2015 Superfund Research Program Annual Meeting

San Juan, Puerto Rico | November 18-20

Hosted by:

PROTECT
Puerto Rico Testsite for Exploring Contamination Threats

NIH National Institute of Environmental Health Sciences
Superfund Research Program

Contents

Agenda

Day One: Wednesday, November 18, 2015

Joint Session of RTC-CEC and Training Programs

Time	*Event*	*Location*
7:30-8:30	**Breakfast Buffet** **Registration**	Ballroom Foyer
8:30-8:45	**Welcome** *On behalf of NIEHS:* • Danielle Carlin: Health Scientist Administrator, NIEHS • Michelle Heacock: Health Scientist Administrator, NIEHS • Alicia Lawson: Health Specialist, NIEHS *On behalf of PROTECT SRP:* • Thomas Sheahan: PROTECT SRP Training Core Leader and Professor of Civil and Environmental Engineering, Northeastern University • Phil Brown: PROTECT SRP Research Training Core Leader and Community Engagement Core co-Leader, and University Distinguished Professor of Sociology and Health Sciences, Northeastern University	San Cristobal Ballroom
8:45-10:00	**Environmental Contamination in Puerto Rico: Perspectives from Diverse Community Organizations** *Welcome* – Colleen Murphy: Trainee, University of Puerto Rico (PROTECT SRP) *Moderator* – Carmen Milagros Velez-Vega: Associate Professor of Public Health, University of Puerto Rico (PROTECT SRP) *Panelists:* • William Ramirez Cacho: Obstetrician & Gynecologist, Perinatologist, and Director of Obstetrics-Gynecology Department at Manatí Medical Center and Obstetrics-Gynecology at PRYMed (Federally Qualified Health Center, Ciales, PR) • Ranier Crespo: Member, COTICAM (Steering Committee for Environmental Quality) • Adriana Gonzalez: Coordinator and National Representative, Sierra Club of Puerto Rico and Representative of Basura Cero (Zero Waste) of Puerto Rico • Cristobal Jimenez: Vice-President, Board of Directors, Coalition for the Northeast Ecological Corridor of Puerto Rico • Emilio Font: Member, Co-Management Committee of the Natural Reserve, Coalition for the Northeast Ecological Corridor of Puerto Rico	San Cristobal Ballroom
10:00-10:15	**Break** • Training Program reconvenes in Tropical Salon at 10:15 • RTC-CEC program reconvenes in Salon del Mar at 10:30	Refreshments served in Tropical Salon and Salon del Mar

Training Program (continued from above)

Time	*Event*	*Location*
10:15-11:20	**Rethinking Scientific Presentations: the Assertion-Evidence Approach** *Introduction* – Jonathan Toro: Trainee, University of Puerto Rico (PROTECT SRP) Michael P. Alley: Associate Professor of Engineering, Pennsylvania State University	Tropical Salon

Day One: Wednesday, November 18, 2015 continued

11:20-11:30	**Break**	
11:30-12:15	**SRP Graduate Career Panel** *Moderator* – TBA *Panelists:* • Ingrid Padilla: Arizona SRP alumna and Professor of Civil Engineering, University of Puerto Rico (PROTECT SRP) • Xabier Arzuaga: Kentucky SRP alumnus and Toxicologist, U.S. Environmental Protection Agency • Veronica Vieira: Boston University SRP alumna and Associate Professor of Public Health, University of California – Irvine • Andres Cardenas: Oregon SRP alumnus and Postdoctoral Fellow, Harvard T.H. Chan School of Public Health	Tropical Salon
12:15-1:00	**Lunch**	Las Olas
1:00-2:15	**DISC Personality Session** *Introduction* – Norma Torres: Trainee, University of Puerto Rico (PROTECT SRP) Steven McGonagle: Professor of Practice in Engineering Leadership, Gordon Engineering Leadership Program, Northeastern University	Tropical Salon
2:15-3:15	**Connecting Your Ideas in Science through Writing** *Introduction* – Jonathan Toro: Trainee, University of Puerto Rico (PROTECT SRP) Michael P. Alley: Associate Professor of Engineering, Pennsylvania State University	Tropical Salon
3:30	**Reconvene for Main Meeting**	San Cristobal Ballroom

RTC-CEC Program (continued from previous page)

Time	***Event***	***Location***
10:30-10:45	**Introductions**	Salon del Mar
10:45-12:00	**Work Groups** Four workgroups will meet, as per prior discussions and interaction.	Salon del Mar
12:00-1:00	**Lunch** Box lunch to facilitate quick assembly into lunch discussion, with choice of (1) continuation of workgroups (including potential for people to move into a second workgroup), (2) further discussion with each of 4 community group speakers from first session, or (3) on your own	Las Olas
1:00-1:30	**Presentation on current state and future directions of SRP** William Suk: Director, Superfund Research Program, NIEHS	Salon del Mar
1:30-3:15	**Risk Communication** *Moderator* – Liza Anzalota del Toro, Human Subjects and Sampling Core Program Director, University of Puerto Rico (PROTECT SRP) *Panelists:* • Julia Brody: Executive Director, Silent Spring Institute (PROTECT SRP) • Ben Gerhardstein: Public Health Advisor, Agency for Toxic Substances and Disease Registry • Ted Emmett: SRP Community Engagement Core Leader and Professor of Occupational Medicine, University of Pennsylvania • Anna Hoover: SRP Research Translation Core co-Leader and Research Assistant Professor, University of Kentucky	Salon del Mar
3:30	**Reconvene for Main Meeting**	San Cristobal Ballroom

Day One: Wednesday, November 18, 2015 continued

Main Program

Time	*Event*	*Location*
1:00-8:30	**Registration Open**	Ballroom Foyer
3:30-3:45	**Welcome** • Akram Alshawabkeh: Snell Professor of Engineering, Northeastern University and co-Director/PI, PROTECT SRP • José Cordero: Patel Distinguished Professor in Public Health, University of Georgia and co-Director, PROTECT SRP • William Suk: Director, Superfund Research Program, NIEHS • Rick Woychik: Deputy Director, NIEHS	San Cristobal Ballroom
3:45-4:25	**Invited Talk 1: {Big} Data as a Catalyst for Collaboration and Innovation** *Introduction* - Rick Woychik: Deputy Director, NIEHS Philip E. Bourne: Associate Director for Data Science, National Institutes of Health	San Cristobal Ballroom
4:25-5:40	**Scientific Session 1: SRP Big data and data science applications** *Moderators:* • William Suk: Director, Superfund Research Program, NIEHS • Thomas Hampton: Trainee, Dartmouth SRP *Presenters:* • *Developing a computational framework for identifying and classifying modes of actions of chemical carcinogenicity in liver using gene expression profiling* Amy Li: Trainee, Boston University SRP • *Prenatal Exposure to Mercury and Arsenic and DNA Methylation in Umbilical Cord Blood* Andres Cardenas: Oregon SRP alumnus and Postdoctoral Fellow, Harvard T.H. Chan School of Public Health (KC Donnelly Externship Award Recipient 2014) • *The PROTECT Data Management and Modeling Core: Impacting Environmental Health Through Data Management and Analytics* David Kaeli: Professor of Electrical and Computer Engineering, Northeastern University (PROTECT SRP) • *Reporting Data to Participants in Biomonitoring and Household Exposure Studies: Its Use in the PROTECT Study (Puerto Rico Test Site to Explore Contamination Effects)* Julia Brody: Executive Director, Silent Spring Institute (PROTECT SRP) • *The Effects of Inter-Individual Variability on a Dose-Response Relationship: 2,3,7,8-tetracholorodibenzo-p-dioxin-induced Suppression of CD40L-activated Human Primary B Cells* Peter Dornbos: Trainee, Michigan State University SRP	San Cristobal Ballroom
5:40-5:50	**Break**	
5:50-7:20	**Poster Session 1 + Reception** • Light refreshments available • Poster presenters listed on page 14	San Geronimo Ballroom
7:20-8:45	**Dinner**	Las Olas

Day One: Wednesday, November 18, 2015 continued

Administrators' Program[1]

4:25-5:40	**Administrator Session 1** Led by: Mindy Sickels/Lisa Archer Edwards/Michelle Victalino/George Tucker • Introductions and Welcome • Icebreaker/Meet and Greet/Informal Survey	Salon del Mar

Day Two: Thursday, November 19, 2015

Main Program

Time	***Event***	***Location***

8:00-9:00	**Main meeting registration and breakfast**
	• Sub-group meetings:
	  ○ Presentation by EPA: Flamboyan Room
	  ○ Others TBA
		Ballroom Foyer

9:00-9:40	**Invited Talk 2: Science and Technology advances –opportunities to support Superfund sites** *Introduction* – Akram Alshawabkeh: Snell Professor of Engineering, Northeastern University and co-Director/PI, PROTECT SRP Jeff Heimerman: Associate Director, Technology Innovation and Field Services Division, US Environmental Protection Agency	San Cristobal Ballroom
9:40-10:55	**Scientific Session 2: Remediation** *Moderators:* • John McKernan: Environmental Health Specialist, U.S. Environmental Protection Agency • Angela Gutierrez: Trainee, University of Kentucky SRP *Presenters:* • *Geochemical Conditions Affect Corrinoid Pools that Control Dehaloccoides mccartyi Reductive Dechlorination Activity* Burcu Simsir: Trainee, University of Tennessee • *Effects of Activated Carbon Amendments on the Bioavailability and Methylation of Various Types of Inorganic Mercury* Heileen (Helen) Hsu-Kim: Associate Professor of Environmental Engineering, Duke University SRP • *In situ electrochemically-induced oxidation of contaminants in groundwater: Pilot scale testing* Ljiljana Rajic: Associate Research Scientist, Northeastern University (PROTECT SRP) • *Development of a Dual-Biofilm Reactive Barrier for Treatment of Chlorinated Benzenes at Anaerobic-Aerobic Interfaces in Groundwater and Sediments* Michelle Lorah: Research Hydrologist, U.S. Geological Survey (• *Arsenic and trichloroethene co-contamination effects on dechlorination activities of Dehalococcoides mccartyi-containing cultures* Sara Gushgari: Trainee, University of California – Berkeley SRP	San Cristobal Ballroom
10:55-11:15	**Break**	Ballroom Foyer

[1] Administrators participate in the main program except as noted in the Administrative Program.

Day Two: Thursday, November 19, 2015 continued

Main Program continued

11:15-12:30	**Scientific Session 3: Detection, Exposure, and Biomarkers** *Moderators:* • Dibakar Bhattacharyya: Alumni Chair Professor and SRP Project Leader, University of Kentucky • Gopi Gadupudi: Trainee, University of Iowa SRP *Presenters:* • *Detection of Biomarkers of Inflammation in newborns using filter paper blood samples from metabolic screening* Andrea González: Trainee, University of Puerto Rico (PROTECT SRP) (KC Donnelly Externship Award Recipient 2014) • *Coupling biotransformation of 2,4-dinitroanisole (DNAN) in anaerobic soil solutions to a multidimensional toxicity assay using zebrafish embryos* Christopher Olivares: Trainee, University of Arizona SRP (KC Donnelly Externship Award Recipient 2014) • *Maternal genotype for arsenic (+3 oxidation state)-methyltransferase AS3MT is associated with arsenic metabolism and newborn birth outcomes with interactions between fetal sex* Rebecca Fry: Associate Professor of Environmental Science and Engineering, University of North Carolina – Chapel Hill SRP • *Exposure Assessment of Three Dimensional (3D) Printer Emissions* Robert Herrick, Senior Lecturer on Industrial Hygiene, Harvard University • *Proof of Concept: Using Passive Sampling Polymers to Monitor Mercury and Methyl Mercury in Estuarine Waters* Vivien Taylor: Trainee, Dartmouth College (KC Donnelly Externship Award Recipient 2014)	San Cristobal Ballroom
12:30-1:30	**Lunch**	Las Olas
1:30-2:45	**Scientific Session 4: SRP Advances in Environmental Biomedical Sciences** *Moderators:* • Xabier Arzuaga: Toxicologist, U.S. Environmental Protection Agency • Lauren Johns: Trainee, University of Michigan (PROTECT SRP) *Presenters:* • *Effects of arsenic on macrophages and immune function* Fenna Sille: Trainee, University of California – Berkeley SRP • *Deletion of fibrocytes in mice attenuates CCl4-induced liver fibrosis* Jun Xu: Trainee, University of California – San Diego SRP • *The role of the intestine in dioxin-mediated fatty liver disease in mice* Kelly Fader: Trainee, Michigan State University SRP • *Spatial distribution of hepatic metals following PCB126 exposure* William Klaren: Trainee, University of Iowa (KC Donnelly Externship Award Recipient 2014) • *Biological and Environmental Interactions of Emerging Two-Dimensional Nanomaterials* Zhongying Wang: Trainee, Brown University SRP	San Cristobal Ballroom
2:45-3:15	**Wetterhahn Award Presentation**	San Cristobal Ballroom
3:15-3:45	**Break**	
3:45-5:15	**Poster Session 2 + Reception** • Light refreshments available • Poster presenters listed on page 19	San Geronimo Ballroom

Day Two: Thursday, November 19, 2015 continued

Main Program continued

5:15-7:00	**Break**	
7:00-9:00	**Dinner "on your own," or as part of following groups (pre-registration required):** • Directors' Dinner • Trainees' Dinner • RTC-CEC Dinner • Administrators' Dinner	Indicated at left

Administrators' Program[2]

Time	***Event***	***Location***
9:00-9:40	15 min one-on-one sessions with NIEHS GMS staff Lisa Archer Edwards and Michelle Victalino	Salon del Mar and Flamboyan
9:40-10:55	**Administrator Session 2** Led by: Lisa Archer Edwards/Michelle Victalino/George Tucker • NIH/NIEHS Updates • Carryover Requests • Uniform Guidance policy updates	Salon del Mar
10:55-11:15	**Break**	Outside Salon del Mar

11:15-12:30	**Administrator Session 3**
	• Part I: 11: 15-11:50 am Led by: Danielle Carlin
	  ○ 11:15 am – 11:30 am: Updates on CareerTrac
	  ○ 11:30 am – 11:50 am: "Life of an RFA/PA": what is the NIEHS process for establishing a new/revised RFA, what decisions must be made, what goes into completing and preparing an RFA for release?
	• Part II: 11:50am – 12:20 pm Led by: Linda Bass, Leroy Worth, Janice Allen, Alfonso Latoni: "The Application: From Submission to Summary Statement"
	• Part III: 12:20pm – 12:30pm Q & A
		Salon del Mar

12:30-1:30	**Lunch**	Las Olas
1:30-2:45	**Administrator Session 4** Led By: Heather Henry and Alicia Lawson • 1:30pm - 1:45pm - New funding opportunities that may be of relevance to Superfund scientists (moderator: Heather Henry) • 1:45pm - 2:00pm - R13 Funding Mechanisms for Conference Support—policy changes and updates (moderator: Alicia Lawson) • 2:00pm -2:20pm - RPPR changes/updates (moderator: Heather Henry) • 2:20pm - 2:45pm – Q & A	
2:45	**Rejoin Main Program**	San Cristobal Ballroom

[2] Administrators participate in the main program except as noted in the Administrative Program.

Day Three: Friday, November 20, 2015

Main Program

Time	*Event*	*Location*
7:45-8:30	**Main meeting registration and breakfast**	Grand Salon Los Rosales CDE
8:30-9:10	**Invited Talk 3: Linking Citizen Science and Social Equity to Advance Public Health: What's the Connection** *Introduction* – José Cordero: Patel Distinguished Professor in Public Health, University of Georgia and co-Director, PROTECT SRP Rachel Morello-Frosch: Professor of Public Health and Environmental Science, Policy and Management, University of California – Berkeley	Grand Salon Los Rosales AB
9:10-10:25	**Scientific Session 5: Sustainable Communities** *Moderators:* • Carmen Milagros Velez-Vega: Associate Professor of Public Health, University of Puerto Rico (PROTECT SRP) • Andres Cardenas: Oregon SRP alumnus and Postdoctoral Fellow, Harvard T.H. Chan School of Public Health *Presenters:* • *Development of a Fish Liver Microtissue Model to Characterize the Toxicity of Aromatic Hydrocarbons and Nanoparticle-Based Dispersants* April Rodd: Trainee, Brown University SRP • *The Meaning of a Superfund Site to an Affected Community* Edward Emmett: Professor of Occupational Medicine, University of Pennsylvania SRP • *Assessing the sewer gas to indoor air pathway at hazardous waste sites* Kelly Pennell: Assistant Professor of Civil Engineering, University of Kentucky SRP • *Overcoming the Barriers to Testing and Treating Arsenic in Private Well Water in New Hampshire* Mark Borsuk: Associate Professor of Engineering, Dartmouth College SRP • *Identifying intermediary pulmonary effects among Bangladeshi adolescents with known life stage water arsenic exposure* Tiffany Sanchez: Trainee, Columbia University SRP	Grand Salon Los Rosales AB
10:25-10:45	**Break**	Grand Salon Los Rosales Foyer

Day Three: Friday, November 20, 2015 continued

Main Program continued

10:45-12:00	**Scientific Session 6: Mixtures** *Moderators:* • Thomas Webster: Professor of Environmental Health and SRP Project co-Leader, Boston University • Danielle Carlin: Health Scientist Administrator, NIEHS *Presenters:* • *Polybrominated diphenylethers (PBDEs) in ambient air samples at the electronic waste (e-waste) reclamation site* Ajit Ghimire: Trainee, Louisiana State University SRP • *Flame Retardants in Housedust Antagonize Human TRβ Signaling* Erin Kollitz: Trainee, Duke University SRP • *Generalized Concentration Addition modeling of PPARγ activation by phthalate compounds in the ToxCast data set* James Watt: Trainee, Boston University SRP • *Statistical modeling approaches for mixtures of environmental toxins* Jordan Perkins: Trainee, University of Kentucky SRP • *Subchronic Inhalation Toxicity Study of a Complex PCB Mixture Representing Urban Air* Peter Thorne: Professor of Occupational & Environmental Health, University of Iowa SRP	Grand Salon Los Rosales AB
12:00-12:30	**Awards and Closing Comments**	Grand Salon Los Rosales AB
12:30-2:00	**Lunch** • Tote bags available for pick up for those traveling or attending field trips • Field Trips leave at 1pm	Las Olas
2:00	Adjourn	

Administrators' Program[3]

Time	***Event***	***Location***
8:30-9:10	15 min one-on-one sessions with NIEHS GMS staff Lisa Archer Edwards and Michelle Victalino	Caribe and Flamboyan

9:10-10:25	**Administrator Session 5**
	Led by: Erin Knight, Superfund Administrator
	• My NCBI
	  ○ 9:10-9:40am: My NCBI Publications-Webinar
	  ○ 9:40-9:50am: Q & A
	• Annual Meeting 2016 Preliminary Planning
	  ○ 9:50-10:25am: Vote Chair/Co-Chair for next year
	  ○ Brainstorming session for next year's agenda topics	

10:25-10:45	**Break**	Grand Salon Los Rosales Foyer

[3] Administrators participate in the main program except as noted in the Administrative Program.

Day Three: Friday, November 20, 2015 continued

Administrators' Program continued

10:45-12:00	**Administrator Session 6**
	Led by: Superfund Administrators
	• Best Practices Group Discussions:
	• Part I: 10:45-11:15am Subaward grant management
	  ○ Tracking of expenses for individual projects
	  ○ Carryover Requests/other Prior Approval requests
	• Part II: 11:15-12:00 pm Tips for Motivating Scientists to tackle Administrative tasks
	  ○ Diffusing heated discussions in meetings
	  ○ Delegating tips for Administrators who "do it all"
		Grand Salon Los Rosales AB

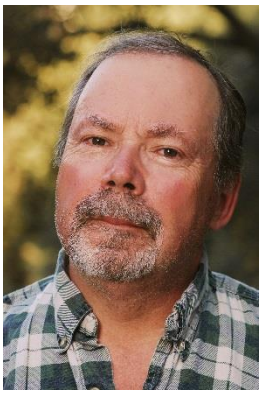
12:00	**Rejoin Main Program**	Grand Salon Los Rosales AB

Invited Talks

{Big} Data as a Catalyst for Collaboration and Innovation

Philip E. Bourne, PhD: Associate Director for Data Science, National Institutes of Health

Abstract: Data has always been at the foundation of the scientific enterprise. However data that are both "big" and digital present new challenges and opportunities which I will discuss. Examples are: (I) the opportunities for new discoveries resulting from looking at signals in large amounts of sensor data while being challenged to sustain such data activities; (ii) the difficulty of integrating disparate types of data but the scientific outcomes that result when achieved; and (iii) matching the demand for trained biomedical data scientists against the supply. I will illustrate these generalizations with specific work from the Big Data to Knowledge initiative (BD2K) with the intent of discussing how these developments can translate to SRP.



Bio: Philip E. Bourne, PhD, is the Associate Director for Data Science (ADDS) at the National Institutes of Health. Formally he was Associate Vice Chancellor for Innovation and Industry Alliances, a Professor in the Department of Pharmacology and Skaggs School of Pharmacy and Pharmaceutical Sciences at the University of California San Diego, Associate Director of the RCSB Protein Data Bank and an Adjunct Professor at the Sanford Burnham Institute.

Bourne's professional interests focus on service and research. He serves the national biomedical community through contributing ways to maximize the value (and hence accessibility) of scientific data. His research focuses on relevant biological and educational outcomes derived from computation and scholarly communication. This implies algorithms, text mining, machine learning, metalanguages, biological databases, and visualization applied to problems in systems pharmacology, evolution, cell signaling, apoptosis, immunology and scientific dissemination. He has published over 300 papers and 5 books, one of which sold over 150,000 copies.

Bourne is committed to maximizing the societal benefit derived from university research. Previously he co-founded 4 companies: ViSoft Inc., Protein Vision Inc., a company distributing independent films for free and most recently SciVee. Bourne is committed to furthering the free dissemination of science through new models of publishing and better integration and subsequent dissemination of data and results which as far as possible should be freely available to all. He is the co-founder and founding Editor-in-Chief of the open access journal PLOS Computational Biology. Bourne is committed to professional development through the Ten Simple Rules series of articles and a variety of lectures and video presentations.

Bourne is a Past President of the International Society for Computational Biology, an elected fellow of the American Association for the Advancement of Science (AAAS), the International Society for Computational Biology (ISCB) and the American Medical Informatics Association (AMIA).

Science and Technology advances –opportunities to support Superfund sites

Jeff Heimerman: Associate Director, Technology Innovation and Field Services Division, US Environmental Protection Agency

Abstract: One hallmark of the U.S. clean-up marketplace is the diffuse decision making that permeates that space. Another hallmark is risk, not just legal risk, but risk of failure meaning a financial risk. So how does an individual or start-up company supplying that space with new science and technologies get the right people to listen and act. There is no yellow brick road, but some still end up in Oz. This presentation will expand on these thoughts and suggest ways to get traction. It will also take stock of EPA/NIEHS efforts to integrate these advances into Superfund site work.

Bio: Jeff Heimerman is the Associate Director in the Technology Innovation and Field Services Division of the U.S. EPA Superfund program. The mission of the Technology Innovation and Field Services Division (TIFSD) is to provide world class technology information and expert field and laboratory support to customers that respond to emergency releases of hazardous materials and manage longer-term site assessment and remediation projects. TIFSD provides primary support to the Superfund Program as well as to other EPA programs including the Office of Solid Waste; Office of Emergency Management; Office of Underground Storage Tanks; and Office of Brownfields and Land Revitalization. TIFSD also partners with other federal and international agencies; other countries; and those in state, tribal, local, and private organizations to improve site remediation practices. As national and international leaders in innovation for laboratory, field, and remediation practices, TIFSD branches identify, develop, and/or advocate promising state-of-the-art technologies, innovative business practices, or tools for streamlining and improving the cost effectiveness and performance of assessment and cleanup strategies.

In addition to his managerial responsibilities, Jeff has been a principal developer on TIFSD's major technical assistance and information dissemination efforts. He and his staff are responsible for the development and operation of the Hazardous Waste Clean-Up Information (CLU-IN) website, the Brownfields Technical Support Center and CLU-IN's popular Internet Seminar Series. TIFSD has supported the NIEHS Risk-eLearning Webinars since 2002. His division also distributes the monthly email listserv, TechDirect, which now reaches more than 35,000 remediation practitioners in more than 70 countries. Jeff has been with EPA since 1987 after serving in the U.S. Peace Corps for two years in the Fiji Islands. He received his Masters from the Duke University School of the Environment. He received his Bachelor's degree in biology from Lawrence University in Appleton, Wisconsin.

Linking Citizen Science and Social Equity to Advance Public Health: What's the Connection?

Rachel Morello-Frosch: Professor of Public Health and Environmental Science, Policy and Management, University of California – Berkeley

Abstract: Policy makers and advocates are increasingly concerned about the origins and persistence of environmental health disparities across racial and class lines. Research also suggests that more unequal societies have more polluted and degraded environments, which may partially explain why more unequal societies are often less healthy. Addressing these social equity and sustainability challenges requires interdisciplinary research that characterizes the adverse impacts of social and physical environmental exposures with particular attention to their combined effects on diverse populations. Yet, although social science research has demonstrated the adverse effects of social stressors such as poverty, discrimination, and income inequality on health and well-being, there has been minimal cross-pollination between the social science and environmental health fields. Recently environmental justice advocates have pushed scientists to broaden lines of inquiry and undertake eco-social and community-engaged approaches to examine how inequality and chronic psycho-social stressors enhance susceptibility to the adverse health effects of environmental exposures, particularly among communities of color and the poor. This talk examines the scientific evidence underlying the cumulative effects and potential interactions of exposures to environmental hazards and social stressors, which has been referred to as a form of "double jeopardy, and the critical importance of using participatory methods in this research. Ultimately, community engagement in this work can reshape environmental policy in ways that improve health and that move public health science from an emphasis on translational research to one of transformational research.

Bio: Rachel Morello-Frosch is Professor in the School of Public Health and the Department of Environmental Science, Policy and Management at UC Berkeley. Her research examines race and class determinants of environmental health disparities among diverse communities in the US with a focus on environmental chemicals and climate change. In collaboration with researchers, regulatory scientists, and community partners, she has developed scientifically valid and transparent tools for assessing the cumulative impacts of chemical and non-chemical stressors to improve regulatory decision-making and advance environmental justice in California. Rachel is co-author of Contested Illness: Citizens, Science and Health Social Movements. Her research is supported by NIEHS, NSF, Cal-EPA, the California Breast Cancer Research Program and private foundations.

Poster Presentations

#	Classification	Name	Organization	Title
Day 1 - 1	non-RTC/ non-Trainee	Andrew Morris	University of Kentucky SRP	Environmental exposures as a determinant of diet and nutrition based interventions for cardiovascular disease risk reduction
Day 1 - 2	non-RTC/ non-Trainee	Ann Aschengrau	Boston University SRP	Occurrence of unintentional head injuries following prenatal and early childhood exposure to tetrachloroethylene (PCE)-contaminated drinking water
Day 1 - 3	non-RTC/ non-Trainee	Benjamin Bostick	Columbia University SRP	Insights from a Kinetics-Based Model Describing Aqueous Arsenic Concentrations at Superfund Sites
Day 1 - 4	non-RTC/ non-Trainee	Brian Jackson	Dartmouth College SRP	Fast ion chromatography-ICP-QQQ for arsenic speciation analysis
Day 1 - 5	non-RTC/ non-Trainee	Brian Mailloux	Barnard College (Columbia University SRP)	Metagenomic and Radiocarbon Analysis of PLFA, DNA, RNA, and Proteins to better understand Arsenic Impacted Aquifers in Bangladesh
Day 1 - 6	non-RTC/ non-Trainee	Catherine Larsen	University of California - San Diego SRP	Urban Agriculture Site Suitability Analysis in San Diego
Day 1 - 7	non-RTC/ non-Trainee	Clementina Mesaros	University of Pennsylvania SRP	Effects of asbestos exposure on the cellular redox state and mitochondrial dysfunction
Day 1 - 8	non-RTC/ non-Trainee	Jared Goldstone	Woods Hole Oceanographic Institution (Boston University SRP)	The PXR “gene battery” in zebrafish
Day 1 - 9	non-RTC/ non-Trainee	Molly Kile	Oregon State University SRP	The effects of arsenic, manganese, and lead on neurodevelopmental outcomes among children in Bangladesh
Day 1 - 10	non-RTC/ non-Trainee	Rita Loch-Caruso	University of Michigan (PROTECT SRP)	Trichloroethylene Metabolite S-(1,2-Dichlorovinyl)-L-Cysteine but not Trichloroacetate Inhibits Pathogen-Stimulated TNF-α in Human Extraplacental Membranes In Vitro
Day 1 - 11	non-RTC/ non-Trainee	Tania Busch Isaksen	University of Washington SRP	Sustainable Technologies, Alternative Chemistry – Training and Education Center
Day 1 - 12	RTC	Brad Upham	Michigan State University SRP	Technology transfer enabling a participatory research project of a high school community to assess microbial populations involved in dioxin degradation and antibiotic resistance
Day 1 - 13	RTC	Catherine Larsen	University of California - San Diego SRP	The UCSD Brownfield Project and the application of safe gardening practices
Day 1 - 14	RTC	Craig Just	University of Iowa SRP	The Iowa Superfund Research Program, Ecolotree, and the Town of Altavista Expand a Partnership
Day 1 - 15	RTC	Dana Haine	University of North Carolina - Chapel Hill SRP	Enhancing the capacity of biology teachers to incorporate SRP research findings into life science instruction
Day 1 - 16	RTC	David Stone	Oregon State University SRP	A Conceptual Framework to Support Exposure Science Research and Complete the Source-to-Outcome Continuum for Risk Assessment
Day 1 - 17	RTC	Dawn Brewer	University of Kentucky SRP	Level of Concern Regarding Harmful Health Effects of Environmental Contaminants among Older Adults Participating in Kentucky’s Congregate Meal Site Program and their Understanding of the Protective Role of Good Nutrition

#	Classification	Name	Organization	Title
Day 1 - 18	RTC	Dawn Brewer	University of Kentucky SRP	Land-Grant Institution's Cooperative Extension Service serves as a valued partner in UK-SRC's Community Engagement Core efforts
Day 1 - 19	RTC	Ellen Cooper	Duke University SRP	The Duke Superfund Foam Project: Preliminary Flame Retardant Findings After One Year of Testing
Day 1 - 20	RTC	Fernando Pantoja-Agreda	University of Puerto Rico (PROTECT SRP)	Spatiotemporal Dynamics of Nitrates in Karst Groundwater
Day 1 - 21	RTC	Frances Barg	University of Pennsylvania SRP	Unintended Consequences of Environmental Risk Research at Superfund Sites: Implications for Integrating Community Involvement into Risk Assessment and Reuse Planning
Day 1 - 22	RTC	Gretchen Kroeger	Duke University SRP	Engaging Stakeholders to Assess Human Exposure to Contaminants via Recreational Fishing in the Elizabeth River Watershed, Virginia
Day 1 - 23	RTC	Ilya Zaslavsky	University of California - San Diego SRP	Analyzing, mapping and visualizing diverse environmental data: New online tools for civically engaged research and healthy place making
Day 1 - 24	RTC	Jessica Meeker	University of Pennsylvania SRP	A New Model for Cumulative Risk Assessment and its Application to Superfund Sites
Day 1 - 25	RTC	Joseph Hamm	Michigan State University SRP	Michigan State University Superfund Research Project Community Engagement Core
Day 1 - 26	RTC	Kathleen Gray	University of North Carolina - Chapel Hill SRP	Partnering with USEPA to Improve Community Understanding of Metals Bioavailability
Day 1 - 27	RTC	Keith Pezzoli	University of California - San Diego SRP	Healthy City Planning: An integrated approach to reducing cumulative impacts in disadvantaged communities
Day 1 - 28	RTC	Kelly Pennell	University of Kentucky SRP	UK SRC Research Translation Core: A Multidirectional Bridge for Stakeholders and Resources
Day 1 - 29	RTC	Komal Basra	Boston University SRP	Science to Stakeholders: Research Translation and Community Engagement Collaborations
Day 1 - 30	RTC	Laurie Rardin	Dartmouth College SRP	Using Evaluation to Measure the Effectiveness of the C-MERC Model to Bring SRP Science to Policy Stakeholders
Day 1 - 31	RTC	Marcella Thompson	University of Rhode Island (Brown SRP)	The Namaus (All Thing Fish) Project: Multidisciplinary Collaboration in Community Engaged Research with the Narragansett Tribe and the Role of the Knowledge Broker
Day 1 - 32	RTC	Margaret Reams	Louisiana State University SRP	Engaging Community Partners and Public Agencies in the Scientific and Regulatory Challenges Associated with an Emerging Contaminant: Environmentally Persistent Free Radicals
Day 1 - 33	RTC	Margaret Reams	Louisiana State University SRP	Toxic landscapes, environmental justice and the community: An assessment of citizen participation in Superfund site remediation in the EPA's 6th region.
Day 1 - 34	RTC	Molly Kile	Oregon State University SRP	Communicating the results of dietary exposures and metabolism of PAHs from a tribally important food
Day 1 - 35	RTC	Phil Brown	Northeastern University (PROTECT SRP)	Community Engagement and Research Translation Cores Working Together to Foster Healthy Pregnancy in Puerto Rico
Day 1 - 36	RTC	Julia Brody	Silent Spring Institute (PROTECT SRP)	Reporting Data to Participants in Biomonitoring and Household Exposure Studies: Its Use in the PROTECT

#	Classification	Name	Organization	Title
				Study (Puerto Rico Test Site to Explore Contamination Effects)
Day 1 - 37	RTC	Sarah Wilkinson	University of Arizona SRP	The Center for Environmentally Sustainable Mining: An Industry-Academic Cooperative to Promote Environmental Stewardship of Mining Sites
Day 1 - 38	RTC	Sarah Yelton	University of North Carolina - Chapel Hill SRP	Fostering Effective Science Communication Skills: A Building Block for Collaboration and Innovation
Day 1 - 39	RTC	Stuart Braman	Columbia University SRP	Collaboration to reduce arsenic exposure from private well water in New Jersey
Day 1 - 40	RTC	Wael Al-Delaimy	University of California - San Diego SRP	Community Gardens: a global view of the balance of harm from toxicants and public health benefits
Day 1 - 41	RTC	Yan Zheng	City University of New York (Columbia University SRP)	Arsenic in Private Well Water – Collaboration on Community Engagement in Maine
Day 1 - 42	RTC	Yan Zheng	City University of New York (Columbia University SRP)	Tackling Arsenic Exposure from Private Well Water in Rural American Communities
Day 1 - 43	RTC	Vilda Rivera	University of Puerto Rico (PROTECT SRP)	Spatiotemporal Assessment of the Link between the Karst Groundwater Sources and the Tap Water Point of Use
Day 1 - 44	RTC and Trainee	Lisandra Santiago Delgado **(KC Donnelly recipient, 2015)**	Oregon State University SRP	Metabolism and Excretion Rates of Parent and Hydroxy-PAHs in Urine Collected After Consumption of Traditionally Smoked Salmon For Native American Volunteers
Day 1 - 45	Trainee	Gloria Garcia	Oregon State University SRP	Discovery of a Conserved Long Noncoding RNA Upregulated in Response to the Xenobiotic Activation of the Aryl Hydrocarbon Receptor
Day 1 - 46	Trainee	Alexandra Goetz	University of California - San Diego SRP	The Role of the NMD RNA Degradation Pathway in Arsenic-Induced Cell Death
Day 1 - 47	Trainee	Amira Aker	University of Michigan (PROTECT SRP)	Association between Phenols and Parabens & Reproductive and Thyroid Hormones
Day 1 - 48	Trainee	Andrew Cooper	University of California - San Diego SRP	Identification of new components in cadmium-specific signaling networks
Day 1 - 49	Trainee	Angela Gutierrez	University of Kentucky SRP	Development of Magnetic Nanocomposite Materials for the Rapid Removal of PCBs from Contaminated Water Sources
Day 1 - 50	Trainee	Anna Chlebowski	Oregon State University SRP	Developmental Toxicity and AHR Induction of Nitrated PAHs
Day 1 - 51	Trainee	Anthony Oliveri	Duke University SRP	Early-life exposure to organophosphate flame retardants alters behavior across the lifespan in zebrafish
Day 1 - 52	Trainee	Arjun Venkatesan	University of Florida	Molecular changes in fathead minnows induced by single and multiple contaminant exposures
Day 1 - 53	Trainee	Ashlyn Harmon	Louisiana State University SRP	Pulmonary inflammation and injury caused by environmentally persistent free radicals is mediated through activation of the aryl hydrocarbon receptor
Day 1 - 54	Trainee	Balamurugan Subramanian	Louisiana State University SRP	The Effect of the Nature of Metal Oxide on the Formation and Persistency of Environmentally Persistent Free Radicals
Day 1 - 55	Trainee	Britton Goodale	Dartmouth College SRP	Arsenic mixture exposure modulates innate immune signaling in human primary bronchial epithelial cells

#	Classification	Name	Organization	Title
Day 1 - 56	Trainee	Carsten Prasse	University of California - Berkeley SRP	Linking Remediation to Toxicology – Screening for Toxic Transformation Products Formed During Oxidative Treatment of Superfund Contaminants
Day 1 - 57	Trainee	Chun Shi Lin	Salk Institute (UCSD SRP)	RORγ: the Nexus of Liver Metabolism, Mitochondrial, Bioenergetics, and Acetaminophen Toxicity
Day 1 - 58	Trainee	Craig Menges	Fox Chase Cancer Center (UPenn SRP)	SRP Project 4: Animal models of asbestos-induced mesothelioma
Day 1 - 59	Trainee	Eduardo Alvarez Martinez	University of Puerto Rico (PROTECT SRP)	Spatial Distribution of Hydraulic Conductivities in Heterogeneous Media
Day 1 - 60	Trainee	Elisabeth Feld	Louisiana State University SRP	The Role of Sulfur as an Environmentally Persistent Free Radical (EPFR) Suppressant
Day 1 - 61	Trainee	Eric Rodriguez	University of Iowa SRP	Hydroxylated and Sulfated Metabolites of Commonly Observed Airborne Polychlorinated Biphenyls Display Selective Toxicity in N27 and SHSY5Y Neuronal Cells
Day 1 - 62	Trainee	Genevieve Ryan	University of California - San Diego SRP	Androgen Action in Pituitary Gonadotropes
Day 1 - 63	Trainee	Hao Wang	University of Washington SRP	The effects of Cadmium on adult neurogenesis and hippocampus -dependent memory in mice
Day 1 - 64	Trainee	Hongyi Wan	University of Kentucky SRP	pH-responsive Membrane Immobilized Iron-Based Particle Systems for PCB Degradation
Day 1 - 65	Trainee	Irmarie Cotto	University of Puerto Rico (PROTECT SRP)	Partitioning Coefficient of DEHP between Methylene Chloride and Water
Day 1 - 66	Trainee	Jeffrey Farner Budarz	Duke University SRP	Photoreactive TiO_2 nanoparticles for Chlorpyrifos Degradation: Synergies and Antagonisms in Nano-Bio Based Remediation Strategies
Day 1 - 67	Trainee	Jessica Laine	University of North Carolina - Chapel Hill SRP	Placental Cadmium Exposure Increases Preeclampsia Risk
Day 1 - 68	Trainee	Jinpeng Li	Michigan State University SRP	2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)-mediated Impairment of Human Hematopoietic Stem Cells (HSCs) to Pro-B Cell Development
Day 1 - 69	Trainee	Jongeun Rhee	Harvard School of Public Health	A Case-Control Study of Multiple Occupational Exposures and Lung Cancer Risk in the Northeastern USA
Day 1 - 70	Trainee	Julie Krask	Virginia Institute of Marine Science	Efficacy of sediment remediation efforts on PAH contaminant flux via porewater advection at the sediment-surface water interface
Day 1 - 71	Trainee	Kate Buckman **(KC Donnelly recipient, 2015)**	Dartmouth College SRP	Influence of temperature and organic carbon on methylmercury bioaccumulation in a mesocosm
Day 1 - 72	Trainee	Kathryn Crawford	Boston University SRP	Using computational toxicology and spatial analysis to inform in vivo toxicity testing: Identifying obesogenic compounds in New Bedford Harbor and Buzzards Bay, Massachusetts
Day 1 - 73	Trainee	Lauren Johns	University of Michigan (PROTECT SRP)	Associations between environmental phthalate exposure and maternal thyroid hormone levels during pregnancy
Day 1 - 74	Trainee	Lei Wu	University of Pennsylvania SRP	Dynamics and mechanisms of asbestos-fiber aggregate growth in water
Day 1 - 75	Trainee	Liwei Weng	University of Pennsylvania SRP	Metabolomics of asbestos exposure-structure identification of upregulated metabolites

#	Classification	Name	Organization	Title
Day 1 - 76	Trainee	Mallory LeBlanc	Harvard School of Public Health	Diacetyl, a Flavoring Chemical Associated with "Popcorn Lung", is in Many Flavored E-cigarettes
Day 1 - 77	Trainee	Marisa Salomon Beltran	University of Iowa SRP	Novel Tools for Targeting PCBs/PCB metabolites using DNA Aptamers
Day 1 - 78	Trainee	Matthew King	University of Arizona SRP	Measurement of threshold friction velocities at the Iron King Mine tailings site and other potential dust sources in semi-arid regions
Day 1 - 79	Trainee	Meng Bi	University of Tennessee	Identification of purine-cobamide as a novel corrinoid cofactor of tetrachloroethene reductive dehalogenases in Desulfitobacterium
Day 1 - 80	Trainee	Michael Petriello	University of Kentucky SRP	EGCG prevents PCB-induced endothelial cell inflammation via epigenetic modifications of NF-κB target genes
Day 1 - 81	Trainee	Mitra Geier	Oregon State University SRP	Developmental Toxicity of Parent and Methylated Polycyclic Aromatic Hydrocarbons in Embryonic Zebrafish
Day 1 - 82	Trainee	Natalia Kovalova	Michigan State University SRP	Effects Of DNA Sequence Variation In Aryl Hydrocarbon Receptor (AHR) On The Sensitivity Of Human Immune System to Suppression by Dioxin
Day 1 - 83	Trainee	Nika Larian	University of Kentucky SRP	Pyocyanin and indirubin, pathogen-associated ligands of the aryl hydrocarbon receptor, reduce differentiation of 3T3-L1 adipocytes
Day 1 - 84	Trainee	Noushin Fallahpour	Northeastern University (PROTECT SRP)	Electrochemical dechlorination of TCE in the presence of natural organic matter, metal ions and nitrates in a simulated karst aquifer
Day 1 - 85	Trainee	Oluwadamilare Adebambo	North Carolina State University	Synergistic Induction of Metal-Responsive and Oxidative Stress Gene Biomarkers in Placental JEG-3 Cells by Arsenic & Cadmium Mixtures from Hazardous Waste Sites
Day 1 - 86	Trainee	Rance Nault	Michigan State University SRP	Pyruvate kinase isoform switching and the metabolic reprogramming of central carbon and amino acid metabolism by the environmental contaminant 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)
Day 1 - 87	Trainee	Rohit Bhandari	University of Kentucky SRP	Functionalized Magnetic Nanoparticle Systems for the Capture of PCBs
Day 1 - 88	Trainee	Roya Nazari	Northeastern University (PROTECT SRP)	Sono-electro-Fenton Degradation of 4-Chlorophenol in Aqueous Media
Day 1 - 89	Trainee	Rui Yu	University of North Carolina - Chapel Hill SRP	Inhaled versus Endogenous Formaldehyde Exposures: Are They Both Misestimated?
Day 1 - 90	Trainee	Scott Coffin	University of California - Riverside	Use of solid phase microextraction (SPME) and laboratory models to estimate risk of SDDT from consumption of fish from contaminated sediments in Palos Verdes, California
Day 1 - 91	Trainee	Shirin Hojabri	Northeastern University (PROTECT SRP)	Modeling of transient pH condition during the water treatment by electrochemical process
Day 1 - 92	Trainee	Sridhar Jaligama	University of Tennessee Health Science Center (LSU SRP)	Combustion Derived Particulate Matter Exposure Suppresses Pulmonary Host Defense through Regulatory T cells and IL10
Day 1 - 93	Trainee	Todd Warczak	Dartmouth College SRP	Identification and Characterization of Genes with a Novel Role in Arsenic Detoxification in Plants

#	Classification	Name	Organization	Title
Day 2 - 1	non-Trainee	Dwayne Elias	University of Tennessee	Development of Biomolecular Tools for Quantifying the Mercury-methylation Genes as Biomarkers for Methylmercury Production
Day 2 - 2	non-Trainee	Edward Emmett	University of Pennsylvania SRP	Definition and identification of a community cohort with exposure to asbestos
Day 2 - 3	non-Trainee	Ekihiro Seki	Cedars-Sinai Medical Center (UCSD SRP)	The involvement of fatty liver and mitochondrial functions in toxin-induced liver injury and fibrosis: Role of Ubc13
Day 2 - 4	non-Trainee	Faruque Parvez	Columbia University SRP	Arsenic exposure, non-malignant respiratory outcomes and immune modulation in the Health Effects of Arsenic Longitudinal Study (HEALS) cohort
Day 2 - 5	non-Trainee	Frances Barg	University of Pennsylvania SRP	A historical cohort study of the influence of occupational and non-occupational exposure to asbestos
Day 2 - 6	non-Trainee	Greg Vanichkachorn	University of Pennsylvania SRP	The detection of effects of asbestos exposure using novel biomarkers
Day 2 - 7	non-Trainee	Heileen Hsu-Kim	Duke University SRP	New Methods to Quantify Mercury Bioavailability and Methylation Potential in Contaminated Sediments
Day 2 - 8	non-Trainee	James Ranville	Colorado School of Mines	Development of in-situ methods for simulating sediment recovery post-remediation in a stream affected by acid mine drainage
Day 2 - 9	non-Trainee	Jared Goldstone	Woods Hole Oceanographic Institution (Boston University SRP)	Transcriptomic effects of ortho-PCBs on developing zebrafish
Day 2 - 10	non-Trainee	Judit Marsillach	University of Washington SRP	Adductomics and organophosphorus exposures in communities
Day 2 - 11	non-Trainee	Kurt Varner	Louisiana State University SRP	Environmentally Persistent Free Radicals Increase Systolic Blood Pressure and Block Compensatory Responses to Cardiac Stress in Rats with Ischemic Heart Disease
Day 2 - 12	non-Trainee	Ljijana Rajic	Northeastern University (PROTECT SRP)	Enhanced groundwater flow modeling in karst using drainage feature: case study of the central northern karst aquifer system of Puerto Rico
Day 2 - 13	non-Trainee	Ljijana Rajic	Northeastern University (PROTECT SRP)	Patterns of phthalates in karst aquifers of Northern Puerto Rico
Day 2 - 14	non-Trainee	Luoping Zhang	University of California - Berkeley SRP	Formaldehyde induces toxicity in mouse bone marrow and hematopoietic stem/progenitor cells and enhances benzene-induced adverse effects
Day 2 - 15	non-Trainee	Mary Gamble	University of Illinois - Chicago (Columbia University SRP)	Epigenetic and gene expression effects of arsenic exposure
Day 2 - 16	non-Trainee	Michael Unger	Virginia Institute of Marine Science	Impact of groundwater-surface water dynamics on in situ remediation efficacy and bioavailability of PAH contaminants
Day 2 - 17	non-Trainee	Molly Kile	Oregon State University SRP	Effect of early marriage and arsenic exposure during pregnancy on gestational weight gain and preterm birth in Bangladesh
Day 2 - 18	non-Trainee	Neel Aluru	Woods Hole Oceanographic Institution (Boston University SRP)	Understanding the genomic basis for adaptation to long-term PCB exposure at Superfund sites: Application of genome editing to aryl hydrocarbon receptor (AHR) signaling pathways in fish

#	Classification	Name	Organization	Title
Day 2 - 19	non-Trainee	Peter Thorne	University of Iowa SRP	Exposure to PCBs Not Found in Commercial Mixtures: Evidence from Biomonitoring Among Urban and Rural Adolescents and Their Mothers
Day 2 - 20	non-Trainee	Raina Maier	University of Arizona SRP	A Four-Year Superfund Site Field Study Demonstrates that Direct Planting on Mine Tailings is a Reclamation Alternative to Cap and Plant
Day 2 - 21	non-Trainee	Rebecca Fry	University of North Carolina - Chapel Hill SRP	Metabolomic Characteristics of Arsenic-Associated Diabetes in a Prospective Cohort in Chihuahua, Mexico
Day 2 - 22	non-Trainee	Rita Loch-Caruso	University of Michigan (PROTECT SRP)	Mono-Ethylhexyl Phthalate Stimulates Prostaglandin Synthesis in Human Placental Macrophages and THP-1 Cells
Day 2 - 23	non-Trainee	Roger Giese	Northeastern University (PROTECT SRP)	Discovery of Xenobiotics Associated with Preterm Birth
Day 2 - 24	non-Trainee	Shujuan Chen	University of California - San Diego SRP	Crypt organoids culture as an in vitro model in pharmacological and toxicological studies
Day 2 - 25	non-Trainee	Staci Simonich	Oregon State University SRP	Relative Influence of Trans-Pacific and Regional Atmospheric Transport of PAHs in the Pacific Northwest, USA
Day 2 - 26	non-Trainee	Thomas Webster	Boston University SRP	Statistical Approaches for Assessing Health Effects of Environmental Chemical Mixtures in Epidemiology Studies
Day 2 - 27	non-Trainee	Tracy Punshon	Dartmouth College SRP	Elemental Imaging Capabilities of Dartmouth College's Trace Element Analysis Core Facility: A new program-wide resource
Day 2 - 28	non-Trainee	Upal Ghosh	University of Maryland Baltimore County	Development of In-Situ Mercury Remediation Approaches Based on Methylmercury Bioavailability
Day 2 - 29	non-Trainee	Veena Antony	University of Alabama at Birmingham	Biomarkers in Exhaled Breath Condensate and Serum for Lung Injury caused by Inhaled Mixtures of Heavy Metal: Linking Lung Fibrosis and Emphysema
Day 2 - 30	non-Trainee	Veronica Vieira	University of California - Irvine (Boston University SRP)	Spatial Analysis of Discrete Outcomes via Bayesian Adaptive Thin-Plate Smoothing Splines
Day 2 - 31	non-Trainee	Wayne Backes	Louisiana State University SRP	Environmentally Persistent Free Radicals Inhibit CYP1A2 and CYP2B4 by Different Mechanisms
Day 2 - 32	Trainee	Amin Sobh	University of California - Berkeley SRP	Using CRISPR-Cas9 Genome Editing Technologies to Study Toxicant Susceptibility
Day 2 - 33	Trainee	Anastasia Velalopoulou	University of Pennsylvania SRP	The Synthetic Lignan Secoisolariciresinol Diglucoside (SDG) Inhibits Asbestos-Induced Inflammation and Oxidative Cell Damage in Murine Peritoneal Macrophages
Day 2 - 34	Trainee	Andrea Gonzalez **(KC Donnelly recipient, 2014)**	University of Puerto Rico (PROTECT SRP)	Detection of Biomarkers of Inflammation in newborns using filter paper blood samples from metabolic screening
Day 2 - 35	Trainee	Angel Anaya	University of Puerto Rico (PROTECT SRP)	Hydrodynamic and TCE Transport Characterization of a Karstic Physical Model using Statistical and Time Moment Analysis
Day 2 - 36	Trainee	Anna Chlebowski	Oregon State University SRP	Quantitation and Prediction of PAH and NPAH Sorption to Polystyrene 96-Well Plates

#	Classification	Name	Organization	Title
Day 2 - 37	Trainee	Ansonia Badgett	Louisiana State University SRP	Controlled Polymerization of SiO_2 Shell for the Synthesis of Highly Fluorescent Up-Conversion Environmentally Persistent Free Radical Surrogates
Day 2 - 38	Trainee	Arjun Venkatesan	University of Florida	Development and validation of a novel dual phase water sampler to monitor trace level phenylpyrazole pesticides
Day 2 - 39	Trainee	Asmaa Sallam	University of Tennessee Health Science Center (LSU SRP)	Neonatal PM Exposure Induces a Regulatory Dendritic Cell Phenotype in the Lung via β-catenin signalin
Day 2 - 40	Trainee	Banrida Wahlang	University of Kentucky SRP	Polychlorinated Biphenyl Exposure Changes MicroRNA Expression Profile in Human Endothelial Cells
Day 2 - 41	Trainee	Burcu Simsir	University of Tennessee	The B_{12}-qChip: a high-throughput qPCR tool for monitoring and predicting reductive dechlorination activity of organohalide-respiring Chloroflexi
Day 2 - 42	Trainee	Caitlin Howe	Columbia University SRP	Sex-specific influences of arsenic and nutritional indices on post-translational histone modifications in Bangladeshi adults
Day 2 - 43	Trainee	Cedric Gonneau	University of Pennsylvania SRP	Plant-assisted remediation of asbestos contaminated soils
Day 2 - 44	Trainee	Chuqi Guo	Louisiana State University SRP	Environmentally Persistent Free Radicals (EPFRs) in Airborne Particular Matter (PM) – Sampling Artifacts
Day 2 - 45	Trainee	Edward Dere	Brown University SRP	Molecular alterations in sperm are sensitive indicators of testicular dysfunction
Day 2 - 46	Trainee	Elizabeth Corteselli	University of North Carolina - Chapel Hill SRP	Characterization of a novel soil bacterium capable of degrading high molecular weight polycyclic aromatic hydrocarbons
Day 2 - 47	Trainee	Emilie Lefevre	Duke University SRP	Effect of activated carbon and biochar on TBBPA biodegradation efficiency, and characterization of the microbial communities responsible in anaerobic sludge digesters
Day 2 - 48	Trainee	Erika Holland	University of California - Davis SRP	Defining the neurotoxic potential of nondioxin-like polychlorinated biphenyls present in fish from US lakes using a ryanodine receptor-based equivalency scheme.
Day 2 - 49	Trainee	Erin Madeen	Oregon State University SRP	Cyp1b1 status modulates PAH induced reproductive toxicity in male mice transplacentally exposed to dibenz[def,p]chrysene
Day 2 - 50	Trainee	Gopi Srinivas Gadupudi	University of Iowa SRP	PCB126-induced disruption in gluconeogenesis and fatty acid oxidation precedes fatty liver in male rats
Day 2 - 51	Trainee	Irfan Ahmad	University of Kentucky SRP	Direct UV Excitation of PCBs for Coupled Fluorescence Detection
Day 2 - 52	Trainee	Jagila Wesley	University of Tennessee Health Science Center (LSU SRP)	The Effects of Air Pollution on Severity of Respiratory Illness
Day 2 - 53	Trainee	Jessica Cox	Columbia University SRP	Arsenic exposure and global %5mc and %5hmC in a population of Bangladeshi adults
Day 2 - 54	Trainee	Jessie Hoffman	University of Kentucky SRP	Table grape consumption reduces body fat accumulation, hepatic steatosis, and inflammation in mice fed a butter-rich diet: a potential nutritional approach for PCB protection

#	Classification	Name	Organization	Title
Day 2 - 55	Trainee	Jing Sun	Columbia University SRP	Use of Oxalic Acid for Mobilizing Arsenic from Contaminated Sediments and Decreasing Vulnerability to Reduction
Day 2 - 56	Trainee	Jing Sun	Columbia University SRP	Use of Reactive Transport Modeling for Understanding and Designing the Magnetite Based Arsenic Immobilization Strategy
Day 2 - 57	Trainee	Jonathan Toro	University of Puerto Rico (PROTECT SRP)	Hydraulic and Salt Tracer Studies to Assess Flow and Transport Regions in an Intermediate Karstified Lab-Scale Physical Model
Day 2 - 58	Trainee	Jordan Kozal	Duke University SRP	Mechanisms underlying transgenerational toxicity of benzo(a)pyrene in Danio rerio
Day 2 - 59	Trainee	Jun Yan	University of Tennessee	Cobamide lower bases control dechlorination rates and extents in organohalide-respiring Dehalococcoides mccartyi
Day 2 - 60	Trainee	Juyoun Kim	University of California - San Diego SRP	Role of TNF Signaling in de novo Lipid Synthesis Upon Hypernutrition
Day 2 - 61	Trainee	Komal Basra	Boston University SRP	Fishing bans and consumption advisories along New Bedford Harbor: A qualitative and quantitative analysis of their efficacy
Day 2 - 62	Trainee	Lauren Czaplicki	Duke University SRP	Scanning Two Eastern Creosote Sites for Potentially Useful Fungi
Day 2 - 63	Trainee	Lauren Redfern **(KC Donnelly recipient, 2015)**	Duke University SRP	PAH-exposure related differences in the sediment profiles and the prokaryotic gut communities of Atlantic killifish (Fundulus heteroclitus)
Day 2 - 64	Trainee	Leryn Reynolds	University of Kentucky SRP	Maternal Polychlorinated Biphenyl 126 Exposure Has Lasting Effects on Offspring
Day 2 - 65	Trainee	Marvic Carmona-De Jesus **(KC Donnelly recipient, 2015)**	University of Puerto Rico (PROTECT SRP)	The Resilience of DNAPLs in Karst Systems
Day 2 - 66	Trainee	Michael Murphy	Brown University SRP	Uncovering Historical Environmental Health Threats at Mashapaug Pond, Rhode Island
Day 2 - 67	Trainee	Mitchell Cheung	Fox Chase Cancer Center (UPenn SRP)	Animal models of asbestos-induced mesothelioma
Day 2 - 68	Trainee	Nerida De Jesus	University of Puerto Rico (PROTECT SRP)	Engagement and Empowerment of Communities on Water Quality Ramifications in Rural Areas: The Case of Non-PRASA Communities in Puerto Rico
Day 2 - 69	Trainee	Norma Torres	University of Puerto Rico (PROTECT SRP)	Influence of hydrogeological variables on the distribution of phthalate contamination in the karst groundwater systems of northern Puerto Rico
Day 2 - 70	Trainee	Olga Novikov	Boston University SRP	Regulation of AhR activation in triple negative breast cancer cells by tryptophan metabolites
Day 2 - 71	Trainee	Ralph Pietrofesa	University of Pennsylvania SRP	Flaxseed Lignans Enriched in Secoisolariciresinol Diglucoside (SDG) Inhibit Asbestos-Induced Peritoneal Inflammation in Mice
Day 2 - 72	Trainee	Rengyi Xu	University of Pennsylvania SRP	Comparison of Statistical Methods for Identifying Biomarkers of Asbestos Exposure and Mesothelioma
Day 2 - 73	Trainee	Rohit Bhandari	University of Kentucky SRP	The Protective Role of Polyphenol-Functionalized Nanoparticle Systems in Environmental Toxicant Exposure

#	Classification	Name	Organization	Title
Day 2 - 74	Trainee	Rosemarie de la Rosa	University of California - Berkeley SRP	Stressogens: An exposomic approach to assessing cumulative risk
Day 2 - 75	Trainee	Rui Shen	Brown University SRP	Indoor Contaminant Vapor Intrusion – Numerical Modeling and Field Data Analysis
Day 2 - 76	Trainee	Ryan Sun	Harvard School of Public Health	Testing for Gene-Environment Interaction under Environment Misspecification
Day 2 - 77	Trainee	Sanjay Mohanty	University of Pennsylvania SRP	Effect of weathering on toxicity and mobility of asbestos fibers in soil
Day 2 - 78	Trainee	Sebastian Hernandez	University of Kentucky SRP	Synthesis and Evaluation of nanoparticle membrane-supported systems for Degradation of Trichloroethylene
Day 2 - 79	Trainee	Shirin Hojabri	Northeastern University (PROTECT SRP)	Quantifying fate and transport of contaminant in surface water connected to karst aquifers in the northern region of Puerto Rico
Day 2 - 80	Trainee	Shohreh Farzan	Dartmouth College SRP	Maternal urinary arsenic and cardiometabolic outcomes in a New Hampshire pregnancy cohort
Day 2 - 81	Trainee	Thomas Hampton	Dartmouth College SRP	Arsenic Associated Antagonism In The Transcriptomic Response To Osmotic Shock In The Atlantic Killifish
Day 2 - 82	Trainee	Victoria Parker	University of Iowa SRP	Metabolites of Commonly Occurring Airborne Polychlorinated Biphenyls Inhibit Steroid Hormone Sulfation Catalyzed by Human Cytosolic Sulfotransferases
Day 2 - 83	Trainee	Vivien Taylor **(KC Donnelly recipient, 2014)**	Dartmouth College SRP	Influences of temperature and carbon loading on methylmercury bioavailability in estuaries
Day 2 - 84	Trainee	William Klaren **(KC Donnelly recipient, 2014)**	University of Iowa SRP	Progression of micronutrient alteration and hepatotoxicity following acute PCB126 exposure
Day 2 - 85	Trainee	Xia Guan	Louisiana State University SRP	Iron and Copper Synergy in the formation of PCDD/Fs
Day 2 - 86	Trainee	Yuanli Liu	University of California - San Diego SRP	Detection of Arsenic in Water by an Enzymatic catalysis System
Day 2 - 87	Trainee	Zhenyu Tian	University of North Carolina - Chapel Hill SRP	Towards identifying unknown genotoxic compounds in bioremediated soil using metabolomics-like methods and effect-directed analysis

Field Trip Information

All tours will leave on Friday 11/20 at 1pm.

Cueva Ventana Tour

This tour allows you to explore a cave in the northern karst region of Puerto Rico.

Located between the Arecibo and Utuado municipalities, Cueva Ventana is a limestone cave, part of the northern karst area of Puerto Rico. The cave is almost on the summit of an 800-foot high cliff. The tour consists of brisk hiking trail showing little caves on the side. Then, you enter to the main cave where you follow a path to the large opening view (approximately 35 feet in diameter) where you can see the Arecibo River Valley approximately 700 feet below.

Recommendations: wear sneakers or hiking type shoes, bring water and an extra shirt (in case you get muddy).

Duration of tour: 3.5 hours (1 hour of tour plus 2.5 hours round-trip travel)

San Juan Estuary Bay Water Tour

This is an opportunity to enjoy a boat ride in one of the most important estuaries on the island, learning about the ecosystem and the communities living near or within it.

The boat tour will travel through the San Jose, Corozos, and Torrecilla lagoons within the eastern part of the San Juan Bay Estuary. Appreciate the flora and fauna present in the area, as well as the environmental conditions of the estuary, while learning about the Caño Martin Peña community that surrounds the Estuary Bay.

Recommendations: bring water, sunscreen and mosquito repellent

Duration of tour: 3.5 hours (2.5 hours of tour plus 1 hour round-trip travel)

Caño Martin Peña Community Tour (Urban Waterway Pollution Tour)

This is a non-Superfund community directly affected by water pollution. The community must pursue actions to improve their surroundings, clean up the contaminated water and give support to redevelop a sustainable, and better ecosystem. Tour participants will be able to see the environmental conditions in which some marginalized communities live, their struggles, and environmental justice and community engagement at its core.

This is a walking tour through the community living at Caño Martin Peña. Stops at different points throughout the community will be held to show actual conditions of the area. The history of the contaminated site, the problems faced by the community, and their engagement to solve the problems will be explained. These low income communities have been working very hard to get governmental and non-governmental agencies to work together towards one goal: the dredging and restoration of the Caño Martín Peña, an urban channel. The local guide will help understand what these thousands of family have to struggle with every day, see the worst of the present condition and the hope of a better future.

Recommendations: wear sneakers, bring water, sunscreen and mosquito repellent

Duration of tour: 3 hours (2 hours of tour plus 1 hour round-trip travel)

Oral Abstracts

Session 1: SRP big data and data science applications

Developing a computational framework for identifying and classifying modes of actions of chemical carcinogenicity in liver using gene expression profiling

Amy Li[1,2], Francesca Mulas[2], Daniel Gusenleitner[1,2], Scott Auerbach[5], David Sherr[3,4], Stefano Monti[2]

[1] Department of Bioinformatics, Boston University

[2] Division of Computation Biomedicine, Boston University School of Medicine

[3]Department of Environmental Health, Boston University School of Public Health

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Despite the ever-increasing effort aimed at advancing cancer treatment research in recent years, cancer prevention, specifically in cancers attributable to chemical pollutants, remains a challenging field of research. Fewer than two percent of the more than 80,000 environmental, industrial and commercial chemicals have been tested for their ability to cause cancer. The limited number of chemicals tested is partially attributable to the high cost and time associated with the gold-standard approach for carcinogenicity testing, which relies on a 2-year rodent bioassay. This effort can be accelerated through the adoption of more cost-effective short-term chemical perturbation gene expression profiling assays paired with computational predictive models of chemical carcinogenicity. Here we analyze gene expression profiles of *in vivo* and *in vitro* models following short-term exposure to more than 300 chemicals properly stratified into known liver carcinogens and non-carcinogens. We focus on identifying gene biomarkers predictive of the adverse phenotypes of carcinogenicity and genotoxicity. In addition, we move beyond the identification of individual gene biomarkers, and we present a network-based analysis approach for the identification of gene modules or pathways associated with chemical-induced carcinogenesis, toward the elucidation of the molecular mechanisms underlying the adverse phenotype. Preliminary findings show that groups of chemicals with similar functions and carcinogenicity and genotoxicity profiles exhibit similar gene module networks. Furthermore, gene modules with significant gain or loss of connectivity in chemical group-specific networks compared to the control network are enriched for pathways that are relevant to the chemical group's mechanisms of action. This computational framework allows for subtyping the different modes of action of chemical carcinogenesis and may benefit research groups focused on studying individual Superfund toxicants by providing experimentally testable hypotheses.

Prenatal Exposure to Mercury and Arsenic and DNA Methylation in Umbilical Cord Blood (KC Donnelly Externship Award Recipient 2014)

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Mercury and arsenic are known developmental toxicants. Prenatal exposures are associated with adverse childhood health outcomes that could be in part mediated by epigenetic alterations and immune disruption. We investigated the association between prenatal mercury exposure, on both DNA methylation and white blood cell composition of cord blood, and evaluated

the interaction with prenatal arsenic exposure in 138 mother-infant pairs. Postpartum maternal toenail mercury and prenatal maternal urinary arsenic levels were measured using ICP-MS. DNA methylation and white blood cell composition estimates were assessed in cord blood using the Illumina Infinium HumanMethylation450 array. A doubling in toenail mercury concentration was associated with a 2.5% decrease (95% CI: 5.0%, 1.0%) in the estimated monocyte proportion. An increase of 3.5% (95% CI: 1.0, 7.0) in B-cell proportion was observed for females only. Among the top 100 CpGs associated with toenail mercury levels (ranked on *P*-value), there was a significant enrichment of loci located in North shore regions of CpG islands (P=0.049), and the majority of these loci were hypermethylated (85%). Among the top 100 CpGs for the interaction between arsenic and mercury, there was a greater than expected proportion of loci located in CpG islands (P=0.045) and in South shore regions (P=0.009) and all of these loci were hypermethylated. Individual loci were nominally associated with exposure but did not reach a Bonferroni threshold for statistical significance. This work supports the hypothesis that mercury may contribute to epigenetic variability and immune disruption, and suggests that prenatal exposure to mercury and arsenic may interact to impact the epigenome. As part of translating our research educational videos on arsenic and mercury exposure are available online from the Dartmouth SRP website.

The PROTECT Data Management and Modeling Core – Impacting Environmental Health through Data Management and Analytics

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The PROTECT Data Management and Modeling Core (DMMC) is responsible for the cleaning, security, curation and management of human subject, biological, chemical, survey and environmental data via an online, integrated and indexed database system. The fact that PROTECT is a geographically distributed Center, with partners in Massachusetts, Michigan, West Virginia and Puerto Rico just adds another layer of challenges to the effective management of data.

In this presentation we will provide an overview of the PROTECT DMMC, focusing on our successful strategy to develop effective tools to manage over 4 billion data points, representing a diversity of data from 5 different PROTECT projects/cores. We will discuss our work to adapt commercial tools for our framework that include EarthSoft's EQuIS, RedCap, Dropbox and PROTECT-developed utilities.

In the second half of this presentation we will focus on our ongoing efforts to develop appropriate data analytics as we move forward in our data collection campaign and address a number of project/core/program aims. We will cover our comprehensive data model used to integrate diverse datasets across the Center. We will also discuss some of the machine learning tools and approaches being developed that address the high dimensionality, mixed sparsity, and diverse data types (e.g., numerical, categorical, free-form text) under analysis in our Center.

Reporting Data to Participants in Biomonitoring and Household Exposure Studies: Its Use in the PROTECT Study (Puerto Rico Test Site to Explore Contamination Effects)

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Environmental exposure assessment in health studies and public health monitoring programs is shifting increasingly from testing for pollutants in air, soil, and water to personal exposure and biomonitoring methods that detect ever lower concentrations of a growing array of chemical contaminants -- in blood, urine, breast milk, umbilical cord blood, breathing zone air, house dust, hair, and hand wipes. Often, the health implications of these personal exposure measurements and the effectiveness of exposure reduction strategies are uncertain. As a result, personal exposure research raises ethical questions

about whether and how researchers should report individual results to study participants while adhering to and balancing the goals of ethical guidelines for human subjects research: specifically, respecting participants' autonomy, maximizing benefit, and avoiding harm. Scientists and IRBs must weigh the value of reporting results, which may inform and empower participants to change personal behaviors and contribute to community health policies, versus the potential for harm, for example, from misplaced worry, stigma, or ineffective action. They must also consider legal or financial issues that may arise, particularly when contaminants are detected in private spaces, such as a home.

Our Community Engagement Core's prior work in this field includes 2 studies of our own, re-interviews of participants in 8 other studies, and development of innovate print and digital report-back materials. We find that nearly all participants want to learn their results and do not experience psychological distress from that. Participants report being pleased to learn their personal exposures, have a high degree of understanding of the data, use the data for personal changes in consumption, and employ the data for social change in matters such as permitting and regulation. We find that report-back fulfills the promise of full and informed consent, and supports a democratic right-to-know process. Report-back benefits for researchers are increased research participation and retention, as well as greater public trust in the specific project and in science in general.

This background provides the model for reporting back data to participants in the PROTECT Study (Puerto Rico Test Site to Explore Contamination Effects), a cohort of more than 800 women that continues to add participants, in an attempt to find effects of contaminants on pre-term birth. Puerto Rico has a pre-term birth rate of 20%, 1.5 times that of the US, and there is exposure to contamination from a long history of pharmaceutical and other industries, with 150 contaminated sites that include 14 active Superfund sites on the island. Developing report-back materials and administering them to participants has been effective in unifying PROTECT's Human Subjects and Sampling Core that recruits participants and gather data from them, the research projects that use the human subjects data and gather additional environmental data, the Data Management and Modeling Core that helps assemble data for the report-back process, the Community Engagement Core that will conduct the report-back process, and the Research Translation Core that will disseminate findings and help other Superfund Research Program and other environmental health researchers to understand the importance of report-back and develop their own techniques. Report-back packages are presently being developed. When participants receive their data they will also be interviewed to learn their responses to and use of the material.

The Effects of Inter-Individual Variability on a Dose-Response Relationship: 2,3,7,8-tetracholorodibenzo-p-dioxin-induced Suppression of CD40L-activated Human Primary B Cells

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Understanding of the dose-response relationship (DRR) for any given chemical lies at the heart of risk assessment. Traditional toxicological studies have limitations with regard to their usefulness for risk assessment. Such studies usually rely on a small number of individuals, inbred mouse strains, or a single human or rodent cell line. The data must then be extrapolated to obtain useful information in managing risk associated with chemical exposures within the human population. Given these limitations, it is not surprising that little is known regarding the effect of inter-individual variability on DRRs in heterogeneous populations. A recent report from the National Research Council (NRC) suggests that, when accounting for inter-individual variation in responses, traditionally assumed nonlinear DRRs would better be explained with a linear model within the low-dose region. Notably, the NRC's hypothesis is not supported by adequate data. To address this knowledge gap, this project focused on assessing the DRR between 2,3,7,8-tetracholorodibenzo-*p*-dioxin (TCDD) exposure and immune suppression in a cohort of human donors. Human B cells were isolated from 50 unique donors and exposed to increasing levels of TCDD on a

logarithmic scale (0 through 30 nM TCDD). Two endpoints sensitive to increasing levels of TCDD were assessed: 1) number of IgM secreting B-cells and 2) amount of IgM secreted. Results indicate that increasing dose of TCDD has a significant suppressive effect on both endpoints (p value < 0.05). More importantly, model comparison results suggest the DRR in our dataset fits better to a non-linear statistical model as opposed to a linear model. Such results have potential to better inform risk-management decision-making for not only for TCDD, but for other receptor-mediated processes as well.

Research Translational Component: The results from the research will be translated to stakeholders (state/local/federal government, small and large business, and communities) by publication in peer-reviewed journals and presentations at professional conferences.

Session 2: Remediation

Geochemical Conditions Affect Corrinoid Pools that Control Dehaloccoides mccartyi Reductive Dechlorination Activity

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Chlorinated solvents such as tetrachloroethene (PCE) and trichloroethene (TCE) are toxic groundwater contaminants, probable human carcinogens, and TCE may contribute to the development of Parkinson's disease. Biodegradation plays a major role in the detoxification of chlorinated ethenes, and *Dehaloccocoides mccartyi* (*Dhc*) is the keystone bacterial group involved in complete reductive dechlorination of chlorinated ethenes to benign ethene. The key catalysts for breaking the carbon-chlorine bonds are reductive dehalogenases (RDases), which require a corrinoid cofactor. Remarkably, *Dhc* strains lack ability for *de novo* corrinoid biosynthesis. Although methanogens, acetogens, and other bacterial groups abundant in groundwater aquifers produce corrinoids, *Dhc* strains have specific requirements and not all corrinoid types support *Dhc* activity. Our work explores if the prevailing geochemical conditions and the associated microbiology determine the predominant type of corrinoid produced, and hence control over *Dhc* reductive dechlorination activity. To test this hypothesis, microcosms were established using sediment collected from a chlorinated solvent-contaminated site in Knoxville, TN. Sulfate-reducing, iron-reducing, nitrate-reducing, manganese (IV) oxide-reducing, methanogenic, acetogenic/fermentative, and organohalide-respiring conditions were established by amending the microcosms with sulfate, amorphous FeOOH, nitrate, MnO_2, lactate, lactate + 2-bromoethane sulfonate, and PCE, respectively. Sediment-free enrichment cultures were obtained after repeated transfers while maintaining the same redox conditions. Corrinoids were extracted and are being characterized using liquid chromatography and mass spectrometry-based techniques. *Dhc* pure cultures will be augmented with the different corrinoids to explore which types fulfill *Dhc*'s nutritional requirement and support reductive dechlorination activity. Improved understanding how geochemical conditions affect the corrinoid pool, and consequently *Dhc* reductive dechlorination activity will provide valuable information for refined decision-making and the implementation of efficient bioremediation treatment for achieving cleanup goals and protecting humans from exposure to harmful groundwater contaminants.

Effects of Activated Carbon Amendments on the Bioavailability and Methylation of Various Types of Inorganic Mercury

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One of the major challenges in evaluating the risk potential of soils and sediments contaminated with mercury is the lack of simple, reliable, environmentally-relevant methods to predict methylmercury formation. Methylmercury is more toxic than inorganic mercury and its accumulation in aquatic organisms, through dietary consumption of fish higher in the food chain, poses a health risk for humans. In anoxic soils and sediments, mercury is transformed to methylmercury via certain types of bacteria carrying mercury-methylating genes. The primary objectives of this study were to compare the bioavailability of different types of inorganic mercury that occur naturally in sediments and understand how carbon amendments might affect mercury methylation potential. A glutathione selective leaching test was used to indicate mercury bioavailability, because glutathione is produced by bacteria and has a high affinity for mercury. We hypothesized that glutathione-leached mercury will correlate with methylmercury production, and that the addition of activated carbon will decrease both mercury bioavailability and methylation rate.

The experiments involved sediment-water microcosms amended with four forms of isotopically-labeled inorganic mercury: dissolved Hg2+, Hg sorbed to iron sulfide (Hg-FeS), nanoparticulate and microparticulate HgS. Total mercury, methylmercury, glutathione-leachable mercury, abundance of bacterial mercury-methylating genes, and important water chemistry parameters in the microcosms were analyzed periodically over 14 days. The results show that total mercury leached from each form by glutathione decreased in the order Hg2+ ≅ nano-HgS > Hg-FeS > micro-HgS. The addition of activated carbon decreased both the leachable mercury concentration and methylmercury production.

This research has broader implications for assessing methylation potential of mercury-contaminated sites, as well as providing evidence for the efficacy of activated carbon as an in situ remediation method.

In situ electrochemically-induced oxidation of contaminants in groundwater: Pilot scale testing

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Electrochemical technologies for groundwater treatment use low-level direct current through electrodes in wells. Electrolysis allows manipulation of groundwater chemistry to create conditions favorable for either reduction or oxidation of the contaminants. We investigated electrochemical oxidation, as the transformation mechanism of contaminants, by generation of reactive oxygen species (hydroxyl radicals) through Fenton reaction using inert electrodes and in the presence of palladium catalyst. We developed pilot scale electrochemical set up to investigate the parameters affecting the *in situ* application of the technology. The pilot scale setup contained the electrochemical reactor connected to the submersible pump in the barrel (190 L) in order to optimize the reactor design, test the long term electrodes performance and test the pump performance. During 30 days of treatment the electrodes performance maintained the same; the deposits on the cathode occurred after this period and the cleaning was performed by electrode polarity reversal. In the similar set up, we tested the reactor performance to remove Reactive Blue 19 (model contaminant) and monitor pH, redox potential, dye concentration, total organic carbon and hydrogen peroxide formation during the treatment. The dye concentration decay measured by the changes of the absorbance at 591 nm, showed that 92% of dye was removed after 72 h of treatment. It was found that the main removal mechanism was oxidation via hydroxyl radicals formed through Fenton reaction. The further investigation is required to confirm and improve the reactor design and performance towards contaminants removal for submersible application.

Research Translation: The goal of the pilot scale optimization is to apply the technology in the field. We started establishing collaborations with consulting, engineering, construction, and operations companies to support and improve the implementation of the technology for the treatment of the selected contaminated sites.

Development of a Dual-Biofilm Reactive Barrier for Treatment of Chlorinated Benzenes at Anaerobic-Aerobic Interfaces in Groundwater and Sediments

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A USGS study in cooperation with EPA to evaluate bioremediation in a wetland at a Delaware Superfund site led to an ongoing collaborative NIEHS study to develop an innovative reactive barrier utilizing an anaerobic dechlorinating culture (WBC-2) and a native aerobic culture to simultaneously degrade a suite of chlorinated benzenes and benzene. In situ microcosms amended with 13C-labelled chlorobenzene, measurement of targeted microbial populations, and flow-through laboratory bioreactor tests indicated that both anaerobic and aerobic pathways naturally co-occurred in the wetland sediment and could be enhanced with WBC-2 addition. Thus, granular activated carbon (GAC) seeded with the two cultures and mixed with sand or directly into the wetland sediment is proposed to form a surface reactive barrier that not only sequesters the chlorinated benzenes to reduce their bioavailability, but also facilitates their transformation to innocuous end products over short groundwater flowpaths.

Study objectives include determining sorption/desorption interactions between biofilms, GAC, and site sediment and defining degradation processes and rates for the dual-biofilm barrier in laboratory and field tests. Genetic sequencing verified biofilm attachment to GAC with no loss of major microbial species. In GAC-biofilm microcosms, about 85 % of added chlorobenzenes were removed in 24 hours, and comparison to controls indicated removal by biodegradation in addition to sorption. Sorption isotherms determined for 1-3 substituted chlorobenzenes on GAC will be compared to those in the presence of biofilms and site water constituents. Initial column experiments are underway to evaluate the dual-biofilm barrier designs with site sediment and water. Use of the Delaware site and continued interaction with EPA allows direct application of research to an effective remediation design for protection of the surrounding environments and communities.

Arsenic and trichloroethene co-contamination effects on dechlorination activities of Dehalococcoides mccartyi-containing cultures

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Arsenic and trichloroethene (TCE) are two of the most widespread groundwater contaminants, but little is known about how co-contamination of these two constituents affects bioremediation strategies. These co-contaminants are especially an issue at sites where reductive dechlorination is promoted by the addition of fermentable substrates to generate a reducing environment, since reduced arsenic (As(III)) is more soluble than oxidized As(V). Here, we assess the effects of arsenic exposure on the TCE reducing activities of *Dehalococcoides mccartyi* strain 195 and *D. mccartyi*–containing microbial communities. Sodium arsenite (As(III)) and sodium arsenate (As(V)) at 50 µM, 100 µM, and 200 µM concentrations were amended to *D. mccartyi* 195 and *D. mccartyi*-containing communities with 65 µmol TCE, 5mM acetate, and vitamins, including 100 $\mu g L^{-1}$ cobalamin. When exposed to As(III), *D. mccartyi* 195 cells were immediately inhibited, exhibiting incomplete dechlorination of TCE. QPCR analysis indicated that while the control with no amended arsenic exhibited robust cell growth (36 x 10^7 cells/mL), concentrations of 100 µM and 200 µM As(III) completely inhibited cell growth (3.3 x 10^7 cells/mL and 5.3 x

10^7 cells/mL, respectively), and 50 µM As(III) significantly inhibited cell growth (8.5 x 10^7 cells/mL). When exposed to As(V), incomplete dechlorination was observed after 3 amendments of TCE. The observed results indicate that the presence of arsenic at TCE bioremediation sites can result in incomplete TCE reduction and inhibited *Dehalococcoides* cell growth. Similar experiments were conducted with *D. mccartyi*-containing enrichment cultures. Transcriptomic and metabolomic analyses are currently being conducted to determine changes in RNA and metabolite profiles resulting from arsenic co-contamination. Results from this study improve our understanding of potential inhibition of *D. mccartyi* caused by arsenic and can help us to develop mechanisms for improved bioremediation.

Research Translation: This work is directly applicable to Superfund Research Project stakeholders because the results of this research can be synthesized to suggest remediation strategies for TCE/arsenic co-contaminated sites. This work will be published in peer-reviewed journals routinely read by bioremediation professionals and regulators. In addition, the enrichment culture studied in this project was originally enriched from a superfund site in New Jersey, USA.

Session 3: Detection and Exposure

Detection of Biomarkers of Inflammation in newborns using filter paper blood samples from metabolic screening (KC Donnelly Externship Award Recipient 2014)

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As a 2014 KC Donnelly Externship Award recipient, I worked on a project to expand and develop the scope of PROTECT. Despite advances in access to maternal health care services and education, Puerto Rico (PR) maintains the highest rate of preterm birth (PTB) of all United States jurisdictions. This along with PR's high concentration of Superfund Sites makes the island a prime site for the study of environmental contaminants and their role in PTB. PROTECT conducts targeted and non-targeted analysis to aid in understanding cumulative risk factors for PTB. The methodology and sample collection characteristic of metabolic newborn screening holds particular promise regarding the understanding of environmental contaminants and their possible role in PTB. For instance, exposure to environmental contaminants like phthalates has been shown to trigger inflammation responses, and inflammation is one of the pathways that may pose a risk for PTB. Therefore, the development of an assay to detect biomarkers of inflammation in newborns that uses readily available dried blood spots (DBS) of newborn metabolic screening could significantly impact our understanding of the mechanisms of PTB. Mass spectrometry (MS) and Luminex were used to detect the inflammatory biomarker C-reactive protein (CRP). CRP is a proven biomarker for cardiovascular disease that has also been shown to increase as a result of environmental exposures. Our results show Luminex can be used to detect CRP in DBS in a comparable way to traditional detection in serum. Additionally, preliminary results show a way towards the detection of inflammatory biomarkers in DBS through MS, in turn highlighting the versatility of newborn screening as a means of understanding PTB mechanisms and risk factors.

Coupling biotransformation of 2,4-dinitroanisole (DNAN) in anaerobic soil solutions to a multidimensional toxicity assay using zebrafish embryos (KC Donnelly Externship Award Recipient 2014)

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This work was performed thanks to the 2014 KC Donnelly Externship award. 2,4-dinitroanisole (DNAN) is an insensitive munitions compound, developed to replace conventional munitions such as 2,4,6-trinitrotoluene (TNT), because they are more stable and safer to handle. Although DNAN is manufactured and used, there is little information about the environmental fate and toxicity of this nitroaromatic compound. We have characterized the relative abundance of products from DNAN (bio) transformation in anaerobic submerged soil microcosms using liquid chromatography quadrupole time-of-flight mass spectrometry in order to determine the transformation pathway and fate of DNAN in anaerobic soil environments. DNAN was shown to be reduced to aromatic amines, and during biotransformation coupling reactions formed azo dimers and oligomers. A library of these compounds and best available surrogates were tested for acute toxicity in a multipoint *in-vivo* developmental and behavioral toxicity zebrafish (*Danio rerio*) embryo model. DAAN (640 µM) affected swimming motion in the behavioral photoresponse assay, and dimer L caused significant developmental toxicity effects at six endpoints for concentrations as low as 6.4-64 µM. Moreover, toxicity changes of the aqueous fraction of DNAN degradation products at different stages of biotransformation were assessed to provide a simulation of environmental exposure of bioavailable products in anaerobic soil environments.

Maternal genotype for arsenic (+3 oxidation state)-methyltransferase AS3MT is associated with arsenic metabolism and newborn birth outcomes with interactions between fetal sex

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Arsenic (+3 oxidation state) methyltransferase (*AS3MT*) is the key enzyme in the metabolism of inorganic arsenic (iAs). Polymorphisms of *AS3MT* have been shown to influence adverse effects associated with exposure to iAs in adults, but little is known about its role in iAs metabolism in pregnant women and newborn birth outcomes. The relationship between seven single nucleotide polymorphisms (SNP) of *AS3MT* and concentrations of inorganic iAs and its methylated arsenic metabolites were assessed in mother-baby pairs of the Biomarkers of Exposure to ARsenic (BEAR) cohort in Gomez Palacio, Mexico. Six of seven SNPs were associated with urinary concentrations of iAs metabolites, while one was associated with birth outcomes/measures. When stratified by the infant sex, mothers who were pregnant with males showed a significant correlation between maternal SNPs of *AS3MT* and both maternal arsenic metabolite concentrations and birth outcomes. These data highlight the role of arsenic metabolism in human health outcomes.

Exposure Assessment of Three Dimensional (3D) Printer Emissions

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The use of the three dimensional (3D) printer is a rapidly emerging technology that has greatly advanced since its creation in the 1980's. Unfortunately, research on exposures associated with 3D printing and potential health effects is scarce. This study assessed airborne contaminants generated from 3D printers by simultaneously evaluating fine particle (FP), ultrafine particle (UFP), and volatile organic compound (VOC) exposures. A standardized cube design was printed on one stereolithography (SLA) printer, two fused deposition modeling (FDM) printers, and one multijet modeling (MJM) printer to represent commonly used printer technologies. A photopolymer resin was used for SLA, acrylonitrile butadiene styrene and polylactic acid used for FDM, and an acrylic photopolymer utilized for MJM printing. One background sample (no printer use) and one printing sample were collected for each printer and compared using the Wilcoxon Rank-Sum test. Statistically significantly elevated FP and VOC levels were found for all four printers. The mean background FP level was 3.3 µg/m3, while mean concentrations of 4.6 µg/m3, 5.5 µg/m3, and 4.4 µg/m3 were measured for the SLA, FDM, and MJM printers respectively. The average printing cycle resulted in 1.4 (SLA), 2.1 (FDMs), and 4.5 (MJM) times greater VOC concentration levels than the background. Additionally, statistically significantly elevated UFP levels were measured for FDM printers (average range of 3531 – 6961 UFP counts per cm3). Our data showing that 3D printers can be significant sources of particle and VOC exposures has been translated to the scientific and lay audiences through a student poster presentation at the 2015 American Industrial Hygiene Conference, and the findings were also featured in the SRP e-Posted Notes Issue 138 (July 6, 2015).

Proof of Concept: Using Passive Sampling Polymers to Monitor Mercury and Methyl Mercury in Estuarine Waters (KC Donnelly Externship Award Recipient 2014)

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Passive sampling techniques allow *in situ* monitoring of contaminants in estuaries by mimicking the uptake of contaminants into fish, which are a major pathway of human exposure. Polymer strips have been widely applied as passive sampling materials for monitoring fat-soluble contaminants. By this technique, polymer films are deployed in the water column over several weeks, until a steady state between contaminant concentrations in the water column and the sampler are reached. Metal contaminants tend not to be fat soluble, but are taken up into the foodweb in their unbound, ionic form; as such, gel-based devices which bind metal ions are used as *in situ* monitors for metals. Mercury is a unique metal, having both mildly lipophilic and ionic properties. While diffusive gel samplers show promise for *in situ* mercury monitoring, preparing gel phases and assembling the devices is expensive and their interpretation can be complicated. In this study, we evaluated the use of polymer-based passive samplers as *in situ* monitors for mercury and its more toxic form, methylmercury. Preliminary studies evaluated the accumulation of mercury species into five polymers; all polymers were found to accumulate mercury linearly over time, whereas polymers which contained sulfur were also found to efficiently take up methylmercury. Significant partitioning of methylmercury to polymers suggests these materials may be used as passive samplers, but further testing is required to determine whether accumulation of mercury into these samplers provides a proxy for uptake into marine organisms. Preliminary field tests of these devices are being conducted at the Penobscot Superfund site, and findings of this research are being communicated to Superfund site managers.

Session 4: Advances in Environmental Biomedical Sciences

Effects of arsenic on macrophages and immune function

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In an early-life arsenic exposed population in Chile, our research group observed *the* greatest increases in young adult mortality ever associated with an early-life environmental exposure. Mortality increased ~7-fold for lung cancer; ~18-fold for bladder cancer and bronchiectasis; and notably ~2-fold for tuberculosis, up to 40 years after arsenic exposures have ended. However, the mechanisms for these prolonged effects remain unknown. With millions exposed to arsenic worldwide and with more tuberculosis today than at any time, the global health burden of arsenic may be much greater than anticipated. We hypothesize that early-life arsenic exposure permanently impacts immune development and increases the risks of various immune-related (infectious) diseases later in life. Here we focus on macrophages, immune cells known to influence the development of both tumors and tuberculosis. We assessed the effects of different doses of various arsenic compounds, both during and after the development of cultured mouse macrophages. Our results revealed significant dose and time-dependent changes in the expression of various signaling proteins (cytokines/ chemokines), in both resting and activated macrophages. Of interest are changes in the secretion of cytokines/ chemokines critical for the immune response against tuberculosis. Additionally, we found that arsenic caused dose- and time-dependent changes in the expression of signaling metabolites (lipids), several known to play a role in tumor development and the immune response against tuberculosis. Our preliminary data with human macrophages suggests that arsenic treatment also influences the capacity of macrophages to control *Mycobacterium tuberculosis* infections. We are currently investigating how arsenic-induced alterations in macrophages influence tumor growth and *Mycobacterium tuberculosis* infections in culture and *in vivo*. Finally, we will validate our findings in macrophages from early-life arsenic exposed individuals.

Deletion of fibrocytes in mice attenuates CCl_4-induced liver fibrosis.

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BACKGROUND: Bone marrow (BM) fibrocytes, designated as $CD45^+$ and Collagen type I^+ (Col1a1) cells, are recruited to the injured liver, however, their role in liver fibrosis remains unclear. **AIM:** To determine the role of fibrocytes in pathogenesis of liver fibrosis. **METHODS:1)**The contribution of fibrocytes to liver fibrosis was studied in BM chimeric mice devoid of fibrocytes (ΔFibrocyte mice), in which fibrocyte death was induced by expression of DTA. Specifically, tamoxifen-inducible $Col1a1^{ER\text{-}Cre}$ mice were crossed with $Rosa26^{flox\text{-}Stop\text{-}flox\text{-}YFP}$ reporter mice ± $Rosa26^{flox\text{-}Stop\text{-}flox\text{-}DTA}$ mice, and used as donors for BM transplantation into wt mice to generate wt and ΔFibrocyte mice.**2)**The role of Col1a1 in regulation of fibrocyte function was studied in BM chimeric **$Col1a1^{5'SL\text{-}/\text{-}}$-into-wt mice**, in which mutation of 5'stemloop ($5'SL^{-/-}$ mice) prevented proper Col1a1 translation in fibrocytes. **RESEARCH TRANSLATION:1)**All mice were subjected to CCl_4 for 6w. The therapeutic potential of Serum Amyloid P (**SAP**), a natural inhibitor of fibrocytes, was tested.**2)**For humans, the role of fibrocytes as prognostic biomarker was evaluated in patients with liver cirrhosis. **RESULTS**:Fate mapping revealed that 20% of fibrocytes become myofibroblasts, while 80% become myeloid cells, which is a significant source of TGFβ1,and IL-1β1 in CCl_4 treated mice. Deletion of fibrocytes/progeny in ΔFibrocyte mice resulted in inhibition of CCl_4 induced liver fibrosis. Fibrocyte ablation also resulted in suppression of pro-inflammatory macrophages (M1) and promote proliferation of anti-inflammatory macrophages(M2), suggesting that fibrocytes regulate M1/M2 macrophage polarization. Liver fibrosis was reduced in $Col1a1^{5'SL\text{-}/\text{-}}$into-wt mice, and was associated with impaired proliferation of BM fibrocytes. In support, the number of

circulating fibrocytes in patients correlated with the stage of liver fibrosis, and with low levels of serum SAP. Administration of SAP ameliorated liver fibrosis in CCl_4-wt mice.

The role of the intestine in dioxin-mediated fatty liver disease in mice

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2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) is a ubiquitous environmental contaminant that elicits fat accumulation in the liver, inflammation, and progression to more severe liver diseases. To investigate intestine – liver interactions that contribute to TCDD-elicited fatty liver disease, we examined the dose-dependent effects of TCDD (0.01 – 30 μg/kg) on intestinal gene expression in mice treated every 4 days for 28 days. Whole genome microarray analysis of the intestinal lining identified 439 differentially expressed genes (DEGs; |fold change| ≥ 1.5, P1(t) ≥ 0.999) across one or more doses, many related to fat processing and the immune response. Specifically, DEGs were associated with fat digestion, fatty acid/cholesterol absorption and transport, and vitamin A metabolism, consistent with increased fat accumulation in the liver. Moreover, several immune cell markers were repressed, coincident with decreased populations of immune cells in the intestinal wall, suggesting migration of immune cells out of the intestine. Reciprocal increases in immune-related gene expression and immune cell populations in the liver lead us to speculate that these cells may be migrating from the intestine to the liver. Furthermore, TCDD treatment increased permeability of the stomach and colon 2.4- and 2.0-fold, respectively, which could promote the translocation of bacteria across the intestinal wall. TCDD also prolonged the excretion of feces from 2.5 to 4.1 hours without affecting daily food consumption, suggesting decreased gut motility which may lead to bacterial overgrowth in the intestine. Collectively, these results demonstrate that TCDD elicits changes that support fat accumulation in the liver, immune cell migration, and the progression to more severe liver diseases.

Spatial distribution of hepatic metals following PCB126 exposure (KC Donnelly Externship Award Recipient 2014)

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Several animal studies have shown that exposure to the environmental pollutant and AhR agonist 3,3',4,4',5-pentachlorobiphenyl (PCB126) causes alterations in hepatic metals and micronutrients, in particular: copper, zinc, and manganese. Previous investigations into these effects used acid digested liver tissue employing inductively coupled plasma mass spectrometry (ICP-MS) or a similar analytical techniques. Although informative, these techniques lack the spatial distribution of the metals, within the tissue. Investigations have shown that the hepatotoxicity of PCB126 is particularly focused on specific areas. This suggests that the greatest degree of metal disruption may be in the region nearest to this localized hepatic injury. X-ray fluorescence microscopy (XFM) is a powerful technique that allows for the spatial distribution of metals to be ascertained on a tissue/cellular level. Male, 75-100 g Sprague-Dawley rats were fed a modified AIN-93G diet for three weeks, to reach micronutrient equilibrium. The rats were then given a single intraperitoneal injection of either tocopherol-stripped soy oil (5mL/kg), 1 umol/kg PCB126 or 5 umol/kg PCB126 in soy oil. After two weeks of exposure, the animals were sacrificed and organs collected. Unstained, formalin fixed, paraffin embedded, sections were placed on silicon-nitride grids and dried in a desiccator. XFM was carried out at the Advanced Photon Source at Argonne National Laboratory.

Metal gradients between the central vein and portal triad were seen, especially with copper and iron. Interestingly, clusters of high concentrations of zinc were seen which appear to be outside the hepatocytes. Differences were seen in animals exposed to PCB126. XFM proves to be a dynamic tool for exploring the micronutrient disruption within a tissue and how toxicants, in particular PCB126, can disrupt this distribution. (P42 ES013661)

Biological and Environmental Interactions of Emerging Two-Dimensional Nanomaterials

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We are witnessing a revolution in materials science centered on the creation and use of two-dimensional (2D) sheet-like materials of atomic-scale thickness. In addition to the discovery of graphene in 2004, the 2D material family now includes a wide range of inorganic materials that include metal oxides, sulfides, selenides, and layered double hydroxides. Very little is known about the potential implications of these emerging 2D nanomaterials on human health or the natural environment. Because of the great chemical diversity in 2D materials, traditional toxicity testing methods will not be suitable for risk management or safe design across the entire material family on a time scale that keeps pace with material development. Toxicity testing and risk management is further complicated by various material transformations that may happen in biological media. Here we evaluate simple theoretical models to screen and predict transformation and biological reactivity of 2D nanomaterials based on their fundamental chemical properties. The oxidation and reduction potentials of 2D nanomaterials are calculated and used to predict the stability of 2D nanomaterials in relevant aqueous solution. We also use a recently developed band-structure based framework to identify 2D materials that are likely to have pro-oxidant activity in biological systems. Finally, we use MoS_2 as an example 2D material to illustrate how biological transformations and reactivity can be studied, and suggestions are offered for grouping 2D materials into chemical classes for prioritization in risk management.

Session 5: Sustainable Communities

Development of a Fish Liver Microtissue Model to Characterize the Toxicity of Aromatic Hydrocarbons and Nanoparticle-Based Dispersants.

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Engineered nanoparticles can assemble at water-oil interfaces to stabilize oil droplets into an emulsion, and are under development for use as dispersants following oil spills. This project focuses on the potential impacts of environmental exposures to these nanoparticles on aquatic organisms. Using a fish liver cell line, PLHC-1, in a three-dimensional (3D), scaffold-free microtissue model, we are examining the environmental impacts of co-exposure to polycyclic aromatic hydrocarbons and surface-engineered carbon black as a model nanoparticle dispersant. 3D cultures can provide the benefits of tissue-like cell-cell interactions and the opportunity for longer term cultures, but also present challenges associated with imaging, maintaining viability, and adapting two dimensional assays to 3D systems. For this novel fish liver microtissue model, assays to determine the toxicity of aromatic hydrocarbons and nanoparticles, including biomarkers of stress and xenobiotic metabolism, were optimized in monolayer and then adapted for use in 3D with toxicants. To characterize the fish liver spheroids, changes in viability, differentiation, and response to toxicants were measured during long term cultures of spheroids.

Research Translation Component: This model is applicable for testing real-world contaminant mixtures, and is being developed as a sensitive screening assay for low-level chronic or cumulative exposures. In collaboration with sociology

graduate student Michael Murphy in the Community Engagement Core, we are developing this microtissue model to evaluate adverse environmental impacts of the Gorham/Textron Brownfield site near Mashapaug Pond in Providence, RI.

The Meaning of a Superfund Site to an Affected Community

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Community knowledge, attitudes and perceptions of environmental health issues are often determined by survey instruments designed by investigators. However these are necessarily subject to the predetermined constructs of the investigators and may lead to a masked representation of the priorities, or the range of interests, concerns, or desires of the impacted communities.

We studied community members around the Ambler PA, superfund sites whose principal hazard is asbestos-containing waste. To determine the "meaning " of the sites to the community we used an inductive methodology; we collected 25 in –depth and broad ranging life histories with individuals in Ambler from diverse backgrounds, professions, ethnic backgrounds and degree of civic involvement. The life histories were then analyzed by two different investigators, one from the field of Environmental Health Science, and one from cultural Anthropology. The life histories contained nine domains: time, space, activities (especially related to asbestos exposure), perceptions of government agencies and \or superfund processes, community input and the Community Advisory Group (CAG), attitudes to asbestos and risk, the optimum remediation solution, research role and needs, and lessons for other communities. The findings were amalgamated to produce a final product.

In many domains there was a surprising degree of homogeneity in community views and experiences. In general there was a high degree of environmental health literacy. However there were a few domains including attitudes to risk and optimum remediation where there were varied and even extremely disparate views. We were able to develop some novel insights into community perceptions. There were also insights into ways governmental agencies lost trust in their relationships with communities. The findings suggest new directions are needed for risk communication.

Research Translation Component: Application of these findings is central to our CEC's present and planned involvement with the community. We have been undertaking activities to help the community understand and deal with areas of conflict, by helping in the appreciation of view of other stakeholders, including through the use of multimedia.

Findings are being shared with regulatory agencies and disseminated to the environmental health sciences community. Further research will focus on gaining a clearer understanding of the factors important in developing community perceptions and community decision making.

Assessing the sewer gas to indoor air pathway at hazardous waste sites

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Nationally, the challenges that aging sewer lines pose for modern cities is widely acknowledged. An emerging issue related to deteriorated sewer systems involves the transport of chemicals from hazardous waste sites. Once contaminated water (and vapors) from hazardous waste sites enter deteriorated sewer lines, sewers can serve as preferential pathways transporting contaminated water and vapors long distances. When the chemicals volatilize within the sewer, the vapor-phase chemicals can be transported into indoor spaces. This process, known as the "*sewer gas to indoor air pathway,"* is gaining national

attention, and was specifically highlighted in the USEPA Finalized Vapor Intrusion Guidance, which was released in June 2015. This presentation will summarize the recent research results of an inter-collaboration of SRPs (Boston University, Brown University and the University of Kentucky) that helped identify the sewer-gas to indoor-air pathway (results were cited in the USEPA guidance, Pennell *et al* 2013). In addition, the presentation will discuss current research being led by the University of Kentucky in collaboration with USEPA to develop assessment approaches to evaluate the sewer-gas to indoor air pathway. This research uses a multi-pronged approach including GIS mapping, computational modeling and field sampling to develop improved assessment methods.

Pennell, K.G., Scammell, M.K., McClean, M.D., Ames, J., Weldon, B., Friguglietti, L., Suuberg, E. M., Shen, R., Indeglia, P.A., Heiger-Bernays, W. J. (2013) "Sewer Gas: An Indoor Air Source of PCE to Consider During Vapor Intrusion Investigations." *Ground Water Monitoring and Remediation*, 33(3): 119-126.

Overcoming the Barriers to Testing and Treating Arsenic in Private Well Water in New Hampshire

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In New Hampshire, more than 40 percent of the population depends on private wells for their water supply. It is estimated that 1 in 5 of these wells contain arsenic levels above EPA's maximum contaminant level (MCL) for public water. In spite of this worrisome situation, testing and treating well water for arsenic is not a priority for many residents. Over the past two years, the Dartmouth College Toxic Metals Superfund Research Program, in partnership with the NH Department of Environmental Services, has conducted research focused the motivation and barriers for household water testing. Year one included four focus groups, a statewide survey, and an exposure risk assessment. Results indicate that almost 40% of residents living in towns with a higher risk of high arsenic levels have not tested. Those who did test tended to be those who have discussed water quality with a friend or family member or have previously received information about arsenic testing. However, of those who decided to treat their water, almost half believe their treatment systems remove arsenic when they do not. Those who have the correct treatment system in place are those who worked with a water treatment professional. Year two of our project focused on creation and utilization of community-vetted communication materials and the planning and implementation of three distinct community interventions in six towns. Preliminary results for year two indicate the need for consistent, clear messaging regarding arsenic in well water, and that the more invested community partners are in the process, the more successful the intervention. We conclude by identifying proactive steps communities can take themselves to encourage well water testing and treatment.

Identifying intermediary pulmonary effects among Bangladeshi adolescents with known life stage water arsenic exposure

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Arsenic exposure can detrimentally affect the respiratory system throughout the lifespan. Here we present an update on our ongoing study examining the respiratory health effects of early-life arsenic exposure among Bangladeshi adolescents. Eligible adolescents, with well-characterized arsenic exposure from conception to present day, have been born to mothers who have

continuously participated in the Health Effects of Arsenic Longitudinal Study (HEALS) since 2000. We describe our novel study population and provide available demographics on enrolled participants. We present preliminary findings on the relationship between water arsenic (wAs) exposure and lung function (spirometry) among adolescents. Finally, we explore potential modes of action, by investigating whether wAs exposure is associated with novel airway-specific markers of increased oxidative stress (8-isoprostane) and inflammation (pH), via exhaled breath condensate; and by describing how air pollution (urinary 1-OHP) and As may influence possible pulmonary function deficits.

We intend to communicate these results to the Bangladeshi community and US policy makers. Non-malignant respiratory effects is one of the health endpoints of concern the EPA is appraising in their upcoming toxicological assessment on inorganic arsenic. Further, of the eligible study participants, 264 have lifetime wAs exposure below both the EPA MCL for exposure (10ppb). This study has a considerable number of potential participants who are exposed to arsenic levels relevant to the US population and we anticipate sharing our results with the appropriate stakeholders. We also plan to communicate our results in Bangladesh. Understanding how prenatal arsenic exposure affects intermediary pulmonary endpoints in adolescence not only may help to determine if and how arsenic exposure causes the development of later-life diseases, but also may provide avenues for early intervention.

Session 6: Mixtures

Polybrominated diphenylethers (PBDEs) in ambient air samples at the electronic waste (e-waste) reclamation site

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Polybrominated diphenylethers (PBDEs) were used as flame retardants in various building materials, plastic and other polymers, airplanes, electronics etc. All or some of their congeners have been already banned in many countries, due to their extreme health effects on human beings via bioaccumulation. In this study, we are focusing on the dangers related to e-wastes as a source of emission of PBDEs in ambient air during reclamation.

The ambient air particulate matter samples were collected by our collaborators from Chulabhorn Research Institute in Bangkok, Thailand. Results showed the presence of various PBDE homologues from Tri, Tetra, Penta, Hexa, and Penta PBDEs on both PM2.5 and PM10 samples. The comparison of samples from e-waste reclamation site and control side indicated elevated levels of PBDE at e-waste site. Interestingly, a shift in the congener pattern was observed with lower brominated PBDEs being more prevalent on those samples. The total Penta PBDE concentration is about double on e-waste site PM2.5 compared to control site samples. For PM10, no clear differences are present for lower brominated PBDE, but penta-hepta congeners are at higher concentrations at e-waste sites. Overall a clear trend can be observed indicating a debromination of PBDEs to more toxic congeners during reclamation process. At the same time PBDEs are being translocated from treated materials to ambient air PM.

This work indicates potential hazards related to the reclamation of e-wastes and remediation of sites containing PBDEs. In particular, thermal treatment methods can lead to congener transformation and increased emissions of toxic PBDEs.

Flame Retardants in Housedust Antagonize Human TRβ Signaling

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Flame retardants (FRs) are applied to a variety of consumer and household products to delay the spread and onset of fire. They can leach from products over time due to normal weathering and aging and accumulate in household dust. Inadvertent dust ingestion is a major route of exposure to PBDEs, especially for young children. Some FRs, particularly polybrominated diphenyl ethers (PBDEs) are known to disrupt normal thyroid regulation, possibly due to structural similarities with native thyroid hormones. It has been hypothesized that PBDEs compete with native thyroid hormones for binding to targets, including the thyroid hormone receptors (TRα and TRβ). However, the ability of PBDEs to disrupt TR activity is not well understood. In this study we investigated the ability of FR mixtures present in household dust to disrupt TRβ signaling. House dust samples were collected from study participants and were extracted and analyzed for 28 FRs, including 22 PBDEs, two brominated flame retardants, and four organophosphate flame retardants. A cell-based reporter assay for TRβ was utilized to characterize the antagonist activity of each extract and of individual FRs. Antagonism was observed in 23 out of 52 samples, and ranged from 18-80% of the T3 EC_{50} control. Preliminary correlation analyses conducted between individual FR concentrations measured in dust and inhibition levels observed in dust extracts suggest that BDE-209 may be responsible for a majority of the observed antagonism ($p < 0.001$, $r = 0.72$). A comparable range of antagonism (19-61%) was observed when BDE-209 was run individually. Our results indicate that household dust may be an important source of contaminants that antagonize TRβ signaling and further research is essential to identify the molecular mechanisms involved.

Generalized Concentration Addition modeling of PPARγ activation by phthalate compounds in the ToxCast data set

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Current high throughput initiatives such as EPA's ToxCast and Tox21 address the problem of testing the toxic potential of thousands of individual environmental compounds. However, predicting toxicity of chemical mixtures represents a large-scale problem in need of practical analysis tools. In the case of endocrine disrupting chemicals, low dose co-exposures have the potential for significant, additive effects at the molecular level. We previously developed a Generalized Concentration Addition (GCA) model to predict additive mixture effects of nuclear receptor agonists with varying efficacies and potencies. In the current study, we identified phthalate compounds in the ToxCast phase II data set that activate human PPARγ, a primary target of adipogenic endocrine disrupting compounds. Using a PPRE-dependent luciferase reporter assay similar to assays used in ToxCast, we generated empirical data of human PPARγ activation by a binary combination of the partial agonist mono-2-ethylhexyl phthalate and the PPARγ reference compound (and full agonist) rosiglitazone. We constructed a GCA response surface from the individual chemical dose-response data and show it to be a reasonable approximation of the experimental data. Then, we applied the GCA approach to model a complex mixture of minimally active doses of five phthalates (including parent compounds and metabolites), which we tested against experimental mixture data. To explore the feasibility of modeling mixture responses using existing high throughput data, we compared our predicted and empirical results to simulated results generated with model parameters obtained through ToxCast. Our results support the use of Generalized Concentration Addition for modeling nuclear receptor activation by complex mixtures, and we identify advantages and caveats to the use of component-based additive models by regulatory agencies and risk assessors.

Statistical modeling approaches for mixtures of environmental toxins

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Traditionally, due to multiple experimental and statistical challenges, the studies of molecular toxicology and risk assessment have focused primarily on dose response relationships of a single toxicant or a binary mixture. However, real world human exposures are complicated and encompass mixtures of chlorinated persistent organic pollutants, metals, and other poorly defined stressors. To more effectively determine the risk related to environmental pollutants we have developed a full factorial experimental design coupled with a statistical model capable of identifying interactions between multiple toxicants. Polychlorinated biphenyls, lipid soluble persistent organic pollutants, were manufactured as complex mixtures and are now found at measurable concentrations in the majority of Americans. The ubiquity of PCBs in the environment makes these chemicals prime candidates for multiple exposure/mixture analyses. To validate this statistical model/approach, vascular endothelial cells were exposed to tertiary, binary, and single congener combinations of environmentally and physiologically relevant concentrations of polychlorinated biphenyl (PCBs). Inflammatory markers were examined as a surrogate for PCB toxicity. The congeners used included PCB 118, PCB 126, and PCB 153, which represent the three major categories of PCBs (mixed congener, coplanar, and non-coplanar, respectively). The experimental design and statistical approaches used within this study may prove to be effective tools in determining interactions between environmentally relevant mixtures and biomarkers of disease risk. Moreover, a better understanding of mixture statistics in regards to environmental health may result in more effective risk assessment and communication.

Research Translation: This work may uncover previously unknown interactions between environmental pollutants which can be used to create a more specific risk assessment. This will allow stakeholders to be more informed about the effects of their individual exposures.

Subchronic Inhalation Toxicity Study of a Complex PCB Mixture Representing Urban Air

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A lack of rigorous inhalation studies has limited the assessment of health risks of inhalation exposure to polychlorinated biphenyls (PCB). Contemporaneous PCB inhalation exposures were conducted using both whole-body and nose-only exposure methods. Sprague-Dawley female rats were exposed to vapor-phase PCBs (533 ± 93 μg/m^3, 4 h/day, 6 days/week, for 4 weeks) generated from PCB11-supplemented Chicago Air Mixture resembling the Chicago airshed and necropsied after the final exposure. Congener-specific analysis showed higher total PCBs (∑PCBs) in the lungs of nose-only exposed animals than the whole-body exposed. PCB 28/31 and higher-chlorinated congeners dominated PCB profiles in five tissue types in both groups reflecting rapid metabolism of most lower-chlorinated PCBs and slower metabolism of higher-chlorinated PCBs. No toxicity was evident from outcomes such as metabolic enzyme expression, glutathione, or histopathology. However, diminished weight gain and reduced plasma total thyroxine levels were found in both groups compared with controls. Hepatic lipid peroxidation was also elevated in the nose-only group. Research Translation: The US EPA is in the process of revising the risk assessment for PCBs and hopes to include an inhalation reference concentration. Our study along with our prior work provides a lowest observed effect level for inhalation toxicity. Accounting for the somewhat higher dose levels for rats exposed nose-only, similar biological responses were observed between the nose-only and whole-body exposure regimens. This work provides needed data to inform future inhalation toxicology studies for human health risk assessment.

Day 1 Poster Abstracts

(1-1) Environmental exposures as a determinant of diet and nutrition based interventions for cardiovascular disease risk reduction.

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Cardiovascular disease is largely caused by genetic (heritable) and environmental factors. Understanding how these factors intersect to determine individual disease risk is a critical challenge in developing personalized approaches to the diagnosis and treatment of the disease. Appalachian Kentucky has an unusually high incidence of cardiovascular disease which is associated with a similarly high prevalence of cardiovascular disease risk factors. These include so called "lifestyle-dependent" determinants of cardiovascular disease risk- smoking, obesity and physical inactivity and their co morbid conditions of diabetes and hypertension. Increased cardiovascular disease risk in Appalachian individuals is likely underpinned by genetic determinants and may be modified by exposures to environmental pollutants. Interventions that emphasize dietary modifications, for example by reducing the consumption of saturated fats and increasing consumption of grains fruits and vegetables are effective at mitigating cardiovascular disease risk. However the field of nutritional epidemiology is currently hindered by a lack of reliable quantitative methods to monitor diet composition, consumption and compliance. Development of suitable methods to identify molecular profiles and biomarkers of food and nutrient intake might identify bioactive constituents of these that are responsible for health benefits, enable monitoring of diet composition and study compliance and illuminate the basis for differences in responses to these cardiovascular disease risk reducing interventions between individuals. We will report data from a study measuring serum levels of environmental pollutants (polychlorinated biphenyls) and diet-derived biomarkers or potentially protective mediators in individuals undergoing dietary interventions for cardiovascular disease risk reduction.

(1-2) Occurrence of unintentional head injuries following prenatal and early childhood exposure to tetrachloroethylene (PCE)-contaminated drinking water

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Tetrachloroethylene (PCE) is a well-recognized neurotoxicant in adults. Now there is emerging evidence that exposure early in life has neurological consequences such as diminished visuospatial function, impaired motor skill, attention deficits[1] and an increase in risk-taking behaviors.[2] Thus, early life exposure could plausibly increase the likelihood of unintentional injuries. We investigated whether prenatal and early childhood exposure to PCE-contaminated drinking water influenced subsequent occurrence of unintentional head injuries. A total of 1,372 participants in a retrospective cohort study were studied, including 828 with early life exposure to PCE from the vinyl-liner of water distribution pipes in Cape Cod, Massachusetts. Participants provided information on unintentional head injuries, demographic and psychosocial characteristics, and a residential history in a self-administered questionnaire. PCE exposure was assessed using water system modeling software. Overall, 27.8% of participants reported at least one unintentional head injury. We found no evidence of an increased risk among exposed participants for any type of head injury, including those involving a doctor's visit or loss of consciousness. For example, the risk ratio for a head injury involving loss of consciousness was 1.0 (95% CI: 0.7-1.4). No dose-response relationship was observed in relation to increasing PCE exposure. Adjustment for confounding variables including psychosocial factors did not alter these results. In conclusion, this study did not find evidence of an increased risk of unintentional head injuries among participants

exposed to PCE during gestation and early childhood even after adjusting for psychosocial factors. Limited information on contextual factors at the time of the head injury (e.g., alcohol and seatbelt use) should be considered when evaluating these results, as they are relevant for an underlying hypothesis about increased risk-taking.

Research Translation Component: Our epidemiologic research is communicated regularly to stakeholders, including government officials, local water companies, and study participants. We have presented our research methods and findings in an NIEHS webinar, a partnership call with Collaborative on Health and the Environment, and several activities in association with the Boston Museum of Science. Most recently, we developed brief research summaries for local water companies and study participants.

References:

1. Janulewicz P, White RF, Martin B, et al. Adult Neuropsychological Performance Following Prenatal and Early Postnatal Exposure to Tetrachloroethylene (PCE)-contaminated Drinking Water. *Neurotox Teratol*, 2012; 34:350-359.

2. Aschengrau A, Weinberg JM, Janulewicz PA, et al. Affinity for Risky Behaviors Following Prenatal and Childhood Exposure to Tetrachloroethylene (PCE)-contaminated Drinking Water. *Environ Health,* 2011; 10(1):102.

(1-3) Insights from a Kinetics-Based Model Describing Aqueous Arsenic Concentrations at Superfund Sites

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More than 50% of National Priorities List (NPL, "Superfund") sites are contaminated with arsenic. In many of these environments, arsenic is reductively released into groundwater by the biological reduction of arsenic-bearing iron oxides. A better understanding of the processes that regulate aqueous arsenic concentrations at these sites is needed to predict arsenic release, transport, and to better understand what controls environmental exposures. Despite considerable efforts, it is still difficult to predict the aqueous concentration of arsenic in the transitional redox environments where arsenic release occurs, or in the reduced sediments through which it is transported. Equilibrium-based partitioning models include adsorption-desorption, and to varying extents, and complete characterization of the minerals present and their surface properties, yet are often no more accurate that simple adsorption isotherms or partition coefficients in these environments. Here, we evaluate a novel kinetics-based approach that incorporates knowledge of the solid-phase speciation, and the microbial rates of sediment reduction, to better predict arsenic concentrations. This model is effective for a number of Superfund sites, and implies that iron mineralogy, which controls the rate of iron reduction and the speciation of arsenic, which affects readsorption rates, are the dominant variables controlling As retention.

Research Translation: There is no more important variable than aqueous concentration in drinking water to describing human exposure to arsenic and other metals. This generalizable model is capable of doing so in many locations, including contaminated sites. This predictive model also can be incorporated into reactive transport models to improve predictions of how arsenic concentrations will change in space and time, allowing us to evaluate the long term stability of Superfund sites during remediation.

(1-4) Fast ion chromatography-ICP-QQQ for arsenic speciation analysis

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Arsenic Speciation analysis is essential in biological, environmental and food samples to differentiate between the carcinogenic inorganic arsenic species and the less toxic organic forms. Most current methods require > 10 minutes per sample for analysis which severely hinders sample throughput and method development. Faster chromatographic methods can be achieved by using smaller chromatography columns with smaller particle size. In this study I demonstrate the use of a small particle size (5 µm), short (50 mm) Hamilton PRP-X100 anion exchange column to separate arsenic species with chromatographic run times of as low as 2 minutes. The use of the ICP-QQQ affords low detection limits by detecting As as the AsO at m/z 91 after reaction with oxygen in the reaction cell. These methods have been applied to arsenic speciation in urine, and food and seaweed extracts.

Jackson, BP. 2015. Fast Ion Chromatography-ICP-QQQ for arsenic speciation. Journal of Analytical Atomic Spectroscopy. 2015,30, 1405-1407

(1-5) Metagenomic and Radiocarbon Analysis of PLFA, DNA, RNA, and Proteins to better understand Arsenic Impacted Aquifers in Bangladesh.

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Microbial respiration drives the release of arsenic from the sediment to the water in drinking water in reducing aquifers. There are still two questions regarding this process that have only begun to be answered. The first question is the relative importance of Fe(III) versus As(V) reduction. The second question is the source of organic carbon for microbial growth and respiration. We have made progress on both fronts by coupling metagenomic and radiocarbon analyses but results were initially limited. Continued focus on co-located sediment and water samples from two well nests in Bangladesh are expanding our knowledge of these processes. Coupled mineralogical and molecular analyses have indicated that sediment arsenic is fully reduced before arsenic is mobilized and that arsenic reducing microbes are present within the sediment. These results do not preclude the importance of Fe(III) reduction but indicate that arsenate reduction is a critical step during arsenic mobilization. Radiocarbon analysis of phospholipid fatty acids (PLFAs), proteins within cellular walls, have further demonstrated that microbes preferentially use carbon sources younger than the sediments and that dissolved organic carbon could be an important carbon source. We have also developed methods to collect samples to enable analyses using next generation sequencing technologies in addition to analysis of proteins. Coupling of these new methods to radiocarbon signatures should enable us better understand processes occurring within high arsenic aquifer systems.

Research Translation: Metagenomic and Radiocarbon analyses are improving our understanding of microbial release of arsenic from sediment to water in aquifers. These results will enable us to better predict arsenic release and transport.

(1-6) Urban Agriculture Site Suitability Analysis in San Diego

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It is estimated that there are more than 450,000 brownfield sites in the U.S. In Southeast San Diego (SES) there are 65 acres or more of vacant or underdeveloped land, some of which are believed to be brownfields. The SES community is a lower socioeconomic area where many of the neighborhoods are considered food deserts. Utilizing these vacant lots for urban agriculture is a way to clean-up, re-invest, and revitalize these areas while improving food security, increasing access to fresh produce, and mitigating storm water run-off. The specific aim of this project is to conduct an urban agriculture and community garden "site suitability analysis" of vacant and underdeveloped land parcels in SES, utilizing *CommunityViz* scenario planning software. Suitability factors in our analysis will include physical, economic, social, and environmental using LIDAR data, GIS data layers, and field surveying. Storm water flow path models will also be factored into the analysis in order to optimally select areas for green infrastructure. The results of this analysis will be an urban agriculture suitability map that can be utilized by the city of San Diego to focus brownfield remediation and redevelopment resources as well as local community gardening network groups that pair up gardeners with available land.

(1-7) Effects of asbestos exposure on the cellular redox state and mitochondrial dysfunction

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Asbestos exposure is a pervasive occupational health hazard as well as a major public health concern. In order to better monitor subjects who are at risk for developing asbestos-related diseases prior to disease onset, it is necessary to identify cellular biomarkers of asbestos exposure that are mechanistically relevant to disease pathogenesis. Currently, the mechanisms by which asbestos induces tissue damage and lung diseases remain unclear. A large body of evidence supports the hypothesis that asbestos increases the cellular oxidative stress burden. In the context of chronic asbestos exposure, this oxidative stress is thought to induce tissue damage and inflammation which can contribute to carcinogenesis. As such, it would be tempting to monitor previously validated biomarkers of oxidative stress in individuals suspected of asbestos exposure. However, such biomarkers are not unique to asbestos, and could therefore be confounded by comorbidities or lifestyle choices such as smoking status.[1] Thus, the use of cell culture models to examine the effects of asbestos on mitochondrial metabolism may lead to the elucidation of biomarkers exclusive to asbestos exposure. An attractive class of metabolites are the coenzyme A thioesters (acyl-CoAs), which are involved in a number of metabolic pathways including the Krebs Cycle, fatty acid oxidation, and sterol biosynthesis. Based on a previously developed liquid chromatography mass spectroscopy (LC-MS) method we monitored how asbestos exposure altered the levels of acyl-CoAs in a lung carcinoma cell line. We also assessed cellular redox state by quantifying the cellular antioxidant glutathione in both its reduced (GSH) and oxidized (GSSG) forms. Our results—though preliminary—could contribute to the elucidation of biomarkers that are unique to asbestos exposure thereby facilitating intervention prior to disease onset.

1. Mesaros C, Worth A, Snyder NW, Christofidou-Solomidou M, Vachani A, Albelda SM et al. Bioanalytical techniques for detecting biomarkers of response to human asbestos exposure. *Bioanalysis* 7(9),1157-1173 (2015).

(1-8) The PXR "gene battery" in zebrafish

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The pregnane X receptor (PXR) (nuclear receptor NR1I2) is a ligand activated transcription factor, mediating responses to diverse xenobiotic and endogenous chemicals. The properties of PXR in fish are not fully understood. Teleost fish lack CAR (NR1I3), a closely related receptor in tetrapods that is involved in the response to many xenobiotics, magnifying the potential role of PXR in fish. *In vitro* studies using isolated ligand binding domains (LBDs) in COS cells have indicated differences in ligand binding between human and zebrafish PXRs. However, these *in vitro* methods do not adequately reflect the complexity of transcription factor activation in vivo, where full length protein occurs in the normal cell context. Here we report on zebrafish *pxr* expression *in vivo*, including transcriptome analysis by RNA-Seq, regulation of *pxr* and the Pxr target gene *CYP3A65* by human PXR agonists, and the generation of CRISPR-Cas knockout strains. The combination of pregnenolone dosing and morpholino knock-down of *pxr* was used to define the Pxr gene battery in zebrafish. Differentially regulated genes include 179 genes assigned as Pxr-regulated, including *pxr*, *CYP2K6*, *CYP3A65,* and *abcb5*. The prototypical human and mouse PXR agonist hyperforin downregulated the expression of both *pxr* and *CYP3A65*, with an IC50 less than 500 nM. Other human PXR agonists downregulated *CYP3A65* but not *pxr* expression, including nifedipine and triclosan, but not pregnenolone sulfate. The description of the Pxr gene battery in zebrafish has implications for assessing the action of PXR ligands in fish, including many pollutants.

(1-9) The effects of arsenic, manganese, and lead on neurodevelopmental outcomes among children in Bangladesh

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Background: The objective of this study was to investigate associations between environmental exposure to arsenic (As), manganese (Mn), and lead (Pb) and neurodevelopmental outcomes among children in Bangladesh, a country currently experiencing an epidemic of arsenic poisoning through contaminated drinking water.

Methods: We evaluated 812 children who are members of an ongoing prospective birth cohort established to study the health effects of prenatal and early childhood arsenic exposure in the Sirajdikhan and Pabna Districts of Bangladesh. As and Mn were measured in water collected from each child's primary drinking water source, and Pb was measured in blood. Water was collected during the first trimester of pregnancy, ages 1 month, 12 months and 2 years. Blood was collected at age 2 years. Neurodevelopmental outcomes were assessed at approximately age 2 years using a translated and culturally-adapted version of the Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III).

Results: The BSID-III scores were significantly lower in Pabna for all domains except expressive language. After adjusting for other significant predictors (e.g. maternal education, birth measurements), increased Mn and Pb exposures were associated with decreased cognitive scores in Sirajdikhan, an area where these levels are high and As levels are low. Increased As was associated with decreased cognitive scores in Pabna, an area with high As levels. Increased Mn was associated with decreased expressive language scores in both regions.

Conclusion: Increased exposures to As, Mn, and Pb are associated with decreased neurodevelopmental outcomes. Different effects are observed at high and low exposure levels. This study provides information for future risk assessment regarding the health effects associated with high water As and Mn concentrations and blood Pb.

(1-10) Trichloroethylene Metabolite S-(1,2-Dichlorovinyl)-L-Cysteine but not Trichloroacetate Inhibits Pathogen-Stimulated TNF-α in Human Extraplacental Membranes In Vitro

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Trichloroethylene (TCE) is a common drinking water contaminant associated in humans and laboratory rodents with adverse pregnancy outcomes. Metabolism of TCE to trichloroacetate (TCA) and *S*-(1,2-dichlorovinyl)-L-cysteine (DCVC) is mechanistically linked to TCE toxicity. During pregnancy, extraplacental membranes define the gestational compartment for the developing fetus and provide a barrier to infectious microorganisms ascending the mother's reproductive tract. We tested the hypothesis that bioactive TCE metabolites decrease pathogen-stimulated cytokine responses of human extraplacental membranes that are critical for resistance for infection. Tissue cultures of extraplacental membranes were treated for 4, 8, and 24 h with TCA or DCVC in the absence or presence of lipoteichoic acid (LTA) or lipopolysaccharide (LPS), components of gram positive and gram negative bacterial cell membranes, respectively, to simulate infection. Additional extraplacental membranes were cocultured with DCVC and live bacteria (Group B *Streptococcus*; GBS). DCVC (5-50 µM) inhibited LTA-stimulated mRNA expression and release of the cytokine TNF-α from cultured tissue as early as 4 h ($p \leq 0.05$). Similarly, GBS-stimulated release of TNF-α, IL-1β, and IL-8 was suppressed by co-exposure to 5 or 10 µM DCVC. In contrast, 24-h exposure to TCA (up to 500 µM) did not inhibit LTA-stimulated TNF-α release from tissue cultures. Exposure to DCVC or TCA alone did not significantly increase cytokine release from extraplacental membranes. These results show for the first time that a TCE metabolite inhibits gestational tissue responses critical to tissue defense against microorganisms, and suggest that TCE exposure could potentially modify susceptibility to infection of the gestational compartment during pregnancy. Such microbial-toxicant interactions may warrant further consideration in risk assessment analyses. These findings were reported previously (Boldenow et al. Reprod Toxicol 52:1, 2015).

(1-11) Sustainable Technologies, Alternative Chemistry – Training and Education Center

Dr. Michael Yost and Dr. Tania Busch Isaksen: University of Washington, Department of Environmental and Occupational Health Sciences

The *Sustainable Technologies, Alternative Chemistry – Training and Education Center (STAC-TEC)*, located within the University of Washington's Department of Environmental and Occupational Health Sciences, focuses on developing awareness of potential workplace health and safety risks associated with biotechnology, nanotechnology and green landscaping through undergraduate and graduate course work and Occupational & Environmental Health and Safety (OEH&S) professional continuing education. Additionally, the Center plays a leading role in promoting green chemistry principles both on and off campus. The Center's main aims are to: develop and pilot test materials to augment existing courses of instruction; develop and deliver OEH&S professional training materials; develop certificate programs for both professional and graduate-level training; and evaluate the Center's effectiveness in design and deliver of educational materials. STAC-TEC is one of three R25 awards funded under the Superfund Research Program. This poster is being submitted to summarize the Center's work to-date.

(1-12) Technology transfer enabling a participatory research project of a high school community to assess microbial populations involved in dioxin degradation and antibiotic resistance.

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The Research Translation Core, Project 4, and Project 5 from Michigan State University – Superfund Research Program Center are collaborating in developing a participatory research project of a high school community to assess microbial groups involved in dioxin degradation and antibiotic resistance. Routine complexities in molecular diagnostics, such as sample processing, can be circumvented with a previously developed hand-held DNA analysis device, termed Gene-Z, that can be used by relatively untrained personnel under field conditions. High school students are being recruited to examine zones of human pollution in river-water samples. As an alternative to direct measurements of pollutants, microbial genetic markers associated with environmental pressures from human imposed activities are being developed. A number of functional genetic targets are being studied in parallel including antibiotic resistance genes, mobile genetic elements (*intI1*), and functional genes related to dioxin degradation (*bph*). Complementing the Gene-Z device, loop mediated isothermal amplification (LAMP), which is less influenced by inhibitors compared to PCR is being used for molecular amplification without DNA extraction/purification. Assay validation includes testing both type strains and surface water samples spiked with type strains, and testing via LAMP on the Gene-Z and qPCR on a conventional thermal-cycler. Validated assays and Gene-Z devices are being provided to high-school students for field based testing of water and sediment along the Tittabawassee River in Midland, MI. Taken together, these tools offer: i) a simplistic means for field-friendly quantification of genetic markers, ii) community engaged activities for molecular diagnostics, and iii) demonstrate the use of microbial targets for quantifying zones of human pollution.

(1-13) The UCSD Brownfield Project and the application of safe gardening practices

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[1]UC San Diego Superfund Research Center

Communities are utilizing urban agriculture and community gardens as a means to improve food security and revitalize their neighborhoods. When neighborhood Brownfields are redeveloped to use for growing food, exposure to potentially contaminated soil is of concern. The UCSD Brownfield project is a community-university partnership, aiming to fill the knowledge and policy gaps that can create roadblocks for brownfields redeveloped for urban agriculture, by transforming a brownfield into a community garden, now called the *Ocean View Growing Grounds (OVGG)*. At OVGG a phase 1 Environmental Site Assessment (ESA) was completed with the funding support of the UCSD SRC. Results of the ESA Phase 1 enabled OVGG to apply for and secure funding from the city of San Diego's EPA Brownfield Redevelopment Grant for a Phase 2 ESA. The Phase 2 ESA measured organic and heavy metal toxicants in samples collected in each area of the garden (10 areas total). Elevated DDT, lead, and arsenic soil concentration levels were found in a few select areas of the garden. Since there are no definitive standards for soil contaminant levels specifically for food production that can be applied to urban agriculture sites, interpretation and application of the results must be made taking many factors into consideration. This poster will present the results of the Phase 2 ESA at OVGG, the interpretation and implementation of the results taking into consideration soil guidelines and safe soil practices to minimize direct exposure, and the application of soil amendments to reduce the

bioavailability of the heavy metals in the soil. The UCSD Brownfield project can serve as a model for brownfield and vacant lot remediation, revitalization, and reuse for urban agriculture.

(1-14) The Iowa Superfund Research Program, Ecolotree, and the Town of Altavista Expand a Partnership

Craig Just

David Osterberg

Scott Spak

A relatively new collaboration between the Town of Altavista, Ecolotree, Inc., the Iowa Superfund Research Program (isrp) Projects 4 and 5, and the isrp CEC and RTC has been expanded. Altavista, Virginia is the location of a PCB-contaminated lagoon that has emerged as a desirable site for studying the field-scale use of poplar trees for PCB remediation (isrp Project 5). Altavista is seeking isrp guidance on how to remediate the PCB-contaminated lagoon to minimize airborne exposures (isrp Project 4) and to save millions of dollars compared to traditional remediation strategies. Ecolotree, Inc. is an Iowa-based engineering company that designs, installs, and maintains engineered forests at regulatory-permitted sites, such as landfills and chemical spill sites. The stakeholders in the partnership include isrp researchers, the isrp engagement coordinator, the isrp research translation coordinators, a small business, town facilities managers, elected officials, state regulators and federal regulators. A workshop titled *Altavista's 6-acre Petri Dish: Testing Sustainable Solutions for PCB Contaminated Sediments* was held in June of 2015 in Danville, VA. The workshop highlighted lab and field work results from 3 years of *in-situ* PCB degradation and containment in Altavista. The workshop featured presentations by isrp Project 5 leader, Jerald Schnoor, and isrp partner from Ecolotree, Louis Licht. The workshop was sponsored by the U.S. Environmental Protection Agency which sought to "share knowledge on the state of the practice of PCB degradation as demonstrated in field scale trials". The long term goal is to engage in a sustainable and mutually beneficial relationship that promotes fundamental research while solving a real environmental problem that will protect human health and enhance a small business.

(1-15) Enhancing the capacity of biology teachers to incorporate SRP research findings into life science instruction

Dana Haine, MS; Sarah Yelton, MS; Kathleen Gray, MSPH, Rebecca Fry, PhD, James Swenberg, DVM, PhD

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In recent years, the UNC SRP RTC has expanded its teacher professional development offerings to include content that extends beyond a pollution/remediation focus to reach a new audience: biology teachers. By developing activities that introduce the topics of epigenetics, the endogenous exposome and bioavailability, the RTC has enhanced the capacity of biology teachers to incorporate current UNC SRP research findings into their life science instruction. Partnering with SRP scientists to develop activities that deepen teacher content knowledge, while also promoting student engagement with real data, cultivates increased awareness of how chemicals in the environment impact DNA structure and function and ultimately human health.

This poster highlights strategies for effectively engaging scientists in developing scientifically rigorous, STEM-focused educational activities that are aligned to state and national science standards and also address the realities of the science classroom. Collaborating with SRP scientists and translating their research into classroom activities is an approach that becomes more pertinent with the advent of the Next Generation Science Standards (NGSS). Specifically, the UNC SRP's biomedical research projects provide biology students with relevant learning experiences that promote integration of science and engineering practices as well as demonstrate links among engineering, technology, science, and society, an NGSS disciplinary core idea (DCI). Thus, the UNC SRP RTC is providing biology teachers with resources to support NGSS-aligned instruction while also promoting the research of the UNC SRP to stakeholders in the education community. The featured

activities have been disseminated to hundreds of teachers nationally through conference presentations for the National Science Teachers Association and the National Association of Biology Teachers.

(1-16) Aggregate Exposure Pathways:A Conceptual Framework to Support Exposure Science Research and Complete the Source-to-Outcome Continuum for Risk Assessment

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Two recent National Academy of Sciences Reports articulated complimentary visions for the fields of toxicology and exposure science to meet increasing regulatory demands for more efficient and accurate risk assessments. For exposure science, an expanded technological base and infrastructure would support the characterization of exposure to all endogenous and exogenous chemicals (stressors) across the life-time of an organism or community of interest. A predictive framework, with the ability to forecast exposures with improved accuracy, was a necessary element of the evolved exposure science paradigm envisioned by the committee. Data and information emerging from an invigorated and expanding field of exposure science would need to be organized in a framework that not only promoted forecasting of exposures, but provided the necessary linkages between source and dose (tissue exposure) to inform environmental health decisions based on effects initiated by tissue exposure, or controlling sources of chemical exposures. Fortuitously, most of these elements of the NRC vision for an organizing framework for exposure science are incorporated within the increasingly successful and maturing Adverse Outcome Pathway (AOP) framework. Here we propose an extension of the AOP concept, to its natural companion in the exposure sciences. The aggregate exposure pathway (AEP) framework offers an intuitive approach to successful organization of exposure science data, identifying data gaps, finding and ranking common critical exposure pathways and setting the stage for prediction, within physical and biological elements or across these elements. Here we articulate the framework and present an example for PAHs emerging from the Oregon State University Superfund Research Program and how this framework promotes translation of research between projects, programs and ultimately, into the regulatory environment.

(1-17) Level of Concern Regarding Harmful Health Effects of Environmental Contaminants among Older Adults Participating in Kentucky's Congregate Meal Site Program and their Understanding of the Protective Role of Good Nutrition

Emily Dickens, Dawn Brewer, Tammy Stephenson and Lisa Gaetke

The University of Kentucky's Superfund Research Center's (UK-SRC's) Community Engagement Core (CEC) distributed surveys to older adults (N=64) participating in the Older American's Act (OAA) Congregate Meal Site Program in four different senior centers to gain insight into the concern they have about environmental contaminants impacting health and the protective role of good nutrition. Participation in the OAA Program is restricted to community-dwelling older adults aged 60 years and older. The age of respondents was 76[62,93] with 81% white females. On a scale of 0 to 10 with 10 being very concerned, older adults ranked their concern as being serious 9[0,10] in regards to exposure to pollution where they perform everyday activities, and 8[0,10] with their concern pertaining to people getting sick because they don't eat the right foods to protect against pollution. Additionally, 77% agreed that a healthy diet can reduce negative health effects of pollution ($p \leq 0.05$), but only 33% reported altering their diet because of their concern of contaminants in food ($p \leq 0.05$). Interestingly, only those with self-reported cancer and diabetes had greater concern with pollution exposure compared to those without those diseases ($p \leq 0.05$).

In general, there is a need and great interest among older adult to learn dietary strategies that protect against environmental contaminants. The OAA Congregate Meal Site Program is an appropriate platform to deliver this type of health education program because nutrition education is a required component of the OAA program. In Kentucky, the Family and Consumer Science Cooperative Extension staff delivers nutrition education activities to senior centers monthly. The potential reach of such an education program is vast because senior centers are located in each of Kentucky's 120 counties.

(1-18) Land-Grant Institution's Cooperative Extension Service serves as a valued partner in UK-SRC's Community Engagement Core efforts

Dawn Brewer, Hannah Clifton and Lisa Gaetke

The University of Kentucky's Superfund Research Center's (UK-SRC's) Community Engagement Core (CEC) provides educational support pertaining to nutrition, environmental issues, and other perceived areas of concern by people affected by environmental pollutants. UK-SRC's researchers have shown that nutrition may modulate the toxicity of Superfund chemicals. Since 2000, UK, a land-grant institution, has been one of the CEC's strongest partners through Kentucky Cooperative Extension Service (Extension). Extension agents, who relay knowledge and research generated by public universities to citizens of the state through educational programs, are found in all 120 Kentucky counties. Extension agents specialize in nutrition, food, and environmental issues. Agents live and work in the county and are trusted community members that facilitate bidirectional communication between CEC and communities. To respond to community requests to learn specific dietary changes that can reduce harmful effects of environmental pollutants the CEC is expanding their Extension partnership by developing a curriculum of nine sets of healthy lifestyle-focused activities. Dietitians and students of the CEC are expanding materials to include activities that encourage increased consumption and variety of fruits and vegetables; increase physical activity; consumption of more fermented foods for gut health, healthier fish, nuts, and seeds; increasing the use of herbs and spices; decreasing processed foods, high-fat meat, and dairy products; and modifications to food preparation techniques to decrease exposure to contaminants. Each topic comes with a facilitator's guide, evaluation materials, participant handouts, an activity and healthy recipe sample. These community-initiated activities delivered through the partnership between UK-SRC CEC and Extension are an important public health strategy that offers nutrition and health strategies to reduce body burden of contaminants which decreases chronic disease development throughout Kentucky.

(1-19) The Duke Superfund Foam Project: Preliminary Flame Retardant Findings After One Year of Testing

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Flame retardant (FR) chemicals are often applied to consumer products to meet flammability standards; however, products are not labeled with specific information on FR content and consumers have no way to determine what FR treatments are applied to products. Concern over persistence, bioaccumulation and toxic potential of one class of FRs, polybrominated diphenyl ethers (PBDEs) led to their voluntary phase-out in the US (2005). Post-2005, use of alternative chemical FRs has increased, and information on the types and amounts of chemicals used, their specific applications, and potential toxicities is not well understood. In early 2014, we developed a program to test polyurethane foam for 7 flame retardant chemicals, free of charge, for the public (accessible at http://pratt.foam.duke.edu). As of May 2015, >650 samples across a variety of product types have been analyzed, 53% of which contained an identifiable FR. Prevalence of FRs across all products was generally of the following frequencies: Tris(1,3-dichloroisopropyl) phosphate(TDCPP) > Firemaster ®550 > Tris (chloropropyl) phosphate (TCPP) > PentaBDE (a PBDE commercial mixture). No products known to be purchased after 2005 contained PentaBDE, reflective of the global wide phase-out. FR type varied with product category. Of the foam submitted from child car seats, 69% tested positive for a FR, and TDCPP (45%) and TCPP (19%) were detected most frequently. A wider variety of FRs were observed in sofas and love seats containing FRs (62%). In mattress pads, type of FR used also varied, but use was only

observed in 32% of samples. These results provide insight on trends in the use of FR chemicals in consumer products and demonstrate the value of the data collected through Duke Superfund's online testing service.

(1-20) Spatiotemporal Dynamics of Nitrates in Karst Groundwater

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The presence of high nitrate levels in groundwater is of concern due to their impact of public health and remedial challenges. High nitrate concentrations in water has been associated with the blue baby syndrome, but their effect on remedial actions and other health issues when present in complex mixtures still need to be determined. Groundwater contamination with nitrates may result from domestic, agricultural and industrial activities. Although not directly due to nitrate concentrations, several superfund sites in the karst region of northern Puerto Rico have shown elevated levels of nitrates in groundwater, in association with other superfund-related contaminants. This is of major concern as the population in this region relies on groundwater for drinking purposes. This work aims at determining the spatio-temporal dynamics of nitrates levels in the karst groundwater of northern Puerto Rico. The work involves sampling and analysis of 12 groundwater sites. General water quality parameters are assessed with a Hydrolab DS4a multi-probe. Common ions, including nitrates, are analyzed using high-pressure liquid ion chromatography. Nitrates are present in all sampled sites, many of which are also associated with chlorinated volatile organic compounds and phthalates, indicating the presence of complex mixtures. The concentration of nitrate for the entire study averages 7.98 mg l^{-1}, and ranges from 0.7 to 21.5 mg l^{-1}. Thirty three percent of the sites show levels above maximum concentrations level. Concentrations in many sites show a decreasing trend, and may be associated with lower rainfall patterns. The infiltration and runoff of the water could generate a health risk due to the high mobility of nitrates in zones of karst origin.

RESEARCH TRANSLATION: This work interacts strongly with community members where wells and springs are sampled. The interaction involves communicating the sampling activities and providing feed back of the water quality results. Results are also disseminated to the broader scientific community through publications (under preparation) and presentations.

(1-21) Unintended Consequences of Environmental Risk Research at Superfund Sites: Implications for Integrating Community Involvement into Risk Assessment and Reuse Planning;

Britt Dahlberg, PhD

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BACKGROUND: The EPA Superfund process requires involving stakeholders in research and decisions that affect them. At some sites, staff observe that residents from neighborhoods most affected by the contaminated site are least represented in public meetings to discuss EPA's risk assessment and reuse planning. As part of a larger dissertation project, I explored how the EPA's community involvement process operates in practice, with implications for engaging communities in research like the EPA's risk assessment and reuse planning. METHODS: I conducted in-depth interviews with residents (n=46) and staff from EPA and partner agencies (n=32), and participant-observation of meetings of community groups, agency staff, and joint public meetings, at the BoRit Asbestos Site in Ambler, Pennsylvania, during the first four years after site listing (2009-2013). RESULTS: Factors influencing participation included: 1) Residents were aware of and interested in the consequences of EPA's investigation, not just the direct findings; (2) Letting a small range of people determine the scope of concerns to be discussed at public meetings and incorporated into planning. IMPLICATIONS: Future environmental health research at contaminated

sites - by agencies as well as other researchers - should seek to: (1) integrate community engagement into risk assessment at the early stage of defining the scope of concerns to incorporate into research design, and allow space for new concerns to arise; (2) allow time for and intentionally support a longer stage of encouraging dissent, perhaps with an active facilitator or mediator, in order to make space for dialogue in which to raise multiple priorities; (3) consider and discuss the other impacts risk assessment can have, and openly discuss ways to mitigate consequences with residents.

RESEARCH TRANSLATION: Preliminary findings helped to inform the approach taken by the University of Pennsylvania SRP # P42 ES023720; focus areas for the research cores emerged out of concerns raised by residents. This work has been incorporated into a report written and presentation for the EPA (citation below). Other portions of this project have been translated to stakeholders through a newspaper insert, online exhibit, and a play and Q&A discussion performed on site in Ambler, PA through a SEPA Grant Funded Collaboration between the University of Pennsylvania and the Chemical Heritage Foundation. See: http://reachambler.chemheritage.org/

(1-22) Engaging Stakeholders to Assess Human Exposure to Contaminants via Recreational Fishing in the Elizabeth River Watershed, Virginia

Gretchen Kroeger, Savannah Volkoff, Joe Rieger, Dr. Richard Di Giulio

Duke University's Superfund Research Center (SRC) studies the effects of pollution on fish populations in Virginia's Elizabeth River, as industrial activity on the river has led to significant PAH and PCB contamination. In response to current concern over possible PCB contamination in red drum and speckled trout in the Elizabeth River, Duke SRC partnered with the Virginia's Department of Environmental Quality (VDEQ) and Department of Health (VDH), and the Elizabeth River Project (ERP) to carry out two activities: PCB analyses in these sport fish and survey anglers to assess fish consumption patterns. Red drum and speckled trout, caught within designated areas and donated by local anglers, are being analyzed for PCB concentrations. We developed the angler survey with guidance from our partners and administered the survey to local anglers (65 in-person and 350 online), collecting information on angler's catch and consumption, knowledge of consumption advisories, and demographics. PCB tissue data and angler surveys are currently being analyzed; however, preliminary findings show that online survey respondents represent a different angler community than in-person respondents: online respondents were predominantly white (94% vs. 58%) with at least a college degree (57% vs 20%) and a household income of over $100,000 (44% vs. 16%). We anticipate finding similar differences between respondents' fish consumption and knowledge of advisories. We are developing a collaborative approach for educating anglers in the Elizabeth River watershed on the existing fish consumption advisories and overall risks and benefits of fish consumption. This work, recently expanded to using *Fundulus heteroclitus* to identify sources of PCBs and the relationship to land use patterns, will inform VDEQ's PCB regulations and VDH's issuance and communication of fish consumption advisories.

(1-23) Analyzing, mapping and visualizing diverse environmental data: New online tools for civically engaged research and healthy place making

Ilya Zaslavsky, San Diego Supercomputer Center, UCSD

Keith Pezzoli, Urban Studies and Planning Program and Communication Department, UCSD

This poster presents a new approach—including online tools for data integration, mapping and visualization—being developed at the University of California, San Diego as part of the Superfund Research Center (SRC) funded by the National Institute of Environmental Health Sciences (NIEHS). The SRC has partnered with the San Diego Supercomputer Center's Spatial Information Systems Lab to improve methods of research translation and community engagement. The approach joins the environmental health sciences with urban and bioregional planning. This is an integral part of a new paradigm called bioregionalism, which emphasizes sustainability of social/natural systems through active maintenance and restoration of

locally-unique patterns of interaction between social, economic, cultural and natural aspects of the environment. To make this vision a reality, local sustainability efforts need to be based on a bioregion-wide integration of information about different aspects of coupled human and natural systems, and develop an online collaboration and exploration space where diverse, multiscalar data and results can be analyzed, shared and discussed.

This poster describes several online technologies that enable user-friendly interactive data analysis and visualization. This includes SuAVE (Survey Analysis via Visual Exploration), a new online tool that uses intuitive graphical design and interactive animations to present information on regional health surveys and on local areas available for development. Applications of SuAVE take advantage of various large-scale data integration and community engagement tools being explored in the course of NSF EarthCube initiative. Background and recent accomplishments of this initiative relevant for SRP Big data and information integration agenda are also presented.

(1-24) A New Model for Cumulative Risk Assessment and its Application to Superfund Sites

Jessica Meeker, MPH[1] and Richard Pepino, MS[1]

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In 2003 the U.S. Environmental Protection Agency (EPA), National Center for Environmental Assessment proposed the Framework for Cumulative Risk Assessment. This document was prepared in response to reports highlighting the importance of understanding the effect of an accumulation of risks from a myriad of environmental stressors on human health. Such reports included the National Research Council's 1994 report, “Science and Judgment in Risk Assessment”, and the 1997 report by the Presidential/Congressional Commission on Risk Assessment and Risk Management entitled, “Risk Assessment and Risk Management in Regulatory Decision-Making”. These reports have demanded a population-based approach to assessing human health risks from environmental contaminants.

Through our research we will summarize the current EPA approach to Cumulative Risk Assessment. We will then present a cumulative risk model that we are generating with EPA Region 3 staff at a Superfund site in Philadelphia. The EPA site assessment currently focuses on volatile compounds and other toxics that are being emitted from the National Priorities List site to a community that may also be experiencing cumulative exposures from local highway traffic patterns, the airport, and an oil refinery within the planning area. Our model will assess the population that is exposed to potential risks from the Superfund site. It will also seek to identify what additional environmental stressors may exacerbate health effects to this potentially vulnerable population, which may fall under the rubric of an environmental justice (EJ) community. Finally, we will demonstrate the possible application of our model to the BoRit site in Amber, PA, which is the focus of our SRP grant.

(1-25) Michigan State University Superfund Research Project Community Engagement Core

Dearing[1], Upham[2], Hamm[3], Zhuang[1], Cox[1], Cruz[1]

Department of Communication, Michigan State University

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School of Criminal Justice and Environmental Science and Policy Program, Michigan State University

Industrialization of the Tittabawassee River and Saginaw River watershed resulted in the release of dioxins and dioxin-like compounds (DCLs; i.e. furans), and polychlorinated biphenyls (PCBs) in toxic concentrations. Over time, changes in waste management practices and pollution controls have reduced or eliminated point-source releases but these highly chlorinated chemicals persist in the environment and have spread through flooding, resulting in some of the highest environmental dioxin concentrations ever recorded.

The Superfund Research Center at Michigan State University (MSUSRP) has a long-standing program of research that seeks to understand the effects of dioxin and DLCs on human health and their fate in the environment. Recently, the Community Engagement Core (CEC) of the MSUSRP has begun to engage the affected communities in this watershed with the intention of understanding and improving environmental and health literacy. Our primary foci are perceptions of stigma, health numeracy, social networks, and trust, and, especially, examining how these factors affect local residents' exposure relevant behaviors.

Four projects are currently being conducted by the CEC to lay the groundwork for future interventions. Specifically, we are conducting interviews with local residents to understand their affective responses to dioxin contamination and food preparation/consumption behaviors. We have also implemented a survey study with current and previous members of the Midland Community Advisory Group (CAG) members, to investigate their communication with community residents. In addition, a wide variety of stakeholders are being recruited to participate in a case study of previous private property remediation efforts in Midland. Finally, we are helping to develop a survey to evaluate local residents' dioxin exposure via food consumption and usage of contaminated land.

(1-26) Partnering with USEPA to Improve Community Understanding of Metals Bioavailability

Melissa Dreyfus, United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation

Kathleen M. Gray and Dana B. Haine, University of North Carolina at Chapel Hill Superfund Research Program

Sarah T. Wilkinson, University of Arizona Superfund Research Program

Lead and arsenic are two of the most common contaminants of concern found at Superfund National Priorities List (NPL) sites. Both metals can vary in their bioavailability, or the amount of the metal that is absorbed into the body following skin contact, ingestion, or inhalation. For communities impacted by metals contamination, the concept of bioavailability and its implications for cleanup decisions may be unknown or confusing. Yet such understanding is essential for community members to assess site-specific cleanup decisions. The Partners in Technical Assistance Program (PTAP) is an EPA pilot program to expand opportunities for collaboration between EPA and colleges and universities with the shared goal of addressing unmet technical assistance needs of impacted communities near Superfund sites. As PTAP pilot partners, SRP grantees apply their unique research strengths to voluntarily assist EPA in responding to community technical assistance needs. In 2015, the UNC-Chapel Hill and University of Arizona SRPs have collaborated with EPA to better inform community audiences about the relevance of bioavailability to site cleanups and protection of human health. We have developed informational materials and activities that can be used in community settings. Rather than focusing on one Superfund site, this project broadly targets communities that are trying to understand the concept of bioavailability and how it informs site-specific cleanup decisions. In addition to developing interactive exercises and educational materials, which were recently shared with agency staff and community groups at a national community engagement meeting, participation in PTAP has provided an opportunity to foster inter-agency and inter-institutional collaboration.

(1-27) Healthy City Planning: An integrated approach to reducing cumulative impacts in disadvantaged communities.

Keith Pezzoli, Ph.D., University of California, San Diego. Director, Urban Studies and Planning Program; and Professor of Teaching, Department of Communication

This presentation describes a community-university partnership to promote healthy city planning in the San Diego-Tijuana binational border region. The partnership includes UC San Diego's Superfund Research Center; the Center for Sustainability Science, Planning and Design; and the Global Action Research Center (a nonprofit organization). The partnership aims to reduce cumulative impacts (i.e., the burden of multiple stressors) on residents in disadvantage communities via a three

pronged integrated approach: (1) transform strategically selected vacant lots into community gardens and food forests; (2) green the city's infrastructure to deal with stormwater and contaminated urban runoff, and (3) mobilize local residents to enhance civic engagement in neighborhood development. This integrated approach is evidence of an emergent paradigm shift happening worldwide; it is redefining human–ecological relationships in the quest for healthy place making. The presentation critically examines the status of the health sciences in the context of sustainability science, bioregional justice and livable communities; and the role of research universities in fostering problem-solving, solutions-oriented research that can improve environmental public health outcomes in vulnerable communities. The science includes testing soil and edible plant tissue where urban agricultural is taking place on land that is potentially contaminated (brownfields). The science communication includes mapping, visualization, and scenario planning. The US Environmental Protection Agency, City of San Diego, and University of California Global Food Initiative is supporting the effort, which was referenced recently in a report to the Congress and President of the United States (Good Neighbor Environmental Board Report). The community-university partnership driving this effort is providing a model for disadvantaged communities to address interlocking food-water challenges.

Reference: Keith Pezzoli, Justine Kozo, Karen Ferran, Wilma Wooten, Gudelia Rangel Gomez, and Wael K. Al-Delaimy, 'One Bioregion/One Health: An Integrative Narrative for Transboundary Planning Along the Us–Mexico Border', Global Society, 28 (2014), 419-40.

(1-28) UK SRC Research Translation Core: A Multidirectional Bridge for Stakeholders and Resources

Lindell Ormsbee[1], Kelly G. Pennell[1], and Anna G. Hoover[2]

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[2]University of Kentucky, College of Public Health, Preventive Medicine & Environmental Health

The University of Kentucky Superfund Research Center (UKSRC) Research Translation Core (RTC) engages in multidirectional communication with stakeholders, placing strong emphasis on efforts to maintain and strengthen stakeholder relationships. Stakeholder relationships are beneficial to UK-SRC in that they provide opportunities for developing partnerships, transferring technology and sharing of research results—requirements set forth by NIEHS for all RTCs. However, in order for the relationship to result in meaningful interactions and multi-directional communication, UK-SRC must be responsive to requests and create opportunities for continual stakeholder engagement. This poster will highlight ways in which UKSRC has leveraged external resources and expertise to ensure RTC efforts are responsive and relevant to stakeholders. As an example, UKSRC has sought inter-SRP collaborations to harness expertise of the greater SRP community when stakeholders express needs that are not necessarily relevant to the overall center theme. In addition, UKSRC has leveraged existing partnerships developed within other university centers, so that long-term relationships are maintained even while stakeholder requests are varied and, at times, inconsistent with UKSRC's overall mission. Broadening responses to stakeholders' diverse needs results in enhanced collaborations, partnerships and technology transfer initiatives.

(1-29) Science to Stakeholders: Research Translation and Community Engagement Collaborations

David Sherr, David Ozonoff, Madeleine Scammell, Wendy Heiger-Bernays, May Woo, Katie Tomsho, Komal Basra

The BU SRP Research Translation Core (RTC) is designed to maximize efficient communication of program research to scientific peers in governmental organizations, the academic and private and public sectors, and other SRPs with an emphasis on open access and a willingness to share new technologies, information, and software. The BUSRP Community Engagement Core (CEC) is an acknowledgement that there is a need, and a responsibility, to respond to individuals and communities living in communities affected by exposures to hazardous substances seeking technical and scientific expertise. Here are some typical examples:

Responding to community concerns about TCE and PCE vapors in two schools in North Carolina in collaboration with UNC SRP RTC and UK SRP RTC. Organizing a peer review of MassDEP's latest draft of Vapor Intrusion Guidance. Contributing a citation by BU SRP and Brown SRP to the Finalized EPA Intrusion Guidance.

Helping to organize and participate in web-assisted national conference calls for the Collaborative on Health and the Environment where SRP researchers (from BU SRP and those from other SRPs we invited) to discuss a variety of SRP-research related topics, including green chemistry and community health studies.

Responding to environmental advocacy community group Hands Across the River Coalition, Inc. concerns by creating the New Bedford Harbor PCB Factsheet. The Factsheet was created in collaboration with the community group and BU SRP CEC partner Alternatives for Community and the Environment in time for it to be distributed to residents at an EPA Public Meeting.

The RTC differs from the CEC in being oriented to public health and scientific professionals while the CEC is oriented to our community partners, but they work together in a coordinated fashion.

(1-30) Using Evaluation to Measure the Effectiveness of the C-MERC Model to Bring SRP Science to Policy Stakeholders

Laurie R. Rardin, MES, Research Translation Coordinator, Dartmouth Superfund Research Program, Dartmouth College
Claire Pendergrast, BS, Research Translation Assistant, Dartmouth Superfund Research Program, Dartmouth College
Celia Chen, PhD, Research Translation Core Leader, Dartmouth Superfund Research Program, Dartmouth College

Measuring the effectiveness of research translation is essential. Did the target audience receive the intended message? Did the audience change their behavior as a result? The Dartmouth RTC is developing a framework for evaluating the effectiveness of science synthesis and communication for policy, based on the Coastal and Marine Mercury Ecosystem Research Collaborative (C-MERC), an innovative model designed to bring Superfund Research Program (SRP) science to inform policy on a regional, national and global scale. We are also using this experience to set up a structure for evaluation of the Collaborative on Food with Arsenic and associated Risk and Regulation (C-FARR) and will compare the outcomes to our C-MERC project.

C-MERC brought together mercury scientists and policy stakeholders to review current knowledge and knowledge gaps relating to the global environmental health problem of mercury contamination in fish. The resulting synthesis papers were published in a special journal issue and a report summarizing the papers was produced and used for policy briefings for US agencies prior to the adoption of the Minimata Convention for Mercury in 2013. Similarly, C-FARR will bring policymakers and arsenic scientists together to review current knowledge and knowledge gaps around the global health problem of arsenic in food. Relevant questions will be identified and discussed with the goal of informing public health policy through the resulting synthesis papers and summary report.

By comparing evaluation metrics from C-MERC and C-FARR, we will measure the effectiveness of using the same innovative approach to bring SRP research to inform policy on two different metal contaminants in food. Our metrics will be both quantitative and qualitative. This evaluation framework will strengthen our future science synthesis projects.

(1-31) The Namaus (All Thing Fish) Project: Multidisciplinary Collaboration in Community Engaged Research with the Narragansett Tribe and the Role of the Knowledge Broker

Marcella Remer Thompson[1, 2], PhD, MS, CSP, RN, COHN-S, FAAOHN, Elizabeth M. Hoover[2], PhD, Dinalyn Spears[3], MS, Scott Frickel[2], PhD

[1]University of Rhode Island, [2]Brown University, [3]Narragansett Tribe

Background. Cultural and economic factors are important determinants of health; importantly, fishing and fish consumption among indigenous populations. While seeking to protect the public from harmful health impacts, fish advisories do not take into account the impact of the absence of fish on indigenous culture. Conversely, continuing tribal fishing traditions in communities where fishing is critically linked to cultural identity has the potential to place tribal members at increased risk for health impacts from environmental contaminants, specifically mercury and polychlorinated biphenyls (PCBs).

Purpose. Assess the impacts of Tribal land and watershed contamination on the Narragansett Tribe, and facilitate informed decision-making regarding fish consumption and fish contamination in Tribal waters.

Method. This multi-year, multi-phased project will employ both quantitative and qualitative research methods. Complex environmental contamination within the contexts of environmental justice requires assembling multidisciplinary teams of academic researchers, state and federal regulators, Tribal government officials, educators, artists, and members of all ages.

Implementation. Talking Circles with indigenous community members will elicit the meaning of fish, fishing, past and current practices and cultural factors influencing these practices. Results from these Talking Circles will be paired with testing the local fish for both contaminants and nutrients. These results will inform a fish consumption household survey. Tribal traditions and current practices regarding fish, fishing and fish consumption as well as how participants think their families and the Tribe have been impacted by environmental pollution will be used to create culturally-sensitive fish advisories. Individual participation in community-based research and group discussion of the risks and benefits of consuming fish have been shown to be effective methods for modifying dietary behaviors.

Conclusion. As knowledge brokers, the SRP Community Engagement Core team ensures the integration of scientific knowledge with the cultural (tacit) knowledge of the Tribal community by creating multidirectional knowledge exchanges, and building the capacity among the Narragansett Tribe for informed decision-making and participation in Tribal environmental health policy and regulatory formulation.

(1-32) Engaging Community Partners and Public Agencies in the Scientific and Regulatory Challenges Associated with an Emerging Contaminant: Environmentally Persistent Free Radicals

Margaret A. Reams, Maud M. Walsh, Slawomir Lomnicki, Tammy R. Dugas, Stephania A. Cormier and Barry Dellinger

Uncertainty concerning the extent to which emerging contaminants may pose risks to public health introduces challenges for research translation and engagement with communities and policymakers. One such contaminant is the Environmentally Persistent Free Radical (EPFR), a central research focus of the LSU SRP. Residents near Superfund sites may be exposed to ultrafine particulate matter (PM) through inhalation of windblown dust and emissions from the on-site thermal treatment of contaminants. Epidemiological evidence supports a link between exposure to airborne PM and an increased risk of cardiovascular and pulmonary diseases. It is well known that during combustion processes, incomplete combustion can lead to the production of organic pollutants that can adsorb to the surface of PM. Recent studies have demonstrated that their interaction with metal centers can lead to the generation of a surface stabilized metal-radical complex capable of redox cycling to produce ROS.

The LSU CEC and RTC have introduced information about EPFR's in their work with the Louisiana Environmental Action Network (LEAN), the Concerned Citizens of Camp Minden, and Baton Rouge residents over the last year. For example, they worked with residents, the EPA, US Army, and state regulators to select a safer disposal option for a large, explosive weapons stockpile in Camp Minden, La. They also worked with residents and local officials concerned about the construction of a proposed barge-cleaning facility along the Mississippi River that would have flared hazardous material several times a day near a park and residential neighborhood. The poster will summarize some of the LSU teams' research concerning EPFRs, their community partnerships, and recent work with residents, regulators and policymakers.

(1-33) Toxic landscapes, environmental justice and the community: An assessment of citizen participation in Superfund site remediation in the EPA's 6th region.

Simone J. Domingue and Margaret M. Reams

Community involvement at federal Superfund sites is rarely conceptualized as an event related to environmental justice despite the role it has in shaping decisions at hazardous waste sites. This study assesses community involvement across 32 Superfund sites in the EPA's 6th region, in light of the EPA's environmental justice commitments. Multinomial logistic regression tested for disparities in community involvement as well as the influence of site-specific variables, including size of the property and potential exposure risks. The results showed no clear evidence of disparities in involvement among minority and low-income communities, and site- specific variables such as hazard-ranking score and the number of operating units (size of the site) were not found to be associated with level of community involvement. Communities with higher urban populations were found to be significantly more likely to have higher levels of community involvement. More rural Superfund communities were found to be less engaged and less likely to participate in decision making concerning the remediation of sites. The findings suggest that community engagement methods may need to be adjusted to account for differences in rural and urban communities. The proposed poster will include a map of the location of Superfund communities within Region 6, photographs of selected communities and a summary of the research methods, findings and implications for community engagement theory and practice.

(1-34) Communicating the results of dietary exposures and metabolism of PAHs from a tribally important food

Diana Rohlman[1,2], Greta Frey[1,2], Molly Kile[1,2], Barbara Harper[1,2], Stuart Harris[3], Anna Harding[1,2], Lisandra Santiago-Delgado[4], Oleksii Motorykin[4], and Staci L. Massey Simonich[4,5]

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The Superfund Research Program (SRP) at Oregon State University (OSU) collaborated with the Confederated Tribes of the Umatilla Indian Reservation (CTUIR) to investigate exposure to polycyclic aromatic hydrocarbons (PAHs). Research projects were designed collaboratively, and effort was made to increase cultural capacity within OSU researchers, and scientific capacity within CTUIR. A previous study found levels of PAHs within traditionally smoked salmon, a tribally important food, to be up to 400 times higher than PAH levels in commercially smoked salmon, raising concerns amongst CTUIR members about their exposure from eating traditionally smoked salmon. To address these concerns, 9 CTUIR tribal members participated in a metabolism study. Each participant ate 50g of traditionally smoked salmon and provided 5 urine samples over a 24 hour period. During the recruitment process, participants requested their individual results. Using best practices, individual reports were designed that were clear, with an emphasis on cultural sensitivity. Results were presented in visual and text form and

individual data was contextualized within the study population. Reports were designed to incorporate feedback from researchers, tribal liaisons and outreach and engagement specialists.

(1-35) Community Engagement and Research Translation Cores Working Together to Foster Healthy Pregnancy in Puerto Rico

Carmen Milagros Velez Vega – University of Puerto Rico

Liza Anazalota del Toro - University of Puerto Rico

Phil Brown, Northeastern University

Julia Brody - Silent Spring Institute

Colleen Murphy - University of Puerto Rico

The Community Engagement Core works with participants to provide materials such as a healthy products brochure "PROTECT Yourself: Keeping Harmful Chemicals Out of Your Life." The CEC maintains ongoing communication and presentations both with participants and clinicians at the community health centers from where we recruit participants. Working with March of Dimes, we participate in their annual march. The CEC made a documentary "36 Semanas" ("36 Weeks") about healthy pregnancy. CEC members present widely at conference, including winning the People's Choice Award at EPA's Community Involvement Training Conference. The CEC works with the Data Core on report-back of participant data to individual participants, as well as aggregate data to community meetings. The Research Translation Core sponsors conferences that bridge many audiences in environmental health: Social Science-Environmental Health Collaborations Conference, Petrochemical America conference, and Reproductive Health and the Environment Symposium (working with the Resilient Sisterhood Project in Boston). The RTC is developing a bulletin on "Environmental Factors in Reproductive Health" to be distributed to health professionals throughout Puerto Rico. The RTC is also surveying physicians about their knowledge of environmental factors in health.

(1-36) Reporting Data to Participants in Biomonitoring and Household Exposure Studies: Its Use in the PROTECT Study (Puerto Rico Test Site to Explore Contamination Effects)

Julia Brody[1], Phil Brown[2], Carmen Milagros Velez Vega[3], and Liza Anzalota del Toro[3]

[1] Silent Spring Institute

[2] Northeastern University

[3] University of Puerto Rico

Environmental exposure assessment in health studies and public health monitoring programs is shifting increasingly from testing for pollutants in air, soil, and water to personal exposure and biomonitoring methods that detect ever lower concentrations of a growing array of chemical contaminants -- in blood, urine, breast milk, umbilical cord blood, breathing zone air, house dust, hair, and hand wipes. Often, the health implications of these personal exposure measurements and the effectiveness of exposure reduction strategies are uncertain. As a result, personal exposure research raises ethical questions about whether and how researchers should report individual results to study participants while adhering to and balancing the goals of ethical guidelines for human subjects research: specifically, respecting participants' autonomy, maximizing benefit, and avoiding harm. Scientists and IRBs must weigh the value of reporting results, which may inform and empower participants to change personal behaviors and contribute to community health policies, versus the potential for harm, for example, from misplaced worry, stigma, or ineffective action. They must also consider legal or financial issues that may arise, particularly when contaminants are detected in private spaces, such as a home.

Our Community Engagement Core's prior work in this field includes 2 studies of our own, re-interviews of participants in 8 other studies, and development of innovate print and digital report-back materials. We find that nearly all participants want to learn their results and do not experience psychological distress from that. Participants report being pleased to learn their personal exposures, have a high degree of understanding of the data, use the data for personal changes in consumption, and employ the data for social change in matters such as permitting and regulation. We find that report-back fulfills the promise of full and informed consent, and supports a democratic right-to-know process. Report-back benefits for researchers are increased research participation and retention, as well as greater public trust in the specific project and in science in general.

This background provides the model for reporting back data to participants in the PROTECT Study (Puerto Rico Test Site to Explore Contamination Effects), a cohort of more than 800 women that continues to add participants, in an attempt to find effects of contaminants on pre-term birth. Puerto Rico has a pre-term birth rate of 20%, 1.5 times that of the US, and there is exposure to contamination from a long history of pharmaceutical and other industries, with 150 contaminated sites that include 14 active Superfund sites on the island. Developing report-back materials and administering them to participants has been effective in unifying PROTECT's Human Subjects and Sampling Core that recruits participants and gather data from them, the research projects that use the human subjects data and gather additional environmental data, the Data Management and Modeling Core that helps assemble data for the report-back process, the Community Engagement Core that will conduct the report-back process, and the Research Translation Core that will disseminate findings and help other Superfund Research Program and other environmental health researchers to understand the importance of report-back and develop their own techniques. Report-back packages are presently being developed. When participants receive their data they will also be interviewed to learn their responses to and use of the material.

(1-37) The Center for Environmentally Sustainable Mining: An Industry-Academic Cooperative to Promote Environmental Stewardship of Mining Sites

Sarah T. Wilkinson, Denise Moreno Ramírez, Karletta Chief, Julia W. Neilson, Mark L. Brusseau, Janick Artiola, Raina M. Maier

University of Arizona Superfund Research Program

Mining companies are realizing that effective mitigation of environmental impacts from their operations will require innovative and sustainable solutions. In recognition of this need, the University of Arizona Superfund Research Program (UA SRP) has partnered with the UA Lowell Institute of Mineral Resources, a global center of excellence in mining, to create the Center for Environmentally Sustainable Mining (CESM), an industry-academic cooperative. The CESM is designed to bring researchers together with mining industry stakeholders to examine environmental stewardship of mining sites. The mission is to develop research initiatives and educational and professional trainings that address environmental issues related to mining activities in arid and semi-arid environments. A technical advisory committee (TAC) composed of experts from the mining industry has worked with us to prioritize industry needs and direct the activities of the CESM. The UA SRP Research Translation Core is working with the CESM TAC to develop new technologies in the prioritized areas of: 1) mining waste revegetation; 2) remote real-time water monitoring and remediation; 3) dust monitoring, modeling, and mitigation; and 4) development of mining modules for educational needs ranging from communities to continuing education. Two examples of UA SRP-CESM efforts include a revegetation initiative which has led to support from three major mining companies to examine biogeochemical indicators of vegetation success on their sites. Additionally, we are developing and piloting mining and environmental educational modules targeted to tribal colleges with the goal of increasing student interest in obtaining education in STEM and mining-related fields. This industry-academic cooperative expands the impact of UA SRP research and is effecting change in current mining industry practices to better protect human health and the environment.

(1-38) Fostering Effective Science Communication Skills: A Building Block for Collaboration and Innovation

Sarah Yelton, MS; Kathleen Gray, MSPH; Dana Haine, MS

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Increasingly, scientists are called upon to communicate their research results to the public to inform decision-making around specific issues and improve scientific literacy more generally. Despite being well trained in their science disciplines, often they are inexperienced in communications. To address this gap and with support from an NIEHS supplemental grant, the UNC SRP RTC staff developed a short course on science and risk communication, preparing SRP graduate and postdoctoral trainees to effectively communicate research findings with non-academic audiences.

Following three skill-building sessions, UNC SRP trainees participated in two professional development workshops for science teachers as well as a large public science festival on the UNC campus. Collaboration between UNC SRP PIs and RTC staff was essential, and resulted in activities featuring current research and translation efforts aimed at understanding how North Carolinians can be exposed to toxic metals like arsenic and how their bodies respond to that exposure. Drawing on their individual research backgrounds, SRP trainees assisted RTC staff in developing educational materials, shared information generated by the UNC SRP on well water contamination in North Carolina, presented their research, and provided lab tours. Lessons developed by the RTC in conjunction with SRP investigators were also featured during the teacher workshops.

These science and risk communication experiences, which were a highlight of our training activities this year, built trainee confidence in interacting with non-academic audiences and created a skilled cohort of trainees ready to engage in future translation and engagement activity. These efforts have also opened doors to future collaboration around science communication training with SRPs at Kentucky and Duke.

(1-39) Collaboration to reduce arsenic exposure from private well water in New Jersey

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Arsenic is naturally occurring in the groundwater aquifers of northern NJ at levels often unsafe for human consumption. Over one million people rely on private well water for drinking in NJ. Since 2011 a collaborative partnership between Columbia's SRP and NJ state and local agencies has been growing and evolving based on the fully shared long-term objective of reducing unhealthy levels of arsenic exposure from well water. Collaboration has opened channels of communication and led to a range of small projects and joint activities for which partners have demonstrated a willingness and creativity to leverage collective resources for mutual public health and research interests. For example, collaboration between RTC and NJ partners to develop a series of educational arsenic videos led to a joint NJDEP-RTC-CEC project to survey private well owners in NJ, similar to a CEC survey in Maine, with the goal of better understanding the socio-behavioral and structural factors that influence well testing and treatment behavior and, consequently, arsenic exposure through drinking water. This survey has now led to a second, focused on the same population, including a well testing component. Future joint projects include development of a smartphone app to guide NJ well owners on testing based on nearby well testing results. SRP has been a steady partner for groundwater arsenic work in NJ, recently providing support for a NJ Department of Health application for CDC funding over 5 years to expand work on private well water quality issues, including an annual budget for further collaboration with Columbia on research and outreach projects focused on arsenic testing and treatment by private well owners and extending partnerships through a NJ private well consortium.

(1-40) Community Gardens: a global view of the balance of harm from toxicants and public health benefits

Al-Delaimy WK, Webb M.

University of California San Diego, UCSD Superfund P42 ES010337.

Community gardens improve diet and physical activity by encouraging the members of the garden to be involved in the activity of gardening and getting educated about healthy fruits and vegetables. However, there are other complex factors that would impact the perceived public health benefits. Balancing the harms and benefits of community gardens and recommendations for further research in this area is needed. Toxicants in soil have been shown to be absorbed by plants and staples such as rice in such soils. There is also discrepancy in psychosocial studies that either report concerns by gardeners about these toxicants or report complete lack of education about it. While in less developed countries the community gardens provide some sustenance and income for growers and are stigmatized as being associated with poverty, they are viewed more positively and serve to decrease weight and improve life style in the more developed countries. There is evidence of a significant decrease in BMI and increase in education and consumption of fruits and vegetables among those involved in community gardens. Community gardens serve as an encouragement to eat less processed, highly calorific foods, and eat more fresh produce with less preservatives and calories. It also serves as empowerment and a source of cohesion among the community with positive psychological impact. If the soil toxicants can be properly addressed or avoided, community gardens offer a clear advantage and a tangible solution to the epidemic of obesity, especially in the urban areas of the more developed countries. Basic science research is needed to develop accurate and cheap measures of soil toxicants and population research is needed to evaluate the health benefits of community gardens.

(1-41) Arsenic in Private Well Water – Collaboration on Community Engagement in Maine

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Since 2006 the Columbia University Superfund Research Program has been collaborating with state agencies in Maine on the issue of arsenic in groundwater; reduction of arsenic exposure from private wells in Maine has been a focus of the Community Engagement Core since 2012. Roughly half the population of Maine obtains their drinking water from a private source and in at least 44 towns of Maine more than 25% of wells tested exceed the arsenic MCL of 10 µg/L. Our 2013 survey with partner Maine Geological Survey (MGS) of 452 private well households identified several factors significantly associated with arsenic testing behavior; messages targeted to these factors may help to motivate well owner testing. In order to assess the effect of different motivational messages on well testing, a mass mailing intervention was developed in collaboration with MGS and the Maine Center for Disease Control and Prevention (CDC). The focus of the intervention is Waldo County of Maine, where about 78% of residents rely on private well water and state lab testing reveals town arsenic occurrence rates as high as 37% and wells with concentrations as high as 280 µg/L. Different versions of a mailer were developed to alternately emphasize arsenic risks, local norms (both for well contamination and for testing behavior), and to strengthen ability beliefs. These mailers will be sent by Maine CDC to 2000 randomly selected addresses in July 2015. Return postcards will track requests for more information and for a subset, requests for test kits, and a mailed follow-up survey in November will seek self-reported testing behavior change and feedback on the mailer content. Lessons learned will inform future motivational materials and outreach.

(1-42) Tackling Arsenic Exposure from Private Well Water in Rural American Communities

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In the United States, the health risks from the well-known As hazard in private well water are overlooked. All American taxpayers contribute to the costs associated with the regulatory process embodied in the Safe Drinking Water Act. However, 43 million Americans, mostly from rural areas and relying on private wells, do not receive the benefits of having guaranteed safe drinking water. Despite regulations on testing for As in a few states, the responsibility to ensure water safety of private wells still falls on well owners.

Not rare in the Earth's crust, geogenic As in well water above the EPA's Maximum Contaminant Level of 10 microgram per liter can often affect 20 to 30 percent of wells, and thus, the population in many rural communities. At present, the prediction of individual well water As level is fraught with high uncertainty, even in areas where detailed hydrogeochemical studies have been done. Thus, testing to identify individual households at risk is the first step of several corrective actions. However, persistent optimistic bias against testing and other barriers including cost for treatment mean that a large percentage of the population remains exposed. In areas with high As occurrence, there will always be households either unaware of their exposure due to not testing, or be aware of their exposure but remain exposed due to not treating or switching to bottled water. To ensure vulnerable populations, such as low income families with children and pregnant women, are not exposed to As in their drinking water, interventions such as public assistance with As exposure reduction and encouraging alternative low-As water supplies may be required. The efficacy of these interventions warrants further research.

(1-43) Spatiotemporal Assessment of the Link between the Karst Groundwater Sources and the Tap Water Point of Use

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Karst water systems have a long and extensive history of contamination. Heterogeneity of karst terrains, high water productivity of karst aquifer, and easy entry of chemicals into the system pose significant risks for exposure and lead to potential public health impact. Of particular concern is the pollution with chlorinated volatile organic compounds (CVOC) and phthalates because they are ubiquitous in the environment and have been identified as potential precursors of preterm birth. This study aims at determining the link between contamination in karst groundwater sources and pollution in the tap water point of use via statistical analysis. GIS technology is used to assess spatiotemporal changes of the target contaminants in the groundwater and the tap water samples. The analysis integrates data gathered from regulatory agencies and current groundwater and tap water samples collected from residential homes. Results show higher detection frequencies and concentrations of CVOC in groundwater samples than tap water. Phthalate contaminants, on the other hand, show greater detection frequencies and concentrations in tap water than groundwater. Lower CVOC detection and concentrations in tap water are indicative of dilution processes and contaminant losses. Higher detection frequencies and concentrations of phthalates in tap water suggest additional contaminant sources. These results indicate that the relation between contaminants in the source water and tap water depends on the type of contaminant and their sources. Future research will develop statistical correlation models between groundwater and tap water pollution, and will assess additional sources of contamination.

RESEARCH TRANSLATION: This work has developed strong relationships with owners and users of groundwater wells, as well as members of the pregnant women cohort where tap water is sampled. Information is provided to them about the sampling and analysis processes, the results, and meaning of these results in the context of health impacts. As part of this, a brochure was developed about tap water quality to increase topic awareness. This brochure is handed to the members of the cohort, as well as other community members. Our work also generates and provides reports on the quality of groundwater at sampled sites. Results are also communicated to the broader scientific and regulatory community in form of publications and presentations. The findings of this research have been presented in different events to diverse audiences such as: the 2014 EPA Region 2 Citizen Science Workshop, 2014 SACNAS Conference and the Hatillo Community from the Añasco municipality.

(1-44) Metabolism and Excretion Rates of Parent and Hydroxy-PAHs in Urine Collected After Consumption of Traditionally Smoked Salmon for Native American Volunteers (KC Donnelly Externship Award Recipient 2015)

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There are limited studies presenting data about the excretion rates of polycyclic aromatic hydrocarbons (PAHs) and hydroxy-polycyclic aromatic hydrocarbons (OH-PAHs) after oral exposure. This study investigated metabolism, excretion rates, and half-lives of 4 parent PAHs and 10 OH-PAHs after the consumption of Native American traditionally smoked fish. Nine members of the Confederated Tribes of the Umatilla Indian Reservation consumed 50g of traditionally smoked salmon for breakfast and 5 urine samples were collected over a period of 24hr. The concentration of OH-PAHs increased with maximum values after 3 to 6hr post-consumption. Maximum values detected in urine ranged from 349ng/g creatinine for 1-OH-pyrene to 43.9µg/g creatinine for 2-OH-naphthalene. Although volunteers followed a controlled diet, there appeared to be secondary sources of naphthalene and fluorene, which led to excretion efficiencies greater than 100%. Parent PAHs were detected in urine and excretion efficiencies ranged from 13% for phenanthrene (and its metabolites) to 240% for naphthalene (and its metabolites). The half-lives for PAHs ranged from 1.4hr for retene to 3.3hr for pyrene. The half-lives for OH-PAHs were higher and ranged from 1.7hr for 9-OH-fluorene to 7.0hr for 3-OH-fluorene. The concentrations of most parent PAHs and OH-PAHs returned to the background concentrations 24hr post-fish consumption.

(1-45) Discovery of a Conserved Long Noncoding RNA Upregulated in Response to the Xenobiotic Activation of the Aryl Hydrocarbon Receptor

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The aryl hydrocarbon receptor (AHR) is necessary for vertebrate embryonic development, but can be inappropriately activated by a diverse group of chemicals. Understanding the downstream transcriptional events that occur after activation of AHR and play a causal role in toxicity pathways is a necessary advancement to accurately impact and guide remediation strategies. To identify downstream AHR targets, RNA was isolated from 48hpf zebrafish embryos (exposed to 10uM 7,12-

benz[a]anthracene quinone) and sequenced using Illumina sequencing. One of the most elevated transcripts was a novel long noncoding RNA (lncRNA), we named Sox9b-lncRNA due to its adjacency 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 predominant Sox9b-lncRNA transcript has been sequenced, contains 3 exons, and is 467nt long. The genomic architecture of the lncRNA relative to Sox9 is conserved in mammals, suggesting similar mechanisms of regulation. Putative AHR response elements have also been identified in the Sox9b-lncRNA promoter. We hypothesize that the conserved Sox9-lncRNA is a direct AHR target gene that transcriptionally represses Sox9 upon induction by strong AHR ligands to produce target organ-specific toxicity. In support of this hypothesis, developmental exposure to 1nM TCDD in AHR2-null zebrafish lines showed Sox9b-lncRNA induction requires AHR2. Additionally, whole mount *in situ* hybridization showed that Sox9b mRNA and Sox9b-lncRNA are expressed in overlapping tissues during development. Furthermore, Sox9b-lncRNA morphants exposed to 1ng/mL TCDD, have a two-fold increase in Sox9b expression, suggesting a relief in repression.

(1-46) The Role of the NMD RNA Degradation Pathway in Arsenic-Induced Cell Death

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Inorganic arsenic compounds are common toxicants found in the water supply. Prenatal exposure is linked to impaired neural development, learning and memory. Arsenic may act through aberrant activation of homeostatic mechanisms, including 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. We 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. My mentor's laboratory recently showed that 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 (1). Strong ER stress suppresses the magnitude of NMD, allowing for full UPR activation. In my own research, I discovered that arsenic exposure suppresses NMD factor expression in HeLa cells. 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. My findings suggest that NMD raises the threshold for arsenic-induced cell death. Future efforts will be directed towards identifying small molecules that activate NMD in order to protect humans, plants and animals at risk of exposure to high levels of arsenic.

References

1. Karam R, Lou CH, Kroeger H, Huang L, Lin JH, Wilkinson MF. The unfolded protein response is shaped by the NMD pathway. *EMBO Rep*. 2015 May;**16(5):**599-609.

(1-47) Association between Phenols and Parabens & Reproductive and Thyroid Hormones

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Introduction: Phenols and parabens are ubiquitous environmental contaminants. Evidence from animal studies suggest they may be endocrine disruptors. The association of phenols and parabens with reproductive and thyroid hormones was examined in the first 103 pregnant women (148 observations) recruited for the prospective cohort, the Puerto Rico Testsite for Exploring Contamination Threats (PROTECT). Research translation: Ongoing work is carried out with PROTECT's research translation core to translate results to the lay public and relevant stakeholders. Methods: Urinary exposure biomarkers (bisphenol A, triclosan, benzophenone-3, 2,4-dichlorophenol, 2,5-dichlorophenol, butyl, methyl and propyl paraben) and serum hormone levels (estrogen, progesterone, sex hormone-binding globulin, free triiodothyronine, free thyroxine and thyroid stimulating hormone) were measured at two time points during pregnancy (16-20 weeks and 24-28 weeks). Linear mixed models with random intercept were constructed to examine the associations between the hormones and the exposures, controlling for specific gravity, maternal age, BMI and education. Progesterone, thyroid stimulating hormone and all exposure biomarkers were log-transformed. The results were additionally stratified by visit. Results: Sex hormone-binding globulin was positively associated with methyl paraben (p value = 0.02); free thyroxine (FT4) was positively associated with butyl paraben (p value = 0.01) and bisphenol A (p value = 0.04); free triiodothyronine (FT3) was negatively associated with benzophenone-3 (p value = 0.04); and, estrogen was negatively associated with butyl paraben (p value = 0.05). Suggestive, but not statistically significant, associations were also observed in this exploratory analysis. Conclusions: In this group of women, phenols and parabens may be associated with reproductive and thyroid hormones which may lead to adverse health effects, but additional research is required.

(1-48) Identification of new components in cadmium-specific signaling networks

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Uptake of toxic heavy metals and metalloids in plants primarily occurs through transporters designed to import essential molecules, with cadmium uptake mediated by zinc and iron (ZIP) transporters and arsenic uptake through organic phosphate transporters. Therefore plants have developed a complex and dynamic system to detoxify and sequester heavy metals to minimize detrimental effects. Exposure to heavy metals causes rapid and diverse changes in gene expression to control and manipulate the detoxification machinery. While much of the chelation and transport pathway has been identified, the signaling network behind this rapid gene regulation is largely unexplored. In order to uncover components of the cadmium-specific signaling network we generated an Arabidopsis line carrying a cadmium-inducible promoter (SULTR1;2) fused to a luciferase reporter gene, which was then mutagenized using ethyl methanesulfonate (EMS). Mutants were then screened for shifts in luciferase response compared to the parental control. Identified mutants were categorized into three groups based on response: super response to cadmium (SRC), constitutive response to cadmium (CRC), and non-response or reduced response to cadmium (NRC). Two non-response mutants, NRC1 and NRC2, have been mapped and characterized as γ-glutamylcysteine synthetase and glutathione synthetase, respectively, both of which are involved in the generation of

chelators essential for heavy metal detoxification. The NRC2 mutation is the first viable recessive mutation in the glutathione synthetase gene. We are currently working to map and characterize two additional mutants, one super response mutant, SRC1, and one constitutive response mutant, CRC1. We are using bulk segregant analysis to map the mutation through backcrossing with the parental control line. We are also characterizing the mutants for growth phenotypes in heavy metal contaminated and sulfur limited conditions.

(1-49) Development of Magnetic Nanocomposite Materials for the Rapid Removal of PCBs from Contaminated Water Sources

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For the capture of organic pollutants from water sources, polyphenolic-based magnetic nanocomposite systems were developed using two distinct methods. The polyphenolic moieties were incorporated to create high affinity binding sites for PCBs within the nanocomposites. The first method utilized a surface initiated polymerization of poly(ethylene glycol)-based and polyphenolic-based crosslinkers on iron oxide magnetic nanoparticles to create a core-shell nanocomposite. The second method utilized a bulk polymerization method to create macroscale films that were composed of iron oxide nanoparticles incorporated into a polyphenolic-based polymer matrix, and then, these films were processed into microparticles. Both methods produce nanocomposite materials that can specifically bind chlorinated organics, can 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, providing a green and cost-effective alternative for PCB remediation. The polyphenol functionalities used to bind organic pollutants were quercetin multiacrylate (QMA) and curcumin diacrylate (CDA), which are acrylated forms of naturally occurring nutrients with expected affinity for chlorinated organics. These were then crosslinked with poly(ethylene glycol) 400 dimethacrylate (PEG400DMA) to form biomimetic PCB binding domains, as those observed in antibodies in the human body. 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 chlorinated organic pollutant to determine binding affinity and capacity, and this was quantified using GC-ECD. It was demonstrated that the materials effectively bound PCBs, and the addition of the polyphenols was shown to have increased affinity.

(1-50) Developmental Toxicity and AHR Induction of Nitrated PAHs

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Nitrated polycyclic aromatic hydrocarbons (NPAHs) are byproducts of combustion and the reactions of PAHs in the atmosphere. NPAHs are present in the environment, yet pose an unknown risk to human health. The developing zebrafish (*Danio rerio*) model was used to evaluate the toxicity of a structurally diverse set of 27 NPAHs. Additionally, their individual activity towards the aryl hydrocarbon receptor (AHR) was evaluated. We assessed all commercially-available NPAHs, as well as two NPAHs synthesized in-house, which are not commercially available. Zebrafish embryos were exposed from 6 to 120 hours post fertilization (hpf) to a dilution series of individual NPAHs and evaluated for 22 developmental endpoints. AHR activation was determined via CYP1A immunohistochemistry (IHC), and compared to predicted docking scores from *in silico* AHR models. We observed a range of statistically significant morphological changes, including pericardial and yolk sac edemas, delayed developmental progression, axis malformations, and mortality. Some NPAHs did not induce observable

developmental toxic responses, while others produced concentration-dependent toxicity. The tested NPAHs also exhibited a range of AHR binding and activation patterns, as indicated by IHC. We also compared the developmental toxicity of two amino PAHs (potential metabolites of NPAHs) to the corresponding NPAHs, and observed equal or increased toxicity in the amino PAHs compared to the corresponding NPAHs. This indicates the need for further study of NPAHs as environmental contaminants with the potential for adverse human health effects, as well as further investigation into the mechanisms-of-action of NPAHs.

(1-51) Early-life exposure to organophosphate flame retardants alters behavior across the lifespan in zebrafish.

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Exposure to organophosphate flame retardants (OPFRs) is widespread in humans, and the extent of their toxicity and whether it is comparable to the neurotoxicity of organophosphate (OP) insecticides is poorly characterized. This study seeks to examine whether developmental exposure to one of two OPFRs, TPP and TDCPP, can alter behavior at multiple life stages, and to compare these toxicities to those of a well-studied OP insecticide, chlorpyrifos. Zebrafish were exposed to 0.03 or 0.3µM of TPP, TDCPP, or chlorpyrifos from 0-5 days post fertilization. Vehicle control consisted of 0.03% solution of DMSO. At 6 days post fertilization, larvae were tested on a locomotor assay. Separate cohorts of 6 day old larvae that were not tested on the larval assay were allowed to grow to adulthood. At 12 weeks post-fertilization, these adult zebrafish were tested on a battery of behavioral assays that included tests of novel environment exploration, startle habituation, social affiliation, and predator escape. Developmental exposure altered zebrafish behavior across the lifespan. Larval zebrafish exposed to the 0.03µM doses of chlorpyrifos or TDCPP exhibited significant ($p<0.05$) hyperactivity in the locomotor assay. Organophosphate exposure was significantly ($p<0.05$) associated with an altered time course of adult zebrafish behavior in the novel environment, startle habituation, and social affiliation assays. Predator escape behavior was significantly ($p<0.05$) reduced in fish exposed to the 0.3µM dose of TDCPP. Exposure also caused hyperactivity in adult fish, with fish exposed to the 0.3µM dose of TDCPP exhibiting significantly ($p<0.05$) elevated locomotor behavior in the novel environment assay. These findings support broader research implicating organophosphate compounds in developmental neurotoxicity.

Research Translation Component: The research done here adds to our understanding of the risks associated with exposure to flame retardants early in life. This is being conveyed to the broader community via our Research Translation Core.

Recent publications/References: Oliveri AN, Bailey JM, Levin ED. “Developmental Exposure to Organophosphate Flame Retardants Causes Behavioral Effects in Larval and Adult Zebrafish.” Under review.

(1-52) Molecular changes in fathead minnows induced by single and multiple contaminant exposures

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High levels of contaminants of concern are measured in aquatic organisms at contaminated sites around the world, potentially affecting survival, growth and reproduction. Forecasting the biochemical effects of mixture exposure is challenging and was attempted here at the transcriptomic level. We conducted a 21-d feeding study to examine molecular effect endpoints in fish (*fathead minnows*). Fish were fed worms exposed to 5 individual organochlorine chemicals featuring varying K_{ow} values, including triclosan, triclocarban, fipronil, dieldrin and *p,p'*-DDE or two mixtures, one with the organochlorine pesticides (OCPs)

dieldrin and *p,p'*-DDE and a second one with triclosan, triclocarban and fipronil. Uptake patterns of chemicals by fish were not different when fish were fed worms exposed to either single chemicals or a mixture of chemicals showing steady-state levels within 7 to 14 days of feeding. However, there was little overlap in gene expression profiles in mixture experiments compared to the single chemical experiments. For example, the two organochlorine pesticides elicited different modes of action, and this was reflected by an observed lack of overlap in biological processes affected in exposed fish. Treatments with triclosan, triclocarban, and fipronil impacted several shared processes, but each chemical also had an individual set of altered processes. These results suggest that fundamental biochemical processes related to health and reproduction are affected by these contaminants and that single compound exposure information cannot necessarily serve to predict the effect of exposures to mixtures of pollutants.

(1-53) Pulmonary inflammation and injury caused by environmentally persistent free radicals is mediated through activation of the aryl hydrocarbon receptor

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Combustion of waste at Superfund sites results in the formation of environmentally persistent free radicals (EPFRs), which occur when pollutants are chemisorbed to particles containing redox-active transition metals. Residents near Superfund sites are exposed to these EPFRs through windblown dust, ingestion of soil and sediments, and through emissions occurring from the on-site treatment of contaminants. We have shown that EPFRs produce ROS and when inhaled, lead to pulmonary inflammation, epithelial cell injury and oxidative stress. Prior studies demonstrated that human bronchial epithelial cells (BEAS-2Bs) exposed to EPFRs had increased activation of the aryl hydrocarbon receptor (AhR). However, AhR activation was not reduced by inhibiting cellular uptake, suggesting that AhR activation was induced by an intermediate rather than directly by EPFRs. Thus, our hypothesis was that products of oxidative stress occurring after EPFR exposure stimulate AhR activation, and this AhR activation mediates pulmonary inflammation. To test this hypothesis, BEAS-2Bs were treated with EPFRs and IL-6, TNF-α and ROS were measured in the medium. IL-6, TNF-α and ROS were all increased in the medium of cells exposed to EPFRs versus control cell medium. A subset of cells were also co-treated with an antioxidant or an AhR antagonist, to determine whether oxidative stress and/or AhR activation contributed to an increased cytokine production. EPFR induced AhR activation was dependent upon oxidant production, but ROS production was also somewhat regulated by AhR activation. Preliminary data showed that 8-isoprostane, a lipid oxidation product formed during oxidative stress, is increased in cells treated with EPFRs. Ongoing experiments are aimed at determining whether 8-isoprostane activates the AhR to promote the inflammatory responses observed after EPFR exposure.

(1-54) The Effect of the Nature of Metal Oxide on the Formation and Persistency of Environmentally Persistent Free Radicals

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Certain aromatic compounds (chlorobenzenes, chlorophenols, etc.) when adsorbed on metal oxide particles, can form free radicals. These free radicals decay very slowly in the atmosphere and retain significant and measurable free radical activity even after many weeks. These type of free radicals are called environmentally persistent free radicals (EPFR). It was reported

that airborne and combustion generated particles contain EPFR. This particulate matter containing EPFR, upon inhalation, are shown to affect the respiratory and cardiovascular functions in experimental animals.

Here, we present the results of the free radical formation on a model particulate matter. This model was prepared using iron oxide and silica particles upon dosing with chlorobenzenes and substituted phenols at 230°C. The results of the free radical concentration and its lifetime in ambient air, studied using electron paramagnetic resonance (EPR) on particles containing different iron oxide/silica ratio (0.25 -5%), will be presented. The comparison with the results of the copper oxide system dosed with chlorobenzenes and substituted phenols at 230°C at different copper oxide / silica ratio will also be discussed. Iron is usually the dominant transition metal in airborne particles as well as in emissions from some types of combustion sources. Therefore, the results of the formation and stabilization of EPFRs involved in the reaction with iron oxide, will increase our knowledge about the health and environmental impacts of these type of EPFR, formed by the reaction of metal oxide with substituted aromatic compounds.

(1-55) Arsenic mixture exposure modulates innate immune signaling in human primary bronchial epithelial cells

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Arsenic in drinking water increases morbidity and mortality from infectious lung disease at high exposure concentrations, and has been associated with adverse respiratory immune responses in US populations. In addition, arsenic (As) has been shown to induce inflammatory responses in cells and in *vivo*. Inorganic arsenic (iAs) is metabolized *in vivo* to monomethlyarsinous acid (MMA), and dimethylarsinic acid (DMA). MMA and DMA are also present in the US food supply, notably in rice and fruit juices. However, the effects of organic arsenic exposure on respiratory immune function, at levels relevant to the US population, are unknown. We exposed differentiated primary human bronchial epithelial cells (HBECs) to varying concentrations of an As mixture representative of levels detected in human serum (50% DMA, 25 % MMA and 25% iAs). Following 6 days of As exposure, we challenged the airway cells with Pseudomonas aeruginosa (Pa), a gram-negative opportunistic bacterial pathogen, and examined cytokine release and RNA expression in the HBECs. The arsenic mixture alone consistently and significantly increased IL-8, CXCL1 and CXCL2 release in a concentration-dependent manner. Both basal expression and maximal induction of cytokines was variable between donors, but Pa induced robust release of all cytokines in all donors tested (N=3). Preliminary results indicate magnified cytokine response to Pa following exposure to the arsenic mixture, but were not significant across all donors. Neither exposure to the arsenic mixture (0-50 ppb total arsenic) nor Pa was cytotoxic as detected by LDH release. Further work will investigate additional donors, as well as global gene expression in arsenic-exposed HBECs exposed to Pa to identify genes that may underlie adverse effects of arsenic on respiratory function in human populations.

(1-56) Linking Remediation to Toxicology – Screening for Toxic Transformation Products Formed During Oxidative Treatment of Superfund Contaminants

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Strong oxidants, such as persulfate, ozone and hydrogen peroxide, are being used more frequently for the remediation of Superfund contaminants including aromatic compounds, perfluorinated chemicals and chlorinated solvents. Although these techniques offer the possibility of cost-effective in situ remediation, oxidation processes produce transformation products that are often more polar and mobile than the contaminants undergoing remediation. In some cases, the transformation

products include functional groups that are known to be toxic, such as aldehydes, nitrosamines, quinones and quinone imines, The large variety of potential transformation products and their occurrence as complex mixtures makes investigation of all possible transformation products impractical. By focusing on transformation products that are expected to be toxic it may be possible to simplify these efforts. To identify transformation products of concern, we are developing assays for reactive transformation products by investigating reactions of compounds with proteins and DNA. The approach is being validated by subjecting common contaminants, such as benzene and aniline, to different oxidative remediation processes. The reactions of transformation products with protein and DNA substructures (e.g. glutathione, deoxy-guanosine), whole proteins (e.g., albumin) and whole proteomes (e.g. mouse liver proteome) are assessed by screening for adduct formation. Liquid chromatography tandem mass spectrometry and high-resolution mass spectrometry are employed in combination with state-of the art approaches, such reactivity-based protein and Cys^{34} adduct profiling, to identify the transformation products produced by each remediation process and assess their potential toxicity.

(1-57) RORγ: the Nexus of Liver Metabolism, Mitochondrial, Bioenergetics, and Acetaminophen Toxicity

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RORγ is one of the core circadian regulators that controls gene expressions to meet metabolic demands throughout the day. Additionally, cistrome of RORγ has showed that it is also one of the key activators for bioenergetics and anti-oxidation defenses. Mice with conditional knock of RORγ in liver are viable under normal conditions but vulnerable to administration of acetaminophen. The underlying pathological mechanisms of acetaminophen toxicity include compromised mitochondrial function and fitness, depletion of endogenous anti-oxidation defenses, and opening of mitochondrial transition pore (MPTP). Respiration and mitochondrial membrane potential are suppressed, while the oxidative stress is increased in the KO mice treated with acetaminophen. Upon the initiation of MPTP, mitochondrial contents such as mitochondria DNA and cytochrome C can be detected in circulation in KO mice. The spewed mitochondrial components trigger and direct innate immune response via activation and recruitment of neutrophils to liver. The combination of MPTP-mediated cell death and overactivation of neutrophils leads to irreversible inflammation and heptatic damage in the RORγ KO mice. These experimental observations illustrate a novel function of RORγ that is likely independent of circadian rhythm. More importantly, the central role of RORγ in mediating cellular bioenergetics and acetaminophen metabolism paves the way for potential therapeutics for acetaminophen toxicity and liver injury.

(1-58) SRP Project 4: Animal models of asbestos-induced mesothelioma

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Malignant mesothelioma (MM) is a highly aggressive, notoriously treatment-resistant cancer usually caused by exposure to asbestos fibers. With estimates of >20 million individuals at risk worldwide, new approaches in disease management and prevention are badly needed. In Ambler, Pennsylvania, there is an elevated incidence of MM linked to decades of asbestos manufacturing, and the presence of an asbestos-contaminated waste site continues to jeopardize the health of residents living in the vicinity. The genetic basis for MM has historically focused on somatic mutations of the tumor suppressor genes *CDKN2A* and NF2 as key alterations influencing initiation and progression. More recently, *BAP1* has been strongly implicated as a major player in MM based on the discovery of germline *BAP1* mutations in two families with a high incidence of MM and other cancers. Moreover, *BAP1* mutations are common in sporadic (non-familial) cases of MM, as well. Previous *in vivo* carcinogenicity studies with crocidolite-exposed heterozygous (+/mut) *Nf2;Cdkn2a* and *Bap1* knockout mice have revealed

that induction of MM is accelerated in these mice compared to that of similarly exposed wild-type littermates. RNA extracted from the peritoneal cavity of crocidolite-exposed *Bap1+/-* mice are being used to identify temporal expression changes connected with asbestos exposure. In an ongoing collaborative chemoprevention study, our *Nf2*;*Cdkn2a* mouse model is being used to determine if flaxseed lignan can delay or lower MM incidence. Finally, we will validate if asbestos remediated via iron chelation results in reduced carcinogenicity in asbestos-exposed mice. These studies represent a comprehensive approach bringing together tumor biology/genetics with epigenetic regulation, which will yield basic insights into mechanisms/interactions that drive MM development and progression, with translational implications for understanding tumor susceptibility and prevention.

(1-59) Spatial Distribution of Hydraulic Conductivities in Heterogeneous Media

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The heterogeneous and anisotropic nature of karst groundwater systems results in varied groundwater flow patterns in space and time, which greatly influence the mobility, persistence, and potential pathways of contaminants toward exposure zones. Hydraulic conductivity is a bulk property of porous media that is used to describe fluid flow through pore spaces or fractures. Thus, its spatial variations reflect the heterogeneity and anisotropic character of the media. This study aims at characterizing spatial variations of saturated hydraulic conductivity (K_s) in karst media as a function spatial scale and flow conditions. Hydraulic conductivities are determined by measuring pressure at various locations under steady-state flow conditions within a saturated confined karst physical lab model at flows ranging from 25 to 750 mL/min. Pressure data is used to calculate hydraulic gradients at various distances. These gradients are used in conjunction with flow data to compute K_s by applying Darcy's Law. Preliminary results show that K_s in the karst media vary greatly over distance and display variable spatial distributions. The distributions differ as a function of flow conditions due to variations in regions of preferential flow paths. The spatial distribution of K_s in laboratory scale models can be ultimately used to identify where contaminants are likely to be mobilized and where they are likely to be stored for later release.

RESEARCH TRANSLATION: This research will generate spatial distribution maps that will aid the visualization of flow, fate and transport characteristics in karst media. These maps serve to facilitate the understanding of complex systems at a basic level for regulatory and community stakeholders. The research, which is its infant stage, will also be disseminated to the scientific community through publications and presentations.

(1-60) The Role of Sulfur as an Environmentally Persistent Free Radical (EPFR) Suppressant

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Environmentally persistent free radicals (EPFRs) are extremely stable radicals that exhibit lifetimes on the order of hours, days and weeks[1]; these radicals cause oxidative stress in biological systems[2] and are an intermediate to polychlorinated-dibenzo-p-dioxin/dibenzofurans (PCDD/F) formation[3]. It is known that sulfates suppress PCDD/F formation[4], though the mechanism of the action is not clear. Within this study we are testing the hypothesis that sulfates suppress EPFR formation.

Presenting experiments are based on the analysis of fly ashes from different incinerators and their comparison with reactions over synthetic "surrogate fly ashes". Two sets of fly ashes were thoroughly characterized for composition, indicating the presence of sulfates. One set, from the U.S. EPA showed a high EPFR concentration, while the other set from China did not.

Since the major compositional difference between the two types of samples was the presence of calcium and sulfur [on the China samples], sulfur was identified as a potential suppressing agent.

Surrogate fly ashes, made to model the composition of the real world samples, were used to study the effect of sulfur addition in both solid and gaseous forms. Development of a procedure/agent preventing formation EPFRs is highly desired, particularly for the thermal remediation of superfund soils.

Research Translation: The Superfund Research Center at LSU focuses on the properties of EPFRs from the chemical and biomedical perspectives. The focus of this work helps form a better picture of the damage caused by EPFRs and how to potentially prevent them from continuing to harm ourselves and future generations. This work is then communicated to the community, teachers and students through a series of workshop presentations relating air pollution and chemistry using Legos.

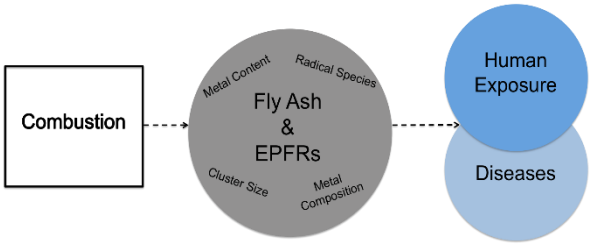
1. Lomnicki, S.; Truong, H.; Vejerano, E.; Dellinger, B., Environmental Science & Technology 2008, 42 (13), 4982-4988.

2. Dellinger, B.; Loninicki, S.; Khachatryan, L.; Maskos, Z.; Hall, R. W.; Adounkpe, J.; McFerrin, C.; Truong, H., Proceedings of the Combustion Institute 2007, 31, 521-528.

3. Dellinger, B.; Truong, H.; Wu, H.; Lomnicki, S.; McCarley, R. L.; Poliakoff, E. D., Abstracts of Papers of the American Chemical Society 2006, 231.

4. Ryan, S. P.; Li, X.-D.; Gullett, B. K.; Lee, C. W.; Clayton, M.; Touati, A., Environ. Sci. Technol. 2006, 40 (22), 7040-7047.

5. Lin, X.; Zhan, M.; Yan, M.; Dai, A.; Wu, H.; Li, X.; Chen, T.; Lu, S.; Yan, J., Chemosphere 2015, 133, 75-81.



(1-61) Hydroxylated and Sulfated Metabolites of Commonly Observed Airborne Polychlorinated Biphenyls Display Selective Toxicity in N27 and SHSY5Y Neuronal Cells

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Polychlorinated biphenyls with lower numbers of chlorine atoms (LC-PCBs) are present in both indoor and outdoor air samples. They are generally more susceptible to metabolic transformations than higher chlorinated congeners, resulting in differences in toxicologic profiles. PCB-exposure is known to cause effects on neurodevelopmental cognition and motor function, and potential roles in neurodegenerative diseases have been proposed. Hydroxylated PCBs and PCB sulfates bind with high affinity to human transthyretin, a major carrier of thyroxine in the central nervous system and in the developing fetus. Furthermore, hydroxylation and subsequent sulfation of the monochlorinated PCB 3 in the rat accounts for more than half of its metabolic fate. We hypothesize that LC-PCBs and their metabolites have toxic effects in neuronal cells, and that these effects differ with cell type. We have studied two neuronal cell lines, the rat-derived dopaminergic N27 and the human-derived SHSY5Y, and compared their toxic responses to treatment with four PCBs that are commonly observed in air (PCBs 3, 8, 11, and 52) and their hydroxylated and sulfated metabolites. Responses in the human hepatocyte HepG2 cell line were also compared, with cell viability determined by the reduction of MTT. Initial results indicated that the hydroxylated PCBs were usually more toxic to all tested cells than either the corresponding parent PCB or PCB sulfate, with greater effects seen in the

N27 cells. PCB 52 sulfate was, however, an exception, since its toxicity in N27 cells was similar to that seen with the hydroxylated congener. This work highlights the importance that hydroxylated and sulfated PCB metabolites may have when considering exposures and risks of neurotoxicity of airborne PCBs.

(1-62) Androgen Action in Pituitary Gonadotropes

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Androgens such as testosterone, which act through androgen receptor (AR), are critical for many aspects of male reproductive function. In males, androgens are produced by the testis in response to pituitary hormones, which in turn are produced in response to secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus. GnRH and its receptor, GnRHR, are essential for fertility. In male mice, androgens act in the pituitary to increase expression of GnRHR, sensitizing the pituitary to GnRH stimulation; conversely, removal of endogenous androgens by castration reduces GnRHR. To further investigate the role of pituitary AR in male reproductive function, we utilized Cre-loxP technology to selectively delete AR from pituitary gonadotropes and thyrotropes (PitARKO). Male PitARKO mice experience delayed puberty, but exhibit normal sperm count, serum hormone levels, and copulatory behavior. However, the effect of castration on GnRHR mRNA levels observed in wildtype mice is not seen in PitARKO males, indicating a physiological role for AR in regulating GnRHR expression. To determine the mechanism through which AR regulates GnRHR, we utilized the LβT2 immortalized cell line, which represents mature pituitary gonadotropes. We mapped induction of GnRHR by AR to the -600 bp region of the GnRHR promoter, and identified two hormone response element half sites at -159 and -499 bp that are required for this effect. Both the ligand- and DNA-binding domains of AR are required for induction of GnRHR, suggesting that AR binds directly to the GnRHR promoter to regulate its expression. Understanding the function of pituitary AR in male reproduction, including its regulation of GnRHR, will provide insight into the mechanisms through which environmental androgenic compounds may disrupt normal endocrine function.

(1-63) The effects of Cadmium on adult neurogenesis and hippocampus -dependent memory in mice

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Adult neurogenesis occurs in the subgranular zone (SGZ) of the dentate gyrus in the hippocampus and subventricular zone (SVZ) along the lateral ventricles in mammalian brains[1]. It plays an important role for hippocampus-dependent memory and olfaction[1]. The effect of neurotoxicants on adult neurogenesis is just beginning to be elucidated. Cadmium (Cd) is a heavy metal with a long biological half-life in humans (from ten to thirty years) and common to Superfund hazardous waste sites. Cd is a neurotoxicant and its exposure may be associated with cognitive and olfactory impairment in humans[2-5]. However, little is known regarding the molecular and cellular mechanisms of Cd neurotoxicity. The goal of our study is to investigate the effects of cadmium on olfaction and cognitive function with a focus on its effects on adult neurogenesis. We found that exposure of low concentrations of Cd decreases cell number and cell proliferation, but increases apoptosis in cultured adult neural stem cells. By using MAP Kinases signaling pathway inhibitors and adult neural stem/progenitor cells (aNPSCs) prepared from JNK3 knock-out mice, we found that the JNK and p-38 MAPK signaling pathways are critical for Cd neurotoxicity in aNPSCs. Furthermore, in vivo Cd exposure also significantly decreases the survival of aNPSCs and impairs short-term spatial memory in adult mice. Our data suggests that Cd exposure can impair adult neurogenesis and hippocampus-dependent cognitive function. These studies provide new insights concerning molecular and cellular mechanisms of Cd neurotoxicity, and partially fulfill UW SRP's mission of mechanistic-based toxicology studies on neurotoxic heavy metals.

1. Altman, J.; Das, G. D., Autoradiographic and histological evidence of postnatal hippocampal neurogenesis in rats. J Comp Neurol 1965, 124, (3), 319-35.

2. Mendez-Armenta, M.; Rios, C., Cadmium neurotoxicity. Environ Toxicol Phar 2007, 23, (3), 350-358.

3. Alessandria, I.; Pennisi, M.; Cataudella, E.; Frazzetto, P. M.; Malaguarnera, M.; Rampello, L.; Rampello, L., Neurotoxicity in Cadmium-Exposed Workers. Acta Medica Mediterr 2012, 28, (3), 253-256.

4. Ciesielski, T.; Bellinger, D. C.; Schwartz, J.; Hauser, R.; Wright, R. O., Associations between cadmium exposure and neurocognitive test scores in a cross-sectional study of US adults. Environ Health-Glob 2013, 12.

5. Mascagni, R.; Consonni, D.; Bregante, G.; Chiappino, G.; Toffoletto, F., Olfactory function in workers exposed to moderate airborne cadmium levels. Neurotoxicology 2003, 24, (4-5), 717-724.

(1-64) pH-responsive Membrane Immobilized Iron-Based Particle Systems for PCB Degradation

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The remediation of PCBs is a critical issue for human health due to their toxic nature and extreme chemical persistence. Despite being prohibited by 170 countries in 2008, about 0.2 million tons of PCBs still remain in the environment. The combination of reductive and oxidative pathway for conversing PCBs to less-toxic or non-toxic products has been demonstrated an effective way for PCBs degradation.

Zero-valent iron has been largely studied in reducing COCs in groundwater, second metal (Pd or Ni) can be added to form bimetallic nanoparticles (NPs) for PCBs dechlorination. The hydrogen, generated from redox reaction between iron and water, gets activated by Pd for hydrodechlorination. The dechlorination of PCB 126 (0.01 mM) is 69% after 4hrs. However, the final product biphenyl still shows little toxicity. In order to reduce biphenyl, the further oxidative pathway was combined. Biphenyl was decomposed in the iron oxide NPs immobilized membranes by the addition of H_2O_2. The heterogeneous Fenton reaction (near neutral pH) catalyzed by iron oxide can break down the aromatic ring and eventually form organic acids, which reducing the toxicity significantly. In addition, we report the sulfate radical pathway (using persulfate catalyzed by iron) based degradation results for PCBs.

The polyvinylidene fluoride (PVDF)-poly acrylic acid (PAA) membrane platform shows good capacity in preventing NPs loss, aggregation, and iron precipitation on surface. Due to the ionization of PAA, membrane pore size was controlled by the environmental pH. The pH-responsive behavior was simulated as well as the extent of PCBs degradation in convective flow experiment.

(1-65) Partitioning Coefficient of DEHP between Methylene Chloride and Water

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Phthalates are pollutants, frequently detected in water, that threaten public health and the environment. For this reason, monitoring and analysis is vital to minimize their adverse effects. One of the most commonly known phthalates pollutants is Di-(2-ethylhexyl)phthalate (DEHP), a compound used in PVC plastics, medical devices and materials, wiring cables, and even in a variety of food and beverage packaging. The Environmental Protection Agency suggests a liquid-liquid extraction method that uses methylene chloride as the preferred organic solvent for the extractions to determine the concentration of these semi-volatile organic compounds. Due to the wide variability of recoveries observed in previous phthalates studies, this

research seeks to find the distribution coefficient of DEHP between methylene chloride and water. This in turn, generates data to further understand this distribution for different samples and solvent volumes, and relate this with the sample extractions efficiency of the methods. Research results indicate that DEHP is in fact distributed between water and methylene chloride with an average value of K= 1.24. Furthermore, a statistical analysis between three different tests concludes that the sample and solvent volumes have no effect on the distribution coefficient but do have an influence on efficiency. The tests also show higher extraction efficiencies for lower DEHP concentrations and higher extraction volumes.

RESEARCH TRANSLATION: This work has significant impact on the methods suggested for analysis of phthalates in water. As such, it has opened formal and informal communications between our research group and the EPA Region 2: Feedback has been obtained from and given to managers at the Regional EPA Laboratory regarding our results. Results from this work have also been presented at the EPA Caribbean Science Consortium Symposium (September 2014), and included in a publication that is under review.

(1-66) Photoreactive TiO_2 nanoparticles for Chlorpyrifos Degradation: Synergies and Antagonisms in Nano-Bio Based Remediation Strategies

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Pesticide contamination of surface waters has been a monitored concern since the early 1970s. Chlorpyrifos (CPF) is a widely used organophosphate with both environmental and human health concerns. Photocatalytic oxidation using UV-illuminated titanium dioxide nanoparticles has emerged as a promising technology for treating contaminated waters. However, partial degradation of CPF does not necessarily correspond to reduced toxicity. CPF oxon, one of the primary degradation products has shown significant acute toxicity in human neural cells. As such, it is important to evaluate not only the efficiency of photocatalytic remediation, but also the impact that CPF and its degradation products may have on naturally occurring bacteria that may participate in bio-attenuation.

In this work we investigate the potential for photocatalytic remediation CPF in water and aim to identify the interactions between photocatalytic nanoparticles and microorganisms during contaminant degradation that would either help or hinder nano-remediation efforts. CPF loss from suspension is observed to be a combination of sorption to NPs and degradation. Dark controls indicate that significant loss is due to sorption, though degradation was observed upon UV illumination. Neither CPF nor its primary degradation products exhibited bacterial toxicity, however the photodegradation treatment itself strongly impacted bacterial viability due to the production of hydroxyl radicals.

Results from this work will be used to consider the viability and optimization of TiO_2 photodegradation technologies in contaminated water remediation. Additionally, as the strong affinity of CPF for suspended particulate matter may increase the lifetime and transport vector of the pesticide, this work suggests that implementation of remediation techniques will need to consider the bioavailability of the pesticide and degradation products following the employment of nanoparticle related technologies.

(1-67) Placental Cadmium Exposure Increases Preeclampsia Risk

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Environmental exposure to heavy metals is a potentially modifiable risk factor for preeclampsia (PE). There are known interactions between the heavy metal cadmium (Cd) and essential metals such as selenium (Se) and zinc (Zn), as these metals can protect against the toxicity of Cd. The aims of this study were to measure placental levels of Cd, Se, and Zn in a cohort of 172 pregnant women from across the southeast US and to examine associations of metals levels with the odds of PE. Logistic regressions were performed to assess odds ratios (OR) for PE with exposure to Cd controlling for confounders, as well as interactive models with Se or Zn. Mean placental Cd levels were 3.6 ng/g (range 0.52-14.5 ng/g). There was an increased odds ratio of PE in relationship to placental levels of Cd (OR= 1.5; 95% CI: 1.1-2.2). The Cd-associated odds ratio for PE increased when analyzed in relationship to low (<median) placental Se levels (OR= 2.0; 95% CI: 1.1-3.5) and decreased with sufficient Se (OR= 0.98; 95% CI: 0.5-1.9). Similarly, under conditions of low placental Zn, the Cd-associated odds ratio for PE was elevated to (OR= 1.8; 95% CI: 0.8-3.9), whereas under sufficient Zn it was reduced (OR= 1.3; 95% CI: 0.8-2.0). The results from this study suggest that Se and Zn may play an important role in reducing the risk of preeclampsia. Results from this work will be shared with the community through the Superfund Research Program research translation core at the University of North Carolina to continue to inform the community of the toxic properties of Cd exposure.

(1-68) 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)-mediated Impairment of Human Hematopoietic Stem Cells (HSCs) to Pro-B Cell Development

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TCDD exposure has been epidemiologically associated with decreased B cell competence and increased incidence of B cell lymphomas. Previous studies have shown that TCDD suppresses antibody responses of human mature B cells; however, the effects of TCDD on early stages of human B cell development from HSCs has not been extensively investigated. To fill this knowledge gap, an *in vitro* human B cell development model system was established using human cord blood HSCs. To investigate the effects of TCDD on human B cell development, HSCs were treated with TCDD (1, 10 or 30nM) or vehicle (0.02% DMSO). TCDD-treatment decreased the expression of the stem cell marker CD34 in a concentration-dependent manner. Likewise, TCDD-treatment decreased the intracellular expression of CD79α, an essential signaling accessory molecule of the B cell receptor, and CD179α, a component of pre-B cell receptor surrogate light chain. Hence, TCDD decreased the generation of CD79α^+CD179α^+ pro-B cells from HSCs. Given the expression of CD79α and CD179α are regulated by a critical transcription factor, Early B-Cell Factor 1 (EBF1), we also found both the mRNA and protein levels of EBF1 were significantly suppressed by TCDD. Structure-activity relationship studies demonstrated a correlation between the aryl hydrocarbon receptor (AHR) binding affinity of dioxin-like compounds and the magnitude of CD79α and EBF1 suppression, suggesting the involvement of AHR in TCDD-mediated effects. In addition, binding of the ligand activated AHR to the putative dioxin response elements (DREs) in *EBF1* promoter were demonstrated by EMSA-Western assay. Taken together, this study demonstrates for the first

time, the impairment of early human B cell development by TCDD, and suggests that transcriptional alterations of *EBF1* by AHR is involved in the underlying mechanism.

(1-69) A Case-Control Study of Multiple Occupational Exposures and Lung Cancer Risk in the Northeastern USA

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Objective: To investigate the relationships between occupational exposures to multiple substances and the risk of lung cancer in a Northeastern US population.

Methods: A hospital based case-control study was conducted from 1992 to 2012. The risk of lung cancer in relation to exposure to multiple occupational substances was examined in two different ways: total carcinogenic score based on the classifications by IARC and total number of occupational exposures (substances) reported. The association between occupational exposures and lung cancer was modeled, adjusting for smoking and second hand smoking history.

Results: There was an increased risk of lung cancer in relation to total carcinogenic score (OR=1.17, 95% CI: 1.01 1.35, per unit). Overall, the exposure of an increasing number of suspected lung carcinogens was significantly associated with positive trend in risk (p-value= 0.10). Exposure to traffic exhaust was a significant risk factor of lung cancer (OR=1.89, 95% CI: 1.12 3.18).

Conclusions: There was an increased risk of lung cancer with increasing occupational exposure to total lung carcinogens as measured by a cumulative score, and with increasing number of occupational exposures to known or suspected carcinogens.

Our study focused on the risk associated with several occupational substances and their combined effects on the risk of developing lung cancer. Hence, this study mirrors real–world carcinogenic risks in occupational settings as most of substances (asbestos, chromium, fiberglass, and diesel exhaust) we examined coexist in different industries.

(1-70) Efficacy of sediment remediation efforts on PAH contaminant flux via porewater advection at the sediment-surface water interface

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Groundwater advection at the sediment-surface water interface is an important biogeochemical mechanism controlling the transport and bioavailability of contaminants in estuaries. At sites along the Elizabeth River (VA, USA) where the subterranean environment is heavily contaminated with polycyclic aromatic hydrocarbon (PAH)-rich dense non-aqueous phase liquid (DNAPL), consideration of groundwater-surface water dynamics and associated chemical exchange is critical for effective remediation. Preliminary data suggest that porewater advection in permeable sediments at this location is controlled by a host of physical forcing mechanisms that correspond with total flow estimates of up to 15,000 centimeters/year. Here, the efficacy of sediment remediation strategies, including dredging and capping DNAPL-laden sediments as well as implantation of a groundwater-blocking sheet pile wall, was evaluated at specific sites within a remediated cap with respect to groundwater and contaminant fluxes using naturally-occurring radionuclide tracers and a PAH antibody-based biosensor. Comparison of these data with results from similar analyses conducted at neighboring sites targeted for future remediation was provided to environmental managers to help guide future remediation efforts. Preliminary results revealed total PAH concentrations of up to >400 µg/L in groundwater at subsurface depths up to 80 centimeters in the unremediated zone and corresponding salinity measurements of 5 –8 ppt, compared with a surface water salinity of 18 ppt. Groundwater samples from sediment depths up to 120 centimeters at the recently remediated location had comparably low salinities and elevated PAH

concentrations. These data provided strong evidence for the role of fresh groundwater contaminated with DNAPL as a major mode of PAH transport and suggest the need to devise additional, innovative strategies to mitigate porewater-associated contaminant flux at specific sites within the remediation area.

(1-71) Influence of temperature and organic carbon on methylmercury bioaccumulation in a mesocosm (KC Donnelly Externship Award Recipient 2015)

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Climate change is predicted to manifest in multiple ways in coastal marine ecosystems with increases in temperature, productivity and biomass, and watershed inputs of nutrients and contaminants. Mescocosm experiments were designed to test the influence of water temperature and sediment organic carbon concentration on the availability and uptake of methylmercury to estuarine organisms. Juvenile oysters (*Crassostrea virginica*) and sediment-dwelling amphipods (*Leptocheirus plumulosus*) were exposed to sediment containing mercury for 30 days at a combination of high (25°) or low (15°) temperature and high (13% LOI) or low (4-5% LOI) sediment carbon treatments. Temperature treatments were chosen to span the range observed in our recent field studies, and inclusive of predicted climate change driven increases in sea surface temperature in New England. Sediment carbon concentrations were also within the range we have observed in field studies throughout New England. The experiment was designed test hypotheses that higher temperatures will lead to increased bioaccumulation and that mercury in lower carbon sediments is more bioavailable. Methylmercury was measured in the sediment, particulates, filtered water, and in the animal tissues. We predicted that we would see the greatest tissue concentrations of methylmercury in animals that lived in the high temperature, low carbon treatment. The data indicate that temperature can influence methylation and bioaccumulation under some conditions, but that carbon in the sediment has greater impact on methylmercury dynamics and subsequent uptake into biota when sediment is the only source of mercury to the system. The findings allow us to better understand how changing environmental variables interact to influence mercury fate, and will be incorporated into models that will allow us to predict how environmental changes will alter human exposure.

(1-72) Using computational toxicology and spatial analysis to inform in vivo toxicity testing: Identifying obesogenic compounds in New Bedford Harbor and Buzzards Bay, Massachusetts.

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Historic land use in New Bedford Harbor (NBH), located in Buzzards Bay, in southeastern Massachusetts, has led to significant pollution, rendering NBH the oldest and largest marine Superfund site. Declining fisheries and the movement of industrial jobs out of the region have taken their toll on communities surrounding NBH, several of which are recognized as environmental justice communities. Polychlorinated biphenyls (PCBs) are the most prevalent pollutants in NBH, followed by polycyclic aromatic hydrocarbons (PAHs) and metals. Scientific inquiry into toxicological effects of these compounds continues to identify new physiological targets and biochemical mechanisms of toxicity. Several of these compounds have been associated with a class of endocrine disrupting chemicals that alter metabolic processes, including lipid and glucose homeostasis, appetite and basal metabolism, termed environmental obesogens. EPA's ToxCast™ database contains information on more than 2,000 chemicals that have been evaluated for biological activity in high throughput *in vitro* or *in vivo* systems. To test the hypothesis that chemicals with obesogenic properties are present in NBH and Buzzards Bay, sediment quality data were compiled from multiple sources and assessed for quality and temporal trends. Measured compounds were compared to

chemicals in ToxCast™ identified in the Toxicological Priority Index (ToxPi) as having obesogenic characteristics. The concentration and spatial distribution of obesogenic compounds were mapped with ArcGIS. Measured compounds were also ranked based on their potency and concentration using ToxPi to identify suspected environmental obesogens for *in vivo* toxicological studies in Atlantic killifish, *Fundulus heteroclitus*, an ecologically and biomedically relevant species native to NBH. Findings from this study will be shared with other Superfund Research Program members studying the effects of contaminants on human and fish health.

(1-73) Associations between environmental phthalate exposure and maternal thyroid hormone levels during pregnancy

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We previously reported that environmental phthalate exposure may be associated with maternal thyroid hormone alterations in a preliminary cohort of pregnant women participating in the Puerto Rico Testsite for Exploring Contamination Threats (PROTECT) Project, which is aimed at identifying novel risk factors for preterm birth. Here, we examined similar associations in a larger, comparison population participating in a nested case-control study of preterm birth. We specifically investigated whether urinary phthalate metabolites were associated with maternal thyroid hormone levels (thyroid-stimulating hormone [TSH], total triiodothyronine [T3], and free and total thyroxine [T4]) measured at multiple time points during pregnancy. We measured 9 phthalate metabolite concentrations in urine samples collected from up to four study visits per subject during pregnancy. We also measured a panel of thyroid function markers in plasma collected at the same four time points per subject during pregnancy. Using data from all time points, we observed that increases in several urinary phthalate metabolites were significantly associated with increases in plasma total T3 as well as total and free T4. In contrast, an increase in urinary mono-isobutyl phthalate (MiBP) was significantly associated with a decrease in plasma TSH. Cross-sectional analyses showed that the strength and direction of these relationships varied by time point of sample collection during gestation. These results suggest that urinary phthalate metabolites are associated with altered maternal thyroid hormone levels in pregnancy. Furthermore, the potential thyroid-disrupting effects of phthalates may vary by timing of exposure during gestation. Our findings have implications for public health interventions aimed at reducing the risks of hormone-mediated adverse birth outcomes – environmental phthalate exposure may represent a potentially modifiable risk factor in pregnant women.

(1-74) Dynamics and mechanisms of asbestos-fiber aggregate growth in water

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Most colloidal particles including asbestos fibers form aggregates in water, when solution chemistry provides favorable conditions. To date, the growth of colloidal aggregates has been observed in many model systems under optical and scanning electron microscopy; however, all of these studies used near-spherical particles. The highly elongated nature of asbestos fibers may cause anomalous aggregate growth and morphology, but this has never been examined. Here we have studied solution phase aggregation kinetics of asbestos fiber using a liquid-cell by *in situ* microscopy. Experiments revealed that diffusing fibers join by cross linking but that such linking is sometimes reversible. Our new finding is that aggregates are very

sparse and non-compact, with morphologies and growth rates that differ dramatically from near-spherical particles. We also find that the growth of aggregates depends strongly on solution pH, but is surprisingly insensitive to salinity. This direct method for quantitatively modeling aggregate growth is a first step for us to accurately predict asbestos fiber aggregate size distributions in water. By studying this fundamental aggregation process, we provide insights into the transport and fate of asbestos fibers in the natural environment that will translate into improved strategies for containment at asbestos disposal sites, such as Ambler and other Superfund and Brownfields sites. In addition, our results may be generalized to help understand the transport behavior of asbestos fibers in some *in vivo* studies.

(1-75) Metabolomics of asbestos exposure-structure identification of upregulated metabolites

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Industrial use of asbestos has resulted in a wide range of exposures in human populations, which is known to cause cancers. The health and economic impacts of asbestos exposure are well documented and being felt by many today. The exceptionally long latency periods of most asbestos related diseases has hampered preventative and precautionary steps thus far. Therefore, there remains a large unmet need for the evaluation and quantification of asbestos exposure on an individual basis. Accurate evaluation of exposure levels would aid in identifying at risk individuals as well as distinguishing asbestos exposure and mesothelioma. Although there have been reports of proteins serving as biomarkers of asbestos exposure, thus far these markers lack sufficient sensitivity and specificity. Identification and implementation of small molecules biomarkers are likely to contribute to evaluating asbestos exposure across human populations. Herein, we analyzed serum samples obtained from three groups of people: healthy controls (C) (n=40), asbestos exposed (A) (n=40), and mesothelioma (M) (n=40). Following serum process using a modified Folch extraction, the organic phase was concentrated and subjected to high-resolution nanospray LC-HRMS (liquid chromatography-high resolution mass spectrometry) under both positive and negative modes. The analysis of the data by the software platform SIEVE 2.0 (Thermo Scientific) identified three novel lipids that were up-regulated in asbestos-exposed individuals and mesothelioma patients. The specific biomarkers can potentially not only distinguish mesothelioma patients from asbestos exposure, but also assist regulatory agencies to evaluate remediation strategies.

(1-76) Diacetyl, a Flavoring Chemical Associated with “Popcorn Lung”, is in Many Flavored E-cigarettes

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Background: There are over 7,000 e-cigarette flavors currently marketed. Flavoring chemicals gained notoriety in the early 2000’s when inhalation exposure of the flavoring chemical diacetyl was found to be associated with a disease that became known as “Popcorn Lung.” There has been very little research on flavoring chemicals in e-cigarettes.

Objective: To estimate the total mass of flavoring chemicals diacetyl, 2,3-pentanedione, and acetoin in e-cigarettes.

Methods: We selected 51 types of flavored e-cigarettes sold by leading e-cigarette brands. E-cigarette contents were fully discharged and the air stream was captured and analyzed for total mass of diacetyl, 2,3-pentanedione, and acetoin, according to OSHA Method 1012.

Results: At least one flavoring chemical was found in 47 of 51 unique flavors tested. Diacetyl was detected in 69% of flavors, ranging from <LOQ to 239 µg/e-cigarette. 2,3-pentanedione and acetoin were detected in 41% and 82% of flavors at concentrations up to 64 and 529 µg/e-cigarette, respectively.

Conclusion: Due to the associations between diacetyl, bronchiolitis obliterans and other severe respiratory diseases, urgent action is recommended to further evaluate this new widespread exposure via flavored e-cigarettes.

(1-77) Novel Tools for Targeting PCBs/PCB metabolites using DNA Aptamers

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Polychlorinated biphenyls (PCBs) are environmental chemicals that persist in the environment and bioaccumulate in the human body. Mono-hydroxylated polychlorinated biphenyls (OH-PCBs) are PCB metabolites found commonly in human blood and environmental water and sediment samples. Determination of the levels of PCBs and their OH-PCB metabolites, along with studies of their adverse health effects is vital for the field of toxicology. However, the detection of small amounts of these compounds in biological matrices from epidemiological and laboratory studies remains a challenge. Here we introduce the application of aptamers as a means to identify PCBs and OH-PCBs. Aptamers are short oligonucleotides used for the detection of analytes ranging from proteins to small environmental molecules. They are selected for a particular application via a process known as Systemic Evolution of Ligands by EXponential enrichment (SELEX) and, like antibodies, have a high affinity and specificity for the selected analyte. Our hypothesis is that aptamers can be used to identify PCB metabolites in environmental and biological samples. To test this hypothesis, two OH-PCBs, 4-OH-PCB72 and 2-OH PCB106, were attached to beads with carboxylic acid as functional groups attached on their surface. Covalent binding to the beads was confirmed by FTIR spectroscopy. *In vitro* assays were performed to demonstrate the binding of two aptamers to the OH-PCB-coated beads. Additionally we explored if these aptamers have the ability to distinguish structurally different OH-PCB congeners and other environmental pollutants. Our studies are important for the detection of low levels of PCBs and their metabolites in biological samples and will aid in the development of novel methods for the identification of protein modifications by hydroxylated PCBs.

(1-78) Measurement of threshold friction velocities at the Iron King Mine tailings site and other potential dust sources in semi-arid regions

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The threshold friction velocities of potential dust sources in the US Southwest were measured in the field using a Portable Wind Tunnel, which is based on the Desert Research Institute's Portable In-Situ Wind Erosion Laboratory (PI-SWERL). A mix of both disturbed and undisturbed surfaces were included in this study. It was found that disturbed surfaces, such as those at the Iron King Mine tailings site (which is part of the EPA's Superfund program), and contains surface contaminants of arsenic and lead concentrations reaching as high as 0.5% (w/w), had lower threshold friction velocities (0.32 m s^{-1} to 0.40 m s^{-1}) in comparison to those of undisturbed surfaces (0.48 to 0.61 m s^{-1}). The Iron King Mine tailings site in particular had a threshold friction velocity within the range of the disturbed surfaces (0.35 m s^{-1} to 0.40 m s^{-1}). Surface characteristics, such as particle size distribution, also had effects on the threshold friction velocity (smaller grain sized distributions resulted in lower threshold friction velocities). Overall, the threshold friction velocities of disturbed surfaces were within the range of natural wind conditions, indicating that surfaces disturbed by human activity are more prone to causing dust storms. This means that contaminated dust particles from superfund locations like the Iron King Mine tailings site can be emitted into the atmosphere without extreme wind related weather events.

(1-79) Identification of purine-cobamide as a novel corrinoid cofactor of tetrachloroethene reductive dehalogenases in Desulfitobacterium

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Corrinoids carrying a variety of lower bases are essential cofactors for reductive dehalogenases (RDases), which catalyze reductive dechlorination reactions in organohalide-respiring bacteria (OHRB). Some members of the genus *Desulfitobacterium* are capable of *de novo* corrinoid biosynthesis and assembly of catalytically functional PceA RDases implicated in the degradation of tetrachloroethene (PCE) and trichloroethene (TCE). The nature of the lower base attached at the ribose moiety can affect OHRB activity; however, the specific lower base produced by *Desulfitobacterium* spp. has not been identified. Initial high mass resolution LC-MS characterization indicated that several PCE-dechlorinating *Desulfitobacterium* isolates produced a novel corrinoid carrying an unknown type of lower base with a molecular weight of 120.11. ^{15}N isotope labelling experiment using *Desulfitobacterium hafniense* strain Y51 cells grown with ^{15}N-NH_4Cl as the only nitrogen source resulted in corrinoid molecular weight shift of 14.95, indicating that the lower base is not a derivative of the well-known lower bases adenine, benzimidazole or phenol. Two-dimensional (2D) ^{1}H-, and ^{15}N-NMR correlation spectra were collected on unlabeled or N^{15}-labled corrinoid produced by strain Y51, and these data were used along with the mass spectrometry information to assign the structure of the lower base. The results of these analyses are consistent with purine as the lower base produced by organohalide-respiring *Desulfitobacterium* spp. Purine has not been identified as a lower base in naturally occurring corrinoids, and this finding expands understanding of corrinoid diversity. Experiments to determine if *Coα*-purinyl-cobamide supports growth and reductive dechlorination activity of organohalide-respiring *Chloroflexi* are ongoing.

(1-80) EGCG prevents PCB-induced endothelial cell inflammation via epigenetic modifications of NF-κB target genes

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Anti-inflammatory polyphenols, such as epigallocatechin-3-gallate (EGCG), have been shown to protect against the toxicity of environmental pollutants. We recently have demonstrated that diets enriched with green tea extracts protect against PCB toxicity in mice, which might involve epigenetic regulation. It is known that bioactive nutrients such as polyphenols may exert their protection by modulating inflammatory pathways regulated through nuclear factor-kappa B (NF-κB) signaling. EGCG has been reported to have anti-NF-κB transactivation activity. We hypothesize that EGCG can protect against PCB-induced endothelial inflammation in part through epigenetic regulation of NF-kB-regulated inflammatory genes. In order to test this hypothesis, vascular endothelial cells were exposed to physiologically relevant levels of coplanar PCB 126 and/or EGCG, followed by quantification of NF-kB subunit p65, histone acetyltransferase (HAT) p300 and histone deacetylases (HDACs) 1-3 accumulation through ChIP assay in the promotor region of inflammatory genes. In addition, the enrichment of the acetylated H3 (ac-H3) was also quantified. Exposure to PCB 126 increased the expression of vascular inflammatory mediators, including interleukin (IL)-6, C-reactive protein (CRP), intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and IL-1α/β, which was prevented by pre-treatment with EGCG. This inhibitory effect by EGCG correlated with abolished nuclear import of p65, decreased chromatin binding of p65 and p300, as well as increased chromatin binding of HDAC1/2. Furthermore, EGCG induced hypoacetylation of H3, which accounts for deactivation of downstream genes. These

data suggest that EGCG-induced epigenetic modifications can decrease vascular endothelial toxicity of PCB 126 (NIH/NIEHS P42ES007380).

Research Translation: Understanding the molecular mechanisms of nutritional modulation of PCB-induced inflammation may lead to more effective biomedical interventions which, ultimately, may decrease associated risks of environmental pollutants in susceptible populations.

(1-81) Developmental Toxicity of Parent and Methylated Polycyclic Aromatic Hydrocarbons in Embryonic Zebrafish

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Polycyclic Aromatic Hydrocarbons (PAHs) are ubiquitous Superfund site contaminants that occur in complex mixtures. Many PAHs are known or suspected mutagens and carcinogens, and the relative carcinogenic potency of parent PAHs has been well characterized. However, very little data exists on the potential developmental toxicity of individual PAHs, which is needed to understand the toxicity of environmental mixtures. Parent and methylated PAHs were assessed for developmental toxicity using our high-throughput embryonic zebrafish assay. Additionally, each PAH was evaluated for AHR activation, by measuring CYP1A protein expression using whole animal immunohistochemistry (IHC). There was structurally-dependent variation in the responses to different PAHs. High-molecular weight PAHs were significantly more developmentally toxic than the low-molecular weight PAHs. Of the PAHs tested, methylation generally did not alter the toxicity relative to the toxicity of the individual parent compounds. IHC data also showed differential patterns of CYP1A, but mainly restricted to the vasculature, liver, and skin. High-molecular weight PAHs generally induced more robust CYP1A expression and in multiple tissue types compared to the lower low-molecular weight PAHs. Interestingly, the methylated PAHs consistently induced higher relative CYP1A expression compared to their parent compounds. These data demonstrate the advantages of using a whole animal model to define PAH structure activity relationships, and provides a platform for assessing the hazards of individual PAHs and complex PAH mixtures.

(1-82) Effects of DNA Sequence Variation In Aryl Hydrocarbon Receptor (AHR) On The Sensitivity Of Human Immune System to Suppression by Dioxin

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2,3,7,8-tetraclorodibenzo-*p*-dioxin (TCDD, dioxin) is a high affinity aryl hydrocarbon receptor (AhR) ligand known to directly suppress immune responses, including antibody production by white blood cells, termed, B-lymphocytes. Interestingly, people differ in their sensitivity to the dioxin-produced suppression of IgM secretion. We hypothesized that small differences (one nucleotide) in DNA code for the AHR gene contribute to differential susceptibility to dioxin-mediated immune system toxicity in the human population. We modified a human B cell line that does not express the AHR, through genetic engineering, to express either a “wild type” form or one of the known polymorphic forms of the AHR (P517S, R554K, V570I, V570I+P517S, R554K+V570I and P517S+R554K+V570I). We confirmed AHR is expressed in these new cell lines and measured the ability of different forms of the AHR to induce the expression of genes known to be influenced by dioxins (such as Cyp1A2 and Cyp1B1) as well as the ability of dioxin to suppress antibody production in these cell lines. Our findings demonstrate that the R554K human AhR SNP alone altered sensitivity of human B cells to TCDD-mediated induction of Cyp1B1 and Cyp1A2 metabolizing enzymes. By contrast, attenuation of TCDD-induced IgM suppression required a combination of all three SNPs: P517S, R554K, and V570I.

(1-83) Pyocyanin and indirubin, pathogen-associated ligands of the aryl hydrocarbon receptor, reduce differentiation of 3T3-L1 adipocytes

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The aryl hydrocarbon receptor (AhR) is a ligand-activated transcription factor known for regulation of genes involved in xenobiotic metabolism of environmental toxins, such as polychlorinated biphenyls (PCBs). Several biological compounds have been shown to interact with AhR to regulate immune and inflammatory responses. Previously, we demonstrated PCB-induced activation of AhR regulated adipocyte differentiation *in vitro* and promoted adipose inflammation in mice with diet-induced obesity. Recent studies demonstrated that AhR senses bacterial pigments, suggesting a link between the microbiome, PCBs and AhR activation. The purpose of this study was to determine if pathogen-associated AhR ligands regulate differentiation of 3T3-L1 adipocytes. Preadipocytes were incubated with increasing concentrations of pyocyanin, kynurenic acid, FICZ, indirubin, from day 0 throughout differentiation. Pyocyanin (100 µM) significantly reduced 3T3-L1 differentiation (vehicle: 0.88 ; pyocanin: 0.42 ; absorbance of Oil Red O; $P<0.0001$). Indirubin also significantly decreased adipocyte differentiation (vehicle: 1.02; indirubin 1 µM: 0.75; indirubin 10uM: 0.75 ; absorbance of Oil Red O in mature adipocytes; $P<0.01$). Results demonstrate that pathogen-associated AhR ligands regulate adipocyte differentiation. Future studies will determine if these effects are AhR-mediated. Discovery of nutritionally-derived AhR agonists could serve as new targets to control obesogenic effects of environmental toxins.

(1-84) Electrochemical dechlorination of TCE in the presence of natural organic matter, metal ions and nitrates in a simulated karst aquifer

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A small-scale flow-through limestone column was used to evaluate the effect of common coexisting organic and inorganic compounds on TCE dechlorination. In the absence of humic acid (organic matters) and dichromate, selenate, and nitrate (inorganic matters), 90% of initial TCE was dechlorinated under optimum conditions (90 mA current, 1 mL/min flow rate, and 1 mg/L initial TCE concentration). As humic acid competes for the reactive sites on iron anode with TCE, its presence inhibits TCE reduction to some extent. Hexavalent chromium was completely reduced to trivalent chromium due to the ferrous species from iron anode. Chromium precipitates could cover the iron anode surface and prevent further anode reaction, which provides a reducing environment for TCE dechlorination. With dichromate, TCE reduction rate decreased by 1.5 times. Selenate effects are less pronounced than dichromate on TCE remediation, as selenite presence reduced the TCE removal efficiency by 10%. In addition, selenate complexation with dissolved iron released due to iron anode corrosion result in aggregates, which may coat the iron surface and reduce dechlorination rate. Although the system is capable of significantly remediating TCE, it is not efficient to treat nitrate as well as metal ions.

Research Translation: The aim of this study is to investigate the TCE removal efficacy in the presence of other groundwater contaminants and natural organic matters. We present the application of a simulated karst aquifer with an iron anode as an e-barrier system to remediate TCE in the presence of dichromate, selenate, nitrate, and humic acid. This system can be engineered to treat TCE co-contamination with a relatively wide variety of contaminants.

(1-85) Synergistic Induction of Metal-Responsive and Oxidative Stress Gene Biomarkers in Placental JEG-3 Cells by Arsenic & Cadmium Mixtures from Hazardous Waste Sites.

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Exposure to elevated levels of the toxic metals inorganic arsenic (iAs) and cadmium (Cd) represents a major global health problem. These metals often occur as mixtures in the environment, creating the potential for interactive or synergistic biological effects different from those observed in single exposure conditions. In the present study, environmental mixtures collected using a passive sampling device from two waste sites in China, and identical mixtures prepared in the lab were tested for toxicogenomic response in placental JEG-3 cells. These cells serve as a model for evaluating cellular responses to exposures during pregnancy. One of the mixtures was predominated by iAs and one by Cd. The gene biomarkers heme oxygenase 1 (*HO-1)* and metallothionein isoforms *(MT1F* and *MT1G)* previously shown to be preferentially induced by exposure to either iAs or Cd, and metal transporter genes aquaporin-9 *AQP9* and ATPase, beta polypeptide *ATP7B* were measured in order to evaluate the effects from the metals mixtures using dose and time course experiments. There was a significant increase in the mRNA expression levels of *HO-1, MT1F* and *MT1G* in mixture-treated cells compared to the iAs or Cd only-treated cells. Notably, the genomic responses were observed at concentrations significantly lower than levels found at the environmental collection sites. These data demonstrate that metal mixtures increase the expression of gene biomarkers in placental JEG-3 cells in a synergistic manner. Taken together, the data suggest that toxic metals that co-occur may induce detrimental health effects that are currently underestimated when analyzed as single metals.

(1-86) Pyruvate kinase isoform switching and the metabolic reprogramming of central carbon and amino acid metabolism by the environmental contaminant 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)

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TCDD is an environmental contaminant that elicits a number of liver effects including fatty liver, inflammation, and fibrosis. To further investigate the underlying mechanisms associated with these responses, we looked at gene expression and metabolites from female mice exposed to TCDD (0.01 – 30 μg/kg) every 4 days for 28 days, and integrated the data into metabolic pathways using CytoKEGG. Complementary dioxin response element (DRE) location and aryl hydrocarbon receptor (AhR), the target of TCDD, binding data was used to elucidate putative direct AhR responses. Overall, 3,406 differentially expressed genes, and ~50 metabolite changes were identified and mapped to more than 15 metabolic pathways. Dose-dependent effects included changes in central carbon and amino acid metabolism characterized by the induction of pyruvate kinase muscle (PKM) protein levels, *Pkm* expression isoform switching from *Pkm1* to *Pkm2*, and increases in glutamine, glucose 6-phosphate, and 3-phosphoglycerate levels due to the expression of GAC isoform of glutaminase (*Gls1*), and the redirection of glucose metabolism intermediates to the pentose phosphate pathway, and serine biosynthesis – metabolic changes typically associated with cancer cells. We propose that this metabolic reprogramming represents an AhR-mediated response to TCDD in defense of oxidative stress to increase NADPH production in support of anti-oxidant counter-measures.

Collectively, these results suggest TCDD induces AhR-mediated metabolic reprogramming, reminiscent of the Warburg effect in cancer cells.

(1-87) Functionalized Magnetic Nanoparticle Systems for the Capture of PCBs

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Polychlorinated biphenyls (PCBs) represent a stable and toxic class of environmental pollutants that has been persistently found in soil and groundwater. The presence of PCBs at many superfund sites across US has been related to adverse health effects among people living nearby these contaminated sites. In our group, we are developing a variety of magnetic nanocomposite systems based on iron oxide nanoparticles for binding and capture of PCBs. Here, a novel approach involving the direct coating of different functionalities onto iron oxide nanoparticles *in situ* in a single step reaction is presented. Polyphenolic antioxidants such as curcumin and quercetin were incorporated onto the surface of magnetic iron oxide nanoparticles, and in addition, other functionalities, such as hydroxybenzoic acid and β-cyclodextrin, were also explored as the moieties on the nanoparticle surface. The functionalized coating interacts and binds PCBs in solution, whereas the magnetic iron oxide core enables magnetic decantation after PCB binding. All functionalized nanoparticle systems were fully characterized using Fourier transform infrared spectroscopy (FTIR), transmission electron microscopy (TEM), dynamic light scattering (DLS), X-ray diffraction (XRD), thermogravimetric analysis (TGA) These nanoparticle systems were then employed for the binding studies with model PCB 126 system, where they demonstrated effective binding at low PCB concentrations.

(1-88) Sono-electro-Fenton Degradation of 4-Chlorophenol in Aqueous Media

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Advanced oxidation processes (AOPs) have shown great potential in degrading bio refractory organic compounds. Sono-electro-Fenton process (SEF), an AOP process, developed about a decade ago has drawn great interests for chloro-organics treatment in water in the recent years. In this study, degradation of 4-chlorophenol (4-CP) was investigated by SEF technique. Because 4-CP has hydrophilic properties and its treatment with sonolysis alone can be delayed or inhibited in the presence of more hydrophobic compounds, it is an ideal chemical to work with for SEF process. Batch experiments are conducted to investigate interfering variables in 4-CP removal at room temperature. Main objective was to understand different pathways of 4-CP degradation and studying the effects of different parameters on removal efficiency. Critical parameters (including, current, ferrous iron concentration and Pd/Al catalyst presence) for electro-Fenton (EF) treatment of 4-CP were first optimized in a two electrode (Ti/MMO) batch system, then the optimum conditions were used along with a pulsing 20KHz, ultrasound wave to degrade 4-CP and to optimize pulsing frequency and sonifiers amplitude. Preliminary EF tests with a 200 ppm 4-Cp initial concentration, 1 gr Pd/Al catalyst, a 10 mM Na_2SO_4 as background electrolyte and varying ferrous ion concentration (19,40,80, and 160 ppm) and current have been conducted. In the presence of 80 ppm ferrous ion concentration, 120 mA was the optimum current intensity. Increased 4-CP degradation is expected to occur in the presence of ultrasound wave. Results of optimum parameters for EF and SEF processes along with the degradation efficiencies and energy consumptions will be presented.

Research Translation: This study investigates feasibility of sonoelectro-Fenton process for 4-chlorophenol remediation and corresponding mechanisms in batch systems, which is important and necessary for application of this technology in the field.

(1-89) Inhaled versus Endogenous Formaldehyde Exposures: Are They Both Misestimated?

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Formaldehyde was classified as a known human and animal carcinogen according to IARC in 2006. However, formaldehyde is also an essential metabolic intermediate in all living cells. N^2-HOMe-dG is the main inhaled formaldehyde-induced DNA mono-adduct, which together with DNA protein crosslinks and toxicity-induced cell proliferation play important roles in mutagenesis and carcinogenesis. We have recently found N^2-HOMe-dG to be the dominant degradation product of several DNA-protein crosslinks, demonstrating that N^2-HOMe-dG represents an excellent biomarker for both DPC and direct adduction of inhaled formaldehyde to DNA.

With the support of ultra-sensitive liquid chromatography-tandem mass spectrometry, endogenous and inhalation-derived exogenous N^2-HOMe-dG adducts were successfully differentiated in the 28-day 2-ppm exposure rat study as well as in the 2-day 6-ppm exposure monkey study. The purpose of this study is to provide the distribution pattern of exogenous DNA adducts, elucidate accumulation of exogenous adducts, the time to reach steady state, and the half-life for the repair/loss of exogenous adducts *in vivo*, as well as to further tell whether or not inhaled formaldehyde can reach tissues distant to sites of initial contact. Fanconi anemia (FA) mice that are deficient in formaldehyde catabolism ($ADH5^{-/-}$) and/or acetaldehyde catabolism ($ALDH2^{-/-}$) were also studied to determine if sufficient endogenous aldehydes accumulate to cause DNA damage.

This study also adds greatly to several of the issues raised by the National Research Council (NRC) of the National Academies. The NRC raised five issues that needed to be addressed in revisions of the draft assessment related to Toxicokinetics and Modes of Action of Formaldehyde after conducting an independent scientific review of the IRIS draft released by The USEPA in June 2010.

Recent Publications: Yu R, et al. (2015) Toxicol. Sci. 146 (1): 170-182.

(1-90) Use of solid phase microextraction (SPME) and laboratory models to estimate risk of ΣDDT from consumption of fish from contaminated sediments in Palos Verdes, California

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DDT and its primary metabolites are a major source of concern in the Palos Verdes Shelf (PVS). Biota-sediment accumulation (BSAF) and biomagnification (BMF) were modeled in a laboratory setting using PVS sediments, the benthic polychaete worm, *Neanthes arenaceodentata* and the demersal flatfish, *Pleuronichthys verticalis* and compared to SPME values to estimate bioavailability of DDT in sediments from PVS. Using human seafood-consumption data specific to anglers for California halibut (*Paralichthys californicus*), cancer and non-cancer risks were calculated and compared to previous assessments by the Los Angeles County Sanitation District (LACSD) using field data. Comparisons were made for the general public as well as high-risk groups. The calculated BMF and BSAF values in this study (4.09 ±0.82 and $1.4x10^{-3}$ $±7.0x10^{-4}$, respectively) were comparable to LACSD values (4.06 and $2.6x10^{-3}$ $±9.0x10^{-4}$, respectively). Cancer risk to the general public (50^{th} percentile) and at-risk groups (private boat anglers, 95^{th} percentile) were $1.21x10^{-8}$ $±6.27x10^{-11}$ and $1.49x10^{-7}$ $±7.78x10^{-10}$ respectively, and of similar magnitude relative to earlier studies ($2.48x10^{-8}$ $±8.9x10^{-9}$ and $3.08x10^{-7}$ $±1.1x10^{-7}$, respectively). The calculated non-cancer hazard quotient values for general public and private boat anglers from this study ($4.14x10^{-4}$ $±2.15x10^{-6}$ and $5.13x10^{-3}$

±2.67x10^{-5}, respectively) were also of similar magnitude to the LACSD values (8.51x10^{-4} ±3.04x10^{-4} and 1.06x10^{-2} ±3.78x10^{-3}, respectively) indicating estimates of bioavailability using SPME could be used to determine risk to ΣDDT from contaminated sediments. Regulatory stakeholders include California Fish and Game, USEPA region 9, National Marine Fisheries (NOAA), US Fish and Wildlife, and CalEPA. Other stakeholders include Heal the Bay, the Santa Monica Bay Restoration Commission and the Fish Contamination Education Collaborative.

(1-91) Modeling of transient pH condition during the water treatment by electrochemical process

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Abstract: Electroremediation involves using direct current across porous electrodes to intercept and transform contamination in groundwater through oxidation and reduction reactions. The system undergoes significant changes in pH due to electrolysis reactions. Considering that pH is one of the important parameters that controls the reactions and influences on transformation mechanisms, a theoretical model can be a decent tool to monitor the change of pH during the process and to adjust the system for a full-scale implementation. However, developing new models is challenging due to multicomponent species transport. Here we present a theoretical model to describe pH changes with the use of inert (mixed metal oxide, MMO) and reactive (iron) anodes during electrochemical processes. Active anodes participate in electrolysis and influence the chemical reaction directly in the anolyte solution, while non-active anodes are used only to transfer electrons into the solution. Experimental data has shown that, pH within the system can alter depending on the type of electrodes which are been using. We developed the theoretical model which includes chemical reactions, water auto-ionization, and electrolysis to describe the dynamic changes in chemistry across the cell. We found a good correlation between the theoretical results and observed data from an experimental study on electrochemical remediation.

Research Translation Component: This model can be used as a tool to measure the energy consumption and treatment efficiency of the system, which gives a good estimation of the cost efficiency of the system for a full-scale implementation.

(1-92) Combustion Derived Particulate Matter Exposure Suppresses Pulmonary Host Defense through Regulatory T cells and IL10.

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Exposure to elevated levels of particulate matter (PM) is associated with adverse respiratory health in infants and increased risk of morbidity and mortality due to respiratory tract viral infections. We have previously shown combustion derived PM (CDPM) induced immunosuppression allowing for enhanced influenza disease severity and mortality in neonatal mice. Current studies address the mechanism of this immunosuppression. Neonatal mice (3 days old) were acutely exposed to DCB230, a CDPM and during exposure, mice were infected with influenza virus. Pulmonary T cell phenotypes including regulatory T cells (Tregs) were analyzed by flow cytometry. A significant increase in pulmonary Tregs and immunosuppressive cytokines IL10 and TGF-β was observed in PM exposed and influenza infected (DCB/Flu) mice, which peaked at 10 days post exposure compared to air exposed and influenza infected mice (Air/Flu). This coincided with decreased Th1 and Tc1 responses that play an important role in protecting against influenza infection. Further, Tregs were depleted in PM exposed mice by administering anti-CD25 antibody (PC61) and infected with influenza (PC61/DCB/Flu). Significant increase in both Th1 and Tc1 cells was observed in PC61/DCB/Flu mice compared to DCB/Flu mice. To further study the role of IL10, air exposed neonatal mice were treated with recombinant IL10 (rIL10) and subsequently infected with influenza (rIL10/Flu). rIL10/Flu mice had increased incidence of morbidity and pulmonary viral load compared to Air/Flu mice. Furthermore, IL10 deficient mice (IL10KO) exposed

to PM and infected with influenza (IL10KO/DCB/Flu) exhibited significant reductions in pulmonary viral load and inflammation indicative of enhanced protection against influenza. Together, these studies demonstrate that PM induced Tregs and IL10 suppress adaptive T cell responses leading to increased influenza severity in infected neonatal mice.

(1-93) Identification and Characterization of Genes with a Novel Role in Arsenic Detoxification in Plants

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Arsenic often enters our food chain via the roots of staple crops. Rice, the worlds second most produced staple crop, transports more of this toxic metalloid from soil to seeds compared to other grains. Previous research has shown plant roots have the capacity to efflux some imported arsenic back into the soil. Efforts to identify an arsenic epidermal plasma membrane effluxer have focused on a subfamily of the Multidrug Resistance Protein (MRP) superfamily, the ATP-Binding Cassette (ABC) transporters, due to their critical function in sequestering arsenic into vacuoles. Despite these efforts, the effluxer(s) responsible for returning arsenic to the soil remains elusive. Using bioinformatics, we have identified several candidate genes that may encode arsenic efflux proteins. To determine whether any of these proteins participate in arsenic detoxification, *O. sativa* as well as closely related *A. thaliana* genes are being characterized in arsenic sensitive *S. cerevis*iae strains and *A. thaliana* lines. This work may ultimately help breeders and agriculture scientists to not only prevent arsenic from reaching the edible seed, but also possibly remove arsenic from the crop entirely, reducing human exposure to arsenic in our diet.

Day 2 Poster Abstracts

(2-1) Development of Biomolecular Tools for Quantifying the Mercury-methylation Genes as Biomarkers for Methylmercury Production

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Two genes (*hgcAB*) that are essential for biological mercury (Hg)-methylation are uniquely positioned to be used as biomarkers for Hg-methylation potential. The development of tools to detect and quantify these biomarkers is the first step in using genetic, genomic and geochemical data to be able to determine the Hg-methylation potential of at-risk environments. Universal polymerase chain reaction (PCR) primers spanning *hgcAB* were developed to ascertain microbial community organismal diversity and were validated using 32 pure cultures spanning the functional groups of fermentors, sulfate- and Fe(III)- reducing bacteria as well as methanogens. All known Hg-methylators were positive and known non-methylators were negative. Positive gene products were purified, sequenced, mapped back to their respective genome to confirm the correct product. Given the different Hg-methylation extents for different functional groups, we developed and fine-tuned group-specific quantitative-PCR primers focusing only on *hgcA*. For each template, amplification efficiencies were calculated, melt curves were analyzed and products were electrophoresed within an agarose gel. Each group-specific qPCR primer set only amplified *hgcA* within its group. Finally, to mimic an environmental sample, cells from all groups were combined in different combinations and ratios to assess qPCR primer efficiency and specificity. The development and validation of these highly specific and quantitative molecular tools is the first step towards rapid and accurate risk management assessment in any environment. Moving forward, these tools will be used as part of the assessment of remediation strategies such as the

development of black carbon (Ghosh, PI) for the removal of Hg(II) and methylmercury as well as being part of the effort to *establish a 3-dimensional relationship between Hg bioavailability, hgcAB abundance and methylmercury production rate (Hsu-Kim, PI).*

(2-2) Definition and identification of a community cohort with exposure to asbestos

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Epidemiologic studies of cohorts with exposures to environmental agents are attractive as they have the ability to simultaneously track different mortality or morbidity outcomes, minimize effects of out-migration and in-migration on patterns of diseases with long latency patterns, and facilitate study of socio-economic variables at the time of exposure. Cohort studies of asbestos-exposed workers have defined elevated mortality from asbestosis, lung cancer and mesothelioma. Cohort studies of family members of asbestos have defined outcomes in those with domestic “paraoccupational” exposure.

To study the effects of chrysotile asbestos exposure on past residents of the Ambler PA community, the largest US asbestos product manufacturing site from 1900-1940 we used a variety of novel methods to identify the exposed cohort and relevant mortality records. Boundaries of the asbestos exposure riskscape in 1930 were defined spatially using Sanborn Fire Insurance maps, with information on the sites of asbestos production and disposal and interviews of residents to establish community exposure sources. 1930 census data allowed identification of those with occupational, para-occupational and community exposure.

Mortality records from 727 data-bases were accessed through Ancestry.com, including US Social Security Death index, death certificates from states, the US grave index and other data. Novel "crowd-sourcing” techniques employed University students to search the large number of records. We assembled a cohort of 4,524 residents within the riskscape in 1930: 474 with occupational exposure, 1,164 paraoccupational exposure, 2886 with community exposure. African–Americans had higher rates of occupational and paraoccupational exposure.

Mortality records have been obtained for most participants. Demographics and outmigration patterns of the demographic groups are described. Studies of mortality characteristics of sociological and exposure groups are continuing.

Research Translation Component: The research project arose out of the affected community’s questions as to the role of community, as opposed to occupational and paraoccupational exposures in the increased incidence of mesothelioma observed in Ambler. Residents and former residents have participated in collecting research data. Updates are presented to the community periodically. The results will be shared with the community and are expected to assist in future policy development for this and other superfund sites.

(2-3) The involvement of fatty liver and mitochondrial functions in toxin-induced liver injury and fibrosis: Role of Ubc13.

Yoon Seok Roh[1,2], Ryosuke Uchiyama[2], Hiroshi Matsushita[1,2], Janice Yang[2], Jihoon Kim[5], Majid Gjassemian[4], Michael Karin[3], David A. Brenner[1], Ekihiro Seki[1,2]

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The prevalence of obesity and fatty liver disease is increasing in the world. Our superfund program previously demonstrated that decreased expression of TAK1, a MAP3K upstream of NF-κB and JNK, contributes to enhanced toxin-induced liver fibrosis in fatty liver disease. We continue to investigate the molecular mechanisms underlying enhanced toxin-induced liver fibrosis in fatty liver.

Acute exposure of carbon tetrachloride (CCl_4), a superfund toxicant, induces liver injury and chronic exposure develops liver fibrosis. high fat diet-fed mice developed more liver fibrosis as demonstrated by increased collagen deposition and fibrogenic gene expression than normal chow-fed mice after exposure to CCl_4. Mice fed with HFD or genetically obese mice showed reduced protein levels of Ubc13, an E2 ubiquitin ligase involved in TAK1 activation in the liver. We hypothesize that the decreased Ubc13 and TAK1 function in fatty liver disease enhances CCl_4-induced liver fibrosis. To examine the effect of decreased Ubc13 in the liver, we generated hepatocyte-specific Ubc13-deficient (Ubc13KO) mice. Upon CCl_4 exposure, Ubc13KO mice had exacerbated liver injury and fibrosis as demonstrated by increased collagen deposition, serum ALT levels and hepatic fibrogenic gene expression. We facilitated proteomics analyses on the livers from WT and Ubc13KO mice treated with CCl_4. Upon CCl_4, WT, but not Ubc13KO livers, showed significantly altered pathways of estrogen biosynthesis, LXR/RXR, FXR/RXR, PXR/RXR, xenobiotic metabolism, aryl hydrocarbon receptor, bile acid biosynthesis and β-oxidation pathways. Mitochondrial function of Ubc13KO livers was significantly suppressed compared to that of WT livers as assessed by oxygen consumption rate through Seahorse machine. Since Ubc13 may participate in the ubiquitination of mitochondria and mitophagy, we suggest that Ubc13 controls mitochondrial function, which protects livers from toxin-induced injury and fibrosis.

(2-4) Arsenic exposure, non-malignant respiratory outcomes and immune modulation in the Health Effects of Arsenic Longitudinal Study (HEALS) cohort

Faruque Parvez, Yu Chen, Mahbub Yunus, Christopher Olopade, Scott Burchiel, Rabiul Hasan, Alauddin Ahmed, Tariqul Islam, Vesna Slavkovich, Joseph H. Graziano, Habibul Ahsan

Limited evidence exists on the effects of arsenic (As) exposure on non-malignant pulmonary outcomes, particularly among those exposed to low-to-moderate levels of As exposure or without skin lesions. We conducted population-based studies to evaluate the association between As exposure, measured in well water and urine samples, and pulmonary infection, lung function, incident of lung diseases and mortality in 20,033 Heath Effects of Arsenic Longitudinal Study (HEALS) participants in Araihazar, Bangladesh who are exposed to wide range of water with As concentrations (0.1-1,517 μg/L). In a prospective analysis, we observed an association between baseline water As and respiratory infections among 784 individuals. As compared to those at the lowest quintile of well As level (<=6 μg/L), the HRs (hazard ratios) for having respiratory infections were 1.2 (95% CI: 1.0-1.5), 1.2 (95% CI: 0.9-1.4) and 1.4 (95% CI: 1.1-1.9) for the 2nd-4th quartiles of baseline water As concentration (6-46, 46-116, and >116 μg/L), respectively, in model adjusted for age, gender, BMI, smoking, and socioeconomic status and skin lesion status. A slightly stronger relationship was observed between baselines urinary As. In a pilot study (N=12), among never-smokes we observed dose dependent suppression of PHA stimulated PBMC T-cell

proliferation associated with urinary arsenic (β=-0.36, p=0.1) and MMA (β=-0.42, p=0.2) and a number of cytokines including (TNFα, IL4, IL6, and IL1β) particularly significantly negatively with IL17 (r=-0.92, p=0.02) as observed in animal study. Our findings suggest that arsenic may affect immune markers in humans.

(2-5) A historical cohort study of the influence of occupational and non-occupational exposure to asbestos

Atu Agawu[1], Shabnam Elahi[1], Luke Basta[1], Douglas J Wiebe[1], Edward Emmett[1], Anil Vachani[1], Frances K. Barg[1]

[1]University of Pennsylvania

Context: Asbestos exposure is most widely studied as an occupational phenomenon. However, there is emerging evidence of asbestos-related diseases among non-occupationally exposed individuals. Using Ambler, Pennsylvania (PA), a community with substantial occupational and community exposure to asbestos, we aimed to characterize non-occupational exposure to asbestos and its resultant mortality.

Methods: Using publically available census records to identify individuals living in Ambler, PA in 1930, we extracted names, address, gender, race, occupation and industry. Occupational exposure was defined on the basis of an individual's occupation and industry. Paraoccupational exposure was defined as having the same address as an individual with occupational exposure. We calculated summary statistics of demographic variables, tabulated exposures, and used chi-square tests to describe associations among exposure variables and race/gender.

Results: 4,524 individuals were identified with a median age of 32 years and an interquartile range of 37. Half were male (50.6%), predominantly white (87.6%) with a small Black population (12.4%). Only 9.6% of the population had occupational exposure, whereas approximately one third had paraoccupational exposure (36.2%). A smaller proportion of women had occupational exposure compared to males (2.5% vs. 18.3%, p<0001), although the trend was reversed for paraoccupational exposure (38.9% for females, 33.5% for males, p<0.001). A higher proportion of Blacks had occupational (15.7%) and paraoccupational (57.3%) exposure compared to Whites (9.7% occupational, 33.2% paraoccupational) and the differences were statistically significant for both (p<0.001).

Conclusions: In this large cohort of individuals living near an asbestos manufacturing plant we found significant paraoccupational exposure to asbestos. Additionally, Blacks had significantly higher occupational and paraoccupational exposure to asbestos. Future efforts will focus on characterizing mortality in the cohort as function of occupational and paraoccupational exposure.

(2-6) The detection of effects of asbestos exposure using novel biomarkers.

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Ian Blair, Ph.D, University of Pennsylvania Superfund Research Program

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Rationale: Screening for asbestos exposure relies heavily on the development of clinical disease, long after the exposures have occurred. The early detection of subclinical changes resulting from asbestos exposure can provide additional medical intervention time and possibly facilitate elimination of the connection between environmental exposure and disease.

Recently, there has been evidence that serum biomarkers can be used to detect asbestos exposure. Previously, we have demonstrated that asbestos exposure can result in a unique lipidome signature. This study hypothesizes that exposure to asbestos and mesothelioma can result in a specific lipidome.

Hypothesis: Novel lipids can serve as early biomarkers of asbestos exposure and mseothelioma.

Study Population: Serum samples from patients exposed to chrysotile asbestos in Ambler PA and patients with mesothelioma.

Methods: Serum metabolomics analysis will be performed on serum samples using ultra-high resolution liquid chromatography & high resolution mass spectrometry**.** Results will be analyzed using LipidView and MarkerView.

Research Translation: The question "have I been exposed to asbestos in a way that could cause long-term health effects" is one that is repeated in many communities across the US, especially in the Superfund areas such as Libby, Montana and Ambler, Pennsylvania. The findings of this study could benefit all communities by providing better identification of those at risk.

(2-7) New Methods to Quantify Mercury Bioavailability and Methylation Potential in Contaminated Sediments

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Mercury (Hg) contamination persists in numerous sediment sites worldwide, and this contamination becomes a problem if the metal is converted to monomethylmercury (MeHg), the highly bioaccumulative form that can impart neurotoxic effects to humans and wildlife. Strategies for remediation generally aim to minimize MeHg production by benthic microorganisms native to the sediments. However, the factors that influence MeHg production in sediments have been poorly understood and difficult to quantify. Moreover, these processes that control Hg methylation can differ between sites. Therefore, methylation potential of Hg at a site needs to be quantified prior to the selection of a remediation strategy.

This presentation will summarize the challenges of mercury contamination in the aquatic environment and offer strategies for assessing risk and appropriate remediation methods. These strategies are based on research to delineate the two major factors that control the net production of MeHg in sediments: the activity of the methylating microbial community and the bioavailability of inorganic Hg for these microorganisms. Genetic-based methods to quantify mercury methylating microorganisms have been combined with chemical leaching methods to quantify Hg bioavailability in sediments. These methods were applied to sediment slurry microcosm experiments in which the type of Hg and the growth of methylating microorganisms were carefully controlled. The results demonstrate that under conditions of low microbial growth, Hg methylation is limited by the productivity of these organisms. While under conditions of high microbial growth, MeHg production is sensitive to the speciation and bioavailability of Hg. The use of these indicators will be discussed in the context of management and in-situ remediation of contaminated sediments.

(2-8) Development of in-situ methods for simulating sediment recovery post-remediation in a stream affected by acid mine drainage

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The North Fork of Clear Creek (NFCC), located in central Colorado, is an aquatic system that is currently receiving drainage from legacy mine waste. After mine drainage metals are deposited onto stream sediment, several factors including water chemistry, stream flow and dissolution kinetics will control the recovery following remediation of the overlying water planned

for 2017. We modified a previously existing method for examining benthic community recovery in-situ, to examine potential sediment recovery rates in the NFCC. Standardized trays filled with cleaned stones and cobbles were anchored in a contaminated stretch of stream below mine drainage inputs. The trays were allowed to accumulate metal coatings and particulates for one month. To simulate probable post-restoration conditions they were subsequently transported upstream of the drainage inputs to a reference site and sampled over several time points. In 2012, after 7 days upstream the average iron concentration in the samples decreased about 30%, and the average copper concentration decreased about 35%. In 2013, after 10 days upstream the average iron concentration in the samples decreased about 10%, and the average copper concentration decreased about 28%. This decreased percent removal in 2013 reflects methodological improvements that reduced metal particulate loss from the trays when removing them from the stream. These improved methods will provide a means to more accurately represent the biological and chemical recovery of contaminated stream sediment. These tools allow for stakeholders to predict future improvements in water quality that will accompany remediation.

(2-9) Transcriptomic effects of ortho-PCBs on developing zebrafish

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Developmental effects of PCBs are among the most important and least well-understood concerns in PCB toxicology. *Ortho*-substituted PCBs are far more abundant than the dioxin-like PCBs but effects, especially on development, are poorly known. Zebrafish embryos were exposed to 3 μM of poly-*ortho* PCB153 for two different lengths of time during development, beginning at 48 hpf and extending 6hrs or 24hrs. Transcriptomic responses were examined using Illumina RNA-Seq. After mapping to the zebrafish genome, differential gene expression analysis found that 1182 genes were significantly differentially expressed after 6 hrs of exposure (186 up- and 996 down-regulated), while 265 were differentially expressed after 24 hrs of exposure (90 up- and 175 down-regulated). CYP activity, glycolysis/gluconeogenesis, and lipid binding and transport were among the downregulated functional gene clusters at both timepoints. Wound-healing, immune function, and endopeptidase inhibitor activity genes were downregulated at short time scales, while cation homeostasis was downregulated only after 24 hrs of exposure. CYP2AAs were prominently downregulated at both time periods, as well as in independent experiments over longer exposure times. In contrast, thioredoxin redox homeostasis and iron dependent oxygenases (not P450s) were upregulated at short and longer timescales, respectively. Similar results were found for exposures to the poly *ortho* PCB95, and PCB52. This research is highly relevant for risk and ecological analyses of the New Bedford Harbor Superfund Site, where extensive PCB contamination has led to the selection of PCB-resistant fish populations that accumulated large concentrations of ortho-PCBs, with the potential for trophic transfer. Research translation to Boston University SRP partners has included the Museum of Science, the Collaborative on Health and the Environment, and the Society for Risk Analysis.

(2-10) Adductomics and organophosphorus exposures in communities

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Half of the insecticides used in the United States are organophosphorus (OP) compounds. OPs poison insects and mammals by impairing the function of serine hydrolases, resulting in detrimental effects in the central and peripheral nervous system. Agricultural workers and community members are at high risk of OP exposures. Of greater concern are OP exposed children, to whom low level exposures can impair proper brain development. The assays used for biomonitoring OP exposures (Ellman enzymatic activity assays) present several drawbacks. Therefore, there is an urgent need for improved assays for biomonitoring OP exposures.

A major aim of our research in the last funding period was to study the individual sensitivity to OP exposures by characterizing modified biomarker proteins.

We use adductomics to profile covalent bonds created between the OP and the active-site serine of biomarkers of exposure, such as plasma butyrylcholinesterase, red blood cell acylpeptide hydrolase and acetylcholinesterase, or monocyte carboxylesterase. The method developed, which combines magnetic bead immunoprecipitation with mass spectrometry (LC-MS/MS), is so sensitive that measurements can be done with dried blood spots. Additional advantages of our adductomics approach include the no requirement of a baseline measurement, the biomonitoring of any serine hydrolase and any OP, the usefulness for monitoring chronic low-level exposures, and the generation of information on the OP of exposure.

Samples from an agricultural community in the Washington State have been analyzed to validate our approach. The developed methods have already been shared with the CDC and the ATSDR. As this adductomics approach can easily be automated, we envision its translation to clinical laboratories to rapidly monitor any OP exposure, with the potential to replace the Ellman assays currently used.

(2-11) Environmentally Persistent Free Radicals Increase Systolic Blood Pressure and Block Compensatory Responses to Cardiac Stress in Rats with Ischemic Heart Disease

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Increases in particulate matter (PM) are linked to increased mortality from cardiac ischemia. PM contains environmentally-persistent free radicals (EPFRs) that form when halogenated hydrocarbons chemisorb to the surface of transition metal oxide-coated particles. EPFRs are capable of sustained redox cycling in the environment. We showed that EPFRs exacerbate left ventricular (LV) dysfunction produced by ischemia-reperfusion injury. Here we tested the hypothesis that inhalational exposure to EPFRs would degrade LV performance in rats with preexisting ischemic disease. Myocardial infarction (MI), or Sham MI were performed 3 weeks before exposure to EPFRs or vehicle. Radio telemetry continuously recorded arterial pressure (AP) and heart rate (HR) before and after exposure. Pressure-volume catheters were used to assess LV function. Exposure to EPFRs (DCB230; 460 µg max/day) or vehicle 60 min/day, 5 days/week for 3 weeks was by nose-only inhalation. Before exposures each day, resting AP and HR were similar in the MI and Sham MI groups. AP and HR were not significantly different in sham rats exposed to DCB230 or vehicle. However, after 2 weeks of exposure, mean- and systolic AP were significantly greater in MI+DCB230 rats than in MI+vehicle rats. HR and diastolic AP were the same in both MI groups. MI evoked contractile compensation at baseline to maintain LV function. During dobutamine infusion, MI+DCB230 rats failed to increase preload recruitable stroke work (PRSW), stroke volume or stroke work indicating reduced contractile reserve. PRSW responses following β-blockade suggest alterations in sympathetic input in the MI+DCB230 group. In conclusion, EPFRs appear to increase systolic AP and reduce compensatory mechanisms in the ischemic heart which, may help to explain the correlations between $PM_{2.5}$ and ischemic heart-related mortality. Support P42ES013648; P30GM106392

(2-12) Enhanced groundwater flow modeling in karst using drainage feature: case study of the central northern karst aquifer system of Puerto Rico

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Abstract: Karst aquifer systems in central Northern Puerto Rico (NPR) are highly productive but also demonstrate high levels of heterogeneity. The subsurface conduit networks with unknown characteristics, and surface features such as springs, rivers, lagoons and wetlands drain the coastal karst aquifers. Due to existence of high permeability pathways, the NPR karst system is considered highly vulnerable to contamination from Superfund sites within the study area. While the field data sparsity often limits the ability to locate and characterize the conduit system, a method is introduced in this study for modeling the heterogeneities of flow in karst aquifers by assigning arrays of adjacent model cells with drains to simulate conduits. Connecting sinkholes and springs, such drain lines can improve the developed regional model by simulating the drainage effects of conduit networks on local groundwater table. Implemented in an Equivalent Porous Media (EPM) regional model, the MODFLOW drainage feature is also able to roughly reproduce the spring discharge hydrographs in response to rainfall. Hydraulic conductivities are found to be scale dependent and significantly increase with higher test radius, indicating scale dependency of the EPM approach. The analysis of historical slug test data suggests that the central NPR aquifers are more karstified that others in northwestern, eastern, and southwestern Puerto Rico. Similar to other karst regions in the world, hydraulic gradients are steeper where the transmissivity values are lower approaching the coastline.

Research Translation Component: This study enhances our current understanding of the hydrodynamics behavior and complex flow patterns in karst aquifers which are important in identifying contaminant transport pathways. The results suggest that using drainage feature may improve modeling results where available data on conduit characteristics are minimal.

Recent publications:

Ghasemizadeh R, Hellweger F, et al. (2012) “Review: groundwater flow and transport modeling of karst aquifers, with particular reference to the North Coast Limestone aquifer system of Puerto Rico” Hydrogeology Journal, 20(8): 1441-1461.

Yu X, Ghasemizadeh R, et al. (2015) “Spatiotemporal changes of CVOC concentrations in karst aquifers: Analysis of three decades of data from Puerto Rico” Science of The Total Environment, 511:1–10.

(2-13) Patterns of phthalates in karst aquifers of Northern Puerto Rico

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Abstract: We investigated phthalate contamination in aquifers particularly karst aquifers in Northern Puerto Rico (NPR), an area with high preterm birth rates. We compiled phthalate concentration data sets from historical studies and our current field sampling campaign. Multiple linear regressions, factor analysis, and logistic regression model were used to examine the causes of phthalate detections and concentrations. The concentrations (mean ± standard deviation) of the total phthalates were 1.45±4.43 μg L^{-1}, and ranged from 0-58.4 μg L^{-1}. The most positively detected phthalates included di(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), and diethyl phthalate (DEP). Among the 176 sampling sites, 159 or 90% were detected with at least one type of phthalates. Overall, 54% of the samples were positively detected with phthalate. The cause analysis identified two principal factors that significantly affecting the detections and concentrations of phthalates: source factor (closeness to Superfund sites, Toxic Release Inventory industries and Resource Conservation and Recovery Act, site elevation, and land use patterns) and hydrogeology factor (aquifer coverage, sinkhole, spring or well types). The greater odds for higher detections and concentrations of phthalates were corresponded to closer distance to Superfund sites, more forest coverage, larger aquifer area, more sinkholes, and in dry seasons.

Research Translation Component: This study improves understanding of the spatial variability and fate of phthalates in karst aquifers, which is important to fill the scientific gap in studying the occurrence of phthalate in karst aquifer as fundamentals for better understanding the link between preterm birth and groundwater contamination.

Recent publications:

Yu X, Ghasemizadeh R, et al. (2015) “Sociodemographic patterns of household water use in Puerto Rico” Science of The Total Environment, 524/525:300–309.

Yu X, Ghasemizadeh R, et al. (2015) “Spatiotemporal changes of CVOC concentrations in karst aquifers: Analysis of three decades of data from Puerto Rico” Science of The Total Environment, 511:1–10.

(2-14) Formaldehyde induces toxicity in mouse bone marrow and hematopoietic stem/progenitor cells and enhances benzene-induced adverse effects

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Formaldehyde (FA) is a human leukemogen and is hematotoxic in human and mouse. The biological plausibility of FA-induced leukemia is controversial, however, because few studies have reported bone marrow (BM) toxicity, and no studies have

reported BM stem/progenitor cell toxicity resulting from FA exposure. We sought to comprehensively examine FA hematoxicity *in vivo* in mouse peripheral blood, BM, spleen and myeloid progenitor cells. We included the leukemogen and BM toxicant, benzene (BZ), as a positive control, separately and together with FA as co-exposure occurs frequently. We exposed BALB/c mice to 3 mg/m^3 FA in air for 2 weeks in a scenario mimicking occupational exposure. We measured complete blood counts (CBC), nucleated BM cell count, spleen index, and myeloid progenitor colony formation. We also investigated potential mechanisms of FA toxicity, including reactive oxygen species (ROS) generation; apoptosis; and levels of key hematopoietic growth factors and their receptors. FA exposure significantly reduced mature cells and myeloid progenitor cells in BM, increased ROS and apoptosis, and altered levels of hematopoietic growth factors and receptors. Separately, FA and BZ exerted similar degrees of toxicity on BM stem/progenitor counts, BM ROS, and apoptosis in CFU-GM and had differential effects on other endpoints. Co-exposure was more potent for several endpoints. FA is toxic to the mouse hematopoietic system, including BM stem/progenitor cells, and it enhances BZ-induced toxic effects. These findings are the first report of BM stem/progenitor cell toxicity caused by FA inhalation in mice, which suggest that FA may induce leukemia by affecting myeloid progenitor growth and survival through oxidative damage and altered cytokine receptor levels. This study may improve risk assessment and management decisions on FA.

Recent Publications

Lan Q, Smith MT, Tang X, Guo W, Vermeulen R, Ji Z, Hu W, Hubbard AE, Min S, McHale CM, Qiu C, Liu S, Reiss B, Beane Freeman L, Blair A, Ge Y, Xiong J, Li L, Rappaport SM, Huang H, Rothman N, **Zhang L** (2015). Chromosome-Wide Aneuploidy Study (CWAS) of cultured circulating myeloid progenitor cells from workers occupationally exposed to formaldehyde. *Carcinogenesis*. 36(1):160-7. PMID: 25391402. PMCID: PMC4291049.

Seow WJ, **Zhang L**, Vermeulen R, Tang X, Hu W, Bassig BA, Ji Z, Shiels MS, Kemp TJ, Shen M, Qiu C, Reiss B, Beane Freeman L, Blair A, Kim C, Guo W, Wen C, Li L, Pinto LA, Huang H, Smith MT, Hildesheim A, Rothman N, Lan Q (2015). Circulating immune/inflammation markers in Chinese workers occupationally exposed to formaldehyde. *Carcinogenesis.* 36(8):852-7. PMID: 25908645.

Ye X, Ji Z, Wei C, McHale CM, Ding S, Thomas R, Yang X, **Zhang L** (2013). Inhaled formaldehyde induces DNA-protein crosslinks and oxidative stress in bone marrow and other distant organs of exposed mice. *Environ Mol Mutagen.* 54:705-718. PMID: 24136419.

(2-15) Epigenetic and gene expression effects of arsenic exposure

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While arsenic is a known human carcinogen as well as associated with a number of other adverse health outcomes, its mechanism of toxicity remains unknown. Aberrant epigenetic and gene expression pathways have been suggested to underlie arsenic toxicity; however, molecular epidemiological studies of arsenic exposure are still sparse. Therefore, among a sample of 400 adult participants in Bangladesh, we evaluated the association between arsenic exposure and epigenome-wide DNA methylation and genome-wide gene expression in cross-sectional analyses. Participants, aged 25-65 years at enrollment, have been chronically exposed to naturally-occurring arsenic through the consumption of groundwater. Individual-level arsenic exposure was measured by urinary total arsenic and blood arsenic concentrations. DNA methylation status was assessed from whole blood DNA using the Illumina Infinium HumanMethylation450 BeadChip, which measures methylation of >485,000 CpG sites. Gene expression was assessed from peripheral blood mononuclear cell RNA using the Illumina HumanHT-12 v4

Expression BeadChip, which measures expression of >47,000 mRNA transcripts. Linear regression models were used to examine the associations between arsenic with each CpG site or mRNA transcript, adjusted for sex, age, and batch. Bonferroni correction was applied to the level of significance to account for multiple comparisons. In adjusted analyses, we observed several significantly differentially methylated CpG sites as well as differentially expressed genes in relation to arsenic exposure. Through integrated analyses, we additionally identified a subset of genes, which showed evidence of gene regulation through epigenetic mechanisms in relation to arsenic exposure. Our findings indicate novel genes and pathways that may be associated with arsenic toxicity and should be examined in relation to risk of arsenic-related diseases.

Recent publications: Argos M et al. Gene-specific differential DNA methylation and chronic arsenic exposure in an epigenome-wide association study of adults in Bangladesh. Environmental Health Perspectives. 2015; 123(1):64-71.

(2-16) Impact of groundwater-surface water dynamics on in situ remediation efficacy and bioavailability of PAH contaminants

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Lipophilic contaminants such as polycyclic aromatic hydrocarbons (PAH) concentrate in sediments and may accumulate in biota, posing a significant human health risk. This project is utilizing new radiological and biosensor based methods to evaluate the biogeochemical mechanisms controlling the transport of dense non-aqueous phase liquids (DNAPL) and dissolved PAH within groundwater and at the groundwater-surface water interface at contaminated sites. Recent work has shown that groundwater-surface water interactions include numerous advection mechanisms such as tidal and wave driven processes that operate independently of canonical groundwater flow. In situ caps placed during remediation efforts are designed to resist physical disturbance by erosion and bioturbation, and are composed primarily of coarse granular material, which is highly permeable. As a result, porewater advection may be orders of magnitude higher than expected from groundwater considerations alone. Contaminant flux may be a better estimate of the PAH bioavailability than sediment concentrations at these sites. Results from field and laboratory studies are being used to evaluate how advection processes determine the efficacy of in situ remediation methods. Measurement of PAH concentrations in porewater samples by biosensor allowed spatial profiling of PAH concentrations within sediments. Concentrations ranged from < 1 to over 500 μg/L and total pore water advection estimates by radionuclide tracer were up to 4400 – 15000 cm/y.

This study is providing new techniques for evaluating shallow advection rates and porewater PAH concentrations for site characterization to guide in situ remediation. We are working directly with remediation managers to evaluate the effectiveness of capped areas and to advise them on ways to improve remediation methods and cap design where groundwater advection processes are active.

(2-17) Effect of early marriage and arsenic exposure during pregnancy on gestational weight gain and preterm birth in Bangladesh.

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Background: In-utero arsenic exposure, early marriage, and low gestational weight gain (GWG) are known risk factors for preterm birth. However, the effect of arsenic and early marriage on preterm birth is direct or mediated through pathways related to GWG remains unknown.

Objective: To evaluate the relationship between in-utero arsenic exposure, early marriage, and preterm birth considering GWG as a mediator.

Methods: Total 1,181 singleton live births from a prospective birth cohort in Bangladesh were included in the analysis. Arsenic was measured in drinking water during the first trimester. Age of marriage and other socio-demographic information were collected using structured questionnaire. GWG during the second and third trimesters (lb/week) was measured. Mediation analysis was used to estimate the direct and indirect effects of arsenic and early marriage on preterm birth. GWG was considered a common mediating variable.

Results: The risk of preterm birth increased with increased natural log water arsenic (RR=1.10; 95% CI:1.02−1.16) after adjusting for confounders; most of which was the direct effect of arsenic (RR=1.09; 95% CI:1.02−1.15), only 11.5% was mediated through decreasing GWG (RR=1.01; 95% CI:1.00−1.02). Women married before age 18 had twice the risk of preterm birth (RR=2.08; 95% CI:1.10−2.81) compared to women married ≥18 years. The effect of early marriage on preterm birth among underweight and normal weight women could have been eliminated by nearly 10% and 14% respectively, had they gained the U.S. Institute of medicine (IOM) recommended mean weight during the second and third trimesters.

Conclusion: In-utero arsenic exposure, early marriage and gestational weight gain were associated with preterm birth. However, the effect of arsenic and early marriage on preterm birth appears to be direct and partly mediated through GWG.

(2-18) Understanding the genomic basis for adaptation to long-term PCB exposure at Superfund sites: Application of genome editing to aryl hydrocarbon receptor (AHR) signaling pathways in fish.

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Multi-generational exposure to high levels of contaminants at Superfund sites can have profound effects on natural populations, imposing strong selective pressure that can dramatically change allele frequencies at multiple loci, with far-reaching physiological and ecological consequences. One example is the evolution of tolerance or resistance to dioxin-like chemicals (DLCs) that has occurred in populations of the Atlantic killifish (*Fundulus heteroclitus*) inhabiting several sites

contaminated with polychlorinated biphenyls (PCBs) and other DLCs. Previous research has implicated the aryl hydrocarbon receptor (AHR) signaling pathway in the mechanism of DLC resistance. AHR signaling is impaired in DLC-resistant fish, but the underlying molecular mechanisms, including the relative roles of the four killifish *ahr* genes and other genes involved in AHR-dependent signaling, have proved elusive. To better understand the factors controlling the sensitivity of AHR pathways, we are engineering germ-line mutant killifish and zebrafish (*Danio rerio*) to test hypotheses about the role of multiple fish AHRs and other AHR pathway members in the evolved resistance to DLCs. We are using the transformative CRISPR-Cas technology to generate null alleles of these genes in killifish and zebrafish as well as to introduce candidate single-nucleotide polymorphisms (SNPs) to test hypotheses about their role in the resistant phenotype. Elucidating the mechanisms of adaptation to long-term DLC exposure will inform ecological risk assessment at Superfund sites and contribute to a fundamental understanding of mechanisms underlying differential sensitivity to chemicals.

Recent publications:

Aluru, N., Karchner, S.I., Franks, D.G., Nacci, D., Champlin, D., Hahn, M.E. (2015) Targeted mutagenesis of aryl hydrocarbon receptor 2a and 2b genes in Atlantic killifish (*Fundulus heteroclitus*). *Aquat Toxicol* **158**, 192-201.

Proestou, D.A., Flight, P., Champlin, D., Nacci, D. (2014) Targeted approach to identify genetic loci associated with evolved dioxin tolerance in Atlantic killifish (Fundulus heteroclitus). *BMC Evolutionary Biology* **14**, 7.

Reitzel, A.M., Karchner, S.I., Franks, D.G., Evans, B.R., Nacci, D.E., Champlin, D., Vieira, V.M., Hahn, M.E. (2014) Genetic Variation at Aryl Hydrocarbon Receptor (AHR) Loci in populations of Atlantic Killifish (*Fundulus heteroclitus*) inhabiting Polluted and Reference Habitats. *BMC Evolutionary Biology* **14**, 6.

(2-19) Exposure to PCBs Not Found in Commercial Mixtures: Evidence from Biomonitoring Among Urban and Rural Adolescents and Their Mothers

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Although production of PCB commercial mixtures has long been banned, they are still being produced as byproducts through modern manufacturing processes. Our prior studies have shown that the non-Aroclor, PCB11, is prevalent in indoor and outdoor air, sediment, and detected in human serum. We have now found that additional non-Aroclor PCB congeners, defined as congeners represented at ≤0.20 wt % in Aroclors, represent a substantial proportion of the PCBs in serum collected from urban and rural cohorts. Sera were extracted and analyzed for 209 PCB congeners quantified as single or co-eluting PCBs in 174 chromatographic peaks using GC-MS/MS. A list of 70 non-Aroclor PCB congeners was determined by measurement of original Aroclors 1016, 1221, 1242, 1248, 1254, 1260 or 1262. PCB 11, 14, 35 and 209 were identified as the most frequently detected congeners and appeared in the highest concentrations. PCB 14 and 35 have not been previously reported for environmental matrices. Adolescents had significantly lower total non-Aroclor PCBs concentrations than mothers in East Chicago ($p<0.001$) and Columbus Junction ($p=0.008$). However, we found significant differences in non-Aroclor PCBs between the East Chicago and Columbus Junction communities ($p<0.001$). Non-Aroclor PCBs represented a mean of 10% of total PCBs measured in serum and for some individuals as much as 50%. An average of half, and as much as 100%, of these concentrations may be attributed to aryl azo and phthalocyanine paint pigments. Research Translation: The notion of PCBs as solely legacy pollutants is false. Adults and children are currently being exposed to new PCB congeners that are being produced now. Since they have not been previously recognized as important pollutants, we know very little about their toxicity.

(2-20) A Four-Year Superfund Site Field Study Demonstrates that Direct Planting on Mine Tailings is a Reclamation Alternative to Cap and Plant

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EPA estimates that future mine tailings remediation costs will exceed US $50 billion using present technologies based on constructing an inert or biological cap on the tailings. Both approaches require large amounts of capping materials that can be difficult and expensive to obtain especially for sites several thousand hectares in size. An alternative technology is direct planting into tailings. However, direct planting alone is not feasible for many legacy sites due to extreme acidity and high metal content which prevent plant germination and growth. Therefore the process must be "assisted" through the addition of amendments such as compost. Here we present results from the first four years of a field study at the Iron King Mine and Humboldt Smelter Superfund site demonstrating the feasibility of compost-assisted direct planting. Parameters measured during the field study included: canopy cover, pH, nutrient content, plant metal uptake, metal(loid) speciation, mineral analysis, microbiome analysis, and plant root-metal-microbe interactions. Integrated analysis of these parameters suggests that even in this "worst-case scenario" mine tailings site (pH 2.5; As and Pb each exceeding 2 g kg^{-1}), we have created a sustainable system. In this system, phyto-catalyzed stabilization of inorganic contaminants in the root zone is driven by plant root exudates and the associated rhizosphere microbial community. Further, the vegetative cap acts to reduce dust emissions, a major route of contaminant transport off the site. This research is being translated through our Superfund Research Center partner, the Center for Environmentally Sustainable Mining, to industry stakeholders with the result that we are now working with three mining companies on similar projects on their sites.

(2-21) Metabolomic Characteristics of Arsenic-Associated Diabetes in a Prospective Cohort in Chihuahua, Mexico

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Chronic exposure to inorganic arsenic (iAs) has been linked to an increased risk of diabetes, yet the specific disease phenotype and underlying mechanisms are poorly understood. The objective of this study was to identify iAs exposure-associated

metabolites with altered abundance in non-diabetic and diabetic individuals in an effort to understand the relationship between exposure, metabolomic response and disease status. A nested study design was used to profile metabolomic shifts in urine and plasma collected from 90 diabetic and 86 non-diabetic individuals matched for varying iAs concentrations in drinking water, BMI, age and sex. Diabetes diagnosis was based on measures of fasting plasma glucose and 2-hour blood glucose. Multi-variable models were used to identify metabolites with altered abundance associated with iAs exposure among diabetic and non-diabetic individuals. A total of 132 metabolites were identified to shift in urine or plasma in response to iAs exposure characterized by the sum of iAs metabolites in urine (U-tAs). While many metabolites were altered in both diabetic and non-diabetic subjects, diabetic individuals displayed a unique response to iAs exposure with 59 altered metabolites including those that play a role in tricarboxylic acid cycle and amino acid metabolism. In conclusion, these data highlight the broad impact of iAs exposure on the human metabolome, and demonstrate some specificity of the metabolomic response between diabetic and non-diabetic individuals. These data may provide novel insights into the mechanisms and phenotype of diabetes associated with iAs exposure.

(2-22) Mono-Ethylhexyl Phthalate Stimulates Prostaglandin Synthesis in Human Placental Macrophages and THP-1 Cells

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Diethylhexyl phthalate (DEHP) is commonly used to increase flexibility in polyvinyl chloride plastics. Although DEHP exposure is associated with increased odds of preterm birth, mechanisms underlying this association remain unclear. Because macrophages are important sources of prostaglandins and because cyclooxygenase-2 (COX-2)-dependent prostaglandin synthesis is implicated in labor onset, we evaluated mono-2-ethylhexyl phthalate (MEHP), a bioactive metabolite of DEHP, on prostaglandin E_2 (PGE_2) synthesis and COX-2 expression in isolated human placental macrophages and a human macrophage-like cell line, THP-1. Cells were treated for 2, 4, 8, or 24 h with MEHP concentrations ranging from 10-180 µM. Prostaglandins were measured in culture medium using ELISA, and COX expression was determined by western blot. A 24-h treatment with 180 µM MEHP significantly increased PGE_2 and $PGF_{2\alpha}$ release, and 90 µM MEHP significantly increased $PGF_{2\alpha}$ release. Co-treatment with 180 µM MEHP and the non-selective COX inhibitor indomethacin or the COX-2 selective inhibitor NS-398 reduced MEHP-stimulated PGE_2 production. Western blot analysis revealed significantly increased COX-2 expression in cells treated with 180 µM MEHP but no changes in COX-1 expression. These results show that a bioactive metabolite of the widely used phthalate DEHP stimulates placental macrophage production of prostaglandins through a mechanism that includes increased expression of the prostaglandin synthesis enzyme COX-2. Given the relevance of these prostaglandins in parturition onset, these findings may be of interest to regulatory scientists for assessing potential risks of DEHP to human pregnancy. These findings were reported previously (Tetz et al. Reprod Biol Endocrinol 13:56, 2015).

(2-23) Discovery of Xenobiotics Associated with Preterm Birth

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Preterm birth is a major health problem, and its incidence is high in Puerto Rico, an island with many Superfund sites. In this project, we are conducting nontargeted analysis of environmental (water) and biological (urine, placenta) samples from Puerto Rico, seeking to discover xenobiotics that contribute to preterm birth. To provide convenient extraction of large water samples in Puerto Rico for analysis in Boston, we have developed a loop solid phase extraction device. Similarly, we have developed a stirring solid phase extraction device (termed a “porous extraction paddle or PEP) for extracting xenobiotics from

large urine samples. With this latter device, we have set up a method for the urine nonpolar sulfateome. The rational for this is that many bioactive xenobiotics are nonpolar and metabolized to some degree to sulfates. We have detected the masses of 1129 sulfates in a collection of 6 pregnancy urines, ranging from 549 to 711 sulfates in the individual samples. In the prior literature, the sulfateome value was about 15. To detect the placental DNA adductome, a new technique, utilizing a cationic mass tag termed "CAX-B" is under development. Research translation: (1) the PEP device is being developed by a company for purification of water, beverages and pharmaceutical reaction mixtures; (2) CAX-B is being developed further by a grant from the Department of Agriculture for discovery of carcinogens in food.

(2-24) Crypt organoids culture as an in vitro model in pharmacological and toxicological studies

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Xenobiotic Processing Genes (XPGs) play an important role in chemical bioactivation, metabolism, and detoxification. The gastrointestinal (GI) tract is the largest absorption organ in the body and is also enriched with many of the *XPGs*; however, an appreciation for the role of the GI track in drug metabolism has been under estimated, leading to inaccuracies in evaluating its role in pharmacological and toxicological applications. Recently, our lab has established an *in vitro* tissue culture model of crypt organoids and the application in both pharmacological and toxicological aspects. Crypt cells were isolated from mouse intestinal tissue, suspended into matrigel, and cultured in the advanced DMEM/F12 medium supplemented with growth factors. Following continuous budding, crypts were further expanded to create organoids. Each organoid contains multiple crypt domains surrounding a central epithelium villus domain. Approximately five days after plating, organoids were treated with vehicle (control) or different prototypical agonists of xenobiotic nuclear receptor (XNR), including the AhR agonist TCDD, PXR agonist PCN, CAR agonist TCPOBOP, PPARα agonist Wy14643, and LXRα agonist T0901317. Twenty four hours after chemical exposure, cells were collected for RNA preparation and followed by real time PCR. Results from the quantitative analysis demonstrated that in response to the activation of different XNR agonists, the representative downstream target genes, including *Cyp1a1* (by TCDD), *Cyp3a11* (by PCN), *Cyp2b10* (by TCPOBOP), *Cyp4a10* (BY Wy14643), and *Abca1* (T0901317) were largely induced. This study suggests that as an *in vitro* model crypt organoid culture is suitable for studying the impact of xenobiotics on intestinal *XPGs*, which will be useful for both pharmacological and toxicological studies.

(2-25) Relative Influence of Trans-Pacific and Regional Atmospheric Transport of PAHs in the Pacific Northwest, USA

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The relative influences of trans-Pacific and regional atmospheric transport on measured concentrations of polycyclic aromatic hydrocarbons (PAHs), PAH derivatives [Nitro- (NPAH) and Oxy-(OPAH)], organic carbon (OC), and particulate matter (PM) less than 2.5 µm in diameter ($PM_{2.5}$) were investigated in the Pacific Northwest, USA in 2010-2011. Ambient high volume $PM_{2.5}$ air samples were collected at two sites in the Pacific Northwest: 1.) Mount Bachelor Observatory (MBO) in the Oregon Cascade

Range (2763 m above sea level (asl)) and 2.) Confederated Tribes of the Umatilla Indian Reservation (CTUIR) in the Columbia River Gorge (CRG) (954 m asl). At MBO, the 1,8-dinitropyrene concentration was significantly positively correlated with the time a sampled air mass spent over Asia, suggesting that this NPAH may be a good marker for trans-Pacific atmospheric transport. At CTUIR, NOx, CO_2, and SO_2 emissions from a 585 MW coal fired power plant, in Boardman OR, were found to be significantly positively correlated with PAH, OPAH, NPAH, OC, and $PM_{2.5}$ concentrations. By comparing the Boardman Plant operational time frames when the plant was operating to when it was shut down, the plant was found to contribute a large percentage of the measured PAH (67%), NPAH (91%), OPAH (54%), $PM_{2.5}$ (39%) and OC (38%) concentrations at CTUIR and the CRG prior to Spring 2011 and likely masked trans-Pacific atmospheric transport events to the CRG. Upgrades installed to the Boardman Plant in the spring of 2011 dramatically reduced the plant's contribution to PAH and OPAH concentrations (by ~72% and ~40%, respectively) at CTUIR and the CRG, but not NPAH, $PM_{2.5}$ or OC concentrations.

S. Lafontaine, J. Schrlau, J. Butler, Y. Jia, B. Harper, S. Harris, L. Bramer, K. Waters, A. Harding, S. Massey Simonich. **2015**. "Relative Influence of Trans-Pacific and Regional Atmospheric Transport of PAHs in the Pacific Northwest, U.S.". *Environmental Science and Technology*, ASAP on-line.

(2-26) Statistical Approaches for Assessing Health Effects of Environmental Chemical Mixtures in Epidemiology Studies

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Analysis of exposure to environmental chemical mixtures is a well-known issue in toxicology and environmental epidemiology. New methods for epidemiologic analysis of mixtures are being developed, but it is not known how well they perform or how they compare with conventional epidemiologic approaches. With partial support from the Superfund Research Program, NIEHS held a workshop in July 2015 bringing together toxicologists, epidemiologists and statisticians with experience in developing and comparing approaches to assess the human health effects of mixtures. Prior to the workshop, researchers analyzed simulated data sets with a health outcome and multiple exposures and submitted their results. As the method used to create the synthetic data sets was known only by workshop organizers, comparisons could be made to the this gold standard. Researchers were then asked to analyze a simplified but real world data set where the answer is not known. Questions of interest include the following: 1) Which exposures are associated with the outcome and what is the size of their effect? 2) Is there evidence of interaction between exposures or not? 4) What is the cumulative effect of exposure to the mixture? A variety of approaches were used by over 30 groups of enthusiastic researchers, including several SRP groups, ranging from variable selection methods to response surface analysis. We will discuss the data sets and preliminary results of the workshop, including strengths and weaknesses of groups of types of approaches, and recommendations for future mixtures studies. While no single method performed best in all situations, there were a number of common themes, e.g., the need for reducing the complexity of the data, particularly the number of exposure variables.

Research Translation Component: Synthetic data sets will be maintained on the NIEHS website, providing other researchers an opportunity to compare methods. Analysts attending the workshop provided a copy of their computer code. We anticipate that these resources and papers coming out of the workshop will advance the field of mixtures analysis in epidemiology and ultimately lead to improved risk assessment.

(2-27) Elemental Imaging Capabilities of Dartmouth College's Trace Element Analysis Core Facility: A new program-wide resource.

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In addition to measuring how much of a metal is present in a sample, being able to see where metals are located, and their oxidation state in the context of the sample is critical and hypothesis-generating information. In biological tissue this can show the specific organ, tissue, cell and even organelle with which metals are associated. Elemental imaging accurately captures the distribution, abundance and (in some cases) speciation of multiple metals simultaneously in a wide range of sample types, from geological to biological specimens, often with minimal sample preparation. We established elemental imaging as a key method in genetic studies of metal homeostasis (1), but its applications to the environmental and health sciences have yet to be fully exploited. In addition to traditional, high-resolution bulk elemental analysis such as inductively coupled plasma mass spectroscopy and liquid chromatographic speciation techniques, Dartmouth's Trace Element Analysis core has recently expanded its analytical expertise to offer several spatially resolved techniques, including in-house laser ablation ICP-MS (LA-ICP-MS), and synchrotron X-ray fluorescence mapping, spectroscopy and diffraction. Our expertise and collaborations with multiple synchrotron beamlines allows us to make these techniques available to the Superfund Research Program. We present a range of elemental images collected at the TEA, from teeth, brain tissue and cereal grains (2) to nematodes(3), marine amphipods (4), plants (5) and placenta (6) that demonstrate the breadth of scientific questions elemental mapping can address. Our primary aim is to facilitate collaboration between Superfund Programs, provide expertise and access to cutting-edge scientific techniques, and ultimately to drive innovations in these techniques forward.

1. Punshon T, et al. Methodological approaches for using synchrotron X-ray fluorescence (SXRF) imaging as a tool in ionomic characterization: Examples from whole plant imaging of Arabdiopsis thaliana. Metallomics. 2013;5(9):1133-45

2. Carey A-M, et al. A review of recent developments in the speciation and location of arsenic and selenium in rice grain. Analytical and Bioanalytical Chemistry. 2011;402:3275-86

3. Jackson BP, et al. Evidence for biogenic pyromorphite formation by the nematode Caenorhabditis elegans. Environ Sci Technol. 2005;39:5620-5

4. Jackson BP, et al. Bioavailability, toxicity, and bioaccumulation of quantum dot nanoparticles to the amphipod Leptocheirus plumulosus. Environ Sci Technol. 2012;46(10):5550-6.3353010.

5. Punshon T, et al. The role of CAX1 and CAX3 in elemental distribution and abundance in Arabidopsis seed. Plant Physiol. 2012;158(1):352-62

6. Punshon T, et al. High-resolution elemental mapping of human placental chorionic villi using synchrotron X-ray fluorescence spectroscopy. Anal Bioanal Chem. 2015

(2-28) Development of In-Situ Mercury Remediation Approaches Based on Methylmercury Bioavailability

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Mercury in sediments can pose a significant human health risk when it is converted by microorganisms to the more toxic methylmercury, which enters organisms at the base of the food chain and ultimately accumulates in the top predatory fish. Critical research needs include improved understanding of mercury methylation and the development of treatment strategies to reduce organism exposure. The first aim of this research project is to develop a model of the microbial processes involved

in mercury methylation and demethylation. Studies are underway to investigate the factors controlling this balance, including microbial community structure, conversion rate constants, and the spatial distribution of organisms in sediments. The results will be used to develop a model to predict the overall methylation capacity of a site and help design more effectively targeted treatments. The second aim of the work is to develop black carbon as a viable strategy for reducing methylmercury bioavailability in the field. Application of black carbon to sediment is an increasingly popular strategy to treat sites contaminated with persistent organic pollutants. However, to date only preliminary, lab- and pilot-scale studies have been performed for in-situ treatment of methylmercury contamination. Experiments currently underway are characterizing sorption on carbons, the effects of treatment materials on microbial methylation, demethylation, and bioavailability of methylmercury under a variety of geochemical conditions. The results will be used to develop a statistical model to predict treatment effectiveness at contaminated sites. Overall, this work will result in significantly improved tools for stakeholders making risk assessment and remediation design decisions for mercury-contaminated sites.

(2-29) Biomarkers in Exhaled Breath Condensate and Serum for Lung Injury caused by Inhaled Mixtures of Heavy Metal: Linking Lung Fibrosis and Emphysema.

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Mixtures of heavy metals have been found to contaminate ambient air especially around coal fired power plants. The dominant metals among these mixtures include cadmium, manganese and arsenic. We have recently demonstrated in mice that exposure to cadmium causes severe emphysematous changes in the lung parenchyma through microvascular endothelial cell apoptosis and that heme oxygenase-1, a cytoprotective molecule, protects from the development of this emphysema through the induction of autophagy in endothelial cells[1]. Exposure to mixtures also caused extensive peribronchiolar fibrosis.

People living in an urban environment around coal fired power plants may be exposed to similar mixtures of heavy metals. We obtained exhaled breath condensate (EBC) from 65 people living within in a 6000 yard radius of a coal fired power plant and 20 age and smoking history matched control subjects from a rural unexposed environment. We also obtained serum from 120 patients diagnosed with lung fibrosis, 50 patients with COPD and 50 age-matched control patients with normal spirometry. Compared to controls, patients living around the coal fired power plants exhibited high levels of fragmented vimentin, a type III intracellular filament in their EBC. They also had heavy metals in their EBC on atomic absorption spectroscopy. Patients with pulmonary fibrosis had the highest levels of vimentin compared to those with COPD or controls in their serum. Anti-vimentin IgG antibodies were also detected in serum by both immunoblots and ELISA with the relative higher levels in patients with pulmonary fibrosis versus both cohorts with COPD and controls. These data suggest that factors obtained noninvasively from EBC or serum may serve as biomarkers for lung injury in people living around coal fired power plants.

References:

1. Surolia R, Karki S, Kim H, Yu Z, Kulkarni T, Mirov SB, Carter AB, Rowe SM, Matalon S, Thannickal VJ, Agarwal A, Antony VB. Hemeoxygenase-1 mediated autophagy protects against pulmonary endothelial cell death and development of emphysema in cadmium treated mice. Am J Physiol Lung Cell Mol Physiol. 2015 [Epub ahead of print] PMID: 26071551

(2-30) Spatial Analysis of Discrete Outcomes via Bayesian Adaptive Thin-Plate Smoothing Splines

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In epidemiological research, spatial analysis is generally conducted by smoothing longitude and latitude. Common smoothing approaches assume the amount of smoothing to be equal across the study region, which may lead to under-smoothing some geographic areas, while over-smoothing others. As part of the Boston University Superfund Research Program (Project 2), we build on previous work of Yue et al (2010) and propose a hierarchical Bayesian adaptive thin-plate spline that allows for spatial smoothing of continuous, binary and count outcomes. The method allows for the amount of smoothing to flexibly vary depending on the local extent of spatial effect by using nonstationary spatial Gaussian Markov random fields while accommodating adjustment for potential confounders. Performance of the approach is evaluated via simulation and the methodology is applied to an epidemiologic study investigating spatial heterogeneity in the risk of preterm birth in Massachusetts. Our methodology is made available to our stakeholders through the MapGAM R package.

(2-31) Environmentally Persistent Free Radicals Inhibit CYP1A2 and CYP2B4 by Different Mechanisms

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Combustion of Superfund wastes containing metals and aromatic organic chemicals results in the formation of particulates containing phenoxy- and/or semiquinone-type radicals that are stabilized by the metal center. These radicals exist in the environment, have half-lives of up to weeks, and are referred to as environmentally persistent free radicals (EPFRs). EPFR exposure can trigger harmful immune responses and oxidative stress, ultimately leading to cardiovascular and pulmonary damage. Cytochromes P450 (P450) from families 1, 2 and 3 catalyze the mixed function oxidation of endogenous and foreign lipophilic compounds to more water-soluble products. Our lab has shown that EPFRs derived from the combustion of fine silica and 5% copper oxide (CuO-Si), and either 2-monochlorophenol (MCP230) or 1,2-dichlorobenzene (DCB230) potently inhibit P450s from each of these families relative to non-EPFR-containing particles. In this study, we examined effects of MCP230, CuO-Si, silica, and silica heated at low temperatures with 2-monochlorophenol (MCP50) on metabolism mediated by purified CYP1A2 and CYP2B4. Metabolism of 7-ethoxy-4-trifluoromethylcoumarin and 7-benzyloxyresorufin by CYP2B4 was noncompetitively inhibited. In contrast, metabolism of 7-benzyloxy-4-trifluoromethylcoumarin and 7-ethoxyresorufin by CYP1A2 was inhibited competitively. For both enzymes, MCP230 was about 10-fold more potent as an inhibitor than CuO-Si and 50-fold more potent than silica and MCP50. Because each P450 was inhibited by different mechanisms, the effects of particulates on metabolism of a CYP2B4 substrate by the mixed CYP1A2-CYP2B4 complex was assessed in order to determine the relative contribution of each P450 to metabolism by the mixed complex. CuO-Si competitively inhibited metabolism of the CYP2B4 substrate by the mixed complex suggesting that the CYP2B4 moiety is catalytically silent when it is in a complex with CYP1A2.

(2-32) Using CRISPR-Cas9 Genome Editing Technologies to Study Toxicant Susceptibility

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Genome-editing technologies have emerged as powerful tools to study toxicant susceptibility in model organisms. Nowadays, the CRISPR/Cas9 system can be considered one of the most powerful approaches to study toxicity mechanisms in mammalian cells. Genome-wide functional screening, which involves generating libraries of mutant cells, allows the identification of genes that increase the susceptibility or the resistance of cells to a given toxicant. In our work, we use lentiviral constructs to express, in mammalian cells, Cas9 nuclease in addition to guide RNA (sgRNA) sequences that can escort the nuclease to break double stranded DNA within the exons of specific genes resulting in their inactivation. Alternatively, we use constructs that express Cas9 fusion proteins, also guided by sgRNA, that can activate or repress the expression of specific genes. Construct libraries can be used to perform functional screening in mammalian cells. Individual activation or inactivation of genes that are relevant to the mechanism of toxicity could modify the cell sensitivity to the studied toxicant thus altering the cell viability or proliferation rate in the presence of this toxicant. During library screening, mutant cells will be cultured under different toxicant conditions. The relative abundance of a specific mutant in each condition is reflected by the abundance of the corresponding guide sequence, which can be identified and quantified by next generation sequencing. We use this approach to study a variety of toxicants including acetaldehyde, arsenic, benzene and heavy metals such as lead and mercury. By identifying toxicant susceptibility genes, our approach can provide valuable information about mechanisms of toxicity.

(2-33) The Synthetic Lignan Secoisolariciresinol Diglucoside (SDG) Inhibits Asbestos-Induced Inflammation and Oxidative Cell Damage in Murine Peritoneal Macrophages

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Background: The interaction of asbestos fibers with macrophages drives two key processes that are linked to malignancy: 1) the generation of reactive oxygen/nitrogen species and 2) the generation of acute and chronic inflammation, with IL-1ß and TNFα playing key roles. Secoisolariciresinol diglucoside (SDG) is non-toxic, pluripotent and has anti-inflammatory and antioxidant properties and can thus function as a chemopreventive agent. **Rationale**: We evaluated SDG in asbestos-exposed elicited murine peritoneal macrophages. **Methods**: To determine the kinetics of cytokine release and markers of oxidative/nitrosative stress, thioglycollate-elicited mouse macrophages (MFs) were exposed to crocidolite asbestos fibers and evaluated at various times post-asbestos for levels of IL-1ß, TNFα, malondialdehyde (MDA), and nitrite in the supernatant. We then evaluated the ability of SDG to mitigate asbestos-induced inflammation and oxidative/nitrosative stress by administering SDG at various times post-asbestos. **Results**: We observed a significant (p<0.05), time-dependent increase in the release of proinflammatory cytokines (IL-1ß and TNFα) and levels of MDA and nitrite in the supernatant. While levels of IL-1ß and TNFα rapidly increased from 0.5 to 8 hours post-asbestos exposure, with sustained levels measured 24 hours post asbestos, levels of MDA and nitrite linearly increased over time. SDG significantly reduced levels of IL-1ß by 26-47% and TNFα by 31-34%, while decreasing levels of MDA and nitrites by 56-73% and 55-59%, respectively. **Conclusions**: SDG reduced proinflammatory

cytokine release and markers of oxidative and nitrosative stress in murine peritoneal macrophages and may impede the asbestos-induced inflammatory cascade on the way to malignancy.

(2-34) Detection of Biomarkers of Inflammation in newborns using filter paper blood samples from metabolic screening (KC Donnelly Externship Award Recipient 2014)

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As a 2014 KC Donnelly Externship Award recipient, I worked on a project to expand and develop the scope of PROTECT. Despite advances in access to maternal health care services and education, Puerto Rico (PR) maintains the highest rate of preterm birth (PTB) of all United States jurisdictions. This along with PR's high concentration of Superfund Sites makes the island a prime site for the study of environmental contaminants and their role in PTB. PROTECT conducts targeted and non-targeted analysis to aid in understanding cumulative risk factors for PTB. The methodology and sample collection characteristic of metabolic newborn screening holds particular promise regarding the understanding of environmental contaminants and their possible role in PTB. For instance, exposure to environmental contaminants like phthalates has been shown to trigger inflammation responses, and inflammation is one of the pathways that may pose a risk for PTB. Therefore, the development of an assay to detect biomarkers of inflammation in newborns that uses readily available dried blood spots (DBS) of newborn metabolic screening could significantly impact our understanding of the mechanisms of PTB. Mass spectrometry (MS) and Luminex were used to detect the inflammatory biomarker C-reactive protein (CRP). CRP is a proven biomarker for cardiovascular disease that has also been shown to increase as a result of environmental exposures. Our results show Luminex can be used to detect CRP in DBS in a comparable way to traditional detection in serum. Additionally, preliminary results show a way towards the detection of inflammatory biomarkers in DBS through MS, in turn highlighting the versatility of newborn screening as a means of understanding PTB mechanisms and risk factors.

(2-35) Hydrodynamic and TCE Transport Characterization of a Karstic Physical Model using Statistical and Time Moment Analysis

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Karst aquifers are associated with high productivity, physical complexity, and susceptibility to contamination. Hydrogeological settings and extreme flows control spatial-temporal heterogeneities on transport processes. Hydrodynamic transport characterization is very useful in kinetic modeling and pollutant assessment analysis. However, the huge uncertainty of karst aquifers consumes high time-machine resources, particularly on inverse computational models. Statistical mixed models (SMM) and time moment analysis (TMA) apply data analysis tools to understand spatial-temporal transport features. SMM can model physical anisotropy using statistical correlation structures. TMA simplifies heterogeneity and transient behavior into break through curves (BTCs) analysis with steady state characteristics. The general objective of this work is to characterize transport processes of Trichloroethylene (TCE) in a dual porosity system under variable flow conditions using SMM and TMA. Experiments are conducted in a laboratory-scale karstic physical model (LSKPM) by injecting tracer and TCE solutions into the

LSKPM and monitoring flow, pressure, and solute concentration in sampling well ports. CaCl tracer and aqueous TCE solutions are injected at a rate of 375 ml/min, followed by a flushing period using uncontaminated groundwater at the same flow rate. Results from the SMM allow us to identify spatial preferential, mass-transfer limitation and non-flow zones. The hydrodynamic characterization by TMA shows a highly heterogeneous system resulting in large preferential flow components and specific mass-transfer limitations zones, especially in diffuse flow areas. Diffusional and advective variables calculated along the limestone block confirm spatial and temporal flow patterns suggested by a statistical model based in a geo-statistical mixed model approach and experimental data BTCs.

RESEARCH TRANSLATION: This research advances our understanding of flow and transport processes in karst systems. The results are communicated to the engineering, regulatory, and broader scientific communities to assist in making the best decisions that can reduce exposure and impact of contaminants to the environment and the public. Results are presented in the form of publications (2 under review) and presentations at national forums.

(2-36) Quantitation and Prediction of PAH and NPAH Sorption to Polystyrene 96-Well Plates

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The field of toxicology is increasingly moving towards high throughput screening of small molecules in multi-well plastic plates, and assumptions are often made that the added concentrations of diverse test materials are equally available to the biological test system. We hypothesized that chemical properties influence sorption behavior. This study investigated the sorptive behavior of polycyclic aromatic hydrocarbons (PAHs) and nitrated PAHs (NPAHs) to uncoated polystyrene plates typically used for zebrafish (*Danio rerio*) testing. We measured the percent sorption in the presence and absence of zebrafish embryos at two exposure concentrations, as well as using two different procedures for the addition of the compounds of interest to the polystyrene plates. Following exposure, the plates were extracted with hexane and the extracts were analyzed using gas chromatography coupled with mass spectrometry.

The average percent sorption of PAHs and NPAHs in the presence of zebrafish embryos was 4.8-52% and 13-47% at the high exposure concentration, and 1.5-68% and 17-91% at the low exposure concentration respectively. Allowing 24 hours of equilibration between the addition of analytes and embryos did not significantly impact the percent sorption. Generally, the percent sorption was 5% higher for PAHs and 25% higher for NPAHs in the lower exposure concentration than the higher exposure concentration in the presence and absence of zebrafish embryos.

We developed a model to predict sorption of PAHs and NPAHs to polystyrene, based on partition coefficients between the polystyrene plate and aqueous exposure solution. While PAH sorption was significantly correlated with log K_{ow}, NPAH sorption did not correlate with any of the properties investigated. This indicates the need for better understanding of the sorptive behavior of hydrophobic compounds, such as PAHs and NPAHs, to plastics such as polystyrene, as well as the need to be able to account for sorptive losses during zebrafish exposures.

(2-37) Controlled Polymerization of SiO_2 Shell for the Synthesis of Highly Fluorescent Up-Conversion Environmentally Persistent Free Radical Surrogates

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Environmentally persistent free radicals (EPFRs) are found on the surface of metal oxides associated with particulate matter (PM). Several studies have shown correlations between ultra-fine particulate matter (PM0.1) exposure and adverse

pulmonary health effects, wherein it was found PM0.1 reaches deep in the alveoli of the lungs, suggesting PM uptake by cells is the causative path. At this time, a mechanism for cellular uptake of ultra-fine PM has been hypothesized but not yet confirmed, as there are no existing traceable materials resembling EPFRs/PM.

To address this limitation, our laboratory is exploring the synthesis of a highly fluorescent surrogate EPFR probe based on upconversion nanoparticles (UCNPs). The latter are unique photoluminescent materials, because of their ability to be excited with near-infrared radiation, with subsequent emission of visible light. Presented here is work on the development of a fluorescent EPFR probe consisting of an UCNP core coated with silica, which is modified with metal oxides characteristic of EPFR/PMs. The 55-nm diameter UCNPs, containing Yb3+ as the sensitizer and Er3+ as the activator, have emission peaks at 520.5, 540.5, and 654.5 nm. Further surface modification of the UCNPs was achieved by forming a silica shell, 19-nm thick, via controlled polymerization (modified Stöber method). Such traceable EPFR/PM materials will be useful in moving toward creating surrogate EPFRs for cellular imaging.

Research Translation: The focus of this work is to provide insight into the mechanism of cellular uptake of EPFR/PM and offer a better understanding of how they alter cellular function and possibly stop the adverse health affects associated with these pollutants. These findings can then be used to inform the community through hands-on chemistry demonstrations, as well as seminars.

(2-38) Development and validation of a novel dual phase water sampler to monitor trace level phenylpyrazole pesticides

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Accurate determination in pore and bulk water of concentrations of hydrophobic organic chemicals (HOCs) is essential for the estimation of mobile, bioaccessible contaminant masses present in aquatic sediments and overlaying surface waters. This study, performed in collaboration with a municipal water department, reports on the design and evaluation of a novel active sampling device, the *in situ* sampler for bioavailability assessment (IS2B). The initial IS2B design enabled simultaneous sampling of bulk surface water and porewater using a low-flow, 6-channel pump that delivered water to an array of solid-phase extraction (SPE) cartridges. Validation of the sampler was performed using five fiprole pesticides (fipronil, fipronil sulfide, fipronil amide, fipronil-desulfinyl, and fipronil sulfone) as targets. The absolute extraction recoveries of analytes in the sampler ranged from 82±14 to 110±18%, and their limits of detection ranged from 40-480 pg/L. The novel device was used to extract fipronil at a wastewater-impacted wetland, and analysis yielded bulk surface water and pore water fiprole concentrations ranging from 9.9 ± 4.6 ng/L to 18.1 ± 4.6 ng/L and 9.1 ± 3.0 ng/L to 12.6 ± 2.1 ng/L, respectively. Design improvements were subsequently implemented to maintain the dual-phase sampling capability of the original design while creating a more compact unit with onboard power, eliminating the need for external peripherals. The principal advantages of the new IS2B active sampler include: dual-phase sampling capability, detection limits in the pg/L range, mitigation of sample handling losses, elimination of the need to transport either water or sediment, and customizable deployment timeframes to enable time-averaged sampling.

(2-39) Neonatal PM Exposure Induces a Regulatory Dendritic Cell Phenotype in the Lung via β-catenin signalin

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Infants represent a population particularly susceptible to the effects of elevated levels of ambient particulate matter (PM), and epidemiological studies correlate high airborne PM levels with increased infant hospital visits due to severe respiratory viral infection. Our laboratory has previously demonstrated that exposure of neonatal mice (< 7 days of age) to combustion-derived PM induces a tolerogenic immunophenotype. This phenotype correlated with disruption of the E-cadherin-mediated integrity of the airway epithelium. The interplay between airway epithelium and dendritic cells (DCs) is crucial for determining the fate and function of DCs and hence, the ensuing immune response. We hypothesized that β-catenin accumulation in DCs upon PM-induced disruption of E-cadherin contacts is responsible for the generation of regulatory DCs and immune tolerance. Using an in vitro air-liquid interface (ALI) co-culture model of neonatal mouse tracheal epithelial cells (mTECs) and lung DCs, we observed the PM-mediated effects on the epithelium:DC interaction and subsequent DC maturation and active β-catenin accumulation. Our preliminary data show that PM exposure disrupts E-cadherin-mediated adhesions and leads to the development of a regulatory DC phenotype. Moreover, DCs show activation of the β-catenin signaling pathway after PM exposure. Our co-culture model is the first to provide direct age- and tissue-specific evidence that disruption of E-cadherin mediated adhesion activates the β-catenin signaling pathway in neonatal DCs, and suggests that such disruption following PM exposure is also responsible for inducing regulatory DCs.

(2-40) Polychlorinated Biphenyl Exposure Changes MicroRNA Expression Profile in Human Endothelial Cells

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Epidemiologic studies have correlated polychlorinated biphenyl (PCB) exposure with multiple vascular complications including endothelial cell dysfunction, myocardial infarction and atherosclerosis. Aryl hydrocarbon receptor activation was attributed as one of the mode(s) of action for PCB-induced activation of the vasculature, subsequently leading to oxidative stress and induction of pro-inflammatory cytokines and adhesion proteins (VCAM-1, ICAM-1). Furthermore, these proteins are also regulated by small, endogenous oligonucleotides known as microRNAs that interact with messenger RNA. MicroRNAs control gene expression/protein turnover, making them biomarkers and causal factors for diseases. Critically, microRNAs are an acknowledged component of the epigenome, but the role of environmentally-driven epigenetic changes such as toxicant-induced changes in microRNA profiles are currently understudied. Therefore, the objective of this study is to determine the effects of PCB exposure on microRNA expression profile in primary human endothelial cells using two commercial PCB mixtures (Aroclor 1260 and 1254) at physiological relevant concentrations. Samples were analyzed using Affymetrix GeneChip® miRNA 4.0 arrays for high throughput detection and relative expression of selected microRNA genes was validated (RT-PCR). Microarray results revealed that 272 microRNAs were changed with PCB exposure (120 were upregulated and 152 were downregulated). Further validation showed that the Aroclors increased miR-21, miR-31 and miR-126 expression levels. Upregulated miR-21 has been reported in cardiac injury while miR-126 and miR-31 modulate leukocyte trafficking in inflammation. Our results demonstrated evidence of altered microRNA expression with PCB exposure, thus providing novel insights into mechanisms of PCB toxicity.

Research translation: The current study implicates the relevance of microRNAs as potential biomarkers for environmental toxicant-induced diseases. Importantly, this is an applicable approach for disease prognosis and diagnosis in PCB-exposed human cohorts.

Recent publications

Identification of environmental chemicals associated with the development of toxicant associated fatty liver disease in rodents. Al-Eryani L, **Wahlang B**, Falkner KC, Guardiola JJ, Clair HB, Prough RA, Cave MC. Toxicol Pathol. 2015, 43(4), 482-97.

Evaluation of Aroclor 1260 exposure in a mouse model of diet-induced obesity and non-alcoholic fatty liver disease. **Wahlang B**, Song M, Beier JI, Cameron Falkner K, Al-Eryani L, Clair HB, Prough RA, Osborne TS, Malarkey DE, Christopher States J, Cave MC. Toxicol Appl Pharmacol. 2014, 279(3), 380-390.

(2-41) The B_{12}-qChip: a high-throughput qPCR tool for monitoring and predicting reductive dechlorination activity of organohalide-respiring Chloroflexi

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Organohalide-respiring *Chloroflexi* including *Dehalococcoides mccartyi* (*Dhc*) and *Dehalogenimonas* spp. (*Dhgm*) are keystone dechlorinating bacterial groups involved in detoxification of chlorinated contaminants. Reductive dehalogenase (RDase) enzyme systems involved in this process require a corrinoid cofactor for breaking the carbon-chlorine bonds. Interestingly, *Dhc* and *Dhgm* lack the ability for *de novo* corrinoid biosynthesis and depend on corrinoid scavenging. Different microbial groups synthesize corrinoids in anoxic environments, and *Dhc* and *Dhgm* possess genes encoding dedicated corrinoid uptake systems as well as enzymes involved in corrinoid remodeling. Laboratory experiments demonstrated that corrinoid limitations impact reductive dechlorination rates and extents and the expression level of genes implicated in corrinoid uptake and remodeling. The goal of this effort is to develop a quantitative real-time PCR (qPCR) array plate (i.e., the B_{12}-qChip) for high-throughput monitoring of genes and transcripts implicated in corrinoid uptake and remodeling by organohalide-respiring *Chloroflexi*. *Dhc* and *Dhgm* genome analysis identified genes implicated in corrinoid uptake and remodeling, and comparative metatranscriptomics studies performed on trichloroethene-to-ethene-dechlorinating consortia. Transcripts abundance of *Dhc* genes implicated in corrinoid metabolism were analyzed over the course of dechlorination. Metatranscriptomics approach revealed temporal expression dynamics of genes implicated in corrinoid uptake and remodeling, and identified potential biomarker genes. For example, *cobT*, *cobS* and *cobC* genes are involved in corrinoid remodeling, and transcripts of these genes were upregulated in *Dhc* at early stage of growth in trichloroethene-ethene-dechlorinating consortia. Further, the *cobU* gene implicated in corrinoid uptake was upregulated in *Dhc* experiencing corrinoid limitations at later stage of growth. Eight identified corrinoid biomarker genes from 11 *Dhc* strains and 1 *Dhgm* strain have been selected for primer and probe design, and designed assays met the requirements of the QuantStudio Flex Real-Time PCR nanofluidics system. This tool is being validated to quantify biomarker genes and transcripts in an attempt use biomarker transcript-to-gene ratios to indicate corrinoid-limiting conditions. This tool can be readily applied to groundwater samples, and we will test if sites where corrinoid availability limits reductive dechlorination performance can be identified. If successful, the B_{12}-qChip can be readily applied to many site samples, refine biostimulation approaches, and improve bioremediation efficacy.

(2-42) Sex-specific influences of arsenic and nutritional indices on post-translational histone modifications in Bangladeshi adults

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Exposure to arsenic (As) is associated with numerous adverse health outcomes, with susceptibility differing by sex. Although the mechanisms underlying this are unknown, As induces epigenetic dysregulation, including alterations in post-translational histone modifications (PTHMs), and there is evidence that these effects differ by sex. Nutritional methyl donors also influence PTHMs and may prevent or reverse epigenetic dysregulation. However, the effects of As and nutritional methyl donors on PTHMs have been largely unexamined in human populations.

We evaluated the sex-specific influences of As and nutritional indices on global (%) levels of three PTHMs (%H3K36me2, %H3K36me3, and %H3K79me2), which are dysregulated in human cancers. %PTHMs were measured in peripheral blood mononuclear cells collected from As-exposed Bangladeshi adults enrolled in a randomized trial of folic acid and creatine supplementation. We also examined the stability of %PTHMs after the use of As-removal water filters for 12 weeks. Associations between As exposure (measured in urine) and %H3K36me2 differed by sex (P = 0.01); As was associated with higher levels of %H3K36me2 in men (P = 0.03), but not women (P = 0.19). The use of As-removal water filters also led to reductions in %H3K36me2 (P<0.01), suggesting that As-induced alterations in %H3K36me2 may be reversible. Associations between nutritional indices (folate, choline, B12, homocysteine) and %PTHMs also differed by sex. These findings suggest that As and nutritional methyl donors influence %PTHMs in a sex-dependent manner, underscoring the importance of considering sex/gender in the design of both mechanistic studies of As toxicity and nutritional interventions in As-exposed populations. The results of this study also have important policy implications, as nutritional interventions may offer low-risk, low-cost opportunities to reduce As toxicity in As-exposed populations.

(2-43) Plant-assisted remediation of asbestos contaminated soils.

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Health risks from asbestos fiber exposure stems from oxidative stress and seems to scale with asbestos fiber iron content. Health risks arise from exposure to airborne fibers. The most commonly used methods for clean-up activities (e.g., capping, burial) primarily aim to minimize asbestos exposure without regard to treating the asbestos *in situ*. We aim to assess plants' roles in weathering and altering the physical and chemical properties of asbestos fibers, thereby contributing to long-term treatment. Soil samples were collected from the BoRit Site (Ambler, PA) where waste-materials from a nearby manufacturing plant containing asbestos were disposed of. Asbestos product waste is currently only visible near a reservoir at the site because other parts of the site have been capped with an uncontaminated excavated soil (or cap soil). We collected soil samples from the reservoir sediments and the stream banks. Firstly, we measured soils properties including pH and iron leachate. Secondly, we tested germination of a grass species on reservoir sediments, stream banks, and two controls (sand and organic substrate) in a greenhouse. All soils exhibited alkaline pH: values for reservoir sediments, stream banks and cap soil were 7.62, 8.13 and 8.36, respectively. Iron leachate did not vary significantly between three locations. Seven days after sowing, seed germination was significantly inhibited in contaminated soil compared to controls: the final germination

percentage was 40% for SB and 65% for reservoir sediments, compared to 85% for both controls. This experiment is continuing during the summer to evaluate plant ecotoxicology. In particular, by measuring iron concentrations in substrates and plants, we will determine if plants can remove iron from asbestos particles and propose new remediation strategy of asbestos-contaminated sites.

(2-44) Environmentally Persistent Free Radicals (EPFRs) in Airborne Particular Matter (PM) – Sampling Artifacts

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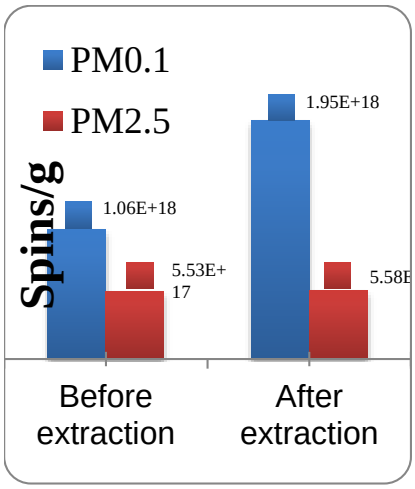

Figure 1: Spins concentration of EPFRs on $PM_{2.5}$ and $PM_{0.1}$ samples retrieved from poly urethane foam during multistage collection experiments.

Environmentally persistent free radicals (EPFRs) can generate reactive oxygen species (ROS) which could induce oxidative stress in biological systems. Particulate matter provides a good breeding ground for EPFRs' formation. When EPFRs are formed during combustion processes on the surface of particulate matter, especially on $PM_{0.1}$ ($\leq$0.1 μ m), and are transported through the blood system to internal organs, risks of damage caused by them to human body are highly increased.

In this study we investigated the presence of EPFRs on ambient air PM. Figure 1 presents average EPFRs concentration on $PM_{2.5}$ and $PM_{0.1}$ collected at the same time using multistage collector. $PM_{0.1}$ has 2-4 fold higher concentration of EPFRs compared to $PM_{2.5}$ with similar spectral parameters (g= 2.0032-2.0038). This g-value range indicates the dominant presence of phenoxyl type EPFRs.

We have developed a new methodology using "fitosampling" method. Hairy surface of leaves can trap PM. Such trapped particles are subject to the same environmental factors as those suspended in air thus are more representative to the radical speciation in ambient PM compared to those collected in a sampler. The overall g-value of EPFRs on such particles is higher (g=2.0035-2.005) indicating that particles collected from air sampler are dominated by phenoxyl EPFRs, while fitosampled PM are dominated by semiquinone type EPFRs.

Future studies will evaluate the difference in oxidative stress potential between samples collected by 2 different methods using vitro cell experiments. Methods used in my research can be applied to analyze particles in the emissions from thermal treatment of superfund sites.

(2-45) Molecular alterations in sperm are sensitive indicators of testicular dysfunction

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The human testis is sensitive to toxicant-induced injury, yet the available tools for detecting exposure effects are limited, insensitive and unreliable. Animal studies use sensitive endpoints to assess toxicity but these are invasive and not translatable to humans. More sensitive and reliable molecular biomarkers of testicular injury that can be used to both monitor human reproductive function and compare animal studies with human exposures are in development. In this study, sperm from adult male rats exposed for 12 weeks to a Sertoli or germ cell toxicant, carbendazim (CBZ; 0, 30, 50, or 70 mg/kg/day) or

cyclophosphamide (CPP; 1.4, 3.4, or 5.1 mg/kg/day) respectively, were used to evaluate reproductive toxicity and assess changes in sperm mRNA abundance on a mRNA PCR-array. CBZ resulted in a dose-dependent decrease in body, testis and epididymis weights, while CPP resulted in a decrease in only body and epididymis weights. Histologic and morphometric evaluation found only CBZ caused a significant increase in homogenization resistant spermatid and retained spermatid heads. A custom developed PCR-array panel was used to assess CBZ- and CPP-induced changes in sperm mRNA content. Ptgds and Tmeff1 were significantly elevated by the highest doses of both CBZ and CPP, and Abi2 and Gimap4 were increased only by CPP treatment. The levels of injury correlated with specific changes in transcript abundance, indicating a utility for these mRNAs as translatable biomarkers for male reproductive dysfunction. These sperm mRNA transcripts are sensitive markers of testicular toxicity in rats capable in distinguishing between Sertoli and germ cell toxicants, and can used as biomarkers to further investigate other testicular toxicants.

(2-46) Characterization of a novel soil bacterium capable of degrading high molecular weight polycyclic aromatic hydrocarbons

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The previously uncultivated bacterial strain Ca6 was recently isolated from an aerobic bioreactor treating contaminated soil collected from a former manufactured gas plant in Charlotte, NC. Stable isotope probing (SIP) of that soil had previously identified several undescribed, phylogenetically distinct groups of high molecular weight (HMW) PAH-degraders including "pyrene group 1" (PG1), of which Ca6 is a member. Strain Ca6 is a rod-shaped betaproteobacterium belonging to a novel lineage within the *Rhodocyclaceae* family, with optimal aerobic growth under mesophilic and neutral pH conditions. Of the organic compounds tested, strain Ca6 grew on a very limited number of common substrates. However, Ca6 is capable of growing on either phenanthrene or pyrene as a sole source of carbon and energy and can mineralize chrysene. The genome of Ca6 consists of a single circular chromosome of 2.9 Mbp containing eight ring-hydroxylating dioxygenase (RHD) genes, which code for enzymes that catalyze the first step of aerobic PAH metabolism. Six of the RHD genes were previously heterologously expressed and demonstrated to transform PAHs. In addition, Ca6 contains several genes putatively involved in the degradation of other monocyclic and polycyclic aromatic compounds. Experiments to classify Ca6 as the type strain of a novel genus, to investigate its degradation of benzo[*a*]pyrene, and to identify the genetic basis for HMW PAH degradation continue. The frequent presence of gene sequences highly similar to those in Ca6 at other contaminated sites worldwide suggests Ca6-type organisms may be important and ubiquitous degraders of hazardous aromatic compounds.

(2-47) Effect of activated carbon and biochar on TBBPA biodegradation efficiency, and characterization of the microbial communities responsible in anaerobic sludge digesters.

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Tetrabromobisphenol A (TBBPA) is the most widely used flame-retardant in the production of plastic polymers and electronic equipment worldwide. Its detection in the environment has raised concerns related to its toxicity towards wildlife and human health. However, knowledge regarding efficient *in situ* remediation strategies that could be implemented at contaminated sites is still limited. The aim of the present study was to compare the efficiency of three remediation strategies: natural bioremediation, and addition of activated carbon or biochar. Bench scale anaerobic sludge digesters spiked with TBBPA were

periodically sampled over the course of 70 days for chemical and microbial analysis. LC-MS was used in order to measure TBBPA and byproducts concentrations, and microbial community composition was characterized using Ion Torrent next-generation sequencing. By day 29, 90% of the TBBPA in the untreated reactors was degraded, while amendment material-treated reactors still had more than 60% of the spiked TBBPA. TBBPA degradation was accompanied by the accumulation of 3,3',5-tribromobisphenol, 3,3'-dibromobisphenol, 3-bromobisphenol A, and bisphenol A (BPA), and the mass balance accounted for changes in parent and metabolite concentrations. By Day 63, all reactors showed nearly complete degradation of TBBPA to BPA. Microbial community composition changed markedly over the course of the experiment, however, compared to control reactors without TBBPA, the community was not significantly different, suggesting that multiple microbial taxa have the capacity to degrade TBBPA. In conclusion, sediment material amendment strategies do not enhance TBBPA degradation compare to natural microbial remediation, suggesting that focus need to be directed towards microbial management remediation strategies, such as bioaugmentation or biostimulation.

(2-48) Defining the neurotoxic potential of nondioxin-like polychlorinated biphenyls present in fish from US lakes using a ryanodine receptor-based equivalency scheme

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Polychlorinated biphenyl (PCB) risk assessment is largely based on dioxin equivalents (TEQ) assessing the relative potency of 209 congeners at the aryl-hydrocarbon receptor (AhR) to predict organismal toxicity. Neurotoxic non-dioxin-like (NDL) PCBs have little to no activity towards AhR and their risk of promoting developmental neurotoxicity is underestimated by the current assessment scheme. Here, we aimed to establish a neurotoxic equivalency (NEQ) scheme based on the potency of NDL PCBs towards ryanodine receptor (RyR) Ca^{2+} channel activation. We utilized [^{3}H]Ryanodine ([^{3}H]Ry) binding analysis and single channel voltage clamp to measure the relative RyR activity of PCB congeners with two to eight chorine substitutions. Receptor based toxicity is compared to that predicted in a previous quantitative structure-activity relationship (QSAR) in order to establish NEQ values that can be applied to environmental PCB concentrations. We found that the toxicity of individual PCBs at the RyR followed the general pattern predicted by the QSAR; however, experimental assessments displayed higher potency. Notably, the tetra-*ortho* PCB 202 was found to be the most potent congener at the RyR, increasing channel open probability with an effective concentration at 100 pM. Applying PCB202 based NEQs to PCB concentrations found in fish from US lakes demonstrated that more than 20% of US lakes have fish containing significant PCB neurotoxic equivalents. This work validates predictive assessments of NDL PCB activity toward the RyR and demonstrates that an NEQ based on RyR-sensitization, combined with the established dioxin TEQ, could provide a more inclusive measure of risk presented by environmental PCB mixtures.

(2-49) Cyp1b1 status modulates PAH induced reproductive toxicity in male mice transplacentally exposed to dibenz[def,p]chrysene

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Dietary exposure to PAHs has been shown to account for nearly 70% of total PAH exposure and over 90% of exposure to the higher molecular weight PAHs, such as DBC and benzo[a]pyrene (BaP), in non-smokers. DBC is genotoxic and can cross the placental barrier. We hypothesize that maternal gavage of DBC (15, 12, 6.5, and 0 mg/kg) on gestation day (GD) 17 will result in reproductive toxicity in the male F1 generation through oxidative stress via the cytochrome P450 (CYP) 1B1 metabolic pathway. Additionally, a maternal diet rich in the anti-oxidant phytochemical indole-3-carbinol (I3C; 500 ppm) may reduce DBC oxidative damage. At 21 days postpartum, the exposed male F1 generation had reduced testes size ($p<0.001$), reduced tubule counts ($p<0.01$), and tubules depleted of spermatocytes. I3C supplementation of maternal diet did not prevent reduction in the size and tubule count in weanlings, but was effective in minimizing spermatocyte depletion. CYP1B1 null F1 pups did not suffer the reproductive toxicity seen in wild-type cohorts as a results of DBC transplacental exposure. Together these data indicate that a single *in utero* exposure to DBC at GD17 results in reproductive toxicity in wild type male F1 mice and that these effects are dependent upon CYP1B1 bioactivation of DBC as null mice are not susceptible to gonad toxicity. Intervention with I3C in the maternal diet prevents the extent of spermatocyte depletion. Ongoing studies will examine the extent of spermatocyte depletion, oxidative stress biomarkers, and histopathology at 10 months of age.

(2-50) PCB126-induced disruption in gluconeogenesis and fatty acid oxidation precedes fatty liver in male rats

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Co-planar polychlorinated biphenyls (PCBs) such as PCB126 are associated with metabolic diseases, including non-alcoholic fatty liver disease (NAFLD)[1,2]. PCB126, an aryl hydrocarbon receptor (AhR) agonist, has been implicated in the disruption of carbohydrate and lipid metabolism as underlying causes of wasting disorders[3-5]. However the mechanisms are unclear. Since liver, the principal organ for metabolic homeostasis, is a target of PCB toxicity, we hypothesized that early disruption of glucose and lipid homeostasis will contribute to later manifestations like hepatic steatosis. To evaluate this time course of events, groups of male Sprague-Dawley rats, fed an AIN-93G diet, were injected (i.p) with a single bolus of PCB126 (5 µmol/kg) at various time intervals between 9 h and 12 days prior euthanasia. The control group of animals received a soy oil vehicle. Spontaneous decrease in the serum glucose level and a gradual decrease in serum triglycerides were observed over the time course. Liver lipid accumulation was most severe at 6 d and 12 d post exposure. Transcript levels of cytosolic phosphoenol-pyruvate carboxykinase (PEPCK-C) and glucose transporter (GLUT2) involved in gluconeogenesis and hepatic glucose

transport, were time and dose-dependently downregulated. Additionally, the transcription of PPARα, and its targets acyl-CoA oxidase (ACOX1) and hydroxy-3-methylglutaryl-CoA synthase 2 (HMGCS2), were also downregulated. These PPARα target enzymes play critical roles in peroxisomal fatty acid oxidation and ketogenesis. Further studies with rat hepatocytes showed that PCB126-induced effects on PEPCK-C are AhR dependent. These results indicate that PCB126 induced wasting and steatosis are preceded initially by a) decrease in the blood glucose caused by decreased hepatic glucose production, followed by b) decrease in peroxisomal fatty-acid oxidation (NIEHS P42 ES013661).

1 Cave, M. et al. Polychlorinated biphenyls, lead, and mercury are associated with liver disease in American adults: NHANES 2003-2004. Environ Health Perspect 118, 1735-1742, doi:10.1289/ehp.1002720 (2010).

2 Everett, C. J. et al. Association of a polychlorinated dibenzo-p-dioxin, a polychlorinated biphenyl, and DDT with diabetes in the 1999-2002 National Health and Nutrition Examination Survey. Environmental research 103, 413-418, doi:10.1016/j.envres.2006.11.002 (2007).

3 Peterson, R. E., Theobald, H. M. & Kimmel, G. L. Developmental and reproductive toxicity of dioxins and related compounds: cross-species comparisons. Crit Rev Toxicol 23, 283-335, doi:10.3109/10408449309105013 (1993).

4 Swedenborg, E., Ruegg, J., Makela, S. & Pongratz, I. Endocrine disruptive chemicals: mechanisms of action and involvement in metabolic disorders. Journal of molecular endocrinology 43, 1-10, doi:10.1677/jme-08-0132 (2009).

5 Hectors, T. L. et al. Insulin resistance and environmental pollutants: experimental evidence and future perspectives. Environ Health Perspect 121, 1273-1281, doi:10.1289/ehp.1307082 (2013).

(2-51) Direct UV Excitation of PCBs for Coupled Fluorescence Detection.

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The exposure to the halogenated persistent organic pollutants (POPs), such as polychlorinated biphenyls (PCBs), has been linked to numerous inflammatory diseases, including diabetes, cancer, liver damage and lowered immune response. 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 gas chromatography–mass spectrometry (GC-MS), screen-printed electrodes (SPCEs), surface-enhanced Raman scattering (SERS), surface plasmon resonance (SPR), electrochemical impedance sensors, whole cell sensors, and micro-flow immunosensor chips. While these systems are exciting possibilities for quantifying and detecting PCBs in environmental standards, none have become a standard of detection owing to the limited flexibility, and are too costly to be a survey approach. [1-5]. As such, there is still a need for an inexpensive robust field detection technique for the PCBs. In this work, we describe a potential new sensing method based on resonance energy transfer. Using a suitable fluorescent dye with the excitation wavelength falling in the region of PCBs emission wavelength, Förster Resonance Energy Transfer (FRET) to the dye can occur, enhancing the resultant fluorescence signal of the dye while suppressing the PCBs intensity signal. The change in the signal of the dye is proportional to the concentration of the PCBs in the solution. In this work, potential fluorescence pairs have been screened and identified for successful detection of PCBs in solution. Potential for these for fluorescent probes to be immobilized onto polymeric supports as a detection platform is also discussed.

References:

1. Lawruk, T.S., et al., Quantitative determination of PCBs in soil and water by a magnetic particle-based *immunoassay.* Environmental Science & Technology, 1996. 30(2): p. 695-700.

2. Endo, T., et al., Fluorescence-based assay with enzyme amplification on a micro-flow immunosensor chip for monitoring coplanar polychlorinated biphenyls. Analytica Chimica Acta, 2005. 531(1): p. 7-13.

3. Del Carlo, W. and M. Mascini, Immunoassay for polychlorinated biphenyls (PCB) using screen printed electrodes. Field Analytical Chemistry and Technology, 1999. 3(3): p. 179-184.

4. Roberts, M.A. and R.A. Durst, INVESTIGATION OF LIPOSOME BASED IMMUNOMIGRATION SENSORS FOR THE DETECTION OF POLYCHLORINATED-BIPHENYLS. Analytical Chemistry, 1995. 67(3): p. 482-491.

5. Turner, K., et al., Hydroxylated polychlorinated biphenyl detection based on a genetically engineered bioluminescent whole-cell sensing system. Analytical Chemistry, 2007. 79(15): p. 5740-5745

(2-52) The Effects of Air Pollution on Severity of Respiratory Illness

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Exposure to airborne particulate matter (PM) has been shown to cause adverse health effects[1] and numerous epidemiologic studies in infants and children exposed to PM show increased visits to the emergency department and hospitalization for acute respiratory infection[2-6]. Despite animal data which show exposure to PM exacerbates pneumonia in mouse models[7], there does not appear to be much human data on severity measures associated with PM exposure such as prolonged hospitalization, admission to the intensive care unit, and use of mechanical ventilation during hospitalization. In this multidisciplinary collaborative study we will use the pediatric population from the Center for Disease Control (CDC) Etiology of Pneumonia in the Community (EPIC) study[8] to assess if exposure to elevated PM levels is a predictor of severe pneumonia in children hospitalized with pneumonia. In addition we will determine if exposure to elevated PM levels predisposes children to bacterial pneumonia and more complications. Air quality standards for PM are measured by the Environmental Protection Agency (EPA), using air quality monitors which measure concentrations of PM throughout the country[9]. Preliminary data show $PM_{2.5}$ Air Quality Index (AQI) data for the city of Memphis, 1 of 3 cities sampled in the EPIC study and currently the only site with geocoded data, were moderately elevated 75% of the time for noted daily values (EPA cutoff is 35ug/m3 daily[9]) during the study period. In addition, there was significant correlation between $PM_{2.5}$ Air Quality Index (AQI) values and incidence of pneumonia (p=0.000 for a 2-tailed test).

References

Olmo NRS, Saldiva PHN, Braga ALF, An Lin C, Santos UP, Pereira LAA. A review of low-level air pollution and adverse effects on human health: implications for epidemiological studies and public policy. *Clinics*. 2011;66(4):681-690

Woodruff TJ, Parker JD, Schoendorf KC. Fine particulate matter (PM2.5) air pollution and selected causes of postneonatal infant mortality in California. *Environ Health Perspect* 2006. 114:786–790.

Saldiva PH, Lichtenfels AJ, Paiva PS, Barone IA, Martins MA, Massad E, Pereira JC, Xavier VP, Singer JM, Böhm GM. Association between air pollution and mortality due to respiratory diseases in children in São Paulo, Brazil: a preliminary report. *Environ Res.* 1994 May;65(2):218–225.

Woodruff TJ, Grillo J, Schoendorf KC. The relationship between selected causes of postneonatal infant mortality and particulate air pollution in the United States. *Environ Health Perspect.* 1997 Jun;105(6):608–612.

Ritz B, Wilhelm M, Zhao Y. 2006. Air Pollution and Infant Death in Southern California, 1989–2000. *Pediatrics* 118:493–502.

Conceição GMS, Miraglia SGEK, Kishi HS, Saldiva PHN, Singer JM. Air pollution and Child Mortality: A Time Series Study in São Paulo, Brazil. *Environ Health Perspectives*. 2001;109:347–50.

Zelikoff JT, Chen LC, Cohen MD, Fang K, Gordon T, Li Y, Nadziejko C, Schlesinger RB. Effects of inhaled ambient particulate matter on pulmonary antimicrobial immune defense. *Inhal Toxicol.* 2003 Feb;15(2):131-50.

Jain et al. Community-Acquired Pneumonia Requiring Hospitalization among U.S. Children. *N Engl J Med* 2015; 372:835-845

EPA http://www.epa.gov/airquality/particlepollution/

(2-53) Arsenic exposure and global %5mc and %5hmC in a population of Bangladeshi adults.

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Roughly 70 million people in Bangladesh drink water contaminated with inorganic arsenic at levels greatly exceeding the current World Health Organization guideline of 10 µg/L. Arsenic is a carcinogenic metalloid associated with increased risk for malignancies of the skin, liver, lung, bladder and kidney, in addition to melanosis and keratosis skin lesions. While the mechanisms of arsenic toxicity are not fully understood, emerging evidence suggests one pathway may be through changes in global DNA methylation. DNA methylation in the form of 5-methylcytosine (5mC) typically occurs at CpG sites and is associated with gene dormancy. Five-hydroxymethylcytosine (5hmC) is a mark generated by the oxidation of 5mC by TET enzymes. It is considered an intermediate in DNA demethylation pathways and is associated with gene activation; loss of 5hmC has been shown to be a hallmark of melanoma. Previous work in our lab showed significant sex-specific effects of As exposure on global levels of %5mC and %5hmC in circulating PBMCs from Bangladeshi adults. Here we provide an update on our ongoing work to identify similar sex-specific differences of As exposure on 5mC/5hmC in 600 participants from our 6 month randomized controlled trial of folic acid and/or creatine supplementation. Further, we will evaluate 5mC/5hmC stability over time and relationships between these marks and intermediates of one-carbon metabolism, a pathway essential for the generation of methyl groups used in DNA methylation. We believe that findings from our work will contribute to mounting evidence that arsenic may increase cancer risk by altering global DNA methylation patterns.

(2-54) Table grape consumption reduces body fat accumulation, hepatic steatosis, and inflammation in mice fed a butter-rich diet: a potential nutritional approach for PCB protection.

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Obesity is a global health concern affecting approximately 300 million adults worldwide and is associated with chronic inflammatory conditions (e.g., type 2 diabetes, hypertension, and cardiovascular disease). The objective of this study was to

examine the extent to which consuming polyphenol-rich, table grapes reduces adiposity, hepatic steatosis, and inflammation in mice fed a high-fat diet (34% kcals from fat). Male, C57BL/6J mice were fed a low fat diet or butter-rich diet with or without 3% or 5% grapes for 11 weeks. Total body and inguinal fat content were reduced in mice fed both levels of grapes compared to their high-fat, sugar controls. Mice fed 5% grapes had lower liver weights, liver triglycerides, and inflammatory gene expression in inguinal fat compared to 5% controls. Additionally, hepatic lipogenic gene expression was lower in mice fed both levels of grapes compared to controls. Interestingly, exposure to lipophilic environmental pollutants such as polychlorinated biphenyls (PCBs) is an emerging risk factor for the development of type 2 diabetes, cardiovascular disease and obesity. Previous studies at the UK-SRC have shown that nutritional intervention using green tea extracts (e.g., high in EGCG) can protect against PCB induced toxicity. Because PCBs are lipophilic and accumulate in adipose tissue, decreasing adiposity by nutritional means is critical in the management of overall PCB body burden. Since we have demonstrated the ability of grapes to reduce body fat, hepatic steatosis, and inflammatory gene expression in high-fat fed mice, it is possible that grapes could provide an affordable and easily obtainable nutritional means to aid in the elimination of PCBs from adipose tissue stores and reduce related inflammation and toxicity.

(2-55) Use of Oxalic Acid for Mobilizing Arsenic from Contaminated Sediments and Decreasing Vulnerability to Reduction

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Pump-and-treat (P&T) is widely used for groundwater remediation. However, P&T often requires long-term implementation due to incomplete desorption and other factors. Oxalic acid has the potential to increase the effectiveness of P&T for arsenic groundwater contamination. Oxalic acid enhances arsenic mobilization by dissolving arsenic host minerals and competing for sorption sites. This study combines batch, column, and microcosm experiments to identify the conditions that favor efficient arsenic mobilization by oxalic acid from contaminated sediments with different arsenic input sources and redox conditions from the Dover Municipal Landfill and the Vineland Chemical Company Superfund sites. It also examines the stability of residual arsenic to redutive dissolution, the most common mechanism of arsenic release in contaminated aquifers. Oxalic acid mobilized arsenate preferentially from both Dover and Vineland sediments most effectively at pH <3 and high oxalic acid concentrations. The residual arsenic in both Dover and Vineland sediments after oxalic acid treatment was less vulnerable to microbial reduction than before the treatment.

Research Translation: P&T systems often demand costly long-term implementation. Periodic injections of oxalic acid could improve the extraction efficiency for arsenic, making them both more effective and less expensive to implement. This study helps identify the conditions that would be most effective, and also indicates that factors such as arsenic redox state and iron mineralogy affect both extraction efficiency, and the long-term stability of residual arsenic. At sites with limited quantities of reactive iron(III) such as the Dover site or sites that have little chance of becoming highly reducing, residual arsenic after oxalic acid treatment would not be easily mobilized, and thus groundwater arsenic remediation via enhanced P&T would be most promising.

(2-56) Use of Reactive Transport Modeling for Understanding and Designing the Magnetite Based Arsenic Immobilization Strategy.

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Groundwater arsenic (As) contamination is currently a concern at hundreds of U.S. Superfund sites. *In situ* mineral precipitation can be an effective means of minimizing the risks of this contamination. Magnetite is stable under a wide range of aquifer conditions, including Fe(III) reducing conditions often associated with groundwater As contamination, and thus is an attractive host-mineral. Our previous laboratory studies suggest that the formation of nanoparticulate magnetite can be achieved by the oxidation of ferrous Fe with nitrate. During formation, magnetite is capable of trapping As into its structure, in which case desorption and As(V) reduction are less likely. After formation, nanoparticulate magnetite is also an effective As adsorbent, and thus is a reactive filter when contamination passes through the treatment zone. The present study integrates the magnetite based *in situ* immobilization strategy by Fe(II)-nitrate injection into a reactive transport model, using the numerical code PHT3D. The results of such modeling suggest that the ratio between Fe(II) and nitrate in the injectant regulates the formations of magnetite and ferrihydrite, and thus regulates the long-term evolution of the effectiveness of the strategy. Larger-scale models have also been developed to assess the potential Fe(II)-nitrate injection scenarios for field implementation. The modeling framework supports alternative injection method that effectively introduces amendments needed to induce mineralogical changes and subsequent As retention. Modeling, therefore, improves our understanding of the complex biogeochemical and physical interactions that control magnetite formation and the fate of As.

Research Translation: This method of reactive transport modeling allows us to scale laboratory results to field environments and thus results can be used to inform remediation options at many Superfund sites affected by As.

(2-57) Hydraulic and Salt Tracer Studies to Assess Flow and Transport Regions in an Intermediate Karstified Lab-Scale Physical Model

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Karst terrain provides high capacity to transport and store large amounts of water. It is also characterized for its high heterogeneity and anisotropy. These characteristics make karst vulnerable to potential contamination of hazardous chemical substances. Furthermore, it is challenging to delineate and predict fate and transport properties of pollutants that might be present in groundwater systems. Previous studies have shown wide interest to characterize the heterogeneity of karst systems, however, the validation of these results have been difficult due to simplistic assumptions or the absence of experimental procedures. For this reason, an intermediate karstified lab-scale physical model (IKLPM) was developed to study fate and transport and to assess viable tools to characterize the heterogeneities within karst at several scales. Hydraulic and salt tracer tests were conducted to assess flow and transport regions, respectively. Preliminary results confirmed high heterogeneities for medium base flow experiments. These results will lead to the characterization of preferential flow path zones of potential pollutants such as PCE and TCE in karst groundwater systems, which affect human health and the

environment. The development of these technologies to predict fate and transport of contaminants will contribute to mitigate its exposure to the communities and reduce public health impacts.

RESEARCH TRANSLATION: Results from this research will lead to understanding fate and transport processes at various scales in karst groundwater systems. They will be used by the scientific community to scale up processes from laboratory-scale to field-scale studies. Conversations are already under way with community members near spring-discharge sites and non-governmental organizations (NGOs), including the Speleological Society and the Conservation Trust of Puerto Rico, for participatory involvement in the field-scale studies. The results will be communicated to local and federal agencies, as well as the community members living near these sites.

(2-58) Mechanisms underlying transgenerational toxicity of benzo(a)pyrene in Danio rerio

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Mitochondrial function and mitochondrial DNA (mtDNA) integrity are essential to the health and survival of all aerobic organisms. Mitochondria are targets of environmental contaminants such as polycyclic aromatic hydrocarbons (PAHs), especially due to metabolic activation by cytochrome P450s and lack of DNA repair mechanisms— mtDNA is maternally inherited and undergoes a bottleneck during early development, potentially leading to transgenerational effects from maternal exposure. This study evaluates transgenerational effects of the PAH benzo(α)pyrene. Reproductively mature female zebrafish (F0) were exposed to 0.25, 2.5, or 25 µg/g (BaP/body weight) per day via their diet for 21 days. The exposed females were bred with naïve males, and the embryos (F1) were collected for subsequent analyses. Mitochondrial function, nuclear and mtDNA damage, mtDNA copy number, and oxidative stress responses are being characterized in F1 embryos. Preliminary findings suggest altered mitochondrial function and metabolic partitioning in F1 embryos. DanioVision®, a high-throughput system for tracking zebrafish larvae, showed that maternal exposure to BaP results in altered larval locomotor activity and adaptation to changing environmental stimuli, suggesting neuro-behavioral effects of maternal exposure. To determine whether adverse effects in the F1 generation were correlated with bioenergetic impairment in the ovaries of the exposed F0 females, we are characterizing oxidative stress responses, nuclear and mtDNA damage, mtDNA copy number, and mitochondrial function *ex vivo* in ovaries using a novel method with the XF^{e}24 Extracellular Flux Analyzer.[1] Overall, this study provides mechanistic insights into how maternal exposure to benzo(a)pyrene may have persistent transgenerational effects. Broader implications of this study are being communicated to the community surrounding Atlantic Wood Industries Superfund site in collaboration with the Duke Superfund Research Translation Core.

[1]Jayasundara, N., Kozal, J.S., Arnold, M. Chan, S.L. and Di Giulio, R.T. (2015). High-throughput tissue bioenergetics analysis reveals identical metabolic allometric scaling for teleost hearts and whole organisms. PLOS ONE -*Accepted*.

(2-59) Cobamide lower bases control dechlorination rates and extents in organohalide-respiring Dehalococcoides mccartyi

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Corrinoid auxotrophic organohalide-respiring *Dehalococcoides mccartyi* (*Dhc*) strains are keystone bacteria for reductive dechlorination of toxic and carcinogenic chloroorganic contaminants. We demonstrate that the lower base attached to the essential corrinoid cofactor of reductive dehalogenase (RDase) enzyme systems affects dechlorination rates and extents. Amendment of 5',6'-dimethylbenzimidazolyl-cobamide (DMB-Cba) to *Dhc* strain BAV1 and strain GT cultures supported *cis*-1,2-dichloroethene-to-ethene reductive dechlorination at rates of 107.0 ($\pm$ 12.0) and 67.4 ($\pm$ 1.4) µM Cl^- released day^{-1}, respectively. Strain BAV1, expressing the BvcA RDase, reductively dechlorinated VC to ethene, albeit at up to 5-fold lower rates in cultures amended with cobamides carrying 5'-methylbenzimidazole (MeBen), 5'-methoxybenzimidazole (MeOBen), or benzimidazole (Ben) as the lower base. In contrast, strain GT harboring the VcrA RDase failed to grow and dechlorinate VC to ethene in medium amended with MeOBen-Cba or Ben-Cba. The amendment with DMB to inactive strain GT cultures restored the VC-to-ethene-dechlorinating phenotype and intracellular DMB-Cba was produced, demonstrating cobamide remodeling. The observed *Dhc* strain-specific responses to cobamides implicate that the lower base controls *Dhc* reductive dechlorination rates and extents (i.e., detoxification), and therefore the dynamics of *Dhc* strains with distinct RDase genes. These findings emphasize that the role of the corrinoid/lower base synthesizing community must be understood to predict strain-specific *Dhc* activity and achieve efficacious contaminated site cleanup.

(2-60) Role of TNF Signaling in de novo Lipid Synthesis Upon Hypernutrition

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Obesity-associated tissue inflammation is thought to be an important cause of decreased insulin sensitivity and glucose intolerance that are the key pathophysiological characteristics of cardiovascular diseases and non-alcoholic steatohepatitis (NASH).

In this study, we will investigate the hypothesis that TNF activates SREBP1 through caspase2 (Casp2) and this can lead to elevated *de novo* lipogenesis in liver. Casp2 is highly activated in HFD-fed *MUP-uPA* mice, which develop NASH, and its activation is largely reduced upon TNFR1-ablation (i.e. in *Tnfr1*$^{-/-}$*MUP-uPA* mice). Moreover, activation of SREBP1 in HFD-fed *MUP-uPA* mice is completely blocked in Casp2-ablated *MUP-uPA* mice, suggesting that Casp2 cleaves/activates SREBP1 in response to TNFR1 signaling in HFD-fed *MUP-uPA* mice. Noteworthy, we found that Casp2 is also activated in livers of patients with NASH but not in those with milder non-alcoholic fatty liver disease (NAFLD), suggesting that Casp2 plays a significant role in the pathogenesis of inflammation-associated metabolic diseases. To better understand Casp2 function, we will use genetically engineered mice, molecular biological studies, and metabolic studies to investigate the mechanism of SREBP1 activation by Casp2 and evaluate the mechanism and pathogenic impact of Casp2-mediated SREBP1 activation in NASH progression and exacerbation of liver metabolic complications.

This study will provide a new insights to the molecular mechanisms by which TNF signaling stimulates SREBP1 processing via Casp2, leading to aberrant lipid accumulation during NASH progression and offer new opportunities for development of drugs

that ameliorate the pathogenesis of NASH, one of the most severe outcomes of the metabolic syndrome and cardiovascular diseases.

(2-61) Fishing bans and consumption advisories along New Bedford Harbor: A qualitative and quantitative analysis of their efficacy.

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Located in Bristol County, Massachusetts, New Bedford Harbor (NBH) has been listed as a Superfund Site since 1983 due to contamination of polychlorinated biphenyls (PCBs) and heavy metals from industrial pollution. To protect public health in 1979, Massachusetts Department of Public Health (MA DPH) promulgated state regulations prohibiting taking and/or consumption of any fish or shellfish from three distinct areas of NBH. In the early 2000s, EPA Region 1, MA DPH, and the Massachusetts Department of Environmental Protection (MassDEP) partnered to implement EPA Region 1's Fish Smart campaign to raise the general public's awareness of health risks from eating PCB-contaminated seafood from NBH. This effort includes outreach to the local fishing community and multi-language signage along the harbor in popular fishing locations. According to USEPA's website, the "greatest concern is the possibility of people eating contaminated locally caught seafood" from NBH. The goal of this study is to characterize the fishing landscape along the shore of NBH—including what fishing advisory signage exists, and to characterize the fishing motivations, behaviors, risk perceptions, and attitudes of the local fishing community. Using qualitative and quantitative research approaches, the project has the following specific aims:

1. Assess fishing advisory materials for number, location, visibility, language, messaging;

2. Develop and administer an interview guide for people who fish in NBH s;

3. Conduct observations of fishing activities;

4. Translate our findings to relevant stakeholders.

(2-62) Scanning Two Eastern Creosote Sites for Potentially Useful Fungi

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Historic creosote disposal and treated wood drying practices have resulted in large-scale soil contamination around the world. Creosote is a mixture of over 30 different polycyclic aromatic hydrocarbons (PAHs), including numerous carcinogens and mutagens. In the U.S., over 600 sites on the National Priorities List are contaminated with PAHs. The heavy PAHs sorb strongly to soils making them especially difficult to treat. As a result, the only effective methods are expensive and resource-intensive. Moving forward, environmental and fiscal concerns push for more sustainable options. The usual sustainable option, traditional bioremediation, relies on bacteria that often have difficulty accessing the heavy PAHs sorbed to soils. As fungi have different metabolism than bacteria, they are not limited by heavy PAHs' low bioavailability and some have degraded heavy PAHs in the laboratory. This possibility of mycoremediation (expanding bioremediation to rely on fungi) has motivated the current work on heavy PAH-contaminated soils from two eastern Superfund sites, Atlantic Wood Industries and Holcomb Creosote. The current work represents an innovative methodology that leverages next generation sequencing technology to scan soils for fungal candidates of mycostimulation. Preliminary results suggest fungi inhabit contaminated soils with total PAH concentrations ranging from 180 µg/g to more than 18000 µg/g soil. Furthermore, Atlantic Wood Industries soils contain fungi similar to those known to possess degradation capacity. The proportion of candidate fungi seems to

increase with total PAH concentrations at Atlantic Wood Industries. Thus, a targeted mycoremediation strategy may be able to encourage their growth and result in contaminant degradation. This would lead to a sustainable remedy for these Superfund soils and others contaminated with creosote.

(2-63) PAH-exposure related differences in the sediment profiles and the prokaryotic gut communities of Atlantic killifish (Fundulus heteroclitus) (KC Donnelly Externship Award Recipient 2015)

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The introduction of high-throughput sequencing has allowed for the detection and quantification of environmental microbial diversity. This has resulted in a greater understanding of anthropogenic impact on microbiota and consequently, its effects on ecosystem health. Here we used high-throughput sequencing to comparatively analyze the composition of gut and sediment prokaryotic communities that have been chronically exposed to polycyclic aromatic hydrocarbons (PAHs). Subpopulations of Atlantic killifish (*Fundulus heteroclitus)* and sediment grabs were collected from an uncontaminated reference site and the former Republic Creosoting Company site in the Elizabeth River, VA. Prokaryotic DNA was isolated, amplified and indexed, and sequenced on the Illumina MiSeq platform. A total of 1,841,027 sequences were filtered, trimmed, and sorted into 1,990 unique operational taxonomic units (OTUs). Archaea representing 2 phyla (*Crenarchaeota* and *Euryarchaeota*) and bacteria representing 25 phyla (top OTUs being *Proteobacteria*, *Actinobacteria*, *Firmicutes*, *Cyanobacteria, Bacteroidetes*) were identified. The control and contaminated site contain many of the same major OTUs, but the Republic Creosote samples have significantly higher abundance of taxa including the benzene degrader *Pseudomonas benzenivorans* (p=0.019), the antiviral *Acinetobacter antiviralis* (p= 0.039), and the radiation-resistant *Streptomyces radiopugnans* (p=0.039). This study shows the responsive bacterial and archaeal taxa associated with high-level chronic PAH exposure, and suggests that some of the lower abundance taxa maybe associated with contaminant tolerance and/or degradation.

(2-64) Maternal Polychlorinated Biphenyl 126 Exposure Has Lasting Effects on Offspring

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Maternal exposure to polychlorinated biphenyls (PCBs) can impart detrimental health effects on fetuses and neonates by crossing the placenta and/or contaminating breast milk. We demonstrated that PCB126 exposed mouse fetuses have increased markers of oxidative stress and inflammation. However, the long term effects of maternal PCB exposure on offspring obesity and glucose homeostasis are mostly unknown. Thus, we followed female offspring to 9 months of age and examined body composition and glucose tolerance. Female mice were gavaged with 1 μmole/kg PCB126 or vehicle once prior to mating, once during pregnancy, and once during nursing. Glucose tolerance and body composition were measured as the offspring aged from 7 weeks to 9 months. Additionally, male offspring were not included at 6 and 9 months due to issues associated with aggressive behavior. Male ($p<0.05$), but not female ($p=0.1$), PCB exposed offspring at 7 weeks of age demonstrate impaired glucose tolerance. However, PCB exposed female offspring have higher fasting blood glucose compared to controls ($p<0.05$). Male and female 7 week PCB exposed offspring have reduced lean mass and female offspring elevated percent body fat ($p<0.05$). Six and 9 month old PCB exposed female offspring have impaired glucose tolerance ($p<0.05$) but normal body composition compared to control mice ($p>0.05$). These results provide evidence for long-term deleterious effects of maternal PCB exposure on adult female offspring glucose homeostasis. While maternal PCB exposure does not impart long term effects on body composition, we approach these results with caution as male offspring were not included in this analysis.

Future studies will follow male offspring and delve into mechanisms of metabolic dysfunction initiated by maternal PCB exposure in both sexes.

(2-65) The Resilience of DNAPL in Karst Systems (KC Donnelly Externship Award Recipient 2015)

Marvic Carmona De Jesús, Ingrid Y. Padilla

Dense non-aqueous phase liquids (DNAPLs) have been a serious contamination problem since production increased to industrial quantities. Its recurrent use has become an environmental issue concerning frequent accidental and intentional spills, especially in karst groundwater areas. Karst are characterized by a high permeability zone, preferential pathways, and porous-matrix providing an excellent medium for water supply but it also can be a potential zone of rapid exposure and a store for prolonged contamination. Therefore, this research studies fate and transport of DNAPLs in a real karstic medium. Experiments are conducted using a karstified limestone physical model (KLPM), a limestone block enclosed in stainless steel tank simulating a saturated confined karst aquifer. After injecting TCE solvent into a steady groundwater flow field, samples are taken and analyzed spatially and temporally. Data shows pure TCE volumes present in many of the sampling ports including those that are distant from the injection port and along preferential flow paths. Results from temporal distributions curves exhibit spatial variations related to the limestone block heterogeneity. Moreover, rapid response to TCE concentrations is associated with preferential flow paths and slow response with long tailing is indicative of diffusive transport in the rock matrix and mass transport rates limitations. Overall, results indicate that karstified limestone has a high capacity to rapidly transport, as well as store and slowly release TCE pure and dissolved phase.

During the academy year 2014-15 I worked both laboratory task and translational component. I presented my research at SRP 2014, AGU 2014 annual meetings and PRoTECT Retreat 2015. Also, exposing my work have giving me the opportunity to ignite the interest on stakeholders to publish in their journals.

(2-66) Uncovering Historical Environmental Health Threats at Mashapaug Pond, Rhode Island

Michael Murphy and Scott Frickel

Brown University

American cities have experienced significant changes in land and water use patterns during the past century. Environmental social scientists have begun to investigate how these changes to urban ecosystems influence the dispersion and concentration of industrially produced contaminants spatially and over time. This on-going pilot study develops a historical approach for understanding the relationship between the socio-ecological conditions of cities today and the urban industrial past. We center data collection efforts on Mashapaug Pond, an urban pond and superfund site in Providence, Rhode Island. Mashapaug is the third pond of a four-pond system that drains into Narragansett Bay. The pond is fed by six storm drains from the surrounding neighborhood and nearby industrial park, and is fed indirectly by ~~the~~ storm drain systems that feed two other upstream ponds. Historical and contemporary information on the built and natural hydrology of the pond and drainage systems were collected to identify boundaries of the Mashapaug Pond watershed. Within the watershed, we next identified historical and contemporary street names and located historical sites of industrial facilities and commercial retail sites such as gas stations and dry cleaners using old manufacturing directories, telephone books, and title deeds. Once potential historical sources of contaminants were identified and mapped, an inventory of possible contaminants was assembled, giving environmental toxicologists valuable information about contaminants that they should be testing for at the Mashapaug pond site. While the methods used here are specific to an urban pond, they can be modified for other sites of interest.

(2-67) Animal models of asbestos-induced mesothelioma

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Malignant mesothelioma (MM) is an aggressive cancer causally linked to asbestos exposure. Approximately 3000 new cases of MM are diagnosed yearly in the United States. Prognosis for this disease is usually dismal because of resistance to chemotherapy, radiation, and surgical intervention. Due to the long latency of disease development after asbestos exposure, the incidence of MM will remain relatively constant over the next few decades despite efforts to curtail and/or ban asbestos use. In Ambler, Pennsylvania, there is an elevated incidence of MM linked to decades of asbestos manufacturing, and the presence of an asbestos-contaminated waste site continues to jeopardize the health of residents living in the vicinity. As with cancer generally, MM is a genetic disease involving multistep genetic and epigenetic alterations occurring during disease progression. Studies conducted by us, and others, implicated the *CDKN2A*, *NF2, and BAP1* tumor suppressor genes in MM development. Moreover, we recently discovered *BAP1* germline (inherited) mutations in families with a high incidence of MM. We have utilized mouse models to demonstrate the importance of these genes in promoting MM onset and progression. Compared to wild type (WT) mice, heterozygous knockout of any one of these tumor suppressor genes in mice results in increased susceptibility to MM development after chronic crocidolite asbestos injections. Using these accelerated tumor suppressor knockout mice, we are evaluating the carcinogenic potential of chyrsotile, the predominant asbestos found at the Ambler superfund site. Together, these animal models will allow us to gain basic insights into mechanisms/interactions that drive MM development and progression with translational implications for understanding tumor susceptibility and prevention.

(2-68) Engagement and Empowerment of Communities on Water Quality Ramifications in Rural Areas: The Case of Non-PRASA Communities in Puerto Rico

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There are more than 200 communities in Puerto Rico that do not have access to drinking water made available by the Puerto Rico Aqueduct and Sewer Authority (PRASA); a corporation directly regulated by the local Department of Health and the Environmental Protection Agency (EPA). These Non-PRASA communities rely on their own water systems, which feed from local water sources and commonly have no or limited treatment or disinfection processes. If available, the use of chlorine tablets is the only method for treatment and there is no treatment for chemical contaminants. Wastewater from these communities is disposed in septic system, which can contaminate the water source. This projects aims at (1) determining the water quality of source water and tap water in these communities, (2) empowering communities to understand water quality issues and alternatives, (3) training local community members and students in field methods, and (4) engaging trustful interaction between these communities, academia, and the government. Because this project is at its initial stages, the presentation will focus on the later 3 objectives, although some water quality measurements will be provided. The work is conducted at the Non-PRASA Hatillo Community, Añasco, PR. In addition to common water quality parameters, this works also looks at superfund-related contaminants, including chlorinated volatile organic compounds and phthalates. Preliminary interactions have shown very positive and trustful response from the community, the academic sector, and the government. Student trainees have learned to organize site visits, communicate with and train community members, prepare IRBs, conduct sampling, and analyze samples. Ultimately, this work will identify health threats, address community concerns, and assist them with technical issues related to treatment processes and system maintenance.

RESEARCH TRANSLATION: This work focuses on direct interactions between rural community members, academia, and government agencies, including the PR Department of Health and the EPA. It has resulted in the award of an EPA Greater

Research Opportunity Award, and has won support from all sectors. Indeed, the EPA has committed equipment to community members for training and water quality monitoring. The current collaboration is promoting the sharing of resources among sectors, furthering the search for community resources, engaging citizens on their water systems, and establishing the path to ensure healthy water systems for rural communities.

(2-69) Influence of hydrogeological variables on the distribution of phthalate contamination in the karst groundwater systems of northern Puerto Rico

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Karst aquifers have a high capacity to store and convey contaminants to zones of potential exposure. Historical assessment of groundwater contamination in the northern karst aquifers of Puerto Rico has shown significant distribution of contaminants beyond demarked sources of contamination. Many of these contaminants, including phthalates and other emerging contaminants of concern, have been related to long-lasting health problems. This work aims at developing spatial-temporal distributions of phthalates in the karst aquifers of northern Puerto Rico, and determining statistical correlations between different hydrogeologic factors and phthalate contamination. Geographic Information Systems (GIS) technologies and statistical models are applied to attain these objectives. Results show that the karsts groundwater resources are extensively contaminated with phthalates, both as single entities and mixture components. Statistical analyses show that the presence of phthalates is significantly related to sinkholes density, hydraulic conductivity of the aquifers and time. The extensive spatio-temporal contamination suggests that contaminants can persist in the environment for long periods of time, and that hydrogeological factors are important in the presence of those contaminants in karst systems.

RESEARCH TRANSLATION: This work involves significant bidirectional engagement with state and federal government institutions (GIs), scientific and local communities, and non-governmental organization (NGOs). Data collected from GIs is digitalized into a comprehensive database and provided back as digital records. Local communities and NGOs are engaged in water sampling and provided with report-back narratives. Analyzed data and model outcomes have been communicated in the context of environmental and public health impacts and remedial alternatives. Results of this research have been included in two publications (under review) and presented in several forums, including: the EPA Caribbean Science Consortium Symposium (September 2014); Conservation Thrust of PR Meetings (November 2014); Community Engagement Core Advisory Committee Consultations (November 2014); and the Speleological Society of PR Board Meeting (June 2015), among others.

(2-70) Regulation of AhR activation in triple negative breast cancer cells by tryptophan metabolites.

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Historically, activation of the aryl hydrocarbon receptor (AHR) by environmental ligands is thought to lead to DNA-damaging products, leading to cancer initiation. Recent evidence suggests that tumor cells themselves produce molecules that hyper-activate the AHR and this hyper-active AHR contributes to breast cancer progression. Our goal is to identify these "endogenous AHR ligands" in particularly aggressive "triple negative" breast cancer and to determine how environmental AHR ligands can disrupt their production and function. We found that tryptophan metabolites kynurenine and its downstream xanthurenic acid are present in a malignant "triple negative" Hs578T breast cancer cell line, at levels capable of engaging the AHR and increasing a hallmark characteristic of tumor aggressiveness, cell migration. Hs578T cells overexpress TDO, an enzyme required for production of these metabolites. Manipulation of TDO levels in breast cancer cells revealed that AHR activity and cell migration are at least partially dependent on TDO activity. Treatment with environmental AHR ligands, TCDD (dioxin) and B[a]P (an aromatic hydrocarbon), both common at Superfund sites, increased tumor cell migration,

demonstrating that environmental AHR ligands can mimic endogenous AHR ligands in promoting malignancy. Moreover, AHR activity regulates *Tdo* expression, suggesting a feedback loop in which AHR hyper-activity sustains production of its own ligands through up-regulation of TDO. Public dataset analyses revealed that *Tdo* expression is abnormally elevated in primary human tumor samples, underscoring a translational clinical implication of our findings, i.e., that the AHR and TDO can be targeted for treatment of breast cancers. In conclusion, we propose that environmental AHR-activating pollutants may exacerbate breast cancer by (1) mimicking endogenous AHR ligands and (2) driving AHR activity that leads to production of excess endogenous AHR ligands.

(2-71) Flaxseed Lignans Enriched in Secoisolariciresinol Diglucoside (SDG) Inhibit Asbestos-Induced Peritoneal Inflammation in Mice

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Background: Malignant mesothelioma (MM), linked to asbestos exposure, is a highly lethal form of thoracic cancer with a long latency period, high mortality and poor treatment options. Chronic inflammation and oxidative tissue damage caused by asbestos fibers are linked to MM development. Flaxseed lignans, enriched in secoisolariciresinol diglucoside (SDG), have antioxidant, anti-inflammatory and cancer chemopreventive properties. **Rationale**: As a prelude to chronic chemoprevention studies for MM development, we tested the ability of flaxseed lignan complex (FLC) to prevent acute asbestos-induced inflammation in MM-prone *Nf2*$^{+/mut}$*;Cdkn2a*$^{+/mut}$ mice. **Methods**: Mice (n=8-10 per group) were placed on control (CTL) or FLC-supplemented diets initiated 7 days prior to a single intraperitoneal bolus of 400 µg of crocidolite asbestos. Three days post-asbestos exposure, mice were evaluated for abdominal inflammation, proinflammatory and profibrogenic cytokine release, WBC gene expression changes, and oxidative and nitrosative stress in peritoneal lavage fluid (PLF). **Results**: Asbestos-exposed mice fed CTL diet developed acute inflammation, with significant (p<0.01) elevations in WBCs and proinflammatory/profibrogenic cytokines (IL-1ß, IL-6, TNFα, and active TGFß1) relative to baseline (BL) levels. Alternatively, asbestos-exposed FLC-fed mice had a significant (p<0.01) decrease in PLF total WBCs and proinflammatory/profibrogenic cytokine levels relative to CTL-fed mice. Importantly, PLF WBC gene expression of cytokines (IL-1ß, IL-6, TNFα, and TGFß1) and cytokine receptors (TNFαR1, and TGFßR1) were also down-regulated by FLC. FLC also significantly (p<0.01) blunted asbestos-induced nitrosative and oxidative stress. **Conclusions**: FLC reduces acute asbestos-induced peritoneal inflammation, nitrosative and oxidative stress, and may thus prove to be a promising agent in the chemoprevention of MM.

(2-72) Comparison of Statistical Methods for Identifying Biomarkers of Asbestos Exposure and Mesothelioma

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Background: Biomarkers of asbestos exposure and mesothelioma can help identify potential cases early and understand the mechanism of the disease. Many statistical methods are available to select biomarkers that distinguish asbestos exposed subjects and mesothelioma patients from controls. **Methods**: We compared the performance of least absolute shrinkage and selection operator (LASSO) logistic regression model, stepwise multiple linear regression and multivariate adaptive regression splines (MARS) in selection of discriminatory serum lipids biomarkers. All methods were applied to a dataset of 40 mesothelioma patients, 40 asbestos-exposed subjects and 40 controls. Discrimination of a model was evaluated using the area

under ROC curve. **Results**: Comparing mesothelioma patients to controls, LASSO-based penalized regression identified 6 lipids with m/z ratio of 244.23, 372.31, 494.32, 782.57, and 829.68 and area under the curve (AUC) of 1. Stepwise procedure based on Akaike information criterion selected lipids with m/z of 367.34 and 377.27 (AUC=1). Logistic regression using MARS basis functions identified lipids with m/z ratio of 353.27, 355.28, 372.31, 671.58, 798.57, 829.68 (AUC=0.948). When comparing asbestos-exposed patients to controls, 3 lipids with m/z ratio of 362.29, 548.38 and 820.36 were selected by all three methods. The AUCs using LASSO, stepwise and MARS were 1, 0.999, and 0.782, respectively. **Conclusion**: Several lipid biomarkers for asbestos exposure and mesothelioma were identified. Three statistical approaches under investigation have selected different sets of lipids but the selection may be equivalent because many selected lipids are highly correlated with each other. Issue of collinearity should be addressed before applying multivariate regression and variable selection methods. LASSO and stepwise tend to overfit the model. Results of the current study will warrant additional validation using independent samples.

(2-73) The Protective Role of Polyphenol-Functionalized Nanoparticle Systems in Environmental Toxicant Exposure.

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Polychlorinated biphenyls (PCBs) are a class of organic environmental pollutants that are ubiquitously present in the soil and groundwater. Although banned for over three decades, they continue to persist in the environment due to their thermodynamic and chemical stability. PCB exposure has been correlated to vascular endothelial cell dysfunction including oxidative stress and inflammation. The objective of the current study is to evaluate the protective role of polyphenol-based iron oxide (Fe_3O_4) nanoparticle system in PCB-mediated endothelial toxicity. The nanoparticles were initially designed to capture and remove PCBs from Superfund sites, but the presence of polyphenols (curcumin and quercetin) may also provide protection against PCB toxicity in biological systems; hence giving them a dual role. Cell viability assays were performed in human umbilical vein endothelial cells to assess the effective concentration of the nanoparticles. Cells were then pretreated with nanoparticles for 0, 12 and 24h and exposed to PCB126 at varying concentrations. Target gene expression was measured using RT-PCR. Cells exhibited decreased basal expression of pro-inflammatory cytokines (IL-6, VCAM-1) when pretreated with nanoparticles for 24h. Furthermore, cells pretreated for 12h and exposed to PCB126 had lower IL-6 mRNA levels *vs.* their untreated, exposed counterparts, suggesting protection against PCB-induced inflammation. Potential mechanisms include PCB binding and adsorption to the nanoparticle surface through pi-pi interactions, resulting in lesser amount of PCBs available for interacting with their biological target receptors. Hence a nanoparticle system that has a dual approach in terms of PCB remediation in cleanup sites and simultaneously exerting biological protection against PCB-induced toxicity has been presented.

NB: The current study is an inter-disciplinary collaboration between Project 1 (biomedical) and Project 4 (non-biomedical) of the UK Superfund Center.

(2-74) Stressogens: An exposomic approach to assessing cumulative risk

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Populations are often exposed to multiple chemical and non-chemical stressors at both the community and individual level. Novel approaches are necessary to identify candidate environmental chemicals that enhance vulnerability to disease via

interactions with the social environment. We have developed a framework where exposomics could be used to measure the combined internal dose of these non-genetic environmental stressors and assess their cumulative impact on health. Cortisol, secreted by the adrenal gland in response to psychosocial stress, activates the glucocorticoid receptor (GR) and has systemic effects on the endocrine, metabolic, cardiovascular, immune, reproductive, and central nervous systems. We propose that environmental chemicals that mimic cortisol can disrupt stress response pathways and homeostasis through altered GR signaling. We define these environmental chemicals that alter stress response pathways as "stressogens." By developing a functional bioassay that measures total glucocorticoid receptor (GR) activity we are able to identify stressogens that perturb the stress response by exerting either agonistic or antagonistic effects on GR. Exposomic discovery of stressogens and detection of endogenous stress response mediators is essential for developing models of disease, particularly among vulnerable populations with substantial mixing of multiple chemical and non-chemical exposures.

(2-75) Indoor Contaminant Vapor Intrusion – Numerical Modeling and Field Data Analysis

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In 2015, the US EPA issued the official guidance on vapor intrusion. There has, over the last two decades, been significant progress in understanding the transport processes of relevance in vapor intrusion of volatile organic compounds (VOCs) of health concern from soil into buildings. These studies have included mathematical modeling of fate and transport of the contaminants. Most such models have until now simplified the prediction of indoor air contaminant vapor concentrations by employing a steady state assumption, which often results in difficulties in reconciling these results with field measurements that show time dependence on many different timescales. This paper focuses on two major factors that may be subject to significant transients in vapor intrusion situations, including the indoor air pressure and the air exchange rate in the subject building. A well-mixed chamber model has been employed with consideration of daily and seasonal variations in these factors, such that the phenomena may be quantitatively analyzed. From the modeling results, the variations of air exchange rate are seen to contribute to orders of magnitude variations in indoor air contaminant vapor concentrations, consistent with the reports from field studies.

(2-76) Testing for Gene-Environment Interaction under Environment Misspecification

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Complex relationships between genetic and environmental risk factors characterize the etiology of many diseases, but there exist very few validated gene-environment interaction (GxE) findings in literature. The standard GxE study repeatedly fits a single-marker model that contains a linear term for the genetic, environmental, and interaction effects. This model is often misspecified because we generally do not know the correct functional form of the environment term in the true data-generating mechanism. For example, if we are interested in the interaction between genes and toxic metals, it is not clear how to introduce metals into the model – should we measure the amount in our blood, in our food, in our water, or some other quantity entirely? We study the impact of misspecification on inference for the interaction effect by investigating the asymptotic bias and variance of estimates from the misspecified working model. When naïve model-based variance estimates are incorrect, we provide an alternative testing procedure that has better small sample properties than a commonly proposed model-robust estimator. Performance of our methods is demonstrated through simulation studies and analysis of a GxE investigation for effect of lead exposures on neurodevelopment outcomes.

Research Translation Component: The results of this work will be very important in helping scientists design future gene-environment interaction studies. Many communities/municipalities are believed to have elevated risk of certain diseases due

to unique, localized environmental factors. Currently, a sizeable amount of funding is spent to understand the interaction between these environmental factors and genetics, but researchers have been largely unsuccessful in finding strong results. We believe environment misspecification has contributed significantly to the lack of progress. With our work, scientists can better understand the potential pitfalls of searching for GxE interactions, and they can design studies that have a higher chance of success.

(2-77) Effect of weathering on toxicity and mobility of asbestos fibers in soil

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Abstract: Asbestos waste poses serious health risks because exposure to asbestos fibers can cause asbestosis and lung cancer. A common practice to remediate asbestos contaminated sites has been capping the site to minimize exposure to airborne asbestos fibers. This practice, however, does little to treat asbestos *in situ*. Furthermore, mobility of asbestos fibers in subsurface and groundwater—an alternative exposure pathway—is unknown. Our research examines how geochemical processes, some of which are mediated by plants and fungi, contribute to asbestos weathering and change the fiber mobility in soil. Firstly, we examined the removal of iron from chrysotile, the most common asbestos mineral, in the presence of several plant and fungi exudates including six organic acids and a siderophore—a particular exudate with a strong affinity to iron. Secondly, we packed asbestos contaminated soil from a superfund site (BoRit Site, Ambler, PA) in columns and applied intermittent wetting cycles to examine the mobility of asbestos fibers through soil. Our results showed that the siderophore increased the removal of iron from asbestos fibers, and addition of organic acids further enhanced iron removal. The removal rate depended on pH and concentration of exudates.

Collaborating with the biomedical research team working on animal models of mesothelioma at the University of Pennsylvania SRP Center, we evaluate the toxicity of the altered asbestos fibers. Results from the column experiment inform and validate the findings from other studies at the SRP Center that examine the aggregation dynamic of asbestos fibers in water. Collectively, these results will help develop a sustainable remediation technology for asbestos contaminated sites and assess the conditions that either increase or decrease the fiber mobility at the sites.

(2-78) Synthesis and Evaluation of nanoparticle membrane-supported systems for Degradation of Trichloroethylene

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Functionalization of polymeric membranes of polyvinylidene fluoride (PVDF) for water purification is an extensive field of study. Most studies of functionalization have been done in flat sheet membranes for pH and temperature responsive applications. In order to improve the detoxification of water, it is necessary to explore different platforms such as hollow fiber (HF) or thicker (spongy-like) flat sheet (FS) microfiltration membranes. HF functionalization has been made on other materials different than PVDF and there are relatively very few studies describing this application as well in thicker membranes.

This work explores the dechlorination of TCE in aqueous solution using iron/palladium nanoparticles (NPs) immobilized in HF and FS membranes functionalized with a functional polymer (polyacrylic acid). The applicability of these systems has been proven in scale-up modules in water polluted with chloro-organic compounds. These systems prevent nanoparticle loss and have a high surface-area that increases their reactivity. Changing the pH of the functionalization process has an impact in the

particle size and inter-particle distance as well in the swelling behavior during the dechlorination reactions. It is worth mentioning that functionalization of HF membranes with functional polymers and nanoparticles have not been applied in detoxification studies. TCE degradation with NPs (174 to 280 nm) follows a first-order rate law. The surface-normalized-area rate constants are 0.08 and 0.39 L/ (m^2·h) for HF and FS, respectively. Up to 75% of TCE degradation is achieved.

(2-79) Quantifying fate and transport of contaminant in surface water connected to karst aquifers in the northern region of Puerto Rico

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Puerto Rico has more than 200 contaminated sites that include 16 active Superfund sites. Risk of exposure to contaminants is aggravated by unlined landfills lying over the karst regions, highly mobile and dynamic nature of the karst aquifers, and direct contact with surface water through sinkholes and springs. Much of the population in the island is getting water from natural springs or artesian wells that are connected with many of these potentially contaminated karst aquifers. Mobility of contaminants such as TCE, through surface water flows and reservoirs are largely known and are highly correlated with the variations in hydrologic events and conditions.

To quantify and characterize Puerto Rico's surface waters, we use hydrologic modeling, satellite and radar remote sensing and field measurements. Streamflow measurements are available from 27 U.S. Geological Survey (USGS) gauging stations with drainage areas ranging from 2 to 510 km^2. Hillslope River Routing (HRR) model is used to simulate hourly streamflow from watersheds larger than 1 km^2 that discharge to ocean. HRR model simulates vertical water balance, lateral surface and subsurface runoff and river discharge. The model consists of 4418 sub-catchments with a mean model unit area (i.e., sub-catchment) of 1.8 km^2. Using gauged streamflow measurements for validation, we first assess model results for simulated discharge using three precipitation products: TRMM-3B42 (3 hour temporal resolution, 0.25 degree spatial resolution); NWS stage-III radar rainfall (~ 5 min temporal resolution and 4 km spatial resolution); and gauge measurements from 37 rainfall stations for the period 2001-2011. We then explore methods for combining each product to improve overall model performance. Effects of varied spatial and temporal rainfall resolutions on simulated discharge are also investigated.

Research Translation Component: In this study, we quantify the spatial and temporal distribution of Puerto Rico's surface water stores and fluxes to better understand potential impacts on the distribution of groundwater contamination.

(2-80) Maternal urinary arsenic and cardiometabolic outcomes in a New Hampshire pregnancy cohort

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Accumulating evidence indicates that arsenic, a potent environmental toxicant, may adversely affect glycemic control, blood pressure, systemic inflammatory markers, vascular endothelial function and CVD occurrence at high levels of exposure. However, the effects of arsenic at lower levels of exposure are uncertain and little is known about the effects of arsenic exposure during pregnancy. Pregnancy is a time of particular vulnerability to environmental insults, not only for the fetus, but the mother as well, and signifies a time when cardiometabolic risks may begin to manifest in the mothers. For example, women who experience cardiovascular-related complications during pregnancy are at greater risk of later life cardiovascular disease. As part of the New Hampshire Birth Cohort Study, we recently reported that arsenic exposure during pregnancy was related to greater increases in blood pressure over the course of pregnancy. Building upon this work, we are investigating

whether exposure to arsenic during pregnancy may impact additional markers of cardiometabolic disease in pregnant women. We are examining the association between arsenic exposure and levels of early markers of cardiovascular dysfunction, systemic inflammation and endothelial dysfunction in plasma samples. Additionally, we are testing whether higher arsenic exposure influences cardiometabolic disease risk factors in pregnant women, including altered glucose metabolism. To our knowledge, our study is among the first to evaluate these cardiometabolic markers in relation to arsenic exposure in pregnant women particularly in a US population. Our work is helping to fill a critical knowledge gap by evaluating the effects of As exposure during pregnancy on cardiovascular risk factors among mothers in our ongoing US prospective study.

(2-81) Arsenic Associated Antagonism In The Transcriptomic Response To Osmotic Shock In The Atlantic Killifish

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Arsenic is an environmental toxicant whose many effects are most evident in the presence of other stressors. We analyzed gene expression in the killifish gill during rapid changes in salt concentration. 100 ppb arsenic significantly impairs salinity acclimation, though this low dose affects very few genes in stable salinity. During salinity acclimation, arsenic antagonistically interacts with known salinity response genes and upstream regulators, consistent with arsenic's ability to block salinity acclimation at higher doses. Finally, although variability in gene expression normally decreases during salinity acclimation, the presence of arsenic during high salt stress instead results in a significant increase in gene expression variability. These findings suggests that arsenic's mechanisms of action in the context of multiple stressors may include interference with gene regulatory networks as well as specific genes, helping to explain arsenic's diverse toxicological footprint.

Research Translation Component: My role is to assess potential health benefits of reducing arsenic exposure. I also serve as the statistician on this project.

Shaw, J. R., Hampton, T. H., King, B. L., Whitehead, A., Galvez, F., Gross, R. H., et al. (2014). Natural selection canalizes expression variation of environmentally induced plasticity-enabling genes. *Molecular Biology and Evolution*, *31*(11), 3002–3015. http://doi.org/10.1093/molbev/msu241

Naujokas, M. F., Anderson, B., Ahsan, H., Aposhian, H. V., Graziano, J., Thompson, C., & Suk, W. A. (2013). The Broad Scope of Health Effects from Chronic Arsenic Exposure: Update on a Worldwide Public Health Problem. *Environmental Health Perspectives*, *121*(3), 295–302. http://doi.org/10.1289/ehp.1205875

(2-82) Metabolites of Commonly Occurring Airborne Polychlorinated Biphenyls Inhibit Steroid Hormone Sulfation Catalyzed by Human Cytosolic Sulfotransferases

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Exposure to polychlorinated chlorinated biphenyls (PCBs) has been associated with the risk of developing cancer, thyroid dysfunction, neurotoxicity, diabetes, and other disease states. PCBs are persistent, lipophilic environmental toxins. Our studies on the lower chlorinated PCBs and their metabolites are particularly relevant to understanding the toxicities and risks associated with current exposures to these PCBs in urban and indoor air. Sulfation is catalyzed by cytosolic sulfotransferases (SULTs) and represents an important process both for transport and for signal termination of steroid hormones. Sulfotransferases SULT1E1 and SULT2A1 participate in regulating the homeostasis of estrogens and androgens, respectively. We hypothesize that inhibition of the catalytic activity of these enzymes by hydroxylated and sulfated metabolites of commonly encountered airborne PCBs will inhibit the catalytic activity of these sulfotransferases with steroid hormones. We found that the sulfotransferase activity of SULT1E1 was decreased at nanomolar concentrations of hydroxylated PCBs (OH-PCBs), and the activity of SULT2A1 was decreased at micromolar concentrations of OH-PCBs. The PCB-sulfates were less inhibitory. Thus, the inhibition of SULT1E1 and SULT2A1 by these and other related OH-PCBs may have implications for alterations in steroid hormone signaling. We are beginning to explore such changes in a cell culture model of human adipocyte differentiation, since previous reports indicate that SULT1E1 plays an important role in adipogenesis. Our preliminary findings with cytosolic preparations from these cells indicate that OH-PCB 11 is effective in inhibiting SULT1E1 activity at nanomolar concentrations. Future studies will focus on determining the intracellular effects of this inhibition of SULT1E1 by OH-PCB 11 and other metabolites of airborne PCBs and understanding the potential effects of this inhibition on adipogenesis.

(2-83) Influences of temperature and carbon loading on methylmercury bioavailability in estuaries (KC Donnelly Externship Award Recipient 2014)

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Climate change is predicted to elevate water temperature and cause increases in nutrient and carbon loading in coastal marine ecosystems. In this study, effects of differences in temperature and organic carbon were investigated in a field study in the Northeastern United States. Field sampling was conducted at two estuarine sites at each of three different latitudes (Chesapeake Bay, MD, Long Island Sound, CT and Mount Desert Island, ME), with low and high sediment organic matter subsites at each location. Geochemical analyses included Hg speciation in sediment, porewater and surface water. Primary and secondary consumers were collected from benthic and pelagic zones in the intertidal region at each subsite. Concentrations of methylmercury in mummichog (Fundulus heteroclitus), Atlantic silversides (Menidia menidia) and shrimp (*Palaemonetes pugio /* Crangon septemspinosa*) were significantly correlated with both dissolved and particulate methylmercury concentrations in the water column across sites.*

Methylmercury concentrations in Atlantic silversides decreased from northern to southern latitude sites, and concentrations in ME and CT (north and mid-latitude) were significantly higher than in MD (southern latitude). The observed higher

*methylmercury concentrations in the northern latitude sites may have been due to higher mercury loading in the sediment and water column, confounding the predicted effects of temperature on uptake. Methylmercury bio*accumulation was significantly higher at low carbon subsites in *mummichog, shrimp and silversides. These findings suggest that mercury loading should be monitored when managing carbon loading to estuarine sites, as an unintended consequence of reducing carbon loading may be to increase mercury bioavailability. Conclusions of this work have been presented at regional and international meetings focusing on mercury release and exposure.*

(2-84) Progression of micronutrient alteration and hepatotoxicity following acute PCB126 exposure (KC Donnelly Externship Award Recipient 2014)

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Polychlorinated Biphenyls (PCBs) are industrial chemicals that have become a persistent threat to human health due to ongoing exposure. A specific set of PCBs, known as dioxin-like PCBs, pose a special threat given their potent hepatic effects. Micronutrient homeostatic dysfunction is commonly see after exposure to dioxin-like PCBs. This study investigates whether the micronutrient alteration is the byproduct of the ongoing hepatotoxicity, or a concurrent, yet independent event of hepatic damage. A time course study was carried out using male Sprague-Dawley rats with treatments of PCB126, the prototypical dioxin-like PCB, resulting in 6 different time points. The animals were fed a purified diet, based on AIN-93G, for three weeks to ensure micronutrient acclimatization. A single IP injection of either tocopherol-stripped soy oil vehicle (5 mL/kg) or 5 umol/kg PCB126 dose in vehicle was given at various time points resulting in exposures of 9 hr, 18 hr, 36 hr, 3 days, 6 days, and 12 days. Mild hepatic vacuolar change was seen as early as 36 hours with drastic changes at the later time points, 6 and 12 days. Micronutrient alterations, specifically Cu, Zn, and Se, were not seen until after day 3 and only observed in the liver. No alterations were seen in the duodenum, suggesting that absorption and excretion may not be involved. Micronutrient alterations occur with ROS formation, lipid accumulation, and hepatomegaly. To probe the mechanistic underpinnings, alteration of gene expression for several copper chaperones was investigated; only metallothionein appeared elevated. In all, the data suggest that the disruption in micronutrient status is a result of the hepatic injury elicited by PCB126 and is mediated in part by metallothionein.

(2-85) Iron and Copper Synergy in the formation of PCDD/Fs

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Transition metals in fly ash play an active role in the formation of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs.) Transition metals assist the formation of surface-associated phenoxyl-type radicals, which subsequently undergo condensation reactions to yield PCDD/Fs in the postflame, cool zone of combustors. Dioxins are of great concern because of their highly toxic potential. The influence of copper and iron oxides on the formation of PCDD/Fs has been shown before. However, in fly ash, iron and copper oxide co-exist and their synergistic/antagonistic effects can be anticipated. To our knowledge such studies have not been reported. In this study we evaluated fly ash surrogate systems containing both copper and ion oxides with varied ratios of Fe_2O_3 and CuO on a silica substrate: 4%Fe_2O_3:1%CuO, 2.5%Fe_2O_3:2.5%CuO, and 1%Fe_2O_3:4%CuO in PCDD/F formation at 200-550^oC under both oxidative and pyrolytic conditions. Under oxidative conditions,

oxidation of 2-monochlorophenol dominated, few byproducts formed including low yields of PCDD/Fs. Under pyrolytic conditions, however, yields of up to 5% PCDD/Fs were observed. Higher yields of PCDD/Fs formed by the bimetallic surrogates indicate synergistic effects between iron and copper oxides. X-ray photoelectron spectroscopy of fresh and used bimetallic surrogates indicates a shift of the binding energy of copper ions towards lower values. This indicates increased propensity of copper to reduction. Since the PCDD/F precursors on the surface are surface bound radicals formed by the electron transfer from adsorbate to copper, increased reducibility of copper will result in more stable radicals and potentially more efficient condensation process.

We conclude that in oxygen rich conditions bimetallic systems do not produce significant amounts of PCDD/Fs. In the pyrolytic pockets of incinerators such systems can generate large quantities of PCDD/Fs.

(2-86) Detection of Arsenic in Water by an Enzymatic Catalysis System

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Abstract: Arsenic (As) is a highly toxic element that exists in environment in different chemical forms. The detection of arsenic in natural water remains a challenging task for analytical chemists. Work will be presented on an existing chemical arsenic sensor, as well as a new detection method for arsenic in aqueous solution, based on an enzyme-catalyzed reaction. The detection range of arsenic is determined by monitoring the change of fluorescence. The preliminary experiments has successfully detected arsenic at ppm range even with very low concentration of the enzyme (1.6µg/mL). This method holds great potential for detection of arsenic with concentration down to the standard level adopted by the Environmental Protection Agency (10ppb in drinking water).

(2-87) Towards identifying unknown genotoxic compounds in bioremediated soil using metabolomics-like methods and effect-directed analysis

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In previous experiments on soil contaminated with polycyclic aromatic hydrocarbons (PAHs), the chicken DT-40 B-lymphocyte cell line and its isogenic DNA repair-deficient mutants were used to assess the effect of bioremediation on toxicity and genotoxicity. While cytotoxicity was reduced after treatment, increased genotoxicity was observed after treating the soil in a laboratory-scale, aerobic bioreactor, implying that certain genotoxic products (metabolites) were formed in the bioremediation process.

The extracts from untreated and bioreactor-treated soils were analyzed by high resolution mass spectrometry (HPLC-qTOF). Inspired by methods in metabolomics, the data were processed using different software and algorithms; peaks with substantially greater signals in extracts from bioremediated soil than in extracts from untreated soil were selected as candidate genotoxic compounds. One peak corresponding to a compound with the formula $C_{15}H_8O_2$ is consistently detected in all bioreactor-treated soil samples but not in untreated soil samples. By comparing with synthetic reference standards of the same formula, the unknown compound is tentatively identified as a PAH *o*-quinone that has never been reported and whose structure is still under investigation. Quinones derived from PAHs are known to be genotoxic and are known to be produced by aerobic bacteria unable to metabolize the parent compound completely.

In ongoing work we are separating the soil extracts into fractions with different chemical properties and using effect-directed analysis (EDA) with the DT-40 bioassay to select the fractions that are causing the most significant genotoxicity. Fractions will

continue to be refined to narrow the possible range of compounds responsible for increased genotoxicity after aerobic bioremediation. Once the correlation between increased genotoxicity and the candidate compounds is confirmed, further structure elucidation and toxicity analysis will be conducted.

Research translation component: Because our work involves remediation of soil from a contaminated field site and examines the effects of bioremediation beyond the removal of the regulated priority pollutant PAHs, it has implications for how bioremediation contributes (or not) to overall risk reduction. This research provides a good example of assessing the effect of bioremediation for contaminated sites using advanced bioassays, which could be applied to other remediation processes. Our research also presents a metabolomics-like method to identify unknown compounds from a complex mixture according to the observed biological effect, an approach that can be applicable to a wide range of environmental and remediation systems.

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