase were measured using gas chromatography-mass spectrometry (GC-MS). To permit calibration of the method, involving corrections for possible bio-fouling and differences in compound sampling rates, equilibrium dynamics were established using the loss of deuterated PAH reference compounds impregnated in the LDPE prior to deployment. Results using the LDPE samplers suggest that PAH concentrations previously determined by water grab-samples may overestimate the equilibrium water content of PAHs of concern. Results suggest the value of use of passive samplers in oil-spill contaminated sites, as an alternative to simple water grab samples.

LAY ABSTRACT

Passive Samplers: A New Way to Measure Spilled Heating Oil in Water

Fuels, such as home heating oil, gasoline, and diesel are sometimes accidentally spilled or leaked into lakes, ponds, rivers and the ocean. This can damage water quality and the health of plants and animals that live in or near the polluted water. Passive samplers are a relatively new way to measure the amount of spilled fuel (and other pollutants) in water. In this study, we made passive samplers out of plastic drop cloth purchased at a local hardware store. We placed the passive samplers underwater in a Massachusetts river that is heavily polluted with spilled heating oil. We left the passive samplers underwater for 1 month to allow some spilled heating oil to absorb into the plastic drop cloth. We then collected the samplers, brought them back to the lab, and measured the amount of oil that had absorbed into the plastic drop cloth. These measurements were then used to calculate the actual amount of spilled heating oil in the river. We found that passive samplers may work better than other, more traditional measurement methods in locations where water is heavily contaminated with fuel oil.

EKIHIRO SEKI
Associate Professor, University of California San Diego, ekseki@ucsd.edu
Health Sciences

Yoon Seok Roh1, Shuang Liang1, Bi Zhang1, Ekihiro Seki1
1University of California San Diego, Department of Medicine

SPEAKER BIOGRAPHY

Dr. Seki has been trained as a gastroenterological-hepatobiliary surgeon in Japan. After completion of his residency and training in surgery, Dr. Seki started his research career on the study of Toll-like receptors (TLRs), which are essential signal sensors recognizing microbial products to initiate innate immunity, in liver diseases. As his graduate study, Dr. Seki has studied regulatory mechanisms of how TLR4 signaling and inflammasome activation contribute to liver disease development. Dr. Seki did his postdoctoral training at Columbia University in New York, and worked on the role of TLR4 signaling in hepatic stellate cell (HSC) biology and liver fibrosis. Dr. Seki determined a new role of TLR4 signaling in HSCs in the crosstalk with fibrogenic TGF-Î² signaling in liver fibrosis. Dr. Seki has also uncovered the interaction between Kupffer cells and HSCs in liver fibrosis through the chemokine-chemokine receptor interaction. Currently, Dr. Seki is conducting his research at UC San Diego. His group investigates the effect of toxin exposure to fibrogenic response in the individuals with underlying liver disease, such as fatty liver disease and hepatitis.

TECHNICAL ABSTRACT

The underlying mechanism of enhancement of toxin-induced liver fibrosis in fatty liver disease

The prevalence of obesity and non-alcoholic fatty liver disease (NAFLD) has been significantly increased in the last decades. Our superfund program previously demonstrated that the development of toxicant-mediated hepatocellular carcinoma (HCC) is augmented in obese mice. Here, we investigated whether NAFLD affects toxin-induced liver fibrosis and its underlying mechanisms.

Chronic exposure of carbon tetrachloride (CCl4), a superfund toxicant, induces liver fibrosis. HFD-fed mice developed more liver fibrosis as demonstrated by increased collagen deposition and fibrogenic gene expression than normal diet-fed mice after exposure to CCl4. Mice fed with HFD or genetically obese mice showed reduced hepatic expression of TAK1, a MAP3K upstream of NF-ÎºB and JNK. Therefore, we hypothesize that the decreased TAK1 function in fatty liver disease enhances CCl4-induced liver fibrosis. To examine the effect of decreased TAK1 in the liver, we generated hepatocyte-specific TAK1-deficient (TAK1KO) mice. Upon exposure to CCl4, TAK1KO mice had exacerbated liver fibrosis as demonstrated by increased collagen deposition, serum ALT levels and hepatic fibrogenic gene expression. TAK1-deficient hepatocytes showed Smad2/3 overactivation, which

LAY ABSTRACT

Fatty liver disease changes the sensitivity to toxin exposure that enhances liver fibrosis.

Nowadays, obesity and fatty liver disease are serious health concerns in the developed countries. These metabolic diseases shorten life expectancy by worsening various underlying diseases, such as diabetes, cardiovascular disease, and various cancers including liver cancer. In human liver cancer, the underlying liver fibrosis/ cirrhosis significantly influences the incidence and the growth of liver cancer. We know acute and chronic exposure to environmental and industrial toxicants, such as carbon tetrachloride (CCl4), causes liver damage and fibrosis. However, we do not know whether people with fatty liver disease will be more sensitive to toxin exposure that causes liver fibrosis. We tested by using animal model, and found that high fat diet-fed mice showed the enhancement of toxin-induced liver fibrosis. To explore its underlying mechanism, we found that an intracellular protein kinase TAK1 expression is decreased in fatty liver disease and is further reduced by chronic exposure to CCl4. In addition, we found that endogenous TAK1 prevents cytokine and toxin-induced hepatocyte damage and fibrogenic response in the liver. Autophagy is a key process to maintain cellular homeostasis to eliminate unfolded long-lived proteins and damaged organelle, such as mitochondria. TAK1 also controls autophagy induction in hepatocytes to maintain cellular homeostasis to prevent hepatocyte

increased susceptibility to TGF-Î²-mediated hepatocyte death and expression of connective tissue growth factor, contributing to enhanced liver fibrosis. In addition, TAK1-deficiency is associated with autophagy defects in hepatocytes. Restoration of autophagy by rapamycin attenuated the development of liver fibrosis in TAK1KO mice, suggesting that autophagy suppression caused by the loss of TAK1 may play a role in the development of liver fibrosis. In conclusion, the decreased TAK1 expression is a mechanism of enhanced CCl4-induced liver fibrosis in fatty liver disease.	damage. Our research revealed a part of the mechanisms of how TAK1 maintains hepatocyte homeostasis and survival. Fatty liver disease causes the changes in hepatic TAK1 expression, which enhances the sensitivity of livers to environmental and industrial toxin exposure.

CRAIG STEINMAUS
Associate Adjunct Professor, University of California Berkeley, craigs@berkeley.edu
Health Sciences

Steinmaus C (1,2), Castriota F (3), Ferreccio C (4), Smith AH (1,2), Smith MT (1,2)
1. Arsenic Health Effects Research Group. University of California, Berkeley
2. University of California, Berkeley Superfund Research Program
3. Columbia University
4. Pontificia Universidad Catolica de Chile

SPEAKER BIOGRAPHY

Dr. Steinmaus is a board-certified physician in Occupational and Environmental Medicine with over 10 years of clinical experience. He is also an Associate Professor of Epidemiology at the University of California, Berkeley (UCB), an Assistant Professor at the School of Medicine and the Global Health Sciences Program at the University of California, San Francisco (UCSF), and a Public Health Medical Officer III (Epidemiology) in the California Environmental Protection Agency's (Cal EPA) Office of Environmental Health Hazard Assessment (OEHHA). He has been involved in epidemiologic research on the health effects of chemical contaminants in drinking water for the last 15 years. He has been the Project Director or Principal Investigator (PI) for six large NIH-funded studies on arsenic and other contaminants with a focus on factors conferring susceptibility including diet, genetics, metabolism, and early life exposure. He has been the PI of two recently completed, NIH-funded R01 studies on early life exposure to arsenic in drinking water and cancer and non-malignant respiratory effects in Chile; is the PI of a newly funded R01 study on early-life arsenic exposure and cancer; and is the PI on an R01 study of perchlorate and thyroid hormone levels in 2000 pregnant women from San Diego County. He currently teaches three graduate level courses on occupational and environmental epidemiology at UCB and UCSF, has served on several NIH and CDC study sections, was a panelist for US EPA's most recent Integrated Risk Information System (IRIS) workshop on arsenic, and was an invited speaker at the National Academy of Science's 2013 Inorganic Arsenic Workshop. He is also involved in risk assessment for Cal EPA and has contributed to risk assessment documents on drinking water perchlorate, chromium 6, nitrate, and fluoride.

TECHNICAL ABSTRACT

The combined effects of arsenic exposure and obesity on lung and bladder cancer risks in a uniquely exposed population in northern Chile

Background: Obesity is a major risk factor for cardiovascular disease, diabetes, cancer, and other common diseases. The chronic inflammatory state induced by obesity has been proposed as a possible mechanism for these effects. Millions of people worldwide drink arsenic contaminated water, and arsenic has also been linked to inflammation and cancer. Methods: We used a unique exposure scenario in northern Chile involving high arsenic drinking water exposures and good data on past exposure to investigate possible interactions between arsenic and obesity on lung and bladder cancer risks. Information on self-reported body mass index (BMI) at various life stages, smoking, diet, and lifetime arsenic exposure was collected from 532 cancer cases and 634 population-based controls.

LAY ABSTRACT

The combined effects of arsenic exposure and obesity on lung and bladder cancer risks in a uniquely exposed population in northern Chile

Rates of several types of cancer are higher in people with obesity. Obesity causes a low-grade inflammation in the body and this inflammation has been hypothesized to be one of the mechanisms by which obesity may increase cancer risks. Like obesity, exposure to arsenic also increases both inflammation and cancer. Given these common effects, it seems possible that cancer risks may be especially high in people who are both exposed to arsenic and are obese. In this study, we obtained information on past height and weight, smoking, diet, and arsenic exposure in 532 people with bladder and lung cancer and comparison group of 634 people without cancer. In those people who had a body mass index (BMI, a measurement commonly used to evaluate excess weight) in the top 10 percent, we found that the

Results: In subjects with BMIs below the 90th percentile at age 20, the odds ratios (OR) for lung and bladder cancer combined for arsenic water concentrations of <100, 100-800 and >800 Âµg/L were 1.00, 1.64 (95% CI, 1.19-2.27), and 3.12 (2.30-4.22). In subjects with BMIs above the 90th percentile, the corresponding ORs were higher: 1.00, 1.84 (0.75-4.52), and 9.37 (2.88-30.5), respectively (synergy index=4.04, 95% CI, 1.27-12.8). Evidence for synergy was not seen for elevated BMIs beginning in later adulthood. Conclusion: Although sample sizes were small in some analyses, these findings provide novel evidence that an elevated BMI in early adulthood may result in major increases in arsenic-associated cancer risks later in life. Additional research is needed to identify dose-response relationships, further define critical exposure periods, and explore potential mechanisms.	estimated risks of arsenic-related cancer were up to four-times higher than the risks in those subjects with lower BMIs. We found that these increased risks were higher in those who had an elevated BMI in early adulthood (i.e., at age 20) compared to those whose BMIs were only elevated as older adults. Overall, although some of our analyses contained only a small number of subjects, these findings suggest that arsenic and obesity may combine to cause especially high cancer risks. Future studies may help determine whether these associations occur at low arsenic levels, help identify the critical ages for these effects, and explore exactly how these two factors (obesity and arsenic) might cause these combined effects.

MICHAEL STOVERN
Graduate Student, University of Arizona, stovern@email.arizona.edu
Environmental Sciences and Engineering

Michael Stovern
University of Arizona

SPEAKER BIOGRAPHY

Michael Stovern was born and raised in Minnesota where he received his bachelors of science in Meteorology from Saint Cloud State University in 2008. He then attended the University of Arizona and received a Masters degree in Atmospheric Sciences in 2011. Michael will be completing his Ph.D. from the University of Arizona, Department of Atmospheric Sciences this fall. Michael's dissertation focuses on the transport of contaminants such as arsenic and lead from storage piles using computational models and in situ observations. During his graduate studies Michael was elected graduate student representative of the Department of Atmospheric Sciences for several years and chaired the interdepartmental research colloquium "EarthWeek". In his free time, which is very limited, Michael is an avid outdoors man who loves hunting, fishing and hiking.

TECHNICAL ABSTRACT

Development of a PM27 dust deposition forecast model for a mine tailings impoundment

Wind erosion, transport and deposition of contaminated particulate matter can have significant impacts on the environment especially in semiarid and arid regions. Mining operations including tailings impoundments are an important anthropogenic source of windblown dust in these regions. This study is focused on emissions, dispersion and deposition of windblown dust from the Iron King mine tailings in Dewey-Humboldt, Arizona, a Superfund site. The tailings impoundment is heavily contaminated with lead and arsenic and is located directly adjacent to the town of Dewey-Humboldt. The study includes the development of a windblown dust deposition forecasting model (DFM) that predicts deposition patterns of fugitive PM27 tailings dust.
The DFM uses in situ observations from the tailings and idealized particle simulations of aerosol transport to parameterize the model. The DFM was initialized using the operational Weather Research and Forecasting (WRF) model over several month-long observational periods. The forecast deposition patterns were compared to inverted-disc samples through gravimetric, chemical composition and lead isotopic analysis. Results from comparing transects of arsenic and lead tracers measured by the samplers to the DFM PM27 forecast indicated that the DFM was able to accurately capture the regional deposition patterns of the tailings dust up to 1 km. Lead isotopes were used for

LAY ABSTRACT

Development of a dust deposition forecast model for a mine storage pile

Wind erosion, transport and deposition of particulate matter can have significant impacts on the environment. Windblown dust is especially prominent issue in the desert southwest U.S. where the dry climate and sparse vegetation increase the natural potential to produce dust. Mining operations including tailings impoundments are an important anthropogenic source of windblown dust in this region. This study is focused on emissions, dispersion and deposition of windblown dust from the Iron King mine tailings in Dewey-Humboldt, Arizona, a Superfund site. The tailings impoundment is heavily contaminated with lead and arsenic and is located directly adjacent to the town of Dewey-Humboldt. The study includes the development of a windblown dust deposition forecasting model (DFM) that predicts deposition patterns of windblown dust originating from the tailings impoundment.
The DFM uses in situ observations from the tailings and theoretical simulations of aerosol transport to parameterize the model. The DFM was verified over several month-long observing periods via the implementation of inverted-disc deposition samplers. The DFM was initialized using data from an operational Weather Research and Forecasting (WRF) model and the forecast deposition patterns were compared to the inverted-disc samples through gravimetric, chemical composition and lead isotopic analysis. Results from the sampling periods indicated that the DFM was able to accurately capture the

source apportionment and showed spatial patterns consistent with the DFM and the observed weather conditions. By providing reasonably accurate estimates of contaminant deposition rates, the DFM can improve the assessment of human health impacts caused by windblown dust from the Iron King tailings impoundment.	regional deposition patterns of the tailings dust up to 1 km. By providing reasonably accurate estimates of contaminant deposition rates, the DFM can improve the assessment of human health impacts caused by windblown dust from the Iron King tailings impoundment.

ERIC M. SUUBERG
Professor, Brown University, Eric_Suuberg@brown.edu
Environmental Sciences and Engineering

Eric M. Suuberg
Brown University

SPEAKER BIOGRAPHY

Prof. Suuberg has been Associate Director of the Brown SRP since its inception, also serving as a Project Leader and Research Translation Core Director in that Center. He was a co-founder of Brown's Chemical Engineering program, as well as a cofounder of Brown's undergraduate concentration in Business, Entrepreneurship and Organizations, and the Masters Program in Innovation Management and Entrepreneurship. A registered professional engineer, he is also a frequent consultant on problems related to environmental pollution and its causes. He is a Fellow of the American Chemical Society, in which he serves as a Trustee of the Energy and Fuels Division. He serves as a principal editor of the journal Fuel. His research focus has been in the areas of chemical thermodynamics, kinetics and transport. Recently, this has involved experimental examination of thermodynamic properties of relevance to fate and transport processes for organic contaminant mixtures such as tars, oils and halogenated hydrocarbons. He has also been actively involved in studying the processes that characterize the vapor intrusion process, and leads a group that has been developing mathematical tools for describing this problem.

TECHNICAL ABSTRACT

Vapor Intrusion- Environmental Health Risks, Technical and Regulatory Challenges

Vapor intrusion (VI, or sometimes, soil vapor intrusion, SVI) is a problem whose scope is not always fully realized or appreciated, and whose investigation and management offer major challenges to environmental regulators and engineers. The complexity of the problem defies simple analysis or regulatory response. At the present time, there exists a patchwork of different regulations throughout the US, and what is considered as acceptable risk varies tremendously, and the regulatory landscape is continually changing. This paper will discuss what the group at Brown has learned through mathematical modeling of the VI phenomenon, and consider how such advanced tools might help better address the problem going forward. It will also examine the general structure of mathematical models of vapor intrusion, and how these will have to continue to evolve. Examples will be given regarding the conclusions that can be drawn from examination of the US EPA's database on vapor intrusion phenomena, and what sorts of issues can confuse simple application of models. The use of simplified analyses, such are part of present site screening processes, will also be examined in the context of what the more complete engineering models offer in terms of development of full site conceptual models.

LAY ABSTRACT

Vapor Intrusion- Environmental Health Risks, Technical and Regulatory Challenges

Vapor intrusion (VI, or sometimes, soil vapor intrusion, SVI) is a problem whose scope is not always fully realized or appreciated, and whose investigation and management offer major challenges to environmental regulators and engineers. Starting almost two decades ago, warnings began to be issued about VI from both petroleum and non-petroleum (especially chlorinated solvent) sources. Over a decade ago, the US EPA began preparing draft guidance on the issue, but has yet to finalize it. The complexity of the problem defies simple analysis or regulatory response. At the present time, there exists a patchwork of different regulations throughout the US, and what is considered as acceptable risk varies tremendously. Moreover, the regulatory landscape is continually changing. What was once a field dominated by concern about excess cancer risk is now increasingly concerned with non-cancer endpoints (especially with trichloroethylene, TCE). Re-opening investigations on sites previously deemed as â€œcleaned upâ€ is common. The scientific understanding guiding how to investigate sites is under continual challenge; in certain instances the role of natural attenuation processes is now believed to be much more significant than it was in the past. On the other hand, there is much greater temporal variability in residential exposures than was recognized or believed earlier, leading to important questions about how to be truly protective of health. This paper will discuss what our group has learned in the process of performing mathematical modeling of VI, and speak to how such advanced tools might help better address the problem going forward.