SRP GRANTEE MEETING
Monday, December 5, 2016

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Please refer to the NIEHS Environmental Health Science FEST webpage for more information about area restaurants and EHS FEST events on December 6-8.
**Agenda**

*Unless otherwise noted, all events will take place at the Grand Ballroom, Durham Convention Center, Durham, NC

**Monday, December 5, 2016**

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<td>7:00 – 9:00 a.m.</td>
<td>Graduate Student Posters Set-Up</td>
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<td>7:00 – 9:00 a.m.</td>
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<td><strong>Moderator: William Suk</strong></td>
<td>9:00 – 9:10 a.m.</td>
<td>Welcome/Opening Remarks</td>
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<td>9:10 – 9:20 a.m.</td>
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<td>9:20 – 9:40 a.m.</td>
<td>Plenary Talk</td>
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<td><strong>Moderator: Gwen Collman</strong></td>
<td>9:40 – 10:15 a.m.</td>
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| **Moderator: Rick Woychik** | 10:30 – 11:40 a.m. | Data Science Panel Discussion | David Sherr (Boston University)  
Illya Zaslavsky (UC San Diego)  
MaryLou Guerinot (Dartmouth College)  
Allen Dearry (NIH) |
| 11:40 a.m. – 1:00 p.m. | Lunch (on your own) Poster Viewing          | Area Restaurants             |
| 12:00 – 1:00 p.m. | Optional meeting with Sally Darney, Editor, Environmental Health Perspectives | Junior Ballroom D |
Agenda Continued

**Moderator: Phil Brown**
1:00 – 1:20 p.m.
What happened at the Gold King Mine Spill and to the Navajo People?: University Response to assist through Navajo Project Partnerships

**Moderator: William Suk**
1:20 – 1:50 p.m.
KC Donnelly Winners (10 min. each)
Kate Buckman (Dartmouth College)
Marvic Carmona De Jesus (University of Puerto Rico/Northeastern)
Lisandra Santiago Delgado (Oregon State University)

1:50 – 3:50 p.m.
Poster Session
Graduate Students – please stand by your poster for the competition judging
Junior Ballroom C

**Moderator: Danielle Carlin**
3:50 – 4:30 p.m.
KC Donnelly Winners cont. (10 min. each)
Erika Fritsch (UC-Davis)
Zhilin Guo (University of Arizona)
Miao Li (University of Iowa)
Lauren Redfern (Duke University)

4:30 – 4:45 p.m.
Closing Remarks
William Suk (SRP/NIEHS)

4:45 – 5:00 p.m.
Group Photo
Steve McCaw (OCPL)

5:00 – 5:15 p.m.
Poster Breakdown
Junior Ballroom C

5:00 – 6:00 p.m.
Directors Meeting
Junior Ballroom B

5:30 – 6:30 p.m.
Trainee Reception
Tyler’s Restaurant and Taproom (324 Blackwell St.)

6:30 – 8:30 p.m.
Open Reception/Award Announcements
Tyler’s Restaurant and Taproom (324 Blackwell St.)
Map to Reception

Monday December 5, 2016

Trainee Reception 5:30 – 6:30 p.m.

Open Reception 6:30 – 8:30 p.m.

Tyler’s Restaurant and Taproom (324 Blackwell St.)
Administrator’s Meeting Agenda

Monday, December 5th
Location: Junior Ballroom D

1:00 – 1:15 p.m.  Introductions and Welcome

1:15 – 1:30 p.m.  Discuss and Update SRP Administrative List Serve

1:30 – 2:30 p.m.  NIEHS Best Practices

*Lisa A Edwards and Bryann Benton*

Carry Forward, Escalating F&A Rate Including Supplements and Carry Forward, Sub Award Monitoring as it Relates to the Progress Report and RPPR, PubMed for RPPR, Genomic Data Sharing; and Other Support Documentation

2:30 - 4:00 p.m.  Round Table Discussion

*Jennifer Moore and Eve Marion*


4:00 p.m.  Administrator’s Group Photo

Location: TBD (Steve McCaw)

7:00 p.m.  Administrator’s Dinner (for Center Administrators only)

Location: Dos Perros, 200 N Mangum Street

One on One Meetings:
Sign up for One on One meetings with NIEHS Grants Management Staff and SRP Program Administrators at the Resource Room. Sign-ups are at the Registration Desk.

Tues 12/6, 11:15 a.m. – 12:45 p.m.: Lisa Edwards, Bryann Benton, and Erin Knight (MyNCBI Expert)

Tues 12/6, 3:45 – 5:15 p.m.: Lisa Edwards and Erin Knight

Wed 12/7, 10:45 a.m. – 12:15 p.m.: Lisa Edwards, Danielle Carlin, and Erin Knight

Wed 12/7, 3:15 – 4:45 p.m.: Lisa Edwards, Heather Henry, and Erin Knight
What happened at the Gold King Mine Spill and to the Navajo People? --
University Response to assist through Navajo Project Partnerships

Karletta Chief, Assistant Professor
Dept. of Soil, Water, & Environmental Sciences
University of Arizona

On August 5, 2015, 3 million gallons of acid mine drainage was released from the Gold King Mine, eventually reaching the San Juan River – the lifeblood of the Navajo Nation. Many Native American communities have subsistence livelihoods and strong spiritual beliefs that are deeply connected to the natural environment. As a result, environmental contamination from catastrophic mine spills severely impacts indigenous people to the core of their spiritual and physical livelihoods and there is potential for unique exposure pathways and greater health risks. This talk will explain what happened with the Gold King Mine Spill and how it impacted the Navajo Nation. Through a listening session that was held, five themes arose from the discussion and include 1) mistrust of outside entities conducting research, 2) concern that research findings won’t come back to the community, 3) anxiety around whether water is safe for subsistence (irrigation, livestock, washing), 4) concern for lack of decision-making protocols, and 5) recognizing cumulative and future impacts to the Animas-San Juan watershed. The Navajo people have been spiritually, emotionally, economically, and psychologically stressed by the Gold King Mine Spill. The Dine’ people say they need clean-up, security from future contaminations, and more accountability in the data collection and results communication. People were disappointed and frustrated by the response of the federal and tribal response to the Gold King Mine Spill. This talk will also share the experiences of building community partnerships to develop and implement a time-sensitive proposal to National Institute of Environmental Health Sciences entitled “Tó’lìtsó, the water is yellow: Investigating short term exposure and risk perception of Navajo communities to the Gold King Mine Spill” and the Agnese Nelmes Haury Foundation Challenge Grant. This is a partnership between the Navajo Community Health Representatives (CHR) Program, University of Arizona (UA) and Northern Arizona University (NAU), Dine’ College, To’ Bee Nihi Dzill and Fort Lewis College. Into the future, the Navajo community members expressed goals of a hydrological water plan, to continue farming, to be more involved, to have water treatment plants, more voice, more involvement of the community and connection, more awareness of the situation, and protection of the river for future generations.
Biography (231 words)

Dr. Karletta Chief (Diné) is an Assistant Professor and Specialist in Soil, Water, and Environmental Sciences at the University of Arizona (UA). Her research focuses on understanding, tools, and predictions of watershed hydrology, unsaturated flow in arid environments, and how natural and human disturbances impact water resources. As an extension specialist, she works to bring relevant science to Native American communities in a culturally sensitive manner by providing hydrology expertise, transferring knowledge, assessing information needs, and developing applied science projects. Dr. Chief is a member of a national climate change network of indigenous and non-indigenous scientists and is working with the Navajo Nation on impacts of the Gold King Mine spill. Dr. Chief is Diné from Black Mesa, AZ and was raised without electricity or running water. She is a first generation college graduate. Dr. Chief received a B.S. and M.S. in Civil and Environmental Engineering from Stanford University in 1998 and 2000 and a Ph.D. in Hydrology and Water Resources from UA in 2007. She completed her post-doctorate at Desert Research Institute in Las Vegas, NV. In 2011, Dr. Chief was named American Indian Science and Engineering Society Most Promising (AISES) Scientist/Scholar, 2013 Stanford University Distinguished Alumni Scholar award, and 2015 Native American 40 under 40. She recently received the 2016 AISES Professional of the Year which will be awarded at the AISES National Conference in Minnesota in November 2016.
Formation of Oxy- and Hydroxy-PAHs during Bench-scale Thermal Remediation of Superfund soil

Lisandra Santiago Delgado¹,², Eva L. Davis³, and Staci L. Massey Simonich¹,²

¹Department of Chemistry, Oregon State University, Corvallis, OR, USA
²Department of Environmental and Molecular Toxicology, Oregon State University, Corvallis, OR, USA
³Ground Water and Ecosystems Restoration Division, US EPA, Ada, OK, USA

Polycyclic aromatic hydrocarbons (PAHs) are environmental contaminants produced mainly from the incomplete combustion and pyrolysis of organic matter. PAHs are among the major contaminants at Superfund sites and are present at over 800 sites nationwide. Thermal remediation employs the use of heat to mobilize and recover pollutants, and is used as a method to remediate soils contaminated with PAHs. Steam enhanced extraction (SEE) is an in-situ thermal remediation technique which relies on the addition of steam (heat) to soil in order to increase the removal efficiency and recovery of volatile and semi-volatile contaminants. However, limited information is available regarding formation of PAH breakdown products during and after thermal remediation. This is due to the inability to predict transformation products, the historical lack of standards, and challenges in the analysis of PAHs and their breakdown products in complex environmental mixtures. Breakdown products seem to be more mobile than PAHs in the environment, and some are more toxic to humans, animals, and plants, compared to the corresponding PAHs. There is an urgent need to develop analytical methods that can accurately quantify these PAH breakdown products, specifically hydroxy PAHs (OHPAHs). In this study, we optimized a gas chromatography/mass spectrometry (GC/MS) method for the analysis of OHPAHs, and identified and quantified non-substituted PAHs, OHPAHs, oxygenated PAHs and nitrated PAHs in creosote contaminated soil before and after SEE from the Wyckoff/Eagle Harbor Superfund site.
Case study of using the stochastic method for contaminant transport in groundwater

Zhilin Guo\textsuperscript{a}, Jose Lopez, Graham Fogg\textsuperscript{b}, Mark Brusseau\textsuperscript{a}

\textsuperscript{a}School of Earth and Environmental Sciences, University of Arizona, Tucson, Arizona, USA
\textsuperscript{b}Department of Land, Air, and Water Resources, University of California-Davis, Davis, California, USA

A recent National Research Council report has stated that most sites with large groundwater plumes comprising contaminants such as chlorinated solvents (e.g., trichloroethylene, tetrachloroethylene, carbon tetrachloride), 1,4-dioxane, methyl tertiary-butyl ether (MTBE), and perchlorate, will require many decades or longer before cleanup will be achieved under current methods and standards. Porous-medium heterogeneity is one of the important factors that contributes to the plume persistence. Enormous funds are spent to characterize sites before the remediation methods are applied, while it is still impossible to obtain detailed information for parameters (e.g. hydraulic conductivity) everywhere because of spatial variability. Stochastic methods have been used to decrease the uncertainties of parameters. The establishment of an appropriate numerical model can help to better delineate and quantify the impact of the various persistence factors, which can provide more information to improve remediation efforts. This study will include a case study that used the stochastic method, Transition Probability Geostatistical Software (T-PROGS), and the mathematical models MODFLOW and the advanced random walk particle method (RWhet) to simulate contaminant transport at the Tucson International Airport Area (TIAA) federal Superfund site. Advantages using T-PROGS and RWhet will be discussed. This work will lead to improve understanding of contaminant transport and plume persistence, and in turn will enhance site characterization and site management for contaminant sites with large plumes.
Finding the Needle in the Haystack - Applying SILAC and RBPP to Identify Protein Adducts of PCB Metabolites

Miao Li\textsuperscript{1,2}, Breanna Ford\textsuperscript{3}, Susanne Flor\textsuperscript{2}, R.M. Pope\textsuperscript{4}, Daniel K. Nomura\textsuperscript{3},
L.W. Robertson\textsuperscript{1,2}, G. Ludewig\textsuperscript{1,2}

\textsuperscript{1}Human Toxicology, \textsuperscript{2}Dept. Occupat. & Environ. Health, \textsuperscript{4}Proteomics Core Facility, University of Iowa, Iowa City, IA 52242
\textsuperscript{2}Program in Metabolic Biology, Dept. Nutritional Sciences & Toxicology, University of California, Berkeley, Berkeley, CA 94720

Polychlorinated biphenyls (PCBs) have been found in inner city air, and also in public school buildings in the US and Europe. The observation of high levels of airborne PCBs in old school buildings raises concerns of inhalation exposure and toxicity of these predominantly lower chlorinated PCBs (LC-PCBs). LC-PCBs are subject to biotransformation which may lead to reactive epoxide, hydroxyl and/or quinone metabolites, but few studies have explored the toxicity of these compounds. In vitro and in vivo studies revealed that reactive metabolites of LC-PCBs form covalent adducts with DNA and proteins. Profiling the target proteins of reactive PCB metabolites could help to better understand the toxic mechanism of LC-PCBs, but no such study was found. The goal of this study was to identify target proteins of PCB3 (4-monochlorobiphenyl) quinone (PCB3-Q) metabolites using traditional and novel techniques. MALDI-TOF and LC-QTOF analysis of experiments with cell lysates in vitro did not show the expected PCB3-Q adducts on cysteine residues. Incubating trypsin pre-digested albumin with PCB3-Q revealed cysteine adducts. The adducts decreased significantly during incubation in pH 7 buffer at 37 °C, but the ‘un-adducted’ peptides did not reappear, suggesting that the ‘instability’ of these adducts may be caused by further redox reactions of quinones and crosslinking. Therefore, the Stable Isotope Labeling by Amino acids in Cell culture (SILAC) method was used where amounts of heavy and light-labeled proteins serving as sample and control, respectively, are compared to indirectly identify the target proteins based on the disappearance of one of the twin peaks. In vitro exposure to cell lysates revealed GAPDH, Annexin A2 and Peroxiredoxin-1 may be the targets for PCB3-Q. The KC Donnelly award made it possible to further increase detection sensitivity by applying the Reactivity-Based Protein Profiling (RBPP) method, developed and refined by Dr. Nomura’s lab at UC Berkeley. Preliminary results suggest adduct formation on DNA topoisomerase 2-beta. These results show that the multiple preparation steps involved in classical proteomics methods may lead to a disappearance of cysteine adducts and false negative results, while the more sensitive, indirect SILAC and RBPP methods will provide evidence of adduction that can be used to identify target proteins and reactive metabolites.

(Funded by NIEHS P42 ES013661 (Iowa) and ES004705 (Berkeley))
Effects of maternal transfer of mercury on larval fish movement: learning how to measure a behavioral endpoint

Kate Buckman\textsuperscript{a}, Bryan Clark\textsuperscript{b}, Denise Champlin\textsuperscript{b}, Ian Kirby, Joseph Bishop, Celia Chen\textsuperscript{a}, Diane Nacci\textsuperscript{b}

\textsuperscript{a}Biology Department, Dartmouth College, Hanover, New Hampshire, USA.
\textsuperscript{b}U.S. Environmental Protection Agency, Office of Research and Development, National Health and Environmental Effects Research Laboratory, Atlantic Ecology Division, Narragansett, Rhode Island, USA.

Buckman spent her externship at the Narragansett (RI) EPA laboratory where she and the members of the Nacci lab collaborated to run a preliminary experiment examining the effects of maternal transfer of mercury on larval fish behavioral endpoints. The execution of this experiment allowed for the development of a framework for future experiments relating early life exposures to later life ecological effects.

Mummichogs (\textit{Fundulus heteroclitus}) from two wild populations with differing native mercury exposures were utilized for the experiment and fed either a high or low methylmercury diet. Fish were strip spawned every two weeks during the feeding period. Adult fish were sampled for tissue total mercury concentration at the start and end of the experiment. Unfertilized eggs were utilized to measure egg methylmercury concentration from each spawning event. Danioscope software was used to assess the heart rate of developing embryos at 10 days post fertilization. A dark:light movement assay determined differences in behavior of larvae between treatments at three and 10 days post hatch using Ethovision software. Tissue analysis indicated successful maternal transfer of mercury to eggs in the high mercury feed treatment through our feeding method. Heart rate and movement assays could be conducted despite large variation in fertilization success, and indicate potential population level differences in baseline behavior. Buckman will present preliminary experimental results as well as discuss her learning experiences and opportunities to collaborate afforded by the KC Donnelly externship.
Use of Passive Sampler Devices for Deployment and Sampling of Spring Water in the Northern Karst Aquifer of Puerto Rico

Marvic Carmona De Jesús\textsuperscript{a}, Ingrid Y. Padilla\textsuperscript{b}, Kim Anderson\textsuperscript{c}, Perla Torres\textsuperscript{d}

\textsuperscript{a}Civil Engineering and Surveying Department, University of Puerto Rico at Mayaguez, PR, USA
\textsuperscript{b}Director of EEL\textsuperscript{*}, Civil Engineering and Surveying Department, University of Puerto Rico at Mayaguez, PR, USA
\textsuperscript{c}Director of FSES\textsuperscript{**}, Environmental and Molecular Toxicology Department, Oregon State University, Corvallis, OR, USA
\textsuperscript{d}Research Assistant of EEL\textsuperscript{*}, Civil Engineering and Surveying Department, University of Puerto Rico at Mayaguez, PR, USA

As a tropical island in the Caribbean, Puerto Rico receives significant amount of rainfall. The northern region of the island, which in its vast majority is underlain by karst terrain, has an annual precipitation of 1,550 mm. In the northern karst region, a significant amount of the rainfall is routed through an underground drainage system containing sinkholes, highly porous rock matrix, fractures, and conduits. During heavy rainfall events, underground flow increases and persistent organic pollutants (POPs) can rapidly enter the groundwater via runoff and pore-matrix exchange. The traditional grab sampling methods used to monitor pollution may, however, miss peak contaminant concentrations because of the lack of sample collection during these events. To circumvent these limitations, new and more sensitive technologies have been developed to measure time-weighted average (TWA) concentrations over long periods of time. These include passive sampling devices (PSDs) that allow for monitoring of multiples contaminants at very low concentrations at a TWA. This study uses modified PSDs developed at the Oregon State University SRP Center to monitor polycyclic aromatic hydrocarbons (PAHs) in two spring in the karst region of northern Puerto Rico. The threat for sustained and/or intermittent exposure to contaminants in this region is being evaluated by the Puerto Rico Testsite for Exploring Contamination Threats SRP Center. Supported by the KC Donnelly Externship Award and National Institute of Environmental Health Sciences (NIEHS) Grant Award No. P42ES017198, the work involved technology transfer and training, development of modified PSDs and methods appropriate for spring sampling and analysis, deployment of PSDs into the springs, and chemical analysis. A total of 10 PSDs were deployed for 21 days, 5 at each spring. Chemical compounds were extracted from the PSDs using hexane and analyzed in a GC-MS equipped with a VF-5ms column. Results show that the PSDs are applicable for monitoring of POPs in dynamic spring flows. Overall, the PSDs are less expensive for water pollution detection and quantification than traditional grab-sampling methods, but they only provide TWA measurements and limit assessment of temporal contaminant distributions. To have a better resolution, it is best to integrate the information for both methods.

\textsuperscript{*} EEL is the Environmental Engineering Laboratory Civil Engineering and Surveying Department, University of Puerto Rico at Mayaguez, PR, USA

\textsuperscript{**} FSES is the Food Safety and Environmental Stewardship, Program Environmental and Molecular Toxicology Department, Oregon State University, Corvallis, OR, USA
Novel molecular tool to monitor the biodegradation of co-contaminants 1,4-Dioxane and PAHs

Lauren K. Redfern, Lisa Alvarez-Cohen, Claudia K. Gunsch

Pratt School of Engineering, Department of Civil and Environmental Engineering, Duke University. Durham, NC 27713
Department of Civil and Environmental Engineering, University of California, Berkeley
Berkeley, CA 94708

Microbial communities that have adapted to live at heavily contaminated Superfund sites occupy a specific niche and these naturally adapted populations may be exploited for bioremediation. During my KC Donnelley work, we developed a molecular tool to monitor the dissemination of PAH- and dioxane-degrading catabolic genes in environmental samples. This enables the monitoring through quantification and temporal tracking of biodegradation potential during bioremediation. In this study, we focused on PAHs and 1,4-dioxane, which co-occur at many sites such as landfills and former drum disposal sites. Sets of microcosms were used to assess the efficacy of co-augmentation as a strategy for improving bioremediation and to demonstrate the ability of unique qPCR Taqman probes as a bioremediation monitoring tool. *Pseudomonas putida* G7 (PpG7) was used as a model naphthalene-degrading microorganism. PpG7 carries the IncP NAH7 plasmid, which is a catabolic and self-transmissible plasmid capable of completely degrading naphthalene. It also associated with the degradation of other PAHs, such as anthracene and phenanthrene. *Pseudonocardia* CB1190 (CB1190) was used as a model 1,4-dioxane-degrading microorganism, as it can degrade 1,4-dioxane as its sole carbon source and also harbors catabolic plasmids. From these microcosms, it was shown that the Taqman probes allow for the rapid and simple identification of an increase in catabolic genes normalized to an increased in microbial growth (i.e., an increase in overall biodegradation potential) in contaminated and complex environmental matrices. This work has implications for optimizing and monitoring bioremediation at Superfund sites.
Characterizing ryanodine receptor and FK506 binding protein isoforms in the Atlantic killifish (Fundulus heteroclitus): A phylogenetic and population based comparison.

Erika B. Holland\textsuperscript{a,b,c,*}, Jared V. Goldstone\textsuperscript{b}, Isaac N. Pessah\textsuperscript{c}, Andrew Whitehead\textsuperscript{d}, Sibel I. Karchner\textsuperscript{b}, Mark E. Hahn\textsuperscript{b} and John J. Stegeman\textsuperscript{b}

\textsuperscript{a}Department of Biological Sciences, California State University of Long Beach, Long Beach CA, USA
\textsuperscript{b}Department of Biology, Woods Hole Oceanographic Institution, Woods Hole MA, USA
\textsuperscript{c}Department of Molecular Biosciences, University of California Davis, Davis CA, USA
\textsuperscript{d}Department of Environmental Toxicology, University of California Davis, Davis CA, USA

Abstract:
Polychlorinated biphenyls (PCBs) remain an environmental and human health concern and are commonly found at Superfund National Priority Sites (NPS). Non-dioxin-like PCBs (NDL-PCBs) activate the ryanodine receptor (RyR) and this activity is associated with neurotoxicity. There is currently a lack of information regarding whether RyR genetic variability may contribute to differential RyR toxicity. We utilize large sequence datasets in Atlantic killifish (\textit{Fundulus heteroclitus}) to compare \textit{RyR}-isoforms and isoforms of \textit{FK506} binding protein 12kDa (FKBP1), known to be involved in NDL-PCB RyR disruption, between killifish and mammals. We also investigated genetic variation between PCB exposed killifish from the NPS at New Bedford Harbor (NBH) compared to the reference killifish population from Scorton Creek (SC). Findings demonstrate that teleost species have 6 \textit{RyR}-isoforms and 2-4 FKBP1 isoforms displaying tissue and age specific expression. The presence of six \textit{RyR}-isoforms, compared to three in mammals (\textit{RyR1-3}), included an uncharacterized duplicate \textit{RyR3}. The additional \textit{RyR3}, herein named \textit{ryr3b}, displayed the highest expression in killifish brain, with limited expression in heart and skeletal muscle. RNA-sequencing data also revealed a prominent single nucleotide variant in \textit{ryr3b} from NBH killifish at E1457D (D1553 in rabbit \textit{RyR3}) that was limited in SC killifish. This amino acid is upstream of residue S1582 an important site for FKBP-RyR interactions. This research helps establish the killifish as an important model for \textit{RyR} related neurotoxicity and suggests that residue 1457 maybe important for defining species or individual NDL-PCB sensitivity, which requires further investigation (NIEHS SRP UCD P42ES04699 EBH and INP; BU-P42ES007381 JJS and JVG)
Poster Session Abstracts

1. The role of Oxidative Stress and MT1F in the Toxicity of Cadmium & Arsenic Mixtures from Hazardous Waste Sites in Placental JEG-3 cells

Oluwadamilare Adebambo, North Carolina State University
oadebam@ncsu.edu

Abstract:
The occurrence of cadmium (Cd) and inorganic arsenic (iAs) as mixtures poses unique challenges because of the little known health effects. This work builds on our initial study demonstrating a significant synergistic increase in mRNA expression levels of metal-responsive and oxidative stress genes - metallothioneins (MT1A, MT1F and MT1G) and heme-oxygenase 1(HO-1) in Cd and iAs environmental mixture-treated cells compared to the Cd or iAs only-treated cells. Oxidative stress in the placenta, and dysregulated transforming growth factor beta (TGF-β) pathway signaling in the maternal vasculature, have been investigated for their contribution to improper placentation and the pathogenesis of certain pregnancy complications. Hence, we measured oxidative stress in placental JEG-3 cells treated with environmental metal mixtures versus single metals and controls, and corresponding TGF-β pathway gene levels. The highest level of reactive oxygen species (ROSs) was measured in metal-mixture treated cells. Conversely, co-treatment with the antioxidant N-acetyl cysteine (NAC) reduced oxidative stress levels with a concomitant down-regulation of MT and TGF-β pathway genes. Furthermore, MT1F knockdown was carried out and expression of TGF-β pathway genes, sEng and sFlt1 were measured. Our results indicate that increased oxidative stress and inhibition of metallothionein contribute to the down-regulation of critical pathways required for proper placentation during early pregnancy.

Contributing Authors:
Damian Shea, NC State University
Rebecca Fry, University of North Carolina, Chapel Hill
2. Iron-graphene oxide nanocomposite (Fe-GO) membranes for remediation of chloro-organics by oxidative pathway

Ashish Aher, University of Kentucky
ashish.aher@uky.edu

Abstract:
Decomposition of organics by sulfate radicals generated from persulfate salts have gained attention for remediation of various toxic organic compounds. Graphene, reduced graphene and nitrogen doped graphene have emerged as promising candidates for persulfate activation. In this study, we synthesized graphene oxide membranes with a trace amount of iron present in the matrix using pressure assisted self-assembly technique on commercial microfiltration PVDF membranes. With the presence of trace amount of iron in the GO matrix, 73% degradation of Trichloroethylene was observed in a batch study over 2 hours. TCE adsorption isotherm of Fe-GO membrane was also investigated. The Fe-GO membranes were characterized for the presence of iron, stability and membrane performance. Our result suggests that trace amount of Iron can significantly enhance the catalytic activity of the GO membranes in the decomposition of toxic organics through the oxidative pathway.

Contributing Authors:
Dibakar Bhattacharyya, University of Kentucky
Mainak Majumder, Monash University
3. Polyphenolic Molecules Based Fluorescence Detection of PCBs.

Irfan Ahmad, *University of Kentucky*
irfan.ahmad@uky.edu

**Abstract:**
The exposure to the halogenated persistent organic pollutants, such as polychlorinated biphenyls (PCBs), has been linked to numerous inflammatory diseases. Owing to these health concerns, it is ideal to have a system that can readily detect their presence with high selectivity and sensitivity. A number of techniques have been developed to sense PCBs, including GC-MS, surface-enhanced Raman scattering, surface plasmon resonance and micro-flow immunosensor chips. While these systems have certain benefits for quantifying and detecting PCBs, none have become a standard of detection owing to limitations, including limited flexibility, too costly to be a survey approach, etc. As such, there is still a need for an inexpensive robust field detection technique for PCBs. In this work, we describe a potential new sensing method based on the capturing of fluorescent dye by the polyphenolic molecules containing polymer particles and displacement of the dye by PCBs. A suitable dye is selected that makes an interaction pair with the polyphenolic molecule, which can be verified using the FRET. This dye can be captured by the polymer particles containing the polyphenolic molecules, which suppresses fluorescence and upon exposure to the PCBs containing solution, this dye is displaced by the PCBs into the solvent, resulting in the emergence of a fluorescent signal. In this work, different polyphenolic molecules have been investigated for successful detection of PCBs in solution.

**Contributing Authors:**
Irfan Ahmad, *University of Kentucky*
Zach Hilt, *University of Kentucky*
Thomas Dziubla, *University of Kentucky*
4. Association between Pesticide Biomarkers and Reproductive and Thyroid Hormones in Pregnant Women

Amira Aker, University of Michigan
aaker@umich.edu

Abstract:
Pesticide prenatal exposure may be associated with health effects, including changes in maternal hormone levels, potentially leading to adverse birth outcomes. The association of pesticides with reproductive and thyroid hormones were examined in the first 44 pregnant women (86 observations) recruited for a Puerto Rican prospective cohort study. Serum hormone levels (estrogen, progesterone, sex hormone-binding globulin (SHBG), free triiodothyronine (FT3), free thyroxine (FT4) and thyroid stimulating hormone (TSH)) and urinary pesticide biomarkers (parathion, a pyrethroid metabolite, three DEET metabolites, and five organophosphohate (OP) metabolites) were measured at two visits during pregnancy (16-20 and 24-28 weeks). Dichotomous or ordinal pesticide variables were used depending on the percent of measurements below the limit of detection. We used linear mixed models with a random intercept to examine associations between the exposures and hormones. TSH was positively associated with pyrethroid and a DEET metabolite (β 0.15, 95% CI (-0.00, 2.30); β 0.21, 95% CI (0.07, 0.35)), but negatively associated with malathion and OP metabolites (-0.48 (-0.85, -0.11); -0.18 (-0.35, -0.01)). Progesterone was positively associated with two OP metabolites (0.09 (-0.00, 0.19); 0.08 (-0.02, 0.18)), but negatively associated with another two OP metabolites (-0.17 (-0.33, -0.00); -0.06 (-0.14, 0.03)). DEET metabolites were negatively associated with FT3 and FT4.

Contributing Authors:
Offie P. Soldin, Georgetown University
Liza Anzalota Del Toro, University of Puerto Rico Graduate School of Public Health
Akram N. Alshawabkeh, Northeastern University
Jose F. Cordero, University of Puerto Rico Graduate School of Public Health
John Meeker, University of Michigan School of Public Health
Hydrochemical Signature and Contaminant Distribution in Springwater from Karst Regions

Eduardo Alvarez Martinez, *University of Puerto Rico, Mayaguez*
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**Abstract:**
Well-developed conduits and high permeability zones make karst aquifers highly productive, but also very vulnerable to contamination. As a consequence, these aquifers can serve as significant routes of contaminant exposure. Contaminants in karst groundwater move through fractures, conduits, and the rock matrix. Conduits connected to surface features, such as sinkholes and sinking streams, serve as direct input of water and contaminants into the groundwater system. This study evaluates the hydrochemical signature of 5 different springs in the karst region of northern Puerto Rico. Springs are monitored for chlorinated volatile organic compounds (CVOCs), phthalates, nitrates, common ions, and standard water quality parameters. Flow in the springs vary spatially and temporally depending on rainfall distribution and the spring’s watershed and conduit characteristics. Springwater is highly mineralized, indicating high interaction with the rock matrix. Major cations and anions are dominated by calcium, sodium, chloride, and bicarbonate, but their proportion and response to rainfall events vary spatially and temporally. CVOCs are found in springs located downgradient of major contaminated sites (including superfunds), but phthalates and nitrates are detected in all springs. Results show that contaminant distributions in karst waters are related to hydrologic conditions, contaminant inputs, and system characteristics that are reflected in the hydrochemical signatures of the springs.

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6. Thyroid hormone parameters during pregnancy in relation to urinary bisphenol A concentrations: a repeated measures study

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Abstract:
Maternal thyroid hormones during pregnancy serve a critical role in fetal development. Although animal and in vitro studies provide evidence that bisphenol A (BPA) exposure may disrupt circulating thyroid hormones, there is still a lack of evidence in human studies during pregnancy. We aimed to explore the associations between urinary BPA concentrations and plasma thyroid hormone parameters during gestation in pregnant women, and also investigated potential windows of vulnerability. Our study population included 116 cases of preterm birth and 323 controls from a nested case-control study. We measured BPA in urine and thyroid hormone parameters were measured in plasma samples collected at up to four study visits during pregnancy (median for each visit: 9.71, 17.9, 26, and 35.1 weeks gestation). We used linear mixed models for repeated measures analyses, and multivariate linear regression models stratified by study visit to explore potential windows of susceptibility. In our repeated measures analysis, BPA and thyroid stimulating hormone (TSH) were inversely associated. An interquartile range (IQR) increase in BPA was associated with a 7.92 % decrease in TSH (95% confidence interval [CI]: -14.1, -1.27). BPA and TSH were also inversely associated in our cross-sectional analyses at visits 1, 3, and 4. Future studies should further explore the interactions between BPA and the thyroid axis because of the potential health effects it may have on fetal development.

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7. **Fetal-Sex Dependent Expression of Immune Genes in the Circulating Lymphocytes of Arsenic-Exposed Pregnant Women in New Hampshire**

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**Abstract:**
Exposure to inorganic arsenic (iAs) during pregnancy has been previously associated with a range of health outcomes both present at birth and emerging later in life. At the molecular level, prenatal iAs exposure is related to epigenetic and genomic reprogramming, particularly of genes involved in innate and adaptive immune functioning. In order to investigate whether similar disruptions occur in the maternal transcriptome, we conducted a targeted analysis of immune-related gene expression in pregnant women from the New Hampshire Birth Cohort Study. A set of 31 unique genes were identified in association with urinary total arsenic (U-tAs; n=3), urinary iAs (U-iAs; n=28), urinary monomethylated arsenic (U-MMAs; n=1) and urinary dimethylated arsenic (U-DMAs; n=19). Notably, when analyses were stratified based on the sex of the infant, maternal gene expression signatures differed across the groups. Women carrying male infants showed a robust inflammatory gene expression response in association with U-tAs (n=307), while women carrying female infants showed a moderate change in association with U-MMAs (n=11). Further, genes differentially expressed in association with urinary arsenic measures were significantly related to birth outcomes, including genes negatively associated with birth length, birth weight, and gestational age and positively associated with the ponderal index. This study highlights the importance of the maternal iAs-induced inflammatory response in fetal outcomes.

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8. Purinyl-cobamide serves as cofactor of tetrachloroethene reductive dehalogenases in Desulfitobacterium

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Abstract:
For carbon-chlorine bond cleavage, reductive dehalogenases (RDases) of organohalide-respiring bacteria require corrinoid cofactors. Some members of the genus Desulfitobacterium synthesize corrinoid de novo and assemble catalytically functional RDases implicated in reductive dechlorination of tetrachloroethene (PCE). The lower base attached to the corrin ring structure can affect RDase function, but the specific lower base produced by Desulfitobacterium has not been identified. Ultra performance liquid chromatography-high resolution mass spectrometric characterization indicated that PCE-dechlorinating Desulfitobacterium isolates produced a novel corrinoid carrying an unknown lower base with a molecular weight of 120.11. An isotope labeling experiment using Desulfitobacterium hafniense strain Y51 grown with 15NH4Cl resulted in a corrinoid molecular weight shift of 14.95, indicating that the lower base contains four N atoms. The combined results of 2-D 1H- and 15N-NMR correlation spectra and mass spectrometric information are consistent with purine as the lower base produced by organohalide-respiring Desulfitobacterium spp. Purinyl-cobamide supported PCE reductive dechlorination by corrinoid-auxotrophic Dehalobacter restrictus but did not support dechlorination activity of Dehalococcoides mccartyi. Purine has not been recognized as a lower base and this finding expands understanding of the diversity of naturally occurring corrinoids.

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**Abstract:**
Air pollution is an important factor influencing determinants of health and promoting healthy communities. In Puerto Rico, air quality is monitored collaboratively by federal and local agencies in order to ascertain regulatory compliance. Despite the widely recognized importance, there has not been a study investigating air pollution levels and social determinants of health in Puerto Rico. This study utilizes a unique dataset of air pollution exposures estimates for three metropolitan municipalities. We include the annual fall-out location of 6 air criteria contaminants, from 10 EPA monitors, at the census block level, for the years 2010-2014. These annual estimates of exposure were matched with census data to calculate trends in exposure for different social groups. Results show that exposure to air toxins have decreased for the years considered. Nonetheless, exposures remain high and this population is additionally challenged by economic hardship. We suggest that expanding the sampling area and placing monitors in industrial areas may be helpful in further analyzing differential exposure amongst marginalized populations in Puerto Rico. These efforts will play a role in promoting environmental justice throughout Puerto Rico. Further research should prioritize focus on air pollution measurement methods that capture exposure levels in marginalized populations.

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10. Multiphase Fate and Transport of TCE in Karst Media

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Abstract:
Contamination of karst groundwater systems (KGWS) with chlorinated solvents is of particular concern because of their high polluted for long-term exposure and adverse impacts to public health and the environment. High mobility in karst conduits results in rapid movement and large exposure of contaminated area. Strong storage capacity in porous matrix retains contaminants and slowly released over long period of time. Among the chlorinated solvents, TCE is of particular concern because of it ubiquitous in the environment. This research studies the contribution of TCE NAPLs to the mobility and persistence of TCE dissolved phase in a KGWS under different flow regimes. Experiments are carried in a karstified limestone physical model (KLPM). After injection of pure TCE solvent into a steady groundwater flow field, samples are taken spatially and temporally and analyzed volumetrically for TCE NAPL and analytically with a HPLC. Generally, the NAPL moves vertically and at an angle along the flow path, but ultimately is stored at bottom of the unit and regions of low permeability. TCE dissolved concentrations tend to increase rapidly after the injection, reach a maximum, and decrease thereafter. Rapid increase is associated with initial rapid dissolution and mass transfer into advecting water and slow mixing. While decrease concentrations after a maximum indicate slower dissolution transfer, dilution with incoming clean-water, higher mixing and higher sorption.

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11. Developmental Toxicity and Mechanistic Investigations of Nitrated and Heterocyclic PAHs

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Abstract:
Nitrated polycyclic aromatic hydrocarbons (NPAHs) and heterocyclic PAHs (HPAHs) are recognized environmental pollutants; however, the health risks of NPAHs and HPAHs to humans and environmental systems are not well-studied. The developmental zebrafish (Danio rerio) model was used to evaluate the toxicity of a structurally diverse set of 27 NPAHs and 10 HPAHs. Zebrafish embryos were exposed from 6 to 120 hours post fertilization (hpf) to a dilution series of individual compounds and evaluated for 22 developmental endpoints. The potential target tissues of AHR was determined via a transgenic GFP/CYP1A reporter zebrafish line. Some compounds did not induce observable developmental toxic responses, while others produced statistically significant concentration-dependent toxicity. All compounds were screened computationally through molecular docking into previously developed AHR models of zebrafish isoforms 1A, 1B, and 2, with a predictive success rate of 74%. The tested compounds also exhibited a range of AHR binding and CYP1A induction patterns, which we determined using morpholino oligonucleotide knockdown to be due to distinct isoforms of the AHR. Furthermore, we investigated mRNA expression of oxidative and cardiac stress genes at 48 and 120 hpf, investigating potential mechanisms-of-action for NPAHs. This indicates the need for further studies of NPAHs and HPAHs as environmental contaminants with the potential for adverse human health effects.

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12. Dual-biofilm reactive barriers: passive destruction of chlorobenzenes polluting anaerobic groundwater

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Abstract:
Groundwater at the Standard Chlorine of Delaware Superfund Site is contaminated with a persistent source of dissolved chlorobenzenes (CBs) and discharges into an adjacent wetland surface water system, posing potential health risks for the local ecosystem and community. This research aims to demonstrate the concept of a “dual-biofilm” reactive barrier, a passive in-situ remediation technology designed to sequester and degrade organic pollutants in groundwater before exiting the subsurface. Leveraging the aerobic-anaerobic interface present in wetlands, bioaugmented microbial consortia of anaerobic reductive dechlorinators and aerobic CB degraders can sequentially mineralize chlorobenzenes recalcitrant to degradation under natural conditions. In this work, we compare the ability of both aerobic and anaerobic bacterial cultures to transform and mineralize CBs individually and sequentially. We demonstrate the capability of the commercial dechlorinating culture WBC-2 to transform trichlorobenzenes to monochlorobenzene in fixed film and sediment-free culture. In addition, we enriched aerobic bacteria from the contaminated site groundwater to stably grow in low pH environments (pH >2) utilizing only 1 - 3 substituted CBs as a carbon source. Utilizing customized upflow column systems to simulate the anaerobic-aerobic gradient commonly seen at wetland surfaces, we evaluate a model dual-biofilm barrier compared to single-biofilm and uninoculated systems.

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13. Identifying components of the Arabidopsis thaliana cadmium response regulatory system

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**Abstract:**
The EPA lists several toxic heavy metal(loid)s among its highest priority hazardous substances; specifically, arsenic, lead, mercury, and cadmium. Toxic metal(loid)s are high priorities due to extensive soil and water contamination, and extreme impact on human health, including increasing cancer rates and causing learning disabilities. Uptake of toxic metal(loid)s in plants primarily occurs through essential nutrient transporters. Once inside the plant toxic metal(loid)s can be bound by thiol-based ligands which inhibit toxicity and allow for transport and sequestration. However, these toxic metal(loid)s remain available to organisms by ingestion providing a major source of human exposure. While components of the heavy metal(loid) detoxification pathway are known, and a rapid heavy metal(loid)-induced transcriptional response has been shown, the transcriptional regulators remain largely unknown. To identify components in this pathway we generated a heavy metal(loid) reporter Arabidopsis line and performed a forward genetic screen using EMS mutagenesis. The mutants were classified based on shifts in luciferase response and include Super-Response (SRC) and Constitutive Response (CRC) mutants. We are currently using both SSLPs and whole-genome deep sequencing to map these mutations. SSLP mapping has identified a 3.6 Mb region of the Arabidopsis genome containing an SRC mutation. In addition, data will be presented showing specific heavy metal(loid) responses in a CRC mutant.

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14. Trust, Risk Perception, and Fish Consumption on a Dioxin Contaminated River: A Michigan Inquiry

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**Abstract:**
Environmental contamination is a critical public health issue in the world. A number of institutions have taken active roles in protecting the public from the adverse health effects of these contaminants and trust in these institutions has been shown to be very important, especially for the effectiveness of their efforts to reduce the likelihood of exposure through risky behaviors. What remains to be seen is the relative impact of trust in these institutions. Thus, it may be that trust in some institutions is relatively more important than trust in others for keeping the public safe. Our research used data collected from a survey of 351 anglers along the Tittabawassee and Saginaw Rivers in Michigan to test the relative predictive influence of trust in nine groups on self-report consumption of fish with a high potential for contamination. The results suggest especially critical roles for trust in state authorities, especially the Michigan Department of Natural Resources. The impact of trust in the US EPA and environmental groups, however, was much more limited. Trust in the institution responsible for the pollution is related to risky fish consumption, such that more trust leads to more risky behavior. Practical implications of this work include an emphasis on state agencies as effective risk communicators, and a need to evaluate the relationship between the original polluter and at-risk populations to understand why increased trust in them leads to increased risk of exposure.

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15. Using fish to simultaneously study the ecological and human health impacts of Superfund chemicals in New Bedford Harbor, Massachusetts

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Abstract:
Fish using the New Bedford Harbor (NBH), Massachusetts, marine Superfund site as habitat provide an important link in assessing both ecological and human health risks. Certain polychlorinated biphenyl (PCB) congeners and tributyltin (TBT) are among the contaminants of concern that bioaccumulate in NBH fish. PCBs and TBT belong to a growing class of metabolism-disrupting compounds associated with obesity, liver steatosis, and Type 2 diabetes. In fact, short-term exposure to PCBs and TBT produced elevated levels of liver triglycerides in laboratory-reared killifish (Fundulus heteroclitus), an ecologically-important NBH fish. Exposure to these compounds also produced skeletal deformities in developing killifish. These biological effects suggest perturbations to metabolic and bone homeostasis, and future genomic analyses of experimental fish tissues may provide clues about the underlying molecular mechanisms of toxicity for these compounds. To estimate human health risks of dietary exposure to harbor-based Superfund chemicals, we are also evaluating temporal changes in PCB congener patterns in human-consumed fish species from NBH. This combination of mechanistic studies using fish and assessment of potential fish-consumption exposure will help to define both ecological and human health risks of exposure to NBH Superfund chemicals.

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16. Empowering mining-impacted tribal communities with educational modules

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Abstract:
Tribal lands in the United States contain a tremendous amount of natural resources (e.g. copper, coal, uranium) with millions of acres already mined. Tribes are often excluded in decision-making processes regarding natural resource extraction that impact their culture, livelihoods, health, and environment. Participation of tribal communities is essential, as they can be subject to adverse environmental and socioeconomic impacts as a result of mining. The University of Arizona Superfund Research Program (UA SRP) is developing educational modules to empower Native American communities with tribal-specific information regarding mining. Educational module topics include copper mining and processing (finalized and published), environmental impacts, mining waste reclamation, and sociocultural impacts. These adaptable modules are designed to augment K-12, tribal college, and non-tribal education. Each module contains an instructional guide, corresponding PowerPoint presentations, and hands-on activities to enhance understanding of mining concepts and are technically reviewed by experts and tribal representatives. UA SRP incorporates science education, in-depth discussion, exchange of ideas and experiences, tribal college student involvement, and local tribal community involvement. Future steps include online publication of finalized modules, development of a uranium mining module, and an evaluation in the effectiveness of learning using the mining educational modules project.

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17. Development and characterization of a stable cell-based bioassay to rapidly screen chemicals and human serum for altered glucocorticoid receptor activity

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Abstract:
The glucocorticoid receptor (GR) has systemic effects on the endocrine, metabolic, cardiovascular, immune, reproductive, and central nervous systems. Therefore, environmental chemicals that disrupt GR signaling may have adverse effects on human health. A major challenge in identifying environmental chemicals that alter GR signaling in humans is a lack of screening methods. To address this, we constructed a bioassay to measure GR activity by stably transfecting a human breast cancer cell line, MDA-MB-231, with a luciferase reporter driven by three copies of glucocorticoid response element. We used this bioassay to screen several environmental compounds for either agonistic or antagonistic effects on GR. We also optimized this bioassay to measure total GR activity in human serum. GR activity was measured in serum collected from 12 healthy volunteers at four time points distributed over a one-year period with an average intra-assay CV of 6.2% and inter-assay CV of 5.4%. The average GR activity for the 12 participants was equivalent to 173.6 nM of cortisol. Notably, the inter-individual variability for these subjects was much greater than the intra-individual variability (54.5% vs. 16.8%). When compared to the serum GR activity measured by MDA-kb2 cells, we found that both bioassays were highly correlated (r=0.94). This novel GR bioassay can be used to identify environmental chemicals that modulate GR activity and further evaluate how these chemicals influence human disease risk.

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18. Water Quality as Social Determinism: The Case of a Non-PRASA Community in Anasco, Puerto Rico

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Abstract:
Water is a very important resource that can be defined in terms of a service. To further understand water as a service agent in Puerto Rico, it is important to study public water systems, the differences between systems, and water quality standards in terms of filtration methods. In Puerto Rico, systems related to drinking water can be divided into two categories that define the dependency or independency of public water systems to a governmental agency that treat water for the public use. The term Non-PRASA identifies independent aqueduct and sewer systems or equivalently, systems sustained and maintained by the communities themselves. The community of Bo. Hatillo in Anasco, Puerto Rico has a Non-PRASA system and it presents some issues regarding their water quality. Social determinism such as income, age, community sense of ownership, location and access can define water quality concerns. This project aims to provide an opportunity to train students in the field of engineering in the water quality monitoring process and effective community engagement activities, but to primarily empower the community to better understand water quality issues, alternatives, and field sampling methods; and to engage trustful interaction between the community, academia, and public agencies. Ultimately, this work will identify health threats, address community concerns, and assist them with technical issues related to treatment processes and system maintenance.

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Assessing soil-air partitioning of PAHs and PCBs at Superfund and environmental disaster sites at with a new passive fugacity sampler

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Abstract:
Soil-air fugacity of polycyclic aromatic hydrocarbons (PAHs) was calculated using passive sampling devices measuring both air and soil pore air, that is, air that is in close proximity and equilibrium with soil. Existing methods to require collecting soil samples from the hard-to-define top soil layer, and the extraction methods may overestimate the fraction of compounds available for partitioning into air. In this modified in situ sampling design, an air-tight box was placed over polyethylene passive samplers deployed 1 cm above the soil. Passive air samplers were also co-deployed at a height of 1.5 m above the soil. Sampling occurred in three locations: near a former PCB manufacturing facility and national priorities list-caliber site in Anniston, Alabama; on the creosote contaminated Wyckoff Superfund site near Seattle, Washington; and near the site of a recent train derailment and oil spill in Mosier, Oregon. Samplers were analyzed for PAHs with GC-MS/MS. PAHs were depositing at Anniston and Mosier sites, but volatilizing at Wyckoff. Inter-sampler variability was greater among pore air samplers than air samplers, likely due to soil heterogeneity. Polychlorinated biphenyls (PCBs) were also analyzed with dual GC-ECD but levels were too low to evaluate flux. This adapted method of measuring pore air in situ will allow for increased understanding of source-sink dynamics of compounds with potential effects human health at sites with recent and historical contamination.

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20. Use of a Population-Based Approach to Identify Potential Genetic Modulators in a TCDD-induced Dose-Response Curve

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Abstract:
There is remarkable diversity in individual responses to xenobiotics. Recent advances have provided the opportunity to probe the role of genetic variation in modulating stressor responses. Previous reports in our lab have established a large degree of individual variability in 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-mediated suppression of the human B cell. Here, we used a population-based approach to identify potential genetic modifiers leading to such variability. This approach leverages the information inherent within the Collaborative Cross mouse panel to associate variant responses with specific genomic regions while providing the opportunity to control for many factors, such as age and exposure histories. Primary B cells were isolated from the spleens of 14 different inbred mouse strains (n > 4) and exposed increasing levels of TCDD to induce a dose-response. In some strains, such as C57Bl6/J and A/J, we found significant suppression (p < 0.05), while other strains, such as 129SvlmJ and CC041, are nonresponsive to TCDD-induced suppression. While some differences are due to the sequence variation within the aryl hydrocarbon receptor (AHR), the transcription factor that mediates most of TCDD-mediated toxicity, results indicate there are further factors that modulate the immunosuppressive effect. Following identification of genomic regions associated with the variation in response, we hope to assess genes localized within these regions to explain the observed phenotype.

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21. Development of PPARy Ligand Exposure Biomarker

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Abstract:
Peroxisome proliferator activated receptor-gamma (PPARγ) connects metabolic and bone homeostasis through its regulatory role in the balancing differentiation of bone and fat and can be targeted by environmental PPARγ ligands. This research utilized multiple serum samples to develop a novel biomarker of exposure to mixtures of environmental chemicals implicated in obesity and osteoporosis by assessing cumulative PPARγ agonist activity. To validate the Serum PPARγ Agonist Activity Assay as a biomarker, we used a reporter assay and a rosiglitazone standard curve to quantify PPARγ activity in sera from mice dosed with known quantities of PPARγ ligands. Further, human sera from commercial sources and from a cohort with well-defined chemical exposures were analyzed. A Hill function was used to fit a rosiglitazone standard curve, and “Rosiglitazone-Like Equivalents” were calculated for each sample by interpolation from the curve. The measured Serum PPARγ Agonist Activity was highly correlated with the rosiglitazone dose administered to the mice. Additionally, co-exposure to rosiglitazone and the PPARγ antagonist GW9662 or the RXR agonist LG100268 in mice resulted in dose-dependent decreases and increases in Serum PPARγ Agonist Activity, respectively. In commercial human serum samples, a range of Serum PPARγ Agonist Activities were detected. We are currently investigating the relationship between activity in the Danish cohort and the concentrations of known PPARγ ligands.

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22. **Effects of the Trichloroethylene Metabolite S-(1,2-dichlorovinyl)-L-cysteine on Mitochondrial Function in Human Cytotrophoblasts**

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**Abstract:**
Trichloroethylene (TCE) is a widespread environmental contaminant that was recently classified as a “known human carcinogen.” Despite this classification, the specific effects of TCE on pregnancy and adverse birth outcomes remain elusive. TCE causes toxicity through its active metabolites such as S-(1, 2-dichlorovinyl)-L-cysteine (DCVC). This study assessed the effects of DCVC exposure on mitochondrial function in human placental cells. First-trimester human extravillous trophoblast cells, HTR-8/SVneo, were exposed to 10-50µM DCVC for 12 hours. Following exposure, the cellular oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) were measured in real-time time using a Seahorse XF24 analyzer. Following measurement of the basal OCR/ECAR, mitochondrial complex inhibitors oligomycin and antimycin A and uncoupler FCCP were serially injected into the media to target specific elements of the electron transport chain in order to measure key parameters of mitochondrial function. The study revealed that exposure to DCVC for 12 hours significantly decreased multiple key parameters of mitochondrial function in HTR-8/SVneo cells, including basal respiration, oxygen-linked ATP production, maximum and spare respiratory capacity and coupling efficiency. These decreases occurred in a concentration-dependent manner. The TCE metabolite DCVC induces substantial deficits in aerobic mitochondrial respiration in trophoblasts.

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23. The Effect of Metal Speciation in Fly Ash on Environmentally Persistent Free Radical (EPFR) Formation

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Abstract:
EPFRs are surface bound radicals with lifetimes on the order of hours to weeks. They originate typically from the combustion processes and are associated with emitted solids such as fly ash. EPFRs are intermediates to PCDD/F formation in the combustion exhaust but also induce oxidative stress in biological and environmental systems. This study aims at determining the relationship of fly ash composition and EPFR formation. Real world fly ash (RWFA) and synthetically composed fly ash (SFA) were studied to evaluate the relationship between metal oxides, sulfur compounds and EPFR formation. Thorough characterization of RWFA from China & the U.S. EPA revealed large differences in the content of EPFRs. SFA were made to model the RWFA composition and determine a driving element in the EPFR formation or inhibition. Sulfur was determined to be an essential element in controlling EPFR inhibition. Low energy X-ray beam studies performed at LSU CAMD provided detailed information on sulfur speciation. For the SFA containing calcium & sulfur, CaSO4 was the most prominent sulfate but FeSO4 & ZnSO4 were present; however, for the sulfur-only containing SFA, ZnSO4 and FeSO4 were the dominant species. We hypothesize that sulfur rich waste releases sulfur dioxides during combustion, which block the metal active sites for the EPFR formation. The mechanisms explored here can potentially be applied to prevent EPFR formation at superfund sites.

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Reducing exposure to arsenic from private well water: Who benefits most from traditional testing promotion?

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Abstract:
Arsenic is common in groundwater, yet private well water is not regulated to meet federal or state standards for drinking. In the absence of regulation, public health efforts have relied on promoting well testing in affected communities to various degrees of success. Few interventions publish results, focusing more often on the outcome of tested wells rather than who tested, and more importantly, who did not. Through our survey of random addresses in 17 towns of NJ (n=670) we find higher rates of arsenic testing in areas with a history of testing promotion. However, we also see stronger correlation between testing and socioeconomic status (SES) in high promotion areas, suggesting that community engagement activities may be exacerbating SES disparities. When 255 households were offered free tests to overcome many of the usual testing barriers -- awareness, convenience, cost -- only 47% chose to return water samples and those who did were of higher income and education than those who did not. Our findings highlight that while efforts to promote and provide arsenic testing succeed in testing more wells, community interventions risk increasing SES disparities if those with more education and resources are more likely to take advantage of programs. Therefore, testing interventions can benefit by better targeting socially vulnerable communities in an effort to overcome SES-patterned self-selection seen when individuals are left alone to manage their drinking water quality.

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Diminished Phosphorylation of CREB Is a Key Event in the Dysregulation of Gluconeogenesis, Glycogenolysis and fatty acid oxidation in PCB126 Hepatotoxicity

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Abstract: 3,3',4,4',5-pentachlorobiphenyl (PCB126), a aryl hydrocarbon receptor (AhR) agonist, is associated with the prevalence of fatty liver disease. We hypothesized that PCB126 disrupts the homeostasis of carbohydrate and lipid metabolism in liver. Separate rat studies were thus performed to understand the time and dose dependent metabolic disruption after PCB126 administration. PCB126 caused early decreases in the serum glucose at 9 h that worsened over 12 d. Lipid accumulation in the liver increased between 3 d and 12 d. The fatty liver was also dose-dependently aggravated at 1 and 5 µmol/Kg of PCB126 exposure. Both protein and transcript levels of phosphoenolpyruvate carboxykinase (PEPCK-C), the rate-limiting enzyme of gluconeogenesis, were significantly decreased. The decrease in serum glucose results from reduced transcription of gluconeogenic and glycogenolytic enzymes, necessary for hepatic glucose production. The transcript levels of peroxisome proliferator activated receptor α (Pparα) and its targets necessary for fatty-acid oxidation were also time and dose-dependently decreased. As a novel finding, we show that PCB126 significantly decreases the necessary phosphorylation of the nuclear transcription factor cAMP response element-binding protein (CREB), and transcription of coactivators involved in hepatic glucose production. The decreased activation of CREB, thus explain the dual effects of PCB126 on both gluconeogenesis and fatty-acid oxidation in causing hepatotoxicity.

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Abstract:
The aryl hydrocarbon receptor (AHR) is necessary for vertebrate development and can be inappropriately activated by a diverse group of chemicals. To identify downstream AHR targets, RNA was isolated from 48hpf zebrafish embryos (exposed to 10uM 7,12-benz[a]anthracene quinone) and sequenced. Among the most elevated transcripts was a novel long noncoding RNA (Sox9b-IncRNA), which we mapped adjacent to the Sox9b gene (human Sox9 ortholog). AHR-dependent repression of Sox9, a conserved transcriptional regulator, is well established in both mammals and fish; however, the mechanism of repression is unknown. The Sox9b-IncRNA transcript contains 3 exons, is 467nt long, and its secondary structure has been predicted using Selective 2’-hydroxyl acylation analyzed by primer extension. The genomic architecture and putative AHR response elements in the promoter of this IncRNA is conserved in mammals, suggesting similar mechanisms of regulation. We hypothesize that the conserved Sox9-IncRNA is a direct AHR target gene that transcriptionally represses Sox9 upon induction by strong AHR ligands to produce target organ toxicity. In support of this hypothesis, developmental exposure to TCDD in AHR2-null zebrafish lines showed Sox9b-IncRNA induction requires AHR2, whole mount in situ hybridization showed that Sox9b mRNA and Sox9b-IncRNA are expressed in overlapping tissues during development, and sox9b-IncRNA morphants exposed to 1ng/mL TCDD have a significant increase in Sox9b expression.

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27. Hazard Assessment of a Representative PAH Superfund Mixture in the Zebrafish Developmental Toxicity Model

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Abstract:
Human PAH exposure at Superfund Sites occurs as complex mixtures. Traditional risk assessment and management practices focus on the additive toxicities of individuals PAHs, which may be misleading if there are synergistic or antagonistic mixture effects. Construction of sufficiently similar mixtures afford risk assessors and managers a more practical and refined tool for assessing mixture toxicity. Low density polyethylene passive sampling devices were used to determine the freely dissolved concentrations of PAHs at the Portland Harbor Superfund Megasite, and the representative mixture “Supermix 10” (SM10) was constructed from the average relative ratios of the ten most abundant PAHs found. The developmental toxicity of the individual PAHs and SM10 was determined using the high throughput embryonic zebrafish assay. Concentration dependent developmental toxicity was observed for SM10. Exposure concentrations of the individual PAHs at their respective concentrations at the LC50 of SM10 yielded lower incidences of mortality and morbidity. Tissue specificity of CYP1A1 expression was determined with immunohistochemistry for both the individual PAHs and SM10, and AhR dependence of CYP1A expression was assessed for SM10. Partially supported by NIEHS grants # P42 ES016465, T32 ES07060 and P30 ES000210.

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28. Study of oxidation of Polyaromatic Hydrocarbon (PAH) by Environmentally Persistent Free Radicals (EPFRs) in physiological conditions.

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Abstract:
Formation of Polyaromatic hydrocarbons (PAHs) and Environmentally Persistent free radicals (EPFRs) typically occur side by side during combustion-related activities. EPFRs, when reacted with O2 or with aqueous medium either in lungs or in an environment, form Reactive Oxygen Species (ROS). The formed ROS can transform PAHs into oxy-PAHs. Since these oxy-PAHs are more soluble than their parent PAH, they are more bioavailable and effect the physiological activities. It is generally believed that the cytochrome P450 metabolism converts PAHs to their hydroxylated, toxic form. Our hypothesis suggest, that EPFRs on PM can activate and desorb PAHs to a larger extent causing additional biological stress to their ROS generation capabilities. For the studies presented, we analyzed the effect of Fenton’s reagent and EPFR-laden particles on the formation of oxy-PAHs from anthracene adsorbed on particles. Fenton’s solution did not yield any Anthracenol and yielded only one isomer of Anthraquinone. We found the formation of various isomers of Anthracenol and Anthraquinone in the presence of EPFRs in aqueous media, indicating the increased bioavailability of PAHs. Since Fenton’s solution did not produce any Anthracenol, it indicates an important role of EPFRs in PAHs activation. The hydroxyl radical concentration gradient around PM can be a critical factor in this process. Additionally, the PAH activation was distinctly higher if PAHs and EPFRs co-inhabited the same particles.

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The Role of the NMD RNA Degradation Pathway in Arsenic-Induced Neural Cell Death

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Abstract:
Inorganic arsenic compounds are common toxicants in the water supply. Prenatal exposure is linked to impaired neural development and cognitive function. Arsenic activates the unfolded protein response (UPR), which degrades misfolded and overexpressed proteins to maintain cellular health. If sensors of the endoplasmic reticulum (ER) recognize an unfolded protein, the UPR is activated and if not resolved in a timely manner, programmed cell death is triggered. My mentor’s laboratory recently reported that the UPR is shaped by Nonsense-mediated RNA decay (NMD), a highly conserved RNA degradation pathway that selectively degrades specific RNAs. Originally discovered as an RNA surveillance pathway that degrades aberrant mRNAs, NMD has since been shown to degrade specific subsets of normal mRNAs. NMD degrades mRNAs encoding specific UPR components to raise the threshold for UPR activation both in vitro and in vivo, thereby reducing the likelihood of its inappropriate activation in response to innocuous stress. Strong ER stress suppresses the magnitude of NMD, allowing for full UPR activation. In my own research, I discovered that arsenic exposure suppresses NMD activity. Depletion of specific NMD components leads to stronger and more rapid expression of genes in the UPR in response to arsenic exposure, as well as increased cell death in both HeLa and neural stem cells. Together, my findings suggest that NMD plays a protective role in arsenic-induced cell death.

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30. Novel Core-Shell Nanocomposite Materials for On/Off Binding of Organic Pollutants from Contaminated Water Sources

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Abstract:
Polyphenolic nanocomposite materials were developed to capture organic pollutants from contaminated water sources using surface initiated polymerization of polyphenolic-based crosslinkers and co-monomers on the surface of iron oxide magnetic nanoparticles to create a core-shell nanocomposite. The polyphenolic moieties were incorporated to create high affinity binding sites for organic pollutants within the nanocomposites. This method produces nanocomposite materials that can bind chlorinated organics, rapidly separate bound organics from contaminated water sources using magnetic decantation, and can use thermal destabilization of the polymer matrix for contaminant release and material regeneration. The polyphenol functionalities used to bind organic pollutants were quercetin multiacrylate (QMA) and curcumin multiacrylate (CMA), which are acrylated forms of the nutrient polyphenols with expected affinity for chlorinated organics such as polychlorinated biphenyls (PCBs). Particles were characterized using transmission electron microscopy (TEM), dynamic light scattering (DLS), Fourier transform infrared spectroscopy (FTIR), and thermal gravimetric analysis (TGA). Pollutant binding studies were performed using PCB 126 as a model PCB and chlorinated organic pollutant to determine binding affinity and capacity, and was quantified using gas chromatography coupled to electron capture detector (GC-ECD). It was demonstrated that the materials effectively bound PCBs in aqueous media.

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31. Metal-induced olfactory sensory neuron death and regeneration in zebrafish

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Abstract:
Fish rely heavily on olfaction to maintain behaviors essential for survival. Environmental exposures to the metal ions copper (Cu) and cadmium (Cd) are known to cause olfactory toxicity but may have differential effects with respect to toxicity to specific olfactory neuron populations and their regeneration following injury. In this study, zebrafish were utilized as a high throughput model system to study metal-mediated olfactory death and regeneration. Confocal imaging in double-transgenic zebrafish larvae that differentially label ciliated and microvillous olfactory sensory neurons (OSNs) were used to image and analyze OSN changes following metal induced death. Following a 24-hour exposure to Cu at 5 days post fertilization, we observed neuronal cell injury in both ciliated and microvillous OSN populations in a dose-dependent manner. Recovery and regeneration of these OSN populations was observed at 24 and 48 hours after Cu exposures. Cell proliferation assays using BrdU incorporation showed increased cell division following Cu-induced OSN death. Exposure to Cd also resulted in visible ORN death, albeit at higher concentrations. Olfactory-driven behavioral assays were used to correlate morphological changes observed through confocal imaging with behavioral endpoints. Our studies support the use of transgenic zebrafish to understand mechanisms of olfactory injury and recovery that can occur in teleosts exposed to metals at Superfund sites.

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32. Hydrogel-nanoparticle composite membranes for degradation of chlorinated organics in water

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Abstract:
Microfiltration membranes can be used as support matrix and functionalized with pH responsive hydrogels and metallic nanoparticles to provide catalytic properties for reductive/oxidative reactions. The membranes immobilize the catalyst preventing its aggregation and improving its reactivity. To improve degradation, higher loading of catalyst per area is required. This is possible using a different kind of support, like sponge-like membranes. Hollow fiber (HF) and some flat sheet (FS) membranes have this characteristic. Other important aspects are the use of “green” techniques to make the nanocomposite and the inert character of the support. This work uses hydrogels of poly(acrylic acid) synthesized within polyvinylidene fluoride membrane pores to immobilize iron/palladium nanoparticles for degradation of trichloroethylene (TCE) in water. Synthesized hydrophobic HF membranes were hydrophilized with polyvinylpyrrolidone. Large-scale commercial FS membranes and the HFs were used in a quantitative TCE batch degradation, following a pseudo-first order reaction kinetics. Sponge-like membranes have about one order of magnitude higher reaction constants than regular membranes. TCE degradation was achieved with chloride produced close to stoichiometric values, indicating slight intermediate production. Membranes used were from a collaborative work with the Singapore Membrane Technology Center, NTU (Singapore) and Nanostone Water, Inc. (Oceanside, CA).

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33. PCB126 Modulates Fecal Microbial Fermentation of the Dietary Fiber Inulin

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Abstract:
Exposure to environmental pollutants can alter gut microbial populations. Short-chain fatty acids (SCFAs), produced from gut microbial fermentation of dietary fibers such as inulin, exert numerous effects on host energy metabolism. SCFAs are also linked to health-promoting effects, including a reduced risk of inflammatory diseases. We hypothesized that exposure to dioxin-like pollutants modulate gut microbial fermentation processes. Fecal microbes from mice were harvested and resuspended in anaerobic media containing 4 or 10g/L of inulin with or without PCB126 (0.02μM, 0.2μM, or 2μM) and incubated for 48h (37°C). HPLC analysis revealed that PCB126 exposure differentially modulated the production of several SCFA, including succinate and propionate. Exposure to PCB126 at 0.2μM and 2μM reduced succinate production, while exposure to 2μM of PCB126 increased total fermentation acids, and in particular propionate production. It has been demonstrated that bacteria-produced succinate contributes to metabolic benefits by acting as an intestinal gluconeogenic substrate. Furthermore, there is evidence that an excess propionate and total SCFA can contribute to increased energy harvest and hepatic lipogenesis. This evidence supports the idea that pollutant exposure may contribute to alterations in host metabolism through gut microbiota-dependent mechanisms, specifically bacterial fermentation processes.

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34. Modeling reactive species transport under electrolysis in flow-through reactors

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Abstract:
Groundwater electroremediation uses direct electric current across electrodes immersed in groundwater to intercept and transform contaminants through direct and/or indirect oxidation or reduction reactions. Electrolysis induces significant changes in groundwater pH and redox potential, which are the most important parameters that influence the transformation mechanisms. A mathematical model improves understanding these changes and facilitates design for full-scale implementation. However, the model can be challenging due to multicomponent species transport and reactivity. A model to describe pH changes during electrochemical transformation in groundwater is developed. The aqueous phase reactions, such as acid/base reactions, transformation and precipitation/dissolution reactions depend on groundwater composition, as well as electric current and groundwater flow rate. The model includes chemical reactions, water auto-ionization, and electrolysis to describe the dynamic changes in chemistry across the cell. The model accounts for direct electrolysis reactions, the effect of polarity reversal as well as different electrolyte composition. The output is compared with experimental studies where it showed a good correlation (R2=0.7) between the theoretical results and observed data.

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35. Multigenerational Behavioral Effects of Benzo[a]pyrene in Zebrafish

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Abstract:
Benzo[a]pyrene (B[a]P) is a well-studied polycyclic aromatic hydrocarbon that poses a significant risk to humans, specifically during prenatal development where parent and metabolites can cross the blood-placental barrier. B[a]P-associated negative impacts on learning, memory, and anxiety have been reported in children. Using the zebrafish model, we evaluated multigenerational behavioral effects of developmental B[a]P exposure. Embryos were developmentally exposed to 2.5 ppm B[a]P or 0.1% DMSO (control) and tested for behavioral changes using the 120 hpf larval photomotor response (LPR) assay. B[a]P-exposed larvae exhibited hyperactivity compared to their respective controls in the dark, following a light-dark transition. A subset of B[a]P exposed embryos were raised until adulthood, and their offspring (F1) exhibited hyperactivity similar to the directly exposed animals (F0). Larvae from subsequent generations (F2, F3, and F4) also exhibited hyperactivity suggesting that B[a]P induced heritable epigenetic changes manifested as neurophysiological defects. To test this hypothesis, unbiased whole-genome bisulfite sequencing will be conducted in the F4 B[a]P and DMSO lineages. Differentially methylated regions across the two lineages will be used to identify genetic regions and begin to identify targeted genes to gain an understanding of the mechanism contributing to the phenotype. This research was supported by NIEHS grants P30 ES000210 and P42 ES016465.

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36. Evaluating Microbial Bioindicators to Assess Reclamation Progress in Southern Arizona

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Abstract:
Mining activities generate unstable waste materials that frequently present environmental hazards to the health of neighboring communities and ecosystems. Phytostabilization is a remediation technology that utilizes a vegetative cover to contain mine waste against wind and water erosion. We aim to improve revegetation strategies by working with mining companies to develop bio-indicators (BI) that document soil formation improvements during phytostabilization and assess the quality of potential sources of soil capping materials. Soil microbial communities facilitate nutrient cycling critical for phytostabilization and can provide a direct indication of soil ecosystem potential. In this study, three BI were used to compare the microbial status of four reclaimed regions of a mine-site. The test regions were capped with different cover materials and represented distinct stages of reclamation. The BI evaluated included heterotrophic plate counts (HPC), quantitative PCR (qPCR) of the bacterial 16S rRNA gene and total extractable soil DNA. HPC provide a measurement of viable heterotrophic bacteria, bacterial qPCR quantifies total bacteria, and extractable DNA is a soil biomass indicator. The value of each BI was evaluated through comparisons with plant community status. Improved understanding of the impact of microbial community capacity on reclamation success will facilitate the development of microbial technologies to enhance phytostabilization-based mine waste stabilization.

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37. Urinary phthalate metabolite and bisphenol-A concentrations in association with serum vitamin D levels: results from pregnant and non-pregnant women in two US populations

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Abstract:
Vitamin D, a fat-soluble prohormone, plays an essential role in bone metabolism and has been linked to numerous chronic diseases. In pregnant women, low levels of vitamin D are associated with a variety of maternal and neonatal complications. Recent research suggests that certain endocrine-disrupting chemicals may alter vitamin D levels in adult men and women. To date, no studies have investigated the extent to which exposure to phthalates or bisphenol A (BPA) are associated with circulating levels of total 25-hydroxyvitamin D [25(OH)D] in humans. Herein, we explored these relationships in a representative sample of 2,414 U.S. adult women participating in the National Health and Nutrition Examination Survey (NHANES), 2005-2010. In a separate analysis, we examined repeated measures associations between urine and plasma biomarkers, collected at median 10 and 26 weeks of gestation, among 477 pregnant women participating in a nested case-control study of preterm birth in Boston, MA. Among NHANES participants, urinary di(2-ethylhexyl) phthalate (DEHP) metabolites and BPA were inversely related to total 25(OH)D, with significant associations detected among women of reproductive age (20-39 years old). These results were consistent with those found in our repeated measures analysis among pregnant women in Boston, MA. Our findings suggest that environmental exposure to phthalates and BPA may influence circulating vitamin D levels in U.S. pregnant and non-pregnant women.

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38. The use of passive sampling devices to implement the new USEPA bioaccumulation model to protect human health

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Abstract:
The USEPA recently updated ambient water quality criteria (WQC) for human health with a new method to predict the bioaccumulation of 94 chemicals in aquatic food chains. The method uses octanol-water partition coefficients (Kow) for each chemical along with a national database of measured bioaccumulation at different trophic levels to obtain a national food chain multiplier (FCM). This FCM is then combined with site-specific environmental parameters to predict bioaccumulation at different trophic levels of the food chain. Polychlorinated biphenyls (PCBs) are among the 94 chemicals included in the new EPA method and PCBs rank #5 on the ATSDR substance priority list (SPL). We investigated how well the new EPA method predicts measured bioaccumulation of PCBs in the food chain of the PCB-contaminated Ward Transformer Superfund Site at Crabtree Lake, NC. We measured PCBs in water, plankton, freshwater mussels, and different trophic levels of fish. We also measured PCBs in passive sampling devices (PSDs) designed to measure only the bioavailable PCBs in the water. We found that the new EPA method was in good agreement with measured PCBs when PCBs in the water were based on the PSD-derived values, but that PCB bioaccumulation was over predicted when based on direct measurement of PCBs in the water. Our work supports the use of the new EPA FCM method for PCBs, but only when the PCB data are based on the bioavailable fraction of PCBs as measured by the PSDs.

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Prenatal Exposure to Environmental Mixtures and Asthma Risk Among Children

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Abstract:
A number of prenatal exposures can alter fetal immune development and increase subsequent risk of childhood atopic disorders, including asthma. Children exposed to multiple chemical stressors prenatally may be particularly susceptible to asthma. We investigated the association between mixtures of stressors and asthma risk among children born 2000-2005 to mothers living in one of four towns near the New Bedford Harbor, Superfund site in Massachusetts. From the resulting 10,517 births, we identified 418 children who were seen in the emergency department or hospital for asthma through 2010, an indication of persistent and poorly controlled asthma. We estimated prenatal exposure to multiple chemicals using biomarker measurements from the New Bedford Cohort study and building regression models as a function of covariates available in birth records. We examined the joint effects of multiple stressors simultaneously using generalized additive models (GAMs), adjusting for confounders including maternal education and prenatal smoking. Results suggest that children of younger mothers who were also exposed to the highest levels of DDE and lived closest to major roads were at greatest risk of developing asthma. This pattern was not apparent for older mothers. This example illustrates the utility of using GAMs for identifying mixtures of chemical and non-chemical stressors associated with asthma risk that would not likely have been discovered using more traditional epidemiologic models.

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Understanding Tributyltin, An Environmental Obesogen, In Its Engagement of Nuclear Receptor Pathways and Molecular Gene Targets Using Transcriptomics

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Abstract:
Obesogens are environmental chemicals that perturb adipogenesis and have been linked to endocrine disruption and obesity. Tributyltin (TBT) has been shown to interact with peroxisome proliferator-activated receptor Y (PPARY) and retinoid X receptor (RXR) to induce white adipocyte differentiation and to negatively regulate bone formation. Given TBTs ability to regulate multiple nuclear receptor pathways, we evaluated the molecular consequences of TBT exposure during bone marrow multipotent mesenchymal stromal cell (BM-MSC) differentiation by examining the expression of nuclear receptors and enriched molecular pathways in comparison to rosiglitazone (PPARγ agonist) and LG100268 (RXR agonist). Transcriptomic analyses were performed using Affymetrix Mouse Gene 2.0ST Array. Using Gene Set Enrichment Analysis for pathway analyses, pathways related to mitochondrial biogenesis and brown adipocyte differentiation were more significantly upregulated in rosiglitazone-exposed cells than in TBT-exposed cells. Pathways related to osteogenesis were downregulated by all ligands. The differential expression of selected brown adipogenesis-related genes induced by rosiglitazone and TBT in BM-MSCs, 3T3-L1 cells and OP9 cells was validated by qPCR. In summary, we show that TBT does not act specifically as a PPARγ or as a RXR ligand and acts distinctly from rosiglitazone, which has a greater efficacy in activating the expression of genes involved in mitochondrial biogenesis and brown adipogenesis.

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41. Benzo(a)pyrene-induced mitochondrial dysfunction persists across generations in zebrafish

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Abstract:
The potential for polycyclic aromatic hydrocarbons (PAHs) to have effects across generations is an emerging concern in both human and wildlife health. However, the mechanisms underlying the maternal and transgenerational effects of PAHs are poorly understood. To this end, the present study evaluated the role of mitochondria, which are maternally inherited, in the multigenerational toxicity of benzo(a)pyrene following a chronic maternal (F0) exposure using zebrafish. We have previously shown that maternally exposed (ME) F1 individuals exhibit mitochondrial dysfunction and oxidative stress during development at exposure levels that are asymptomatic in the exposed F0 females. Herein, we demonstrate that mitochondrial dysfunction persists later in life in ME F1 fish, including reduced cardiac mitochondrial reserve capacity. ME F1 fish also exhibit altered locomotor activity and reduced fear and anxiety behaviors. Swimming performance, aerobic respiration, and oxidative stress responses are currently being evaluated. Further, ME F1 adults exhibit reduced reproductive success, and their offspring (F2 embryos) have reduced developmental viability. Notably, the F2 embryos also exhibit mitochondrial dysfunction and reduced metabolic plasticity. These data represent the first demonstration that environmental toxicant-induced mitochondrial dysfunction can have persistent effects across generations, with important implications for human disease etiology and organismal ecological fitness.

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42. Generation and analysis of transcriptomic gene signatures and carcinogen-associated pathways in liver carcinogenesis

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Abstract:
The current gold-standard approach for chemical carcinogenicity testing is the two-year rodent bioassay, a time-consuming and costly process that has limited chemical carcinogenicity testing to 1,500 out of ~84,000 chemicals in commercial use today. We utilize a novel, fast and cost-efficient approach to high-throughput gene expression screening, based on chemicals exposures in HEPG2 cells, to predict chemical carcinogenicity and define carcinogen-associated pathways. HEPG2 cell lines were treated with a chemical library of 131 liver carcinogens and 167 non-carcinogens across 6 doses and their transcriptional gene expression profiles were measured using the L1000 assay. Gene signatures were extracted from each profile using moderated z-scores, and summarized at the level of pathway activities using the Kolmogorov-Smirnov based gene-set projection method. The data suggest there are heterogeneous pathways in the carcinogenic response, as well as heterogeneity within specific receptor responses. The gene signatures show enrichment of specific receptor-mediated pathway activities within chemicals of known receptor-mediated classes, such as AHR, PPAR, and ER. AHR related pathway activities are correlated with the strength of the receptor agonists, yielding a separation between strong environmental AHR ligands and weaker endogenous AHR ligands. This finding suggests the potential for the L1000 platform to subclassify the transcriptomic response of receptor-mediated perturbagens.

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43. Toxicity and trade-offs in PAH-resistant and non-resistant Fundulus heteroclitus exposed to creosote-contaminated sediment extract and hypoxia

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Abstract:
Chronic creosote pollution at sites along the Elizabeth River (VA, USA) has resulted in the evolution of polycyclic aromatic hydrocarbon (PAH) resistance in local populations of Atlantic killifish (Fundulus heteroclitus). We have found that a killifish population that resides at the site of a former wood treatment facility, “Republic,” is recalcitrant to both in ovo CYP1A induction and developmental deformities after exposures to simple and complex PAH mixtures compared to the reference site Kings Creek (Severn River, VA, USA). However, there are apparent consequences of PAH-resistance. The goals for this study were to evaluate if evolved resistance against PAH toxicity influences the tolerance of Republic killifish to other environmental stressors. To do so, we exposed killifish embryos to non-teratogenic doses of a sediment extract obtained from a PAH-contaminated site along with diurnal hypoxia, an environmental condition common to estuaries in the United States. Endpoints of interest include mortality, hatch rates, gross morphological deformities, and CYP1A activity. Our results suggest that Republic killifish have reduced maximal metabolic rates and subsequently reduced aerobic scopes (both p<0.05) compared to Kings Creek killifish. This type of fitness trade-off could exacerbate potential toxicity resulting from co-exposures of PAHs and hypoxia in PAH-resistant killifish. This work was supported by NIEHS T32-ES021432 and the Superfund Research Program P42ES010356.

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Hazardous Conditions: Industrial growth and environmental inequality in Rhode Island, 1954-2012

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Abstract:
Uneven spatial patterning of industrial activities has been repeatedly documented by environmental justice scholars at national, state, county, and neighborhood levels. Yet little systemic research investigates the broader historical processes of industrialization that condition such well-known environmentally unequal outcomes. Heeding Pellow’s (2000) call to historicize environmental inequality formation, this study investigates changes in the spatial and temporal distribution of industrial hazards in Rhode Island over six decades (1954-2012). Employing a unique database that combines annual information from Rhode Island manufacturing directories that totals over 23,000 facilities with demographic data from the US Census, we address the relationship between industrial production and the distribution of industrial waste via three analyses: 1) an analysis of industrial churning, which allows us to measure temporal and spatial dynamics of overall industrial growth; 2) an analysis of relict industrial sites, which describes the accumulation of environmental risk; 3) a comparative analysis of the changing spatial configuration of textiles and jewelry manufacturers, which demonstrates key differences in the distribution of environmental risk across different industrial sectors. Together, these analyses highlight the need for historical data collection at different spatial scales and industrial sectors in order to understand the dynamic nature of environmental inequality formation.

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45. Systems-Level Genomic amiRNA Screening Platform Identifies New Genes with Overlapping Functions Mediating Cadmium and Arsenic Resistance

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Abstract:
Traditional forward genetic screens in plants are limited in their ability to identify the numerous homologous genes with overlapping functions: Only ≈10% of A. thaliana genes have been linked to a single gene mutant phenotype [Hauser et al, 2013]. Thus (partial) genetic redundancies greatly limit gene discovery in forward genetic screens in plants. Higher-order mutant analyses have shown overlapping homologous gene functions. To address this problem on a genomic systems level, we computationally designed amiRNA libraries for genome-wide knock-down of homologous gene family members [Hauser et al, 2013]. We generated 10 amiRNA libraries (22,000 amiRNAs total), thus providing a powerful new genomic screening platform [Hauser et al, 2013]. We have pursued systems-level screens of amiRNA plants grown in the presence of cadmium or arsenic to identify new genes that affect toxic metal(loid) resistance. We report here new genes that are key to cadmium and arsenic resistance and accumulation. We have isolated amiRNA lines in MATE efflux family proteins, ERF transcription factors, phosphate uptake transporters and many other interesting homologous gene sets that affect arsenic and/or cadmium sensitivity. Hauser, F., Chen, W., Deinlein, U., Chang, K., Ossowski, S., Fitz, J., Hannon, G.J. and Schroeder, J.I. (2013). A genomic-scale artificial microRNA library as a tool to investigate the functionally redundant gene space in Arabidopsis. Plant Cell. 25: 2848-2863.

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46. **Diffusive Flux of PAHs Across Sediment, Water, and Air Interfaces at Urban Superfund Sites**

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**Abstract:**
Superfund sites are often a source of polycyclic aromatic hydrocarbons (PAHs) to the surrounding environment. In urban locations these sites can also act as PAH sinks from present day anthropogenic activities. Understanding PAH transport across environmental compartments is important for informing remedial and management decisions in the context of mitigating the potential for human exposure to these compounds. In this study, passive samplers were co-deployed in sediment, water, and air within the Portland Harbor Superfund Megasite (PHSM) and the McCormick and Baxter (MCB) Superfund Site. These Superfund sites, located along the Willamette River, have both historical PAH contamination from industrial activities as well as present day PAH inputs from the Portland urban center. Passive sampling was used to determine the freely dissolved water and sediment porewater concentrations as well as the air vapor-phase concentrations of 61 PAHs. Diffusive flux was calculated across the interfaces of the three compartments. Results suggest that the Willamette River acts predominately as a sink for lighter molecular weight PAHs from both the sediment and the air. At most locations, the sediment was also a source of four and five ring PAHs to the river and the river was a source of these same PAHs to the air indicating that legacy pollution may be contributing to human PAH exposure for those living in the Portland urban center.

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47. Voices Unheard: Documenting the Human Experience of Living Near Arizona Superfund Sites

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Abstract:
National Priority List Superfund sites are federally designated lands that pose a risk to human and environmental health due to the presences of hazardous contamination. Each of these sites have a unique history consisting of the experiences of those who have lived in an area of environmental risk, and those who have documented and challenged practices that have led to environmental degradation. However, as time passes, the memory of community members is lost as they age and/or leave the area. An oral history method was selected to preserve this knowledge by community members living near two Superfund sites in Arizona. Archival work has been completed on both sites to establish a historical framework. Need assessment interviews and surveys have also been conducted with key community members to explore the importance of undertaking such a project, how it should be developed, who should be interviewed, and what the outcomes should be. The next steps include: 1) the capture of oral history interviews using audio and video recordings and personal photographs; 2) the collaboration with community members to identify ways to share their histories with a broader audience; and 3) the development of an Arizona Superfund site archive. Overall, the study will inform the fields of environmental communication and social justice by capturing the real world experiences of those residing near contamination and who are engaged in environmental justice advocacy.

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A novel non-selective passive sampling device to measure bioavailable PCBs in water

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Abstract:
Polychlorinated biphenyls (PCBs) are one of the most important toxic substances of concern at EPA Superfund Sites, ranking # 5 on the ATSDR substance priority list (SPL) and PCBs are the primary contaminant of concern at the Alcoa Badin Works Superfund Site in the Yadkin River/Badin Lake watershed in NC. As part of a PCB bioavailability and bioaccumulation study in the Yadkin River, we developed and deployed new types of passive sampling devices (PSDs) designed to accumulate only the bioavailable fraction of PCBs in the water and sediment. We evaluated how well simple “grab samples” of water and several different types of PSDs predict the accumulation of PCBs in freshwater mussels. We found that traditional grab samples had high variability leading to highly variable estimates of PCB bioaccumulation. Conversely, all of the PSDs we tested provided much lower variability and much better agreement with measured PCBs in the mussels. The standard low-density polyethylene (LDPE) PSD was compared to three newer PSD designs developed in our laboratory and all four PSD types showed relatively good agreement. However, the LDPE can only capture hydrophobic chemicals, whereas the newer PSDs capture chemicals with a much broader range of hydrophobicity (having log Kow values from 0.5 -10). Our newer PSDs are comparable to the LDPE for PCBs, while having a very significant advantage of more effective uptake for the less hydrophobic chemicals as well.

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49. Uncovering Historical Environmental Health Threats in the Mashapaug Pond Watershed

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Abstract:
Social scientists have begun to investigate how changes to urban ecosystems influence the dispersion and concentration of industrially produced contaminants spatially and over time. As part of a larger historical study of the relationship between the socio-ecological conditions of cities today and the urban industrial past, we are constructing a historical database of urban hazardous sites. We center data collection efforts on the Mashapaug Pond watershed in the urban context of Providence, Rhode Island. In the first phase of this project, we identified historical sites of industrial facilities using state manufacturing directories, 1950-2015. In the second phase, we used historical city directories for the same time period to identify the location of former hazardous retail sites such as gas stations, auto shops, and dry cleaners. The combined directory-based historical data collection methods revealed 172 unique sites that characterize the contemporary hazardscape lying within the Mashapaug watershed. The current phase of research examines property records and government hazardous site databases to better understand the relationship between these 172 legacy sites and contemporary risk assessment and hazard remediation efforts. When complete, data from this project will be used to inform residents, community groups, and state regulatory agencies, through a free online database and interactive website, as well as multiple community forums.

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50. Attitudes and Knowledge of Healthcare Providers on Environmental Pollution in Puerto Rico

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Abstract:
Despite the Institute of Medicine recommendations to increase awareness of environmental determinants of illness and disease among healthcare providers (HCPs), studies have revealed that while HCPs generally recognize that environmental hazards have the potential to negatively impact the health of patients, many do not take a full environmental exposure history. Many HCPs report being hesitant to discuss environmental health issues with their patients because of uncertainty and lack of knowledge regarding environmental health (EH). Building on existing research that is currently taking place through PROTECT (Puerto Rico Testsite for Contamination Threats), this project provides an ideal location for examining questions about perceptions of HCPs in Puerto Rico (PR) on EH. It is well-suited to investigate perceptions and practices pertaining to emerging environmental contaminants, such as phthalates and trichloroethylene, which have not yet been examined in similar studies in the US or PR. A questionnaire will be distributed to 200 HCPs in order to 1) Identify differences in perceptions of EH issues across HCPs in PR and 2) Examine how HCPs who acknowledge the importance of environmental determinants of health incorporate this knowledge into their professional practice. Analysis will be complete prior to the poster presentation. The findings have implications for the development of a Training Program in Environmental Health for HCPs at health centers in PR.

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51.  The effects of mutations in FOXL2 on FSHβ transcription

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Abstract:
Appropriate regulation of follicle-stimulating hormone (FSH) is required for normal female fertility. Previous studies have shown that the synergistic induction of FSHβ transcription by activin and progesterone requires the binding of SMAD proteins and the FOXL2 transcription factor to the FSHβ promoter. Human mutations in the FOXL2 gene have been identified in premature ovarian failure (POF) and blepharophimosis ptosis epicanthus inversus syndrome (BPES). To understand the involvement of FOXL2 in these reproductive disorders, we modeled human FOXL2 mutations associated with BPES and/or POF in both human and mouse FOXL2 expression vectors. We characterized the effects of these mutations on induction of the mouse FSHβ promoter in a mouse gonadotrope cell line. Our results show that FSHβ basal expression is altered in the presence of FOXL2 mutants. FSHβ induction in response to hormone treatments is also differentially affected by the FOXL2 mutants. Future experiments will involve the testing of FOXL2 binding patterns with proteins involved in the activation of FSHβ. These studies bring new insight into the pathophysiology of human reproductive disorders.

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Abstract:
The UDP glucuronosyltransferase 1A1 (UGT1A1) enzyme is responsible for the glucuronidation of a host of small lipophilic molecules (e.g. Bilirubin), and the gene is regulated by xenobiotic receptors (XenoRs), such as CAR, PPARα, and PXR. Humanized UGT1 mice (hUGT1) develop neonatal hyperbilirubinemia and total serum bilirubin (TSB) levels are readily observable [2]; this facilitates the correlation between in vivo XenoR activation and toxicant exposure. To examine potential XenoR activation by common fire retardants (FR), hUGT1 mice were treated with several compounds (TBBPA, BPA, TPP, and TCEP). The most significant modulator of UGT1A1 activity was the triphenyl phosphate class of FRs, which are common and known to accumulate in the home environment [1]. We have validated the hUGT1 mouse model for in vivo XenoR screening, and show TPP activates CAR as determined by gene expression analysis and TSB levels showing significant increases in hepatic expression of UGT1A1 and Cyp2b10 in hUGT1 mice, but not hUGT1/Car −/−.

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Multi-species meta-analysis of transcriptomic deregulation following PCB126 and PCB153 exposure

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Abstract:
Widely recognized as environmental contaminants, polychlorinated biphenyls (PCBs) are commercially produced chemical congeners implicated in a variety of deleterious health effects including liver damage, reduced immune response, and neurological alteration. Non-ortho-substituted PCBs such as PCB126 activate the ligand-dependent transcription factor, aryl hydrocarbon receptor (AHR), impacting transcription of AHR target genes. Ortho-substituted PCBs such as PCB153 act through other mechanisms that are not well understood. Toxicogenomic analyses of PCB exposure have included transcriptomic studies for a variety of specific PCBs, species, and tissue types. However, the consistency of PCB-induced transcriptome deregulation across studies has not yet been evaluated. In this analysis we combine data from six different sources to produce signatures of differential gene expression after exposure to either PCB153 or PCB126. Signatures were obtained from human, mouse, and rat liver, from killifish brain, and from zebrafish embryos. Enrichment analyses with externally derived gene sets reveal consistent association within liver signatures and functional states including oxidative stress, fatty acid metabolism, cytochrome P450 function, and immune response. Signatures in brain and embryo showed time, dose and strain as modifiers. These findings suggest consistent hepatic response across species and reaffirm PCB contamination as both a human health and environmental hazard.

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54. Determination of PAH flux during groundwater to surface water exchange processes

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Abstract:
Due to the potential toxicity of polycyclic aromatic hydrocarbons (PAHs) to marine organisms and humans, considerable effort has been focused on remediation strategies to reduce the bioavailability of PAHs to marine life and reduce risk for human exposure. Remediation strategies such as in situ capping assume Darcy flow for groundwater movement in sediments and do not account for non-equilibrium groundwater advection mechanisms and their potential effect on PAH transport. In our work, we evaluated methods to quantify PAHs using a near real-time PAH biosensor to assess fine spatial and temporal variability of PAH concentrations. Using the VIMS biosensor along with an in-house developed monoclonal antibody (2G8), we were able to detect 3 to 5 ring PAHs (LOD = 0.2 µg/L) in small volume (1-5 mL) porewater samples collected from piezometers and seepage meters at a Money Point, VA field site. Biosensor PAH concentrations correlated well with GC-MS (R² = 0.99). Groundwater advection rates of 0 to 40 cm/d (mean 16.3 cm/d) were calculated using disequilibrium between parent/daughter nuclides in the Th-Ra-Rn system. Short-term (hours) and long-term (weeks) variability in PAH flux from contaminated sediments were compared at various site locations to evaluate the efficacy of current remediation strategies in controlling PAH transport. Future work will focus on the development of new antibodies to help evaluate the flux of other organic contaminants such as PCB’s.

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55. Associations Between Low Birthweight, Maternal Prenatal Stress, Depression, and Social Support During Pregnancy: a Cohort Study in the Northern Karst Region of Puerto Rico

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Abstract:
Low birthweight (LBW) increases the risks of developing serious morbidities in all ages and stages of life and increases the risk of perinatal mortality. The rate of LBW is perennially higher in Puerto Rico than the United States. In Puerto Rico seven out of ten infant deaths are due to complications of LBW. There is not a consensus in the literature regarding associations between maternal prenatal stress (MPS) and LBW. The aim of this study is to investigate associations between LBW and MPS among a pregnancy cohort in the northern Karst Region of Puerto Rico. The Puerto Rico Test Site for Exploring Contamination Threats (PROTECT) Program is a multi-institutional collaborative that is dedicated to studying health outcomes of pregnant women and their offspring in Puerto Rico. Perceived Stress, Life Experience Survey, Depression Scale and Social Support questionnaires were administered during the second trimester of gestation to examine separately and combined in relation with LBW in women of the cohort between 2011 and 2015. Among the cohort of women, we found that 17% report perceiving high levels of stress during pregnancy and 9.5% of all births were of LBW. Results suggest that exposure to stress-triggers can contribute to the burden of LBW, though causal pathway is unclear. We recommend future studies further explore this association for the development of the most effective interventions at preventing stress during pregnancy.

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Abstract:
Vapor intrusion (VI) describes migration of volatile organic compound (VOC) vapors from subsurface sources to indoor areas. VI has been studied for decades based on the concept of migration of VOC’s vapors through soils into overlying buildings entering through cracks in the foundation. There been recent evidence that other possible routes can act as conduits (alternative pathways) for vapor migration and increase human exposure risks to VOC vapors at VI sites. Recently the role of vapor migration through alternative pathways has been gaining attention and US Environmental Protection Agency’s (USEPA’s) most recent VI technical guidance (2015) mentioned sewers system and drain lines as important exposure pathways. In this study, we investigate the potential of sewer system as a preferential pathway and, investigate routes and conditions that promote human exposures to VOC vapors via this alternate pathway. Results from a numerical model that considers various liquid-gas transfer mechanisms within the sewer system will also be presented.

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57. Antiandrogen treatment ameliorates reproductive and metabolic phenotypes in the letrozole-induced mouse model of polycystic ovary syndrome

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Abstract:
Polycystic ovary syndrome (PCOS) is the most common reproductive disorder in women of reproductive age. PCOS is characterized by elevated androgen levels with absent or infrequent ovulation, and often presents with metabolic comorbidities including obesity. The etiology of PCOS is unknown, but excess androgens are thought to be a key factor driving its pathogenesis. Recently, rodent studies have shown that exposure to environmental compounds can result in reproductive abnormalities that resemble PCOS, suggesting that endocrine disruptors may play a role in the development of this disorder. We previously established a mouse model of PCOS using the aromatase inhibitor letrozole to increase testosterone levels, which recapitulated both reproductive and metabolic aspects of human PCOS. In this study, we treated PCOS and control mice with the androgen receptor antagonist flutamide, to understand how androgen receptor (AR) signaling contributes to the PCOS phenotype. We found that disruption of AR action restored many reproductive and metabolic parameters in PCOS mice. In particular, flutamide treatment normalized expression of key genes in the pituitary (Lhb) and ovary (Fshr), restored normal estrous cycling, and reduced body weight gain. This establishes the letrozole PCOS model as a useful tool in understanding how excess androgens contribute to PCOS, and provides insight into the mechanisms through which environmental androgens may act to disrupt female reproduction.

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58. Degradation of Chlorinated Organics by Temperature Responsive PNIPAm-co-PAA Functionalized MF Membranes with Reactive Nanoparticles

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Abstract:
This study is aimed at evaluating the degradation of chlorinated organics, specifically polychlorinated biphenyl and trichloroethylene. The effect of both temperature and pH were evaluated. PVDF microfiltration membranes were functionalized with poly-N-isopropylacrylamide (PNIPAm) and polyacrylic acid (PAA), and their temperature responsive behavior was studied as it relates to water flux and partitioning of toxic pollutants. The entrapment of reactive Fe/Pd nanoparticles in the PAA polymer domain has been reported. Here, the NPs are entrapped in the temperature responsive PNIPAm-co-PAA polymer network for dechlorination and contaminant degradation of PCBs and TCEs. This study aims to evaluate PCB and TCE degradation by reactive immobilized nanoparticles in a PNIPAm-co-PAA functionalized PVDF MF membrane. Solute concentration is predicted as a function of length through the membrane, and also as a function of time. Increasing the surrounding temperature affects inter-particle spacing and solute adsorption because of the changing PNIPAm conformation, as well as the intrinsic rate constant for the reaction. These effects are predicted, and verified by experimental degradation results. This research is supported by the NIEHS-SRP grant P42ES007380, and by the NSF KY EPSCOR program. Full-scale PVDF membranes were developed through collaborative work with Nanostone-Sepro (Oceanside, CA, USA).

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59. Detected Asbestos Fiber Toxicity Depends on Fiber Grinding Methods

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Abstract:
Asbestos is an umbrella term encompassing a group of naturally occurring fibrous silicate materials, which are known to cause serious health effects including asbestosis, malignant mesothelioma, and both lung and stomach cancer. Studies that investigate the toxic potential of asbestos usually begin by grinding the asbestos ore down to small fibers for use in cell line models, murine models, and other toxicity assays. However, it is unknown whether these various processing methods can themselves affect the fiber toxicity. To examine this, we ground chrysotile ore with or without water for 5-30 min and quantified asbestos induced reactive oxygen species generation in elicited murine peritoneal macrophages as an indicator of fiber toxicity. We discovered that although grinding with or without water did not materially alter the mineralogical properties of the fibers, the toxicity of dry-ground fibers was higher than that of wet-ground fibers. Additionally, dry-ground fibers contained at least 7 times more iron than wet-ground fibers. These results indicate that grinding methods significantly affect the surface concentration of iron, resulting in changes in fiber-induced reactive oxygen species generation or toxicity. Thus, when comparing the reported toxicity of asbestos fibers between relevant studies, it is important to consider the fiber preparation methods.

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60. Development of a novel passive sampling strategy for methylmercury in sediments and soils

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Abstract:
Aquatic mercury can pose a significant risk to ecological and human health when it is converted to the more toxic and bioaccumulative methylmercury by anaerobic microorganisms near the sediment-water interface. Benthic invertebrates exposed in this zone represent an important link in the accumulation of methylmercury in aquatic food webs. As such, measurement of methylmercury’s availability to these organisms is critical for risk assessment of contaminated sites. To date, no sampling strategy has achieved wide acceptance for this purpose. We are developing a novel passive sampling technology to mimic the pseudo-equilibrium mode of accumulation by benthic organisms. Custom polymers containing either thiolated sorbents or activated carbon were prepared and evaluated in increasingly environmentally realistic experiments, with positive results. In contaminated soil slurries, water concentrations estimated by samplers agreed within a factor of one to four with direct measurements of centrifuged pore water. Sampler partitioning was within half an order of magnitude of soil. Ongoing work is aimed at correlating sampler measurements with accumulation by a benthic test organism in sediment microcosms with or without activated carbon amendment. Sampler data will be used as input for a bioaccumulation model to validate the predictive capability of the device. Ultimately, our sampler will enable more accurate measuring and modeling of bioavailability under multiple amendment scenarios.

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Optimization of analytical method for identification and quantification of hydroxy-polycyclic aromatic hydrocarbons in thermally remediated soil

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Abstract:
Polycyclic aromatic hydrocarbons (PAHs) are environmental contaminants produced mainly from the incomplete combustion and pyrolysis of organic matter. PAHs are among the major contaminants at Superfund sites and are present at over 800 sites.1 Thermal remediation employs the use of heat to mobilize and recover pollutants and is used as a method to remediate soils contaminated with PAHs.2 Steam enhance extraction (SEE) is an in-situ thermal remediation technique which relies on the addition of steam (heat) to soil to increase the removal efficiency and recovery of volatile and semi-volatile contaminants.3 Limited information is available regarding formation of PAH breakdown products during and after thermal remediation. This is due to the inability to predict transformation products, the historical lack of standards, and challenges in the analysis of PAHs and their breakdown products in complex environmental mixtures. Breakdown products are more mobile in the environment, and some are likely more toxic to humans, animals, and plants, compared to corresponding PAHs.4 There is an urgent need to develop analytical methods that can accurately quantify these PAH breakdown products, specifically OHPAHs. In this study, we optimized a gas chromatography/mass spectrometry (GC/MS) method for the analysis of OHPAHs, and identified and quantified OHPAHs, OPAHs and NPAHs in creosote contaminated soil before and after SEE.

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Differential gene expression and chronic arsenic exposure in a transcriptome-wide association study of adults in Bangladesh

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Abstract:
Background: Inorganic arsenic is one of the most common naturally occurring contaminants and is associated with impaired development, cancer, cardiovascular disease, diabetes, pulmonary disease and other disorders. The molecular mechanisms underlying these effects remain unknown. Objective: Among a large sample of adult Bangladeshi participants (n=~1,800), we evaluated the association between arsenic exposure, as measured by blood and urinary total arsenic concentrations, and genome-wide gene expression in peripheral blood lymphocytes. Methods: We used linear regression models to examine the associations between arsenic exposure and gene expression, adjusted for sex, age and cell type composition. Differentially expressed genes were subsequently evaluated using gene ontology and pathway enrichment analysis to determine the functional relevance of arsenic-associated gene expression. Results: We identified 496 differentially expressed genes with urinary total arsenic concentration and 134 differentially expressed genes with blood arsenic concentration, based on the Bonferroni-corrected significance threshold of p < 1.5 x 10^-6. These expression patterns demonstrated an overrepresentation of genes involved in immune response and T-cell function. Conclusions: These findings define molecular changes associated with arsenic exposure in human peripheral blood lymphocytes and provide potential targets for intervention in the pathogenesis of arsenic-induced diseases.

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63. Wind Effects on Vapor Intrusion Process and Indoor Air Quality

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Abstract:
The migration of soil gas from a contaminated source to indoor air is known as vapor intrusion (VI). Over the past decade, VI models have been developed to predict vapor transport through the soil and into indoor areas. Most VI models have focused on subsurface processes, however there is a need to modify the existing models by accounting for aboveground parameters that affect vapor intrusion, such as wind speed and direction. In this study, we investigate how wind conditions might influence VOC concentrations in the soil and in indoor air areas. Our model solves the Reynolds-Averaged Navier-Stokes (RANS) equations for turbulent wind flow, above and around a building coupled with the soil gas continuity equation and then solves the chemical transport equation. The results indicate that wind flow can influence both air exchange rate of the building and contaminant concentration distribution in subsurface. Resulting asymmetric pressure profiles around buildings can cause infiltration in the windward side and exfiltration on the leeward side of the building. While the impact on contaminant mass entry rates due to changes in the subsurface pressure profiles is important, the combined effect of mass entry and the influence of wind effects on air exchange rates is ultimately of more importance and is currently understudied in the field of VI exposure risk assessment.

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Breathable Graphene Oxide Toxicant Barriers

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Abstract:
There is tremendous interest in the development of ultrathin graphene and graphene oxide films as molecular transport barriers, or as selective membranes that use molecular sieving properties for small molecular separation or recovery technologies. Graphene oxide films in particular have been shown to be excellent barriers to the transport of small-molecule gases in the dry state, but expand in the presence of water vapor to allow rapid permeation of H2O. Here we explore a new application for GO films as water-breathable barriers for protection of personnel that allow perspiration while protecting from toxicants. The interlayer channels in GO films are sufficiently small to exclude larger toxicants, but some toxicants can fit in the < 1nm transport channels, and are known to be co-transported with water. We have developed a theoretical model and experimental facility suitable for studying vapor permeation in both directions simultaneously, and show results for two model vapors. Ethanol and trichloroethylene (TCE) were chosen due to their widely varying solubility in water. The results point to design parameters that allow both outward water transport and the results suggest that GO can be used to create breathable toxicant barriers as components in wearable devices for chemical and biochemical detection.

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65. Sub-slab depressurization systems for vapor intrusion mitigation - some aspects of design

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Abstract:
This study examines various aspects of design of an active sub-slab depressurization system (ASSD) typically used in mitigation of vapor intrusion scenarios. A three-dimensional finite element model of a typical residential building with a steady influx of vapor contaminant entering the structure via vapor intrusion (VI) was considered. Various VI scenarios were modelled to give a holistic view of the factors that influence the ASSD energy requirements and performance. The importance of the soil and sub-slab characteristics with and without presence of an ASSD were considered. By implementing certain practices during installation of an ASSD and/or construction of a building, it is possible to increase performance of the mitigation system while reducing operational energy costs.

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66. The effect of toxicants on forskolin-induced syncytialization of cytotrophoblasts

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Abstract:
The fusion, or syncytialization, of cytotrophoblast cells is important for providing a barrier to maternal-fetal exchange, potentially preventing pre-eclampsia, and induced by increased intracellular cAMP levels. Though the impact of cAMP-inducing compounds, such as forskolin, on syncytialization has been established, the role of toxicants on forskolin-induced syncytialization has scarcely been investigated. Using the human cytotrophoblast cell line, BeWo, as a cell model that can be syncytialized using forskolin treatment, we investigated the susceptibility of the cells to toxicant co-treatment with forskolin. In this study, we established that monobutyl phthalate (MBP) had little effect on forskolin-induced syncytialization, as evidenced by corresponding syncytin-1 gene expression levels. Mono-(2-ethylhexyl) phthalate (MEHP) and S-(1,2-dichlorovinyl)-L-cysteine (DCVC) decreased forskolin-induced syncytialization, but not to a level as low as that in control conditions. These data have been supplemented with data looking at the effect of toxicants co-administered with forskolin on human chorionic gonadotropin (hCG) production levels. Briefly, toxicant-co-treatment with forskolin decreased hCG production levels to varying extents relative to forskolin only treatment. Overall, this work not only sheds insight on the effect toxicants can have on syncytialization but also informs of potential ways in which toxicants may mechanistically act to produce adverse pregnancy outcomes.

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Effects of Geochemical Perturbations on Dehalococcoides mccartyi-containing Dechlorinating Consortia

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Abstract:
Trichloroethene (TCE) is a commonly detected contaminant at Superfund sites and is frequently listed on the U.S. EPA’s National Priorities List. To date, Dehalococcoides mccartyi (Dhc) strains are the only known organisms that can completely dechlorinate TCE to ethene. In situ bioremediation employing Dhc has become an important process for addressing groundwater contamination with chlorinated solvents. Although much has been learned with respect to the metabolism of Dhc-based microbial communities, the effects of geochemical perturbations on dechlorinating communities are still unknown. As other electron-accepting processes in groundwater environments might impact TCE-dechlorination, the objective of our study is to investigate how dechlorination communities respond to the changes in these conditions by constructing various Dhc-containing consortia in batch and completely mixed flow reactors (CMFRs). The batch experimental results indicated that ferric iron and ferrous iron did not affect TCE dechlorination rates at concentrations up to 10 mg/L. In addition, sulfide generated from sulfate reduction inhibited TCE dechlorination at a concentration of 5mM only in Dhc/Desulfovibrio vulgaris hildenborough co-cultures with excess electron donor. Ongoing experiments are analyzing the toleration for sulfate perturbation in CMFRs. The information gained from this study will contribute to the development of engineered solutions that seek to optimize TCE dechlorination conditions.

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Development of thermally responsive magnetic nanocomposites for the capture and release of environmental pollutants

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Abstract:
Thermally responsive hydrogel based sorbents have gained great attention for environmental remediation, specifically in water treatment, due to their high adsorption capacities and response to external environment change. N-isopropylacrylamide (NIPAAm) is one of the most widely studied thermo-responsive materials, which undergoes reversible phase transition at its lower critical solution temperature (LCST) around 32°C. NIPAAm-based thermally responsive materials can be synthesized with various functionalities, which can provide specific interactions with target environment pollutants (e.g., organic dyes, PCBs). Our group’s recent efforts have focused on applying naturally derived polyphenols, such as curcumin and quercetin, to develop materials with binding affinities to such pollutants. The overall goal of this work was to develop thermally responsive materials for on/off binding of pollutants. Specifically, NIPAAm-based thermally responsive hydrogel films and microparticles have been developed. In addition, magnetic nanoparticles have been incorporated into the hydrogel network to enable magnetic separation. The temperature response of the bulk gels were characterized using swelling studies, and their LCSTs were characterized by DSC. Size and morphology of the gel microparticles were characterized by SEM, the magnetic nanoparticle loading was determined by TGA, the thermo-responsive was characterized by DLS, and the magnetic separation was also demonstrated.

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69. Understanding the Effects of Aging on Bioavailability of Legacy Contaminants using Isotope Dilution Method and 24-hr Tenax Desorption

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Abstract:
Ocean sediments around the world are contaminated with persistent organic pollutants (POPs), such as DDT and PCBs. Many instances of environmental contamination by these compounds are due to historic use and manufacturing from the 1950s up until they were banned in the 1970s. Since these compounds are hydrophobic and are recalcitrant to chemical and physical degradation, they have a strong affinity for both soil and sediment particles. As the properties of these compounds lend them to become persistent in the environment, these compounds have undergone many decades of aging, which may have rendered their residues less bioavailable. This study tests this assumption using sediment cores taken from the Palos Verdes Shelf Superfund Site off the coast of California, where around 44 km2 of sediment is heavily contaminated with DDT and PCBs. These cores were 210Pb dated and two methods to measure relative bioavailability (Isotope Dilution Method (IDM), and Tenax desorption) were used to relate age and the relative bioavailability of these contaminants. Both Tenax and the newly developed IDM have been successfully used to determine the relative bioavailability of several POPs in sediments, including DDT and PCBs. However, the use of IDM for assessing the effects of aging on bioavailability has not been validated. Through this study we hope to validate the use of IDM as a measure to assess, and establish a quantitative relationship between, the effects of aging on bioavailability.

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Molecularly Imprinted Polymers for Selective PCB Capture

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Abstract:
Polychlorinated biphenyls (PCBs) are a toxic class of persistent organic pollutants that are ubiquitous in soil and groundwater, bioaccumulate within the food chain, and have been associated with a variety of pathological processes, including vascular endothelial cell dysfunction. PCBs are thermally and chemically stable molecules, and chronic exposure to coplanar PCBs (e.g. PCB 126) has been shown to result in increased vascular oxidative stress and inflammation. Recently, our group has developed biomimetic magnetic nanoparticles coated with plant-derived polyphenols and demonstrated these to have affinity to PCBs, providing a novel method to capture and sense PCBs. Molecularly imprinted polymers (MIPs), using novel polyphenolic crosslinkers (e.g. curcumin multiacrylate, quercetin multiacrylate, etc.), are a novel method to improve binding specificity of these biomimetic nanoparticles. The objective of the current study is to synthesize these MIPs imprinted for PCBs by polymerizing functional monomers (e.g., styrene) with these novel crosslinkers. Our MIP system may have applications in both environmental and biological settings, by selective capture and removal of environmental pollutants such as PCBs. Hence, these novel materials may be utilized in a dual-purpose manner, to remediate PCB contaminated soils and groundwater, while also providing therapeutic means to decrease PCB-induced toxicity and body burden.

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Non-targeted analysis reveals a novel microbial metabolite of pyrene implicated in genotoxicity of bioremediated soil

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Abstract:
Bioremediation of soil contaminated with polycyclic aromatic hydrocarbons (PAHs) has been shown in some cases to increase its genotoxicity, despite removal of the regulated PAHs. Attempts to elucidate the source(s) of increased genotoxicity have not been successful, although prior work has implicated polar biotransformation products. We pursued a non-targeted analytical approach combining effect-directed analysis (EDA) and metabolite profiling to compare extracts of PAH-contaminated soil before and after treatment in an aerobic bioreactor. The DT 40 DNA damage response assay, high resolution mass spectrometry, and the XCMS Online platform for metabolomics were applied. Results revealed the accumulation of an oxygenated compound (C15H8O2) and four methylated homologs in bioremediated soil. The compound was purified from soil extracts and its cytotoxicity and genotoxicity confirmed. It was identified by nuclear magnetic resonance and mass spectroscopy as a previously unidentified α,β-unsaturated lactone derived from pyrene. The lactone accumulated when bioreactor-treated soil was incubated with pyrene, and it is also a product of pyrene metabolism by a pure bacterial culture known to be a significant degrader of pyrene in PAH-contaminated soils. Overall, non-targeted analysis combined with EDA led to the elucidation of a novel microbial metabolite now implicated as a source of increased genotoxicity resulting from aerobic bioremediation of PAH-contaminated soil.

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The Effects of Resveratrol on the Health Outcomes of Offspring Born to Dams Perinatally Exposed to Polychlorinated Biphenyls

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Abstract:
Polychlorinated biphenyls (PCBs) are persistent environmental pollutants that are known to have detrimental health consequences. PCB126 is a potent activator of the aryl hydrocarbon receptor (AhR) and previous studies by our lab have shown that in utero exposure to this chemical alters offspring body composition and glucose homeostasis. Resveratrol (Resv) is an AhR antagonist that is commonly used as a dietary supplement. This study was aimed at improving body composition and glucose tolerance in mouse offspring born to dams exposed to PCBs by supplementing the maternal diet with Resv. Female mice were fed experimental diet ± Resv from two weeks prior to mating until the pups were weaned. Prior to mating, the dams were further divided into four treatment groups; Control diet ± PCB126 and Resv ± PCB126. The dams were exposed to vehicle or PCB126 by oral gavage at 72 h prior to mating, on day 7 of gestation, and on postnatal day 7. Adult body weight was significantly decreased by maternal PCB exposure, and this difference was caused mostly by a decrease in lean mass. Maternal Resv consumption had minimal effects on body weight and lean mass in offspring. Perinatal PCB exposure caused a significant impairment in glucose tolerance in male offspring while female glucose tolerance was unchanged. Maternal Resv consumption did not significantly alter glucose tolerance in offspring of either sex. In conclusion, Resv did not provide enough benefit for further study in this model.

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Abstract:
The July 25th Appalachian Health and Well-Being Forum improved understanding of health concerns among people in the region while raising awareness about regional efforts to promote a healthier, more resilient Appalachia. Held in rural Whitesburg, KY, the forum was organized jointly by the UK-SRC Research Translation Core, Community Engagement Core, and local community leaders, who recruited a four-member expert panel to share success stories and highlight local, state, and national efforts to promote health and well-being in Eastern Kentucky. During the two-hour forum, panelists responded to attendee questions, of which 58% focused on the effect of the rural Appalachian environment on residents’ health. Other topics included drug abuse, access to healthcare, poverty and chronic disease management. Panel members’ responses pointed participants to existing programs and activities to improve health and well-being, while also acknowledging the continued need for policy, systems, and environmental changes to support improved health outcomes at the individual and community levels. In addition to the forum, the UK-SRC Training Core hosted a team-building retreat that allowed sharing of research ideas among Superfund trainees of UK, Duke University, and Louisiana State University. Trainees assisted with staffing the community forum, providing opportunities for trainees to interact directly with community participants. Research reported was supported by NIEHS/NIH grant P42ES007380.

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Biotransformation of prochiral polychlorinated biphenyls (PCBs): a novel source of chiral PCB metabolite

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Abstract:
PCB congeners with 3 or 4 ortho chlorine substituents and their metabolites exist as stable rotational isomers, or atropisomers, that are non-superimposable mirror images of each other. The toxicity of chiral PCBs can be highly atropselective, with only one atropisomer being active. Theoretically, the meta oxidation of certain axially prochiral PCBs, such as 2,2′,4,6′-tetrachlorobiphenyl (PCB 51) and 2,2′,4,5,6′-pentachlorobiphenyl (PCB 102), results in axially chiral hydroxylated metabolites (OH-PCBs); however, the formation of chiral OH-PCBs from prochiral PCBs to has not been demonstrated experimentally. We investigated whether metabolism of PCB 51 and PCB 102 by different liver microsomal preparations results in the formation of chiral OH-PCBs. Gas chromatographic analysis revealed that PCB 51 and PCB 102 were metabolized to 2,2′,4,6′-tetrachlorobiphenyl-3′-ol (OH-PCB 51) and 2,2′,4,5,6′-pentachlorobiphenyl-3′-ol (OH-PCB 102), respectively, by liver microsomes from male rats pretreated with different inducers; untreated male monkeys, guinea pigs, rabbits, and hamsters; and female dogs. The formation of both metabolites was inducer and species dependent. Moreover, OH-PCB 51 and OH-PCB 102 were chiral and were formed enantioselectively in all microsomes investigated. These findings demonstrate that chiral PCB metabolites can be formed from prochiral PCB congeners, a fact that should be considered when assessing the toxicity of PCB metabolites.

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75. Reproducible Iron/Palladium Nanoparticle Functionalized Membrane System for PCB Degradation from Water

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Abstract:
Polychlorinated biphenyls (PCBs) in groundwater, soil and sludge are of global concern due to their high toxicity, extremely persistence and prevalence in the environment. Zero-valent iron (ZVI) has been largely studied in reducing chlorinated organic compounds in groundwater, noble metal, such as palladium can be introduced for PCBs dechlorination. However, the Fe/Pd nanoparticles method faces difficulties with recycling and reuse. We have integrated nanoparticle catalysts into polyvinylidene fluoride (PVDF) membrane domains for reaction and separation. After functionalized with poly (acrylic acid) (PAA), this membrane platform shows good capacity in preventing metal ion loss and nanoparticle aggregation. Fe/Pd-PAA-PVDF membranes were applied in PCB degradation: In batch study, 97.5% of PCB 126 ([PCB]initial=15 µM) was consumed and 58.1% of consumed PCB was converted to biphenyl in 4 hours; In convective flow study, 96% of PCB 126 was consumed at 26s residence time. Besides degradation aspect, another three objectives have been already achieved: (1) Understanding the correlation between Fe/Pd nanoparticles properties (size, distribution and density) and the depth within the membrane. (2) Demonstration the reusability of functionalized membranes in PCB degradation study. (3) Investigation of PCB degradation kinetics with the help of development of reaction model. This research is supported by the NIEHS-SRP grant P42ES007380.

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76. Cadmium impairs adult neurogenesis, hippocampus-dependent memory and olfactory memory in mice

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Abstract:
Cadmium (Cd) is a heavy metal with a long biological half-life in humans and common to Superfund hazardous waste sites. Cd is a potential neurotoxicant and its exposure is associated with impairments of cognition and olfaction in humans. However, little is known regarding the mechanisms of Cd neurotoxicity. Adult neurogenesis occurs in the subgranular zone (SGZ) of the dentate gyrus in the hippocampus and subventricular zone (SVZ) along the lateral ventricles in adult mammalian brains. It plays an important role for hippocampus-dependent memory and olfaction. The effect of neurotoxicants on adult neurogenesis is just beginning to be elucidated. The goal of our study is to investigate the effects of Cd on cognition and olfaction with a focus on its effects on adult neurogenesis. We found that exposure of low-level Cd can affect adult neurogenesis in vivo. Furthermore, Cd exposure impairs spatial working memory, contextual fear memory, and short-term olfactory memory in adult mice. These results provide new insights concerning the underling mechanisms of Cd neurotoxicity, and partially fulfill UW SRP’s mission of mechanistic-based toxicology studies on neurotoxic heavy metals.

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77. Dietary frequency’s association with urinary phthalate levels among pregnant women in Puerto Rico

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Abstract:
Endocrine disrupting compounds (EDCs), particularly phthalates, are ubiquitous in modern society, posing a risk to pregnant women and the developing fetus. While often found in consumer products, phthalates are also found in the food supply, making diet a major route of exposure. Research has shown associations between previous 24-48 hour diet and phthalate levels, but none has explored how frequency of typical food consumption relates to phthalate body burden. This analysis includes 187 pregnant women, with urinary phthalate samples and who completed the food frequency questionnaire between 2010-2015. Phthalate levels were averaged across three visits, one from each trimester. In unadjusted generalized linear models, MEHHP, MEOHP, MCPP and DEHP were significantly (P<0.05) associated with high intake of meat. While high frequency of fruit intake was significantly associated with lower levels of MEHP, MEHHP, MEOHP, MCNP, MCOP, MCPP and DEHP sum. Increased MCNP levels were significantly associated with higher ice cream consumption frequency, and MEHP with high frequency of poultry consumption (p<0.10). The consistent associations found in this analysis show that typical eating habits, as represented by food frequencies, are associated with the urinary phthalate biomarkers, giving guidance for what foods and what frequency of intake, might increase or lower the body burden of phthalates in pregnant women.

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78. Association between Mesothelioma and Non-occupational Asbestos Exposure: Systematic Review and Meta-analysis

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Abstract:
Objective: To estimate the association between mesothelioma and non-occupational asbestos exposure, and evaluate control recruitment and exposure measurement methods. Methods: A systematic literature review was conducted on PubMed to identify case-control (CC) and cohort studies that examined the association between mesothelioma and non-occupational exposure to asbestos (neighborhood, household/domestic). Meta-analysis was performed to estimate a combined relative risk (RR) and 95% confidence intervals using random-effects models. Subgroup analyses were also conducted by gender, region, and fiber type. Results: 20 CC and 18 cohort studies were selected. Controls in CC studies were mostly matched by sex and age (95%) and selected from general population (70%), otherwise using hospital records. 50% of the cohort studies were retrospective (vs prospective). Multiple methods were used to classify neighborhood exposure (e.g., linear distance and direction of residence from an asbestos factory) and household/domestic exposure (e.g., duration of asbestos-related employment of subject’s spouse). Preliminary meta-analyses suggested a combined RR of mesothelioma of 6.69 (95%CI=5.69, 7.86) from neighborhood exposure and 4.52 (95%CI=3.83, 5.33) from household/domestic exposure. Conclusion: Neighborhood and household/domestic asbestos exposure is associated with an elevated risk of mesothelioma. Further investigation to identify additional studies and sources of bias are underway.

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79. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-mediated Suppression of IgM Secretion Activation Involves an Increase in Lymphocyte-specific Protein Tyrosine Kinase (LCK) in Human Primary B Cells

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Abstract:
The molecular mechanism responsible for TCDD-mediated immunotoxicity has been studied intensely in animal models and in human models. In the mouse models, it has been shown that TCDD markedly suppressed the number of IgM antibody forming cells and the expression of Ig, Ig and IgJ chains upon LPS activation. In humans, recent studies have indicated that TCDD-mediated activation of AHR impaired B cell activation. In our study, TCDD impaired the number of IgM forming cells and the level of IgM. However, the level of the intracellular IgM and the mRNA level of Ig, Ig and IgJ chains were not altered by TCDD. Previously, RNA-seq analysis of pokeweed mitogen-activated (PWM) human B cells treated with TCDD revealed TCDD-mediated upregulation of LCK. LCK is a tyrosine kinase that can phosphorylate critical signal proteins for vesicle secretion in T cells. However, it is little known about the role of LCK in B cell function. We discovered that the protein level of LCK were elevated with TCDD treatment which corresponded with a decrease in secreted IgM on days 7, post activation in vitro. The impairment of IgM secretion, which is well established in virtually every animal species evaluated to date, was rescued when a LCK specific inhibitor was applied. Our preliminary results suggest that the TCDD-mediated activation of AHR leads to an increase of LCK expression which is responsible for the impaired differentiation of naive B cells into antibody secreting plasma cells in human.

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